Health Based Guidance for Air
Environmental Impacts Analysis Unit, Environmental Health Division
651-201-4899

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Air Toxicological Summary for: Perfluorobutanoic acid (PFBA)

CAS: 375-22-4
Synonyms: PFBA, Perfluorobutanoate

Air Exposure Durations:

Acute - dosing duration 24-hours or less
Short-term - repeated dosing for more than 24-hours, up to approximately 30 days
Subchronic - repeated dosing for more than 30 days, up to approximately 8 years (10 percent of a lifespan in humans; more than 30 days up to approximately 90 days in typical laboratory rodent species)
Chronic = repeated dosing for more than approximately 8 years (10 percent of a life span in humans; more than approximately 90 days in typical laboratory rodent species)

Acute Non-Cancer Risk Assessment Advice (RAA_{Acute}) = Not Derived (Insufficient Data)

Non-Cancer Short-term RAA ($RAA_{Short\text{-}term}$) = 10 µg/m^3

= Reference Dose (mg/kg-d) x Route-to-route scaling factor (kg/m^3-d) x (1000 µg/mg)

= 0.0038 (mg/kg-d) x (70 kg/20 m^3-d) x (1000 µg/mg)

= 13.3 µg/m^3 rounded to 10 µg/m^3

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 (t½Human / t½MaleRat = 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 (study did not identify a NOAEL or acceptable BMDL10 for thyroid effects. A multigeneration reproductive study has not been conducted, however the database does include an extended one generation developmental study)
Critical effect:	Decreased cholesterol
Co-critical effects:	Increased relative thyroid weight, decreased serum total thyroxine (TT4), decreased dialysis free thyroxine (dFT4)
Additivity endpoints:	Hepatic (Liver) system, and Thyroid

Non-Cancer Subchronic RAA ($RAA_{Subchronic}$) = 10 µg/m^3

= Reference Dose (mg/kg-d) x Route-to-route scaling factor (kg/m^3-d) x (1000 µg/mg)

= 0.0029 (mg/kg-d) x (70 kg/20 m^3-d) x (1000 µg/mg)

= 10.2 µg/m^3 rounded to 10 µg/m^3

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 (t½Human / t½MaleRat = 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. A multigeneration reproductive study has not been conducted, however the database does include an extended one generation developmental study)
Critical effects:	Liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, decreased red blood cells, decreased hematocrit and hemoglobin
Co-critical effects:	Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol, delayed eye opening
Additivity endpoints:	Developmental, Hematological (blood) system, Hepatic (liver) system, Thyroid

Non-Cancer Chronic RAA ($RAA_{Chronic}$) = 10 µg/m^3

= Reference Dose (mg/kg-d) x Route-to-route scaling factor (kg/m^3-d) x (1000 µg/mg)

= 0.0029 (mg/kg-d) x (70 kg/20 m^3-d) x (1000 µg/mg)

= 10.2 µg/m^3 rounded to 10 µg/m^3

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 (t½Human / t½MaleRat = 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. A multigeneration reproductive study has not been conducted, however the database does include an extended one generation developmental study)
Critical effects:	Liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, decreased red blood cells, decreased hematocrit and hemoglobin
Co-critical effects:	Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol, delayed eye opening
Additivity endpoints:	Developmental, Hematological (blood) system, Hepatic (liver) system, Thyroid

Further detail regarding the MDH 2018 PFBA RfD can be found in the Toxicological Summary for Perfluorobutanoate (https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/pfba2summ.pdf).

Cancer Risk Assessment Advice = Not Applicable

Cancer classification:	Not classified
Inhalation Unit Risk (IUR):	Not applicable
Source of IUR:	Not applicable
Tumor site(s):	Not applicable

Volatile: No

Summary of Guidance Value History: There are no previous PFBA air guidance values.

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	Respiratory
Tested for specific effect?	Yes	No	Yes	No	Yes	Yes
Effects observed?	Yes[1]	--	Yes[2]	--	No[3]	Yes[4]

Comments on extent of testing or effects:

[1] MDH 2018; 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] MDH 2018; 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] MDH 2018; 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.

[4] Morphological changes to the respiratory tract were not induced in rats exposed to gavage doses of ≤184 mg/kd/d for five days, ≤150 mg/kg/d for 28 days, or ≤30 mg/kg/d for 90 days.

References and Resources Consulted

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