Adopted as Rule: August 2018

Toxicological Summary for: Pyrene

CAS: **129-00-0**
Synonyms: Benzo[d,e,f]phenanthrene

Acute Non-Cancer Health Risk Limit ($nHRL_{Acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = Not Derived (Insufficient Data)

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = 90 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.033 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.070 L/kg-d)}^{**}}$$

= 94.3 rounded to **90 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose:	HED/Total UF = 10/300 = 0.033 mg/kg-d (CD-1 mice)
Source of toxicity value:	Determined by MDH in 2015
Point of Departure (POD):	75 mg/kg-d NOAEL (U.S. Environmental Protection Agency, 1989)
Dose Adjustment Factor (DAF):	0.13 Body weight scaling, default (US EPA 2011 and MDH 2011)
Human Equivalent Dose (HED):	POD x DAF = 75 mg/kg-d x 0.13 = 10 mg/kg-d
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics); 10 for intraspecies variability; 10 for database uncertainty due to lack of reproductive/developmental studies and a lack of studies in a second species
Critical effect(s):	Nephropathy in female mice, decreased kidney weight
Co-critical effect(s):	Not applicable
Additivity endpoint(s):	Renal (kidney) system

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 50 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.010 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.044 L/kg-d)}^{**}}$$

= 45.5 rounded to **50 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose:	HED/Total UF = 10/1000 = 0.010 mg/kg-d (CD-1 mice)
Source of toxicity value:	Determined by MDH in 2015
Point of Departure (POD):	75 mg/kg-d NOAEL (U.S. Environmental Protection Agency, 1989, subchronic study)
Dose Adjustment Factor (DAF):	0.13 Body weight scaling, default (US EPA 2011 and MDH 2011)
Human Equivalent Dose (HED):	POD x DAF = 75 mg/kg-d x 0.13 = 10 mg/kg-d
Total uncertainty factor (UF):	1000
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics); 10 for intraspecies variability; 3 for extrapolation from a subchronic study to a chronic study due to the lack of severity of the critical effect; 10 for database uncertainty due to lack of reproductive and developmental studies and a lack of studies in a second species)
Critical effect(s):	Nephropathy in female mice, decreased kidney weight
Co-critical effect(s):	Not Applicable
Additivity endpoint(s):	Renal (kidney) system

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification:	Group D, Not classifiable as to carcinogenicity
Slope factor (SF):	Not Applicable
Source of cancer slope factor (SF):	Not Applicable
Tumor site(s):	Not Applicable

Volatile: Yes (Moderate)

Summary of Guidance Value History:
Pyrene has a 1993 chronic HRL of 200 µg/L. In addition, a Pesticide Rapid Assessment Value of 20 µg/L was derived in 2014 and was lower than the HRL due to the conservative rapid assessment method (MDH 2014). Subchronic and Chronic HBVs of 90 µg/L and 50 µg/L were derived in 2015. The 2015

Chronic HBV was 4 times lower than the 1993 HRL as a result of: 1) the use of new methodology including use of body weight scaling and updated water intake rates; and 2) rounding to one significant digit. In 2016 MDH updated the intake rate values used to derive guidance values. Use of updated intake rates did not result in any changes to the Subchronic or Chronic nHBV values derived in 2015. The updated guidance was adopted into rule as HRLs in 2018.

Summary of toxicity testing for health effects identified in the Health Standards Statute (144.0751):
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. MDH has considered the following information in developing health protective guidance.

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested for specific effect?	No	No	No	No	No
Effects observed?	No	No	No	No	No

Comments on extent of testing or effects: Not Applicable

Resources Consulted During Review:

Australian Natural Resource Management Ministerial Council; Environmental Protection and Heritage Council; and National Health and Medical Research Council. (2008). Australian Guidelines for Water Recycling. Augmentation of Drinking Water Supplies. from http://webarchive.nla.gov.au/gov/20130904200226/http://www.environment.gov.au/water/publications/quality/water-recycling-guidelines-augmentation-drinking-22.html

Dutch National Institue for Public Health and the Environment (RIVM). (2001). Re-evaluation of human-toxicological maximum permissible risk levels.

International Agency for Research on Cancer (IARC). (2010). Monograph 92: Some non-heterocyclic polycyclic aromatic hydrocarbons and some related exposures.

Minnesota Department of Health (MDH). (2008). Statement of Need and Reasonableness (SONAR), July 11, 2008. Support document relating to Health Risk Limits for Groundwater Rules. Retrieved from http://www.health.state.mn.us/divs/eh/risk/rules/water/hrlsonar08.pdf

Minnesota Department of Health (MDH). (2011). MDH Health Risk Assessment Methods to Incorporate Human Equivalent Dose Calculations into Derivation of Oral Reference Doses (May 2011, revised 2017) from http://www.health.state.mn.us/divs/eh/risk/guidance/hedrefguide.pdf

Minnesota Department of Health (MDH). (2014). Report on Pesticide Rapid Assessments. Retrieved from: http://www.health.state.mn.us/divs/eh/risk/guidance/dwec/rapassrept.pdf

U.S. Department of Health and Human Services Agency for Toxic Substances and Disease Registry (ATSDR). (1995). Toxicological Profile for Polycyclic Hydrocarbons. Retrieved from: http://www.atsdr.cdc.gov/toxprofiles/tp69.pdf

U.S. Environmental Protection Agency - IRIS. Integrated Risk Information Systems (IRIS) A-Z List of Substances. from http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showSubstanceList

U.S. Environmental Protection Agency - Office of Research and Development. (1988). Recommendations for and Documentation of Biological Values for Use in Risk Assessment. from http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=34855

U.S. Environmental Protection Agency - Office of the Science Advisor. (2011). Recommended Use of Body Weight¾ as the Default Method in Derivation of the Oral Reference Dose. from http://www.epa.gov/raf/publications/pdfs/recommended-use-of-bw34.pdf

U.S. Environmental Protection Agency - Regional Screening Tables. Mid-Atlantic Risk Assessment - Regional Screening Table. from http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/Generic_Tables/index.htm

U.S. Environmental Protection Agency. (1989). IRIS Summary for Pyrene. Retrieved from: http://www.epa.gov/iris/subst/0445.htm

U.S. Environmental Protection Agency. (2007). Provisional Peer Reviewed Toxicity Values for Pyrene (CASRN 129-00-0). Retrieved from: http://hhpprtv.ornl.gov/issue_papers/Pyrene.pdf

U.S. Environmental Protection Agency. (2010a). Development of a Relative Potency Factor (RPF) Approach for Polycyclic Aromatic Hydrocarbon (PAH) Mixtures (External Review Draft).

U.S. Environmental Protection Agency. (2010b). Development of a relative potency factor (RPF) approach for polycyclic aromatic hydrocarbon (PAH) mixtures. Retrieved from: http://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=194584

U.S. Environmental Protection Agency (EPA) - Office of Research and Development. (2011). Exposure Factors Handbook: 2011 Edition. Retrieved from https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252

U.S. Environmental Protection Agency. (2012). Benchmark Dose Technical Guidance. Retrieved from: http://www.epa.gov/raf/publications/pdfs/benchmark_dose_guidance.pdf

U.S. Geological Survey - Health-Based Screening Levels. from https://cida.usgs.gov/hbsl/apex/f?p=104:1

Viau, C., Bouchard, M., Carrier, G., Brunet, R., & Krishnan, K. (1999). The toxicokinetics of pyrene and its metabolites in rats. *Toxicol Lett, 108*(2-3), 201-207.