# Polycyclic aromatic hydrocarbon (PAH) mixture containing benzo[a]pyrene

| CAS number: | 50-32-8 |
| --- | --- |
| Synonyms: | — |
| Chemical formula: | — |

Workplace exposure standard (new)

| TWA: | **0.13 µg/m3 (as benzo[a]pyrene)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1; DSEN, Sk.** |
| IDLH: | **—** |
| **Sampling and analysis:** The recommended value is likely to be below the current limit of detection for standard sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 0.13 µg/m3 (as benzo[a]pyrene) is recommended to minimise the risk of cancer in exposed workers.

## Discussion and conclusions

PAH are formed during the pyrolysis of organic material when heating in the absence of oxygen or incomplete combustion. Relevant pyrolysis products at the workplace include tar, tar vapours, coke oven emissions as well as emissions or soot from the combustion of coal, electrodes and oil. PAH generally do not exist as discrete compounds and instead are found as complex mixtures of many different concentrations and configurations. Benzo[a]pyrene (B[a]P) is a hazardous component of most PAH mixtures.

The critical effects of exposure to PAHs are lung and skin cancer.

Many PAH compounds, including B[a]P, are considered human carcinogens based on sufficient evidence in humans, supported by positive results in studies in experimental animals (IARC, 2010; NTP, 2016; AIOH, 2016). IARC (2010) concludes that occupational exposures during coal gasification, coke production, coal-tar distillation, paving and roofing with coal-tar pitch, aluminium production are considered carcinogenic to humans.

B[a]P induces tumours locally and systemically (ACGIH, 2018; DFG, 2012). Genotoxic effects induced by PAH are reported in human cells *in vitro* and *in vivo.* Positive mutagenicity results are reported in bacteria. PAH chemicals share a similar mechanism of carcinogenic action; notably due to metabolites that cause DNA adducts (IARC, 2010; DFG, 2012; NTP, 2016). For the purposes of this assessment, PAH mixtures containing B[a]P are assumed to be non-threshold-based genotoxic carcinogens. Comprehensive and detailed reviews and studies on the effect of individual PAH, mixtures of PAH not containing B[a]P and PAH metabolites are widely available from the source documentation.

The recommended TWA is derived using B[a]P as the indicator chemical at a minimal cancer risk level. The recommended TWA of 0.13 µg/m3 is calculated through application of an inhalation slope factor derived from a chronic inhalation study identifying a dose-dependent increase in incidence of upper respiratory and upper digestive tract tumours in male hamsters (US EPA, 2010).

The toxicology of these substances is well catalogued. There are differences in decision making by sources, but the differences are based on individual policies underpinning risk assessments. It is noted that reservations exist about the legitimacy of using B[a]P as the reference chemical with which to base risk assessment on for PAH mixtures. This is due to the variability of PAH mixture profiles, the variability of the total contribution of B[a]P to the PAH mixture and the resulting carcinogenicity and that the contribution to carcinogenicity may not correlate with weight-for-weight percentage of B[a]P in the mixture. Carcinogenicity equivalency factors for selected PAH has been published by DFG (2012) as well as other regulators world-wide, that can be used in the assessment of risk.

## Recommendation for notations

Classified as a category 1 carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Classified as a skin sensitiser and not a respiratory sensitiser according to the GHS.

A skin notation is recommended based on evidence of uptake via the skin, excretion in the urine and the severity of effect in animals and humans.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA NA NA | |
| B[a]P - probable human carcinogen for which there is sufficient evidence to provide a strong presumption that human exposure might result in the development of cancer. Based on appropriate long-term animal studies, limited epidemiological evidence. No further information. |
| ACGIH 2001 Not assigned |
| B[a]P considered a suspected human carcinogen; no TLV-TWA assigned.  Worker exposure by all routes should be carefully controlled to levels as low as possible.  Summary of data:   * The following evidence is based on comments predominantly from reviews; study specifics generally not provided; refers to ATSDR for toxicological review * B[a]P often used as an index of air pollution and of total PAH.   Human data:   * Critical effect is lung cancer *via* inhalation: * skin cancer, dermatitis, photoallergy non-neoplastic respiratory disease and emphysema reported *via* various routes of exposure * Epidemiologic studies indicate a significant correlation between B[a]P and lung cancer mortality: * cigarette smoking, air pollution and occupational exposure are primary means of inhalation exposure * cigarette smoking overwhelming factor in causation of lung cancer * Epidemiological studies generally not quantitative, but obvious increase in B[a]P exposure results in increase of adverse health outcomes * B[a]P was a significant causative agent of lung cancer in epidemiologic studies involving air pollution: * data assumed that exposure indices and B[a]P levels were linearly related particularly in air pollution studies * sometimes B[a]P levels not directly proportional to other pollutants * dose-response estimate derived from general air pollution epidemiology * increase of 1 µg B[a]P per 1,000 m3 of air related to 5% increase in pulmonary cancer death rate * A review of lung cancer death rates among US coke oven workers identified a doubling or 10‑fold excess in lung cancer death rate vs controls: * estimated associated exposure was 2,000 ng/m3 when at work * Epidemiologic data pertaining to workers exposed to diesel emissions showed no positive correlation with lung cancer morbidity: * studies considered inconclusive as they did not allocate for the necessary latency period to measure lung cancer incidence accurately (up to 30 yr) * B[a]P-DNA adducts in human workers by immunoassay: * roofers: lymphocytes 7/28 * foundry workers: lymphocytes 7/28 * smokers/non-smokers: lung tissue 7/23 * lung cancer patients: lung tissue 4/14 * lung cancer controls: lung tissue, 0/13 * B[a]P metabolites shown to bind to DNA in cultured human hepatocytes and in human bladder and tracheobronchial explants * Generally, significant correlation between B[a]P exposure and lung cancer in limited studies.   Animal data:   * B[a]P proven carcinogenic in all animal species tested to date: mouse, rat, hamster, rabbit, guinea pig, duck, newt, dog, monkey and fish * Acts locally as demonstrated by tumour development at site of administration * Repeated administrations of B[a]P (same total dose in small aliquots by the same route) appeared more potent at initiating tumours than a single total dose of the same amount * Rats, subcutaneous injection B[a]P in oil (4 doses at 0.05, 0.1, 0.5 or1 mg); dose–response relationship identified; no threshold observed * Injection of 3 mg into hind legs of rats results in local tumours in area of application in all animals, no further data * Exposure of rats at 10 mg/m3 including increasing SO2 resulted in squamous cell carcinomas: * incidence increases with SO2 exposure * Acts systemically as evidenced by pulmonary adenomas in mice resulting from any route of administration, no further information * Mutagenic in *S. typhimurium* strain TA98: * 0.5 µg/plate caused significantly higher revertant rate than controls * stated 1 of many studies showing mutagenicity in Ames assay. No further information * Mice; oral administration of 2 doses of 1,351 µmol/kg; B[a]P metabolite/DNA adduct formation in liver, lung and forestomach. No further information * Mice; single oral dose of 1 µg/mouse; adduct formation highest in liver>intestine>colon>stomach. |
| DFG 2012 Not assigned |
| No MAK assigned for group of 19 PAH due to carcinogenic potential.  Review based mainly on the monograph on selected PAH by the International Programme on Chemical Safety, WHO.  Summary of additional data:   * PAH formed mainly during the pyrolysis of organic material (heating in the absence of oxygen or incomplete combustion): * relevant pyrolysis products at the workplace are tar, tar vapours, coke oven emissions, emissions or soot from the combustion of coal, electrodes, oil * Skin penetration of individual PAH demonstrated in humans and animal studies * Single doses of 1.25–125 µg/cm2 14C-labelled B[a]P applied to necks of mice: * 6% uptake in 1 h * 40% in 24 h * 93% in 7 d * excreted *via* the hepatobiliary system and in the faeces:   + 35% after 24 h   + 58% after 48 h   + 80% after 7 d. No further information * Evidence in animals suggest tumorigenicity in the respiratory tract may be attributed to range of PAH including B[a]P. No further information * 20 µg B[a]P applied 2–3/wk to depilated skin of mice for 2 yr: * skin tumours observed in treated region in 60% of animals. No further information * Tumour incidences of 0, 37% and 56% reported in the larynx and trachea of Golden hamsters in isolators exposed at 2.2, 9.5 or 46.5 mg/m3 B[a]P, respectively. No further information * Squamous cell carcinoma in 2/21 exposed rats exposed at 10 mg/m3 B[a]P for 1 h/d for 494 d. No further information * B[a]P historically used as reference for carcinogenicity of the PAH mixture and for the assessment of public and occupational health risks; some reservations for this practice are expressed due to variability of the effective fraction and PAH profile in an emission: * carcinogenicity is ~>70–90% caused by the class of PAH with 4 or more rings although almost all of them account for less than 4% w/w of the mixture * contribution of B[a]P to the effect varies widely in the mixtures and does not correlate with the % w/w of this component in the mixture * variability of PAH profile from different sources * List of PAH considered in MAK review and DFG recommended carcinogenicity equivalency factors: * anthanthrene 0.1 * benzo[a]anthracene 0.1 * benzo[b]fluoranthene 0.1 * benzo[j]fluoranthene 0.1 * benzo[k]fluoranthene 0.1 * benzo[b]naphtho[2,1‐d]thiophene 0.01 * benzo[a]pyrene 1 * chrysene 0.01 * cyclopenta[cd]pyrene 0.1 * dibenz[a,h]anthracene 1 * dibenzo[a,e]pyrene 1 * dibenzo[a,h]pyrene 10 * dibenzo[a,i]pyrene 10 * dibenzo[a,l]pyrene 10 * indeno[1,2,3‐cd]pyrene 0.1 * 1‐methylpyrene 0.1 * naphthalene 0.001 * phenanthrene 0.001 * pyrene 0.001 * Genotoxic effects induced by PAH found in human cells *in vitro* and *in vivo* * DNA adducts of dibenzo[*a,l*]pyrene detected in C3H10T1/2 cells; *via* LC/HPLC and 32P‑labelling. No further information * Positive results for DNA damage induced by PAH in various eukaryotes; extensive list * Predominantly positive results for mutagenicity in *S.typhyrium* for benzo[a]anthracene, benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[k]fluoranthene,  benzo[b]naphtho[2,1‐d]thiophene, B[a]P, chrysene, cyclopenta[cd]pyrene, dibenzo[a,h]anthracene, phenanthrene and pyrene. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| AIOH |  | 2016 | * PAH generally do not exist as discrete compounds, but are found as complex mixtures of many different concentrations and configurations * Irritating to eyes and can cause photosensitivity. No further information * Carcinogenicity of 17 PAH compounds has been confirmed (referring to IARC): * many are mutagenic * Increased lung tumour rates linked to exposure found in coke‐oven workers, asphalt workers and workers in aluminium reduction plants. No further information * A study in Australian prebake aluminium smelters found no overall excess of mortality or cancer: * incidence of mesothelioma and kidney cancer risks elevated * Occupational exposures to B[a]P‐containing mixtures associated with lung, bladder, skin, oesophagus, haematolymphatic system, larynx cancers * Noted occupational studies have found no effects for average PAH workplace exposures below 0.25 to 2.5 µg/m3 of B[a]P. No further information * Suggests TWA of 0.2 µg/m3 * B[a]P classified as a mutagen and teratogen according to IARC * Information gaps for health aspects of exposure *via* skin absorption indicate additional research is undertaken to confirm the long‐term health impact *via* this route of entry. |
| IARC |  | 2010 | * Some non-heterocyclic PAH; occupational exposures during coal gasification, coke production, coal-tar distillation, paving and roofing with coal-tar pitch, aluminium production are considered carcinogenic to humans * B[a]P is carcinogenic to humans. |
| NTP |  | 2016 | * 15 individual PAH are reasonably anticipated to be human carcinogens based on sufficient evidence of carcinogenicity from studies in experimental animals * Range of physiological properties based on aromatic ring numbers have influence on the biological activity of PAH * PAH chemicals share a similar mechanism of carcinogenic action; mechanism of carcinogenic action *via* metabolic processes; converted to oxides and diol epoxides: * PAH oxides can form stable DNA adducts * diol epoxides can form stable and depurination adducts with DNA through formation of electrophilic carbonium ions. |
| US EPA |  | 2017 | * The IRIS scientific review a relative potency factor (RPF) approach for PAH mixtures as one approach for assessing cancer risk from exposure to PAH mixtures has been suspended/discontinued and toxicity values will not be added to the IRIS database at present * Epidemiology studies involving exposure to PAH mixtures have reported associations between exposure to B[a]P and B[a]P diol epoxide-DNA adducts * Studies in multiple animal species demonstrate B[a]P is carcinogenic at multiple tumour sites (alimentary tract, liver, kidney, respiratory tract, pharynx, and skin) by all routes of exposure * Mechanistic studies provide strong supporting evidence that links metabolism of B[a]P to DNA reactive agents with key mutational events in genes leading to tumour development * Combination of human, animal, and mechanistic evidence provides the basis for characterisation of B[a]P as carcinogenic to humans; concluded B[a]P is carcinogenic by a mutagenic mode of action * Inhalation unit risk of 6×10−4 per µg/m3 calculated by linear extrapolation (slope factor= 0.1/BMCL10) from a BMCL10 of 0.16 mg/m3 for the occurrence of squamous cell neoplasia in the larynx, pharynx, trachea, nasal cavity, oesophagus, and forestomach chronically exposed for 130 wk by inhalation to B[a]P. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Yes |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Yes |
| **The chemical is a non-threshold based genotoxic carcinogen.** |  |
| Is a cancer slope factor or inhalation unit risk value available? | Yes |
| Inhalation unit risk value (1/(µg/m³)) | 6 x 10-4 |
| Calculated TWA value (µg/m3) | 0.13 |

## Notations

| Source | Notations |
| --- | --- |
| SWA | NA |
| HCIS | NA |
| NICNAS | NA |
| EU Annex | Skin sensitisation – category 1 |
| ECHA | Skin Sens. 1 |
| ACGIH | — |
| DFG | Carcinogenicity – 2, H (skin) |
| SCOEL | NA |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 1 |
| US NIOSH | NA |

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

### Skin notation assessment

| Calculation |
| --- |
| |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | |  |  | Adverse effects in human case study: | yes | 4.00 |  | |  |  | Dermal LD50 ≤1000 mg/kg: |  |  |  | |  |  | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | |  |  | Dermal LD50/Inhalation LD50 <10: |  |  |  | |  |  | *In vivo* dermal absorption rate >10%: |  |  |  | |  |  | Estimated dermal exposure at WES >10%: |  |  |  | |  |  |  |  | **a skin notation is warranted** | | |

### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

|  |  |
| --- | --- |
| Molecular weight: | NA for PAH, 252.32 for B[a]P |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = NA for PAH; 1 mg/m3 = NA for PAH  1 ppm = 10 .34 mg/m3 for B[a]P; 1 mg/m3 = 0.1 ppm for B[a]P |
| This chemical is used as a pesticide: |  |
| This chemical is a biological product: |  |
| This chemical is a by-product of a process: |  |
| A biological exposure index has been recommended by these agencies: | ACGIH  DFG  SCOEL |

## Workplace exposure standard history

| Year | Standard |
| --- | --- |
| Click here to enter year |  |

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [*TLVs® and BEIs® Guidelines section*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

Australian Institute of Occupational Hygienists (AIOH) (2016) Position paper – Polycyclic Aromatic Hydrocarbons (PAHs) and occupational health issues.

Deutsche Forschungsgemeinschaft (DFG) (2012) Polycyclic aromatic hydrocarbons – MAK value documentation.

European Chemicals Agency (ECHA) (2019) Benzo[a]pyrene – REACH assessment.

International Agency for Research on Cancer (IARC) (2012) Benzo[a]pyrene. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Toxicology Program (NTP) (2016) NTP 14th Report on Carcinogens - Polycyclic Aromatic Hydrocarbons.

NTP (National Toxicology Program). 2016. Report on Carcinogens, Fourteenth Edition.; Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service.

Tenth Adaptation to Technical Progress Commission Regulation (EU) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

US Environmental Protection Authority (US EPA) (2017) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Toxicological Review of Benzo[a]pyrene.