Health Based Guidance for Water
Health Risk Assessment Unit, Environmental Health Division
651-201-4899

Adopted as Rule: November 2023

Toxicological Summary for: Fluorene

CAS: **86-73-7**

Synonyms: 9H-fluorene, 2,2'-methylenebiphenyl, diphenylenemethane, O-biphenylenemethane

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 ($nHRL_{Subchronic}$) = 200 µg/L

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

$$= \frac{\text{(0.058 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 156 rounded to **200 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3, and 3-5.

Reference Dose/Concentration:	HED/Total UF = 17.5 / 300 = 0.058 mg/kg-d (CD-1 mouse)
Source of toxicity value:	Determined by MDH in 2019
Point of Departure (POD):	125 mg/kg-d (administered dose NOAEL, US EPA, 1989)
Dose Adjustment Factor (DAF):	0.14 from body weight scaling, study specific (US EPA, 2011 and MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 125 mg/kg-d x 0.14 = 17.5 mg/kg-d
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty to account for the absence of adequate developmental, reproductive, and neurotoxicity studies in the database.
Critical effect(s):	Decreased red blood cells in female mice, decreased packed cell volume in female and male mice, and increased relative spleen weight in male and female mice
Co-critical effect(s):	None identified
Additivity endpoint(s):	Hematological (blood) system, Spleen

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 80 µg/L

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

$$= \frac{\text{(0.018 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.045 L/kg-d)}^{**}}$$

$$= \mathbf{80\ \mu g/L}$$

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3, and 3-5.

Reference Dose/Concentration:	HED/Total UF = 17.5/1000 = 0.018 mg/kg-d (CD-1 mouse)
Source of toxicity value:	Determined by MDH in 2019
Point of Departure (POD):	125 mg/kg-d (administered dose NOAEL, US EPA, 1989 subchronic exposure)
Dose Adjustment Factor (DAF):	0.14 from body weight scaling, study specific (US EPA, 2011 and MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 125 mg/kg-d x 0.14 = 17.5 mg/kg-d (study specific body weight scaling basis)
Total uncertainty factor (UF):	1000
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, 3 for subchronic-to-chronic extrapolation, and 10 for database uncertainty to account for the absence of adequate developmental, reproductive, and neurotoxicity studies in the database.
Critical effect(s):	Decreased red blood cells in female mice, decreased packed cell volume in female and male mice, and increased relative spleen weight in male and female mice
Co-critical effect(s):	None identified
Additivity endpoint(s):	Hematological (blood) system, Spleen

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification:	Not Classified
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:
A non-cancer chronic HRL of 300 µg/L was promulgated in 1993. The 2019 chronic and subchronic nHBVs are lower than the previous HRL as a result of using MDH's most recent risk assessment

methodology. In 2020, MDH incorporated updated intake rates (US EPA 2019). Use of the updated intake rates did not result in any changes to the guidance values. In November 2023, the guidance values were adopted into Minnesota Rules, 4717.7860, as Health Risk Limits (HRLs).

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	Yes	No	No	Yes
Effects observed?	-	No[1]	-	-	No[2]

Comments on extent of testing or effects:

[1] Very little information relating to immunotoxicity is available. One limited acute oral gavage study in male mice did not find any reduction in humoral or cell mediated immunity following exposure to fluorene.

[2] Results from a limited neurobehavioral gavage study in adult male rats did not indicate any adverse effects on locomotor activity or learning ability. A slight, but significant, decrease in anxiety-related behavior was observed in rats exposed to fluorene at a dose approximately 13-fold higher than the current chronic reference dose when tested in the elevated plus maze, although there was no dose response and the biological significance of this finding is unknown. In the subchronic/chronic critical study, increased incidence of salivation and hypoactivity were noted in the fluorene-exposed rats, however, there was no statistical analysis performed on these endpoints and they are not clear indicators of neurotoxicity but may point to central nervous system effects. No other neurotoxicity studies were available. A database uncertainty factor of 10 was applied, in part, to account for possibility of neurotoxic effects.

Resources Consulted During Review:

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