Priority substances for the EU Human Biomonitoring Initiative HBM4EU

Summary

The European Human Biomonitoring Initiative (HBM4EU) is a joint effort of 26 countries and the European Commission (EC), co-funded by the EC research programme Horizon 2020. The main aim of the initiative is to coordinate and advance the measurement of the presence of chemicals in the European population. HBM4EU is expected to provide better evidence of the actual exposure of citizens to chemicals and the possible health effects.

CHEM Trust is one of the stakeholder organisations of the European Human Biomonitoring Initiative. All stakeholders were invited to nominate chemicals or groups of chemicals for the future priority setting in the project.

The project’s first priority list of chemicals already contains many very important groups of priority substances, which are the following:

- Phthalates and DINCH
- Bisphenols
- Per- and polyfluorinated compounds (PFAS)
- Flame retardants
- Cadmium and chromium VI
- Polycyclic aromatic hydrocarbons
- Aniline family
- Chemical mixtures
- Emerging substances

In CHEM Trust’s view the main added value that this project can bring to society is to close specific knowledge gaps aimed at the preparation of regulatory measures to increase human health and environment protection.

For the second prioritisation round CHEM Trust nominated the following 5 substance groups which also include a focus on specific questions for the 3 first re-nominations.

1) Bisphenols
2) Per- and polyfluorinated compounds (PFAS)
3) Flame retardants
4) UV filters (oxybenzones)
5) Methoxycinnamates
Background information on CHEM Trust proposed nominations for priority substances in the 2nd prioritisation round for HBM4EU

Please note that this information was submitted as complementary input to the ongoing deliberations in the HBM4EU project. It is not aimed at providing a complete substance profile.

1. Bisphenols

Summary of nomination: Lead substance: BPA (CAS: 80-05-7)

BPA is still used in many consumer articles despite its classification as being toxic to reproduction. At the same time research finds that other bisphenols in frequent use may be similarly or even more toxic. Our nomination and input provided below intends to complement the information in the official HBM4EU scoping document which summarizes details on hazards, uses and regulatory status. We propose to focus the HBM4EU work on the known common replacements for BPA.

Update on hazard identification:

In addition to its classification as a reproductive toxicant, BPA has been identified as an EDC for human health under REACH in June 2017. Meanwhile Germany has also proposed its identification as EDC for the environment.

Recently Swedish Chemical Agency KEMI identified over 200 substances with a chemical structure similar to bisphenol A. In total, 39 bisphenols were surveyed, 37 of which may have endocrine disrupting properties, KEMI found. Six bisphenols “could be problematic from a risk perspective” due to their properties and uses: BPA, bisphenol F (CAS 620-92-8), bisphenol M (CAS 13595-25-0), bisphenol S (CAS 80-09-1), 2,2-bis(4’-hydroxyphenyl)-4-methylpentane (CAS 6807-17-6), and benzophenone-2 (CAS 131-55-5). Moreover, a recent US study illustrated anti-estrogenic effects of the BPA replacement fluorene-9-bisphenol BPHF (CAS number 3236-71-3) and report findings of BPHF in human plasma.

Update on exposure:

Recent findings in the US have shown that some people’s exposure to BPF can meanwhile be higher than to BPA. It would be important to also explore this trend more in Europe and conduct some new analysis of the occurrence of the most common BPA replacements. In particular women of child-bearing age are a relevant study group given the endocrine disrupting properties of the bisphenols. Furthermore, a recent study by Liu and Martin illustrated that dermal exposure from BPA might still be underestimated.

Policy needs

Following the ban on BPA use in thermal paper, the EU Chemicals Agency ECHA was tasked to only assess whether the presence of bisphenol S in thermal paper could pose a

---

1 http://www.chemtrust.org/bisphenol-a-bpa/
2 http://www.endsreport.com/article/57429/chemical-substitutes-worse-than-bpa
5 https://echa.europa.eu/documents/10162/12d03565-e386-c66d-0f5b-4851d2dd2767
8 https://silentspring.org/blog/results-our-biomonitoring-study-are
9 http://pubs.acs.org/doi/full/10.1021/acs.est.7b03093

http://www.chemtrust.org Twitter: @CHEMTrust
risk to human health\textsuperscript{10}, while there are also other similar substances used as replacements.\textsuperscript{11} No similar request has been given to EFSA even though it is well known that BPS is being used as a replacement for BPA in a wide range of applications.\textsuperscript{12}

Policy approaches should be developed to tackle a reduction of exposures to the whole group, in particular for all known consumer uses or applications reaching the environment. Regarding the activities in HBM4EU we would like to caution against investing too many efforts in developing individual safety values (i.e. assumed and declared safe levels) for substances such as BPS: in particular if more and more analytical data confirm that the general population is co-exposed to several bisphenols at the same time, a safety level for individual substances is highly questionable.

Instead, we would like to see more work invested in policy objective 10 of the HBM4EU scoping document which looks into combined exposures and the need to revisit and change existing approaches and health guidance:

10. To determine the effect of combined exposures to substance mixtures within the bisphenol family and with other families and whether this should impact health guidance (in food contamination, cosmetics, other plasticizers, etc.).

We also very much support an emphasis on the objective no 14 – the importance to eliminate legacy BPA from material cycles (i.e. waste till receipt rolls) when implementing a circular economy in order to protect human health. Danish researchers have just published a novel way of identifying chemicals in paper and board packaging.\textsuperscript{13} Policy proposals should be developed to extend the focus to the whole group of bisphenols.

\textbf{Public concern (examples)}

- [http://www.chemtrust.org/tag/bpa/](http://www.chemtrust.org/tag/bpa/)

\section*{2. Per- and polyfluorinated compounds (PFAS)}

\textit{Summary of nomination: Lead substance: PFOA (CAS: 335-67-1)}

The HBM4EU scoping document already provides a good literature overview and lists many chemicals belonging to this large group of substances. We support the important work in this area and propose to focus the HBM4EU work to develop approaches to tackle this large group in subgroups of very similar structure. The recent German restriction proposal for the group of C9-C14 PFCAs including their precursors and salts is leading the way in the right direction.\textsuperscript{14} This approach could help in more effectively closing regulatory gaps.

One emphasis should be the shorter PFCs, often used to replace the long and medium chained PFCs, one example would be Perfluorohexanesulfonic acid PFHxS (CAS 335-46-4). This substance is also used for surface treatment and water-and stain repellent coating. The

\begin{thebibliography}{99}
\bibitem{10} https://echa.europa.eu/documents/10162/13641/echa_rest_proposals_rubber_granules_en.pdf/1a8a254c-bd4a-47b1-a091-99ae4a94a8c2
\bibitem{11} Maria K. Björnsdotter a,b, Willem Jonker c, Jessica Legradi a, Jeroen Kool c, Ana Ballesteros-Gómez: Bisphenol A alternatives in thermal paper from the Netherlands, Spain, Sweden and Norway. Screening and potential toxicity, Science of the Total Environment 601–602 (2017) 210–221
\bibitem{13} https://chemicalwatch.com/59005/danish-test-finds-phthalates-and-bpa-in-pizza-boxes
\bibitem{14} https://chemicalwatch.com/60552/germany-proposes-eu-restriction-on-pfcas
\end{thebibliography}
same applies to 8:2 DiPAP (CAS 678-41-1) and C8SamPAP (CAS 2965-52-8). All 3 substances have been included in the SIN list (Substitute it now) in 2014.\textsuperscript{15}

The concern regarding exposures to PFAS is well-known and it is high time to extend restrictions beyond PFOS and PFOA in order to protect human health and the environment.

It is highly alarming that all large European rivers are highly contaminated with perfluoroalkyl acids and that European environmental quality standards for PFOS are exceeded in all of them\textsuperscript{16}. At the same time, also the health concerns of PFAS are increasing, for example regarding effects on brain developments, as we highlighted in the CHEM Trust report ‘No brainer’\textsuperscript{17}.

**Need for standardised methods**

The Nordic Council recently came up with very useful recommendations on PFAS, such as the proposal to develop a standardised method for monitoring total organic fluorine with a low detection limit in various matrices\textsuperscript{18} including products and in human blood as well as the need for mechanistic studies of the effects and fate of PFASs in the environment and biota to facilitate read-across and to avoid pseudo-substitutions.

**Policy needs**

The EU Commission announced their intention to develop EU proposals for chemicals in printed paper and board food contact materials.\textsuperscript{19} Therefore a focus of HBM4EU on current exposures of the EU population to chemicals used for food packaging could provide valuable insights and also establish tools for monitoring exposure trends in the future.

A recent study published in September 2017 by the EU Commission in the context of the development of the EU Strategy for a non-toxic environment highlights that ‘The thousands of new short-chain PFAS marketed by producers as “safer” than the long-chain PFOS and PFOA are also extremely persistent.’ It concludes that the ‘evidence of their toxicity and of their presence in the environment is mounting’ and refers to major gaps in EU legislation which need to be closed to better control PFAS (see in particular the sub-study on very persistent compounds).\textsuperscript{20}

The question in policy objective 8 in the scoping document regarding the importance of eliminating legacy PFASs from material cycles in order to protect human health should be clearly answered with yes: The current EU efforts to build a circular economy is an important reminder for stepping up the efforts in reducing the PFAS in supply chains: only a clean circular economy is a sustainable one.\textsuperscript{21}

Given the tremendous policy tasks ahead, current work should focus on developing group approaches for addressing combined exposures to groups of similarly acting PFAS. This should have a priority over setting guidance values for individual chemicals. Moreover, in particular for those PFAS with endocrine disrupting properties and cases of known co-exposures it would not be appropriate to establish individual reference values. The uncertainties for setting safe levels will be extremely high and are thus unlikely to guarantee

---


\textsuperscript{17} http://www.chemtrust.org/brain/

\textsuperscript{18} http://norden.diva-portal.org/smash/record.jsf?pid=diva2%3A1120881&dswid=944

\textsuperscript{19} http://www.chemtrust.org/chemicals-packaging-fcm/


\textsuperscript{21} http://www.chemtrust.org/chemicals-and-the-circular-economy/

http://www.chemtrust.org

Twitter: @CHEMTrust
a high level of protection. Instead, the urgency on minimising exposures needs to be recognised and addressed in regulatory measures.

Public concern (examples)

- http://www.chemtrust.org/tag/pfcs/
- https://www.greenpeace.de/themen/endlager-umwelt/textilindustrie/geschafft

3. Flame retardants

Summary of nomination:

As described very well in the useful HBM4EU-scoping document there is a high need to close knowledge gaps regarding the many novel BFRs that are widely used as replacements for globally banned PBDEs and are suspected of having similar properties of concern.

We agree with the prioritisation of 18 substances (table 9, page 68) and would suggest a strong focus on the presented ‘category B substances’. This corresponds to the priority of our nomination in this group: We propose to generate new human biomonitoring data on the following 5 substances which have been included in the SIN list in 2014. They are also all mentioned in the scoping document (under the prioritised category B).

1. BTBPE (CAS 37853-59-1) found in marine mammals and the Artic environment and it has been detected in humans and shows persistent, bioaccumulative and toxic (PBT) properties
2. Decabromodiphenylethane (CAS 84852-53-9) found in wildlife all over the world and shows PBT properties.
3. BEH-TEBP (CAS 26040-51-7) found in environmental samples from various regions as well as human and wildlife samples and shows PBT properties.
4. TRIS (CAS 13674-87-8) frequently found in children following exposure with house dust. Suspected carcinogen, shows P and T properties
5. Dechlorane Plus (13560-89-9) found in wildlife and humans, shows PBT properties

Studies needed

More systematic assessments of exposure trends among the general EU population for commonly used flame retardants are needed in order to develop better regulatory controls for those substances of high concern with PBT and endocrine disrupting (ED) properties. Given there is a considerable exposure via house dust it would make sense to include analyses from samples of younger age groups.22

Policy questions

Human monitoring data on the occurrence and trends in EU citizens could help develop better regulatory controls for these very problematic substances with PBT and ED properties.

22 http://www.chemtrust.org/dust-not-only-a-nuisance-but-also-a-source-of-hazardous-chemicals/
http://www.chemtrust.org
It is really important to dedicate work to mixtures of flame retardants. The recent study by Martin et al.\(^{23}\) showed that combined exposures to polybrominated diphenyl ethers (PBDEs) may exceed acceptable levels in breastfeeding infants (0–3 months old) and in small children (1–3 years old), even for moderate (vs. high) exposure scenarios. The estimates also suggested that acceptable levels of combined PBDEs may be exceeded in adults whose diets are high in fish. Small children had the highest combined exposures, with some estimated body burdens that were similar to body burdens associated with developmental neurotoxicity in rodents.

As highlighted by EFSA in 2012\(^{24}\) and described in the scoping document, toxicological data for these substances have gaps. Establishing reference values might not be very difficult and in any case it would be important to take a group approach.

Moreover, there is a clear need to develop approaches how HBM data can be used more proactively in decision-making in the future (in EU laws and global conventions) and to end the huge time lag between first analytical findings and regulation. One important societal added value the HBM4EU should therefore bring is to develop approaches to accelerate the current gap between the first findings of anthropogenic substances in wildlife, concerns about their detrimental impacts and the time of imposing some controls for the better protection of nature and people. The Artic Monitoring and Assessment Programme have recently published recommendations for future policy action in this regard in order to tackle this decade-long delay.\(^{25}\)

**Public concern (examples)**


A decision on September 20 by the Consumer Product Safety Commission to look into banning the use of organohalogen flame retardants in several consumer product categories:

- [https://chemicalwatch.com/59151/us-cpsc-moves-to-ban-organohalogenflame-retardants](https://chemicalwatch.com/59151/us-cpsc-moves-to-ban-organohalogenflame-retardants)
- [http://ecostandard.org/category/flame-retardants/](http://ecostandard.org/category/flame-retardants/)

---


\(^{24}\) European Food Safety Authority. EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Emerging and Novel Brominated Flame Retardants (BFRs) in Food. EFSA J. 2012, 10, 125.


[http://www.chemtrust.org](http://www.chemtrust.org)  
Twitter: @CHEMTrust
4. UV Filters – benzophenones

**Summary of nomination: Lead substance: Oxybenzone (benzophenone-3 (BP-3)), CAS: 131-57-7**

There are different UV filters, many of them are widely used in sunscreen, cosmetics and other personal care products but partly also used in plastics and coating and inks.

1. benzophenone (BP), 119-61-9
2. benzophenone-1 (BP-1), 2,4-Dihydroxybenzophenone CAS: 131-56-6
4. benzophenone-3 (BP-3), oxybenzone, CAS: 131-57-7
5. 5-chloro-2-hydroxybenzophenone (BP-7), CAS: 85-19-8
6. 4-hydroxy- benzophenone (4-HBP), CAS; 1137-42-4
7. 4-methyl-benzophenone (4-MBP), CAS: 134-84-9

Recent research findings\(^{26}\) have highlighted the concern over all-year background exposure of Oxybenzone BP-3 (also known as oxybenzone). Benzophenone-3 (BP-3) and its metabolite BP-1 are both suspected endocrine disrupters, as well as many other compounds belonging to this group.

**Knowledge needs**

Ultra violet (UV) filters with known or suspected endocrine disrupting properties are widely used in sunscreens and other personal care products, clothing, food packaging and many other consumer products (probably with other functions than UV protection).

Human biomonitoring studies have confirmed widespread human exposure to certain UV filters. Oxybenzone has been detected in house dust, as well as in blood and urine from people in the US, Europe and China.

There is limited information on concentrations and quantities of the substances in the different types of products, which limits an assessment of the extent to which the different product types contribute to the total exposure of the general population and vulnerable groups such as children and pregnant women.

There are limited biomonitoring data for UV filters and UV absorbers used exclusively for purposes other than cosmetics. Such data could help to identify how much other uses contribute to the overall exposure.

There is a need to clarify exposure routes to children apart from sunscreen: urine samples also contained the chemicals in winter season. More human biomonitoring data from other parts of Europe could provide useful insights and clarify the concern and establish if stricter controls are needed to address the potentially harmful exposure.

**Relevant literature**

- The Danish Environmental Protection Agency: Survey and health assessment of UV filters - Survey of chemical substances in consumer products No. 142, 2015\(^{27}\)
- Glenn C. Morrison, Gabriel Beko, Charles J. Weschler, Tobias Schripp, Tunga Salthammer, Jonathan Hill, Anna-Maria Andersson, Jorn Toftum, Geo Clausen,


\(^{27}\) [https://www2.mst.dk/Udgiv/publications/2015/10/978-87-93352-82-7.pdf](https://www2.mst.dk/Udgiv/publications/2015/10/978-87-93352-82-7.pdf)
and Hanne Frederiksen, Dermal uptake of benzophenone-3 from clothing, *Environ. Sci. Technol.*, 2017, DOI: 10.1021/acs.est.7b02623


**Policy needs**

BP-3 is currently evaluated by Denmark in the context of REACH, the reason being its endocrine disrupting properties and wide dispersive use.\(^\text{28}\) It would be important to evaluate cumulative exposures from different exposure routes to the same UV filter as well as to different, similarly acting UV filters and see what that means for risk assessment and management. More clarity is needed how concerning the current exposure situation is for children and pregnant women.

EU has just further restricted and lowered the permitted concentrations of benzophenone-3 in sunscreen and in other cosmetics with effect from September 2017.\(^\text{29}\)

It would be important to check if exposure will go down and if as a result the exposure to other benzophenone compounds might increase.

Some substances of the proposed benzophenone group have also been included in the SIN list due to concerns over their potential endocrine disrupting properties.\(^\text{30}\)

**Public concern (examples):**

- [https://chemicalwatch.com/58523/clothing-may-increase-exposure-to-uv-filter-benzophenone-3](https://chemicalwatch.com/58523/clothing-may-increase-exposure-to-uv-filter-benzophenone-3)
- [https://biomonitoring.ca.gov/sites/default/files/downloads/FactSheet-Benzophenone3.pdf](https://biomonitoring.ca.gov/sites/default/files/downloads/FactSheet-Benzophenone3.pdf)
- [http://www.ewg.org/sunscreen/report/the-trouble-with-sunscreen-chemicals/#.WcWMmi0M2w](http://www.ewg.org/sunscreen/report/the-trouble-with-sunscreen-chemicals/#.WcWMmi0M2w)
- [http://pubs.acs.org/doi/abs/10.1021/acs.est.6b05211](http://pubs.acs.org/doi/abs/10.1021/acs.est.6b05211)

---


5. UV Filters - methoxycinnamates

**Summary of nomination: Lead substance: OMC (2-ethylhexyl trans-4-methoxycinnamate) CAS: 5466-77-3**

- 2-ethylhexyl trans-4-methoxycinnamate (OMC) – CAS: 5466-77-3:
  - Justification given in Community Rolling Action Plan (CoRAP): suspected PBT and EDC, wide dispersive use (1000-10 000 tpa):
  - Isopentyl p-methoxycinnamate (IPMC) – CAS: 71617-10-2
    - Registered under REACH, used in cosmetics and personal care products:

**Knowledge needs**

2-ethylhexyl trans-4-methoxycinnamate is assessed in the context of the REACH evaluation (CoRAP) on the grounds of being a suspected PBT and suspected endocrine disrupter as well as its wide dispersive use in consumer products.31

It would be important to fill information gaps on current exposure to both 2-ethylhexyl trans-4-methoxycinnamate and isopentyl p-methoxycinnamate from different uses to be able to assess the total exposure of the general population and vulnerable groups such as children and pregnant women.

Furthermore, there are knowledge gaps on the toxicological properties, fate and behaviour and ecotoxicological properties. Given the high production volume and its use in personal care products it makes it a high priority for further assessment.

HBM4EU could provide an added value to more systematically evaluate the exposure of children and women in child-bearing age to these potential endocrine disrupters used in consumer products. It would also be useful to gather more information about other relevant uses besides personal care products.

The use in cosmetics is expected to account for the majority of exposure to OMC. OMC has been identified in biomonitoring studies and it has been measured in drinking water and in the environment, indicating a relatively high consumer exposure not only to sunscreen products, but also to the many other cosmetic products which are used all year round.

**Relevant literature**

- The Danish Environmental Protection Agency: Survey and health assessment of UV filters - Survey of chemical substances in consumer products No. 142, 2015 27
- A study by Manová et al., 2015 on the aggregate consumer exposure to UV filter ethylhexyl methoxycinnamate via personal care products found that children were the highest exposed individuals in that study population.
- The association between use of sunscreens and cosmetics and urinary concentrations of the UV filter ethylhexyl-methoxy cinnamate: A pilot biomonitoring study.

---


[http://www.chemtrust.org](http://www.chemtrust.org)
Policy needs

Ethylhexyl methoxycinnamate (OMC) is registered under REACH for different uses in the tonnage band of 1,000-10,000 tonnes. Another UV filter registered in this high volume is octocrylene (CAS No. 6197-30-4) which is also applied in various consumer uses.

The report by the Danish Environment Agency on UV filters from 2015 illustrated the many different chemical compounds used as UV filters in various applications, many of them in high volumes and with suspected endocrine disrupting properties. There is a general lack of information regarding the effect of daily exposure to multiple UV protective substances with potential endocrine disrupting properties. This issue adds further uncertainty to the risk assessments, since it is still under discussion as to whether thresholds for effects of endocrine disruptors can be assessed with reasonable certainty.

There is also limited knowledge about which UV filters and UV absorbers are contained in articles imported from countries outside the EU such as textiles (clothes, automotive textiles, technical textiles, etc.) or articles of plastic, and quantities of the UV filters and UV absorbers imported with these products.

Some substances of the proposed benzophenone group have also been included in the SIN list due to concerns over their potential endocrine disrupting properties.30

Public concern

- [http://www.ewg.org/sunscreen/report/the-trouble-with-sunscreen-chemicals/#.WcWMmi0M2w](http://www.ewg.org/sunscreen/report/the-trouble-with-sunscreen-chemicals/#.WcWMmi0M2w)
- [https://chemicalwatch.com/55320/echa-updates-substance-assessments-under-pact](https://chemicalwatch.com/55320/echa-updates-substance-assessments-under-pact)
- [https://www.soilassociation.org/media/11393/c4c-report-3.pdf](https://www.soilassociation.org/media/11393/c4c-report-3.pdf)