HBM4EU science and policy for a healthy future

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HBM4EU

POLICY BRIEF

JULY 2022

European Human Biomonitoring Initiative

Benzophenones

This policy brief summarizes the adverse human health effects of benzophenones, their main exposure pathways for humans, and how human biomonitoring (HBM) of benzophenones could be of value in the development of EU policies.

Benzophenones are a group of substances used as UV filters in cosmetics, personal care products, food contact materials, inks, textiles, and other consumer products. Despite widespread usage, there is a knowledge gap regarding health and environmental impacts of benzophenone exposure and growing societal concern regarding their safety. Improved understanding of the risks associated with benzophenones is imperative because the societal concern could encourage consumer avoidance of sunscreens, and thereby increase public health risk of pathologies such as skin burns and skin cancers.

KEY MESSAGES

- Some benzophenones are suspected to cause endocrine disruption (for example BP-3, BP-1), and others are suspected to cause cancer. HBM4EU provided data on human internal exposure to benzophenones at the European level, which was previously limited.
- Within HBM4EU, new data was generated on the exposure of teenagers and adults to BP-1, BP-2, BP-3 and BP-7. While BP-3 and BP-1 were detected in most samples, BP-2 and BP-7 were found in less than 10% of urine samples and the detected concentrations were low.
- Data suggests that women are more exposed to BP-3 than men. Due to the potential impacts on maternal and developmental toxicity, pregnant women are expected to be the most vulnerable group to the adverse effects of benzophenones.
- Societal concern regarding benzophenones may lead to reduced use of sunscreen products, which could adversely impact public health due to increased risk of skin cancer.
- Risk assessment based on newly generated HBM data indicate that BP-3 exposure levels are safe and below the level of concern.

BACKGROUND: HBM4EU

The European Human Biomonitoring Initiative, HBM4EU, running from 2017 to June 2022, is a joint effort of 28 countries, the European Environment Agency and the European Commission, and co-funded under Horizon 2020. The main aim of the initiative is to coordinate and advance human biomonitoring in Europe. HBM4EU has provided a wealth of improved evidence of the actual exposure of citizens to chemicals and their possible health effects. Human biomonitoring allows us to measure our exposure to chemicals by measuring either the substances themselves, their metabolites or markers of subsequent health effects in body fluids or tissues. Information on human exposure can be linked to data on sources and epidemiological surveys to inform research, prevention, and policy with the objective of addressing knowledge gaps and promoting innovative approaches. If you would like to read more about the project itself, please visit the HBM4EU website.

HBM4EU RESULTS

The main outputs from HBM4EU, have been extracted from IPCHEM (the European Commission's Information Platform for Chemical Monitoring), the reference access point for searching, accessing, and retrieving chemical occurrence data collected and managed in Europe.

HBM4EU laid the foundations for a European HBM platform to monitor human exposure to priority chemicals (including benzophenones) and related health effects in a harmonised and quality-controlled way. More information on benzophenones is available in the HBM4EU scoping document. A Quality Assurance/Quality Control Programme was implemented in order to establish a HBM European Platform of candidate laboratories that are equally qualified for exposure biomarker analysis.

To further support current and future HBM studies, HBM4EU has produced a variety of publicly available groundwork materials for a harmonised approach to study planning and conduct in Europe, available in the HBM4EU online library.

- HBM data on benzophenones can be explored and visualized on the HBM4EU interactive dashboard.
- A consolidated literature review on the levels and sources of exposure to BP-3 and a comparison of exposure levels in sub-populations has been performed. Preliminary results showed no significant differences between urinary BP-3 levels in Western, Southern, and Northern Europe.
- A risk assessment of BP-3 was performed based on available HBM data and was updated using new data from HBM4EU Aligned Studies[1]. Based on the preliminary assessment using new HBM data, exposure levels to BP-3 were below the level of concern indicating no health risk at the current state of knowledge. However, some concerns were flagged related to the presence of the unregulated BP-1 in most human samples.
- A review on using HBM data to support risk assessment of cosmetic ingredients was published using BP-3 as an example.

The HBM4EU initiative has been successful in addressing some policy questions on benzophenones, for example on safety of exposure levels. The review of results is available here. These outputs highlight the potential of HBM4EU to provide evidence to answer the policy questions.

EXPOSURE & HEALTH EFFECTS

The main source of exposure for the general population in Europe to benzophenones is likely the direct application of sunscreens and cosmetics, but little is known about the relative importance of other exposure sources such as food contact materials.

Whilst there are many speculative impacts of benzophenones on human health, the most critical hazards are:

- Maternal and reproductive toxicity and the impact on thyroid hormones (BP-3)
- Potential carcinogenicity (BP)
- Liver and kidney impacts (BP)

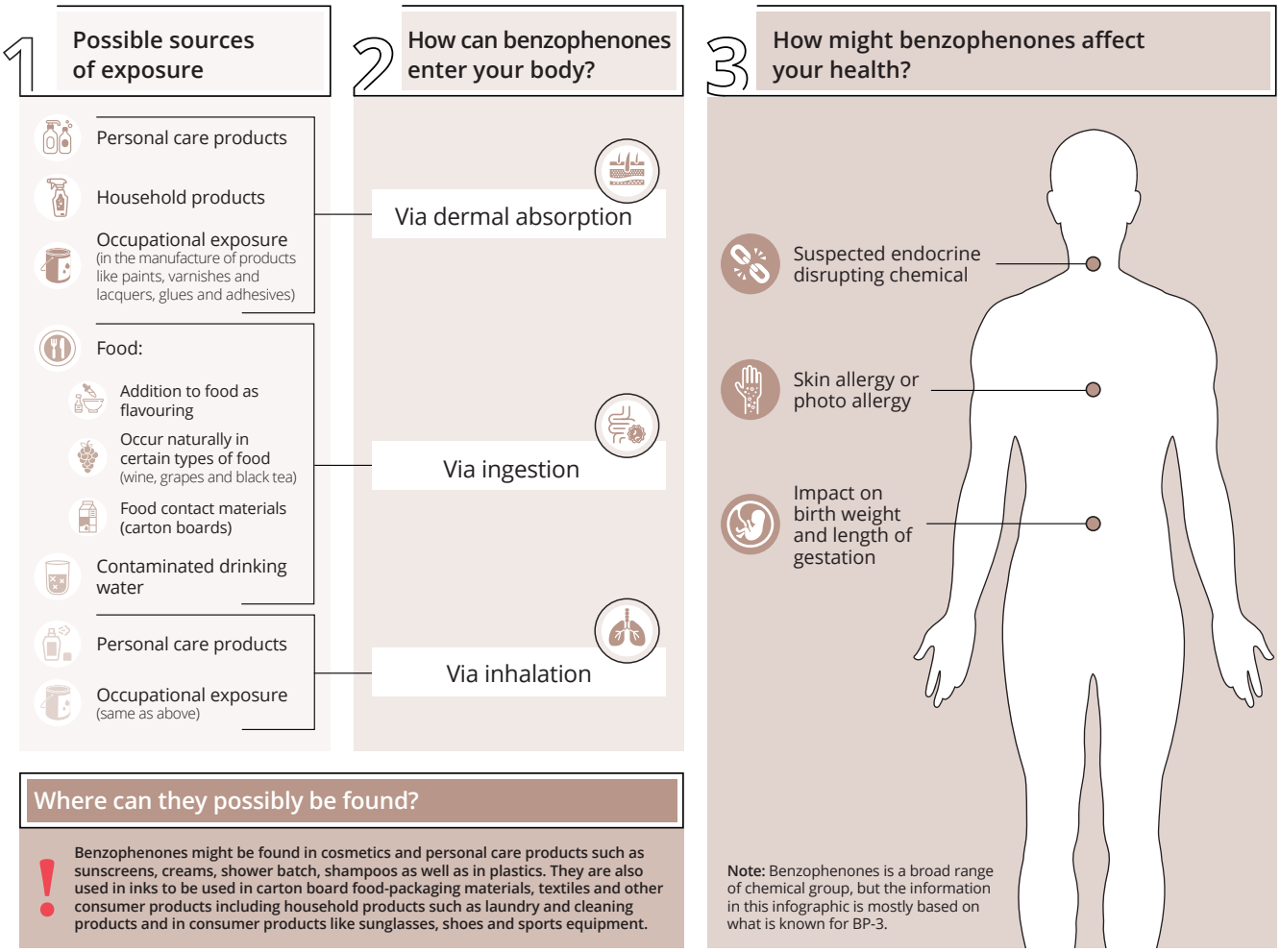
HBM4EU has identified effect biomarkers for benzophenones including reproductive and thyroid hormones which can be used in future studies to explore the adverse health effects of benzophenones.

The strength of evidence translating these potential hazards to real impacts on humans varies and therefore human biomonitoring could be used to explore causal links between benzophenone exposure and human health impacts.

An overview of main sources of exposure (environmental, occupational, consumer), exposure pathways (oral, inhalation, dermal) and health effects is provided in Figure 1.

1 The HBM4EU Aligned Studies are a survey aimed at collecting HBM samples and data as harmonised as possible from (national) studies to derive current internal exposure data representative for the European population/citizens across a geographic spread.

Figure 1. Overview of exposure sources, pathways and health effects of benzophenones



INPUT TO POLICY PROCESSES AND RELEVANT POLICY MEASURES

HBM4EU results have contributed to consultations for the Chemicals' Strategy for Sustainability and the Zero-Pollution Action Plan. These are available in the HBM4EU Science to Policy section.

Several policy measures have already been introduced in the EU to address human exposure to benzophenones and manage potential risks. A report on relevant legislation is available here. In general, the existing EU policies cover regulations on chemicals, consumer products and occupational exposure. In terms of environmental regulations, there is no relevant legislation available yet.

BP registered uses are regulated under Regulation (EC) No 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). BP is subject to EU harmonised classification and labelling under Regulation (EC) No 1272/2008 on classification, labelling and packaging (the CLP Regulation).

Consumer-related EU regulations include the restriction of BP-3 to 6% in cosmetic sunscreen products and to 0.5% in other cosmetic products (Cosmetics Regulation (EC) No 1223/2009) and plastic materials in contact with food (Regulation (EC) 2002/72).

Occupational exposure legislation could be indirectly covered by the pregnant workers directive (92/85/EEC).

POLICY QUESTIONS

The answers to the policy questions below are summarised. For more details, please see the Substance Reports available on the substance specific page of the HBM4EU website.

1 Are sensitive reliable and cost-effective methods and biomarkers available to measure UV filters?

Analytical methods are available to measure benzophenone UV filters in urine. Benzophenone-3 (BP3) is the urinary biomarker most commonly measured in this group.

2 What are current exposure levels to benzophenones in the EU population (cumulative exposure from different exposure sources)?

Aligned studies results (2014-2018) from studies in Germany, Luxembourg, Sweden, Norway, Spain and Poland indicate that there is widespread exposure to BP-3 in adults and teenagers in Europe. Exposure to BP-2 and BP-7 was very limited (detected in less than 10% of urine samples). BP-3 and BP-1 were more commonly measured, with concentrations of BP-3 the double than BP-1.

P50 and P95 of urinary BP-1 concentrations in teenagers are in the range of 0.47-1.66 µg/g crt (1 study with P50 value < detection limit: 0.5 µg/L) and 6.66–26.35 µg/g crt. In adults P50 and P95 are in the range of 0.37–0.69 µg/g crt (1 study with P50 value < detection limit: 0.5µg/L) and 6.85-20.43 µg/g crt in adults.

P50 and P95 of urinary BP-3 concentrations are in the range of 0.88-3.68 µg/g crt (1 study with P50 < detection limit: 2 µg/L and 14.34-68.83 µg/g crt in teenagers and 0.94-2.33 µg/g crt (one study with P50 value < detection limit: 2 µg/L) and 18.97-64.98 µg/g crt in adults.

3 What are the major sources of exposure to benzophenones in the EU population and in vulnerable groups such as children and pregnant women?

Based on the literature review, personal care products are the most common exposure source, mainly sunscreen. This association was difficult to explore in the aligned studies because of missing data.

In terms of personal care products determinants, only deodorant use showed any statistically significant association with UV filters. For both BP-1 and BP-3, higher levels were associated with everyday or almost everyday use of deodorant when compared to the reference of no or rare use of deodorant. No other statistically significant associations or patterns were observed.

4 Do exposure levels differ significantly between different EU countries (possibly related to climate)?

Based on available literature, there are no significant regional differences in BP-3 exposure across Europe. No significant difference in average urinary BP-3 levels between Northern, Western and Southern Europe were observed when adjusting for sex, age and period of sample collection.

5 Do exposure levels differ between different subgroups: elderly, adults, and children? Between males and females? Between adults of different age groups? Between individuals in different ethnic subgroups (perhaps due to differences in use of sunscreen products)?

Based on results from the aligned studies, females have significantly higher BP-3 urinary concentrations than males.

According to the Danish DEMOCOPHES data collection, female children have slightly higher median urinary levels than male children for BP3.

Studies conducted in Northern Europe (literature review) showed no significant difference in reported average BP-3 levels in urine between males and females. Average urinary BP-3 levels were significantly lower in children and adolescents compared to adults.

In addition, a systematic review of BP-3, together with a meta-analysis of human biomonitoring data on BP-3 and BP-1 was performed under HBM4EU. The meta-analysis of HBM studies showed that urinary BP-3 concentrations were around 10- and 20-fold higher in North America compared to Europe and Asia, respectively. Although median urinary BP-3 concentrations usually found in Europe correspond to a low-dose range, top percentiles of population exposure (P90 and P95) were significantly higher, being possibly linked to peak-exposure scenarios after sunscreen and cosmetic use.

6 Are current exposure levels safe in relation to the endocrine and carcinogenic properties of benzophenones? (for the general population and for vulnerable groups such as children and pregnant women?)

The most sensitive endpoint for the hazardous properties of benzophenone-3 was maternal and developmental toxicity.

Risk assessment of BP-3 based on urinary levels and effect levels, in studies from 2010 and 2013 showed that exposure estimates of BP-3 ranged from 0.60 to 4.40 µg/g creatinine for the average exposure, and 16.30 to 392.00 µg/g creatinine for the reasonable worst-case exposure. With the derived provisional HBM guidance value of 333 µg/g creatinine, the exposure estimates of the average exposure did not exceed the guidance value. The exposure estimates of the extensive exposure did exceed the guidance value.

Based on data from the aligned studies in 2014-2018, the average and reasonable worst case scenario exposure levels did not exceed the provisional HBM guidance value. Urinary levels (average <LOQ to 3.68 µg/g and reasonable worst-case exposure 18.97 to 68.83 µg/g) were below the guidance value and were no longer of concern.

This finding implies that in general there is no risk indicated to the population included in the aligned studies. There are notable differences in exposure between the groups investigated, with the most highly exposed groups approaching (but not surpassing) the acceptable risk levels for BP-3.

There is a need to assess BP-1 and BP-3 concentrations in cosmetic products commercialized in Europe, as well as to better characterize human peak-exposure scenarios after sunscreen and cosmetic use.

7 Was the restriction of BP-3 in cosmetics in the EU (September 2017) effective in reducing public exposure? Did exposure to other benzophenone or other UV filter compounds increase as a result?

Yes, urinary levels of BP-3 were lower in 2014-2018 compared to those in 2010-2013. Data is not available to evaluate whether exposure to other UV filters increased during this period.

KNOWLEDGE GAPS

While the HBM4EU Aligned Studies provided data on exposure of teenagers and adults, current data on the exposure of children to benzophenones is lacking in Europe.

Also, while HBM data provides insight into real-life exposures, which can be used to refine regulatory risk assessments and assess the effectiveness of regulation, there is no official guidance on the use of HBM data in regulatory risk assessment of cosmetic ingredients.

Gaps include:

- contribution of different cosmetic products and sunscreens to total exposure
- evidence on food contact materials as a source of exposure
- differences in exposure levels between age groups

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