Prioritised substance group: UV filters (benzophenones)

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Short overview of results of the activities carried out within HBM4EU in 2020 to answer the policy questions with reference to corresponding deliverables.

Policy Question	Short Summary of Results
Are sensitive reliable and cost-effective methods and biomarkers available to measure UV filters?	List of biomarkers, matrices and analytical methods is available (WP 9). UV-filters (benzophenones; BPs) are analysed as total, free or conjugated BPs. Determination of total or conjugated BPs include enzymatic hydrolysis. The extraction procedures consisted of dispersive liquid-liquid microextraction, SPE, and automated online SPE. The automated online SPE systems have the highest throughput. BP3 has been measurd in most laboratories. List of 8 candidate laboratories for analysis of benzophenones is available (WP 9.2). This list includes laboratories in Denmark, Germany, Norway, Sweden and Spain. Several expert laboratories were chosen to participate in Interlaboratory Comparison Investigations for analysis of BP-1 and BP-3. As part of WP8 (fieldwork preparation) AD7.2 included information on stability of BP-3 in urine. It was reported that urinary conjugates of benzophenone-3 (BP-3) are stable for one week when urine is stored at 4°C and for at least six months when stored at -70°C. In contrast, BP-3 conjugates commenced to degrade after three days when the urine was stored at room temperature.
What are current exposure levels to benzophenones in the EU population (cumulative exposure from different exposures sources)?	Harmonised aggregated data and exposure distributions for BP-1, BP-3 and the metabolite 2,2'-dihydroxy-4-methoxybenzophenone (DHMB) in urine, stratified by age and gender is available (WP 10-D10.6). These harmonised aggregated data are obtained from two data collections from Denmark: Democophes with exposure data for children and teenagers, and DYMS (Danish Young Men Study) with exposure data in teenagers; and one from Germany: Environmental Specimen Bank with exposure data in adults. Data is available from these collections on morning urine (Democophes), random spot urine (RegionH) or 24 hr urine (ESB). The heterogeneity of the data collections (different age range, different sampling types, different sampling years) makes it difficult to compare the levels between data collections. It appears that based on the Danish Democophes data collection that female children have slightly higher median urinary levels than male children for BP-3. Report on studies on UV filters in EU in adults, children, adolescents is available (WP7). Based on the 2018 questionnaire, there are 6 studies which included collection of data on UV filters, most of which are in the Northern region. No initiated or planned studied were reported on UV filters in children and adolescents, however one study was initiated in

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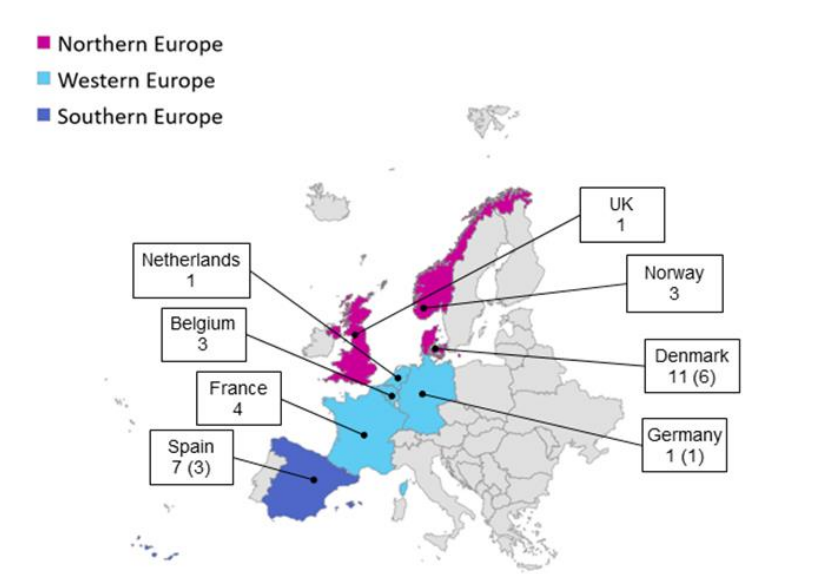
	adults. There were more studies on children and adolescents compared to adults and elderly. Studies reported in the 2018 questionnaire collected data on UV filters in a range of biological samples including blood, saliva, urine, hair and umbilical cord blood. Planning of aligned studies is underway (WP8). The biomarkers included in the aligned studies are BP-1, BP-2, BP-3 and BP-7. Data will be collected in adolescents and adults in Sweden(?), Norway, Poland, Portugal and Spain. Evaluation of exposure levels in available literature on BP-3 as part of the risk assessment is ongoing (WP5.3) Review on the available literature on Benzophenone-3 and -1 (WP13-WP14) includes map showing number of studies from EU countries  European countries for which publications reporting human benzophenone-3 (and -1) were identified. In the boxes the number of publications reporting BP-3 human exposure data is presented for each country. The number in the brackets represents the number of those publications, which provided information on BP-1 concentration as well. *HBM4EU WP13 working group on Benzophenones*
What are the major sources of exposure to benzophenones in the EU population	Development of questionnaires for adults and adolescents was completed (WP7.3). The main variables in the questionnaire for UV filters cover use of cleaning products and scents in the home, consumption of food in food contact materials, use of cosmetics and

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and in vulnerable groups such as children and pregnant women?	hygiene products, type of sunscreen used, and DIY hobbies and activities. The statistical analysis of existing data (WP10 in collaboration with WP13-14) will be based on a meta-analysis and will include a section on main sources of exposure.
Do exposure levels differ significantly between different EU countries (possibly related to climate)?	No., Available data from literature (studies between 2004 – 2017) on average urinary BP-3 levels from studies from Western Europe (4 studies), Southern Europe (1 study) and Northern Europe (19 studies) were compared in a random-effects meta-regression model. No studies with data on urinary BP-3 were identified from Eastern Europe. No significant difference in average urinary BP-3 levels between the three regions were observed when adjusting for sex, age and period of sample collection. (WP13)
Do exposure levels differ between different sub-groups: 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)?	Exposure distributions BP-1, BP-3 and DHMB in urine, stratified by age and gender is available (WP 10, D10.6), however only 3 data collections were obtained. Reported average BP-3 levels in urine stratified by age and gender based on the literature is available for Northern Europe (WP13). No significant difference was seen between males and females in these European studies. Average urinary BP-3 levels were significantly lower in children and adolescence compared to adults.
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)?	Appropriate effect biomarkers were identified (WP 14.1) These include: ○ Reproductive hormones: BP-3 could alter the androgen/estrogen balance based on experimental findings, and urinary exposure to BP-3 was associated with decreased serum TT levels in adolescent males in the NHANES. Thyroid hormones: Exposure to BP-3 is associated with altered thyroid hormone levels in several studies, including both pregnant women and adults. Experimental studies support that benzophenones may alter thyroid hormone balance by influencing their central regulation and metabolism and inhibition of thyroid peroxidase (TPO) appears as a potential mechanism. Moreover, effects may be more pronounced in a context of low iodide availability, still prevalent in many parts of the world. Risk assessment of BP-3 based on urinary levels and effect levels, taking into account the new evaluation of the SCCS is currently ongoing (WP 5.3) WP12 prepared a review of available PBTK models for benzophenones. Three human model PBTK models for benzophenones have been published.
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?	Data is not available to answer this question (no studies identified with sampling after 2017). There was no significant change in average BP-3 levels from 2003-2017 within the Northern European studies. Data from aligned studies may provide data to answer this question. However only BP-3 will be measured in these studies.