Committee for Risk Assessment
RAC

Opinion on scientific evaluation of occupational exposure limits for polycyclic aromatic hydrocarbons

ECHA/RAC/OEL-O-0000007198-66-01/F

1 December 2022

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OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON THE EVALUATION OF THE OCCUPATIONAL EXPOSURE LIMITS (OELs) FOR POLYCYCLIC AROMATIC HYDROCARBONS

Commission request

The Commission asked the advice of RAC to assess the scientific relevance of occupational exposure limits for some carcinogenic chemical substances, in support of the preparation of proposals for amendment of Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens mutagens or reprotoxic substances at work (CMRD)[1].

I PROCESS FOR ADOPTION OF THE OPINION

Following the above request from the European Commission RAC is requested to draw up an opinion on the evaluation of the scientific relevance of occupational exposure limits (OELs) for polycyclic aromatic hydrocarbons with a deadline of 31 December 2022.

Chemical name: polycyclic aromatic hydrocarbons

In support of the Commission's request, and following the scoping study which recommended that benzo-a-pyrene (CAS RN 50-32-8) was a suitable marker of overall PAH exposure[1], ECHA has subsequently prepared a scientific report concerning occupational limit values for polycyclic aromatic hydrocarbons at the workplace.

In the preparatory phase of drafting the scoping study and this report, a call for evidence was opened on 5 July 2021 to invite interested parties to submit comments and evidence by 3 September 2021. The scientific report was made available on ECHA's website at: Occupational exposure limits-Consultations on OEL recommendation on 10 May 2022 and interested parties were invited to submit comments by 11 July 2022.

The Committee for Risk Assessment (RAC) developed its opinion on the basis of the scientific report submitted by ECHA. During the preparation of the opinion on occupational limit values for polycyclic aromatic hydrocarbons, the scientific report was further developed as the Annex to the RAC opinion.

II ADOPTION OF THE OPINION OF THE RAC

Rapporteurs, appointed by RAC:

Thomas Gebel (with support from Kevin Kohns) and

Andrea Hartwig

The opinion was adopted by **consensus** on **1 December 2022.**

[1] https://echa.europa.eu/documents/10162/7399806/scoping_study_pah_report_en.pdf/e4cc1ef4-610d-feb7-8b68-89b2ba50cc97?t=1653474170416

RAC Opinion of the assessment of the scientific relevance of OELs for polycyclic aromatic hydrocarbons

RECOMMENDATION

Benzo-a-pyrene (BaP) is considered as a marker substance for carcinogenic PAH. BaP and PAH containing BaP are non-threshold carcinogens. Consequently, no health-based occupational exposure limit (OEL) can be identified. BaP is classified as a reproductive toxicant in category 1B. Therefore the BOEL for PAH set in the legislative process should also cover the reprotoxic effects.

Below the RAC derived an exposure-risk relationship (ERR) expressing the excess risk for lung cancer as a function of the air concentration of BaP. The ERR is not calculated for BaP alone but for (combustion/pyrolysis-derived) PAH mixtures using BaP as an exposure indicator.

RAC recommends to set a biological guidance value (BGV) for 1-hydroxy pyrene (1-OH-P) in urine based on European background levels, or based on national background levels, if available. Furthermore, RAC recommends to set a biological limit value (BLV) for 3-hydroxy benzo-a-pyrene (3-OH-BaP) in urine, once the air limit value according to the correlation equation presented in this opinion has been decided.

SUMMARY

The tables below present the outcome of the RAC evaluation to derive limit values for the inhalation route and the evaluation for dermal exposure and a skin notation.

Derived Limit Values

OEL as 8-hour TWA:	None
STEL:	None
BLV:	To be confirmed (see text after ERR table below)
BGV:	To be confirmed (see text after ERR table below)

Notations

Notations:	Skin

Cancer exposure-risk relationship (ERR)*

Concentration of BaP (ng/m^3)	Excess (life-time) lung cancer risk (cases per 100 000 exposed)
1	0.56
2	1.1
5	2.8
10	5.6
20	11
50	28
100	56
200	110
500	280
1000	560

* Assuming an 8-hour exposure per day and 5 days per week, over a 40-year working life; the air concentration values for BaP refer to the inhalable fraction.

Biomonitoring of PAH metabolites in urine is also recommended. RAC recommends that the urine levels published for the general population for 1-hydroxypyrene (1-OH-P) are used to set a BGV, corresponding to the background level of the occupationally not PAH exposed, non-smoking general population (BGV) in the EU/EEA area or in the respective member countries.

It is not possible to derive a safe level for a BLV for non-threshold carcinogens such as PAH. However, after a Binding OEL (BOEL) has been recommended by the Working Party on Chemicals (WPC) of the Commission's Advisory Committee on Safety and Health (ACSH), **the level of 3-hydroxybenzo-a-pyrene (3-OH-BaP) in urine corresponding to the air level of BaP should be selected as a BLV.** This is further described in sections 6.2.1 and 6.2.2 of Annex 1). Urinary levels of 3-OH-BaP are far lower than 1-OH-P levels requiring highly sensitive monitoring methods; nevertheless, recent analytical improvements render the measurement possible at all levels corresponding to the ERR.

Annex I of the CMRD currently contains the following entry:

> *"Work involving exposure to polycyclic aromatic hydrocarbons present in coal soot, coal tar or coal pitch"*

It is recommended to review this entry so it that it more comprehensively covers the diverse range of carcinogenic PAH exposures (see section 9.1.5 of Annex 1 for some considerations).

RAC OPINION

Background

This opinion concerns **polycyclic aromatic hydrocarbons** (PAH, see section 1 of Annex 1).

This evaluation takes previous reviews into account, in particular:

- National and International assessments, including those of AGS (2011), AGS (2015), ATSDR (1995), DECOS (2006), DFG (2012 and 2021), ECHA (2018), ECHA (2019), EPA (2017), IARC (2010), IARC (2012), IPCS (1998) and SCOEL (2016).
- A literature search of published papers from 2017 to date, for topics of relevance to this report.

As explained above and in Annex 1, a scoping study was performed by ECHA which recommended BaP as a suitable marker for overall carcinogenic PAH exposure.

Key conclusions of the evaluation

- PAH constitute a large class of compounds, and consist of two or more fused aromatic rings and their mixtures may contain substituents that may influence the toxicity[2].
- PAH form due to incomplete combustion of organic material, such as coal and wood and they are released to the environment from natural and man-made sources. Man-made sources release a much greater volume than natural sources. Some single PAH are commercially produced in Western Europe, Japan and the USA (see section 5.2.1 of Annex 1 for detailed information).
- PAH are readily absorbed through inhalation, dermal and gastrointestinal routes. Although there are no human data for distribution of PAH in the body following dermal exposure, from the limited animal data that are available, it is reasonable to conclude that PAH are distributed after dermal exposure through various internal organs, including the lungs.
- To biomonitor human exposures to PAH the biomarkers most commonly applied are 1-OH-P and hydroxyphenanthrenes. Due to their low toxicity, neither of these markers represent adequately the internal exposure to carcinogenic PAH in quantitative terms. Furthermore, no single metabolite/ biomarker can adequately represent the variability of PAH exposure mixtures. To tackle these drawbacks, metabolites of the toxicologically more relevant 3-OH-BaP as a metabolite of the carcinogenic BaP, and metabolites of other PAH are taken into consideration. BaP is classified as Mutagen 1B and Carcinogen 1B and is the most potent single PAH together with dibenz[a,h]anthracene (see Table 17 and section 7.6 of Annex 1).
- There is sufficient evidence to demonstrate the carcinogenicity of BaP in experimental animals. BaP produced tumors in all species tested for which data were reported following exposure by many different routes.
- Carcinogenic PAH act as non-threshold carcinogens. In relation to occupational exposure to PAH, cancer in the lungs and skin present the main risks. However, there is no quantitative data on skin cancer to conclude on an exposure risk relationship. Therefore, the exposure risk relationship derived is explicitly restricted to excess lung cancer risk.

[2] However, the toxicity of PAH mixtures is not in the scope of this report and consequently the risk estimates produced do not apply to substances with such substituents.

- Acute toxicity of PAH is relatively low. No chronic exposure studies in animal models evaluate nervous system effects. However human neurotoxicity has been identified as a hazard from developmental studies.

  Mixtures of carcinogenic PAH cause skin disorders in humans and animals, although no specific effects in humans of individual PAH, except for BaP, have been reported. Adverse dermatological effects are observed in animals after acute and subchronic dermal exposure to PAH. PAH has also been reported to be a slight eye irritant. Positive skin sensitization effects in humans and animals are reported for certain PAH. However, data are not comprehensively available for various types of PAH.

- Animal studies demonstrated various effects in gestationally and/or early postnatally treated animals. Effects on sperm quality and male fertility have been demonstrated in human populations highly exposed to PAH mixtures.

  Animal studies demonstrate decreases in sperm quality, changes in testicular histology, and hormone alterations following BaP exposure in adult male animals, and decreased fertility and ovotoxic effects in adult females following exposure to BaP.

- BaP is classified as Repro. 1B for effects on fertility and developmental toxicity, according to Regulation (EC) No 1272/2008. Observed effects reported in inhalation studies on reproductive toxicity have thresholds. These study results are not appropriate to derive definite OELs. A worst case estimate for an OEL referring to reproductive toxicity would be slightly above 200 ng BaP/m³ which would be associated with an excess lung cancer risk of more than 110 cases per 100 000 exposed workers. Consequently, a BOEL below this value would cover reproductive toxicity.

- In the absence of an OEL, RAC recommends an Exposure Response Relationship with which to calculate excess risk based on the meta-analyses of Armstrong et al. (2003, 2004). These meta-analyses cover a wide range of industrial settings and include a large variety of job tasks. Thus, they represent an average and quite comprehensive view on published real-life exposures.

Carcinogenicity and mode of action (see sections 7.7 and 8.1 of Annex 1 for full discussion)

Epidemiological evidence

In humans, there is consistent evidence of PAH-related risk of lung cancer. There is also consistent evidence of PAH-related risk of skin cancer after substantial dermal exposure to PAH.
The scientific evidence of PAH-related risk of bladder cancer is not consistent: an increased risk in workers has been observed only in a limited number of PAH-related industrial processes and confounding by other, established bladder carcinogens remains a possibility. There is no consistent evidence of PAH-related risk for cancer in other organs.

Quantitative estimates have been published for lung cancer risk by BaP concentration in the air, based on a meta-analysis of 39 cohort studies representing nine main occupational settings with PAH exposure. Quantitative risk estimates were not identified from human data for any other specific PAH compound.

Animal carcinogenicity studies

RAC concluded that there is sufficient evidence to demonstrate the carcinogenicity of BaP in experimental animals. IARC (1973, 2012) reported that BaP produced tumours in all species tested (mouse, rat, hamster, guinea-pig, rabbit, duck, newt, monkey) for which data were reported following exposure by many different routes (oral, dermal, inhalation, intratracheal, intrabronchial, subcutaneous, intraperitoneal, intravenous). BaP had both a

local and a systemic carcinogenic effect, was an initiator of skin carcinogenesis in mice, and was carcinogenic in single-dose studies and following prenatal and transplacental exposures.
Overall, these animal data clearly showed that carcinogenic PAH act as local and systemic carcinogens.

Mode of action: Metabolism and genotoxicity

RAC recently reviewed the mechanisms of carcinogenic action of PAH mixtures overall and of BaP (ECHA, 2018). The RAC assessment is summarised below, while a detailed description is given in section 8.1. of Annex 1.

Many PAHs share the same genotoxic mechanism of action, i.e. metabolic activation to electrophilic dihydrodiol epoxides and/or quinones which are capable of covalent binding to DNA (IPCS 1998). The DNA adducts thus formed may cause mutations.
The variation in carcinogenic potencies of PAHs is most probably associated with the structural differences between adducts and the subsequent removal by DNA repair mechanisms. However, it could additionally be a result of changes in DNA polymerase activity and incorrect base-pair insertion resulting from translesion DNA synthesis.
Experiments on interactions of PAH in both binary and complex mixtures on DNA adduct levels reported both less-than-additive and more-than-additive effects (see section 8.1 of Annex 1).

The carcinogenicity of BaP, the most extensively studied PAH, is well documented in animal models. The primary mode of action by which BaP induces carcinogenicity is genotoxicity. The general sequence of key events (KEs) associated with the genotoxic mode of action for BaP is as follows:

1. Bioactivation of BaP to DNA-reactive metabolites via three possible metabolic activation pathways: diol epoxide, radical cation and o-quinone;

2. Direct DNA damage by reactive metabolites, including the formation of DNA adducts and ROS-mediated damage;

3. Formation and fixation of DNA mutations, particularly relevant in tumour suppressor genes or oncogenes associated with tumour initiation; and

4. Clonal expansion of mutated cells during the promotion and progression phases of cancer development.

BaP can act as both an initiator and a promoter of carcinogenesis. The available human, animal, and in vitro evidence all supports mutagenicity as the primary mode of action by which BaP induces carcinogenesis (EPA, 2017). In addition to genotoxicity, there are suspected interactions of BaP with various constituents of the proteome. Such non-genotoxic pathways are a matter of recent research.

Overall, a non-threshold mode of action is assumed by RAC for BaP, in agreement with other regulatory bodies considering some specific PAH (e.g., coal tar pitch high temperature (CTPHT)) and more generally for carcinogenic PAH or PAH mixtures (AGS (2011), DECOS (2006), SCOEL (2016), ECHA (2018), ECHA (2019a).

Cancer Risk Assessment (see section 9.1 of Annex 1 for full discussion)

Occupational exposure to PAH concerns almost exclusively exposure to PAH mixtures. These mixtures vary in the content of different PAH, with different carcinogenic potencies. Only a minor fraction of all PAH or of all PAH mixtures has been tested in standard toxicological assays. Even less PAH have been investigated in epidemiological studies. Therefore, the cancer risk assessment of PAH is complex.

Consideration of possible exposure indicators for cancer risk assessment

It is noted that National and International bodies have considered various options for monitoring control of exposure to carcinogenic PAH at workplaces (see section 9.1.1 of Annex 1). For the inhalation route these options can be summarised as (1) using BaP as a unique indicator, (2) using a selection of PAH and applying an approach based on toxic equivalence value and (3) using total PAH (benzene soluble matter).

Having considered various options, RAC concluded that BaP is the most robust marker of PAH-related cancer risk via the inhalation route. This is mainly due to the abundance of quantitative data for cancer risk and the fact that BaP is considered as one of the most potent genotoxic carcinogens and thus an adequate and toxicologically relevant surrogate for the overall PAH risk. The other options suffer from the lack of quantitative cancer risk data and also from interference by non-PAH substances, e.g. in case of the benzene soluble matter approach. Both human and animal studies have clearly shown that PAH penetrate the skin and reach the circulation (see section 5.4. of Annex 1).

With regard to systemic exposure via the dermal route, the urine concentration of 1-OH-P and of 3-OH-BaP have been recommended as suitable indicators by some, but not all bodies. Since skin exposure may contribute significantly to BaP toxicity, RAC proposes a skin notation for PAH.

Although not all PAH mixtures have been investigated in experimental or (observational) epidemiological studies, based on general mode of action considerations, it is concluded that all PAH mixtures should be considered non-threshold carcinogens. BaP is a potent PAH with an abundant human database on cancer risk. Thus, an exposure risk relationship (ERR) is derived to characterise the excess cancer risk for the concentration of airborne BaP. This can then be applied to a variety of PAH resulting from incomplete combustion and pyrolysis (thermal degradation) processes of organic material. A PAH-related excess of lung cancer has been quite consistently observed following exposure to PAH mixtures in various industries. The ERR is thus derived for lung cancer risk.

The ERR is based on meta-analyses of Armstrong et al. (2003, 2004) (see section 9.1.3 of Annex 1). In short, the (linear) lung cancer ERR used the unit relative risk from 39 cohort studies of RR=1.20 for lung cancer from cumulative exposure of 100 µg BaP/m³-years. This cumulative exposure was distributed over a 40-year working career (i.e. average airborne concentration equalling 2.5 µg BaP/m³ per year). The relative risk was converted to absolute excess cases of lung cancer using a life-table approach and EU male population reference rates for lung cancer. These meta-analyses cover a wide range of industrial settings and include a wide variety of job tasks. Thus, they represent an average and quite comprehensive view on published real-life exposures.

As lung cancer rates are higher among males than females, using the male population rates results in more conservative excess risk estimates in comparison to calculations using data on both genders. The same ERR was already used in the context of the authorisation process of Coal Tar Pitch High Temperature (CTPHT), RAC (ECHA, 2018).

Uncertainties

The proposed approach is based on a single indicator substance, BaP, which would be applied to control cancer risk from a variety of PAH mixtures. BaP is a very potent carcinogenic PAH. Therefore the ERR which is derived from a large number of human epidemiological studies representing exposure from a large variety of processes and industries and using a potent indicator substance is considered an adequate and toxicologically relevant proxy of the overall cancer risk of PAH exposure from various combustion and pyrolysis sources.
It is noted that the exposure assessments in a part of the studies included in the Armstrong et al. 2014 analysis were rather poor (exposure was not directly measured at all in 23 of the 39 studies), for which exposure estimates based on measurements in each worker group in other workplaces of the same industries were used as further explained in section

7.7.1.1 of Annex 1). Also, in some occupational settings, the exposure results from PAH contained in the materials used and the content of certain single PAH, including BaP in those products, are already heavily restricted. This results in low workplace concentrations of these restricted PAH while leaving the possibility of exposure to other non-regulated PAH (see e.g. creosote wood impregnation and tyre manufacturing in sections 5.2 and 5.3 of Annex 1).
In such settings it would be preferable to monitor exposure to a wider variety of PAH, e.g., the 16 EPA PAH, even if they were less carcinogenic than BaP. However, the available toxicological and epidemiological data does not allow deriving quantitative ERRs or other benchmarks for such an approach. Nevertheless, the exposure minimisation principle of CMRD should apply to any carcinogenic PAH.

The ERR is derived for lung cancer. There are also indications of an elevated risk of bladder cancer in some industries with PAH exposure. However, the evidence is less consistent than for lung cancer and limited to only a few specific industries some of which also entailed exposure to known bladder carcinogens, e.g. aromatic amines. Therefore confounding from such exposures cannot be excluded. This would mean that an ERR derived for bladder cancer risk by BaP as a proxy of exposure would be confounded and would not correctly describe the cancer risk in all PAH related exposures. Sensitivity calculations indicate that assuming no confounding by other factors would at maximum influence the ERR by a factor of 1.7 (see section 9.1.4 of Annex 1). Also, skin cancer risk is not considered by the ERR. Even though the evidence for skin cancer induction by BaP is conclusive, no quantitative data are available.

Studies by Archibong et al. (2002, 2008, 2012) concerning reproductive toxicity are not considered sufficiently reliable for precise OEL derivation. They are unique because there are no other inhalation studies on reproductive toxicity indicating toxic effects (see section 7.8.2 of Annex 1). All other studies either found no impact on fetal mortality or testes weight and/or used far higher doses via different exposure pathways. OELs could be calculated based on the described LOAECs (i.e. 25 µg/m³ resp. 75 µg/m³) or NOAEC (75 µg/m³) for effects on reproduction/development. The mentioned studies would only provide OELs for the respirable fraction, while the ERR is related to the inhalable fraction. Nevertheless, as no MMADs are given, the respirable and deposited fraction in rats and humans cannot precisely be derived. As a result, OEL derivation from the studies by Archibong et al. must be considered with caution. The lowest OEL from the Archibong studies would be derived as follows:

A LOAEC of 25 µg BaP/m³ for foetal survival was provided from Archibong et al. 2002.

Using default factors for inter- and intraspecies differences, 4 h/d to 8 h/d, LOAEC to NOAEC (i.e. 2.5 × 5 × 2 × 3) x 6.7 m³/10 m³ results in:

human NOAEC = 223 ng BaP/m³ for the respirable dust fraction.

A time extrapolation factor is not needed as the exposure time covered pregnancy/foetal development.

In comparison, the ERR derived from epidemiology is derived from exposures to inhalable dust. Respirable dust is contained in workplace inhalable dust fractions mostly in lower portions, however, it is not possible to set a fixed standard factor for the respirable fraction. Total dust exposure estimates at PAH workplaces were generally reported lying between 1-25 mg/m³ (Armstrong et al. 2004). These higher total dust levels indicate higher mass fractions of inhalable dust. It can be assumed that the current dust exposure levels at PAH workplaces are lower. As the type of work activities at PAH workplaces will not have generally changed also currently substantial exposure to bigger particles must be assumed.

Taken together, it is reasonable to assume that the respirable dust fraction contained in inhalable dust at PAH workplaces contributes considerably less than 100 % (w/w). This means that a putative OEL of 223 ng BaP/m³ for reproductive toxicity related to respirable

dust would be a worst case estimate for inhalable dust and would be associated with an excess (life-time) lung cancer risk of more than 110 cases per 100 000 exposed workers according to the derived exposure risk relationship. Therefore, there is no need to establish a separate OEL for respirable dust connected to reproductive toxicity, which would be expected to be covered by the risk-based binding OEL based on carcinogenic effects provided that the latter will not exceed 200 ng BaP/m³.

Derived Exposure Response Relationship (see section 9.2 of the Annex 1 for full discussion)

BaP and PAH-containing BaP are non-threshold carcinogens and consequently no health-based OELs can be recommended. Instead, an ERR for lung cancer has been derived.

The ERR is not calculated for BaP alone but for (combustion/pyrolysis-derived) PAH mixtures using BaP as an exposure indicator.

Lung cancer exposure-risk relationship after a 40-year working life exposure to a given 8-hour air concentration for five working days a week

Air concentration of BaP (ng/m³)	**Excess life-time lung cancer risk (cases per 100 000 exposed)**
1	0.56
2	1.1
5	2.8
10	5.6
20	11
50	28
100	56
200	110
500	280
1000	560

Analytical feasibility

Methods for monitoring air exposure levels covering the entire ERR are available. These methods cover different analytical techniques validated for a range of particle bound PAH in the inhalable fraction and in the gaseous phase. The LoQ for BaP goes down to 1.6 ng BaP/ m³ air (see section 6.1 of Annex 1).

Short term limit value (STEL)

Most of the available toxicological and epidemiological evidence concerns hazardous effects from long-term exposure, especially lung cancer. There is no obvious evidence indicating a particular hazard from short-term exposure. It is concluded that it is not justified to recommend a STEL for BaP as an indicator substance or for any other specific PAH.

Biological limit values (see sections, 6.2.1, 6.2.2, 9.2.4 and 9.2.5 of Annex 1 for full discussion)

Biomonitoring and Biological Limit Value (BLV)

BaP and PAH are considered non-threshold carcinogens and the Binding OEL will be set later in the legislative process taking into account the ERR and socio-economic aspects. It is strongly recommended by RAC that after the **Binding OEL** has been defined, the correlations between BaP concentrations in the air and 1-OH-P and 3-OHBaP

concentrations in urine are used to set a a **BLV** for 3-OH-BaP and a **BGV** for 1-OHP that correspond to the chosen OEL for BaP.

The most widely and routinely used biomonitoring method for assessing occupational PAH exposure is to measure urinary 1-OH-P, a major metabolite of pyrene. Pyrene has a high thermodynamic stability rendering it one of the most predominant PAH in virtually any mixture of PAHs. As a consequence, it can serve as a universal marker for exposure to PAH. Due to its structure, its metabolism is also less prone to interindividual genetic variation compared to many other PAH. A relatively large proportion of pyrene is excreted in the urine as 1-OH-P, which facilitates its detection. However, pyrene is not carcinogenic and therefore not a direct indicator of cancer risk.

Toxicologically more relevant but more demanding with respect to laboratory equipment would be 3-OH-BaP, a direct metabolite of BaP. A correlation between air levels and 3-OH-BaP has been published by the German MAK Commission (DFG, 2021):

Air **Benzo[*a*]pyrene** **[ng/m³]**	**Urine** **3-hydroxybenzo[a]pyrene (3-OH-BaP)** **(after hydrolysis) - [ng/g creatinine]**
70	0.7
350	2
700	3.5
1,000	5
1,500	7

Sampling time at the beginning of the next shift

In the meantime, an advanced analytical procedure for the more sensitive and specific determination of 3-OH-BaP in human urine has been published (Rögner et al., 2021). This method is based on enzymatic hydrolysis, solid-phase extraction, derivatisation with 2-fluoromethylpyridinium-p-toluene sulfonate, and UPLC-MS/MS analysis. Both the calibration reference substance and the isotope-labelled internal standards were used as glucuronide conjugates (3-OH-BaP-glucuronide, 3-OH-BaP-$^{13}C_6$-glucuronide). The limit of quantification for the method is 50 pg/L urine and is therefore well suited to cover the entire ERR stated above. This method has been validated according to the US Food and Drug Administration (FDA) guideline and will soon be adopted by the working group "Analyses in Biological Materials" of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK commission) in Germany.

Biological guidance value (BGV)

In 2016, SCOEL proposed a value of 0.5 µg 1-OH-P per g creatinine as a Biological Guidance Value (BGV) (SCOEL, 2016). 1-OH-P background levels in urine of occupationally unexposed, non-smoking adults are available for some European countries (HBM4EU Dashboard;https://www.hbm4eu.eu/what-we-do/european-hbm-platform/eu-hbm-dashboard/; accessed 20.12.2022). These indicate 95th percentiles around 0.085-0.74 µg/g of creatinine, with indications of a 2-3-fold difference between non-smokers and smokers.
Such data could be used to define a BGV value contributing to the overall risk management of PAH mixtures, using either the highest value in Europe or – if available – national levels to identify occupational exposure towards PAH.

Groups at extra risk

No groups at extra risk were identified. It is noted that tobacco smoke contains PAH and thus under similar working conditions, smokers would have a higher overall PAH exposure than non-smokers.

Notations

PAH usually occur as mixtures of several PAH. Consequently, dermal absorption of PAH varies, but can be high in certain industries and processes. Therefore, a skin notation is recommended. For reasons outlined in section 9.3 of Annex 1, it is not possible to tailor the assignment of skin notation for different PAH. Therefore it is recommended to assign skin notation to all PAH as a precautionary measure.

BaP has a harmonised classification for skin sensitisation. However, there is no comprehensive information indicating skin or respiratory sensitisation from most of PAH and notation for these properties are not recommended for PAH overall.

ATTACHMENTS:

Annex 1: gives the detailed scientific grounds for the opinion.

Annex 2: provides the comments received on the ECHA scientific report, and responses provided by ECHA and RAC (excluding confidential information).