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## Toxicological Summary for Benzo[a]pyrene

**CAS: 50-32-8**

Synonyms: Benzo(d,e,f)chrysene; 3,4-benzopyrene; 3,4-benzpyrene; 3,4-benzylpyrene; 3,4-benz(a)pyrene; 6,7-benzopyrene; benzpyrene; benz(a)pyrene; 3,4-bp; BP; BaP; BαP; benzo(alpha)pyrene

**Benzo[a]pyrene is an index compound for carcinogenic Polycyclic Aromatic Hydrocarbons (PAHs). Please refer to the MDH guidance “Polycyclic Aromatic Hydrocarbons: Methods for Estimating Health Risks from Carcinogen PAHs” for the potency equivalency factors to estimate risks for carcinogenic PAHs. The MDH guidance can be found at:**  
<http://www.health.state.mn.us/divs/eh/risk/guidance/pahmemo.html>.

**Acute Non-Cancer Health Based Value (nHBV<sub>acute</sub>) = 2 µg/L**

$$\frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Acute intake rate, L/kg/d})}$$
$$= \frac{(0.0013 \text{ mg/kg/d}) \times (0.5) \times (1000 \text{ µg/mg})}{(0.289 \text{ L/kg-d})}$$
$$= 2.2 \text{ rounded to } \mathbf{2 \text{ µg/L}}$$

Reference Dose / Concentration:	0.0013 mg/kg-day (CD-1 mice)
Source of toxicity value:	MDH 2012
Point of Departure:	10 mg/kg-day (LOAEL), MacKenzie and Angevine 1981
Human Equivalent Dose (MDH 2011):	1.3 mg/kg-d [10 mg/kg-d x 0.13]
Total uncertainty factor:	1000
UF allocation:	3 for interspecies extrapolation (to address potential differences in toxicodynamics); 10 for intraspecies variability; 3 for database insufficiencies (neurological effects were not evaluated in the acute critical study but were identified as a concern in the short-term critical study and exposure in the critical 2-generation study only occurred <i>in utero</i> and did not cover the full developmental period); 10 for use of a LOAEL rather than a NOAEL
Critical effect(s):	Decreased pup weight, decreased litter size produced by female offspring; decreased fertility in offspring associated with alterations in gonadal morphology and germ cell development; gonadal effects included: decreased testes weight, testicular damage including tubular injury, hypoplasia in ovarian tissues and follicles and corpora lutea

- Co-critical effect(s): Decreased fertility and interference in female reproductive organ development: decreased ovary weight, decrease in ovarian follicles, and decreased number of corpora lutea (effects observed in offspring exposed *in utero*)
- Additivity endpoint(s): Developmental (male and female reproductive effects)

**Short-term Non-Cancer Health Based Value (nHBV<sub>short-term</sub>) = 0.3 µg/L**

$$\frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Short-term intake rate, L/kg/d})}$$

$$= \frac{(0.0002 \text{ mg/kg/d}) \times (0.5) \times (1000 \text{ µg/mg})}{(0.289 \text{ L/kg-d})}$$

$$= 0.346 \text{ rounded to } \mathbf{0.3 \text{ µg/L}}$$

- Reference Dose / Concentration: 0.0002 mg/kg-d (Wistar rats)
- Source of toxicity value: MDH, 2012
- Point of Departure: 0.02 mg/kg-day (NOAEL) Chengzhi et al. 2011
- Human Equivalent Dose (MDH 2011): Not Applied (study utilized direct dosing to neonatal animals)
- Total uncertainty factor: 100
- UF allocation: 10 for interspecies extrapolation (toxicokinetics and toxicodynamics), 10 for intraspecies variability
- Critical effect(s): Significant alterations in performance in tests designed to evaluate learning and locomotor abilities – animals were exposed as neonates and the neurological effects persisted into adolescence and adulthood
- Co-critical effect(s): None
- Additivity endpoint(s): Developmental (nervous system)

**Subchronic Non-Cancer Health Based Value (nHBV<sub>subchronic</sub>) = Short-term nHBV = 0.3 µg/L**

$$\frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Subchronic intake rate, L/kg/d})}$$

$$= \frac{(0.0002 \text{ mg/kg/d})^{**} \times (0.2) \times (1000 \text{ µg/mg})}{(0.077 \text{ L/kg-d})}$$

$$= 0.52 \text{ rounded to } 0.5 \text{ µg/L}$$

\*\*See the short-term information above for details about the reference dose

**The Subchronic nHBV must be protective of the acute, and short-term exposures that occur within the subchronic period and therefore, the Subchronic nHBV is set equal to the Short-term nHBV = 0.3 µg/L. Additivity Endpoints – developmental (nervous system).**

**Chronic Non-Cancer Health Based Value (nHBV<sub>chronic</sub>) = Short-term nHBV = 0.3 µg/L**

$$\frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Chronic intake rate, L/kg/d})}$$

$$= \frac{(0.0002 \text{ mg/kg/d})^{**} \times (0.2) \times (1000 \text{ } \mu\text{g/mg})}{(0.043 \text{ L/kg-d})}$$

$$= 0.93 \text{ rounded to } 0.9 \text{ } \mu\text{g/L}$$

\*\*See the short-term information above for details about the reference dose

**The Chronic nHBV must be protective of the acute, and short-term exposures that occur within the chronic period and therefore, the Chronic nHBV is set equal to the Short-term nHBV = 0.3  $\mu\text{g/L}$ . Additivity Endpoints – developmental (nervous system).**

**Cancer Health Based Value (cHBV) = 0.06  $\mu\text{g/L}$**

$$= \frac{(\text{Additional Lifetime Cancer Risk}) \times (\text{Conversion Factor})}{[(\text{SF} \times \text{ADAF}_{<2 \text{ yr}} \times \text{IR}_{<2\text{yr}} \times 2) + (\text{SF} \times \text{ADAF}_{2-16 \text{ yr}} \times \text{IR}_{2-16\text{yr}} \times 14) + (\text{SF} \times \text{ADAF}_{16+ \text{ yr}} \times \text{IR}_{16+\text{yr}} \times 54)] / 70}$$

$$= \frac{(1\text{E-}5) \times (1000 \text{ } \mu\text{g/mg})}{[(1.7 \times 10 \times 0.137 \text{ L/kg-d} \times 2) + (1.7 \times 3 \times 0.047 \text{ L/kg-d} \times 14) + (1.7 \times 1 \times 0.039 \text{ L/kg-d} \times 54)] / 70}$$

$$= 0.060 \text{ rounded to } \mathbf{0.06 \text{ } \mu\text{g/L}}$$

Cancer classification: B2 – Probable Human Carcinogen (EPA IRIS 1994)  
 Slope factor: 1.7 (mg/kg-d)<sup>-1</sup> (laboratory animal) (Culp et al. 1998)  
 Source of slope factor: California OEHHA 2010  
 Tumor site(s): Forestomach, esophagus, tongue

**Volatile: No**

**Summary of changes since 1993/1994 HRL promulgation:**

A 1993/1994 HRL was not promulgated for benzo[a]pyrene. In 1995, MDH derived an HBV for benzo[a]pyrene of 0.05  $\mu\text{g/L}$  based on cancer effects utilizing the 1994 EPA IRIS slope factor. The 2012 MDH cancer based HBV of 0.06 is different than the 1995 cancer based HBV because 1) a different slope factor was used, 2) age dependent adjustment factors were applied in 2012 that were not applied in 1995.

**Summary of toxicity testing for health effects identified in the Health Standards Statute:**

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	Yes	Yes	Yes	Yes
Effects?	-	Yes <sup>1</sup>	Yes <sup>2</sup>	Yes <sup>3</sup>	Yes <sup>4</sup>

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers

identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

**Comments on extent of testing or effects:**

<sup>1</sup> Immune effects were observed in short-term oral BaP studies at Human Equivalent Doses (HEDs) that were 8500 -100,000 times higher than the short-term RfD. The immune effects reported in these studies included decreased thymus weight, decreased lymph node weight, atrophy of the spleen and thymus, decreased number of spleen cells and B cells, decreased serum IgA, and reduced white blood cell counts.

<sup>2</sup>Developmental effects were the basis of the acute and short-term RfDs. Developmental effects reported in the acute critical study included decreased pup weight, decreased litter size, and histological gonadal effects in males and females at a Human Equivalent Dose (HED) 300 times higher than the acute RfD.

Neurodevelopmental effects that were selected as the basis for the short-term RfD were observed at doses 1000 times higher than the short-term RfD.

<sup>3</sup>A decreased number of pregnancies and viable litters were observed in female mice exposed to BaP at doses approximately 5000 times greater than the acute RfD.

<sup>4</sup> Neurodevelopmental effects are the basis of the short-term RfD. Neurological effects were observed in the critical short-term study as well as other studies were reported at doses 400-25,000 times higher than the short-term RfD. Neurological effects reported included significant suppression of motor activity parameters, impacts on learning, and significant changes in neuromuscular, autonomic, sensorimotor, and physiological function, and delayed cortical neuronal activity.

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