Understanding Risk to Wildlife from Exposure to PFAS

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Background

- Widespread use of PFAS → global contamination of the environment, wildlife, and humans.
- PFAS are highly persistent, bioaccumulative substances.
- PFOS and PFHxS are the most frequently detected.
- PFOS is a likely driver of risk.
Background

- PFAS are detected in tissues of various species of wildlife.
  - Ringed-billed Gulls;
  - Sea lion;
  - Polar bear;
  - Laysan Albatross;
  - Bottlenose dolphin;
  - Various fish species.

- Effects and environmental dynamics are not well understood.

Background

• Historical AFFF use $\rightarrow$ groundwater contamination.
• Ecological receptors are exposed via diet and directly from media.

Salice et al., Environ Toxicol Chem. 2018; 45(8): 2198-2209.
Characterization of PFOS in an aquatic ecosystem

- Samples were collected near fire-training areas at Barksdale Air Force Base.

![Graph showing log10 concentration vs proportion affected species.]

**TABLE 2: Probability of exceeding benchmark toxicity values**

<table>
<thead>
<tr>
<th>Exposure scenario</th>
<th>Location</th>
<th>SSD HCS (1.12 ppb)</th>
<th>SSD HCS LCL (0.42)</th>
<th>Qi et al. (2011) (0.6 ppb)</th>
<th>Giesy et al. (2010) (5.1 ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>Flat River</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall—likely</td>
<td>All Cooper Bayou</td>
<td>0.17</td>
<td>0.32</td>
<td>0.26</td>
<td>0.050</td>
</tr>
<tr>
<td>Specific location—likely</td>
<td>Weapons Bridge</td>
<td>0.14</td>
<td>0.25</td>
<td>0.21</td>
<td>0.043</td>
</tr>
<tr>
<td>High-end—likely</td>
<td>Cooper Confluence</td>
<td>0.23</td>
<td>0.36</td>
<td>0.31</td>
<td>0.09</td>
</tr>
<tr>
<td>High-end—unlikely</td>
<td>Upper-Tributary Mack’s Bayou</td>
<td>0.37</td>
<td>0.51</td>
<td>0.46</td>
<td>0.19</td>
</tr>
</tbody>
</table>

C5 = 5% hazardous concentration; LCL = 95% lower confidence limit of the HCS from the SSD; SSD = species sensitivity distribution for chronic perfluorooctane sulfonate toxicity generated in the present study (Supplemental Data).
Characterization of PFOS in a terrestrial ecosystem

- Samples were collected near a fluorochemical plant in Flanders, Belgium.
Modeling avian exposure to PFAS

- Modeled exposure of 7 PFAS to birds in aquatic habitats impacted by AFFF.
Risk Assessment Paradigm

Risk = quantification of the likelihood that an effect will happen in response to exposure.

- Hazard identification: Is this toxic?
- **Dose-response assessment**: How toxic is it? How much is safe?
- Exposure assessment: Who is exposed? How often? How long?
- Risk characterization: So what?
- Risk management: What will be done about it?
Dose-response assessment

- **Traditional point(s) of departure:** Point where exposure exceeds an organism’s ability to adapt without eliciting an adverse health effect
  - **No Observed Adverse Effect Level (NOAEL):** Highest data point at which there is not an observed toxic or adverse effect
  - **Lowest Observed Adverse Effect Level (LOAEL):** Lowest data point at which there is an observed toxic or adverse effect
Dose-response assessment

• Modern points of departure
  • **Benchmark Dose:** estimate of the dose that produces a predetermined change in response rate of an adverse effect
  • **BMDL:** 95% lower-bound confidence limit on the BMD

Weibull Model, with BMR of 10% Extra Risk for the BMD and 0.95 Lower Confidence Limit for the BM

Logistic Model, with BMR of 10% Extra Risk for the BMD and 0.95 Lower Confidence Limit for the BM
Pharmacokinetics of PFAS

• Differences in pharmacokinetic disposition among:
  • Different carbon-chain lengths;
  • Different functional groups;
  • Species, strain, sex, and age
    • PPARα
    • Pathways for release (e.g., menstruation, parturition, lactation)

TABLE 1
Serum Levels of PFOA in Adult Sprague-Dawley Rats and CD-1 Mice after Receiving Daily Oral Gavage

<table>
<thead>
<tr>
<th>Species</th>
<th>Dose</th>
<th>Days of treatment</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>10 mg/kg</td>
<td>20</td>
<td>111 ± 10 μg/ml (8)</td>
<td>0.69 ± 0.18 μg/ml* (8)</td>
</tr>
<tr>
<td>Mouse</td>
<td>20 mg/kg</td>
<td>7</td>
<td>181 ± 34 μg/ml (6)</td>
<td>178 ± 19 μg/ml (7)</td>
</tr>
<tr>
<td>Mouse</td>
<td>20 mg/kg</td>
<td>17</td>
<td>199 ± 19 μg/ml (8)</td>
<td>171 ± 15 μg/ml (5)</td>
</tr>
</tbody>
</table>


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Characterizing the toxicity of PFAS

Conduct laboratory studies | Conduct field studies | Extrapolate results

- General toxicological features of PFAS
  - Hepatotoxicity
  - Tumor induction
  - Developmental toxicity
  - Immunotoxicity
  - Neurotoxicity
  - Endocrine disruption


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Model species: *Peromyscus spp.*

- *Peromyscus spp.*
  - Most widespread native, North American mammal (genera);
  - Adapt to the laboratory environment;
  - Have known genetic/disease background;
  - Maintain relevance as an environmental model.
Technical Approach

- **Task 1**: Serum pharmacokinetics
  - Administer PFAS for 28 days.
  - Collect blood samples every 7 days → analyze serum for [PFAS] via LC/MS-MS.

- **Task 2**: Repro/devo toxicity tests
  - Administer PFAS for 28 days.
  - Establish 1:1 mating pairs.
  - Evaluate repro/devo, immune response, and hormones (sex and thyroid).
Effects in *Peromyscus* exposed to PFOS

- Complete mortality at 40 and 20 mg/kg-day
- Tissue weights:
  - Increased liver
  - Decreased thymus
- Serum levels:
  - Unaffected by sex
  - Increased between day 14 and 28

Organ Weights of Animals Exposed to PFOS

Serum levels of PFOS

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Effects in *Peromyscus* exposed to PFOS

Reduced live litter size

Increased total litter loss by PND1

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Effects in *Peromyscus* exposed to PFOS

Reduced T4 in males (A) and females (B)

**A**

- Hormones: E2, P4, Test., T3, T4
- Y-axis: Hormone conc. (ng/ml)
- X-axis: Hormones

**B**

- Hormones: E2, P4, Test., T3, T4
- Y-axis: Hormone conc. (ng/ml)
- X-axis: Hormones

Legend:
- 0 mg/kg-day
- 0.2 mg/kg-day
- 1.0 mg/kg-day
- 5.0 mg/kg-day

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### Summary

<table>
<thead>
<tr>
<th>Critical effect</th>
<th>Peromyscus</th>
<th>Rat</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMD₅ mg/kg-day</td>
<td>BMDL₅ mg/kg-day</td>
<td>BMD₅ mg/kg-day</td>
</tr>
<tr>
<td>Decreased neonatal survival</td>
<td>1.69</td>
<td>0.97</td>
<td>1.06&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Source: Luebker et al., 2005  
<sup>b</sup> Source: Lau et al., 2003
## Recommended PFOS TRVs

### Ingestion TRVs for the Class Mammalia\(^a\)

<table>
<thead>
<tr>
<th>TRV</th>
<th>Dose (mg/kg-day)</th>
<th>Confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRV&lt;sub&gt;LOW&lt;/sub&gt;</td>
<td>0.0327 (male)</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>0.0680 (female)</td>
<td></td>
</tr>
<tr>
<td>TRV&lt;sub&gt;HIGH&lt;/sub&gt;</td>
<td>0.0521 (male)</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>0.0980 (female)</td>
<td></td>
</tr>
</tbody>
</table>

### Ingestion TRVs for the Class Aves\(^b\)

<table>
<thead>
<tr>
<th>TRV</th>
<th>Dose (mg/kg-day)</th>
<th>Confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRV&lt;sub&gt;LOW&lt;/sub&gt;</td>
<td>0.15</td>
<td>Low-Medium</td>
</tr>
<tr>
<td>TRV&lt;sub&gt;HIGH&lt;/sub&gt;</td>
<td>0.64</td>
<td>Low-Medium</td>
</tr>
</tbody>
</table>

### Ingestion TRVs for Terrestrial Amphibian Species\(^c\)

<table>
<thead>
<tr>
<th>TRV</th>
<th>Concentration (mg/L-day)</th>
<th>Confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRV&lt;sub&gt;LOW&lt;/sub&gt;</td>
<td>0.003</td>
<td>Low</td>
</tr>
<tr>
<td>TRV&lt;sub&gt;HIGH&lt;/sub&gt;</td>
<td>0.075</td>
<td>Low</td>
</tr>
</tbody>
</table>

\(^a\) Source: Thomford (2002). TRVs determined by the BMD/BMDL Benchmark Dose approach.

\(^b\) Sources: Newsted et al. (2007), Gallagher et al. (2003a, 2003b, 2003c). TRVs determined by the NOAEL/LOAEL approach.

\(^c\) Source: Ankley et al. (2004). TRVs determined by the NOAEC/LOAEC approach.
Conclusions

• Predicting bioaccumulation and toxicity of PFAS in wildlife is complex.
• Lab studies can be used to generate TRVs.
• TRVs can be used to assess the risks from environmental exposure.
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  – Mike Quinn
  – Emily Lent

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Questions?