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

Adopted as Rule: August 2018

Toxicological Summary for: Perfluorobutanoate

CAS: **45048-62-2 (anion)**
375-22-4 (acid)
Synonyms: PFBA, Perfluorobutanoic Acid, Perfluorobutyric acid, Heptafluorobutyric acid

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

* While a developmental study is available for PFBA, a human equivalent dose (HED) forms the basis of the reference dose and assumes steady state conditions that cannot be achieved from a one-day exposure. Based on a mean human half-life of 3 days steady-state conditions would be established within ~ 9-15 days. At the present time the information necessary to estimate less than steady-state doses is not available. The short-term HRL assessment incorporated information regarding developmental effects.

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 7 µg/L

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

$$= \frac{\text{(0.0038 mg/kg-d) x (0.5)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.285 L/kg-d)}^{**}}$$

= 6.67 rounded to **7 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/Concentration:	HED/Total UF = 0.38/100 = 0.0038 mg/kg-d (rat)
Source of toxicity value:	Determined by MDH in 2008
Point of Departure (POD):	3.01 mg/kg-d ($BMDL_{1SD}$, calculated by Butenhoff, 2007; based on NOTOX 2007a)
Dose Adjustment Factor (DAF):	Chemical-Specific Toxicokinetic Adjustment ($t½_{Human}$ / $t½_{MaleRat}$ = 72 hours / 9.22 hours = 8) (t½ based on Chang et al. 2008, Olsen et al. 2007b)
Human Equivalent Dose (HED):	POD/DAF = 3.01 mg/kg-d / 8 = 0.38 mg/kg-d (chemical specific basis)
Total uncertainty factor (UF):	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty due

	to the lack of a NOAEL or acceptable $BMDL_{10}$ for thyroid effects as well as lack of available immunotoxicity testing. A multigeneration reproductive study has also not been conducted, however the database does include an extended one generation developmental study
Critical effect(s):	Decreased cholesterol
Co-critical effect(s):	Increased relative thyroid weight, decreased serum total thyroxine (TT4), decreased dialysis free thyroxine (dFT4)
Additivity endpoint(s):	Hepatic (liver) system, Thyroid (E)

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = $nHRL_{Short\text{-}term}$ = 7 µg/L

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

$$= \frac{\text{(0.0029 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.070 L/kg-d)}^{**}}$$

= 8.29 rounded to 8 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/Concentration:	HED/Total UF = 0.86/300 = 0.0029 mg/kg-d (rat)
Source of toxicity value:	Determined by MDH in 2008
Point of Departure (POD):	6.9 mg/kg-d (NOAEL, NOTOX 2007b)
Dose Adjustment Factor (DAF):	Chemical-Specific Toxicokinetic Adjustment ($t½_{Human}$ / $t½_{MaleRat}$ = 72 hours /9.22 hours = 8) (t½ based on Chang et al. 2008, Olsen et al. 2007b)
Human Equivalent Dose (HED):	POD/DAF = 6.9 mg/kg-d / 8 = 0.86 mg/kg-d (chemical specific basis)
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty (assessment of thyroid effects was compromised by missing serum hormone data and an immunotoxicity test has not been conducted. In addition, a multigeneration reproductive study has not been conducted, however the database does include an extended one generation developmental study)
Critical effect(s):	Liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, decreased red blood cells, decreased hematocrit and hemoglobin
Co-critical effect(s):	Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol, delayed eye opening

Additivity endpoint(s):	Developmental, Hematological (blood) system, Hepatic (liver) system, Thyroid (E)

The Subchronic nHRL must be protective of the acute and short-term exposures that occur within the subchronic period and therefore, the Subchronic nHRL is set equal to the Short-term nHRL of 7 µg/L. Additivity endpoints: Hepatic (liver) system, Thyroid (E)

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = $nHRL_{Short\text{-}term}$ = 7 µg/L

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

$$= \frac{\text{(0.0029 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.044 L/kg-d)}^{**}}$$

= 13.2 rounded to 10 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/Concentration:	HED/Total UF = 0.86/300 = 0.0029 mg/kg-d (rat)
Source of toxicity value:	Determined by MDH in 2008
Point of Departure (POD):	6.9 mg/kg-d (NOAEL, NOTOX 2007b)
Dose Adjustment Factor (DAF):	Chemical-Specific Toxicokinetic Adjustment ($t½_{Human}$ / $t½_{MaleRat}$ = 72 hours /9.22 hours = 8) (t½ based on Chang et al. 2008, Olsen et al. 2007b)
Human Equivalent Dose (HED):	POD/DAF = 6.9 mg/kg-d / 8 = 0.86 mg/kg-d (chemical specific basis)
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty (assessment of thyroid effects was compromised by missing serum hormone data and an immunotoxicity test has not been conducted. In addition, a multigeneration reproductive study has not been conducted, however the database does include an extended one generation developmental study)
Critical effect(s):	Liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, decreased red blood cells, decreased hematocrit and hemoglobin
Co-critical effect(s):	Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol, delayed eye opening
Additivity endpoint(s):	Developmental, Hematological (blood) system, Hepatic (liver) system, Thyroid (E)

The Chronic nHRL must be protective of the acute, short-term, and subchronic exposures that occur within the chronic period and therefore, the Chronic nHRL is set equal to the Short-term nHRL of 7 µg/L. Additivity endpoints: Hepatic (liver) system, Thyroid (E)

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: No

Summary of Guidance Value History:

MDH promulgated short-term, subchronic and chronic Health Risk Limits (nHRL) of 7 µg/L in 2011. In 2017, MDH re-evaluated the noncancer HRLs. The values did not change as a result of the evaluation and incorporation of MDH's most recent risk assessment methodology. This guidance was adopted 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?	Yes	No	Yes	No	Yes
Effects observed?	Yes[1]	-	Yes[2]	-	No[3]

Comments on extent of testing or effects:

[1] Secondary observations, including decreased T4 levels, altered hyperplasia/hypertrophy of the follicular epithelium of the thyroid, and increased thyroid weight were noted in the 28 and 90 day studies. These effects are identified as critical or co-critical effects for the short-term, subchronic, and chronic duration HBVs.

[2] Developmental delays were observed in offspring of mice exposed during pregnancy. This effect was observed at 2-fold higher than the human equivalent dose, upon which the short-term RfD is based. Developmental effects are identified as secondary effects.

[3] No available neurotoxicity studies. Secondary observations reported in the 28 and 90-day studies include delayed bilateral pupillary reflex for males exposed to a dose > 10-fold higher than the

BMDL used as the basis of the short-term, subchronic, and chronic HBVs. Histopathological assessment of neuronal tissues (including the optic nerve) and motor activity evaluations did not reveal any treatment-related abnormalities.

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