

Adopted as Rule: August 2025

Toxicological Summary for: Perfluorooctanoate

CAS: **45285-51-6 (anion)**
335-67-1 (free acid)
3825-26-1 (ammonium salt, APFO)
2395-00-8 (potassium salt)
335-95-5 (sodium salt)
335-93-3 (silver salt)

DTXSID: DTXSID40892486

Synonyms: PFOA; 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluorooctanoic acid (IUPAC name);
Perfluorooctanoic acid (free acid)

In 2024, the Minnesota Department of Health (MDH) completed a re-evaluation of PFOA that focused on epidemiological data. Recent reviews from the European Food Safety Authority, California Environmental Protection Agency, US Environmental Protection Agency, and National Academies of Sciences, Engineering, and Medicine were utilized as resources. Many toxicity studies in laboratory animals also exist; however, the points of departure are significantly higher than those identified in epidemiology studies. MDH also conducted a literature search for epidemiological studies published between 2021 and December 2022, which focused on potential sensitive endpoints (e.g., development, immune, thyroid), to capture information that postdated the reviews by the agencies listed above. In 2026, MDH updated this document to include a reference to Greene 2024, a publication describing a revised toxicokinetic model developed to derive this guidance.

Short-term, Subchronic, and Chronic Noncancer Health Risk Limit (nHRL) = 0.00024 µg/L (equivalent to 0.24 ng/L or ppt)*

*Due to the highly bioaccumulative nature of PFOA, serum concentrations are the most appropriate dose metric. PFOA has a half-life of approximately 2.5 years, and the bioaccumulated levels within women of reproductive age can be passed on to fetuses and infants through placental and breastmilk transfer. The standard equation used to derive health-based values (HBVs) is not adequate to address the bioaccumulative nature nor the maternal transfer of PFOA. Since 2017, a single PFOA HBV for all durations has been derived using a toxicokinetic (TK) model developed by MDH (Goeden 2019), which assesses a formula-fed infant scenario as well as a breastfed infant scenario. The TK model accounts for the bioaccumulation and maternal transfer of PFOA and more accurately represents real-world exposure scenarios. MDH typically calculates HBVs at the part per billion level with the final concentration rounded to one significant digit. However, serum concentrations are impacted by changes in water concentrations at the part per trillion (ppt) level. As a result, the final PFOA HRL in rule is expressed with two significant digits.

Reference Serum Concentration:	POD/Total UF = 2.8/3 = 0.93 ng/mL (human) <i>This serum level was developed using population-based data and should not be used for clinical assessment or interpreting serum levels in individuals.</i>
Source of toxicity value:	Determined by MDH in 2024
Point of Departure (POD):	2.8 ng/mL (equivalent to $\mu\text{g}/\text{L}$) 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

[#]The POD is based on serum levels in one-year old infants, of whom nearly 80% were exclusively breastfed for at least 4 months. Very little information is available regarding PFOA half-life in infants. To evaluate the potential impact of TK variability, an upper-bounding scenario, in which all model parameters were set to upper percentile values, was evaluated. The maternal, peak infant, and lifetime steady-state serum levels produced by the upper-bounding scenario were <3-fold higher than MDH's selected Reasonable Maximum Exposure (RME) scenario. Since the upper-bounding scenario is considered worst-case and is very unlikely to represent a realistic scenario, the incorporation of an UF to address human TK variability was considered unnecessary. MDH's RME model parameter values used to derive the noncancer water guidance is considered adequately protective of the general population.

Toxicokinetic Model Description (Goeden 2019; Greene 2024):

Serum concentrations can be calculated from the dose and clearance rate using the following equation:

$$\text{Serum Concentration} \left(\frac{\mu\text{g}}{\text{L}} \right) = \frac{\text{Fluid IntakeRate} \left(\frac{\text{L}}{\text{kg} \cdot \text{day}} \right) \times \text{Fluid Concentration} \left(\frac{\mu\text{g}}{\text{L}} \right)}{\text{Clearance Rate} \left(\frac{\text{L}}{\text{kg} \cdot \text{day}} \right)}$$

Where:

Clearance Rate = Volume of Distribution (L/kg body weight) x (Ln2/half-life in days)

Two exposure scenarios were examined: 1) an infant fed with formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water throughout life; and 2) an infant exclusively breastfed for 12 months, followed by drinking contaminated water. In both scenarios, the simulated individuals began life with a pre-existing body burden through placental transfer. The serum concentration of the mother was calculated to be at steady state at the time of delivery, using the equation presented above and a time-weighted average (TWA) 95th percentile intake rate from birth to 30 years of age (sufficient time to attain steady-state).

Consistent with MDH methodology, a 95th percentile water and upper percentile (2 standard deviations above mean) breastmilk intake rates were used along with central tendency estimates for half-life, placental transfer, and breastmilk transfer. Breastmilk concentrations are calculated by multiplying the maternal serum concentration by a PFOA breastmilk transfer factor. For the breastfed exposure scenario, a one-year period of breastfeeding is used as representative of an RME scenario.

Daily post-elimination serum concentrations were calculated as:

$$\text{Serum Concentration} \left(\frac{\mu\text{g}}{\text{L}} \right) = \left[\frac{\text{Previous day} + \text{Today's Intake}(\mu\text{g})}{V_d \left(\frac{\text{L}}{\text{kg}} \right) \times \text{BW}(\text{kg})} \right] \times e^{-k}$$

Where:

V_d = volume of distribution

BW = body weight

e^{-k} = represents clearance

Note: MDH has made several improvements to the TK model published in 2019 (Goeden 2019), including the following:

- The PFOA mass transferred to the infant is now subtracted from the maternal steady-state concentration on day 0 (the day of delivery).
- The daily calculation of the infant's serum concentration is now fully mass-based by adjusting both the current day as well as the previous day's intake by the current day's body weight.
- Maternal lactation was phased in over the first four days of lactation based on data from Neville 1991.
- Water intakes, breastmilk intakes, and body weights were updated with more current information.
- Chemical-specific parameter values (i.e., clearance, half-life, placental transfer, breastmilk transfer, and volume of distribution) were updated to include literature information up to December 2022.

These improvements are detailed further in Greene 2024.

Summary of TK Model Parameter Values Used to Derive Non-Cancer HRL for PFOA

Model Parameter	Value Used
Half-life ($t_{1/2}$)	Central Tendency = 902 days (2.47 years) Mean value from (Li 2022) The TK model estimates serum levels from birth to approximately 50 years of age. Critical lifestage is <4 years of age for which serum half-life information is not available. The overall mean was used for the RME scenario. A 95 th percentile half-life value of 5.4 years was used in the upper-bounding scenario evaluation.
Placental transfer	Central Tendency = 0.83 (mean of mean values from 25 studies) The mean upper percentile value (1.39) was selected as an upper-end value for the upper-bounding scenario evaluation.

Model Parameter	Value Used																																													
Breastmilk transfer	<p>Central Tendency = 0.068 (95th upper confidence limit (UCL) of the mean from 7 studies). Validation testing of model infant serum predictions indicated that use of the overall mean of the 7 studies (0.046) resulted in underestimating breastfed infant serum levels whereas the 95th UCL did not. A value of 0.12 was used as representative of an upper-end value for the upper-bounding scenario evaluation.</p>																																													
Breastmilk Intake Rate (mL/kg-day) and corresponding Body Weight (kg)	<p>Upper Percentile intake for exclusively¹ breastfed infants ((US EPA 2011), Table 15-1). Body weight at birth was set at 3.38 kg (Donahue 2010). Remaining body weights (kg) were calculated from data presented in US EPA's Table 15-1 for each age group (i.e., mL/day ÷ mL/kg-day):</p> <table border="1" data-bbox="430 494 1176 724"> <thead> <tr> <th data-bbox="430 494 584 530">Age Group</th><th data-bbox="584 494 910 530">Intake Rate (mL/kg-d)</th><th data-bbox="910 494 1176 530">Body Weight (kg)</th></tr> </thead> <tbody> <tr> <td data-bbox="430 544 584 580">>Birth to <1 month</td><td data-bbox="584 544 910 580">220</td><td data-bbox="910 544 1176 580">4.3</td></tr> <tr> <td data-bbox="430 595 584 631">1 to < 3 months</td><td data-bbox="584 595 910 631">190</td><td data-bbox="910 595 1176 631">5.2</td></tr> <tr> <td data-bbox="430 646 584 682">3 to < 6 months</td><td data-bbox="584 646 910 682">150</td><td data-bbox="910 646 1176 682">6.7</td></tr> <tr> <td data-bbox="430 696 584 732">6 to < 12 months</td><td data-bbox="584 696 910 732">130</td><td data-bbox="910 696 1176 732">7.7</td></tr> </tbody> </table>	Age Group	Intake Rate (mL/kg-d)	Body Weight (kg)	>Birth to <1 month	220	4.3	1 to < 3 months	190	5.2	3 to < 6 months	150	6.7	6 to < 12 months	130	7.7																														
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Duration (months) of Breastfeeding	<p>Upper percentile = 12 months (Breastfeeding Report Card for 2022 (CDC 2022)) reporting that nearly 70 percent of mothers in Minnesota report breastfeeding at six months, with 36.5 percent still exclusively breastfeeding at six months.</p>																																													
Water Intake Rate (mL/kg-day)	<p>Upper Percentile Intake = Formula-fed infants (up to 2 years old, Table 3-5); for >2 years of age values (Table 3-1); and for lactating women (Table 3-3) (US EPA 2019) were used. Body weights (kg) were calculated from data presented in the aforementioned EPA tables (i.e., mL/day ÷ mL/kg-day):</p> <table border="1" data-bbox="430 1043 1416 1797"> <thead> <tr> <th data-bbox="430 1043 714 1079">Age Group</th><th data-bbox="714 1043 1057 1079">Intake Rate (mL/kg-d)</th><th data-bbox="1057 1043 1416 1079">Body Weight (kg)</th></tr> </thead> <tbody> <tr> <td data-bbox="430 1094 714 1129"><1 month</td><td data-bbox="714 1094 1057 1129">240</td><td data-bbox="1057 1094 1416 1129">3.6</td></tr> <tr> <td data-bbox="430 1144 714 1180">1 to < 3 months</td><td data-bbox="714 1144 1057 1180">290</td><td data-bbox="1057 1144 1416 1180">3.8</td></tr> <tr> <td data-bbox="430 1195 714 1231">3 to < 6 months</td><td data-bbox="714 1195 1057 1231">186</td><td data-bbox="1057 1195 1416 1231">7.0</td></tr> <tr> <td data-bbox="430 1246 714 1281">6 to < 12 months</td><td data-bbox="714 1246 1057 1281">151</td><td data-bbox="1057 1246 1416 1281">8.9</td></tr> <tr> <td data-bbox="430 1296 714 1332">1 to < 2 years</td><td data-bbox="714 1296 1057 1332">119</td><td data-bbox="1057 1296 1416 1332">10.5</td></tr> <tr> <td data-bbox="430 1347 714 1383">2 to < 3 years</td><td data-bbox="714 1347 1057 1383">67</td><td data-bbox="1057 1347 1416 1383">13.4</td></tr> <tr> <td data-bbox="430 1398 714 1434">3 to < 6 years</td><td data-bbox="714 1398 1057 1434">45</td><td data-bbox="1057 1398 1416 1434">18.6</td></tr> <tr> <td data-bbox="430 1448 714 1484">6 to < 11 years</td><td data-bbox="714 1448 1057 1484">41</td><td data-bbox="1057 1448 1416 1484">30.7</td></tr> <tr> <td data-bbox="430 1499 714 1535">11 to < 16 years</td><td data-bbox="714 1499 1057 1535">31</td><td data-bbox="1057 1499 1416 1535">56.8</td></tr> <tr> <td data-bbox="430 1550 714 1586">16 to < 21 years</td><td data-bbox="714 1550 1057 1586">31</td><td data-bbox="1057 1550 1416 1586">71.4</td></tr> <tr> <td data-bbox="430 1600 714 1636">21 to < 30 years</td><td data-bbox="714 1600 1057 1636">47</td><td data-bbox="1057 1600 1416 1636">72.5</td></tr> <tr> <td data-bbox="430 1651 714 1687">30 to < 40 years</td><td data-bbox="714 1651 1057 1687">44</td><td data-bbox="1057 1651 1416 1687">74.5</td></tr> <tr> <td data-bbox="430 1702 714 1738">40 to < 50 years</td><td data-bbox="714 1702 1057 1738">43</td><td data-bbox="1057 1702 1416 1738">78.5</td></tr> <tr> <td data-bbox="430 1752 714 1788">50 to < 60 years</td><td data-bbox="714 1752 1057 1788">42</td><td data-bbox="1057 1752 1416 1788">80.7</td></tr> </tbody> </table> <p>For calculation of maternal serum concentration at time of delivery, a time-weighted average water intake rate was calculated from birth to 30 years of age, resulting in a 95th percentile water intake rate of 48 mL/kg-day.</p>	Age Group	Intake Rate (mL/kg-d)	Body Weight (kg)	<1 month	240	3.6	1 to < 3 months	290	3.8	3 to < 6 months	186	7.0	6 to < 12 months	151	8.9	1 to < 2 years	119	10.5	2 to < 3 years	67	13.4	3 to < 6 years	45	18.6	6 to < 11 years	41	30.7	11 to < 16 years	31	56.8	16 to < 21 years	31	71.4	21 to < 30 years	47	72.5	30 to < 40 years	44	74.5	40 to < 50 years	43	78.5	50 to < 60 years	42	80.7
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Model Parameter	Value Used
Volume of Distribution (L/kg)	<p>Central Tendency = 0.36 (calculated from human clearance rate of 0.28 mL/kg-d (California EPA Office of Environmental Health Hazard Assessment 2023)) and the mean half-life of 902 days (Li 2022):</p> $CR \div (\ln 2 / \text{half-life}) = V_d$ $0.28 \text{ mL/kg-d} \div (\ln 2 / 902 \text{ d}) = 364 \text{ mL/kg or rounded to 0.36 L/kg}$

¹Note: Exclusively breastfed as defined by (US EPA 2011) refers to infants whose sole source of milk is breastmilk and not formula. Exclusively breastfed infants in the studies underlying these USEPA estimates were not excluded from other foods, typically after six months. This definition differs from other sources, which may define exclusive breastfeeding as breastmilk being the only source of nourishment (solid or liquid).

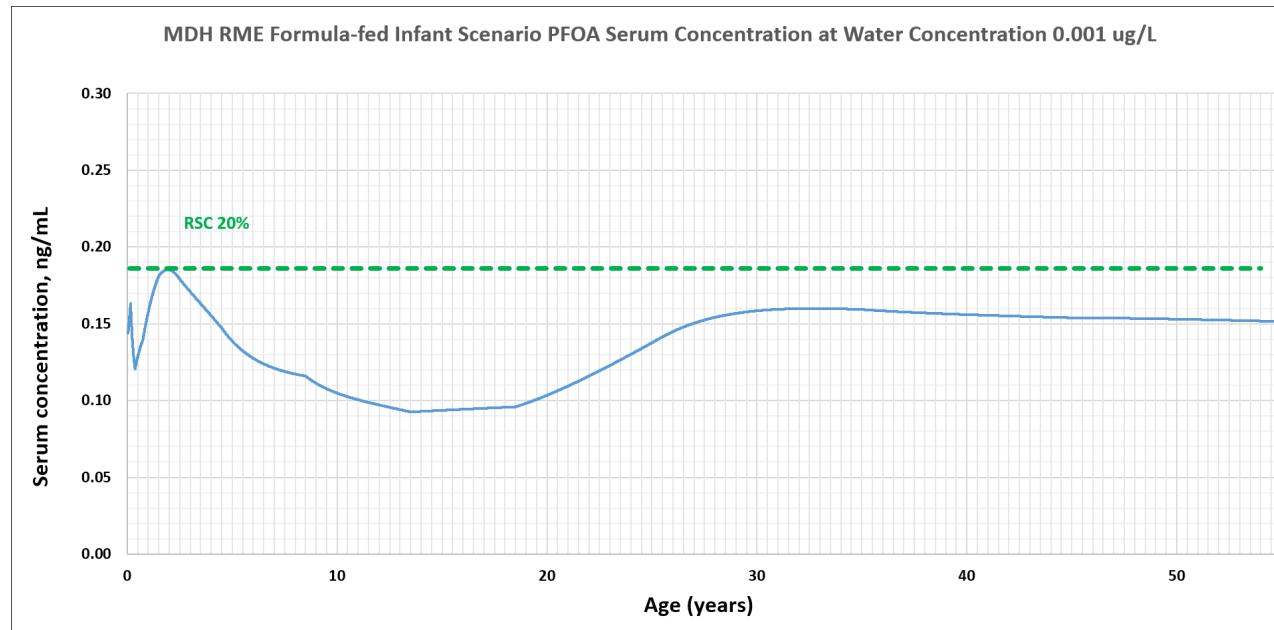
A relative source contribution factor (RSC) is incorporated into the derivation of HRL values to account for exposure sources other than drinking water. MDH utilizes the US EPA 2000 Exposure Decision Tree process to derive appropriate RSCs. The default duration-specific RSCs (0.5, 0.2, and 0.2 for short-term, subchronic and chronic, respectively) are based on the magnitude of contribution of non-drinking water exposures that occur during the relevant exposure duration (Minnesota Department of Health (MDH) 2008). However, in the case of PFOA, application of an RSC needs to account for the long elimination half-life, such that a person's serum concentration at any given age/duration is not only the result of current or recent exposures but also from years past and/or maternal transfer.

Serum concentrations are the best measure of cumulative exposure for PFOA and can be used in place of the reference dose in the Exposure Decision Tree process. Biomonitoring results for the general public reported in the most recent National Report on Human Exposure to Environmental Chemicals (CDC 2021) can be used to represent non-water exposures for older children and adults. The reference serum concentration is 0.93 ng/mL. Both the geometric mean (1.42 ng/mL) and the 95th percentile (3.77 ng/mL) PFOA serum concentration from the most recently available National Report exceed the reference serum concentration. Based on placental transfer data, newborn infants would have PFOA body burdens similar to their mothers. Even at low levels of exposure, PFOA would accumulate in women of reproductive age. Studies assessing young infants (e.g., <6 months of age) who are exclusively breastfed exhibit serum levels that are approximately 3-fold higher than their mothers (e.g., (Fromme 2010), (Gyllenhammar 2018)). It is likely that infants will have similar or, in the case of breastfed infants, higher serum concentrations than their mothers. Consequently, the RSC is set at the floor value of 20% for all life stages.

As mentioned above, two RME scenarios were examined: 1) an infant fed formula reconstituted with contaminated water starting at birth and continuing consumption of contaminated water throughout life; and 2) an infant exclusively breastfed for 12 months by a chronically-exposed mother, followed by consumption of contaminated water throughout life.

For the formula-fed infant, the water concentration that maintains a serum concentration attributable to drinking water below an RSC of 20% throughout life is 0.0010 µg/L (equivalent to 1.0 ng/L or ppt) (Figure 1).

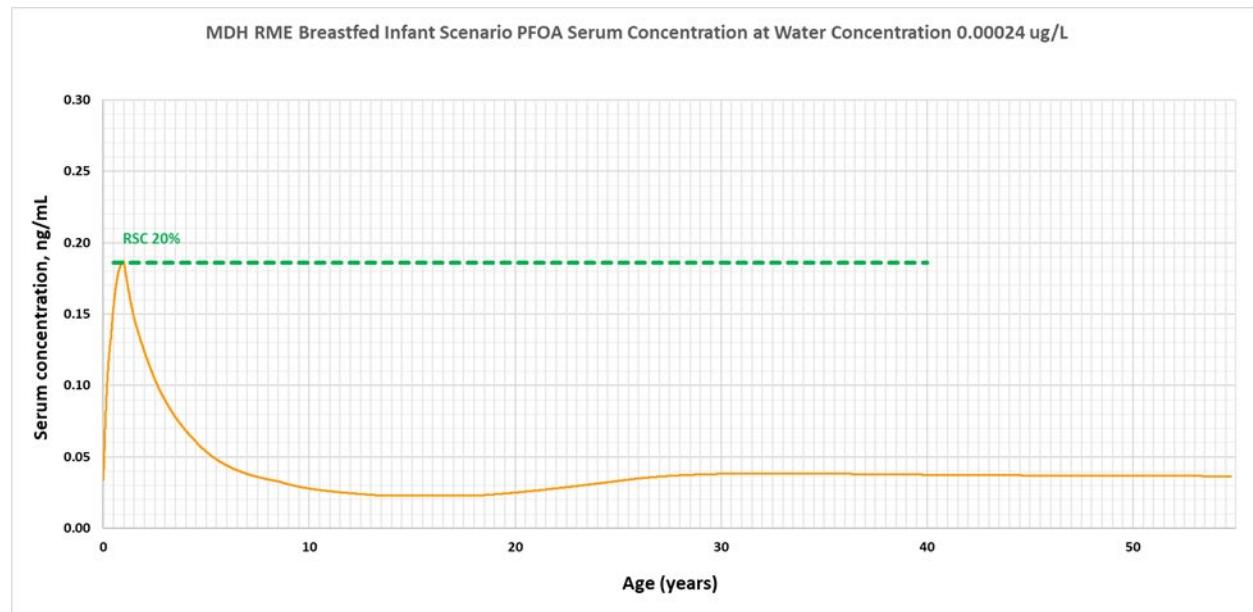
Figure 1. MDH RME Formula-fed Infant Scenario PFOA Serum Concentration at Water Concentration 0.001 ug/L



A sharp decrease in the formula-fed infant serum levels between the 1 to < 3 month and 3 to <6 months is noted. The formula-fed infant water intake drops from 290 to 186 mL/kg-d as body weight increases from 3.8 to 7 kg across the same time period.

Applying this water concentration (1 ng/L) in the context of a breastfed infant results in peak infant serum concentrations that significantly exceed the RSC of 20%. In order to maintain a serum concentration at or below an RSC of 20% for the breastfed infant scenario, the water concentration should not exceed 0.00024 μ g/L (or 0.24 ng/L or ppt) (Figure 2).

Figure 2. MDH RME Breastfed Infant Scenario PFOA Serum Concentration at Water Concentration 0.00024 μ g/L



Due to bioaccumulation in the mother and subsequent transfer to breastmilk, the breastfed infant exposure scenario produces the lower PFOA water concentration. To ensure protection of all segments of the population, the final noncancer HRL for PFOA is set at 0.00024 µg/L (0.24 ng/L).

Cancer Health Risk Limit (cHRL) = 0.0000079 µg/L (0.0079 ng/L or ppt)

(Additional Lifetime Cancer Risk) x (Conversion Factor)

$$[(SF \times ADAF<2 \text{ yr} \times IR<2\text{yr} \times 2) + (SF \times ADAF2-<16 \text{ yr} \times IR2-<16\text{yr} \times 14) + (SF \times ADAF16+ \text{ yr} \times IR16+\text{yr} \times 54)] / 70$$

$$= \frac{(1E-5) \times (1 \text{ µg}/1000 \text{ ng})}{[(0.0126 \times 10^* \times 0.155 \text{ L/kg-d}^{**} \times 2) + (0.0126 \times 3^* \times 0.040 \text{ L/kg-d}^{**} \times 14) + (0.0126 \times 1^* \times 0.042 \text{ L/kg-d}^{**} \times 54)] / 70}$$

= 0.0000079 µg/L (same as 0.0079 ng/L or ppt)

*Age-dependent adjustment factor (ADAF) and Lifetime Adjustment Factor: MDH 2008, Section IV.E.2. ADAFs were maintained because the cohort from the critical cancer study was unlikely to have early-life exposure to PFOA.

**Intake Rate: MDH 2008, Section IV.E.2. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3, and 3-5.

Cancer classification: 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)

Slope factor (SF): 0.0126 per ng/kg-day (renal cell carcinoma in humans) (Shearer JJ 2021)

Source of cancer slope factor (SF): Serum slope factor 0.00325 per ng/mL from (US EPA 2023a,b) converted to 0.0126 per ng/kg-d using a clearance rate of 0.28 mL/kg-d (CalEPA Office of Environmental Health Hazard Assessment 2023)

Tumor site(s): Human: Kidney (basis of guidance), Testicle
Animal: Liver, Pancreas

Volatile: No

Summary of Guidance Value History:

A chronic nHBV of 7 µg/L was first derived in 2002. A revised chronic nHBV of 0.3 µg/L was derived in 2007 and promulgated as a noncancer HRL (nHRL) in 2009. In 2016, EPA released a Health Advisory of 0.07 µg/L for PFOA, which MDH recommended on an interim basis while a re-evaluation was conducted. As a result of the re-evaluation, which incorporated the most recent toxicological information and included the application of the TK model, the 2017 nHBV decreased to 0.035 µg/L for all nonacute durations. The 2017 guidance was adopted as a HRL in 2018. In 2020, MDH classified PFOA as “likely to be carcinogenic at high doses” and added Thyroid (E) and Pancreas as Additivity Endpoints. The 2024 nHBV of 0.00024 µg/L (0.24 ng/L) was lower than previous values as the result of: 1) utilizing epidemiological data as the basis for the POD; and 2) updating the toxicokinetic model, including more recent data on placental and breastmilk transfer. The 2024 cancer HBV of 0.0000079 µg/L (0.0079 ng/L) was a new value, and MDH has revised their

cancer classification to “likely to be carcinogenic”. In August 2025, the HBVs were adopted into Minnesota Rules, Part 4717.7860 as HRLs, and the previous 2018 HRL was repealed from Minnesota Rules, Part 4717.7860.

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	Yes	Yes	Yes	Yes
Effects observed?	Yes ¹	Yes ²	Yes ³	Yes ⁴	Yes ⁵

Comments on extent of testing or effects:

[Note: MDH conducted a re-evaluation that focused on epidemiological data and sensitive health endpoints.]

¹ 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 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 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 prepuberal

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

⁴ 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 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.

Resources Consulted During Review:

1. AAP (2012). "(American Academy of Pediatrics) Breastfeeding and the Use of Human Milk." *Pediatrics*. 129(3).
2. 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.
3. Abraham K, Monien BH. (2022). "Transdermal absorption of ¹³C₄-perfluorooctanoic acid (¹³C₄-PFOA) from a sunscreen in a male volunteer – What could be the contribution of cosmetics to the internal exposure of perfluoroalkyl substances (PFAS)?" *Environ Int.* 169: 107549.
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