1 Prioritised substance group: UV filters

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1.1 Background information

1.1.1 Hazardous properties

Benzophenone 3 (BP-3) displays a low acute toxicity profile. It is not considered as being irritating to the skin and the eyes1. Results from animal studies—primarily dietary studies that affected body weight gain—showed alterations in liver, kidney, and reproductive organs in rats and mice with BP-3 administered dermally and orally[2].

BP-3 is on the Community Rolling Action Plan (CoRAP) list because of potential endocrine disruption3. BP-3 elicited anti-androgenic activity in a human breast carcinoma cell line4 and interferes with functions of human sperm cells in vitro. Critical effects are maternal and developmental toxicity5. In cell cultures, BP-3 (and also BP-8) were found to affect lipid metabolism6. Larval zebrafish exposed to environmental concentrations of BP-3 showed developmental neurotoxicity, altered motor and social behaviors, in addition to changes in cell proliferation and apoptosis in the larval head region7. In female mice, low dose exposure causes long-lasting alterations to mammary gland morphology and function8. Dermal exposure of pregnant mice to low doses of BP-3 (during early pregnancy) resulted in intrauterine growth restriction phenotype and in disturbed sex ratio (more female offspring)9. Prenatal exposure of pregnant mice to BP-3 impairs autophagy, disrupts several signalling pathways and also alters epigenetic and post-translational statuses in brain neurons10. Studies in rat primary cortical neuronal cultures and neuroblastoma cell lines showed decreased cell viability after BP-3 treatment at moderate concentrations11. In addition, exposure at birth of rats to BP-3 perturbs early events of germ cell development, and alters early follicular assembly12.

In a study on young men from Spain, there was a significant positive association between urinary BP-3 concentrations and serum FSH levels13. In male adolescents in the US, urinary BP-3 was associated with lower total testosterone14. In a study of young Danish men, associations between male reproductive health parameters and urinary levels of benzophenones such as BP-3, BP-1 and 4-HBP were observed in filaggrin gene mutation carriers but not in controls15. In a study in healthy, premenopausal women, UV filter factors (BP-1, BP-3) were associated with decreased estradiol, FSH, and LH16. In pregnant women from the Boston area, elevated urinary concentrations of phenols including benzophenone-3 were associated with increases in the urinary oxidative stress biomarkers 8-OHdG and 8-isoprostane17.

Exposure to BP-3 was not associated with preterm birth18, but was associated with decreased birth weight and length (in girls only)19.

Benzophenone is possibly carcinogenic to humans (Group 2B, IARC classification, based on sufficient evidence in experimental animals)4 Benzophenone exerts tumourigenic effects in rats and mice in the liver, the kidney and in the haematopoetic system, including rare histiocytic sarcomas. Available evidence supports that benzophenone is not genotoxic. Benzophenone meets the criteria for classification as carcinogenic in category 2[20]. Benzophenone may alter endocrine signalling through multiple effects on receptors. Critical effects are liver and kidney effects.

Benzophenone-1 (BP-1) is a UV filter and metabolite of BP-3. BP-1 is not irritating nor sensitizing at concentrations that may be found in cosmetic products. The toxicity studies available indicate

low acute and subchronic toxicity of BP-1. BP-1 is not mutagenic. The lowest effect levels were determined for reproductive toxicity with lowest observable adverse effect levels (LOAELs) between 100-625 mg/kg and NOAELs between 100-250 mg/kg. BP-1 is on the European Commission priority list of potential endocrine disruptors[21].

In a study of young Danish men, associations between male reproductive health parameters and urinary levels of benzophenones such as BP-3, BP-1 and 4-HBP were observed in filaggrin gene mutation carriers but not in controls. In a study in healthy, premenopausal women, UV filter factors (BP-1, BP-3) were associated with decreased estradiol, FSH, and LH[15-16]

In the a Spanish sub-cohort from the European Prospective Investigation into Cancer and Nutrition study, a negative trend between BP1 and type 2 diabetes mellitus risk was observed in women[22].

Benzophenone-2 (BP-2) is a UV filter commonly used in personal care products. BP-2 may disturb thyroid hormone homeostasis by inhibiting or inactivating thyroid peroxidase, effects that are even more pronounced in the absence of iodide[23]. Both BP-2 and BP-3 were shown to exert uterotrophic effects and BP2 was shown to bind to estrogen receptors[24]. In fish and mammals, BP-2 induces a variety of reproductive disorders, including feminization of male fish, inhibition of gamete development in fish, reduction of testosterone secretions from testicular tissue, induction of uterotrophic effects in rats, changes in bone density and osteo-regulation, changes in luteinizing hormone, cholesterol levels, fat deposition, and an increased risk of endometriosis[25]. BP-2 was also found in the brains of rats that were dermally exposed to BP-2, this shows that BP-2 passes through the blood-brain barrier[26]. In a study on exposure to UV filters and fertility, male partners' concentrations BP-2 was associated with reduced fecundity[27].

4-Methylbenzylidene camphor (4-MBC) is found in cosmetics and in drinking water. The available data suggest no genotoxicity, mutagenic potential or phototoxicity of 4-MBC. However, this chemical is suspected to have a mild endocrine disrupting effect on the thyroid gland. Experiments in rats found 4-MBC to have development toxicity[21,28]. A recent study that exposed human cell culture (trophoblast cells) to 4-MBC showed that this chemical has the potential to delay the normal growth and survival of tissue and may hamper normal placental formation during early pregnancy[29]. Exposure of zebrafish embryos to 4-MBC induced morphological abnormalities during embryonic development, including notochord curvature, delayed absorption of yolk sac and pericardial oedema, in addition to the decrease in embryo heart rate[30].

3-benzylidene camphor (3-BC) - 3-BC is a potential endocrine disrupter[31]. Experiments in vivo and in vitro revealed oestrogenic activity. In addition, 3-BC was found to interrupt sexual development and maturation in animal models. According to the Scientific Committee on Consumer Safety, hormonal activities of 3-BC have been reported in vitro: estrogenic and anti-estrogenic effects as well anti- androgenic activities. In vivo, the expression of target genes (ERα, ERβ, SRC-1 and PR (progesterone receptor)) has been shown to be altered in both males and females rats[32].

4-hydroxy benzophenone (4-HBP) is used as an industrial UV-filter. 4-HBP has potential to disrupt endocrine activity, and fetal growth. 4-HBP exposure in women carrying a male fetus was associated with increased maternal thyroid hormone concentrations, in addition to decreased birth outcomes (lower weight and shorter head and abdominal circumferences at birth compared to the low exposure group)[33].

4-methylbenzophenone (4-MBP) is used in paints and varnishes, in food packaging but not in cosmetics. According to an assessment by EFSA, the currently available data on 4-methylbenzophenone are insufficient to enable the assessment of this substance with respect to its human toxicological effects. 4-MBP is expected to be a non-genotoxic carcinogen[34].

Hazardous Properties of Benzophenones

	Critical effect	Potential Endocrine Disruption	Other
BP-3	Maternal and reproductive toxicity	Suspected	Developmental neurotoxicity
BP	Liver and kidney	Suspected	Possible carcinogenic in human (IARC)
BP-1		Suspected	
BP-2		Suspected	
4-MBC	Repeated dose: thyroid effects	Suspected	
3-BC		Suspected	
4-HBP		Suspected	
4-MBP			Expected carcinogen (EFSA)

1.1.2 Exposure characteristics

Benzophenone is manufactured and/or imported in the European Economic Area in 1000-10000 tonnes per year; it is used by consumers, by professional workers (widespread uses), in formulations or re-packaging and at industrial sites.

Benzophenones are used in cosmetics and in personal care products, food contact materials, coating products, fillers, modelling clay and finger paints. UV-absorbers and UV filters including benzophenone-1 and benzophenone-3 are added to food packaging to protect the packaging itself and the contained food from harmful UV light[5].

Release to the environment is likely to occur from: industrial use, indoor use (e.g. machine wash detergents, personal care products, paints and coating, fragrances and air fresheners).

Biological half-life (urine) of 16 hours

Human Biomonitoring (HBM) data: pregnant women in US (California)[35], France[36], China[37], Israel[38], general public in Belgium[39], Denmark[40], and the US[46]. Data on exposure in children in available for the US[41], Denmark[42], China[43], Australia[44], and Taiwan[45]. Overal, BP-3/BP-1 exposure data is much more limited for children and adolescents compared to adults.

Several biomonitoring studies (including NHANES) have focused on BP-346. BP-3 has been widely detected in several biomonitoring studies with urinary levels correlated with the use of personal care products. Higher BP3 exposure has been observed in the female population, possible due to its presence in personal care products[46].

In women undergoing fertility treatments, self-reported sunscreen use, physical activity, and time spent on moderate/heavy outdoor work were positively associated with urinary benzophenone-3[47]. In pregnant Chinese women, urinary levels of benzophenones were associated with the refurbishment of homes and household income, and higher levels of benzophenones were

observed in summer than in winter[48]. In women in Michigan (U.S), sunscreen use was strongly positively associated with benzophenone-3 concentrations. Benzophenone-3 concentrations tended to be highest in the summer (25.4%) and lowest in the autumn (−20.5%) compared with winter[49].

1.1.3 Policy relevance

Since September 2017 the use of BP-3 in the EU is restricted to 6% in cosmetic sunscreen products and up to 0.5 % in other cosmetic products[50]. In February 2020, the European Commission requested the SCCS to carry out a safety assessment on Benzophenone-3 in view of new information provided in a "Call for data on ingredients with potential endocrine-disrupting properties used in cosmetic products".

According to the Cosmetics Regulation (EU Regulation 1223/2009), BP-4 and BP-5 are permitted as UV filters in cosmetic products. 4-MBC is allowed as a UV filter in cosmetic products with a maximum concentration of 4% in ready-for-use preparations[51].

According to the Scientific Committee on Consumer Safety, the use of 3-BC as a UV-filter in cosmetic products in a concentration up 2.0% is not safe[32].

Benzophenone is approved as an additive in plastic food contact materials, with a specific migration limit of 0.6 mg/kg[52]. In September 2019, the USA amended food additive regulations to no longer authorise the use of benzophenone as synthetic flavoring substances for use in food and to no longer provide for the use of benzophenone as a plasticizer in rubber articles intended for repeated use in contact with food. According to the FDA, this action was taken in response to evidence that the additive causes cancer in laboratory animals, and despite the determination "that these substances do not pose a risk to public health under the conditions of their intended use"[53].

Inks are not covered by a specific European legislation on food contact materials. The use of printing inks has to comply with the general rules of Regulation (EC) No 1935/2004 and with good manufacturing practice as laid down in Commission Regulation (EC) No 2023/2006.

1.1.4 Technical aspects

BP-3 can be directly measured and quantified in urine in HBM studies. In addition, three oxidative metabolites (2,4-dihydroxylbenzophenone, 2,2′-dihydroxy-4-methoxybenzophenone, and 2,3,4-trihydroxybenzophenone) can also be measured in HBM studies using quantitative analytical methods[54].

On-line TurboFlow-LC-MS/MS method has been developed at Copenhagen University Hospital for simultaneous biomonitoring of nine UV filters in urine (benzophenone, benzophenone-1 benzophenone-2, benzophenone-3, 5-chloro-2- hydroxybenzophenone, 4-hydroxybenzophenone, 4-methyl-benzophenone, 3-(4- methylbenzylidene)-camphor, and 3-benzylidene camphor)[55].

1.1.5 Societal Concern

UV filters, including benzophenones, are widely used in cosmetics, personal care products, food contact materials, inks, textiles and other consumer products. Therefore, there is a high potential for the general public (including vulnerable populations) to be exposed to benzophenones.

While UV filters in sunscreens and cosmetics have been effective in protecting against a variety of UV-related pathologies, such as sunburns and melanomas, growing popularity of sunscreens and increasing potential exposure has led to increased societal concern about their potential impact on the environment and human health.

There are several EU regulations regarding benzophenones, such as the restriction of BP-3 to 6% in cosmetic sunscreen products and to 0.5% in other cosmetic products. However, there are

regulatory gaps regarding benzophenones. There are also knowledge gaps regarding the exposure pathways and health effects in humans of many of the benzophenones. BP-3 was included in the Community Rolling Action Plan list because of potential endocrine disruption and fulfilling exposure criteria[3].

BP, BP-2 and BP-3 are on the SIN ("Substitute It Now") list.

In addition, CHEMTrust nominated this group of chemicals as a priority substance for HBM4EU. In 2018, the Environment Working Group (EWG) reviewed studies and documents regarding UV filters and recommended a thorough investigation of the safety of all ingredients currently in sunscreens to ensure that none of them damage skin or cause other toxic effects in consumers. Because of concerns regarding potential health effects, the EWG has recommended that consumers avoid sunscreens with oxybenzone. It is noteworthy that consumer avoidance of sunscreens because could increase public health risk from UV rays (sunburn and skin cancers); ***therefore risk- benefit analysis and risk communication is especially important with regards to benzophenones.***

Of note, due to reports on adverse effects of UV filters on coral reef, there is societal concern about ecological effects of suncreens.

1.2 Categorisation of Substances

Table 1-1: Substances included in the substance group, listed according to availability of toxicology and human biomarker data, in category A, B, C, D, E substances (see general introduction)

Category	Abbreviation/ Acronym	Systematic name	CAS No.	Regulation
B	BP-3	Benzophenone-3	131-57-7	Cosmetics 2017/238
C	BP	Benzophenone	119-61-9	Plastic materials in contact with food 2002/72
C	BP-1	Benzophenone-1	131-56–6	
C	BP-2	Benzophenone-2	131-55-5	
C	4-MBC	3-(4-methylbenzylidene)-camphor	36861-47-9	
C	3-BC	3-benzylidene camphor	15087-24-8	
C	4-HBP	4-hydroxy-benzophenone	1137-42-4	
C	4-MBP	4-methyl-benzophenone	134-84-9	

Justification of Grouping

We propose to categorise BP-3 in Category B, as European HBM data are available from some countries. Understanding of sources of human exposure is limited. For BP-3, there is a need for improved understanding of exposure levels and potential health impacts to inform policy makers.

For the remaining substances, we propose to categorise them as Category C as HBM data is scarce. While analytical methods have been developed, there is a need for validation and widespread collection of data using validated methods.

1.3 Policy-related questions

1. Are sensitive, reliable and cost effective methods and biomarkers available to measure UV filters?
2. What are current exposure levels to benzophenones in the EU population (cumulative exposure from different exposures sources)?
3. What are the major sources of exposure to benzophenones in the EU population and in vulnerable groups such as children and pregnant women? (cosmetics and personal care products, plastic and other food contact materials, other)
4. Do exposure levels differ significantly between different EU countries (possibly related to climate)?
5. 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)?
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)

1.4 Research Activities to be undertaken

Table 1-2: Listing of research activities to be carried out to answer the policy questions

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
1. Are sensitive, reliable and cost effective methods and biomarkers available to measure UV filters?	Benzophenones	List of biomarkers, matrices, analytical methods, and candidate laboratories is available (WP 9)	**WP9 -** Update list of biomarkers, matrices, analytical methods and candidate laboratories as needed
2. What are current levels of exposure of the EU population to benzophenone UV-filters?	Benzophenones, emphasis on BP-3	There are ~30 published HBM studies reporting BP-3/BP-1 exposure data in European countries, with the largest number of studies in Denmark. BP-3/BP-1 exposure data is much more limited for children and adolescents compared to adults.	**Knowledge gaps: current level of exposure to benzophenones other than BP-3 and BP-1** **WP7** – Update of questionnaires on available data and studies as needed **WP10** - Identifying additional data collections and uploading metadata and aggregated data to IPCHEM **WP12** - Modelling, estimate exposure levels to benzophenones, differences within countries **WP8** - Generate new HBM data from aligned studies to fill identified data gaps
3. Do the exposure levels differ significantly between the countries?	Benzophenones, emphasis on BP-3	No. Available data from literature 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 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)	**Knowledge gaps: Only 1 study identified in Southern Europe, no studies with data on urinary BP-3 were identified from Eastern Europe** **WP13 / WP14** - Publication of a systematic integrative review on BP-3/BP-1 exposure levels **WP8** - Generate new HBM data from aligned studies to fill identified data gaps **WP10** – Statistical analysis plan for data obtained in the aligned study (geographical comparisons, exposure distributions and calculating European exposure values, if possible)
4. What are the main sources of exposure to benzophenones?	Benzophenones	Based on review of limited literature, main exposures sources include sunscreen, make-up products and personal care products. The occurrence of BP-3 at relatively high levels has been described in indoor dust, and to a lower extent in textiles, indoor air and tap water. Although benzophenones could be used in plastics and food contact materials to protect them from UV radiation, there is little published data available.	**Knowledge gaps: Literature available only on BP-3; little available evidence on food contact materials as source of exposure** **WP8** – Collect new data on exposure sources as part of alligned studies **WP10** – Statistical analysis plan for data obtained in the aligned study (exposure determinants) **WP13** – Publish review of available literarue on exposure sources

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
5. Who are the highest exposed groups? Are there statistical differences in concentration between different ages? males and females? Ethnic subgroups? occupational vs. general population exposure.	Benzophenones, emphasis on BP-3	Exposure distributions for BP-1, BP-3 and DHMB in urine, stratified by age and gender is available (WP 10). 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 European studies. Average urinary BP-3 levels were significantly lower in children and adolescence compared to adults.	**Knowledge gaps: Age and gender differences in Southern and Eastern Europe countires not available** **WP8 -** Alligned HBM studies on benzophenone exposure **WP10** – updated report on exposure distributions
6. Are current exposure levels safe?	BP-3 and BP-1	Appropriate effect biomarkers were identified Review on the available literature on Benzophenone-3 and -1 has been performed including evalution of toxicology studies, HBM data and exposure-health data, includes effect biomarker data and health outcome data, in vitro and in vivo data, intervention studies, xenometabolism.	**Knowledge gaps: The current research is not sufficient to answer this question** **WP5**:Risk assessment of BP-3 based on urinary levels and effect levels **WP12**: Development of integrated exposure modelling platform, PBTK modelling **WP13** – Continue review of cohorts available to link BP-3 exposure-health associations **WP13 – WP14** - Comparison of toxic doses and HBM data is ongoing
7. How can HBM4EU results feed into regulatory decisions and risk assessments (ECHA and EFSA)?	UV filters, specifically BP-3		**WP5 –** Risk Assessment started with data from available HBM studies
~~6. How effective was the restriction of BP-3 in reducing exposures in the EU population?~~	~~BP-3 and other benzophenones~~	~~Since September 2017 the use of BP-3 has in EU been restricted to 6% in cosmetic sunscreen products and up to 0.5 % in other cosmetic products~~	~~**WP10**~~ ~~- Compare between exposure to regulated UV-filters (BP-3) and nonregulated UV-filters~~

Table 1-3: Summary of biomonitoring studies on UV filters

Study / Institution	Country	Year of publication	Study Population	Matrix	Analytes	Citation + link
NHANES	USA	2003-2004	General, includes children	Urine	BP-3	Calafat et al.
NHANES	USA	2003-2010 (sample collection)	General, includes children	Urine	BP-3	CDC Report
Bispebjerg Hospital	Denmark	2004	General	Urine, plasma	BP-3, 4-MBC	Janjua et al.
Princess Alexandra Hospital	Australia	2005	Human skin culture	Skin	BP-3, Octocrylene	Hayden et al.
Sahlgrenska University Hospital	Sweden	2006	General	Urine	BP-3	Gonzalez et al.
Southe Korean institutes	South Korea	2010-2011	General	Urine	BP-1, BP-2, BP-3, BP-4, BP-8	Kang et al
Maternal and Infant Environmental Exposure Project (MIEEP)	USA	2010-2011 (sample collection)	Pregnant women and infants	Urine	BP-3	Biomonitoring California
Biomonitoring Exposures Study (BEST) – Pilot Study and Expanded Study	USA	2011-2012 (sample collection)	Adults	Urine	BP-3	Biomonitoring California
State University of New York at Albany	USA	2012	Woman	Urine	BP-1, BP-3, , BP-2, BP-8	Kunisue et al
Institut Albert Bonniot	France	2012	Mothers giving birth	Urine	BP-3	Philippat et al
Nankai University	China	2013	children, adults, and pregnant women	Urine, blood	BP-1, BP-2, BP-3, BP-8, 4OH-BP	Zhang et al
Institut Albert Bonniot	France	2013	Pregnant women	Urine	BP-3	Philippat et al
University of Copenhagen	Denmark	2013	Children	Urine	BP, BP-1, BP-2, BP-3, BP-7, 4-MBP, 4-HBP, 4-MBC, 3-BC	Krause et al
Queensland	Australia	2015	Children and adults	Urine	BP-3	Heffernan et al.

Study / Institution	Country	Year of publication	Study Population	Matrix	Analytes	Citation + link
Several universities	China	2015	Young children	Urine	BP, BP-1, BP-2, BP-3, BP-8, 4-HBP	Gao et al
University of Liege	Belgium	2014	Adults	Urine	BP-3	Dewalque et al.
Several universities	Denmark	2017	General	Urine	BP-1, BP-3	Morrison et al
I-Shou University	Taiwan	2017	Children and adolescents	Urine	BP-3	Chang et al
Copenhagen University Hospital	Denmark	2017	Children and adolescents	Urine	BP, BP-1, BP-2, BP-3, BP-7, 4-HBP, 4-MBP, 4-MBC, 3-BC	Frederiksen et al.
University of Bath	UK	2018	General (samples collected from a festival event)	Urine	BP-1, BP-2 ,BP-3, 3-BC, Homosalate, Octocrylene	Lopardo et al
Pregnant women in Israel	Israel	2018	Pregnant women	Urine	BP-3	Machtinger et al
EURO-MIX study	Norway	2019	Adult population	24 hr urine, blood	oxybenzone/ benzophenone-3	Husoy et al.
Sample pooling/ misclassification	France	2019	Pregnant women	Urine	BP-3	Vernet et al.
LIFECODES	USA	2019	Pregnant women	Urine	BP-3	Ferguson et al.
Environment and Reproductive Health cohort study	USA	2019	Women undergoing fertility treatment	Urine	BP-3	Minguez-Alarcon et al.
Universidade de São Paulo	Brazil	2019	New detection method	Saliva	Benzophenones (3, 1, 2, 8, 4-OH BP)	De Oliveira et al
College of Public Health and Human Sciences	USA	2019	Children and adults (>=6 years old) – exposure profiles	Urine	BP-3	Przybyla et al
South China Normal University	China	2019	Children (4-6 years old)	Urine	BP1, BP2, BP3, BP4	Li et al
University of Granada (GraMo cohort)	Spain	2019	adults	adipose	BP-3	Artacho-Cordónet al.

Study / Institution	Country	Year of publication	Study Population	Matrix	Analytes	Citation + link
Chinese Center for Disease Control and Prevention	China	2019	Pregnant women	Urine	4-OH-BP, BP-1, BP-3, TCS	Li et al.
Huazhong University of Science and Technology, Wuhan, Hubei	China	2019	Pregnant women	Urine	4-OH-BP, BP-1, BP-3	Long et al
HERMOSA study	USA	2019	adolescents	Urine	BP-3	Berger et al
Norwegian Institute of Public Health + Grenoble	France, Norway	2020	Pregnancy + first year (coupled)	Urine	BP-3	Rolland et al.
Study of Environment, Lifestyle, and Fibroids	USA	2020	Women, ages 23-34	Urine	BP-3	Bethea et al.
Copenhagen University Hospital	Denmark	2020	General, young males	Paired urine, serum, and seminal fluid samples	BP-3	Frederikson et al.
Granada EPIC-Spain cohort	Spain	2020		Serum	BP-1, BP-3	Salamanca-Fernandez et al.
Massachusetts General Hospital (MGH) Fertility Center	US	2020	Fertility clinic	Urine	BP-3	Mustieles et al.
Women FFs Biomonitoring Collaborative	US	2020	Women, firefighters and office workers	Serum	"serum suspect screening" BP-3 confirmed	Grashow et al.
Copenhagen University Hospital	Denmark	2020	Young men, Danish population	Urine	BP-3	Frederikson et al.
George Mason University	US	2020	Women of reproductive age	Urine	BP-3, BP-1	Pollack et al.
Southern China	China	2020	Matched maternal-fetal samples	Urine, serum, amniotic fluid	4-OH-BP, BP-1, BP-3, BP-8	Song et al.
SEPAGES study group	France	2020	8 pregnant women	Urine	BP-3	Nakiwala et al.

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