



Adopted as Rule: November 2023

## Toxicological Summary for: Perfluorohexane sulfonate

CAS: 108427-53-8 (anion)

355-46-4 (acid)

3871-99-6 (potassium salt)

Synonyms: PFHxS; perfluorohexanesulfonic acid; 1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorohexane-1-sulfonate

### Short-term, Subchronic and Chronic\* Non-Cancer Health Risk Limit (nHRL) = 0.047 µg/L\*\*

\*Due to the highly bioaccumulative nature of PFHxS within the human body, serum concentrations are the most appropriate dose metric and the standard equation to derive the HRL is not appropriate. Short-term exposures have the potential to stay in the body for an extended period of time. In addition, accumulated maternal PFHxS is transferred to offspring (i.e., placental and breastmilk transfer). A single HRL has therefore been recommended for short-term, subchronic, and chronic durations. The HRL was derived using a toxicokinetic (TK) model previously developed by MDH (Goeden 2019). Model details and results are presented below.

\*\*Relative Source Contribution (RSC): Using the most recent published biomonitoring results (CDC, accessed February 2019) and USEPA's Exposure Decision Tree (USEPA 2000) as outlined in MDH 2008, Section IV.E.1., an RSC of 0.5 (50%) was selected for the peak serum concentration during infancy. The RSC of 0.5 during infancy resulted in chronic (steady-state) serum concentrations at approximately 0.2 of the 'reference' serum concentration.

Intake Rate: In keeping with MDH's peer-reviewed and promulgated methodology, 95<sup>th</sup> percentile water intake rates (Table 3-1, 3-3 and 3-5, USEPA 2019) or upper percentile breastmilk intake rates (Table 15-1, USEPA 2011) were used. Breastmilk concentrations were calculated by multiplying the maternal serum concentration by a PFHxS breastmilk transfer factor of 1.4%. For the breast-fed infant exposure scenario, a period of exclusive breastfeeding for one year was used as representative of a reasonable maximum exposure scenario. [Note: "exclusively breast-fed" intake rates refers to infants whose sole source of milk comes from human breastmilk, with no other milk substitutes (USEPA 2011, page 15-2).]

A simple equation is typically used to calculate HRLs at the part per billion level with results rounded to one significant digit. However, the toxicokinetic model used to derive the HRL for PFHxS showed that serum concentrations are impacted by changes in water concentrations at the part per trillion level. As a result, the HRL contains two digits.

Reference Dose/Concentration:  $HED/Total\ UF = 0.00292/300 = 0.0000097\ mg/kg-d$  (or 9.7 ng/kg-d) (adult Sprague Dawley rats). [The corresponding serum concentration is  $32.4/300 = 0.108\ \mu g/mL$ . Note: this serum concentration is inappropriate to use for individual or clinical assessment.\*\*\*]

Source of toxicity value: Determined by MDH in 2019  
Point of Departure (POD): 32.4 µg/mL (or mg/L) serum concentration (male rats - NTP 2018, MDH modeled BMDL<sub>20%</sub>)

Dose Adjustment Factor (DAF): Toxicokinetic Adjustment based on Chemical-Specific Clearance Rate = Volume of Distribution (L/kg) x (Ln2/Half-life, days) = 0.25 L/kg x (0.693/1935 days) = 0.000090 L/kg-day. (Half-life from Li et al 2018)

Human Equivalent Dose (HED):  $POD \times DAF = 32.4 \text{ mg/L} \times 0.000090 \text{ L/kg-d} = 0.00292 \text{ mg/kg-d}$

Total uncertainty factor (UF): 300

Uncertainty factor allocation: 3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty to address concerns regarding early life sensitivity to decreased thyroxine (T4) levels as well as lack of 2 generation or immunotoxicity studies.

Critical effect(s): decreased free T4

Co-critical effect(s): decreased free and total T4, triiodothyronine (T3), and changes in cholesterol levels and increased hepatic focal necrosis

Additivity endpoint(s): Hepatic (Liver) System and Thyroid (E)

\*\*\*The serum concentration is useful for informing public health policy and interpreting population-based exposure potential. This value is based on population-based parameters and should not be used for clinical assessment or for interpreting serum levels in individuals.

Toxicokinetic Model Description (Goeden 2019):

PFHxS is well absorbed and is not metabolized. Serum concentrations can be calculated from the dose and clearance rate using the following equation.

$$\text{Serum Concentration} \left( \frac{\text{mg}}{\text{L}} \right) = \frac{\text{Dose} \left( \frac{\text{mg}}{\text{kg} \cdot \text{day}} \right)}{\text{Clearance} \cdot \text{Rate} \left( \frac{\text{L}}{\text{kg} \cdot \text{day}} \right)}$$

Where:

$\text{Dose} (\text{mg/kg-day}) = \text{Water or Breastmilk Intake} (\text{L/kg-day}) \times \text{Water or Breastmilk Concentration} (\text{mg/L})$   
 and  
 $\text{Clearance} (\text{L/kg-day}) = \text{Volume of distribution} (\text{L/kg}) \times (\text{Ln } 2/\text{human half-life, days})$

Two exposure scenarios were evaluated: 1) an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life; and 2) an infant exclusively breast-fed 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 of PFHxS (maternal serum concentration x 70%) based on median cord to maternal serum concentration ratios reported in the literature. The serum concentration of the mother at delivery was assumed to be at steady-state and was calculated by using the equation above with a time-weighted 95<sup>th</sup> percentile intake from birth to 30 years of age (0.048 L/kg-d). During lactation a 95<sup>th</sup> percentile water intake rate

of 47 mL/kg-d and a body weight of 65.1 kg ((USEPA 2019), Table 3-3) was used to calculate daily maternal serum concentrations.

Consistent with MDH methodology, 95<sup>th</sup> percentile water intake and upper percentile breastmilk intake rates were used to simulate a reasonable maximum exposed individual. A PFHxS breastmilk transfer factor of 1.4%, based on average breastmilk to maternal serum concentration ratios reported in the literature, was used to calculate breastmilk concentration. According to the 2016 Breastfeeding Report Card (CDC, 2016), nearly 66 percent of mothers in Minnesota report breastfeeding at six months, dropping to 41% at twelve months. MDH chose to use the breastmilk intake rates for exclusively breastfed infants, as reported in USEPA 2011, for one year for the breast-fed infant scenario.

Daily post-elimination serum concentration was calculated as:

$$\text{Serum Conc.} \left( \frac{\text{mg}}{\text{L}} \right) = \left[ \text{Prev. day Serum Conc.} \left( \frac{\text{mg}}{\text{L}} \right) + \frac{\text{Today's Intake}(\text{mg})}{V_d \left( \frac{\text{L}}{\text{kg}} \right) \times \text{BW}(\text{kg})} \right] \times e^{-k}$$

To maintain mass balance, daily maternal serum concentrations and loss-of-chemical via transfer to the infant as well as excretion represented by the clearance rate, were calculated.

#### Summary of Reasonable Maximum Exposure (RME) Scenario Model Parameters

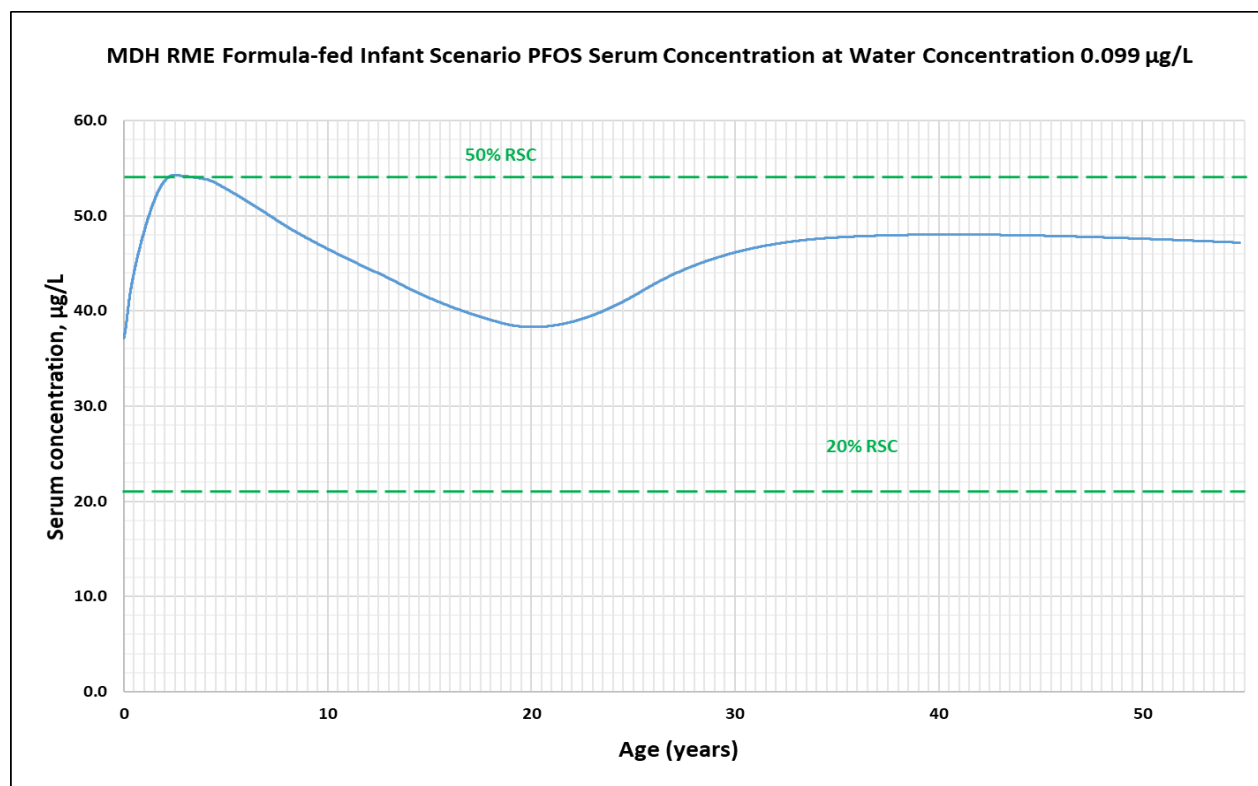
Model Parameter	Value Used
Volume of distribution (Vd)	0.25 L/kg (average of male (0.287) and female (0.213) nonhuman primate Vd, Sundstrom, 2012)
Vd Age Adjustment Factor	2.1 age 1-30 days decreasing to 1.2 age 5-10 years and 1.0 after age 10 years (Friis-Hansen 1961)
Half-life	1935 days (mean value for all ages, Li et al 2018) (5 <sup>th</sup> to 95 <sup>th</sup> percentile range: 1095 – 3358 days)
Elimination rate constant (k)	Calculated from Ln 2/half-life
Placental transfer factor (% of maternal serum level)	70% (mean of median paired maternal:cord blood ratios reported in the literature. Range of mean values 43 – 95%.) (Mean 95 <sup>th</sup> percentile value 110%, range 69 – 168%.)
Breastmilk transfer factor (% of maternal serum level)	1.4% (mean of mean paired maternal serum:breastmilk ratios reported in the literature. Range of mean values 0.8 – 2%.) (No 95 <sup>th</sup> percentile values reported in literature.)
Water Intake Rate (L/kg-d)	95 <sup>th</sup> percentile consumers only (default values, MDH 2008) (Table 3-1 (for ages ≥ 2 yrs), 3-3 (for lactating women), and 3-5 (for ages < 2yr)) (USEPA 2019)
Breastmilk Intake Rate (L/kg-d)	Upper percentile exclusively breast-fed infants (Table 15-1, USEPA 2011)
Body weight (kg)	Calculated from water intake and breastmilk intake rate tables

A relative source contribution factor (RSC) is incorporated into the derivation of a health-based water guidance value to account for non-water exposures. MDH utilizes the Exposure Decision Tree process presented in USEPA 2000 to derive appropriate RSCs. Determination of an appropriate RSC must recognize the long elimination half-life of PFHxS, such that a person's serum concentration at any given age is not only the result of his or her current or recent exposures within the duration of concern, but also from exposure from years past.

Human biomonitoring data provide a quantitative description of the ongoing widespread exposure, but the serum data are not informative as to the specific pathways and exposure routes. The most recently reported 95<sup>th</sup> percentile serum concentrations from CDC (February 2019) range from 1.62 µg/L serum for young children to nearly 5 µg/L serum for older children and adults. This suggests that 'background' exposures, when compared to the 'reference' serum concentration (108 µg/L serum) would not represent significant sources of exposure. Using the most recent published biomonitoring results and USEPA's Exposure Decision Tree (USEPA 2000) as outlined in MDH 2008, an RSC of 0.5 (50%) was selected.

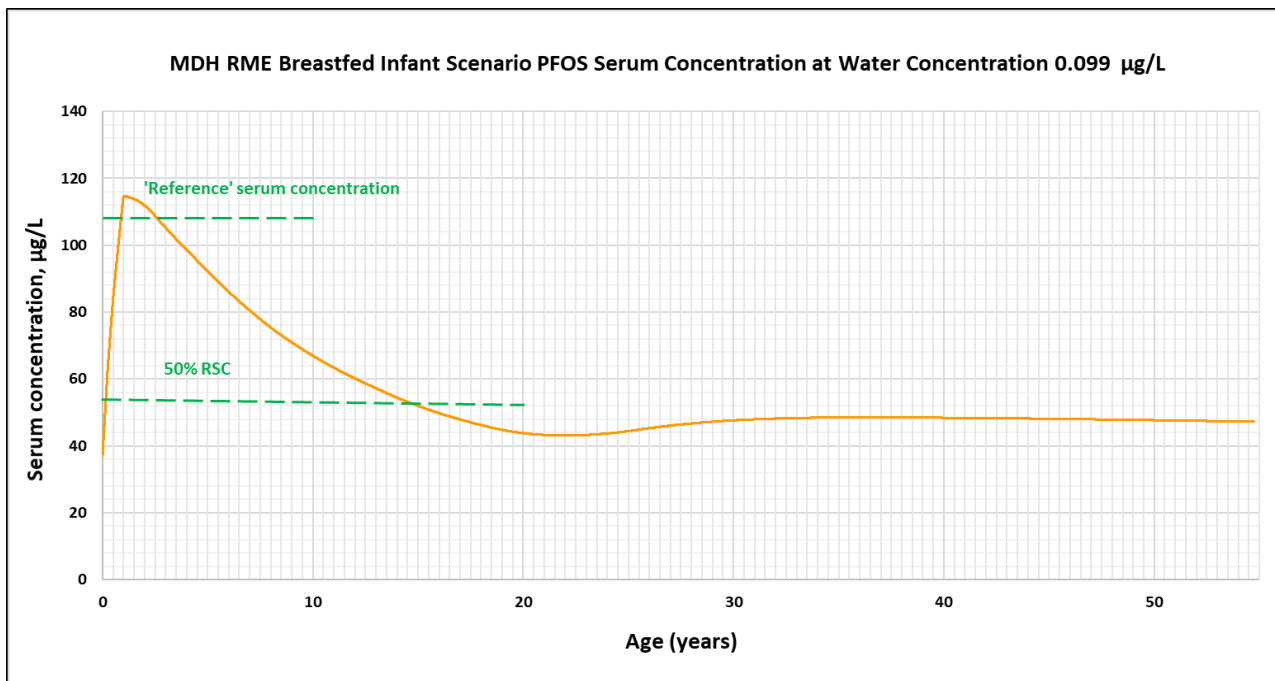
As mentioned above, two exposure scenarios were examined: 1) an infant fed formula reconstituted with PFHxS-contaminated water starting at birth and continuing ingestion of contaminated water throughout life; and 2) an infant exclusively breast-fed for 12 months, followed by drinking PFHxS-contaminated water throughout life. For the first scenario, the formula-fed infant, the water concentration that maintains a serum concentration attributable to drinking water at or below an RSC of 50% is 0.099 µg/L (Figure 1).

Figure 1. Exclusively formula-fed infant scenario serum concentrations over a lifetime, based on MDH's RME and an RSC of 50%.



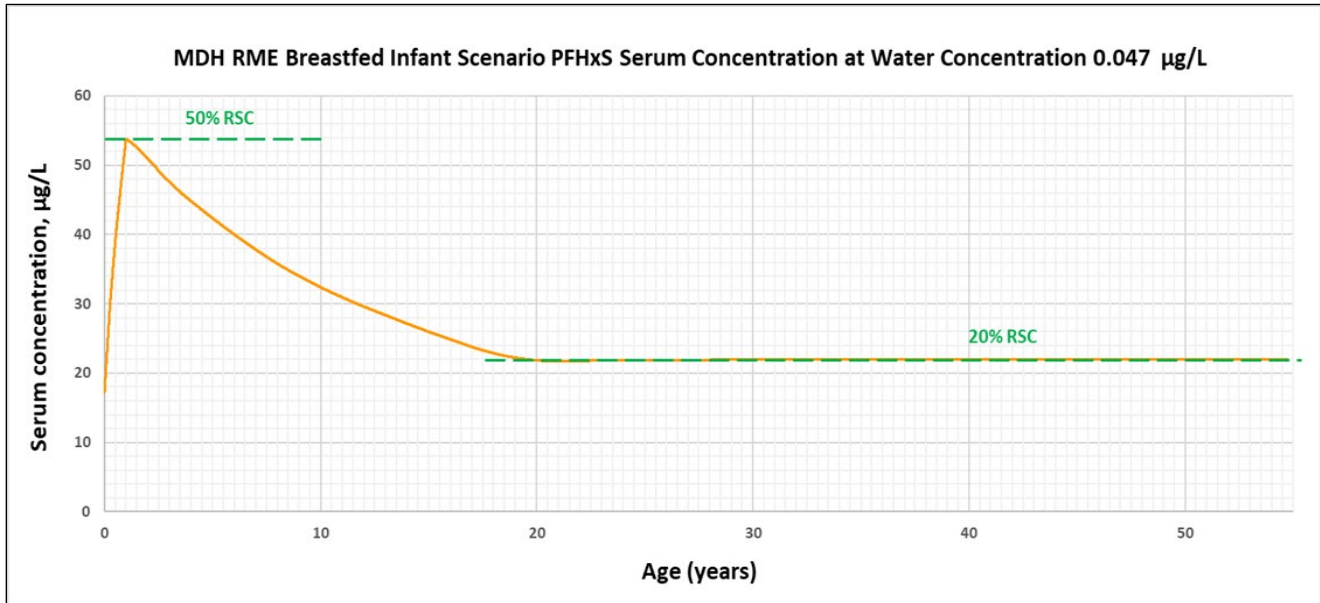
Applying this water concentration (0.099 µg/L) in the context of the breast-fed infant resulted in serum PFHxS concentrations exceeding the 'reference' serum concentration for nearly 2 years, and the 50% RSC threshold for nearly 14 years. See Figure 2.

Figure 2. Breast-fed infant scenario serum concentrations over a lifetime, based on MDH's RME and a water concentration of 0.099 µg/L.



In order to maintain serum concentrations at or below an RSC of 50% for breast-fed infants, the water concentration should not exceed 0.047 µg/L; see Figure 3. This water concentration also produces steady state serum concentrations at approximately 20% of the 'reference' serum concentration.

Figure 3. Exclusively breast-fed infant scenario serum concentrations over a lifetime, based on MDH’s RME, and a water concentration of 0.047 µg/L.



To ensure protection of all segments of the population, the final health-based value for PFHxS is set at 0.047 µg/L.

**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:** Yes (moderate)

**Summary of Guidance Value History:**

MDH first reviewed PFHxS in 2009 and determined that there was insufficient data to derive a value. In 2013, MDH’s Site Assessment and Consultation Unit began using the guidance value for PFOS as a surrogate to assess potential risks from exposure to PFHxS, in the absence of adequate chemical specific data. In 2018 additional toxicokinetic and toxicity information became available. In 2019, MDH derived a noncancer HBV (applicable to short-term, subchronic, and chronic durations) of 0.047 µg/L. In 2020 MDH incorporated updated water intake rates (US EPA 2019). Use of the updated intake rates did not result in changes to the 2018 value. In November 2023, the guidance values were adopted into Minnesota Rules, 4717.7860, as Health Risk Limits (HRLs).

**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	Yes	Yes
Effects observed?	Yes <sup>1</sup>	No <sup>2</sup>	No <sup>3</sup>	Yes <sup>4</sup>	No <sup>5</sup>

**Comments on extent of testing or effects:**

<sup>1</sup> Several human epidemiological studies have evaluated the possible association between serum PFHxS and alterations in thyroid hormone levels. Two studies found an association in women between serum PFHxS and thyroid hormone levels, however, other studies did not find this association. Two general population epidemiology studies have evaluated associations between PFHxS and reproductive hormones, finding no association.

Based on studies in laboratory animals, alterations in serum thyroid hormone levels, in particular thyroxine (T4), appear to be a sensitive effect. The POD is based on decreased serum T4 levels in adult male rats however, decreased serum T4 levels have also been reported in pregnant and lactating rats and pups. Unfortunately, serum PFHxS levels were not measured in pregnant or lactating rats or pups at the NOAEL and LOAEL dose levels, however, study results suggest that pups may be more sensitive than adult nonpregnant animals. A database uncertainty factor (DB UF) has been incorporated into the RfD derivation, in part, due to concerns that early life stages may be more sensitive.

Androgenic effects have also been evaluated in laboratory animals to a limited extent. No changes in adult male reproductive organ weights or sperm parameters were observed at serum levels up to ~600-fold higher than the 'reference' serum concentration. Androgenic activity was also evaluated in pups exposed in utero and through lactation. No significant effects were observed on anogenital distance, nipple retention, or reproductive organ weights at serum levels ~1300-fold higher than the 'reference' serum concentration.

<sup>2</sup> Several epidemiology studies have examined the potential association between PFHxS and suppression of the immune system. Inverse or no associations were observed in these studies. In general, available studies have not found an association between PFHxS and infectious disease resistance or with hypersensitivity outcomes.

Immunotoxicity has not been studied in laboratory animals. A DB UF has been incorporated into the RfD derivation, in part, to address this data gap.

<sup>3</sup> General population epidemiology studies have evaluated potential associations between maternal PFHxS and a variety of birth outcomes. A couple of studies have reported associations with birth weight or neurobehavioral outcome but others found no association.

Reproductive/developmental screening studies in rats and mice have not found treatment related changes in development outcome, including neurobehavioral effects, at serum levels  $\geq$  ~900-fold higher than the 'reference' serum concentration. Neurobehavioral outcomes were also evaluated in a study using a single oral exposure to neonatal mice on postnatal day 10. No serum levels were measured and therefore, the results could not be quantitatively incorporated into MDH's assessment. No 2-generation study has been conducted. A DB UF has been incorporated into the RfD derivation, in part, to address this data gap.

<sup>4</sup> In general, epidemiology studies evaluating potential associations between PFHxS and reproductive measures have not found any associations. A small number of studies have reported associations with earlier menopause or time to pregnancy. However, since menstruation, childbirth, and lactation are potential elimination routes for women this could confound the associations.

Laboratory studies in rats did not find changes in reproductive parameters at serum levels  $\geq$  ~1600-fold higher than the 'reference' serum concentration. A decrease in the number of pups per litter has been reported in mice, however the dose-response curve was flat and there was no difference in the number of pups born to the implant ratio. The 'reference' serum concentration is ~500-fold lower than the serum concentrations at which this effect occurs in mice, therefore the RfD is protective for this potential effect.

<sup>5</sup> Two epidemiology studies have evaluated association between PFHxS serum levels and self-reported memory loss or periods of confusion. One study reported a decrease in risk at the fifth quintile whereas the second study found no association.

Laboratory animal studies have evaluated neurotoxicity using the functional observation battery (FOB) and motor activity assessment. No effects were observed on adult rats and mice at serum concentrations  $\geq$  ~600-fold higher than the 'reference' serum concentration. Potential neurological effects have also been evaluated in rat pups using these same evaluation tools. No effects were observed at serum concentrations up to ~800-fold higher than the 'reference' serum concentration. A neurotoxicity evaluation following a single oral dose to neonatal animals has also been conducted. See footnote #3 above.

#### **Resources Consulted During Review:**

AAP. (2012). (American Academy of Pediatrics) Breastfeeding and the Use of Human Milk. Pediatrics, 129(3).

ATSDR. (2018). Agency for Toxic Substances and Disease Registry. Toxicological Profile for Perfluoroalkyls. Draft for Public Comment. June 2018.

<https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237> .



ATSDR. (2018b). (Agency for Toxic Substances and Disease Registry) Minimal Risk Levels (MRLs) and Environmental Media Evaluation Guides (EMEGs) for PFAS. Retrieved from [https://www.atsdr.cdc.gov/pfas/mrl\\_pfas.html](https://www.atsdr.cdc.gov/pfas/mrl_pfas.html) .

Australian Department of Health And Ageing NICNAS. (2005). Existing Chemical Hazard Assessment Report. Potassium Perfluorobutane Sulfonate.

Axelstad, M. (2019). [Personal Communication Re: Numerical Data for Figure 3A-E of Toxicological Science 2018 Publication.].

Beesoon, S., GM Webster, M Shoeib, T Harner, JP Benskin, JW Martin. (2011). Isomer Profiles of Perfluorochemicals in Matched Maternal, Cord, and House Dust Samples: Manufacturing Sources and Transplacental Transfer. *Environmental Health Perspectives*, 119, 1659-1664.

Bijland, S., PCN Rensen, EJ Pieterman, ACE Mass, JW van der Hoorn, MJ van Erk, KW van Dijk, SC Chang, DJ Ehresman, JL Butenhoff, HMG Princen. (2011). Perfluoroalkyl Sulfonates Cause Alkyl Chain Length-Dependent Hepatic Steatosis and Hypolipidemia Mainly by Impairing Lipoprotein Production in APOE\*3-Leiden CETP Mice. *Toxicological Sciences*, 123(1), 290-303.

Blystone, C. (2019). [Personal Communication. Use of NTP data tables and study protocol (January 2019 email exchange). ].

Butenhoff, J., SC Chang, DJ Ehresman, RG York. (2009). Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. *Reproductive Toxicology*, 27, 331-341.

Cariou, R., B Veyrand, A Yamada, A Berrebi, D Zalko, S Durand, C Pollono, P Marchand, J-C Leblanc, J-P Antignac, B Le Bizec. (2015). Perfluoroalkyl acid (PFAA) levels and profiles in breast milk, maternal and cord serum of French women and their newborns. *Environment International*, 84, 71-81.

CDC (Center for Disease Control). National Report on Human Exposure to Environmental Chemicals. Biomonitoring Data Tables for Environmental Chemicals. Retrieved February 2019 from [https://www.cdc.gov/exposurereport/data\\_tables.html](https://www.cdc.gov/exposurereport/data_tables.html)

CDC. (2016). Centers for Disease Control and Prevention. Breastfeeding Report Card. United States 2016. Retrieved from <https://www.cdc.gov/breastfeeding/pdf/2016breastfeedingreportcard.pdf>

Chang, S., JL Butenhoff, GA Parker, PS Coder, JD Zitsow, RM Krisko, JA Bjork, KB Wallace, JG Seed. (2018). Reproductive and developmental toxicity of potassiumperfluorohexanesulfonate in CD-1 mice. *Reproductive Toxicology*, 78, 150-168.

Chen, F., S Yin, BC Kelly, W Liu. (2017). Isomer-Specific Transplacental Transfer of Perfluoroalkyl Acids: Results from a Survey of Paired Maternal, Cord Sera, and Placentas. *Environmental Science & Technology*, 51, 5756-5763.

Das, K., CR Wood, MT Lin, AA Starkov, C Lay, KB Wallace, JC Corton, BD Abbott. (2017). Perfluoroalkyl acids-induced liver steatosis: Effects on genes controlling lipid homeostasis. *Toxicology*, 378, 37-52.

Donahue, S., KP Kleinman, MW Gillman, E Oken. (2010). Trends in Birth Weight and Gestational Length Among Singleton Term Births in the United States, 1990-2005. *Obstetrics and Gynecology*, 115((2 (pt. 1)), 357-364.

ECHA. (2017). (European Chemical Agency) Member State Committee Support Document for Identification of Perfluorohexane-1-sulphonic Acid and Its Salts as Substances of Very High Concern Because of Their VPVB1 (Article 57 E) Properties. Retrieved from [https://echa.europa.eu/documents/10162/13638/svhc\\_msc\\_support\\_document\\_pfhxs\\_4867\\_en.pdf/1f48372e-97dd-db9f-4335-8cec7ae55eee](https://echa.europa.eu/documents/10162/13638/svhc_msc_support_document_pfhxs_4867_en.pdf/1f48372e-97dd-db9f-4335-8cec7ae55eee)

Felter, S., GP Daston, SY Euling, AH Piersma, MS Tassinari. (2015). Assessment of health risks resulting from early-life exposures: Are current chemical toxicity testing protocols and risk assessment methods adequate? *Critical Reviews in Toxicology*, 45(3), 219-244.

FRANZ. (2017). (Food Standards Australia New Zealand) Hazard Assessment Report - Perfluorooctane Sulfonate (PFOS), Perfluorooctanoic Acid (PFOA), Perfluorohexane Sulfonate (PFHxS).

Friis-Hansen, B. (1961). Body Water Compartments in Children: Changes During Growth and Related Changes in Body Composition. *Pediatrics*, 28(2), 169-181.

Fromme, H., C Mosch, M Morovitz, I Alba-Alejandre, S Boehmer, M Kiranoglu, F Faber, I Hannibal, O Genzel-Boroviczeny, B Koletzko, W Volkel. (2010). Pre- and Postnatal Exposure to Perfluorinated Compounds (PFCs). *Environmental Science & Technology*, 44, 7123-7129.

Fu, J., Y Gao, T Wang, Y Liang, G Qu, B Yuan, Y Wang, A Zhang, G Jiang. (2016). Occurrence, temporal trends, and half-lives of perfluoroalkyl acids (PFAAs) in occupational workers in China. *Scientific Reports*, 6:38039.

Goeden, HM., CW Greene, JA Jacobus. (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>.

Gomis, M., R Vestergren, M MacLeod, JF Mueller, IT Cousins. (2017). Historical human exposure to perfluoroalkyl acids in the United States and Australia reconstructed from biomonitoring data using population-based pharmacokinetic modelling. *Environment International*, 108, 92-102.

Gutzkow, K., LS Haug, C Thomsen, A Sabaredzovic, G Becher, G Brunborg. (2012). Placental transfer of perfluorinated compounds is selective - A Norwegian Mother and Child sub-cohort study. *International Journal of Hygiene and Environmental Health*, 215, 216-219.

Harris, M., SL Rifas-Shiman, AM Calafat, X Ye, AM Mora, TF Webster, E Oken, SK Sagiv. (2017). Predictors of Per- and Polyfluoroalkyl Substance (PFAS) Plasma Concentrations in 6–10 Year Old American Children. *Environmental Science & Technology*, 51(9), 5193-5204.

Hoberman, A., RG York. (2003). Final Report. Argus Research Protocol 418-028. Oral (gavage) combined repeated dose toxicity study of T-7706 with the reproduction/developmental toxicity screening test.

Interstate Technology and Regulatory Council (ITRC). (2018). Regulations, Guidance, and Advisories. Section 4 Tables (Excel). September 15, 2018.

Karrman, A., I Ericson, B van Bavel, PO Darnerud, M Aune, A Glynn, S Lignell, G Lindstrom. (2007). Exposure of Perfluorinated Chemicals through Lactation: Levels of Matched Human Milk and Serum and a Temporal Trend, 1996-2004, in Sweden. *Environmental Health Perspectives*, 115, 226-230.

- Kato, K., L-Y Wong, A Chen, C Dunbar, GM Webster, BP Lanphear, AM Calafat. (2014). Changes in Serum Concentrations of Maternal Poly- and Perfluoroalkyl Substances over the Course of Pregnancy and Predictors of Exposure in a Multiethnic Cohort of Cincinnati, Ohio Pregnant Women during 2003-2006. *Environmental Science & Technology*, 48, 9600-9608.
- Kim, S., K Choi, K Ji, J Seo, Y Kho, J Park, S Kim, S Park, I Hwang, J Jeon, H Yang, JP Giesy. (2011a). Trans-Placental Transfer of Thirteen Perfluorinated Compounds and Relations with Fetal Thyroid Hormones. *Environmental Science & Technology*, 45, 7465-7472.
- Kim, S.-K., KT Lee, CS Kang, L Tao, K Kannan, KR Kim, CK Kim, JS Lee, PS Park, YW Yoo, JY Ha, YS Shin, JH Lee. (2011b). Distribution of perfluorochemicals between sera and milk from the same mothers and implications for prenatal and postnatal exposures. *Environmental Pollution*, 159, 169-174.
- Kim, S., SH Heo, DS Lee, IG Hwang, YB Lee, HY Cho. (2016). Gender differences in pharmacokinetics and tissue distribution of 3 perfluoroalkyl and polyfluoroalkyl substances in rats. *Food and Chemical Toxicology*, 97, 243-255.
- Kudo, N. (2015). Chapter 6. Metabolism and Pharmacokinetics. In J. C. DeWitt (Ed.), *Toxicological Effects of Perfluoroalkyl and Polyfluoroalkyl Substances*. Switzerland: Humana Press, Springer International Publishing.
- Lee, Y., M-K, Kim, J Bae, J-H Yang. (2013). Concentrations of perfluoroalkyl compounds in maternal and umbilical cord sera and birth outcomes in Korea. *Chemosphere*, 90, 1603-1609.
- Li, Y., T Fletcher, D Mucs, K Scott, CH Lindh, P Tallving, K Jakobsson. (2018). Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. *Occupational and Environmental Medicine*, 75, 46-51.
- Liu, J., J Li, Y Liu, HM Chan, Y Zhao, Z Cai, Y Wu. (2011). Comparison on gestation and lactation exposure of perfluorinated compounds for newborns. *Environment International*, 37, 1206-1212.
- Manzano-Salgado, C., M Casas, MJ Lopez-Espinosa, F Ballester, M Basterrechea, JO Grimalt, AM Jimenez, T Kraus, T Schettgen, J Sunyer, M Vrijheid. (2015). Transfer of perfluoroalkyl substances from mother to fetus in a Spanish birth cohort. *Environmental Research*, 142, 471-478.
- MDH. (2008). Minnesota Department of Health. Statement of Need and Reasonableness (SONAR) in the Matter of Proposed Rules Relating to Health Risk Limits of Groundwater. <https://www.leg.state.mn.us/archive/sonar/SONAR-03733.pdf#page=2>.
- MDH. (2015). Minnesota Department of Health. Environmental Health & Biomonitoring Advisory Panel June 9, 2015 Meeting Background Materials. Retrieved from <https://www.health.state.mn.us/communities/environment/biomonitoring/docs/2015Junematerials.pdf>.
- Needham, L., P Grandjean, B Heinzow, PJ Jorgensen, F Nielsen, DG Patterson Jr, A Sjodin, WE Turner, P Weihe. (2011). Partition of Environmental Chemicals between Maternal and Fetal Blood and Tissues. *Environmental Science & Technology*, 45, 1121-1126.
- Nelson, J. (2018b). [Personal Communication - Nov 2017 draft manuscript tables regarding MDH MN (East Metro) PFC biomonitoring project data].

New Hampshire Department of Environmental Services. (2019). Summary Report on the Development of Maximum Contaminant Levels and Ambient Groundwater Quality Standards for PFOS, PFOA, PFNA, and PFHxS.

NTP. (2018). National Toxicology Program. TOX-96: Toxicity Report Tables and Curves for Short-term Studies: Perfluorinated Compounds: Sulfonates. Retrieved from [https://tools.niehs.nih.gov/cebs3/views/?action=main.dataReview&bin\\_id=3874](https://tools.niehs.nih.gov/cebs3/views/?action=main.dataReview&bin_id=3874) .

Olsen, G., JM Burris, DJ Ehresman, JW Froehlich, AM Seacat, JL Butenhoff, LR Zobel. (2007). Half-life of Serum Elimination of Perfluorooctanesulfonate, Perfluorohexanesulfonate, and Perfluorooctanoate in Retired Fluorochemical Production Workers. *Environmental Health Perspectives*, 115, 1298-1305.

Ramhøj, L., U Hass, J Boberg, M Scholze, S Christiansen, F Nielsen, M Axelstad. (2018). Perfluorohexane Sulfonate (PFHxS) and a Mixture of Endocrine Disruptors Reduce Thyroxine Levels and Cause Antiandrogenic Effects in Rats. *Toxicological Sciences*, 163(2), 579-591.

RIVM. (2018). (National Institute for Public Health and the Environment) Mixture exposure to PFAS: A Relative Potency Factor approach. RIVM report 2018-0070. Retrieved from <https://rivm.openrepository.com/handle/10029/622164> .

Schechter, A., N Malik-Bass, AM Calafat, K Kato, JA Colacino, TL Gent, LS Hynan, TR Harris, S Malla, L Birnbaum. (2012). Polyfluoroalkyl Compounds in Texas Children from Birth through 12 Years of Age. *Environmental Health Perspectives*, 120, 590-594.

Sundstrom, M., SC Chang, PE Noker, GS Gorman, JA Hart, DJ Ehresman, A Bergman, JL Butenhoff. (2012). Comparative pharmacokinetics of perfluorohexanesulfonate (PFHxS) in rats, mice, and monkeys. *Reproductive Toxicology*, 33, 441-451.

USEPA. (2000). US Environmental Protection Agency (EPA). Office of Water. Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health. EPA-822-B-00-004. October 2000. Retrieved from <https://nepis.epa.gov/Exe/ZyPDF.cgi/20003D2R.PDF?Dockey=20003D2R.PDF> .

USEPA. (2011). US Environmental Protection Agency - National Center for Environmental Assessment. Exposure Factors Handbook. 2011 Edition. Retrieved from <https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252> .

USEPA. (2016). US Environmental Protection Agency - Office of Water. Drinking Water Health Advisory for Perfluorooctane Sulfonate (PFOS). Retrieved from [https://www.epa.gov/sites/production/files/2016-05/documents/pfos\\_health\\_advisory\\_final\\_plain.pdf](https://www.epa.gov/sites/production/files/2016-05/documents/pfos_health_advisory_final_plain.pdf).

USEPA. (2018). (US Environmental Protection Agency) Public Comment Draft - Human Health Toxicity Values for Perfluorobutane Sulfonic Acid and Related Compound Potassium Perfluorobutane Sulfonate.

U.S. Environmental Protection Agency (EPA) (2019). Exposure Factors Handbook Chapter 3 Update 2019. <https://www.epa.gov/expobox/exposure-factors-handbook-chapter-3>

Verner, M.-A., F Ngueta, ET Jensen, J Fromme, W Volkel, UC Nygaard, B Granum, MP Longnecker. (2016). A Simple Pharmacokinetic Model of Prenatal and Postnatal Exposure to Perfluoroalkyl Substances (PFASs). *Environmental Science & Technology*, 50, 978-986.

Wang, Y., W Han, C Wang, Y Zhou, R Shi, EC Bonefeld-Jorgensen, Q Yao, T Yuan, Y Gao, J Zhang, Y Tian. (2018). Efficiency of maternal-fetal transfer of perfluoroalkyl and polyfluoroalkyl substances. *Environmental Science and Pollution Research*, 26(3), 2691-2698.

Weiss, J., PL Andersson, MH Lamoree, PEG Leonards, SPJ van Leeuwen, T Hamers. (2009). Competitive Binding of Poly- and Perfluorinated Compounds to the Thyroid Hormone Transport Protein Transthyretin. *Toxicological Sciences*, 109(2), 206-216.

Wolf, C., ML Takacs, JE Schmid, C Lau, BD Abbott. (2008). Activation of Mouse and Human Peroxisome Proliferator - Activated Receptor Alpha by Perfluoroalkyl Acids of Different Functional Groups and Chain Lengths. *Toxicological Sciences*, 106(1), 162-171.

Worley, R., SM Moore, BC Tierney, X Ye, AM Calafat, S Campbell, MB Woudneh, J Fisher. (2017). Per- and polyfluoroalkyl substances in human serum and urine samples from a residentially exposed community. *Environment International*, 106, 135-143.

Wu, X., DH Bennett, AM Calafat, K Kato, M Stryner, E Andersen, RE Moran, DJ Tancredi, NS Tulse, I Hertz-Picciotto. (2015). Serum concentrations of perfluorinated compounds (PFC) among selected populations of children and adults in California. *Environmental Research*, 136, 264-273.

Yang, L., J Li, J Lai, H Luan, Z Cai, Y Wang, Y Zhao, Y Wu. (2016a). Placental Transfer of Perfluoroalkyl Substances and Associations with Thyroid Hormones: Beijing Prenatal Exposure Study. *Scientific Reports*, 6, 21699.

Ye, X., K Kato, LY Wong, T Jia, A Kalathil, J Latremouille, AM Calafat. (2018). Per- and polyfluoroalkyl substances in sera from children 3 to 11 years of age participating in the National Health and Nutrition Examination Survey 2013-2014. *International Journal of Hygiene and Environmental Health*, 221, 9-16.

Zhang, T., H Sun, Y Lin, X Qin, Y Zhang, X Geng, K Kannan. (2013). Distribution of Poly- and Perfluoroalkyl Substances in Matched Samples from Pregnant Women and Carbon Chain Length Related Maternal Transfer. *Environmental Science & Technology*, 47, 7974-7981.