

# Benzo[a]pyrene and other polycyclic aromatic hydrocarbons

## Definition of Polycyclic Aromatic Hydrocarbons (PAH)

Polycyclic aromatic hydrocarbons (PAH) are ubiquitous environmental contaminants that are formed by the incomplete combustion of organic materials, such as wood or fossil fuels. PAH molecules are made up of three or more benzene rings, at least two of which are fused with two neighbouring rings sharing two adjacent carbon atoms. In addition to PAH that are composed of carbon and hydrogen atoms only, some PAH contain heteroatoms such as nitrogen and sulphur. PAH form a large and heterogeneous group, but the most toxic members of this family known to-date are PAH molecules that have four to seven rings. In this report, the discussion therefore focuses on the properties of this four- to seven-ring subset of the PAH family of compounds. Table 1 lists some of the most known PAH molecules.

Benzo[a]pyrene (B[a]P) is the most studied of the PAH family of compounds. It is a relatively large unsubstituted five-ring compound. Because of its relatively high environmental levels and high level of toxicity resulting in larger health impact than any other PAH identified in the environment, B[a]P is often selected as a surrogate for other PAH compounds.

### 1. Physico-chemical Properties

The physico-chemical properties of PAH have been reviewed in detail elsewhere (MOE, 1997; ATSDR, 1995). Only a brief summary will be provided here.

The physical and chemical property of PAH is governed by the size (number of carbon atoms) and shape (ring linkage pattern) of the individual molecule. All completely unsaturated PAH are solid at room temperature and have relatively high melting and boiling points.

PAH are soluble in lipid (fat), and are essentially insoluble in aqueous systems. The aqueous solubility decreases with increasing molecular size. Vapour pressure for PAH are low and decrease with increasing molecular size.

A summary of some relevant physico-chemical properties for a number of selected PAH is provided in Table 2.

### 2. Environmental Fate

The environmental fate of PAH has been reviewed in detail elsewhere (MOE, 1997; ATSDR, 1995; CEPA, 1994). Only a brief summary will be provided here.

Table 1. Chemical Identity of Some Polycyclic Aromatic Hydrocarbons (Adapted from ATSDR, 1995)

Characteristic	Acenaphthene	Acenaphthylene	Anthracene
Synonym(s)	1,2-Dihydroacenaphthylene; 1,8-dihydroacenaphthalene; 1,8-ethylenenaphthalene; 1,2-dihydroacenaphthylene	Cyclopenta[d,e]naphthalene; paranaphthalene	Anthracin; green oil;
Chemical	C <sub>12</sub> H <sub>10</sub>	C <sub>12</sub> H <sub>18</sub>	C <sub>14</sub> H <sub>10</sub>
CAS registry	83-29-9	208-96-8	120-12-7b

Characteristic	Benzo[a]anthracene	Benzo[a]pyrene	Benzo[b]fluoranthene
Synonym(s)	BA;benz[a]anthracene;1,2-benzanthracene; benzo[b]phenanthrene;2,3-phenanthrene;2,3-benzophenanthrene; tetraphene,benzo[e]fluoranthene; B[b]F	Benzo[d,e,f]chrysene; 3-4 benzopyrene, 3,4-benzpyrene; benz[a]pyrene;BP;B[a]P ;	3,4-Benz[e]acephenanthrylene; 2,3-benzfluoranthene;3,4-benzfluoranthene;2,3-benzofluoranthene;3,4-benzofluoranthene; benzo[e]fluoranthene; B[b]F
Chemical formula	C <sub>18</sub> H <sub>12</sub>	C <sub>20</sub> H <sub>12</sub>	C <sub>20</sub> H <sub>12</sub>
CAS Registry	56-55-3	50-32-8	205-99-2b

Characteristic	Benzo[e]pyrene	Benzo[k]fluoranthene	Benzo[g,h,i]perylene
Synonym(s)	1,2-Benzopyrene;1,2-benzpyrene; 4,5benzopyrene;4,5-benzpyrene;B[e]P	8,9-benzfluoranthene;8,9-benzofluoranthene;11,12-benzofluoranthene;2,3,1,8-binaphthylene; dibenzo[b,j,k]fluorine	1,12-Benzoperylene
Chemical formula	C <sub>20</sub> H <sub>12</sub>	C <sub>20</sub> H <sub>12</sub>	C <sub>20</sub> H <sub>12</sub>
CAS registry	192-97-2	207-08-9	191-24-2

Characteristic	Benzo[j]fluoranthene	Chrysene	Dibenz[a,h]anthracene
Synonym(s)	10.11Benzofluoranthene ; benzo-12.13 fluoranthene; dibenzo[a,j,k]-fluorene;7.8-benzofluoranthene; B[j]F	1.2-Benzophenanthrene;benzo[a]-phenanthrene;1,2benzphenanthrene; benz[a]phenanthrene; 1,2,5,6-dibenzonaphthalene	Dibenz[a,h]anthracene; DB[a,h]A; DB[a,h]A; DBA;1,2:5,6 dibenz[a]anthracene
Chemical formula	C <sub>20</sub> H <sub>12</sub>	C <sub>18</sub> H <sub>12</sub>	C <sub>22</sub> H <sub>14</sub>
CAS registry	205-82-3	218-01-9	53-70-3

Characteristics	Fluoranthene	Fluorene	Indeno[1,2,3-c,d]pyrene
Synonym(s)	1.2-[1,8-Naphthylene]-benzene;1.2-benzacena-phthene;1.2-[1.8-naphthalenediyl]benzene; benzo[j,k]fluorene	ortho-Biphenylene methane; diphenylenemethane;2,2-methylene biphenyl; 2.3-benzidene	Indenopyrene;IP;ortho-phenylene pyrene;1,10-ortho-phenylene]pyrene; 1,10-[1,2-phenylene]pyrene; 2,3-ortho-phenylene pyrene
Chemical formula	C <sub>16</sub> H <sub>10</sub>	C <sub>13</sub> H <sub>10</sub>	C <sub>22</sub> H <sub>12</sub>
CAS registry	206-44-0	86-73-7	193-39-5

Characteristic	Phenanthrene	Pyrene
Synonym(s)	Phenanthrene; Phenantrin	Benzo[d,e,f]phenanthrene; 8-pyrene
Chemical formula	C <sub>14</sub> H <sub>10</sub>	C <sub>16</sub> H <sub>10</sub>
CAS registry	85-01-8	129-00-00

Table 2. Physical and chemical properties of individual PAH (Adapted from ATSDR, 1995)

Property	Acenaphthene	Acenaphthylene	Anthracene
Molecular weight	154.21	152.20	178.2
Color	White	No data	Colourless with violet fluorescence when pure; yellow with green fluorescence when impure

Property	Acenaphthene	Acenaphthylene	Anthracene
Physical state	Solid (needles)	Solid (prisms/plates)	Solid (tablet or prism)
Melting point	95 °C	92-93 °C	218 °C
Boiling point	96.2 °C	265-275 °C	342 °C, 340 °C
Density at 20 °C	1.225g/cm <sup>3</sup>	No data	No data
Specific gravity	1.0242 at 90 °C/4 °C	0.8988 at 16 °C/ 2 °C	1.25 at 27 °C/4 °C; 1.283 at 25 °C/4 °C
Odour	No data	No data	Weak aromatic odour
Odour threshold: Water Air	0.08 ppm 0.08 ppm	No data No data	No data No data
Solubility: Water Soluble in	1.93 mg/L Alcohol, methanol, propanol, chloroform, benzene, toluene, glacial acetic acid	3.93 mg/L Alcohol, ether, benzene	0.076 mg/L Acetone; benzene, carbon disulphide, carbon tetrachloride, chloroform, ether, ethanol, mthanol, toluene
Partition coefficients: Log K <sub>ow</sub> Log K <sub>oc</sub>	3.98 3.66	4.07 1.40	4.45 4.15
Vapour pressure	4.47x10 <sup>-3</sup> mm Hg	0.029 mm Hg at 20 °C	1 mm Hg at 145 °C; 1.7x10 <sup>-5</sup> mm Hg at 25 °C
Henry's law constant	7.91x10 <sup>-5</sup> atm-m <sup>3</sup> /mol	1.45x10 <sup>-3</sup> atm-m <sup>3</sup> /mol	1.77x10 <sup>-5</sup> atm-m <sup>3</sup> /mol
Autoignition temperature	No data	No data	540 °C
Flashpoint	No data	No data	121 °C (closed cup)
Flammability limits	Dust is moderately flammable	No data	No data
Explosive limits	No data	No data	Lower, 0.6% by volume

Property	Benzo[a]anthracene	Benzo[a]pyrene	Benzo[b]fluoranthene
Molecular weight	228.29	252.3	252.3
Color	Yellow-blue fluorescence	Pale yellow	Colourless
Physical state	Solid (plates or needles)	Solid (plates or recrystall. From benzene/ligroin)	Solid (needles)
Melting point	158-159 °C; 162 °C	179-179.3 °C	168.3 °C
Boiling point	400 °C; 435 °C sublimes	310-312 °C at 10 mm Hg; 495 °C	No data

Property	Benzo[a]anthracene	Benzo[a]pyrene	Benzo[b]fluoranthene
Density	1.274 g/cm <sup>3</sup> at 20 °C	1.351 g/cm <sup>3</sup>	No data
Odour	No data	Faint aromatic odour	No data
Solubility Water	0.010 mg/L	2.3x10 <sup>-3</sup> mg/L	0.0012 mg/L
Organic solvents	Slightly soluble in acetic acid and hot ethanol; soluble in acetone and diethyl ether; very soluble in benzene	Sparingly soluble in ethanol and methanol; soluble in benzene, toluene, xylene, and ether	Slightly soluble in benzene, acetone
Partition coefficients: Log K <sub>ow</sub> Log K <sub>oc</sub>	5.61 5.30	6.06 6.74	6.04 5.74
Vapour pressure	2.2x10 <sup>-8</sup> mm Hg at 20 °C	5.6x10 <sup>-9</sup> mm Hg	5.0x10 <sup>-7</sup> mm Hg at 20-25 °C
Henry's law constant:	1x10 <sup>-6</sup> atm-m <sup>3</sup> /mol	4.9x10 <sup>-7</sup> atm-m <sup>3</sup> /mol	1.22x10 <sup>-5</sup> atm-m <sup>3</sup> /mol

Property	Benzo[e]pyrene	Benzo[k]fluoranthene	Benzo[g,h,i]perylene
Molecular weight	252.30	252.3	276.34
Color	Colourless	Pale yellow	Pale yellow-green
Physical state	Prisms or plates (recrystallized From benzene)	Solid (needles)	Solid (plate)
Melting point	178-179 °C	215.7 °C	273 °C
Boiling point	310-312 °C at 10 mm Hg	480 °C	550 °C
Solubility: Water Organic solvents	6.3x10 <sup>-3</sup> mg/L at 25 °C Acetone	7.6x10 <sup>-4</sup> mg/L at 25 °C Soluble in benzene, acetic acid, ethanol	2.6x10 <sup>-4</sup> mg/L at 25 °C Soluble in benzene, dichloromethane, acetone
Partition coefficients: Log K <sub>ow</sub> Log K <sub>oc</sub>	No data No data	6.06 5.74	6.50 6.20
Vapour pressure	5.7x10 <sup>-9</sup> mm Hg at 25 °C	9.59x10 <sup>-11</sup> mm Hg	1.03x10 <sup>-10</sup> mm Hg at 25 °C
Henry's law constant:	No data	3.87x10 <sup>-5</sup> atm-m <sup>3</sup> /mol	1.44x10 <sup>-7</sup> atm-m <sup>3</sup> /mol

Property	Benzo[j]fluoranthene	Chrysene	Dibenz[a,h]anthracene
Molecular weight	252.32	228.3	278.35
Color	Yellow or orange	Colourless with blue or red-blue fluorescence	Colourless

Property	Benzo[ <i>j</i> ]fluoranthene	Chrysene	Dibenz[ <i>a,h</i> ]anthracene
Physical state	Plates (recrystallized from ethanol) or needles (recrystallized from acetic acid)	Solid (plates)	Solid (plates or leaflets)
Melting point	166 °C	255-256 °C	262 °C
Boiling point	No data	448 °C	No data
Density	No data	No data	1.282 g/cm <sup>3</sup>
Specific gravity	No data	1.274 at 20 °C/4 °C	No data
Solubility: Water Organic solvent(s)	6.76x10 <sup>3</sup> mg/L at 25 °C Slightly soluble in alcohol and acetic acid; soluble in hydrogen sulphide on heating	2.8x10 <sup>3</sup> mg/L Slightly soluble in acetone; carbon disulphide, diethyl ether, ethanol, glacial acetic acid, toluene hot xylene; soluble in benzene	5x10 <sup>4</sup> mg/L Slightly soluble in ethyl alcohol soluble in acetone, acetic acid, benzene, toluene and xylene
Partition coefficients Log K <sub>ow</sub> Log K <sub>oc</sub>	6.12 4.7-4.8	5.16 5.30	6.84 6.52
Vapour pressure	1.50x10 <sup>-8</sup> mm Hg at 25 °C	6.3x10 <sup>-7</sup> mm Hg at 25 °C	1x10 <sup>-10</sup> mm Hg at 20 °C
Henry's law constant	1x10 <sup>-6</sup> atm-m <sup>3</sup> /mol	1.05x10 <sup>-6</sup> atm-m <sup>3</sup> /mol	7.3x10 <sup>-8</sup> atm-m <sup>3</sup> /mol

Property	Fluoranthene	Fluorene	Indeno[1,2,3- <i>c,d</i> ]pyrene
Molecular weight	202.26	166.2	276.3
Color	Pale yellow	White	Yellow plates or needles showing a greenish-yellow fluorescence
Physical state	Solid (needles or plates)	Solid (leaflets or flakes; crystalline plates)	Solid (plates or needles)
Melting point	11 °C	116-117 °C	163.6 °C
Boiling point	~375 °C	295 °C	530 °C
Specific gravity	1.252 at 0 °C/4 °C	1.203 at 0 °C/4 °C	No data
Solubility: Water Organic solvents	0.20-0.26 mg/L Soluble in alcohol, ether, benzene, acetic acid	1.68-1.98 mg/L Soluble in acetic acid, acetone, benzene, carbon disulphide, carbon tetrachloride, diethyl ether,	0.062 mg/L Soluble in organic solvents

Property	Fluoranthene	Fluorene	Indeno[1,2,3-c,d]pyrene
		ethanol, pyrimidine, solution, toluene	
Partition coefficients: Log $K_{ow}$ Log $K_{oc}$	4.90 4.58	4.18 3.86	6.58 6.20
Vapour pressure	$5.0 \times 10^{-6}$ mm Hg at 25 °C	$3.2 \times 10^{-4}$ mm Hg at 20 °C	$\sim 10^{-11}$ - $10^{-6}$ mm Hg at 20 °C
Henry's law constant	$6.5 \times 10^{-6}$ atm-m <sup>3</sup> /mol	$1.0 \times 10^{-4}$ atm-m <sup>3</sup> /mol	$6.95 \times 10^{-8}$ atm-m <sup>3</sup> /mol

Property	Phenanthrene	Pyrene
Molecular weight	178.2	202.3b
Color	Colourless	Colourless, pale yellow plates (recrystallized from toluene) or Slight blue fluorescence (recrystallized from ethanol or sublimation)
Physical state	Solid (plates, crystals or leaflets)	Solid (plates or tablets)
Melting point	100 °C	156 °C
Boiling point	340 °C	393 °C; 404 °C
Density	0.980 g/cm <sup>3</sup> at 4 °C	1.271 g/cm <sup>3</sup> at 23 °C
Specific gravity	No data	1.271 at 23 °C/4 °C
Odour	Faint aromatic odour	No data
Solubility: Water at 25 °C Organic solvents	1.20 mg/L Soluble in glacial acetic acid, benzene, carbon tetrachloride, carbon disulphide, anhydrous diethyl ether, toluene, ethanol	0.077 mg/L Soluble in benzene, carbon disulphide, diethyl ether, alcohol, petroleum ether, toluene
Partition coefficients: Log $K_{ow}$ Log $K_{oc}$	4.45 4.15	4.88 4.58
Vapour pressure	$6.8 \times 10^{-4}$ mm Hg 25 °C	$2.5 \times 10^{-6}$ mm Hg at 25 °C
Henry's law constant	$2.56 \times 10^{-5}$ atm-m <sup>3</sup> /mol	$1.14 \times 10^{-5}$ atm-m <sup>3</sup> /mol

PAH are generally insoluble in water but can be readily solubilized in organic solvents or organic acids. This means that in aqueous environments, PAH are generally found adsorbed on particulates and on humic matter, or solubilized in any oily matter which may contaminate water, sediments and soil. The solubility of PAH in water is inversely proportional to the number of rings it contains. As a result, larger

molecular weight PAH ( $\leq 4$  rings) are almost exclusively bound to particulate matter, while lower molecular weight PAH (3 rings) can also be found dissolved in water.

Since PAH tend to have low vapour pressures, they are usually adsorbed on to particulate matter in the atmosphere. The vapour pressure of PAH is inversely proportional to the number of rings it contains. As a result, the larger molecular weight PAH ( $\leq 4$  rings) are mostly adsorbed onto particulate matter in atmospheric samples, while the lower molecular weight PAH can be found both free in the atmosphere and bound to particulates.

In the atmosphere and in the presence of sunlight, PAH undergo photo oxidation (oxidation catalysed by sunlight). Photo oxidation occurs much faster for particle-free PAH than for particle bound compounds. For example about half of benzo[a]pyrene (B[a]P) will be oxidised in a matter of hours to days. PAH in the air can also be oxidised by ozone, reactive compounds adsorbed on particles, NO<sub>x</sub> and SO<sub>x</sub>.

### **3. Toxicokinetics**

The toxicokinetics of PAH have been reviewed in detail elsewhere by MOE (1997), ATSDR (1995) and CEPA (1994). Only a brief summary will be provided here.

Exposure in humans to PAH is primarily through ingestion and inhalation. Under normal circumstances, dermal contact with PAH is relatively unimportant. Similar to other oil-soluble compounds, PAH are generally well absorbed in the body, but are stored in the body only briefly, primarily in the kidney, liver and spleen. Most of the absorbed dose is then excreted into bile and eventually faeces and to a much lesser extent urine. Most of the PAH are excreted in a metabolised form and only very small amounts of the parent compound find its way into faeces and urine. PAH are highly soluble in fats. In this form they can rapidly enter cells and become virtually unavailable for excretion. Metabolic processes tend to make PAH more water soluble, which facilitates excretion.

A number of metabolic processes compete to produce a variety of different metabolites. Phase I reactions add one or more hydroxyl groups to the parent core and phase II reactions attach highly water-soluble groups to the PAH molecule. Phase I reactions are controlled by enzymes epoxide hydrolase and a subset of cytochrome P-450 mixed-function oxidases called aryl hydrocarbon hydroxylase (AHH). The structures of PAH vary greatly, but the metabolism of these compounds is similar and leads to the formation of homologous metabolites.

Variations in tumorigenicity of these compounds are due to the differences in the location of the metabolic modifications and the activities of the intermediate metabolites formed. Some of the metabolites formed are diol epoxides. A number of these diol epoxides are in turn converted into carbonium ions. The carbonium ions can react with DNA and proteins to form adducts, and induce genotoxic damage. It is these alkylating agents that are thought to be the primary carcinogens, acting as initiators. Initiation is the first step in the development of cancer.

The enzymes required for the conversion of parent PAH compounds into the reactive diol epoxides are found mainly in the liver, but also in the lungs, skin basal cell layer, intestinal mucosa and other tissues.

#### **4. Health Effects**

The health effects of PAH have been reviewed in detail elsewhere (MOE, 1997; ATSDR, 1995; CEPA, 1994; WHO, 1996). Only a brief summary will be provided here.

PAH have been shown to induce a number of toxic effects. Some of them, however, are unlikely to be a cause for concern at environmental levels. Several PAH have been shown to cause death in rodents, for example, after short-term exposure to high doses. On the other hand, no deaths have been reported from short-term occupational exposures to PAH. Since environmental levels are generally much lower than some of the occupational ones, it is extremely unlikely that short-term exposure to PAH in the environment would lead to death. On the other hand, eye irritation, photophobia and skin toxicity such as dermatitis and keratosis, have been demonstrated to be caused by occupational exposures to PAH. Extreme environmental conditions (e.g. heavy exposure to a forest fire smoke) may also trigger the above effects.

Adverse respiratory effects, including acute and subacute inflammation, and fibrosis, have been demonstrated experimentally. With B[a]P, severe and long-lasting hyperplasia and metaplasia were observed as precancerous lesions and are consistent with the general assertion that one of the main targets of PAH toxicity is the respiratory tract. Available data are insufficient to assess the effects of PAH at environmentally relevant concentrations.

Carcinogenic PAH, but not the noncarcinogenic ones, have been reported to suppress immune reaction in rodents. A number of authors have reported immunosuppressive effects in a dose-range similar to that at which carcinogenicity has been observed. Furthermore, there appears to be a rough correlation between the potency of PAH as immunosuppressors and as carcinogens. Immunosuppression may therefore be an important toxic endpoint of PAH. Some authors also suggest that immunosuppression may be involved in the mechanisms by which PAH induce cancer. At present, however, the data on immunosuppression are not sufficient for quantitative dose response assessment.

Exposure to PAH can have a number of adverse effects on both female and male reproductive systems and on fetal development. The largest amount of data is available for rodent fetal development, where reported effects include malformations, stillbirths, resorptions, immunosuppression, clastogenicity, and tumorigenicity. The doses required to produce the developmental effects are generally similar or somewhat higher than those required to elicit a carcinogenic response. Although no human data are available, reproductive and developmental effect may be important in humans. Unfortunately, there are insufficient data to assess these effects quantitatively.

Genotoxic effects for some PAH have been repeatedly demonstrated both in *in vivo* tests in rodents and *in vitro* tests using mammalian (including human) cell lines, as well as in prokaryotes. On the other hand, some PAH appear not to be genotoxic. Most of the genotoxic unsubstituted PAH are not genotoxic themselves, but need to be metabolised first by the AHH system. The diol epoxides that are formed then react with DNA to form DNA adducts, thus inducing genotoxic damage. A genotoxic event is postulated as a required step in the carcinogenicity process and may play a role in some forms of developmental toxicity.

The tumorigenicity and carcinogenicity of individual PAH and PAH-containing mixtures have been widely studied in experimental animals. Only a limited amount of data on carcinogenicity of PAH-containing mixtures in humans is available, while virtually none is found for carcinogenicity of individual PAH in humans. Some individual PAH compounds are found to be carcinogenic in experimental animals, while others have been found to be non-carcinogenic. The evidence that certain PAH-containing complex mixtures are carcinogenic both to humans and experimental animals is strong and convincing. Based on the available evidence, both the International Agency for Research on Cancer (IARC, 1987) and USEPA (1994) classified a number of PAH as carcinogenic to animals and some PAH-rich mixtures as carcinogenic to humans. For example, B[a]P is classified as a probable human carcinogen (Group B2) by USEPA (1994) and as probably carcinogenic to humans (Group 2A) by IARC (1987). Evidence for other PAH varies. Some are ranked the same as B[a]P, while others have lower ranking. For the rest of the PAH, there are insufficient data to determine whether the compounds are carcinogenic or not.

Effects such as skin, eye and respiratory mucosa irritation are more likely to be observed with high occupational exposures rather than with the characteristically lower environmental exposures. There may be exceptions to this conclusion. Exposure to heavily contaminated soils or sediments, for example, may trigger these effects. However, these effects have not been studied well enough to provide adequate data to allow a quantitative assessment to be conducted. PAH-induced immunotoxicity and developmental toxicity may be important toxic endpoints. Unlike carcinogenicity, there is a paucity of human data for immunotoxicity and developmental toxicity. Furthermore, animal data in support of the carcinogenicity endpoint are far more extensive than for immunotoxicity and developmental toxicity. It is not clear whether or not there is a threshold for PAH immunotoxicity and developmental toxicity. It is plausible that at environmentally relevant (low) levels, PAH do not exhibit appreciable immunotoxicity and developmental toxicity. Since it is believed that there is no threshold for the tumour-initiating effects of PAH, there is a finite risk from exposure to PAH even at low doses. For these reasons, carcinogenicity is the endpoint generally considered for dose response assessment.

## **5. Potency Estimates for PAH in Humans**

Overall, there are two primary approaches to risk assessment of PAH fractions. The first method is called Individual PAH method (IPM) or toxic equivalency factor (TEF). This approach first estimates the potency of B[a]P and then express the environmental levels of other PAH as "*B[a]P equivalents*". In order to estimate the potency of a PAH fraction of a mixture, the total number of B[a]P equivalents of the mixture is multiplied by the potency for B[a]P. The result is numerically equivalent to summing up risks attributable to individual PAH in the mixture.

An alternative approach (Whole Mixture Model or WMM) estimates the potency of a PAH fraction of the mixture as a whole. The model assumes that the potency of the PAH fraction of a mixture is proportional to the B[a]P content of the mixture. The potency of the fraction is given by the product of the B[a]P content of the mixture and the typical potency of the PAH fraction of the mixture. B[a]P serves as a surrogate for all other PAH present in the mixture and assumes the potency of the entire PAH fraction. The B[a]P surrogate that has the potency of the PAH fraction is named (B[a]PS).

The two approaches differ significantly from each other in the data used for the assessment, in the assumptions used and in the process of estimating assumptions. The distinction between the two approaches is therefore important.

#### Assessments based on IPM (TEF) Approach

This approach requires establishment of:

- potency for B[a]P
- potency relative to B[a]P for other PAH.

The cancer potencies established by different regulatory agencies for B[a]P via inhalation exposure are listed in Table 3. Inhalation potencies recommended for use by MOE (1997), by California Environmental Protection Agency (Cal EPA, 1993) as well as the withdrawn US EPA value are similar. On the other hand, Health Canada's (CEPA, 1994) potency estimate is substantially lower, even though Health Canada has used a similar methodology as US EPA and Cal EPA to derive the potency.

The US EPA and MOE cancer potency estimates for the oral route of exposure for B[a]P are quite different (see Table 4), primarily due to the use of different methods in their derivation. USEPA estimated the potency in humans by extrapolating from animal ingestion data. In contrast, MOE extrapolated the oral potency from inhalation potency, which was derived based on good quality human data. Extrapolation to the oral route was based on the relative sensitivity of animals to the carcinogenic effect of PAH delivered via the oral versus the inhalation routes in several rodent species. The MOE estimate is therefore associated with lower uncertainty.

To date, only MOE (1997) has published cancer potency for B[a]P via the dermal route of exposure. The basis for its derivation is presented in Table 5.

Relative potencies of individual PAH listed in Table 6 seem fairly consistent from agency to agency. In practice, the combination of B[a]P potency and its relatively high content in PAH-rich mixtures (MOE, 1997) means that this compound contributes more than 60% of the overall potency of a mixture based on the IPM approach. Benzofluoranthenes (b+j+k), on the other hand, contribute about an additional 10%. As a result, any differences in the potencies of the rest of the compounds do not affect the outcome significantly.

Table 3. Inhalation potencies (unit risks) for B[a]P

Lifetime risk (ng B[a]P/m <sup>3</sup> ) <sup>-1</sup>	Derivation Method	Reference
1.5 E-6	Assumed that the relative potency of coke oven emissions derived from human studies and an animal test is the same as the relative potency of B[a]P in humans and in animal studies. The potency of coke oven emissions was derived from US EPA's estimate (US EPA, 1994) which was expressed in terms of risk per unit airborne concentration of benzene soluble fraction of mixture. MOE converted the US EPA estimate into an expression of cancer risk per ng B[a]P/m <sup>3</sup> , assuming 1.7 ng B[a]P in 1 µg of benzene soluble fraction. Animal data were derived from Nesnow <i>et al.</i> (1992). Maximum Likelihood Estimate (MLE). The Upper Confidence Limit (UCL) is about an order of magnitude higher (2.4 E-5/ng B[a]P/m <sup>3</sup> ).	MOE, 1997
1.1 E-6	Based on surface area extrapolation (surface area estimated as (body weight) <sup>2/3</sup> ) using hamster data of Thyssen <i>et al.</i> (1981) via inhalation of B[a]P. Low dose extrapolation by Linearized Multistage Model. A UCL value.	Cal EPA, 1993
1.8 E-6	Based on the assumption of equal risk to hamsters and humans at equal airborne B[a]P levels. Thyssen's B[a]P data (1981) in hamsters by inhalation exposure were used as the starting point. Low dose extrapolation by Linearized Multistage Model. Upper confidence limit.	USEPA, 1984b; has been withdrawn from IRIS
3.2 E-8	Thyssen's (1981) B[a]P data in hamsters via inhalation exposure were used as the starting point. No details were provided on how extrapolation from hamsters to humans was conducted. Potency was originally reported as TD <sub>0.05</sub> , which was converted into a slope factor.	CEPA, 1994

Table 4. Potency of B[a]P by the oral route as established by different regulatory agencies.

<b>Lifetime risk (ng B[a]P/day)<sup>-1</sup></b>	<b>Derivation Method</b>	<b>References</b>
2.6 E-9	Maximum likelihood estimate (MLE). Potency based on UCL would be about 4.2 E-8. Derived from inhalation potency in humans (see table 3) by applying a factor (0.003) equal to the relative potency of B[a]P by oral versus inhalation exposure as established from rodent data.	MOE, 1997
1.0 E-7	Recommended by USEPA. Provisional guidance based on available estimates from Thorslund & Farrar (1990), Schoeny <i>et al.</i> , (1991); Schoeny & Poirier (1993).	USEPA, 1993

Table 5. Potency of B[a]P by dermal route

<b>Lifetime risk (ng B[a]P/day)<sup>-1</sup></b>	<b>Derivation Method</b>	<b>References</b>
1.2 E-7	Maximum likelihood estimate (MLE). UCL estimate would be about 4.2 E-8. Derived from inhalation potency in humans (see table 3) by applying a factor (0.14) equal to the relative potency of B[a]P by dermal versus inhalation exposure as established from rodent data.	MOE (1997)

Table 6. Comparison of relative potencies of PAH developed by different agencies. Relative potency of an individual PAH is the ratio of its potency to the potency of B[a]P.

PAH	MOE (1997)	CEPA (1994)	USEPA (1993)	CalEPA (1993)
acridine	0.0			
anthanthrene	0.28			0.1
benz[a]anthracene	0.014		0.145	0.1
benzo[a]acridine	0.0			
benzo[a]pyrene	1.0			
benzo[b]fluoranthene	0.11	0.06	0.167	0.1
benzo[c]acridine	0.0			
benzo[e]pyrene	0.0			0.01
benzo[c]phenanthrene	0.023			
benzo[ghi]perylene	0.012			0.01
benzo[j]fluoranthene	0.045	0.05		0.1
benzo[k]fluoranthene	0.037	0.04	0.020	0.1
benzo[rs]t]pentaphene	1.1			
chrysene	0.026		0.0044	0.01
chrysene, 6-nitro-				10
cyclopenta[cd]pyrene	0.012			0.1
dibenzo[a,h]acridine	0.11			1.0
dibenzo[a,h]anthracene	0.89		1.11	
dibenzo[a,h]pyrene	1.2			
dibenzo[a,j]acridine	0.0			1.0
7H-dibenzo[c,g]carbazole				1.0
fluoranthene				0.01
fluorene, 2-nitro-				0.01
indeno[1,2,3-cd]pyrene	0.067	0.12	0.055	0.1
5-methylchrysene				1.0
phenanthrene	0.00064			
pyrene	0.0			0.1
pyrene, 1-nitro-	0.0			0.1
pyrene, 4-nitro-				0.1
pyrene, 1,6-dinitro-				0.1
pyrene, 1,8-dinitro-				0.1

### Assessment based on WMM Approach

WMM approach assumes that the PAH profile (i.e. levels of individual PAH relative to B[a]P level) and the potency of the PAH fraction are reasonably similar from mixture to mixture. MOE (1997) has systematically examined many PAH-rich source and environmental mixtures and found these assumptions to be valid. The finding that the potencies of PAH-rich complex mixtures are approximately the same when risk is expressed in terms of B[a]P content supports the use of B[a]PS as the surrogate for the potency of the entire PAH fraction.

The WMM approach requires establishment of cancer potency for B[a]PS. Table 7 lists the potency estimates of B[a]PS by MOE (1997), the Netherlands (NIPHEP, 1989) and World Health Organisation (WHO, 1996) for the inhalation route of exposure. These estimates are similar in value. However, only MOE (1997) has established cancer potencies for the oral and dermal exposure routes for B[a]PS (refer to Table 8) in a manner consistent with inhalation potency. Therefore, the MOE cancer potencies for all three routes of exposure (listed in Table 9) are recommended for use in the conduct of human health risk assessment.

### **Recommendation**

MOE (1997) has extensively reviewed the advantages of the WMM and IPM models. MOE concludes that WMM provides a more realistic estimate for the potency of the PAH fraction of environmental mixtures, while IPM significantly underestimates the true potency of the fraction. Furthermore, the WMM model is more conservative. Therefore, WMM is recommended as the primary model in most circumstances.

Table 7 Unit risks for B[a]PS - inhalation exposure

Lifetime risk (ng B[a]PS /m <sup>3</sup> ) <sup>-1</sup>	Derivation Method	Reference
2.3 E-5	Maximum Likelihood Estimate (MLE). Derived from US EPA (1984) assessment for coke oven workers. Linearized multistage model. UCL estimate would be 3.6 E-4 per ng B[a]PS/m <sup>3</sup> . First, MOE estimated MLE using US EPA (1984) data and an approach homologous to the EPA's approach for estimating UCL. Next, risk expressed per unit mass of benzene soluble fraction was converted to risk per ng B[a]PS/m <sup>3</sup> , assuming 1.7 ng B[a]P in 1 µg benzene soluble fraction (from Albert <i>et al.</i> 1983).	MOE, 1997
1.0 E-4	Based on interpretation of existing assessments (Pike, 1983; WHO, 1986 and Tuomisto & Jantunen, 1987)	NIPHEP, 1989
8.7 E-5	Based on US EPA(1984) UCL estimate of potency of 6.2 E-4 (µg of benzene extractables/m <sup>3</sup> ) <sup>-1</sup> . Converted potency to 8.7 E-5 (ng B[a]PS/m <sup>3</sup> ), assuming B[a]P makes up 0.71% of benzene extractable mass.	WHO, 1996

Table 8 Potency of B[a]PS by oral and dermal route of exposure

Lifetime risk (ng B[a]PS/day) <sup>-1</sup>	Derivation Method	Reference
4.2 E-8	Oral exposure. Derived from inhalation potency (see table 7) by applying a factor (0.003) equal to the relative potency of B[a]P by oral versus inhalation exposure as established from rodent data.	MOE, 1997
2.0 E-6	Dermal exposure. Derived from inhalation potency (see table 7) by applying a factor (0.14) equal to the relative potency of B[a]P by dermal versus inhalation exposure as established from rodent data.	MOE, 1997

Table 9. Recommended potencies for assessment of PAH fractions of complex mixtures.

Lifetime risk	Route	Reference
2.3 E-5 (ng B[a]PS /m <sup>3</sup> ) <sup>-1</sup>	Inhalation	MOE, 1997
4.2 E-8 (ng B[a]PS/day) <sup>-1</sup>	Oral	MOE, 1997
2.0 E-6 (ng B[a]PS/day) <sup>-1</sup>	Dermal	MOE, 1997

## 6. References

ATSDR (Agency for Toxic Substances and Disease Registry), 1995. Toxicological Profile for Polycyclic Aromatic Hydrocarbons (PAHs). U.S. Department of Health & Human Services. Agency for Toxic Substances and Disease Registry, August 1995

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Only the key references related to the risk assessment are presented here. Please obtain the remaining references from MOE, 1997.