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

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Air Toxicological Summary for: Perfluorobutane Sulfonic Acid (PFBS)

CAS: 375-73-5
Synonyms: PFBS, Perfluorobutane sulfonate

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 ($RAA_{Short\text{-}term}$) = 0.3 µg/m^3

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

= 0.000084 (mg/kg-d) x (70 kg/20 m^3-d) x (1000 µg/mg)

= 0.29 µg/m^3 rounded to 0.3 µg/m^3

Reference Dose/Concentration:	HED/Total UF = 0.0084/100 = 0.000084 mg/kg-d (Hsd:Sprague Dawley Rats)
Source of toxicity value:	Determined by MDH in 2022
Point of Departure (POD):	6.97 mg/kg-d (administered dose $BMDL_{1SD}$, (National Toxicology Program 2019))
Dose Adjustment Factor (DAF):	Chemical- and Study-Specific Toxicokinetic Adjustment Half-life$_{FemaleRat}$/Half-life$_{Human}$ = 1.3 hr/1050 hr = 0.0012,

	based on MDH analysis of (Huang, Dzierlenga et al. 2019) for female rats and (Xu, Fletcher et al. 2020) for humans
Human Equivalent Dose (HED):	POD x DAF = 6.97 mg/kg-d x 0.0012 = 0.0084 mg/kg-d
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 a lack of available immunotoxicity and developmental neurotoxicity studies (known sensitive effects of other PFAS) as well as lack of a 2-generation study in a more appropriate species
Critical effects:	Decreased total T4
Co-critical effects:	None
Additivity endpoints:	Thyroid (E)

(E) = Endocrine mediated effect on the specified target organ

Non-Cancer Subchronic RAA ($RAA_{Subchronic}$) = 0.3 µg/m^3

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

= 0.000084 (mg/kg-d)* x (70 kg/20 m^3-d) x (1000 µg/mg)

= 0.29 µg/m^3 rounded to 0.3 µg/m^3

*The calculated MDH subchronic RfD (0.00054 mg/kg-d) results in RAA (2 µg/m^3) that is higher than the short-term RAA (0.3 µg/m^3) which is based on thyroid effects. The RAA must be protective of shorter duration exposures that occur within the subchronic period and therefore, the subchronic RAA is set equal to the short-term RAA of 0.3 µg/m^3 (MDH 2001, 2008).

Non-Cancer Chronic RAA ($RAA_{Chronic}$) = 0.3 µg/m^3

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

= 0.000084 (mg/kg-d)* x (70 kg/20 m^3-d) x (1000 µg/mg)

= 0.29 µg/m^3 rounded to 0.3 µg/m^3

*The calculated MDH chronic RfD (0.00018 mg/kg-d) results in RAA (0.6 µg/m^3) that is higher than the short-term RAA (0.3 µg/m^3) which is based on thyroid effects. The chronic RAA must be protective of shorter duration exposures that occur within the chronic period and therefore, the chronic RAA is set equal to the short-term RAA of 0.3 µg/m^3 (MDH 2001, 2008).

Further detail and specific references regarding the MDH 2022 PFBS RfDs can be found in the Toxicological Summary for Perfluorobutane sulfonate:
(https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/pfbssummary.pdf)

Cancer Risk Assessment Advice = Not Applicable

Volatile: No

Summary of Guidance Value History: There are no previous PFBS 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	Yes	Yes	Yes
Effects observed?	Yes[1]	--[2]	Yes[3]	Yes[4]	Yes[5]	Yes[6]

Comments on extent of testing or effects:

[1] MDH 2022; Male and female rats exposed to PFBS orally had large decreases in various thyroid hormones at a dose 900-fold higher than the Short-Term RfD; the effect on one thyroid hormone (tT4) served as the basis for the Short-Term RfD. A decrease in serum thyroid hormones is an effect consistently observed in other PFAS compounds.

An oral developmental study evaluated female mice exposed in utero to PFBS. Delays in vaginal opening and changes in estrus cycling as well as changes in uterine and ovarian size were reported. Pubertal and adult female offspring exhibited decreases in serum estrogen and progesterone levels with elevation of luteinizing hormone levels. Decreases in serum tT4 and T3 were observed in conjunction with slight increases in TSH in female offspring as well as their mothers. These effects all occurred at doses at least 1400-fold higher than the Short-Term RfD.

[2] MDH 2022; An study evaluated the association between 11 PFAS chemicals and immunological markers in children from Taiwan. Associations of several PFAS chemicals, including PFBS, with asthma and asthma related biomarkers were found. Associations for PFBS were fewer and weaker than those for several other PFAS chemicals. Concentrations of individual PFAS were positively correlated, and therefore it is not possible to determine whether associations apply to multiple PFASs or to only a subset of individual PFAS. A more recent study following a cohort of several hundred children in Shanghai, China found an association between PFBS concentration in maternal cord blood with increased frequency of respiratory tract infections and decreased IgG concentration in 5-year-old children, suggesting that pre/perinatal exposures to PFBS impacts future immune function in children.

No PFBS immunotoxicity studies have been conducted in laboratory animals. Immunotoxicity has been identified as a sensitive endpoint for several other PFAS. A database uncertainty factor of 3 was incorporated, in part, to address the need for immunotoxicity testing.

[3] MDH 2022; Two oral developmental studies (one in rats and one in mice) and a 2-generation study in rats have been conducted. The developmental effects reported in the mouse study included decreased pup body weight, decreased serum thyroid hormones, delayed eye opening, delayed vaginal opening and first estrus as well as smaller ovarian and uterine size in adult offspring. These effects were observed at doses 1400-fold higher than the Short-Term RfD. The developmental study in rats reported decreased fetal body weight at doses >14000-fold higher than the Short-term RfD. In the 2-generation study in rats, no developmental effects were identified at the highest dose tested (14000-fold higher than the Short-Term RfD). However, female rats excrete PFBS much more quickly than humans, which may limit the applicability of this 2-generation study. A database uncertainty factor of 3 was incorporated, in part, to address the lack of a 2-generation study in a more appropriate species.

[4] MDH 2022; Researchers examined the association between PFAS chemicals and endometriosis-related infertility among Chinese reproductive-age women in a case-control study. Women with endometriosis-related infertility had significantly higher median levels of PFBS compared with those without the disease. PFBS was the only PFAS identified with a significant positive association, while several other PFAS chemicals exhibited an inverse association. Limitations of this study include no identification of the time course, disease survey reported levels may not reflect actual exposure, and no physical exam data was measured for controls.

An oral 2-generation study in rats has been conducted. No treatment related effects on female reproductive parameters were noted. Decreased number of spermatids per gram testes (P0) and increased incidence of abnormal sperm (F1) were noted at HED dose levels 37000-fold higher than the Short-term RfD.

[5] MDH 2022; Neurological alterations were reported in the 28-day but not the 90-day oral study in adult rats. The results of the study are difficult to interpret. The longer study did not report any treatment related effects. The effects in the 28-day study occurred at HED dose levels 1400-fold higher than the Short-term RfD.

A database UF was incorporated, in part, to address the need for additional neurological testing, particularly in developmental life stages.

[6] No human studies reporting respiratory effects were found. Gavage doses of ≤900 mg/kg/d for 28 days resulted in no significant effect on gross or microscopic morphology of rat lung or trachea. Gavage dosing rats up to 600 mg/kg/d for 90 days also resulted in no effects to gross or microscopic lung or trachea morphology and no increases in nasal lesions.

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