Substance report

June 2022

Polycyclic Aromatic Hydrocarbons (PAHs)

HBM4EU science and policy for a healthy future

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Table of contents

Authors and Acknowledgements 4
Glossary 5
1 Key messages 7
2 Introduction 7
2.1 How to use this document 7
2.2 Overview of PAHs 7
3 Human exposure to PAHs 8
3.1 Environmental exposure 9
3.2 Consumer exposure 9
3.3 Occupational exposure 10
4 Health impacts of PAHs 10
4.1 Overview of key health impacts from PAHS 10
4.2 Vulnerable target groups 14
4.3 Societal concerns 14
4.4 Evidence bases on use of human biomonitoring 15
5 EU policies on PAHS 15
6 Policy questions for PAHS 15
6.1 What is the current exposure of the EU population to PAHs? 15
6.2 What is the current exposure of different occupational groups? 16
6.3 Is there an association between air quality and human exposure to PAHs? 16
6.4 Does exposure differ between countries? Why? 16
6.5 Can we see a decline in exposure to the eight PAHs restricted under REACH? 16
6.6 Can HBM4EU data inform the development of legislation specifically targeting exposure to PAHs through ambient air? 17
6.7 Do European citizens support human biomonitoring to reduce chemical exposure? 17
7 HBM4EU outputs 18
7.1 Categorisation 18
7.2 Key outputs 19
7.3 Key data gaps and challenges 22
8 Future recommendations 23
9 References 23

Figure 1 Overview of exposure routes and health effects for PAHS 9
Figure 2 Overall answer distribution on issues of higher concern regarding chemical exposure 14
Figure 3 Priority areas in human biomonitoring 18
Figure 5 Challenges 23

Table 4-1: Human health classifications 10
Table 4.2 Overview of CLP classifications for PAHS 12
Table 7-2: Categorisation of PAHs 18

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Glossary

Abbreviations	
BaA	Benzo[a]antracene
BaP	Benzo[a]pyrene
BbF	benzo[b]fluoranthene
BeP	Benzo[e]pyrene
BjF	benzo[j]fluoranthene
BkF	benzo[k]fluoranthene
Biomarker	The primary chemical or its metabolites used to estimate the extent of exposure of an organism.
Carcinogen (Carc.)	A chemical that induces or increases the risk of cancer.
CMD	Carcinogen and Mutagens Directive.
DBAhA	Dibenzo[a,h]antracene
Developmental effects	Effects on the developing offspring from exposure of a parent before conception or during the period of embryonic or fetal development; such effects may include skeletal, soft tissue or functional changes in the offspring and may be observable prenatally, postnatally or at puberty.
ELCR	Excess lifetime cancer risk.
Epigenetic change	is a heritable change in the expression of the genes present in a cell (e.g. in active versus inactive genes) that does not involve any change to the underlying DNA sequence resulting in a change of phenotype without a change in the genotype
Genotoxicity	Process by which an agent produces a deleterious effect on DNA and other cellular targets which control the integrity for genetic material
GM	Geometric mean
HBM	Human Biomonitoring.
IARC	International Agency for Research on Cancer.
LC-MS-MS	Liquid chromatography-tandem mass spectrometry.

LLE	Liquid-liquid extraction.
LoQ	Limit of Quantification. This is the lowest concentration that an analyte can be quantified reliably and also the lowest level that predefined goals for imprecision and bias are met.
mg/m3	Milligram per cubic meter.
Mode of action	Change at the biochemical or cellular level that result from exposure to a chemical or combination of chemicals.
Mutagenic	Term used to define a chemical or other agent that causes permanent change in the amount or structure of the genetic material (DNA) in a cell; such changes may affect the exposed organism or, if the cell exposed is a germ cell, any future generation(s) of offspring.
OELV	Occupational Exposed Limit Value.
PBTK modelling	Physiologically based toxicokinetic modelling. These are quantitative (mathematical) descriptions of the absorption, distribution, metabolism and excretion of a chemical to which an organism is exposed.
PM	Particulate Matter
Reproductive toxicant	Chemicals or other agents (e.g. radiation) that adversely impact the sexual function, fecundity and/or fertility of a parent or the development or viability of an offspring.
RPE	Respiratory Protective Equipment.
PAHs	Polycyclic Aromatic Hydrocarbons
Skin irritation (Skin Irrit.)	The reversible damage of the skin following exposure to the substance of up to four hours.
SPE	Solid phase extraction.

1 Key messages

- Exposure to PAHs, both acute and chronic, can result in or contribute to a range of adverse health effects.
- The contribution of PAHs to cancer is of particular concern, especially for exposed workers.
- Current exposure levels are related to an excessive lifetime cancer risk (ELCR).
- Workers dealing with asphalt and soil remediation are particularly exposed to PAHs.
- The general population is exposed to PAHs via food, ambient air pollution, smoking and consumer products. Dietary exposure accounts for 90% of exposure to PAHs.
- Within Europe, Eastern and Western regions show the highest, and similar levels of exposure based on PAH metabolites measured in urine, followed by Southern Europe, with Northern Europe having the lowest exposure levels observed.
- Many data gaps remain concerning integrated PAH exposure assessment, which can be investigated by additional HBM analyses coupled with analyses of environmental matrices.
- European citizens are concerned about environmental chemical pollutants such as PAHs and largely support the use of HBM for risk assessment and policy, though awareness is still low.

2 Introduction

HBM4EU is a project funded under Horizon 2020, running from 2017 until 2021. It generates knowledge to inform about the safe management of chemicals, and hence protect human health in Europe. HBM4EU uses human biomonitoring (HBM) to monitor the actual human exposure to chemicals and resulting health impacts to build upon existing evidence bases and improve chemical risk assessment. HBM4EU compares data from across Europe which allows an understanding of regional differences and can help to identify vulnerable groups in order to inform targeted measures to reduce exposure. The results of the HBM4EU project are aimed at supporting policy development, by providing a key evidence base in the understanding of exposure and impacts to toxic chemicals.

For more information about the project itself, please visit the HBM4EU website.

2.1 How to use this document

This substance report is based largely on the scoping document for PAHs produced in 2018, an earlier short overview report produced in 2017, the presentation titled “Main results for PAHs” at the Joint Meeting of Chemical Substance Group Leaders and Management Board in October 2019 and the deliverables produced to date. ECHA information from REACH registrations, information in the C&L Inventory, and opinions and decisions from committees or authorities published in the ECHA website have also been used for this substance report.

This document summarises the known and suspected human health effects of exposure to a range of PAHs and indicates where HBM could be of value in the development of future EU policy, along with indicating the remaining challenges in determining PAH exposure.

This substance report is intended to inform policy makers and other interested stakeholders on the potential value of HBM to establish the EU population’s exposure to PAHs.

2.2 Overview of PAHs

Polycyclic aromatic hydrocarbons (PAHs) are a large group of organic compounds comprised of two or more fused benzene rings arranged in various configurations. They are ubiquitous environmental pollutants generated primarily during the incomplete combustion of organic

materials (e.g. coal, oil, petrol, and wood). Emissions of PAHs are also predominantly anthropogenic with some emissions from natural sources. Emissions from anthropogenic activities predominate, including from residential and commercial combustion, industrial combustion, road transport, metal production, waste incineration, cigarette smoke, and other sources. Environmental emissions of PAHs can be broken down as follows: 58% is from biofuel, 17% from wild fires, 7% from consumed product use, 5% from traffic oil, 4% from domestic coal, 2% from coal production and petrol refineries and 1% from waste incineration and other emissions. Nevertheless, some PAHs in the environment originate from natural sources (e.g. open burning, natural losses or seepage of petroleum or coal deposits, and volcanic activities). In areas where local sources are mostly industrial, PAH concentrations show little seasonality because emissions are constant throughout the year. However, in areas where the local sources are related to residential and commercial heating, they show significant seasonality during the year (i.e. they are higher during winter). Part of the PAHs emitted into the atmosphere remain in the gas mix, whereas part of the PAHs get bound to particulate matter and may be deposited into other environmental reservoirs, mainly soil, sediments and other matrices, thus expanding possibilities for human exposure (1) .

3 Human exposure to PAHs

The main source, pathways of human exposure and health effects of PAHs are shown in Figure 1.

For the general population, the main routes of exposure to PAHs are diet and, the environment (i.e. from inhalation of polluted ambient and indoor air). Major inhalation sources of PAHs are smoking and second-hand smoke, residential heating (when combustion and venting into the room is involved) and use of fireplaces. For non-smokers, food and food preparation are the main sources of exposure, including drying, smoking, and high temperature cooking. In addition to environmental exposures, PAHs exposure results from the use of and contact with consumer articles. PAHs can be found in plastics and rubber products primarily as result of additives added during production and manufacturing. Two additives are the main PAH sources through this process: carbon black and extender oils. Workers in a variety of industries are exposed to higher levels of PAHs than the general population. These include the production of carbon black, coal-tar pitch and asphalt, aluminium and coke, petroleum refineries, exhaust fumes from motor vehicles and from dermal contact with synthetic turf.

Emissions of PAHs as air pollution are predominantly anthropogenic with some emissions from natural sources. Environmental emissions of PAHs can be broken down as follows: 58 % is from biofuel, 17 % from wild fires, 7 % from consumed product use, 5 % from traffic oil, 4 % from domestic coal, 2 % from coal production and petrol refineries and 1 % from waste incineration and other emissions.

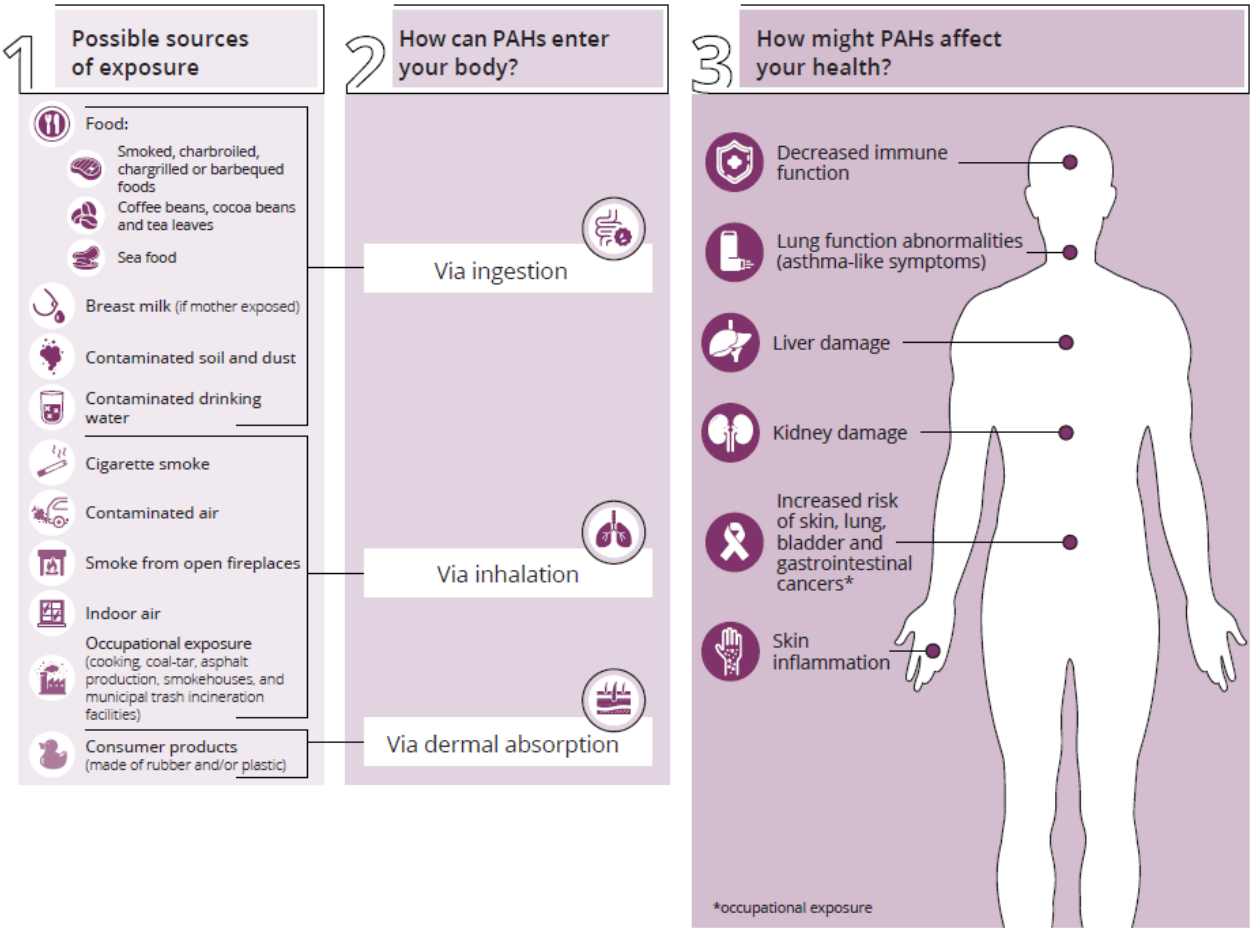

Figure 1 Overview of exposure routes and health effects for PAHS

3.1 Environmental exposure

For the general population, the major route of exposure to PAHs is environmental, specifically through inhalation of ambient and indoor air, and from wider environmental exposure. Major sources of exposure to PAHs for the population are dietary exposure, smoking and second-hand smoke, residential heating (when combustion and venting into the room is involved) and use of fireplaces, carbon black, coal-tar pitch and asphalt production, aluminium and coke production, petroleum refineries, exhaust fumes from motor vehicles and from dermal contact with synthetic turf.

3.2 Consumer exposure

In addition to the environmental exposures mentioned, PAH exposure results from the use of and contact with consumer articles (PAHs are present due to the use of plasticisers or carbon black in manufacturing, for instance in some rubber products). For non-smokers, food and food preparation is the main route of exposure, including drying, smoking, and high temperature cooking. High fat level and presence of smoked or grilled meat and fish products seem to influence the presence of higher levels of PAH in diet (2). Some crops may absorb PAHs which could then be ingested, and PAH intake from soil may occur via ingestion, inhalation or dermal exposure.

3.3 Occupational exposure

There is a variety of occupational activities that may result in workers being exposure to PAHs, particularly those where workers may breather exhaust fumes, but also mining, metallurgy, and oil refining.

4 Health impacts of PAHs

4.1 Overview of key health impacts from PAHS

PAHs are of human health concern as they are either known or suspected of being carcinogenic and/or mutagenic. Eight PAH congeners are classified Carc. 1B (presumed to have carcinogenic potential based on animal data): BaP, BeP, BaA, chrysene, BbF, BjF, BkF and DBAhA BaP and chrysene are also classified for their mutagenic properties (Categories 1B and 2 respectively). . Benzo[a]pyrene (BaP) is a classified Carc. 1.
PAHs are potent immune-suppressants, affecting the development of the immune system, humoral immunity and host resistance. PAHs and their metabolites may also interact with estrogen receptors.
Furthermore, exposure to BaP can affect the central nervous system, cause liver and kidney damage, and birth defects and reproductive disorders. BaP is a classified Repro. 1B (Presumed reproductive toxin based on animal studies) substance. Other PAHs are also classified for their reproductive toxicity; these are discussed in Table 1-1.

The current EU (ECHA C&L Inventory) and/ IARC classification of selected PAHs is given in Table 1-1.

Table 4-1: Human health classifications

PAH substance	Human health classifications	IARC classification
Anthracene	No classified hazards	Carc 3
Pyrene	No classified hazards	Carc 3
Benzo(ghi)perylene	No classified hazards	Carc 3
Benzo(e)pyrene	Carc. 1B	Carc 3
Indeno[1,2,3-cd]pyrene	Carc. 2 (self-classified)	Carc 2B
Benzo[j]fluoranthene	Carc. 1B	Carc 2B
Benzo[b]fluoranthene	Carc. 1B	Carc 2B

Benzo[k]fluoranthene	Carc. 1B	Carc 2B
Chrysene	Carc. 1B, Muta. 2	Carc 2B
Fluoranthene	Acute Tox. 4, Eye Irrit. 2	Carc 3
Benzo[a]pyrene	Skin Sens. 1, Muta. 1B, Carc. 1B, Repr. 1B	Carc 1
Dibenz[a,h]anthracene	Carc. 1B	Carc 2A
Benz[a]anthracene	Carc. 1B	Carc 2B
Acenaphthene	Eye Irrit. 2	Carc 3
1-Methylphenanthrene	Acute Tox. 4, Carc. 2 (self-classified)	Carc 3
Phenanthrene	Acute Tox. 4	Carc 3
Fluorene	Not classified	Carc 3
Naphthalene	Carc. 2, Acute Tox. 4	Carc 2B

Key:

Acute Tox. category 4 (EU classification) – Mild acute toxicity (category 4 is the lowest concern level)

Asp. Tox. category 1 (EU classification) – Aspiration toxicity (category 1 is the highest concern level)

Carc .1B (EU classification) – Substances that are presumed to have carcinogenic potential based on animal data

Carc. 1 (IARC classification) – Substance is carcinogenic to humans

Carc. 2 (EU classification) – Substances that are suspected of causing cancer

Carc. 2A (IARC classification) – Substance is probably carcinogenic to humans

Carc. 2B (IARC classification) – Substance is possibly carcinogenic to humans

Carc. 3 (IARC) - Limited evidence that the substance causes cancer in experimental animals and it is inconclusive.

Muta. 2 (EU classification) – May cause mutagenic (genotoxic) damage

Muta. 1B (EU classification) – Known to cause mutagenic (genotoxic) damage

Repr. category 1B (EU classification) – Presumed reproductive toxin based on animal studies

Repr. 2 category (EU classification) - Suspected reproductive toxin based on limited evidence from animal studies or/and human studies

Skin Irrit. 2 (EU classification) – Category 2 substances are classed as irritants with reversible damage

Skin Sens. Category 1 (EU classification) - Substances in this category may cause an allergic skin reaction

STOT RE category 2 (EU classification) – Presumed to be toxic after repeated exposure from studies in experimental animals

STOT SE category 3 (EU classification) – Reversible effects after single exposure

Table 4.2 Overview of CLP classifications for PAHS

Substance	Properties of concern				Category according to CLP criteria								ECHA info card
	Carcinogenicity (IARC)	Mutagenic	Skin sensitising (SS)	Reproductive Toxicity	Carcinogenicity	Acute Toxicity	Specific target organ tox (repeated exposure)	Reproductive Toxicity	Mutagenic	Eye Damage/ Eye Irritation	Skin Sensitivity	Skin Corrosion/ Irritation	
Anthracene	3				NA								Link
Pyrene	3				NA								Link
Benzo(ghi)perylene	3				NA								Link
Benzo(e)pyrene	3				1B								Link
Indeno[1,2,3-cd]pyrene	2B				2								Link
Benzo[j]fluoranthene	2B				1B								Link
Benzo[b]fluoranthene	2B				1B								Link
Benzo[k]fluoranthene	2B				1B								Link
Chrysene	2B	2			1B				2				Link
Fluoranthene	3				NA		4			2			Link
Benzo[a]pyrene	1	1B	1	1B	1B			1B	1B		1		Link

Dibenz[a,h]anthracene	2A				1B								Link
Benz[a]anthracene	2B				1B								Link
Acenaphthene	3				NA					2			Link
1-Methylphenanthrene	3				2		4						Link
Phenanthrene	3				NA		4						Link
Fluorene	3				NA								Link
Naphthalene	2B				2								Link

* Harmonised classification under the CLP Regulation. (Other classifications are those notified to the CLP inventory but without harmonised EU classification.); ** Based on IARC classification. Blank cells denote a lack of classification.

Confirmed

Suspected

Some data

Most hazardous — Least hazardous

1 2 3 4

4.2 Vulnerable target groups

Considering that gestation and early infancy are periods that are detrimental for later life health, fetuses may be at risk for PAH exposure, since PAH and its metabolites have been shown to cross the placenta in various animal studies (ATSDR, 1995), while due to the fact that PAHs are excreted in breast milk, nursing infants of exposed mothers can be secondarily exposed. In terms of exposure, there are occupational activities that are linked to higher levels of exposure to PAHs, such as chimney sweeps, asphalt workers, soil remediation workers, coke plant workers, bus drivers and waste incinerator workers. On the other hand, people that are smoking are highly exposed to PAHs, as well as the ones living with smokers.

4.3 Societal concerns

A citizen survey was conducted across Europe as part of HBM4EU, with over 5,000 valid responses spanning 30 countries. The objective of the survey was to understand citizens to awareness and concerns regarding chemical exposure and human biomonitoring.

Regarding citizens' concerns on chemical exposure, in all regions, industrial emissions and pollution were ranked the highest concern of all possible chemical exposures, with Pesticides in food and in the environment ranked second and third for overall answers. Contaminants in drinking water and food were also of high concern, followed by chemicals in drinking water and road traffic (see Figure 2).

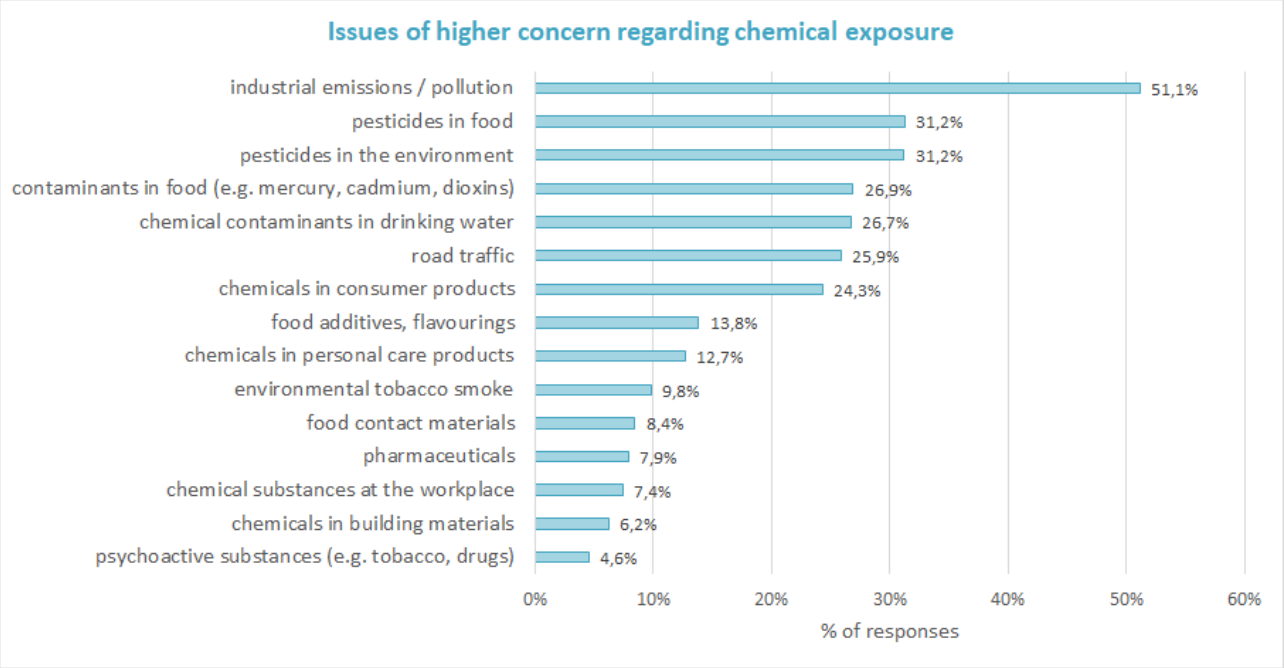

Figure 2 Overall answer distribution on issues of higher concern regarding chemical exposure

While there isn't evidence of specific societal concern directed towards PAHs, insofar as they affect the public via environmental pollution, they would be included in the highest concern category.

4.4 Evidence bases on use of human biomonitoring

HBM sampling to allow measurement of PAH exposure was reviewed. To study the exposure to PAHs, urinary mono-hydroxylated PAHs (OH-PAHs), a group of PAH metabolites, are commonly used as biomarkers. Among the OH-PAHs, 1-hydroxypyrene (1-PYR) is the most commonly used PAH biomarker in both occupational as well as in the general population from various countries.

From the technical point of view, methods already exist for the determination of some PAHs in urine, blood, hair, or breast milk. Sample volume is dependent on the matrix; 2 ml is required for whole blood, 0.1-0.2 g for hair, 10-50 ml for breast milk, 0.03 ml for core blood, and 1-36 ml for urine. Sample preparation is performed using liquid-liquid extraction; solid phase extraction and florosil and silica is also used. Analysis is performed using liquid chromatography and mass spectrometry.

5 EU policies on PAHS

Several policy measures have been introduced in the EU to reduce PAHs exposure. These include measures under REACH and other policy instruments, in particular restrictions under REACH for extruder oils in the production of tyres or parts of tyres. PAHs are also restricted in rubber and in plastic parts of some consumer goods while the eight carcinogenic PAHs are restricted for use in childcare articles and toys. Anthracene oil and coal tar pitch are also subject to authorisation under REACH.

Furthermore, air pollutants including PAHs are regulated under the Ambient Air Quality Directive and the National Emission Ceilings Directive.

6 Policy questions for PAHS

6.1 What is the current exposure of the EU population to PAHs?

WP7 has produced a variety of materials to provide the groundwork for a harmonised approach to study planning and conduct in Europe.

For PAH, questionnaires for adults, adolescents and children are available.

Data prior to HBM4EU allowed to estimate that for most of the countries, median daily intake was around 0.050 µg/kg_bw/d, however, it has to be noted that, the bio samples were not collected in the same year, while analyses were performed by different laboratories, thus, hampering the overall intercomparison (AD12.5).

Based on the data of the aligned studies, the median value of 1-naphthol in urine ranges between 0.13 µg/l in Switzerland to 1. 81 µg/g crt in Poland. Higher values were observed for 2-naphthol in urine where the median value ranges between 1.28 µg/g crt in Germany to 8.03 µg/g crt in Poland. The median values of 2-fluo and 3-fluo in urine vary between 0.10 µg/g crt and 0.02 µg/g crt in Iceland to 0.31 µg/g crtl and 0.11 µg/g crt in France respectively. The highest median value of 9-fluo in urine was observed in France (0.39 µg/l) and the lowest median value was observed in Luxembourg (0.17 µg/l). The median value of 1-phen in urine varies between 0.03 µg/g crt in Czech Republic to 0.17 µg/g crt in France. The median value of 2-phen ranges between 0.04 µg/g crt in Croatia to 0.09 µg/g crt in Czech Republic. The median value of 3-phen in urine, was highest France (0.12 µg/g crt) and the lowest median value was measured in Croatia (0.025 µg/g crt). The median value of 4-phen in urine varies between 0.02 µg/g crt in Iceland to 0.06 µg/g crt in Czech Republic. The median value of 9-phen ranges between 0.05 µg/g crt in France to 0.11 µg/g crt in Czech Republic. Regarding 1-HO-pyr, the highest median value was observed in Poland (0.24 µg/g crt) and the lowest median value was observed in Iceland (0.03 µg/g crt).

6.2 What is the current exposure of different occupational groups?

Asphalt and soil remediation workers have the highest exposure based upon an urinary 1-hydroxypyrene biomarker (GM up to 7 µg/L). This is followed by coke plant workers (GM up to 1 µg/L), bus drivers (GM ~ 0.7 µg/L) and waste incinerator workers (GM ~ 0.2 µg/L; these are discussed in section 1.6 of this brief).

Considering the review (in task T5.3), two main aspects were apparent: i) the exposure levels are still high in some occupational settings; ii) there is need for updated biomonitoring data from recent studies for PAHs exposure in occupational settings and iii) there is a need for developing new occupational studies, applying a set of exposure biomarkers, including a specific biomarker for BaP exposure, which would allow a better risk estimation for exposed workers.

6.3 Is there an association between air quality and human exposure to PAHs?

Exposure reconstruction studies have shown that dietary exposure dominates exposure to PAHs (contributing to almost 90 %) of daily intake, while the contribution of inhalation is lower (about 10 %), except for the cases where significant sources of inhalation exposure such as the proximity to industrial hot spots, heavily trafficked roads, biomass emissions, as well as smoking.

Most studies on PAH exposure from air pollution, report external exposure. In HBM studies, mainly the urinary metabolite 1-OH-PYR is measured, probably because it still represents the best biomarker of occupational exposure to PAHs although it is mainly from dietary exposure except in cases with significant sources of inhalation exposure such as the proximity to industrial hot spots, heavily trafficked roads, biomass emissions, as well as smoking.

6.4 Does exposure differ between countries? Why?

Exposure is higher in the Czech Republic, Greece and Italy than in France, Spain, Germany and Finland (urinary 1-hydroxypyrene: 0.1 to 0.4 µg/L).

The differences in intake levels among the various countries are mostly explained by the differences in dietary intake, which is the result of increased soil contamination and dietary patterns (frequency of eating smoked food) and to a smaller extent to difference in air pollution levels.

In specific studies several exposure modifiers such as age, smoking status and exposure to secondhand smoke, as well as residential location have been identified as key factors affecting the overall intake levels.

6.5 Can we see a decline in exposure to the eight PAHs restricted under REACH?

It is concluded that the most recent values obtained in the HBM4EU aligned studies showed that the levels of internal exposure of the European adult population were similar to those from previous studies published in the literature. There were no indications that the newly obtained HBM data for 1-OHPyr were substantially lower than the ones previously measured and reported in the open literature. In addition, while comparing the risk estimations with the ones formerly estimated and presented in D5.5, the risk levels now estimated are at the same order of magnitude, with an exception of smokers (10-4), when considering solely oral (dietary) exposure. From the health

policies questions perspective, further efforts should be envisaged for reducing intake and potential contamination with PAHs from various sources.

6.6 Can HBM4EU data inform the development of legislation specifically targeting exposure to PAHs through ambient air?

The current levels of exposure to pyrene are in the range of 0.1 µg/kg_bw/day for all age groups and countries. The combination of HBM data exposure reconstruction, and the bottom up assessment of sources contribution, allows us to identify the relative contribution of the various sources to PAHs exposure. Such a comprehensive modelling framework, is able to properly identify differences in HBM data attributable to different sources. Considering that the main source of exposure to PAHs is diet, HBM data can efficiently inform ambient air legislation, if dedicated data of a population with similar sociodemographic characteristics, but living in areas with different air pollution levels (e.g. proximity to industrial units using coal, incinerators or heavily trafficked streets) are recruited and their exposure levels to be evaluated. An alternative option, would be the evaluation of PAHs biomonitored levels accounting for the seasonal variability, that it is expected to be observed between winter and summer, where PM and PAHs levels in ambient air are significantly lower. As a final recommendation, delivery of new HBM data and further stratification that will result in intake estimates that account both for spatial variability (so as to capture air pollution differences between locations characterized by different air pollution levels) and seasonal variability (to capture the seasonal differences in air pollution) are needed.

6.7 Do European citizens support human biomonitoring to reduce chemical exposure?

Concerning the use of Human Biomonitoring of toxic chemicals, 87 % of the respondents of the HBM4EU citizens' survey supported the use of HBM and said it should be used more, with 50 % saying it should be undertaken as regularly as food and water quality tests, with a stronger coordination at the European level, and near 60 % considered it should be included in the National Health Surveys.

Over 65 % of the respondents strongly supported the importance of HBM studies for the purposes of: evaluating chemical exposure of the population, study the health impacts of chemical exposure, the development of health policy that promote the safe use of chemicals, to support occupational health policies and the safe use of chemicals at work, to raise awareness/understanding the impact of chemical exposure amongst the population and to raise awareness/understanding of the impact of chemical exposure amongst health professionals and policy makers.

Overwhelmingly, citizens chose food, the environment and drinking water as priority areas of chemical exposure to be addressed by human biomonitoring studies (see Figure 3)

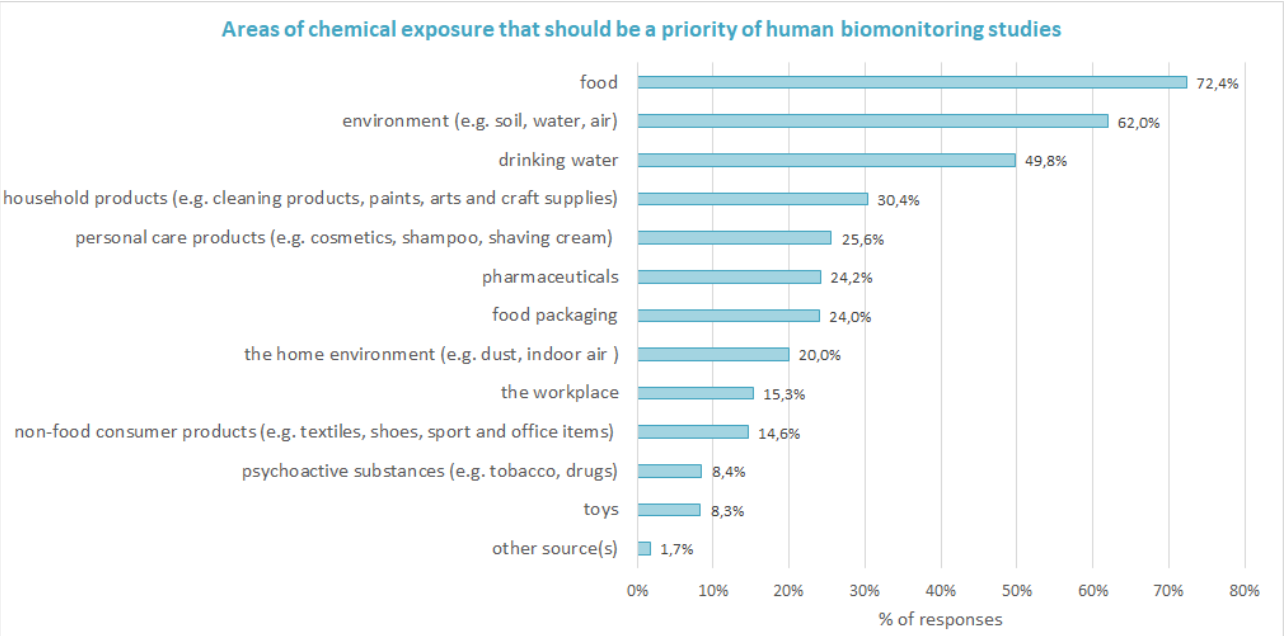

Figure 3 Priority areas in human biomonitoring

It is also noteworthy that, conversely, 13 % of the survey respondents supported the idea that HBM should not be done at all. A round of focus groups in several countries that were also part of the survey provided additional insights. Notably, the level of awareness about human biomonitoring was relatively low across countries and was not related with educational attainment. Moreover, beyond human biomonitoring, the awareness of the potential ill health effects from chemical exposures was also low, underscoring the importance of awareness raising and public education activities and policies.

7 HBM4EU outputs

7.1 Categorisation

Substances under HBM4EU have been categorised depending on availability of HBM data. The categorisation indicates the information gaps allowing the development of targeted activities to fill the knowledge gaps. Substances will pass from Category E over D, C, B towards Category A as more information becomes available. Fully characterised substances should end up as category A substances. PAHs are categorised as category B substances based on the availability of toxicology and biomonitoring data (see Table 7-2). Category B means HBM data exists, but the exposure distribution across Europe is not well known.

Table 7-1: Categorisation of PAHs	
Category	**Substances**
B	Acenaphthene, Acenaphthylene, Anthracene, Benzo(a)anthracene, Benzo(a)pyrene, Benzo(b)fluoranthene, Benzo(e)pyrene, Benzo(ghi)perylene, Benzo(j)fluoranthene, Benzo(k)fluoranthene, Dibenzo(ah)anthracene, Fluoranthene, Fluorene, Chrysene/Benzo(a)phenanthrene, Indeno(123-cd)pyrene, Naphthalene, Phenanthrene, Pyrene, 1-Methylnapthalene, 1-Methylphenanthrene, 2,6-Dimethylnapthalene, 2-

	Methylnapthalene, 7.12-Dimethylbenz(a)anthracene, 2,3,5-trimethylnaphthalene, Benzene, Toluene, Ethylbenzene, Xylene, o-Xylene, m-Xylene, p-Xylene, Formaldehyde, Acetaldehyde

7.2 Key outputs

Exposure of the EU population to PAHs

Exposure to PAHs was addressed using the 1-OH-pyrene data collected from available HBM studies. 1-OH-pyrene is a major metabolite of pyrene and is representative for the PAHs mixtures, while it is the metabolite that is commonly measured in the majority of PAH-related HBM studies. The European HBM dashboard has 18 datasets with PAHs exposure data integrated and in IPCHEM metadata for 40 datasets with PAHs data are available.

A PBTK model was parameterised and validated in Task 12.1 and it was coupled with the exposure reconstruction algorithms developed in Task 12.2. Based on the existing HBM data available prior to HBM4EU, the median value of pyrene exposure ranges between 0.025 µg/kg_bw/d for non-smokers in Belgium to 0.240 µg/kg_bw/d for smokers in Netherlands.

New data for 13 PAH's markers (1-naphthol, 2-naphthol, 1,2 DHN, 2-FLUO, 3-FLUO, 9-FLUO, 1-PHEN, 2-PHEN, 3-PHEN, 4-PHEN, 9-PHEN, 1-PYR and 3-BaP) are available from the HBM4EU Aligned Studies in adults (20-39 years). The Aligned Study data were collected between 2014-2021 across 10 sampling sites in Europe (Iceland, Denmark, Portugal, Croatia, Czech Republic, Poland, France, Switzerland, Luxembourg, and Germany) representing 2609 individuals. Not all biomarkers were analyzed in all contributing studies, therefore number of sampling sites and data points can vary per biomarker.

Exposure of different occupational groups

Based on literature review and exposure reconstruction the following results were obtained. Exposure to the various occupational groups varies based on the specific activities of the related occupational sectors. The highest intake estimates were identified in soil remediation workers (in the range of 0.981 to 1.284 µg/kg_bw/d), followed by asphalt workers (0.093 to 0.325 µg/kg_bw/d) and workers in aluminum and rubber industry (0.035 to 0.100 µg/kg_bw/d).

The lowest intake levels were identified to waste incinerator workers (0.004 to 0.104 µg/kg_bw/d), which is the only reported sector occupying both males and females. On the contrary, in all other sectors (soil remediation workers, asphalt workers, workers in aluminum and rubber industry) only males are being occupied and a differentiation on their intake results from their smoking habits, the time of their shift (pre shift, end of shift, post shift, next pre shift) and the age groups.

The highest intake levels were related to soil remediation workers (1.284 µg/kg_bw/d) during the next pre shift, where pre shift and end of shift reported lower intakes (0.981 and 1.249 µg/kg_bw/d, respectively). For asphalt workers the highest intake was reported in the post shift and the specific age range of 35-52 (all workers were non-smokers). For workers in the aluminum and rubber industries, the lowest intake was reported for non-smokers (0.035 µg/kg_bw/d) comparing to smokers who exhibited a considerably higher intake (0.065 µg/kg_bw/d) (AD12.5).

Based on reported data from PAH metabolites, the highest values were observed for 2-naphthol metabolite in urine across different European countries. The highest median concentrations of 2-naphthol metabolite were identified in skilled agricultural, forestry and fishery workers (7.76 µg/l), professionals (6.88 µg/l) and clerical support (6.10 µg/l) in France. The lowest median concentrations were identified in services and sales workers (4.61 µg/l), technicians and associate professionals (4.52 µg/l), craft and related trades workers (4.33 µg/l) and elementary occupations

(3.81 µg/l). In Croatia, the highest median concentrations of 2-naphthol were observed in craft and related trades workers (7.82 µg/l), elementary occupations (6.9 µg/l), plant and machine operators and assemblers (6.74 µg/l), skilled agricultural (6.47 µg/l), services and sales workers (6.36 µg/l) and clerical support (6.29 µg/l). The lowest median concentrations were observed in professionals (4.64 µg/l), technicians and associate professionals (4.14 µg/l) and managers (1.92 µg/l). Regarding Luxembourg, the median concentrations were higher in elementary occupations (8.83 µg/l), services and sales workers (7.43 µg/l), plant and machine operators and assemblers (6.99 µg/l), clerical support (6.39 µg/l) and craft and related trades workers (5.43 µg/l) while the median concentrations were lower in technicians and associate professionals (3.95 µg/l), professionals (3.92 µg/l) and managers (3.15 µg/l). With regard to Czech Republic, the median concentrations of 2-naphthol vary between 3.96 µg/l in services and sales workers to 2.77 µg/l in clerical support. The median concentrations of 2-naphthol were observed in managers (6.74 µg/l) and services and sales workers and craft and related trades workers (5 µg/l), technicians and associate professionals (4.16 µg/l) and clerical support (3.13 µg/l) in Denmark. As regard Switzerland, the median values of 2-naphthol range between craft and related trades workers (4.48 µg/l), services and sales workers and clerical support (3.69 µg/l) to managers, professionals and technicians and associate professionals (2.53 µg/l). The highest median concentration of 2-naphthol was identified in plant and machine operators and assemblers (5.4 µg/l) in Iceland and the lowest concentrations were observed in services and sales workers and craft and related trades workers (2.46 µg/l). The highest median concentrations of 2-naphthol metabolite were identified in elementary occupations (11.36 µg/l) and clerical support (11.18 µg/l) in Portugal. The lowest median concentrations were identified in services and sales workers (6.75 µg/l), skilled agricultural, forestry and fishery workers (6.01 µg/l) and professionals (5.75 µg/l).

Association between air quality and human exposure to PAHs

From exposure reconstruction studies it was shown that smokers have consistently higher exposure levels to pyrene, resulting to daily intake of between 0.015 to 0.150 µg/kg_bw/d. Regarding hot spots, it is expected that they result in higher pyrene concentrations in the range of 0.005 to 0.01 µg/kg_bw/d. (AD12.5).

Studies on associations with the density of traffic in France, Croatia and Switzerland, reported higher median values for 2-naphthol metabolite in urine of 6.03 µg/l, 5.7 µg/l and 2.84 µg/l respectively in intense traffic compared with light traffic (5.74 µg/l, 5.42 µg/l and 2.56 µg/l). Regarding the indoor use of biomass/coal burning, the median values were higher for 2-naphthol metabolite in Portugal, Czech Republic and Switzerland (6.93 µg/l, 2.68 µg/l and 1.86 µg/l respectively). In connection to recent barbeque activities (last 24h), the highest median values were observed for 2-naphthol metabolite in urine in Croatia (8.2 µg/l) and Switzerland (4.46 µg/l) in comparison to those that didn't take part in barbeque activities (7.64 µg/l and 2.65 µg/l respectively). Regarding fireplace emissions, the highest median value of 2-naphthol was observed in Croatia (6.25 µg/l) compared to controls that didn't sit near to an open fireplace (5.2 µg/l) and the highest median value of 1-naphthol was observed in Switzerland (0.16 µg/l) in comparison to those didn't sit near to fireplace (0.13 µg/l). The highest median values were observed for 2-naphthol metabolite in urine in Czech Republic (3.27 µg/l), Iceland (15 µg/l) and Switzerland (4.19 µg/l) for the subjects with homes near a waste incineration plant.

Differences in exposure across countries

Based on the HBM data available prior to HBM4EU, the highest intake levels were calculated in Netherlands (0.073 to 0.245 µg/kg_bw/d) followed by Germany (0.019 to 0.125 µg/kg_bw/d) and Greece (0.060 to 0.065 µg/kg_bw/d), Denmark (0.041 to 0.095 µg/kg_bw/d), Czech (0.053 µg/kg_bw/d), France (0.022 to 0.078 µg/kg_bw/d) and Italy (0.041 to 0.059 µg/kg_bw/d), Spain

(0.035 µg/kg_bw/d) and Belgium (0.029 µg/kg_bw/d). The lowest intake levels were reported in Sweden (0.013 to 0.036 µg/kg_bw/d).

It has to be noted that In Netherlands, Italy, France and Sweden the intake levels of smokers have been identified much higher compared to the ones of non-smokers (0.245 and 0.073 µg/kg_bw/d, 0.059 and 0.041 µg/kg_bw/d, 0.078 and 0.022 µg/kg_bw/d and 0.036 and 0.013 µg/kg_bw/d, respectively). In Germany the highest intake levels were reported for children of 5-8 years old, living near industrial hot spots (0.125 µg/kg_bw/d) while for children of the same ages living away from industrial hot spots the intake levels were much lower (0.064 µg/kg_bw/d). This is explained by the higher multimedia contamination in the area and the higher contribution to intake of both soil ingestion and ambient air inhalation.

In Greece, living nearby areas with traffic congestion, the intake levels were higher than in urban areas free of traffic (0.065 and 0.060 µg/kg_bw/d, respectively). In Denmark the highest intake levels were reported for bus drivers of 27-60 years of age (0.095 µg/kg_bw/d) while the lowest ones were reported for people working in rural areas (0.041 µg/kg_bw/d) (AD12.5).

However, the reason why differences are reported among the various countries will be further explored when the latest HBM data will be available and the statistical analysis in WP10 will have been completed.

Based on the reported median levels of 2-naphtol in urine: in Poland, Portugal, France, Luxembourg, Denmark, Croatia, Iceland, Switzerland, Czech Republic and Germany, the median levels of 2-naphthol in urine of smokers was higher compared to non-smokers (18.63 µg/l, 11.88 µg/l, 11.83 µg/l, 11.46 µg/l, 8.36 µg/l, 7.58 µg/l, 7.22 µg/l, 5.7 µg/l, 3.45 µg/l, 1.52 µg/l and 7.17 µg/l, 5.99 µg/l, 4.22 µg/l, 3.83 µg/l, 8.36 µg/l, 4.49 µg/l, 2.54 µg/l, 2.3 µg/l, 3.07 µg/l and 1.23 µg/l respectively). The median values of 1-naphthol in urine for smokers were higher in Poland (7.79 µg/l), France (7.02 µg/l), Croatia (5.33 µg/l), Iceland (5.32 µg/l), Denmark (3.91 µg/l), Portugal (3.57 µg/l) and Luxembourg (2.29 µg/l) compared to non-smokers (1.9 µg/l, 0.57 µg/l, 1.18 µg/l, 0.74 µg/l, 1.32 µg/l, 0.63 µg/l and 0.49 µg/l respectively). The rest of PAHs metabolites followed a similar pattern with lower median values.

Regarding secondhand smoking, the highest concentrations were observed for 2-naphthol metabolite followed by 1-naphthol metabolite in urine for secondhand smokers compared to no-secondhand smokers in France, Croatia, Czech Republic, Poland, Switzerland and Germany. The median values of 2-naphthol metabolite in urine for secondhand smokers were higher in Poland (11.83 µg/l), France (8.66 µg/l), Switzerland (5.98 µg/l), Croatia (5.79 µg/l) and Czech Republic (3.96 µg/l) compared to non-secondhand smokers (7.56 µg/l, 4.65 µg/l, 2.52 µg/l, 4.79 µg/l and 2.92 µg/l respectively). Regarding the 1-naphthol metabolite in urine, the highest median values for secondhand smokers were identified in Poland (4.85 µg/l), Croatia (2.27 µg/l), Portugal (2.09 µg/l), France (1.49 µg/l) and Czech Republic (1.13 µg/l) compared to in non-secondhand smokers (1.95 µg/l, 1.19 µg/l, 0.91 µg/l, 0.59 µg/l and 0.98 µg/l respectively).

Trends in exposure to the eight PAHs restricted under REACH

Exposure to PAHs occurs through multiple pathways and routes. This also pertains for the 8 PAHs (benzo[a]pyrene, benzo[e]pyrene, benzo[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[k]fluoranthene and dibenzo[a,h]anthracene) restricted under REACH. Restrictions from REACH are expected to affect the contribution of exposure related mainly to consumer products. It is also likely that the restriction of use will result in a reduction in the overall tonnage that will be reflected in the soil levels, which in turn will be reflected in the food chain and the dietary intake. However, to identify a potential decline, a trend analysis is required.

In HBM4EU estimated intake levels of data available in the HBM4EU dashboard and available in the literature prior to HBM4EU, were compared with HBM data collected in the HBM4EU aligned

studies in adults (20-39 yrs) all over Europe. No real time trend analysis can be calculated as the sampling sites were different and the age groups, but we could compare the aggregated data from the studies to draw some conclusions.

Exposure levels above reference dose or HBM guidance values

The results of the aligned studies were used to update the PAHs risk assessment previously performed within D5.5 that was based on published data. The aligned study cohorts included adults from the general population from France (A_ANSP_ESTEBAN), Czech Republic (A_MU_(C)ELSPAC), Croatia (A_CIPH_HBM in Croatia), Germany (A_UBA_ESB), Iceland (A_UI_DIET_HBM), Luxembourg (A_LNS_Oriscav-Lux2), Poland (A_NIOM_POLAES) and Switzerland (A_SWISS TPH_HBM4EU).

The excess lifetime cancer risk (ELCR) was estimated using two stages. In the first stage, the external exposure was reconstructed, i.e. the probable daily intake (PDI) of pyrene was estimated based on HBM data on 1-hydroxypyrene (1-OHPyr) available in the aligned studies. The PDI of pyrene intake levels were then translated into PAH4 (BaA, BbF, BaP, CHR) intake levels based on the assumption that pyrene intake was a surrogate of PAH4. In the second approach, for comparison, PAH4 dietary intake levels were derived from the country specific food residue and the food consumption data, available in the EFSA reports (2008, 2015c). Derived PAH4 intakes were then used as an input to estimate ELCR, using the ECHA-RAC (2018) formula.

The mean intake of PAH4 derived from the EFSA data on the occurrence of PAHs in food was, in general, one order of magnitude higher than that estimated based on exposure reconstruction from the HBM4EU aligned study data (mean values of 1-OHPyr).

In addition, input is provided (WP12), towards the association of the dose of toxic metabolites in the target tissue, with the observed HBM levels.

7.3 Key data gaps and challenges

Challenges faced in using HBM data to assess exposure to PAHs are summarised in Figure 2. Determining the overall exposure of PAHs needs to be understood as exposure as multiple sources can contribute varying amounts. There are also challenges to overcome in developing AOPs. A further issue is the limited availability of data available across the EU and for population subgroups.

We need more HBM data from different exposure groups (different ages) in conjunction with simultaneously collected data from food and air monitoring these would allow us to better understand the relative contribution from the different exposure routes and major sources to the internal concentrations.

A crucial knowledge gap regarding PAHs regards the robust estimation of the respective burden of disease and of the costs of exposure to these substances. In this regard, in addition to enhancing the exposure estimates, efforts should be made to better understand the immunotoxic effects of PAHs and to enhance the data necessary to unravel the adverse outcome pathways (AOPs) associated with PAH carcinogenicity, immunotoxicity, pro-inflammatory and reproductive toxicity effects.

Challenges faced in using HBM data to assess exposure to PAHs are summarized in Figure 4. Determining the overall exposure of PAHs needs to be understood since exposure of multiple sources can contribute varying amounts. A further issue is the limited amount of data available for the whole population and subgroups across the EU, while more sensitive analytical methods for the quantification of the BaP biomarkers are needed.

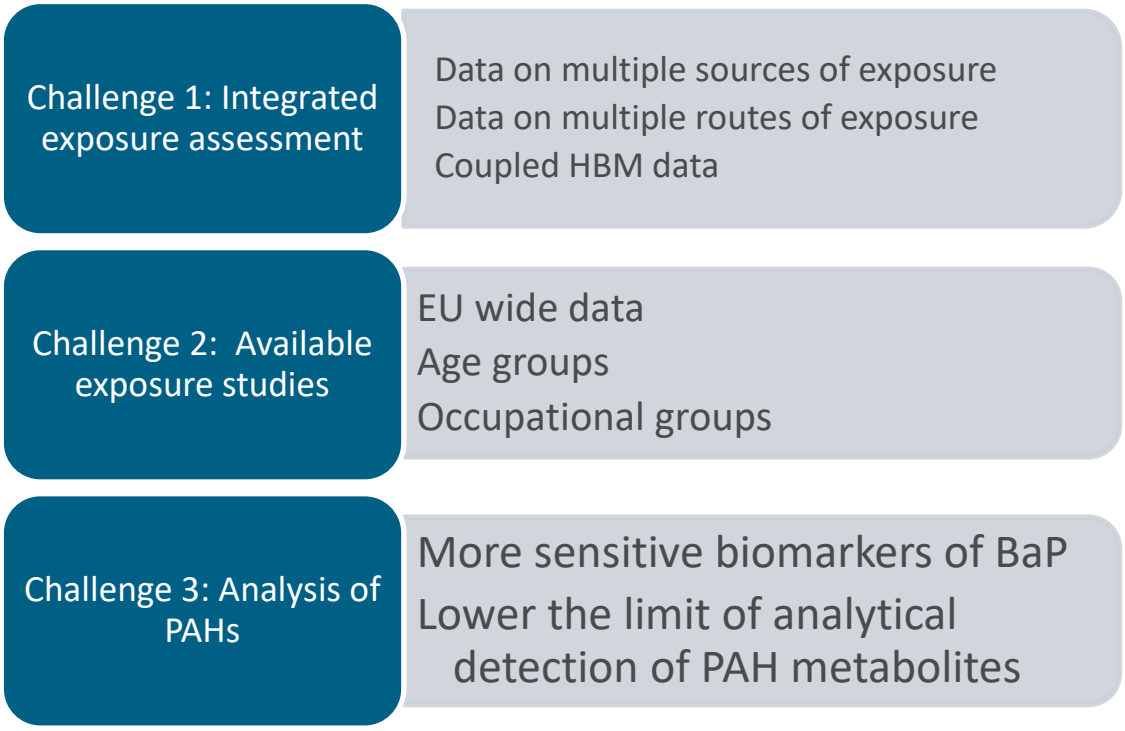

Figure 4 Challenges

8 Future recommendations

Since exposure to PAHs is a typical problem of both cumulative (multiple compounds) and aggregate (multi-pathway and multi-route) exposure, future efforts should focus on the source identification of the PAHs that contribute mostly to adverse health effects. Given the above, HBM should be able to inform for a great variety of compounds with a particular focus on the most toxic ones, namely dibenzo[a,h]anthracene, benzo[a]pyrene (BaP), benzo[a]anthracene (BaA), benzo[b]fluoranthene (BbF), and chrysene (CHR), that comprise the PAH4 group which mainly framed for carcinogenetic related to PAHs. In addition, newer toxicokinetic data of these compounds will result in more accurate PBPK modelling, which in turn will result in (a) more precise exposure reconstruction estimates and (b) more refined estimates of the reactive metabolites in potential target tissues (lung, GI tract). The latter is of particular importance towards the development of quantitative AOPs (qAOPs) and more in particular with AOP networks; future research on exposure and health associations to PAHs should focus on the identification of the intersecting molecular (key) events that are triggered and sustained under cumulative exposure to real-life PAHs mixture composition and levels, in experimental systems (both *in vivo* and *in vitro*). AOP networks focused analysis should aim on filling gaps of key events not only related to carcinogenicity, but also to other endpoints such as immunotoxicity or cardiovascular disease.

9 References

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