Health Based Guidance for Air
Site Assessment and Consultation Unit
Environmental Health Division
651-201-4897

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Air Toxicological Summary for: PERFLUOROOCTANOIC ACID (PFOA)

CAS: 335-67-1
Synonyms: Perfluorooctanoate, PFOA

Air Exposure Durations:
Acute - 1-hour and/ or 24-hours
Intermediate - repeated dosing for more than 24-hours, up to approximately 1 year
Chronic - repeated dosing for greater than 1 year to a lifetime

In 2024, the Minnesota Department of Health's (MDH) Health Risk Assessment (HRA) Unit completed a re-evaluation of health-based guidance for PFOA in groundwater that focused on epidemiological data. The 2024 air risk assessment advice for PFOS is derived from the updated 2024 PFOS groundwater health-based guidance data.

Noncancer Acute Risk Assessment Advice (RAA_{Acute}) = Not Derived (Insufficient Data)

Noncancer Intermediate, Chronic RAA ($RAA_{Intermediate, Chronic}$) = 0.00091 µg/m^3

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

= 0.00000026 (mg/kg-d) x (70 kg/20 m^3-d) x (1000 µg/mg)

= 0.00091 µg/m^3

Reference Dose (RfD):	RfSC * CR = 0.00000026 mg/kg-d (human)
Source of toxicity value:	Determined by MDH in 2024
Reference Serum Concentration (RfSC):	POD/UF = 0.93 ng/mL
Clearance Rate (CR):	0.28 mL/kg-d (California EPA Office of Environmental Health Hazard Assessment 2023)
Point of Departure (POD):	2.8 ng/mL (equivalent to µg/L) serum concentration (California EPA Office of Environmental Health Hazard

	Assessment 2023), $BMDL_{5\%}$ for decreased haemophilus influenzae Type B (Hib) antibodies from (Abraham K 2020)
Dose Adjustment Factor (DAF):	Not applicable (POD is based on human serum level)
Human Equivalent Dose (HED):	Not applicable (POD is based on human serum level)
Total uncertainty factor (UF):	3
Uncertainty factor allocation:	A database UF of 3 was applied to account for remaining database uncertainties regarding potential adverse effects at or near the serum POD concentration (e.g., low birth weight, liver effects, thyroid effects). An UF for human toxicodynamic (TD) variability was not applied because the POD is based on a sensitive lifestage (i.e., young infants). Differences in human TK were determined to be adequately addressed through the exposure scenario and parameter values selected for use in the TK model.[#]
Critical effect(s):	Decreased antibody titers in infants
Co-critical effect(s):	Decreased antibody titers in children, decreased birthweight, increased cholesterol, increased ALT (liver enzyme)
Additivity endpoint(s):	Developmental, Hepatic (Liver) system, Immune system

[#]Further detail regarding the MDH HRA Unit's 2024 PFOA serum concentration and toxicokinetic model can be found on MDH's Human Health-Based Water Guidance Table's Toxicological Summary for Perfluorooctanoate: https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/pfoa2024.pdf

Cancer Risk Assessment Advice = Not Derived (insufficient data)

Cancer classification:	via oral route - Likely to be carcinogenic to humans (US EPA 2023a,b) (MDH 2023); Strong evidence of carcinogenicity (CalEPA Office of Environmental Health Hazard Assessment 2023); and Group 1 (carcinogenic to humans) (IARC 2023)
Tumor site(s):	via oral route - Human: Kidney (basis of guidance), Testicle Animal: Liver, Pancreas

Volatile: No

Summary of Guidance Value History: MDH previously developed air RAA for PFOA in 2021. The 2021 RAA was based on the 2020 MDH groundwater PFOA RfD.

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	Yes	Yes	Yes	Yes	Yes
Effects observed?	Yes[1]	Yes[2]	Yes[3]	Yes[4]	Yes[5]	Yes[6]

Comments on extent of testing or effects:

[1] MDH 2024; Evidence for endocrine effects in humans following PFOA exposure is largely based on increased TSH (thyroid stimulating hormone) and T3 (triiodothyronine) in adults and T4 (thyroxine) in children. However, findings in epidemiology studies were inconsistent, likely due in part to diurnal variations, differential effects across genders and age groups, timing of sampling, and limited number of studies. US EPA (2023) considers the current level of evidence for thyroid effects to be suggestive due to the uncertainty in results. A database uncertainty factor has been incorporated into the reference serum level to reflect the need for more data regarding thyroid effects.

Studies in laboratory animals have demonstrated clear alterations in serum thyroid hormone levels, increased thyroid gland weight, and increased follicular cell hypertrophy in the thyroid gland. Previous MDH guidance was based, in part, on thyroid effects in animals.

[2] MDH 2024; It is widely accepted that PFOA exposure is likely associated with reduced antibody response, especially in infants and children. An immune study in infants forms the basis of the PFOA reference serum concentration used to derive the 2024 nHBV. There is also limited supporting evidence of increased risk of asthma, eczema, and autoimmune disease.

In animal models, there is consistent evidence of decreased antibody response, decreased spleen and thymus weight, and alterations in immune cell function after PFOA exposure.

[3] MDH 2024; It is widely accepted that decreased birth weight is likely associated with maternal PFOA serum levels. This likely association is supported by additional epidemiological evidence of related effects such as decreased birth length and postnatal growth. In general, these effects have been reported around similar serum levels as effects on the immune system, which is the basis of the reference serum concentration.

Among the animal studies, decreased postnatal growth leading to developmental effects (e.g., lower pup body weight, delayed eye opening, delayed vaginal opening, and accelerated preputial separation)

have been observed. Delayed mammary gland development in female mice exposed in utero has also been reported at low dose levels.

[4] MDH 2024; The evidence for male reproductive effects in humans is limited and largely based on suggestive associations between PFOA exposure and testosterone levels in male children and adults and decreased anogenital distance in children. Considerable uncertainties in these associations exist due to inconsistencies across the limited number of studies available.

The evidence for female reproductive effects in humans is limited and largely based on suggestive associations between PFOA exposure and increased odds of preeclampsia, and changes to female reproductive milestones and female reproductive hormonal outcomes. Considerable uncertainties in these associations exist due to inconsistencies across studies and the limited number of available studies. In general, these effects have been reported at doses somewhat higher than effects on the immune system, birth weight, and liver effects.

Among the animal studies, there was no effect of PFOA on reproductive or fertility parameters in female rats. However, it should be noted that female rats have a very high PFOA elimination rate compared to male rats or other species. Increased full litter resorptions and increased stillbirths were observed in pregnant mice exposed to doses resulting in very high serum concentrations. No evidence of altered testicular and sperm structure or function was reported in adult male rats exposed to doses producing high serum concentrations. Increased sperm abnormalities and decreased testosterone were reported at high serum concentrations.

[5] MDH 2024; The evidence for effects on the nervous system in humans is limited and largely based on neurodevelopment, including neuropsychological and cognitive development, executive function, and behavioral problems. There are considerable uncertainties due to inconsistency in magnitude and direction of effects across the limited number of studies available.

Information from animal studies is also quite limited. The offspring of mice fed PFOA throughout gestation had detectable levels of PFOA in their brains at birth. Locomotor activity, anxiety-related or depression-like behavior, and muscle strength were not altered. Circadian activity tests revealed sex-related differences in exploratory behavior patterns.

[6] PFOA studies investigated respiratory effects are limited in animals. Reported acute effects included excessive salivation and eye and nose irritation in rats exposed to 18,600 mg/m^3 for one hour and weight loss and pulmonary edema (disappeared within one week of exposure) in rats exposed to 380 mg/m^3 for four hours. No changes to the lungs or trachea were reported from rats exposed head-only to up to 84 mg/m^3 ammonium perfluorononanoate (APFO) dusts 6 hours/day, 5 days/week for two weeks. Male CD rats exposed nose-only to ≥590 mg/m^3 APFO for four hours exhibited lung noise and labored breathing during exposure and throughout a 12-day recovery period. A monkey study

exposure to APFO via up to 20 mg/kg/d via capsule for 26 weeks reported no sign of respiratory issues or gross or microscopic effects in the lungs and trachea.

Pulmonary function tests and chest roentgenograms conducted on workers potentially exposed to PFOA at the Washington Works fluoropolymers production facility were within normal limits. Another study of workers at this facility did not find an association between estimated cumulative serum PFOA levels and the risk of chronic obstructive pulmonary disease; however, residents living near the facility had an increased risk of chronic bronchitis and shortness of breath (based on health surveys).

References and Resources Consulted

A comprehensive reference list can be found on the health-based guidance for water 2024 PFOA toxicological summary: www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/pfoa.pdf

Abraham K, Mielke H, Fromme H, Völkel W, Menzel J, Peiser M, Zepp F, Willich SN, Weikert C. 2020. "Internal exposure to perfluoroalkyl substances (PFASs) and biological markers in 101 healthy 1-year-old children: associations between levels of perfluorooctanoic acid (PFOA) and vaccine response." *Arch Toxicol*. 94: 2131-2147

Agency for Toxic Substances and Disease Registry (ATSDR). 2021. Toxicological Profile for Perfluoroalkyls. https://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf

California EPA Office of Environmental Health Hazard Assessment. 2023. Public Health Goals, Second Public Review Draft: Perfluorooctanoic Acid and Perfluorooctane Sulfonic Acid in Drinking Water.

Goeden, H. M., Greene, C. W., & Jacobus, J. A. 2019. A transgenerational toxicokinetic model and its use in derivation of Minnesota PFOA water guidance. *Journal of Exposure Science & Environmental Epidemiology*. https://doi.org/10.1038/s41370-018-0110-5

Michigan Dept of Environment, Great Lakes, and Energy. 2018. File for Perfluorooctanoic Acid (PFOA) Cas No. 335-67-1. http://www.deq.state.mi.us/aps/downloads/ATSL/335-67-1/335-67-1_24hr_ITSL.pdf

Minnesota Department of Health. 2001. Statement of Need and Reasonableness; Proposed Permanent Rules Relating to Health Risk Values Minnesota Rules, Parts 4717.8000 to 4717.8600. https://www.health.state.mn.us/communities/environment/risk/docs/rules/hrvsonar.pdf

Minnesota Department of Health. 2024. Toxicological Summary for Perfluorooctanoate. www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/pfoa2024.pdf

New Jersey Department of Environmental Protection. December 19, 2019. Memo--Evaluation of Michigan Department of Environmental Quality's derivation of Initial Threshold Screening Levels for Inhalation Exposure to PFOA and PFOS.

US EPA. 1994. Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry. EPA/600/8-90/066F. https://www.epa.gov/sites/production/files/2014-11/documents/rfc_methodology.pdf

US EPA. 2005. Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001F. March 2005. https://www.epa.gov/sites/default/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf