Guidance for Calculating Benzo(a)pyrene Equivalents for Cancer Evaluations of Polycyclic Aromatic Hydrocarbons

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List of Abbreviations

ADS	Associate Director for Science
ATSDR	Agency for Toxic Substances and Disease Registry
BaP equivalent	benzo(a)pyrene equivalent
BEC	BaP equivalent concentration
CSF	cancer slope factor
CV	comparison value
EPA	U.S. Environmental Protection Agency
EPC	exposure point concentration
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System
IUR	inhalation unit risk
OEHHA	California Office of Environmental Health Hazard Assessment
PAH	polycyclic aromatic hydrocarbon
PEF	potency equivalency factor
PHA	public health assessment
PHAST	Public Health Assessment Site Tool
PHAGM	Public Health Assessment Guidance Manual
RPF	relative potency factor
95UCL	95% upper confidence limit of the arithmetic mean

Note

Since the time when this guidance was originally drafted, the Agency for Toxic Substances and Disease Registry (ATSDR) has developed an online tool that automates the calculations outlined in this document (i.e., ATSDR's EPC Tool). Health assessors are encouraged to use that tool when estimating exposure point concentrations (EPCs) for polycyclic aromatic hydrocarbons (PAHs).

1.0 INTRODUCTION

When multiple chemicals in the same class have similar toxicological properties, potency equivalency factors (PEFs) can be used to express the chemicals' overall carcinogenicity as a single value. PEFs are similar to the toxic equivalency factors used for dioxin and dioxin-like compounds (ATSDR 2019c), but they are specific for the estimation of cancer risk. For multiple polycyclic aromatic hydrocarbons (PAHs), carcinogenicity can be expressed as a benzo(a)pyrene equivalent (BaP equivalent).

This document presents the Agency for Toxic Substances and Disease Registry's (ATSDR's) approach for calculating BaP equivalents. [1] Health assessors can use this approach to reduce environmental data for many PAHs to a single value, expressed as a BaP equivalent, for use in a public health assessment (PHA) when evaluating cancer risk.[2]

Using this Guidance

This guidance presents rigorous methods that health assessors should use for evaluating PAH cancer risk as part of the PHA process. Health assessors should use their professional judgment, consulting with the ATSDR Associate Director of Science (ADS) group and management, to determine if high levels of PAHs or other risk-driving contaminants necessitate immediate public health actions.

The approach for calculating BaP equivalents described in this guidance is based on methods developed by the Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency (OEHHA, 2015). Health assessors should follow this approach when evaluating environmental samples collected with discrete, composite, and incremental methods.

Health assessors can use this guidance to calculate a BaP equivalent with data gathered via any sampling strategy, but they must use sampling-specific guidance to calculate exposure point concentrations (EPCs) for BaP equivalents. ATSDR has developed guidance to calculate EPCs for data collected with discrete sampling (ATSDR 2019a) and composite sampling and incremental sampling methodology (ATSDR 2022). A separate guidance document is also available that provides details on how to properly define exposure units (ATSDR 2019b).

ATSDR's general approach for evaluating PAHs for cancer effects is summarized in the text box on the next page and is applicable to environmental sampling data in all media (e.g., air, soil, water).

[1] Despite similarities, the approach described here is different from ATSDR's approach for handling dioxin and dioxin-like compounds because of statistical considerations tied to addressing non-detects (ATSDR, 2019c). Specifically, the Kaplan-Meier statistic used to sum non-detects on a per-sample basis in that guidance should not be used for PAHs due to the potential for elevated detection limits in high PEF PAHs within this class of chemicals.

[2] PHA is used here to refer to any health assessment conducted by ATSDR, including public health assessments, health consultations, and letter health consultations.

ATSDR's Overall Approach for Evaluating PAHs for Cancer Effects

1. Calculate a BaP equivalent for each sample within the exposure unit using congener-specific PEFs. Screen the maximum BaP equivalent against the cancer comparison value (CV) for benzo(a)pyrene.
2. If the maximum BaP equivalent is greater than the cancer CV, calculate an EPC for each measured PAH congener using results from all environmental samples collected within the exposure unit.
3. Calculate a BaP equivalent EPC using congener-specific PEFs and the EPCs calculated in Step 2.
4. Calculate cancer risk with ATSDR's Public Health Assessment Site Tool (PHAST) using the BaP equivalent EPC and OEHHA's oral cancer slope factor (CSF) for benzo(a)pyrene (i.e., 1.7 $mg/kg/day^{-1}$).

Note: Do not evaluate non-cancer effects with a BaP equivalent. Instead, evaluate each PAH congener separately with available non-cancer CVs or health guidelines, as you would any other contaminant. PHAST currently includes non-cancer CVs or health guidelines for benzo(a)pyrene and naphthalene. Health assessors should check PHAST for other PAHs not shown in Table 1.

Note that this guidance applies to the calculation of BaP equivalents for evaluating cancer effects of PAHs as a class. BaP equivalents do not apply in evaluations of non-cancer health effects. When non-cancer effects for PAHs are evaluated, each PAH congener should be evaluated separately with appropriate and available congener-specific non-cancer comparison values (CVs) or health guidelines.

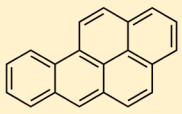
Section 2.0 of this document provides additional background information. Section 3.0 presents ATSDR's approaches for calculating BaP equivalents. Appendix A shows an example of BaP equivalent calculations and Appendix B gives a sensitivity analysis example.

2.0 BACKGROUND

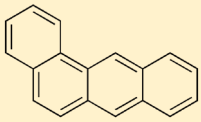
PAHs are a class of more than 100 different chemicals that are formed during the incomplete burning of coal, oil, natural gas, wood, garbage, or other organic substances, such as tobacco or charbroiled meat. PAHs are also found in asphalt, coal tar, crude oil, creosote, and roofing tar. Although PAHs typically occur in these types of sources as mixtures of two or more compounds, they can be manufactured as individual compounds for research purposes (ATSDR 1995). In this guidance, individual PAHs are referred to as "congeners."

PAH congeners are organic compounds composed of multiple aromatic rings, containing only hydrogen and carbon. The chemical structures of several common PAH congeners are shown below.

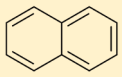
Chemical Structures of Several PAHs



Benzo[a]pyrene



Benzo(a)anthracene



Naphthalene

2.1 Potency Equivalency Factors

Potency equivalency factors (PEFs) provide a way to assess the relative potency of PAH congeners measured in environmental samples as a group. They are particularly helpful when complete toxicological data are not available for all congeners. PEFs are derived for each congener to reflect the

congener's relative toxicity to a benchmark compound and can be combined to estimate a single value that represents the overall carcinogenicity of multiple PAH congeners. In the case of PAHs, the benchmark compound is benzo(a)pyrene — chosen because of the large amount of toxicological data and sampling methods available for this compound, as well as the known frequent human exposure to benzo(a)pyrene (Collins et al. 1998).

Although PAHs comprise more than 100 individual congeners, only some have sufficient data available on carcinogenic effects to derive a PEF. ATSDR currently recommends using the PEFs derived by OEHHA and shown in Table 1[3,4]. Detailed information on the criteria used to develop these PEFs can be found in Appendix G of OEHHA's *Air Toxics Hot Spots Program Guidance Manual* (OEHHA 2015).

In brief, OEHHA derived these PEFs by comparing the relative toxicity of each congener to that of benzo(a)pyrene, based on a detailed scientific review of chemical structures and toxicological databases. Currently, OEHHA's PEF values range from 0.01 to 10. A PEF of 0.1 indicates that the congener is one tenth as toxic as BaP, whereas a PEF of 1.0 indicates that the congener is equally as toxic as benzo(a)pyrene.

Health assessors might find environmental data sets that include measurements for PAH congeners that are not included in Table 1. This is to be expected, as not all PAHs have sufficient evidence for carcinogenicity. Table 2 gives a summary of PAHs, along with weight of evidence classifications for carcinogenicity from the International Agency for Research on Cancer (IARC) and the U.S. Environmental Protection Agency (EPA). Health assessors are referred to Section 3.4 for additional information on congeners that do not have PEFs.

Health assessors should note that OEHHA continues to review literature pertaining to the carcinogenicity and mutagenicity of PAHs. As such, PEFs may be derived for additional PAHs or existing PEFs may be modified based on new data. ATSDR Associate Director for Science (ADS) groups will inform health assessors of any notable future updates.

[3] Naphthalene is not listed in Table 1. This congener should not be included in BaP equivalent calculations; it should be evaluated separately, like any other contaminant considered in the PHA process (see Section 3.3).
[4] ATSDR recognizes that EPA developed relative potency factors (RPFs) for a subset of PAHs in 1993 (EPA 1993). However, health assessors should use the OEHHA PEFs shown in Table 1 of this guidance when evaluating PAHs. Note that OEHHA uses the term "PEF," which is conceptually the same as EPA's "RPFs."

2.2 General Approach for Calculating Benzo(a)pyrene Equivalents

To calculate a BaP equivalent for one or more environmental samples, first multiply the concentration of each PAH congener by that congener's PEF to produce a congener-specific BaP equivalent concentration (BEC). The calculated BECs for all measured congeners are then summed to obtain a total BaP equivalent. The box below shows the two equations used to calculate BaP equivalents. Section 3.0 describes how health assessors should use these equations to calculate BaP equivalents for a PHA and Appendix A presents an example.

General Framework for Calculating a BaP Equivalent

Equation 1:

$$BEC_i = x_i \times PEF_i$$

Equation 2:

$$\text{BaP equivalent} = \sum_{i=1}^{k}(BEC_i)$$

Where:

- BEC_i is the BaP equivalent concentration of the i^{th} individual congener
- x_i is the measured concentration for the i^{th} individual congener
- PEF_i is the potency equivalency factor (PEF) of the i^{th} individual congener
- BaP equivalent is the total BaP equivalent
- k is the number of congeners that make up the total BaP equivalent

Overall, the BaP equivalent framework provides a scientifically justified, accepted method for evaluating carcinogenicity of PAH mixtures. However, it has inherent uncertainties and might not capture the true health risks of all congener exposure scenarios.

3.0 APPROACH FOR CALCULATING BENZO(A)PYRENE EQUIVALENTS FOR HEALTH ASSESSMENTS

This section presents ATSDR's approach for calculating BaP equivalents when evaluating cancer risk for PAHs. The approach for calculating BaP equivalents for screening is described first (Section 3.1), followed by a discussion of how to calculate a BaP equivalent EPC, when necessary (Section 3.2). Health assessors should note that naphthalene should not be included in a BaP equivalent calculation; Section 3.3 describes how to evaluate this particular PAH congener.

Although ATSDR developed this guidance to apply to a broad range of site-specific scenarios, some environmental data sets will present unique challenges for calculating BaP equivalents. Health assessors should consult with the ATSDR ADS group when they encounter any site-specific scenarios or other circumstances not sufficiently covered by the guidance described below.

3.1 Calculating Benzo(a)pyrene Equivalents for Screening

During the PHA process, health assessors must screen maximum detected concentrations against applicable CVs for all identified potential or completed exposure pathways. To do this for PAHs, health assessors should first calculate a total BaP equivalent *for each environmental sample* collected within the exposure unit and then compare the maximum total BaP equivalent against the cancer CV for benzo(a)pyrene (i.e., the cancer risk evaluation guide for benzo[a]pyrene). If the maximum BaP

equivalent exceeds the cancer CV, health assessors must calculate an EPC to further evaluate cancer risk (Section 3.2). If the maximum BaP equivalent is below the cancer CV, health assessors can conclude that the measured concentrations of PAHs within the exposure unit do not pose a health hazard. The text box below outlines this general approach.

ATSDR's Approach for Calculating a BaP Equivalent for Screening

1. For each sample, apply OEHHA's PEFs to each congener to obtain BECs.
2. Sum the congener-specific BECs to determine the total BaP equivalent for each environmental sample.
3. Compare the maximum total BaP equivalent across samples to the cancer CV for benzo(a)pyrene.

Note: Health assessors should replace non-detects with the full detection limit when calculating BaP equivalents during initial screening with cancer CVs. Health assessors should not evaluate non-cancer effects with a BaP equivalent.

Note that during this process, health assessors will often encounter non-detect observations, which are PAH concentrations that are too low to measure with confidence. Laboratories typically present non-detects as being less than a specified limit (e.g., "<25 ng/kg"), either a method detection limit or a quantification limit. When results are presented in this way, health assessors can only conclude that the actual PAH level is somewhere between zero and the specified level. Nonetheless, these observations are considered valid results and should be included in BaP equivalent calculations. As a conservative approach during the initial screening step, ATSDR recommends that health assessors use the full method detection limit when calculating BaP equivalents.

As an example, imagine an exposure unit where 12 samples were collected and analyzed for seven different PAH congeners. The text box on the next page demonstrates how a health assessor would calculate BaP equivalents for one of those samples during the initial screening step. Note that this sample includes one observation that was reported as non-detect, with a detection limit of 60 µg/kg (shown in the table as <60 µg/kg for indeno[1,2,3-cd]pyrene).

The same process would be used to calculate BaP equivalents for the other 11 samples collected within the exposure unit. The maximum BaP equivalent calculated for the 12 samples would then be compared with the cancer CV for benzo(a)pyrene. If the maximum BaP equivalent from these samples was greater than that CV, the health assessor would need to calculate an EPC to further evaluate cancer risk, following the approach described in Section 3.2.

Example BaP Equivalent Calculation for Screening

PAH congener	PEF* (unitless)	Sample 1	
		Measured concentration (µg/kg)	BEC† (µg/kg)
Benzo(a)anthracene	0.1	60	6.0
Benzo(a)pyrene	1	100	100
Benzo(b)fluoranthene	0.1	190	19.0
Benzo(k)fluoranthene	0.1	135	13.5
Chrysene	0.01	80	0.8
Dibenzo(a,h)anthracene	2.4	47	113
Indeno(1,2,3-cd)pyrene	0.1	<60	6.0
		BaP equivalent‡ (µg-BaP/kg) =	**258.1**

*Recommended PEFs are presented in Table 1 at the end of this guidance.

†BEC for each PAH congener = (EPC value) × (PEF).

‡BaP equivalent for sample = sum of the BECs for the seven PAH congeners.

With this example, health assessors should recognize that BaP equivalents are weighted sums of the individual congeners, with weights based on each congener's potency relative to benzo(a)pyrene. Another way to consider the result from the sample shown above is that exposure to the measured concentrations of seven different PAH congeners is equivalent to exposure to 258.1 µg-BaP/kg.

3.2 Calculating Benzo(a)pyrene Equivalents for EPCs

If the maximum BaP equivalent calculated for each sample within the exposure unit is greater than the cancer CV for benzo(a)pyrene, health assessors must calculate a BaP equivalent EPC for a more detailed exposure and cancer risk evaluation. To do so, health assessors should first calculate an EPC for each measured PAH congener across all environmental samples collected within the exposure unit. Health assessors should refer to ATSDR's Exposure Point Concentration Guidance for Discrete Sampling (ATSDR 2019a) or ATSDR's Exposure Point Concentration Guidance for Non-discrete Sampling (ATSDR 2022) for guidance on how to determine the appropriate EPC statistic (e.g., 95% upper confidence limit around a mean [95UCL], maximum detected concentration) based on the sampling method, number of samples, number of detected results, and data distribution of each congener.

After EPCs are calculated for each measured congener in the exposure unit, health assessors should calculate a BaP equivalent by first multiplying each congener's EPC by its respective PEF and then summing the results. The text box below outlines this general approach.

ATSDR's Approach for Calculating a BaP Equivalent EPC

1. Calculate an EPC for each measured PAH congener from the environmental samples collected within an exposure unit.
2. Apply OEHHA's PEFs to each calculated EPC from step 1 to obtain a BEC for each PAH congener.
3. Sum the congener-specific BECs to determine the total BaP equivalent.

As an example, imagine an exposure unit where 12 samples were collected and analyzed for seven different PAH congeners. A health assessor calculated BaP equivalents for each sample during the initial screening step (following the approach described in Section 3.1) and found that the maximum BaP equivalent exceeded the cancer CV. The text box below demonstrates how they should then calculate a BaP equivalent EPC to estimate cancer risk.

In this example, the health assessor calculated EPCs as the 95UCL for each congener by following ATSDR's Exposure Point Concentration Guidance for Discrete Sampling (ATSDR 2019a). These EPCs were multiplied by applicable PEFs to obtain congener-specific BECs and then summed to estimate a BaP equivalent EPC.

Example BaP Equivalent EPC Calculations

PAH Congener	EPC Statistic	EPC Value (µg/kg)	PEF* (unitless)	BEC† (µg/kg)
Benzo(a)anthracene	95UCL	125	0.1	12.5
Benzo(a)pyrene	95UCL	200	1	200
Benzo(b)fluoranthene	95UCL	380	0.1	38
Benzo(k)fluoranthene	95UCL	270	0.1	27
Chrysene	95UCL	160	0.01	1.6
Dibenzo(a,h)anthracene	95UCL	95	2.4	228
Indeno(1,2,3-cd)pyrene	95UCL	120	0.1	12
			BaP equivalent EPC‡ = 519.1 µg-BaP/kg	

*Recommended PEFs are presented in Table 1 at the end of this guidance.

†BEC for each PAH congener = (EPC value) × (PEF).

‡BaP equivalent EPC = sum of the BECs for the seven PAH congeners.

Health assessors should then use the calculated BaP equivalent EPC to evaluate cancer effects, following the general approach outlined in ATSDR's Public Health Assessment Guidance Manual (PHAGM). This involves calculating a BaP equivalent dose from the BaP equivalent and then using that dose to estimate cancer risk. For these steps, ATSDR encourages health assessors to use the agency's Public Health Assessment Site Tool (PHAST).

Note that when estimating cancer risk for a BaP equivalent, ATSDR currently recommends using OEHHA's oral cancer slope factor (CSF) for benzo(a)pyrene of 1.7 $(mg/kg/day)^{-1}$ (OEHHA 2010). This CSF is based on toxicity data from Culp et al. (1998) and was derived in 2010 as part of a public health goal for benzo(a)pyrene in drinking water. ATSDR similarly recommends using OEHHA's IUR for benzo(a)pyrene of $1.1x10^{-3}$ $(µg/m3)^{-1}$ (OEHHA 1993). This IUR is based on toxicity data from Thyssen et al. (1981). PHAST applies OEHHA's oral CSF and OEHHA's IUR for benzo(a)pyrene, along with appropriate age-dependent adjustment factors.

3.2.1 Special Considerations for PAH congeners with All Non-Detect Observations

The approach described above for calculating a BaP equivalent EPC requires health assessors to first determine EPCs (i.e., 95UCLs, maximum detected concentrations) for each measured PAH congener. If there are no detected observations for a given congener, health assessors will not be able to calculate

an EPC for that congener. When this occurs, health assessors should follow the steps below to determine how much of an influence the non-detect PAH congener(s) has on cancer risk estimates. Figure 1 shows a flow chart of this process.

1. Evaluate an upper-bound or "worst-case" BaP equivalent EPC. Health assessors should do this by first setting the EPC value for the non-detect PAH congener(s) to the value of the full detection limit. If there are multiple detection limits for a given PAH, health assessors should use the highest detection limit as a health-protective assumption. EPCs (i.e., 95UCLs or maximum detected concentrations) for the other congeners should be estimated following ATSDR's Exposure Point Concentration Guidance for Discrete Sampling (ATSDR 2019a) or Exposure Point Concentration Guidance for Non-Discrete Sampling (ATSDR 2022). Health assessors should then calculate the upper-bound BaP equivalent EPC based on all congeners and estimate cancer risk in PHAST to determine the potential for cancer health effects.
    - If cancer risk is estimated at a value less than or equal to $1x10^{-6}$, there is no hazard and your evaluation is complete.
    - If cancer risk is estimated at a value greater than $1x10^{-6}$, conduct a toxicological evaluation following PHAGM guidance to further evaluate the potential for harmful effects.
        - If the toxicological evaluation indicates that there is no hazard, your evaluation is complete.
        - If the toxicological evaluation indicates that there is a hazard, continue to step 2.
2. Evaluate a lower-bound BaP equivalent EPC. Health assessors should do this by first setting the EPC value for the non-detect PAH congener(s) equal to zero. EPCs (i.e., 95UCLs or maximum detected concentrations) for the other congeners should be estimated following ATSDR's Exposure Point Concentration Guidance for Discrete Sampling (ATSDR 2019a) or Exposure Point Concentration Guidance for Non-Discrete Sampling (ATSDR 2022). Health assessors should then calculate a lower-bound BaP equivalent EPC based on all congeners and use that result to estimate cancer risk in PHAST.
    - If cancer risk is estimated at a value less than or equal to $1x10^{-6}$, the conclusions from the upper- and lower-bound BaP equivalent EPCs conflict. This indicates that there is uncertainty in the EPC and corresponding cancer risk determination because of non-detect observations. When this occurs, health assessors should report the range of cancer estimates from the upper- and lower-bound EPCs and discuss related uncertainty in the PHA. They should use their professional judgement, supported by PHAGM cancer risk guidance, and consult the ATSDR ADS group for additional support, if needed.
    - If cancer risk is estimated at a value greater than $1x10^{-6}$, conduct a toxicological evaluation following PHAGM guidance to further evaluate the potential for harmful effects.

- If the toxicological evaluation indicates that there is no hazard, the conclusions from the upper- and lower-bound BaP equivalent EPCs conflict. Refer to step 2a above for how to discuss these findings in the PHA.
- If the toxicological evaluation indicates that there is a hazard, the conclusions from the upper- and lower-bound BaP equivalent EPCs agree. Discuss the risk following cancer risk guidance in PHAGM.

Appendix B provides an example of this process. Health assessors are encouraged to consult the ATSDR ADS group if they have any questions or concerns about this process. When summarizing results from this sensitivity analysis, health assessors should refer to PHAGM for additional information on how to discuss results of cancer risk evaluations.

3.3 Special Considerations for Naphthalene

As mentioned above, naphthalene should not be included in the BaP equivalent for screening or the BaP equivalent EPC when evaluating cancer risk. Naphthalene is not mutagenic, whereas the PAHs listed in Table 1 are. BaP equivalents are considered mutagenic and therefore evaluated with age dependent adjustment factors in PHAST. It would be inappropriate to apply PEFs to naphthalene and then combine the results with the other PAH congeners in Table 1 for evaluations of BaP equivalents. Furthermore, there is abundant toxicological data to evaluate this congener on its own without estimating its relative potency to benzo(a)pyrene.

Because of this, naphthene should be evaluated separately, the same as any other chemical considered in the PHA process. Maximum detected concentrations should be compared with the cancer CV for naphthalene, and if appropriate, cancer risk should be calculated using the CSF for this congener. Cancer risk for naphthalene should then be added to cancer risk for the other identified contaminants of concern.

Health assessors should note that evidence for the carcinogenicity of naphthalene via the oral route is limited; they should therefore not include this PAH when evaluating the oral pathway. However, health assessors should include naphthalene when evaluating the inhalation pathway. As mentioned above, naphthalene should be evaluated separately, and not as part of the BaP equivalent, when doing so.

When evaluating non-cancer effects, health assessors should evaluate naphthalene separately with appropriate and available non-cancer CVs or health guidelines.

3.4 PAH Congeners without PEFs

As mentioned in Section 2.1, health assessors might find environmental data sets that include measurements for PAH congeners that do not have PEFs. Table 2 presents a summary of these PAH congeners, along with their IARC and EPA cancer classifications. Most of the congeners in Table 2 do not have PEFs because there is not sufficient evidence demonstrating their carcinogenicity. This includes PAH congeners classified as Group 3 by IARC or Group D by EPA (IARC 2021; EPA 2021). These PAHs are not included in BaP equivalent calculations. It would be inappropriate to consider them in cancer risk evaluations, and therefore, they are not discussed further.

Several of the PAH congeners shown in Table 2, however, have been identified as possible or probable carcinogens by IARC or EPA. This includes all PAH congeners classified as groups 2A or 2B by IARC and

groups B1, B2, or C by EPA (IARC 2021; EPA 2021). As with the other PAH congeners in Table 2, these PAHs are not included in BaP equivalent calculations. When working with measured data for these PAH congeners, health assessors should note that those are excluded from cancer risk evaluations based on BaP equivalents and acknowledge the potential limitations.

Health assessors should also note that none of the PAH congeners identified in Table 2 as being possibly or probably carcinogenic have oral CSFs or IURs in PHAST. As such, those PAH congeners would not be considered as individual congeners in a public health assessment.

Health assessors should consult the ATSDR ADS group if they have any questions on these points.

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Table 1. Potency equivalency factors (PEFs) for polycyclic aromatic hydrocarbons (PAHs)

CAS Number	PAH*	PEF†
50-32-8	Benzo(a)pyrene	1
56-55-3	Benzo(a)anthracene	0.1
205-99-2	Benzo(b)fluoranthen	0.1
205-82-3	Benzo(j)fluoranthene	0.1
207-08-9	Benzo(k)fluoranthene	0.1
218-01-9	Chrysene	0.01
224-42-0	Dibenz(a,j)acridine	0.1
226-36-8	Dibenz(a,h)acridine	0.1
194-59-2	7H-dibenzo(c,g)carbazole	1
192-65-4	Dibenzo(a,e)pyrene	1
189-64-0	Dibenzo(a,h)pyrene	10
189-55-9	Dibenzo(a,i)pyrene	10
191-30-0	Dibenzo(a,l)pyrene	10
193-39-5	Indeno(1,2,3-cd)pyrene	0.1
3697-24-3	5-methylchrysene	1
5522-43-0	1-nitropyrene	0.1
57835-92-4	4-nitropyrene	0.1
42397-64-8	1,6-dinitropyrene	10
42397-65-9	1,8-dinitropyrene	1
7496-02-8	6-nitrochrysene	10
607-57-8	2-nitrofluorene	0.01
53-70-3	Dibenzo(a,h)anthracen	2.4‡
57-97-6	7,12-dimethylbenz(a)anthracene	147‡,§
56-49-5	3-methylcholanthrene	13‡,§
602-87-9	5-nitroacenaphthene	0.08‡

*Naphthalene is not included in this table and should not be included in benzo(a)pyrene (BaP) equivalent calculations. See Section 3.3 for special considerations for naphthalene.

†PEFs are from the California Office of Environmental Health Hazard Assessment (OEHHA) (2015), with the exception of the PEFs for dibenzo(a,h)anthracene, 7,12-dimethyl(a)benzanthracene , 3-methylcholanthrene, 5-nitroacenaphthene, and naphthalene.

‡PEFs are based on the ratio of OEHHA's oral cancer slope factor (CSF) for BaP (i.e., 1.7 $[mg/kg/day]^{-1}$) and OEHHA's cancer potency factors for each PAH: 4.1 $(mg/kg/day)^{-1}$ for dibenzo(a,h)anthracene, 250 $(mg/kg/day)^{-1}$ for 7,12-dimethylbenz(a)anthracene, 22 $(mg/kg/day)^{-1}$ for 3-methylcholanthrene, and 0.13 $(mg/kg/day)^{-1}$ for 5-nitroacenaphthene. OEHHA's CSF for BaP is documented in OEHHA (2010) and the cancer potency factors are presented in OEHHA (2015).

§7,12-dimethyl(a)benzanthracene and 3-methylcholanthrene are not generally measured in environmental samples and are not included in U.S. Environmental Protection Agency's suite of 16 PAHs that are typically analyzed. If they are detected, health assessors should contact the agency that completed the sampling to determine why they were measured.

Table 2. Evidence for carcinogenicity for polycyclic aromatic hydrocarbons (PAHs) without potency equivalency factors (PEFs)

CAS number	PAH*	Current IARC group†	Current EPA group‡	Notes
8001-58-9	Creosotes	2A	—	Probably carcinogenic to humans, based on IARC
494-38-2	Acridine orange	3	—	Not classifiable
4657-93-6	5-Aminoacenaphthene	3	—	Not classifiable
117-79-3	2-Aminoanthraquinone	3	—	Not classifiable
191-26-4	Anthanthrene	3	—	Not classifiable
120-12-7	Anthracene	3	D	Not classifiable
83-32-9	Acenaphthene	3	D	Not classifiable
225-11-6	Benz[a]acridine	3	—	Not classifiable
225-51-4	Benz[c]acridine	3	—	Not classifiable
203-12-3	Benzo[g,h,i]fluoranthene	3	—	Not classifiable
191-24-2	Benzo[g,h,i]perylene	3	D	Not classifiable
195-19-7	Benzo[c]phenanthrene	2B	—	Possibly carcinogenic to humans, based on IARC
192-97-2	Benzo[e]pyrene	3	—	Not classifiable
86-74-8	Carbazole	2B	B2	Possibly carcinogenic to humans, based on IARC, and probable carcinogen, based on EPA
202-98-2	Cyclopenta[c,d]pyrene	2A	—	Probably carcinogenic to humans, based on IARC
215-58-7	Dibenz[a,c]anthracene	3	—	Not classifiable
224-41-9	Dibenz[a,j]anthracene	3	—	Not classifiable
5385-75-1	Dibenzo[a,e]fluoranthene	3	—	Not classifiable
192-47-2	Dibenzo[h,r,s,t]pentaphene	3	—	Not classifiable
105735-71-5	3,7-Dinitrofluoroanthene	2B	—	Possibly carcinogenic to humans, based on IARC
22506-53-2	3,9-Dinitrofluoroanthene	2B	—	Possibly carcinogenic to humans, based on IARC
75321-20-9	1,3-Dinitropyrene	2B	—	Possibly carcinogenic to humans, based on IARC
206-44-0	Fluoranthene	3	D	Not classifiable
86-73-7	Fluorene	3	D	Not classifiable
3351-28-8	1-Methylchrysene	3	—	Not classifiable
3351-32-4	2-Methylchrysene	3	—	Not classifiable
3351-31-3	3-Methylchrysene	3	—	Not classifiable
3351-30-2	4-Methylchrysene	3	—	Not classifiable
1705-85-7	6-Methylchrysene	3	—	Not classifiable
33543-31-6	2-Methylfluoranthene	3	—	Not classifiable

CAS number	PAH*	Current IARC group†	Current EPA group‡	Notes
832-69-9	1-Methylphenanthrene	3	—	Not classifiable
2243-62-1	1,5-Naphthalenediamine	3	—	Not classifiable
602-60-8	9-Nitroanthracene	3	—	Not classifiable
20268-51-3	7-Nitrobenz[a]anthracene	3	—	Not classifiable
63041-90-7	6-Nitrobenzo[a]pyrene	3	—	Not classifiable
892-21-7	3-Nitrofluoranthene	3	—	Not classifiable
86-57-7	1-Nitronaphthalene	3	—	Not classifiable
581-89-5	2-Nitronaphthalene	3	—	Not classifiable
20589-63-3	3-Nitroperylene	3	—	Not classifiable
789-07-1	2-Nitropyrene	3	—	Not classifiable
198-55-0	Perylene	3	—	Not classifiable
85-01-8	Phenanthrene	3	D	Not classifiable
135-88-6	N-phenyl-2-naphthylamine	3	—	Not classifiable
129-00-0	Pyrene	3	D	Not classifiable
217-59-4	Triphenylene	3	—	Not classifiable

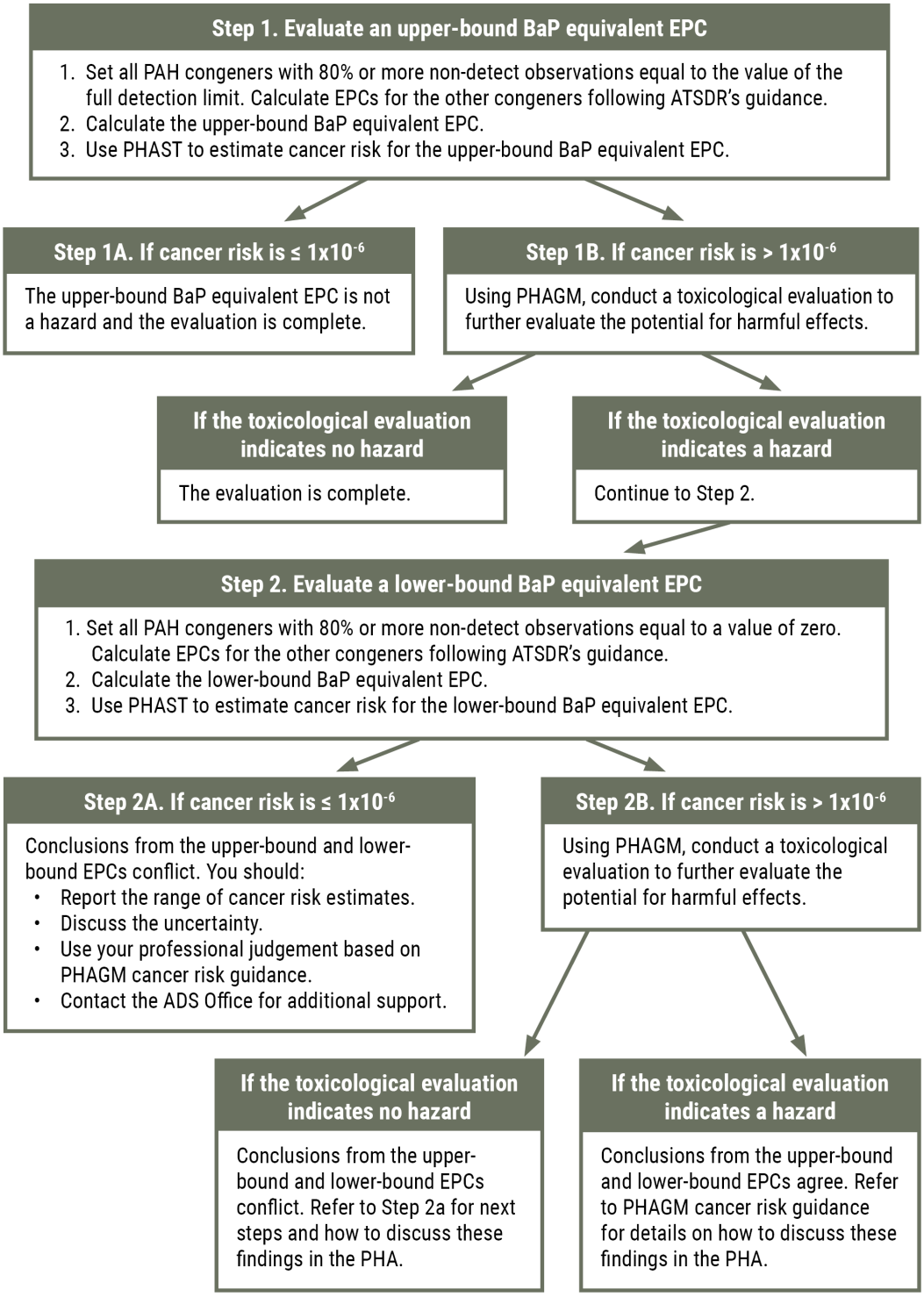
Abbreviations: CAS = Chemical Abstract Service; EPA = U.S. Environmental Protection Agency; IARC = International Agency for Research on Cancer.

* The PAH congeners listed here include those that do not have PEFs, as identified in Table 1.

† IARC classifications are current as of December 2021. Groupings represent the weight of evidence for carcinogenicity in humans and are assigned as follows: 1 = carcinogenic; 2A = probably carcinogenic; 2B = possibly carcinogenic; and 3 = not classifiable as to its carcinogenicity to humans (IARC 2021).

‡ EPA classifications are current as of December 2021. Groupings indicate the weight of evidence for carcinogenicity in humans and are assigned as follows: A = human carcinogen; B1 = probable carcinogen; limited human evidence; B2 = probable carcinogen, sufficient evidence in animals; C = possible human carcinogen; and D = not classifiable (EPA 2021).

Figure 1. Sensitivity analysis for polycyclic aromatic hydrocarbon (PAH) congener(s) with all non-detects



Abbreviations: ADS = ATSDR Associate Director for Science; BaP equivalent = benzo(a)pyrene equivalent; EPC = exposure point concentration; PAH = polycyclic aromatic hydrocarbon; PHA = public health assessment; PHAGM = Public Health Assessment Guidance Manual; PHAST = Public Health Assessment Site Tool.

Appendix A: Example Benzo(a)pyrene (BaP) Calculation

To illustrate the general benzo(a)pyrene equivalent (BaP equivalent) computational approach described in Section 3.0, imagine a community surrounding a large facility that historically pressure-treated wood products with a coal-tar solution and creosote oil. Twenty-five discrete surface soil samples were collected throughout the community and analyzed for seven polycyclic aromatic hydrocarbon (PAH) congeners: benzo(a)anthracene, benzo(b)fluoranthene, benzo(a)pyrene, benzo(k)fluoranthene, chrysene, dibenzo(a,h)anthracene, and indeno(1,2,3-cd)pyrene. PAHs were measured in most samples; however, several PAHs were reported as non-detects. For this example, assume that all non-detects have the same detection limit of 2 µg/kg and that the samples were collected from an area that represents a single exposure unit.

Step 1. Calculate the BaP equivalent for each sample and compare the maximum to the cancer comparison value (CV)

For initial screening and as described in Section 3.1, calculate a BaP equivalent for each environmental sample. Health assessors should do so by first multiplying each congener's concentration by its respective potency equivalency factor (PEF) to obtain congener-specific BaP equivalent concentrations (BECs). They then sum the BECs to obtain the sample BaP equivalent. The text box below shows these calculations for two samples, although in this example health assessors would perform this calculation for all 25 samples collected in the exposure unit.

PAH Congener	Sample 1 (µg/kg)	Sample 2 (µg/kg)	PEF (unitless)	Sample 1 BEC (µg/kg)	Sample 2 BEC (µg/kg)
Benzo(a)anthracene	40	88	0.1	4.0	8.8
Benzo(a)pyrene	60	147	1	60	147
Benzo(b)fluoranthene	129	210	0.1	12.9	21
Benzo(k)fluoranthene	101	199	0.1	10.1	19.9
Chrysene	43	88	0.01	0.43	0.88
Dibenzo(a,h)anthracene	20	69	2.4	48	166
Indeno(1,2,3-cd)pyrene	<2	66	0.1	0.2	6.6
BaP equivalent (µg-BaP/kg) =				**135.6**	**369.8**

In this example, imagine that the maximum BaP equivalent from across all 25 samples collected in the exposure unit is 369.8 µg-BaP/kg (the value shown in the table above for Sample 2). Because the maximum BaP equivalent for these samples exceeds the cancer CV for benzo(a)pyrene (65 µg/kg or 0.065 ppm), health assessors must calculate an exposure point concentration (EPC) to further evaluate cancer risk.

Step 2. Calculate a BaP equivalent EPC

Step 2A. Treat each PAH congener as an individual chemical and calculate an EPC for each measured PAH congener from the environmental samples collected within an exposure unit.

For this example, assume that detected observations were sufficient to calculate a 95% upper confidence limit (95UCL) for each of the seven congeners. Following the Agency for Toxic Substances and Disease Registry (ATSDR) Exposure Point Concentration Guidance for Discrete Sampling (ATSDR 2019a), health assessors should calculate 95UCLs and then complete a series

of quality control checks to ensure that the 95UCLs are appropriate for use. In this example, assume that the calculated 95UCL for benzo(b)fluoranthene was above the maximum concentration. Consistent with the ATSDR guidance (ATSDR 2019a), the maximum detected concentration would therefore be used as the EPC. The EPCs for six congeners are based on 95UCLs and the EPC for one is the maximum, as shown below.

PAH congener	EPC statistic	EPC value (µg/kg)
Benzo(a)anthracene	95UCL	170
Benzo(a)pyrene	95UCL	220
Benzo(b)fluoranthene	Maximum	420
Benzo(k)fluoranthene	95UCL	210
Chrysene	95UCL	220
Dibenzo(a,h)anthracene	95UCL	80
Indeno(1,2,3-cd)pyrene	95UCL	280

Step 2B. Apply California Office of Environmental Health Hazard Assessment (OEHHA) PEFs to each calculated EPC to obtain a BEC for each PAH congener.

Following equations 1 and 2, as shown in Section 2.2, each EPC is then multiplied by its respective PEF to calculate a congener-specific BEC. Calculations for this example are shown below.

PAH Congener	EPC value (µg/kg)	PEF (unitless)	BEC (µg/kg)
Benzo(a)anthracene	170	0.1	17
Benzo(a)pyrene	220	1	220
Benzo(b)fluoranthene	420	0.1	42
Benzo(k)fluoranthene	210	0.1	21
Chrysene	220	0.01	2.2
Dibenzo(a,h)anthracene	80	2.4	192
Indeno(1,2,3-cd)pyrene	280	0.1	28

Step 2C. Sum the BECs to determine the total BaP equivalent.

In this example, the BaP equivalent EPC is 522.2 µg-BaP/kg. Note that this value is presented in units of µg-BaP/kg, consistent with ATSDR's preferred approach for reporting BaP equivalents.

Step 3. Calculate cancer risk in ATSDR's Public Health Assessment Tool (PHAST) using the BaP equivalent EPC

The health assessor should first calculate a BaP equivalent dose from the BaP equivalent EPC estimated in Step 2 and then use that dose to estimate cancer risk for applicable exposure groups. To do so, ATSDR recommends that health assessors use the agency's PHAST. More specifically, health assessors should open the dose calculator in PHAST, select BaP in the Contaminant field, enter the BaP equivalent EPC in the Concentration field, select the correct units in the Unit field, and then select "other" in the Type field and note "BaP equivalent EPC." PHAST will then provide an estimate of cancer risk using OEHHA's cancer slope factor for BaP (i.e., 1.7 $[mg/kg/day]^{-1}$). Additional information on exposure parameters, dose calculations, and

risk calculations can be found in ATSDR's Public Health Assessment Guidance Manual and PHAST.

Note that non-cancer health effects should not be evaluated with BaP equivalent values. Instead, each PAH congener should be evaluated separately with available non-cancer CVs/health guidelines. Of the PAHs listed in Table 1, PHAST currently includes non-cancer CVs or health guidelines for benzo(a)pyrene. PHAST also includes non-cancer CVs for naphthalene (see Section 3.3).

Appendix B: Example Sensitivity Analysis

To illustrate the sensitivity analysis for handling polycyclic aromatic hydrocarbon (PAH) congeners with all non-detect observations, as described in Section 3.2.1, imagine a hypothetical community surrounding an industrial facility that historically manufactured coke and mineral fibers, and contained a biological treatment facility designed to treat wastewater generated at the facility. Fifteen discrete surface soil samples were collected throughout the community and analyzed for seven PAH congeners: benzo(a)anthracene, benzo(b)fluoranthene, benzo(a)pyrene, benzo(k)fluoranthene, chrysene, dibenzo(a,h)anthracene, and indeno(1,2,3-cd)pyrene. For this example, assume that all samples were collected from an area that represents a single exposure unit, and that the maximum benzo(a)pyrene equivalent (BaP equivalent) calculated for these samples exceeded the cancer comparison value (CV) for benzo(a)pyrene during the initial screening step described in Section 3.1. The health assessor therefore needs to calculate a BaP equivalent exposure point concentration (EPC), as described in Section 3.2.

To do so, the health assessor must first calculate appropriate EPCs for each congener following the Agency for Toxic Substances and Disease Registry (ATSDR) Exposure Point Concentration Guidance for Discrete Sampling (ATSDR 2019a). For this example, assume that there were sufficient detected observations to calculate a 95% upper confidence level (95UCL) as the EPC for six of the congeners. For one congener (i.e., dibenzo[a,h]anthracene), all samples were reported as non-detects, with a maximum detection limit of 3.0 µg/kg.

In order to evaluate a BaP equivalent EPC that includes dibenzo(a,h)anthracene, the health assessor must conduct a sensitivity analysis following the approach outlined in Section 3.2.1 and outlined in Figure 1. This involves first evaluating an upper bound BaP equivalent EPC and then, if necessary, evaluating a lower bound BaP equivalent EPC. Example calculations for an upper bound BaP equivalent EPC are provided below.

Calculating an upper-bound or "worst-case" BaP equivalent EPC

To calculate an upper-bound BaP equivalent EPC, the health assessor must set the EPC value for the PAH congener(s) with all non-detect observations equal to the value of the full detection limit. If there are multiple detection limits for a given PAH, health assessors should use the highest detection limit as a health-protective assumption.

In this example, EPCs are based on 95UCLs for six congeners and the maximum detection limit for one congener. Example data are provided in the table below. Note that the EPC value for dibenzo(a,h)anthracene is set to maximum detection limit.

PAH congener	EPC statistic	EPC value (µg/kg)
Benzo(a)anthracene	95UCL	50
Benzo(a)pyrene	95UCL	35
Benzo(b)fluoranthene	95UCL	55
Benzo(k)fluoranthene	95UCL	10
Chrysene	95UCL	70
Dibenzo(a,h)anthracene	Maximum detection limit	3.0
Indeno(1,2,3-cd)pyrene	95UCL	30

The health assessor should then apply the California Office of Environmental Health Hazard Assessment (OEHHA) potency equivalency factors (PEFs) to each congener-specific EPC. Following equations 1 and 2, as shown in Section 2.2, each EPC is then multiplied by its respective PEF to calculate a congener-specific BEC. BEC calculations for this example are shown in the table below.

PAH congener	EPC value (µg/kg)	PEF (unitless)	BEC (µg/kg)
Benzo(a)anthracene	50	0.1	5.0
Benzo(a)pyrene	35	1	35
Benzo(b)fluoranthene	55	0.1	5.5
Benzo(k)fluoranthene	10	0.1	1.0
Chrysene	70	0.01	0.7
Dibenzo(a,h)anthracene	3.0	2.4	7.2
Indeno(1,2,3-cd)pyrene	30	0.1	3.0

Finally, the health assessor should sum the benzo(a)pyrene equivalent concentrations (BECs) to determine the upper bound BaP equivalent EPC. In this example, the upper bound BaP equivalent EPC is equal to 57.4 µg-BaP/kg.

Evaluating an upper-bound or "worst-case" BaP equivalent EPC

After the health assessor has calculated the upper bound BaP equivalent EPC, they can use ATSDR's Public Health Assessment Site Tool (PHAST) to estimate cancer risk for all exposure groups. In this example, health assessors should open the dose calculator in PHAST, select benzo(a)pyrene in the Contaminant field, enter the upper bound BaP equivalent EPC value in the Concentration field (i.e., 57.4), select the correct units in the Unit field (i.e., µg/kg), and then select "other" in the Type field and note "BaP equivalent EPC." PHAST will then provide an estimate of cancer risk using OEHHA's cancer slope factor for benzo(a)pyrene (i.e., 1.7 $[mg/kg/day]^{-1}$).

If cancer risk is estimated at a value less than or equal to $1x10^{-6}$ with the upper-bound BaP equivalent EPC, the evaluation is complete. The health assessor does not need to complete any other steps as part of the sensitivity analysis. They should refer to the ATSDR Public Health Assessment Guidance Manual (PHAGM) for how to discuss this result in the PHA.

If cancer risk is estimated at a value greater than $1x10^{-6}$, the health assessor should use PHAGM guidance to conduct a toxicological evaluation to further evaluate for harmful effects. If no hazard is identified, the evaluation is complete. If a hazard is identified, the health assessor should continue the sensitivity analysis by evaluating a lower-bound BaP equivalent EPC. For this, they should refer to the instructions outlined in Figure 1 and described in Section 3.2.1.

Figure 1. Sensitivity analysis for polycyclic aromatic hydrocarbon (PAH) congener(s) with all non-detects

This image is a flowchart showing the steps for sensitivity analysis for polycyclic aromatic hydrocarbon (PAH) congener(s) with all non-detects. The first box is titled "Step 1. Evaluate an upper-bound BaP equivalent EPC" and has three steps, "1. Set all PAH congeners with 80% of more non-detect observations equal to the value of the full detection limit. Calculate EPCs for the other congeners following ATSDR's guidance. 2. Calculate the upper-bound BaP equivalent EPC. 3. Use PHAST to estimate cancer risk for the upper-bound BaP equivalent EPC."

From this box, there are two arrows pointing to two other boxes. One box says, "Step 1A. If cancer risk is less than or equal to $1x10^{-6}$: The upper-bound BaP equivalent EPC is not a hazard and the evaluation is complete". The second box says, "Step 1B. If cancer risk is greater than $1x10^{-6}$: Using PHAGM, conduct a toxicological evaluation to further evaluate the potential for harmful effects." This Step 1B box has two arrows pointing to two more boxes. The first box says, "If the toxicological evaluation indicates no hazard, the evaluation is complete." The second box says, "If the toxicological evaluation indicates a hazard, continue to step 2." This box has an arrow that points to a box titled, "Step 2: Evaluate a lower-bound BaP equivalent EPC". This box has three steps, "1. Set all PAH congeners with 80% or more non-detect observations equal to a value of zero. Calculate EPCs for the other congeners following ATSDR's guidance. 2. Calculate the lower-bound BaP equivalent EPC. 3. Use PHAST to estimate cancer risk for the lower-bound BaP equivalent EPC. 3. Use PHAST to estimate cancer risk for the lower-bound BaP equivalent EPC." This box has two arrows pointing to two more boxes. The first box is titled, "Step 2A. If cancer risk is less than or equal to $1x10^{-6}$" and says, "Conclusions from the upper-bound and lower-bound EPC's conflict. You should: Report the range of cancer risk estimates. Discuss the uncertainty. Use your professional judgement based on PHAGM cancer risk guidance. Contact the ADS Office for additional support." The other box is titled, "Step 2B: If cancer risk is > $1x10^{-6}$" and the box says, "Using PHAGM, conduct a toxicological evaluation to further evaluate the potential for harmful effects." There are two arrows pointing from this box to two final boxes. The first box says, "If the toxicological evaluation indicates no hazard: Conclusions from the upper-bound and lower-bound EPCs conflict. Refer to Step 2a for next steps and how to discuss these findings in PHA." The second box says, "If the toxicological evaluation indicates a hazard: Conclusions from the upper-bound and lower-bound EPCs agree. Refer to PHAGM cancer risk guidance for details on how to discuss these findings in the PHA."