A Public Health Response to Large-Scale PFAS Contamination in Minnesota

Chris Greene, MSc
Helen Goeden, PhD
James Jacobus, PhD

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Denver, Colorado
• PFAS a known issue in East Metro since 2002
• Contamination zone >150 sq. mi.
• 140,000 residents affected
• 2,700 private drinking water wells sampled
• Over 1,100 drinking water advisories issued
• Biomonitoring of residents
MDH has programs to develop Health-Based Guidance (HBG) for conventional and emerging drinking water contaminants.

2002: derived water guidance for PFOS and PFOA
2007 – 2009: revised PFOS and PFOA values and derived new values for PFBA and PFBS. For PFHxS, PFOS HBG was recommended as a surrogate.

\[
nHBG \left( \frac{\mu g}{L} \right) = \frac{RfD \left( \frac{mg}{kg \cdot day} \right) \times RSC \times 1000 \frac{\mu g}{mg}}{IR \left( \frac{L}{kg \cdot day} \right)}
\]
Drinking Water Guidance in Minnesota

**RfD** = toxicological reference dose; may be developed for multiple exposure durations

**IR** = water intake rate; time-weighted, consumer-only intakes may be applied for short durations or over a lifetime

**RSC** = Relative Source Contribution factor to allocate the RfD across multiple exposure sources, including non-drinking water sources

\[
n\text{HBG} \left( \frac{\mu g}{L} \right) = \frac{\text{RfD} \left( \frac{mg}{kg \cdot day} \right) \times \text{RSC} \times 1000 \frac{\mu g}{mg}}{\text{IR} \left( \frac{L}{kg \cdot day} \right)}
\]

Past PFAS guidance used the standard equation shown, but we had outstanding concerns regarding early life exposures for the bioaccumulative PFAS
**The Challenge of PFAS**

Some PFAS are bioaccumulative

Serum concentrations do not represent recent exposure, but rather an integral of past exposure, attenuated over time

Serum concentrations are better than current intake as a measure of potential for health effects

Placental and breast milk transfer further complicate evaluation through “traditional” methods

<table>
<thead>
<tr>
<th>PFAS</th>
<th>RfD (mg/kg-d)</th>
<th>Equivalent serum conc. (µg/L)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFOA</td>
<td>0.000018</td>
<td>130</td>
</tr>
<tr>
<td>PFOS</td>
<td>To be released ~4/3/19</td>
<td></td>
</tr>
<tr>
<td>PFHxS</td>
<td>To be released ~4/3/19</td>
<td></td>
</tr>
</tbody>
</table>

* Serum concentration is based on population-based parameters and should not be used for interpreting serum levels in individuals or for clinical assessment.
a single-chemical, one-compartment, Excel-based, lifetime-duration, toxicokinetic (TK) model to simulate serum levels of PFAS from birth through adulthood (attainment of steady-state conditions)

- Start at birth with body burden from placental transfer
- Daily intake and elimination
  - Breastfeeding
  - Water Consumption
- 20,000-day simulation period
Governing Equations

Volume of Distribution ($V_d$) is chemical-specific and varies with age

Half-life is chemical-specific

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

where:

$\text{Clearance Rate} \left( \frac{L}{kg \cdot day} \right) = V_d \times k$

$V_d = \text{Volume of Distribution} \left( \frac{L}{kg} \right)$

$k = \frac{\ln(2)}{\text{half-life (days)}}$
Initial Conditions

At Day 1 (birth):

\[
\text{Serum Conc.} \left( \frac{mg}{L} \right) = \text{Maternal serum conc.} \left( \frac{mg}{L} \right) \times \text{placental transfer factor}
\]

For all subsequent days:

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

Daily intake derived from contaminated water of known concentration, and/or breast milk with PFAS concentration calculated from transfer factor

Maternal loss of PFAS during breastfeeding also considered
## Key Parameters

<table>
<thead>
<tr>
<th>Model Parameter</th>
<th>PFOA</th>
<th>PFOS</th>
<th>PFHxS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Half-life</strong></td>
<td>840 days</td>
<td>1241 days</td>
<td>1935 days</td>
</tr>
<tr>
<td><strong>Volume of Distribution ($V_d$)</strong></td>
<td>0.17 L/kg</td>
<td>0.23 L/kg</td>
<td>0.25 L/kg</td>
</tr>
<tr>
<td><strong>$V_d$ Age Adjustment</strong></td>
<td>2.4 at birth, 2.1 age 1-30 days, declines to 1 at age 10 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clearance rate (CR)</strong></td>
<td>0.00014 L/kg-d</td>
<td>0.00012 L/kg-d</td>
<td>0.000090 L/kg-d</td>
</tr>
<tr>
<td><strong>Placental transfer factor</strong> (% of maternal serum level)</td>
<td>87% [range ~70 – 124%]</td>
<td>40% [range ~30 – 60%]</td>
<td>70% [range 43-95%]</td>
</tr>
<tr>
<td><strong>Breastmilk transfer factor</strong> (% of maternal serum level)</td>
<td>5.2% [range ~3 – 11%]</td>
<td>1.7% [range ~1 – 2%]</td>
<td>1.4% [range 0.8 – 2%]</td>
</tr>
</tbody>
</table>
Using the Model

Generic Example—Effect of altering PFAS concentration in water

- Time series of serum concs scales linearly with water conc
- Starting point is product of steady-state conc and transfer factor
Generic Example– Effect of altering elimination half-life

At age 3.5 years, ratio is 15 vs. 8 at steady-state
Using the Model

Generic Example

Serum concentration, µg/L

Age (years)

Max allowable serum concentration

Max allowable serum concentration
Using the Model: RSC

Relative Source Contribution (RSC) factors
Derived by comparing RfD-based serum concentration to known non-water-related serum PFAS levels in the general population (NHANES and Minnesota-specific studies)

When non-water exposures are significant, RSC can be based on (or informed by) a residual value

Example (PFOA):
- Reference serum conc. = 130 µg/L; 80% of this = 104 µg/L
- NHANES 2013-14 indicates P95 serum concentration of 5.57 µg/L
- 104 – 5.57 = 98.4 µg/L, which is about 75% of the reference serum concentration
  This value was lowered to 50% due to uncertainties in the serum data, especially among younger children and infants, and following EPA’s Exposure Decision Tree process for RSC (EPA, 2000)

When non-water exposures are not significant, decision tree process leads to an RSC of 50% (example: PFHxS)
Model Output: PFOA
Model Output: PFOS

RSC = 50% (infants/young children)
RSC = 20% (older)
Model Output: PFHxS

**Formula-fed Infant**

**Breastfed Infant, Reduced Water Concentration**
### Breastfeeding vs. Formula feeding

<table>
<thead>
<tr>
<th>PFAS</th>
<th>Water conc., ug/L</th>
<th>Mother's serum, ug/L</th>
<th>Mother's milk, ug/L</th>
<th>Milk:Water ratio</th>
<th>Half-life, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFOA</td>
<td>0.035</td>
<td>11.7</td>
<td>0.61</td>
<td>17.4</td>
<td>delivery 840</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.3</td>
<td>0.17</td>
<td>4.9</td>
<td>1 year</td>
</tr>
<tr>
<td>PFOS</td>
<td>(R)</td>
<td>(R)</td>
<td>(R)</td>
<td>6.2</td>
<td>1241</td>
</tr>
<tr>
<td></td>
<td>(R)</td>
<td>(R)</td>
<td>(R)</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td>PFHxS</td>
<td>(R)</td>
<td>(R)</td>
<td>(R)</td>
<td>7.4</td>
<td>1935</td>
</tr>
<tr>
<td></td>
<td>(R)</td>
<td>(R)</td>
<td>(R)</td>
<td>5.6</td>
<td></td>
</tr>
</tbody>
</table>

(R) = redacted value pending public release

**Why the big difference between breastfeeding and formula-feeding?**

PFAS concentration in milk can be much higher than the concentration in contaminated water.
Breastfeeding vs. Formula feeding

Mother is effectively “offloading” body burden onto infant

Shape of curve will depend on chemical parameters

MDH still recommends breastfeeding to mothers due to myriad health benefits
Current and Future Steps

✓ PFOA guidance (0.035 ug/L) has been released
✓ Analysis of PFOS and PFHxS is complete

☐ Release of PFOS and PFHxS values and documentation next week

☐ Summer 2019 – anticipating release of NTP report on PFOA; will determine if revision of our PFOA value is warranted

☐ Also considering adapting model to evaluate fish consumption

☐ Monitoring continues around the state
For More Information

• See our recent open-access article in the *Journal of Exposure Science and Environmental Epidemiology*, 29:183-95, 2019. https://www.nature.com/articles/s41370-018-0110-5

• Sign up for notifications about our upcoming guidance for PFOS and PFHxS: https://bit.ly/2HTnRyQ

Chris Greene, christopher.greene@state.mn.us
Helen Goeden, helen.goeden@state.mn.us
James Jacobus, James.jacobus@state.mn.us
Key References

- Vd adjustment factors:

- Model development:

- RSC factors:

- Water and breast milk intake rates:
MDH Model in agreement with human serum data
Placental Transfer has a large impact on serum levels
Ingestion through breastmilk has an even larger impact.