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Per- and polyfluoroalkyl substances (PFAS) in powdered infant formula: potential exposures and health risks

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Abstract

Per- and polyfluoroalkyl substances (PFAS) are a class of human-made persistent, bioaccumulative, and toxic compounds. People can be exposed to PFAS through many different pathways, including food, drinking water, and PFAS-containing consumer products. Infants are recognized as particularly susceptible to the harmful effects of PFAS while also being among the most highly exposed populations. Exposure to PFAS begins *in utero* via placental transfer and can continue after birth from environmental exposures and breastfeeding. PFAS-contaminated water, if used to mix infant formula, is an important potential exposure route for formula-fed infants because they consume more fluid on a per-body-weight basis than older individuals. However, data about potential PFAS exposures from powdered infant formula itself are lacking. To address this data gap, we analyzed 17 powdered infant formulas for 10 different PFAS. Only one type of PFAS, perfluorooctanesulfonic acid (PFOS), was detected in a single dairy-based formula at a reconstituted concentration of 8.9 ng/L. Using our recently updated toxicokinetic model, we estimated serum PFOS concentration curves over the first year of life for various exposure scenarios, including different fluid intake rates, formula reconstituted with uncontaminated and contaminated water, and with and without placental transfer. Our analytical results indicate the single PFOS detection in powdered infant formula is not a major source of PFOS relative to other sources, and our risk assessment comparing various formula-fed

infant scenarios to the Minnesota Department of Health's 2024 PFOS reference serum concentration (2.6 ng/mL) concludes that PFAS from powdered formula likely does not pose a significant risk to infants.

Keywords: Infant formula, baby formula, PFAS, per- and polyfluoroalkyl substances, PFOS, toxicokinetics, childhood exposure, breastmilk

INTRODUCTION

Per- and polyfluoroalkyl substances (PFAS) are a family of approximately 15,000 synthetic chemicals that comprise at least one fluorine atom attached to a linear or branched alkyl chain[1]. This molecular structure results in their stability and resistance to biodegradation[2]. PFAS have been manufactured since the 1950s and are found in products such as stain-resistant and water-repellant products, food packaging, nonstick cookware, some personal care products and cosmetics, and some lubricants, paints and sealants[3]. Due to chemical releases to the soil, air, and water by manufacturers and decades of use of products containing PFAS by the public, PFAS are now ubiquitous in the environment, and human exposure can occur from numerous sources.

The Centers for Disease Control and Prevention's (CDC) National Health and Nutrition Examination Survey (NHANES) has measured 12 PFAS in blood serum in samples dating back to 1999, and four PFAS have been detected consistently in nearly all of the people tested: perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexanesulfonic acid (PFHxS), and perfluorononanoic acid (PFNA)[4]. PFAS are also known to partition into breastmilk[5-8], reaching sufficient concentrations to result in significant exposure to young infants[9-11]

The Minnesota Department of Health (MDH) makes health-based guidance for contaminants found in groundwater (Minnesota Statute §103H.201). A health-based guidance value (HBGV) is the concentration of contaminant in water that poses little to no health risk for those drinking the water[12], including highly exposed or susceptible populations. HBGVs are derived solely on the basis of human health and do not consider technical feasibility or cost of treatment. In 2002, MDH first developed HBGVs for PFOS and PFOA[13]. This guidance was based on extremely limited animal toxicity data. In the subsequent 20 years, scientists have produced a more robust toxicity and toxicokinetic (TK) database for PFOS and PFOA that now includes human epidemiology data. As a result, MDH guidance for PFOS and PFOA has undergone many iterations based on the latest available science, resulting in progressively lower MDH HBGVs with each update[13]. MDH has also developed HBGVs for other PFAS including perfluorobutanesulfonic acid (PFBS), perfluorobutanoic acid (PFBA), perfluorohexanoic acid (PFHxA), and PFHxS[14].

MDH's policy is to protect the most vulnerable populations when deriving HBGVs[12], and for the long-chain PFAS family members, the infant is the most sensitive population. Many PFAS have half-lives lasting years in humans[2]. Due to placental and breastmilk transfer, infants are among the most highly exposed individuals[11,15-17]. While reevaluating the PFOA HBGV in 2017, MDH developed a model to better account for the unique toxicokinetic behaviors of PFOA in humans, particularly pertaining to infant exposures. The model received minor iterative updates since development, and it was subsequently used for deriving HBGVs for PFOS (2017, 2019) and PFHxS (2019)[13,14]. The TK model recently received a major revision and was used in the derivation of MDH's 2024 epidemiology-based HBGVs for PFOA and PFOS[18,19]. The revised model has been described in a recently accepted publication[20].

In the 2017 HBGV, MDH's TK model evaluated two exposure scenarios: an infant exposed to PFOA from formula reconstituted with contaminated water, and an infant exposed to PFOA via breastfeeding from a mother who drinks contaminated water[15]. Breastfed infants had peak PFOA serum levels that were more than four times higher than formula-fed infants[15]. However, the formula-fed infant evaluation assumed that the only source of PFOA in reconstituted formula was contaminated water. This was because little was - and continues to be - known about potential PFAS contamination in powdered formula itself[9,21]. The overall lack of data about PFAS in infant formula results in the possibility of underestimating PFAS exposures for formula-fed infants.

To examine this, we measured the concentrations of 10 PFAS in 17 different powdered formulas sold in the United States. Next, using our recently updated TK model, we estimated serum PFOS concentration curves over the first year of life for several exposure scenarios, including different fluid intake rates, formula reconstituted with uncontaminated and contaminated water, and with and without placental transfer while providing risk context for each scenario.

MATERIALS AND METHODS

Formula selection

Seventeen different types of powdered infant formulas were selected for analysis. Ten were included based on data from MDH's Women, Infants, & Children (WIC) program. The WIC program is a nutrition and breastfeeding program that helps pregnant women and young families with nutrition education and counseling, nutritious food, and referrals to social services[22]. WIC participants are one of the largest groups of purchasers of infant formula, and only certain formulas are available through WIC at a given time. We submitted a public data request to the WIC program for purchasing statistics for the most popular contract (i.e., standard, routine formulas) and medical (i.e., requires a documented medical diagnosis) formulas available through their program from December 2021 to January 2023. These formulas represent some of the most widely used formulas in Minnesota. Additional selections were made to increase coverage of available formula types. The 17 formulas can be characterized in several ways:

- WIC (7 contract, 3 medical), non-WIC (7)
- Dairy (12), Soy (4), Amino acid (1)
- Organic (3), Non-organic (14)
- Dietary need
  - Standard/added rice (for spit-up) (6)
  - Lactose sensitivity (6)
  - Protein sensitivity (1)
  - Premature infants (2)
  - Hypoallergenic (2)

A complete list of formulas tested is shown in Supplementary Table 1.

Sample preparation and analysis

Sample preparation and analysis are slightly modified from Criswell *et al.*[23]. Triplicate samples of powdered formula were weighed on a high-precision balance (Sartorius BCA324I-1S) and reconstituted in ultrapure water to a 20% weight/volume stock solution. The analysis of PFAS in reconstituted formula was performed through protein precipitation followed by centrifugation, concentration, and analysis using liquid chromatography tandem-mass spectrometry (LC/MS/MS). A stable isotope-labeled internal standard solution and cold acetonitrile were added to a 400 µL aliquot of reconstituted formula in microcentrifuge

tubes. The tubes were mixed, stored overnight in a -20C freezer, centrifuged, and an aliquot of supernatant was quantitatively transferred to 96-well plates for concentration via gentle nitrogen. After concentration, the sample was analyzed by LC/MS/MS (Shimadzu Prominence, AB Sciex 5500Q) using electrospray ionization with multiple reaction monitoring (MRM) and retention time windows. Bovine whole milk was used to prepare matrix-matched calibration curves and quantitation was performed via isotope dilution. A minimum of 2 MRM transitions were monitored for each analyte, and unknowns were verified through retention time and ion ratio matching with the calibration curve. A minimum of three quality control (QC) samples were run with each batch of 17 unknowns: a method blank, and low and high concentration levels. The QC materials were prepared in bovine dairy milk (method blank) and fortified human milk. Batches with QC recovery outside of 70%-130% are reanalyzed.

The data are reported as continuous variables from the limit of quantitation (LOQ) up to 5,000 ng/L. Ten PFAS analytes were included in this method [Table 1].

During the development of the analytical method, perfluorobutanoic acid (PFBA), perfluoropentanoic acid (PFPeA), and perfluorododecanoic acid (PFDoA) were also included, but all three had irresolvable technical difficulties. PFBA and PFPeA had interfering coeluates, and PFDoA had a very poor recovery. Therefore, these were not included in the final analysis.

Calculating PFAS concentrations in infant formula powder

Dry-weight PFAS concentrations (ng/g) in powdered infant formula were calculated for each sample with a PFAS detection above the LOQ (Equation 1), where $PFAS_{LCMS/MS}$ equals the mass of PFAS measured in 1 mL of the sample, and V_{stock} and M_{stock} equal the volume and the mass of the associated powdered infant formula stock solution, respectively:

$$\mathrm{PFAS_{DryWeight}}\left(\frac{\mathrm{ng}}{\mathrm{g}}\right) = \frac{\mathrm{PFAS_{LCMS/MS}\ (ng)}}{\mathrm{1\ mL}} \times \frac{\mathrm{V_{stock}\ (mL)}}{\mathrm{M_{stock}\ (g)}} \quad (1)$$

Calculating PFAS amounts in reconstituted infant formula

A scoop of powdered formula was taken from each canister per label directions and weighed. The mass of PFAS in one scoop was then calculated by multiplying the PFAS dry weight by the mass of the formula per scoop, as listed on the formula label (Equation 2):

$$\mathrm{PFAS_{Scoop}(ng) = PFAS_{DryWeight}}\left(\frac{\mathrm{ng}}{\mathrm{g}}\right) \times \mathrm{Formula_{Scoop}\ (g)} \quad (2)$$

Equation 3 was used to determine the final PFAS concentration in the reconstituted formula:

$$\mathrm{PFAS_{ReconstitutedFormula}}\left(\frac{\mathrm{ng}}{\mathrm{L}}\right) = \mathrm{PFAS_{Scoop}(ng)} \times \mathrm{Z}\left(\frac{\mathrm{1\ scoop}}{\mathrm{Volume\ (L)}}\right) \quad (3)$$

where Z refers to the number of scoops used in reconstituting the formula and Volume refers to the volume of water used to reconstitute one scoop of formula, per the label. Infant formula labels list a scoop/water ratio for reconstitution. One scoop of formula per 2 oz of water (0.059 L) is a common ratio, used in 16 out of 17 formulas analyzed in this study. The PFAS concentrations in reconstituted formula represent real-world exposure scenarios and can be used for risk assessment.

Table 1. List of PFAS analytes and associated method reporting levels

CASRN	DTXSID	PFAS		LOQ (ng/L)
307-24-4	DTXSID3031862	Perfluorohexanoic acid	PFHxA	25
375-85-9	DTXSID1037303	Perfluoroheptanoic acid	PFHpA	25
335-67-1	DTXSID8031865	Perfluorooctanoic acid	PFOA	10
375-95-1	DTXSID8031863	Perfluorononanoic acid	PFNA	10
335-76-2	DTXSID3031860	Perfluorodecanoic acid	PFDA	10
2058-94-8	DTXSID8047553	Perfluoroundecanoic acid	PFUnA	25
375-73-5	DTXSID5030030	Perfluorobutanesulfonic acid	PFBS	10
355-46-4	DTXSID7040150	Perfluorohexanesulfonic acid	PFHxS	10
1763-23-1	DTXSID3031864	Perfluorooctanesulfonic acid	PFOS	10
754-91-6	DTXSID3038939	Perfluorooctanesulfonamide	PFOSA	10

CASRN: Chemical Abstracts Service registration number; DTXSID: Distributed Structure-Searchable Toxicity Substance Identifier; LOQ: limit of quantitation; PFHxA: perfluorohexanoic acid; PFHpA: perfluoroheptanoic acid; PFOA: perfluorooctanoic acid; PFNA: perfluorononanoic acid; PFDA: perfluorodecanoic acid; PFUnA: perfluoroundecanoic acid; PFBS: perfluorobutanesulfonic acid; PFHxS: perfluorohexanesulfonic acid; PFOS: perfluorooctanesulfonic acid; PFOSA: perfluorooctanesulfonamide.

Toxicokinetic modeling and risk assessment

PFOS is bioaccumulative, and the serum concentration rather than intake is the best measure of exposure[15,19]. MDH previously published a TK model that calculates daily serum concentrations of bioaccumulative PFAS over a simulated lifetime[15] and which has been used in the derivation of Minnesota health-based guidance values for several bioaccumulative PFAS, including PFOS[14]. The model evaluates two exposure scenarios: an infant exposed to reconstituted formula prepared with contaminated water, and a breastfed infant whose mother consumed (and continues to consume) contaminated drinking water. MDH has updated the TK model[20] and used it in the derivation of the most recent health-based guidance values for PFOA[18] and PFOS[19]. The updated version of the TK model and the reconstituted formula scenario were used in this analysis. A list of the TK parameters used in the updated model and the sources of the values are presented in Table 2.

RESULTS AND DISCUSSION

PFAS detections in infant formulas

No PFAS were detected above the LOQs in 16 of 17 infant formulas tested. In the one formula that had a detection, a dairy-based formula, only PFOS was detected in triplicate samples [Table 3] of a 20% weight/volume solution at an average concentration of 12 ng/L (standard deviation = 0.6), with a calculated concentration in formula reconstituted per label instructions of 8.9 ng/L. PFOS is one of the few PFAS previously determined to accumulate in cow's milk[27-29].

Risk assessment of PFOS exposure from infant formula

Exposure to PFOS from formula alone

To evaluate the impact of formula alone on the serum concentration during an infant's first year of life, we modeled an infant exclusively consuming reconstituted formula with a PFOS concentration of 8.9 ng/L with either a mean or 95th percentile formula intake rate from EPA's Exposure Factors Handbook[25] [Figure 1]. These scenarios assume the infant has no other exposure to PFOS, e.g., no placental transfer, no PFOS in the water used to reconstitute the formula, no household exposures, *etc.*

Since there is no placental transfer considered in this scenario, the serum PFOS concentration at birth in these model runs are zero. Over the course of the first year, serum PFOS concentrations for an infant would increase to 0.33 ng/mL (mean fluid intake) or 0.66 ng/mL (95th percentile fluid intake).

Table 2. Parameters used in PFOS toxicokinetic model - formula-fed infant exposure scenario

Model parameter	Value used and background
Serum PFOS half-life ($t_{½}$)	Central tendency = 996 days (2.73 years)[24] Although the TK model estimates serum levels from birth through a lifetime, the output was limited to 1 year for the purposes of this study. Serum half-life information is not available for children less than 1 year of age, and thus the central tendency from the overall population mean was used
Placental transfer	Central tendency = 0.39 (mean of mean values from 27 studies listed in Supplementary Table 2) For exposure scenarios that include placental transfer, the mother's concentration was set as the most recent (2017/2018) NHANES female median concentration (3.30 ng/mL)
Water intake rate (mL/kg-day)	The model calculates serum levels over a lifetime and uses corresponding age-specific water intake rates and body weights. This study focused on formula-fed infants from birth to 1 year of age and used mean and 95th percentile intake rates (Tables 3-5 of US EPA's Exposures Factors Handbook[25]). Tables 3-5 presents mean and 95th percentile intake rates for indirect in formula (Formula) as well as total direct and indirect (Total), which is the sum of consumption of reconstituted formula and other ingested water

Mean intake

Age group	Formula intake rate (mL/kg-day)	Total intake rate (mL/kg-day)
< 1 month	143	146
1 to < 3 months	124	136
3 to < 6 months	93	101
6 to < 12 months	65	78

95th percentile intake

Age group	Formula intake rate (mL/kg-day)	Total intake rate (mL/kg-day)
< 1 month	240	240
1 to < 3 months	285	290
3 to < 6 months	171	186
6 to < 12 months	136	151

For scenarios where the only PFAS exposure is from powdered formula, Formula intake rates are used. In scenarios with water PFAS contamination, both powdered formula and water contribute to PFAS exposure
The combined PFAS intake from contaminated formula and contaminated water was determined by adding the PFAS concentrations of reconstituted formula and water and using the Formula intake rate. Incidental water ingestion (additional water ingested outside of that used to reconstitute formula) was calculated by subtracting the indirect in formula intake rate from the total direct and indirect intake rate from Tables 3-5 of US EPA's Exposures Factors Handbook[25]

Age group	Mean incidental intake rate (mL/kg-day)	95th percentile incidental intake rate (mL/kg-day)
< 1 month	3	0
1 to < 3 months	12	5
3 to < 6 months	8	15
6 to < 12 months	13	15

For scenarios with PFAS-contaminated water, the additional PFAS exposures from incidental water intake were calculated by running the TK model separately with the water PFAS concentration using the incidental intake rates. Those PFAS intakes were added to intakes from formula reconstituted with contaminated water to calculate overall PFAS serum curves for each scenario

Body weights (kg) were calculated from total water ingestion data presented in Table 3-5 (i.e., mL/day ÷ mL/kg-day):

Mean intake

Age group	Body weight (kg)
< 1 month	3.5
1 to < 3 months	4.6
3 to < 6 months	6.9
6 to < 12 months	8.9

95th percentile intake

Age group	Body weight (kg)
< 1 month	3.6
1 to < 3 months	3.8
3 to < 6 months	7.0
6 to < 12 months	8.9

Volume of distribution (L/kg)	Central tendency = 0.56 (calculated from human CR of 0.39 mL/kg/day[26]) and the half-life CR ÷ [ln(2)/half-life] = V_d 0.39 mL/kg/day ÷ [ln(2)/996 days] = 560 mL/kg, rounded to 0.56 L/kg

PFOS: Perfluorooctanesulfonic acid; NHANES: National Health and Nutrition Examination Survey; $t_{½}$: half-life; TK: toxicokinetic; CR: clearance rate; V_d: volume of distribution.

Table 3. PFOS detection in one dairy-based infant formula powder

PFOS in 20% w/v solution (SD) (ng/L)	PFOS in formula powder (SD) (ng/g)	Formula per scoop (g)	PFOS per scoop (ng)	Water per scoop (L)	PFOS in reconstituted formula (ng/L)
12 (0.6)	0.054 (0.003)	9.8	0.53	0.059	8.9

n = 3. PFOS: perfluorooctanesulfonic acid; SD: standard deviation.

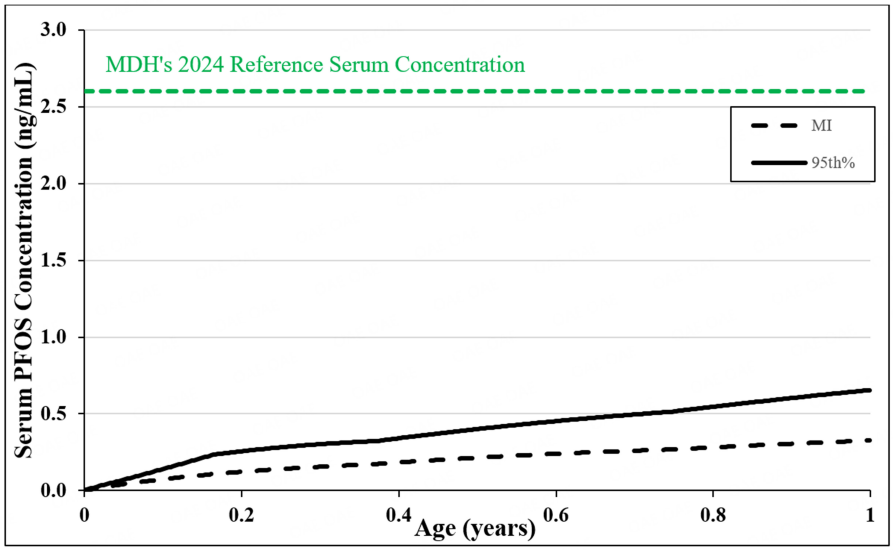

Figure 1. Serum PFOS concentration of an infant exposed to PFOS from drinking contaminated infant formula (8.9 ng/L). PFOS: Perfluorooctanesulfonic acid; MDH: Minnesota Department of Health; MI: mean fluid intake rate; 95th%: 95th percentile fluid intake rate.

In 2024, MDH released an updated PFOS reference serum concentration (RfSC) of 2.6 ng/mL based on epidemiological data[19]. An RfSC is the concentration of a chemical (in this case, PFOS) in the serum without an appreciable risk of noncancer health effects. With no other sources of PFOS exposure, an infant with a mean fluid intake rate consuming formula contaminated with 8.9 ng/L PFOS would have a peak serum concentration equal to 13% of the PFOS RfSC, while an infant with a 95th percentile fluid intake rate would have a peak serum concentration equivalent to 24% of the PFOS RfSC [Table 4].

Exposure to PFOS from contaminated formula plus contaminated water

Powdered infant formula must be reconstituted with water before use, which allows for another possible exposure route[30]. Many states have created health-based and/or regulatory limits on PFOS and other PFAS in drinking water[31,32], and in 2024, the US EPA released Maximum Contaminant Levels (MCLs) for six PFAS, including PFOS, under the Safe Drinking Water Act[33]. MCLs are not strictly health-based and account for factors such as technical feasibility and cost of treatment. The MCL for PFOS is 4 ng/L, the practical quantitation level for PFOS defined by EPA. Public water systems with PFOS levels above 4 ng/L will be required to take action to reduce PFOS below 4 ng/L.

Table 4. Peak serum PFOS concentrations across various exposure scenarios compared to MDH's 2024 reference serum concentration

Formula intake rate	PFOS water conc. (ng/L)	Maternal transfer considered	Serum PFOS conc. at birth (ng/mL)	Peak serum PFOS conc. (ng/mL)	% of MDH's 2024 RfSC at peak serum conc.
Mean	0	No	0	0.33	13%
95th percentile	0	No	0	0.63	24%
Mean	4	No	0	0.50	19%
95th percentile	4	No	0	0.94	36%
Mean	0	Yes	1.29	1.29*	50%
95th percentile	0	Yes	1.29	1.33	51%
Mean	4	Yes	1.29	1.30	50%
95th percentile	4	Yes	1.29	1.44	55%

*Peak serum PFOS concentration occurred at birth as the result of placental transfer from the mother using median 2017-2018 NHANES serum for females. PFOS: Perfluorooctanesulfonic acid; MDH: Minnesota Department of Health; conc.: concentration; NHANES: National Health and Nutrition Examination Survey; RfSC, reference serum concentration.

In the second exposure scenario, we compared an infant drinking formula reconstituted with water containing no PFOS with an infant drinking formula reconstituted with water contaminated with PFOS at the MCL of 4 ng/L [Figure 2]. The shape of the curves matches the first scenario, but the slopes are steeper since the overall concentration of PFOS consumed is higher (8.9 ng/L *vs.* 12.9 ng/L).

Like the first scenario, the serum PFOS concentration at birth is zero. Over the course of the first year, serum PFOS concentrations for these infants would increase to 0.50 ng/mL (mean intake) or 0.94 ng/mL (95th percentile intake) [Table 4].

Impact of placental transfer on serum PFOS levels

For bioaccumulative PFAS like PFOS, the mother's serum PFAS concentrations from prior exposures can have large impacts on the infant. Many PFAS, including PFOS, can both efficiently cross the placenta and accumulate in breastmilk[6,15,34-36]. These can be major exposure pathways for the infant. Although exposure via breastmilk was not considered in this study, MDH's TK model can account for both pathways[15,20]. To complete our exposure scenario, we looked at how placental transfer contributes to infant serum PFOS concentration relative to contaminated infant formula.

To investigate the relative impact of maternal exposure on infant serum PFOS levels, we used data from NHANES to first determine a reasonable proxy for maternal concentration. NHANES has collected serum data on several PFAS for many years; the most recent round of available data on PFOS is from 2017-2018[37]. In females (n = 977), the median serum PFOS was 3.30 ng/mL (95% confidence intervals 2.90-3.70; geometric mean 3.42 ng/mL, 95% confidence intervals 3.08-3.78). The median concentration was used as a measure of central tendency and inputted into the TK model as the maternal serum concentration to establish an infant serum concentration at birth - 1.29 ng/mL [maternal serum × placental transfer factor (0.39), Supplementary Table 2]. We then ran the previous exposure scenarios with the inclusion of placental transfer [Figure 3 and Table 4].

Infants with mean intake rates had peak serum PFOS concentrations at birth, with a sharp decline over the first 4 months and a slower decline over the following 8 months before slightly rising again approaching 1 year. Infants with no water contamination had a serum PFOS concentration of 0.69 ng/mL at 1 year, and infants drinking water at the MCL of 4 ng/L PFOS had a serum PFOS concentration of 0.86 ng/mL at 1 year.

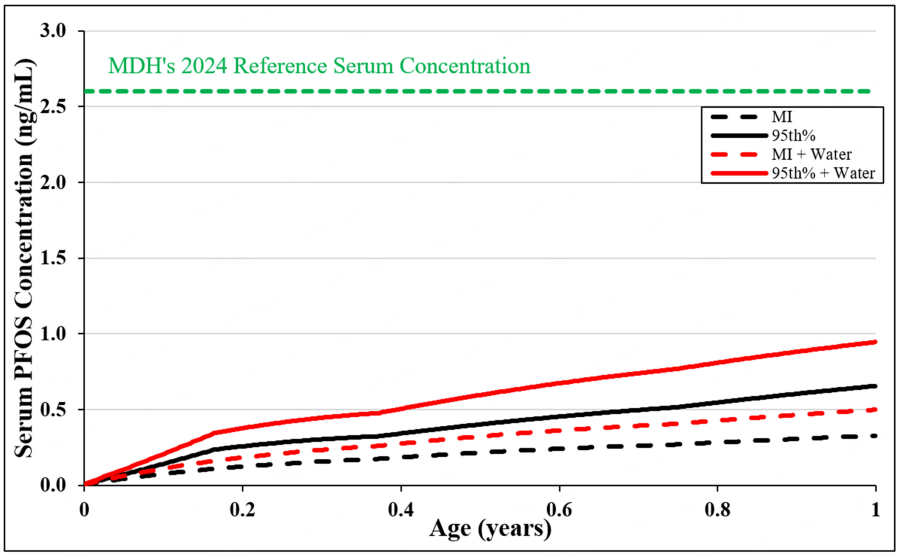

Figure 2. Serum PFOS concentration of an infant exposed to PFOS solely from contaminated infant formula (8.9 ng/L) or from drinking contaminated formula (8.9 ng/L) reconstituted with water contaminated with PFOS at the US EPA MCL (4 ng/L). PFOS: Perfluorooctanesulfonic acid; MCL: maximum contaminant level; MDH: Minnesota Department of Health; MI: mean fluid intake rate; US EPA: United States Environmental Protection Agency; 95th%: 95th percentile fluid intake rate.

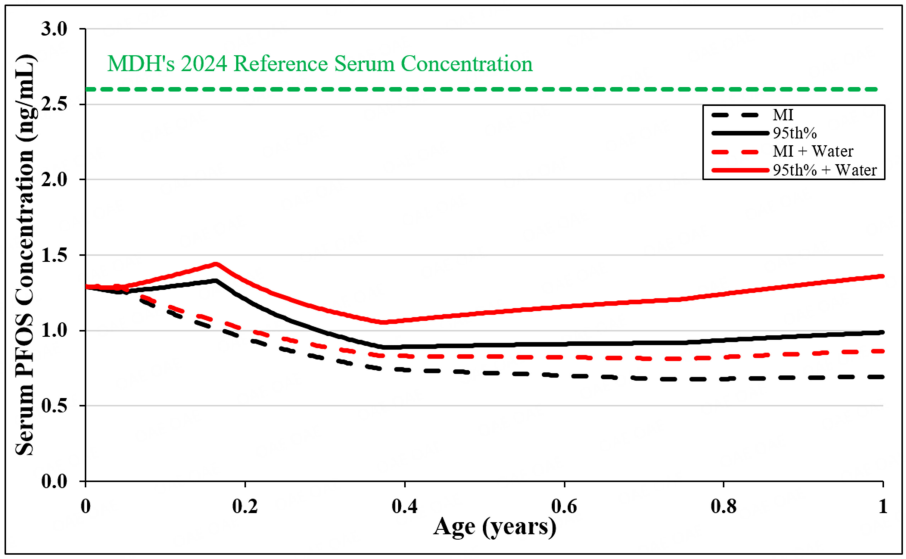

Figure 3. Serum PFOS concentration of infants exposed to PFOS via placental transfer [median 2017/2018 female NHANES serum concentration × placental transfer factor (3.3 ng/mL × 0.39)] and from infant formula contaminated with PFOS (8.9 ng/L) or from drinking formula contaminated with PFOS (8.9 ng/L) reconstituted with water contaminated with PFOS at the US EPA MCL (4 ng/L). PFOS: Perfluorooctanesulfonic acid; MCL: maximum contaminant level; MDH: Minnesota Department of Health; MI: mean fluid intake rate; US EPA: United States Environmental Protection Agency; 95th%: 95th percentile fluid intake rate; NHANES: National Health and Nutrition Examination Survey.

With a 95th percentile intake rate, infants saw an increase in PFOS serum rate after birth, peaking at two months - 1.33 ng/mL for infants without PFOS in their water and 1.44 ng/mL for infants with 4 ng/L PFOS in their water. Serum PFOS declined over the next two months to a minimum before rising again for the rest of the first year. Infants with PFOS only in their formula (i.e, consuming 8.9 ng/mL PFOS) had a final serum PFOS concentration of 0.99 ng/mL at 1 year. Infants with PFOS in their formula and 4 ng/L PFOS in

their water had a serum PFOS concentration of 1.36 ng/mL, nearly reaching the peak concentration at 2 months.

This risk assessment is consistent with previous studies demonstrating that maternal serum PFAS levels have a large impact on the infant's serum level through placental transfer[11,15-17]. For an infant with a mean formula-fed fluid intake rate whose mother's serum PFOS concentration was the 2017-2018 NHANES median, the peak serum PFOS concentration occurred at birth even while drinking formula contaminated with PFOS at 8.9 ng/L for the entire first year, and additional water contamination at EPA's PFOS MCL results in only a very slightly higher peak serum PFOS level soon after birth before decreasing [Table 4].

CONCLUSIONS

Overall, this study suggests that powdered infant formula is likely not a significant source of exposure to PFAS for infants. Across 17 types of powdered infant formulas and 10 PFAS tested, only a single PFAS was detected above the LOQ in a single infant formula. It is possible that LOQs will decrease in the future due to method improvements, and future studies could determine if PFAS contamination exists in infant formula at lower levels. We also note that technical limitations prevented the analysis of three PFAS originally included in this study (PFBA, PFPeA, PFDoA), and that this study focused on perfluorinated carboxylic and sulfonic acids. Other classes of PFAS exist, such as perfluoroether carboxylic and sulfonic acids (PFECAs and PFESAs); PFECAs and PFESAs were often used as replacements for perfluorinated PFAS and should be further investigated in both breastmilk and infant formula. It is also possible that future RfSCs will continue to decrease as more epidemiological and toxicokinetic data become available that recontextualize our understanding of PFAS risk.

While this study indicates that powdered infant formula likely does not constitute a major exposure pathway, infants remain one of the most highly exposed and most sensitive populations to PFAS; many other sources of PFAS exposure remain and must be addressed. A large fraction of infant exposure can come from maternal transfer. NHANES data indicate that almost all Americans have PFAS in their blood[37] at levels above the National Academies of Science, Engineering, and Medicine's serum guidelines for potential adverse effects[38]. The female median serum PFOS concentration used as a proxy for maternal serum in this study is above MDH's 2024 RfSC, indicating potential health concerns for both mother and infant alike.

One of the best solutions for reducing PFAS exposures is to prevent them from entering the environment in the first place by banning their manufacture and nonessential uses in products. "Turning off the PFAS tap" is a major victory for public health, and in 2023, the Minnesota state legislature passed Amara's Law, which, among other things, prohibits the sale or distribution of many products with intentionally added PFAS[39]. However, a patchwork of state laws is insufficient to meet the scale of the problem. Better testing methods and broader testing requirements must be enacted to fully define the scope of PFAS exposures from products. Federal regulation and international agreement are necessary to drastically cut PFAS emissions or enact outright PFAS bans on nonessential uses.

Furthermore, because of their environmental persistence, PFAS released into the environment long ago remain a source of ongoing human exposure. MDH and other Minnesota state agencies have been working with the people and communities of Minnesota on PFAS for decades. MDH has created fact sheets on many topics related to PFAS, including human health and reducing exposures, to help people take personal action to protect themselves and their families. More information is available on MDH's website[3]. In brief, women who are pregnant or are planning to become pregnant can reduce their own exposures and potential health

risks to themselves and their babies by, among other things, limiting the use of consumer products that contain PFAS. Parents who formula-feed their infant and are worried about PFAS exposures can take simple actions to reduce their infant's potential exposures, including preparing infant formula with filtered water or bottled water if their drinking water contains PFAS, and limiting their infant's exposure to PFAS-containing products and household dust.

DECLARATIONS

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Authors' contributions

Conceived of the study: Goeden HM
Designed the study: Goeden HM, Klos KS, Bogdan AR
Prepared the samples: Klos KS, Barry KM, Bogdan AR, Huset CA
Performed the mass spectrometry and wrote the associated "Materials and Methods" section: Huset CA, Barry KM
Performed the toxicokinetic modeling and risk assessment: Bogdan AR, Greene CW
Reviewed the modeling and risk assessment: Bogdan AR, Greene CW, Goeden HM, Klos KS
Wrote the manuscript: Bogdan AR, Klos KS
All authors reviewed and approved the manuscript.

Availability of data and materials

The toxicokinetic model used in this study is described in ref[20] (Greene *et al.* 2024); to obtain a copy, contact the authors.

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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