

Descriptive toxicological approaches to understand health risks of understudied PFAS

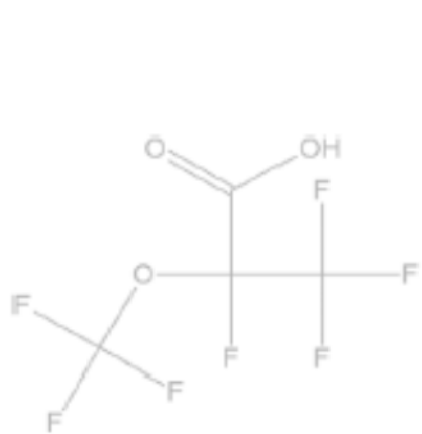
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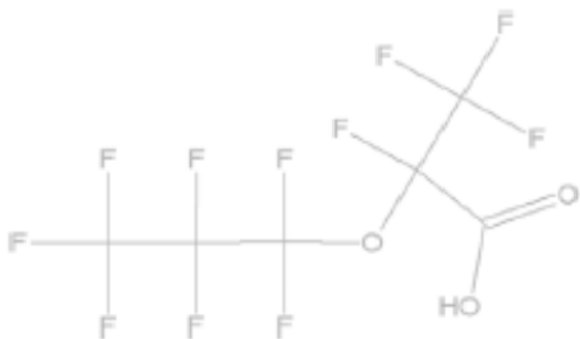
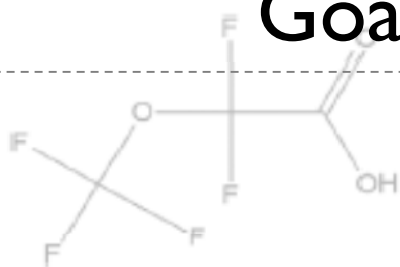
October 23, 2019

Environmental Health Collaborative 2019 Summit
PFAS: Integrating Science and Solutions in NC

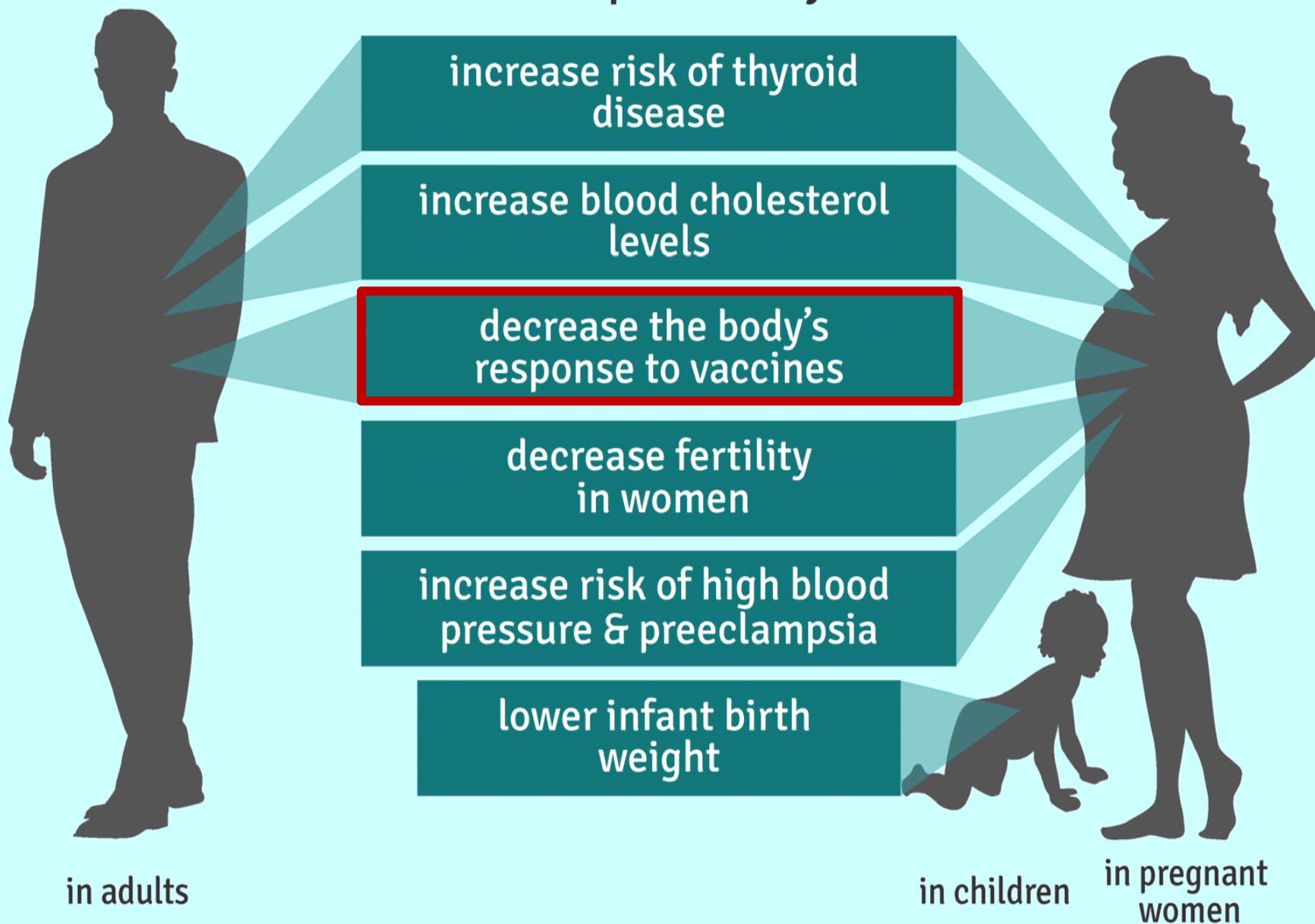




Goals and rationale for our studies.



Human studies suggest PFAS exposure may...



Animal studies suggest PFAS exposure is linked to...



damage to the immune
system

liver damage

birth defects, delayed
development, and newborn
deaths

**Team 5
Applied Research
Opportunities**

DeWitt (ECU)
Fry (UNC-CH)

Team 5C (DeWitt) Goals

In animals exposed to understudied
PFAS specific to NC:

1. Observe animals over a 30-day exposure period.
2. Count major cell subpopulations in immune organs.
3. Assess function of the adaptive immune system.
4. Assess function of the innate immune system.

Rationale

- Basic descriptive toxicological data are essential for decision-making.
- The immune system is one of the systems targeted by exposure to PFAS in both exposed experimental animal models and humans.

Weight of evidence from studies of PFAS-exposed humans experimental animals

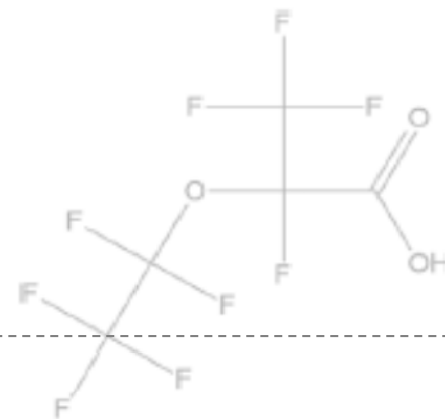
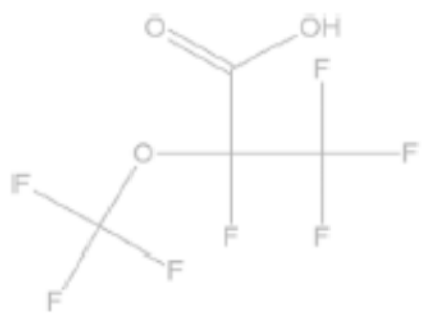


PFOA and PFOS suppress antigen-specific antibody responses in experimental models (high level of evidence) and humans (moderate level of evidence).

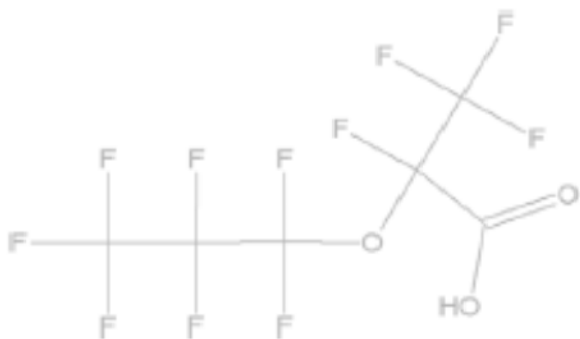
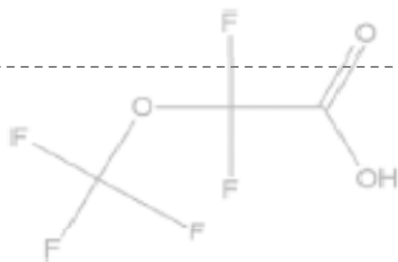


National Toxicology Program
U.S. Department of Health and Human Services

SYSTEMATIC REVIEW OF
IMMUNOTOXICITY ASSOCIATED WITH EXPOSURE TO
PERFLUOROCTANOIC ACID (PFOA) OR PERFLUOROCTANE
SULFONATE (PFOS)



Basic experimental design.



Basic experimental design of toxicity studies for evaluating exposure to PFAS

Orally exposed male and female mice. Three different doses of PFAS delivered in water plus an unexposed group.



We use a “harmonized test guideline” as our experimental design framework.

1

30

Days of exposure.

Daily body weights and in-life observations (what they look like, how they act).

In-life observations.

Urine and feces 24-hr prior to dosing and after 1, 5, and 15 days of dosing.

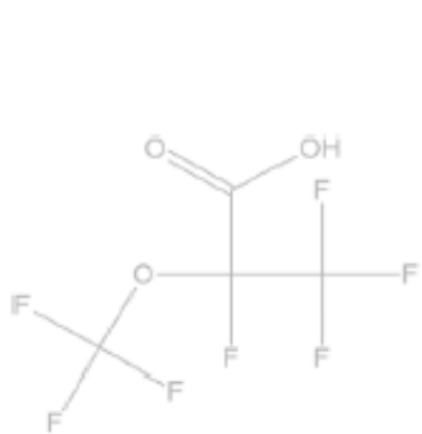
To find internal dose.

“Vaccinations” at 25th day of dosing to stimulate antibody response.

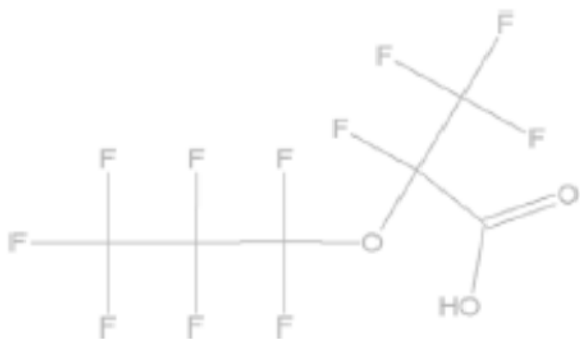
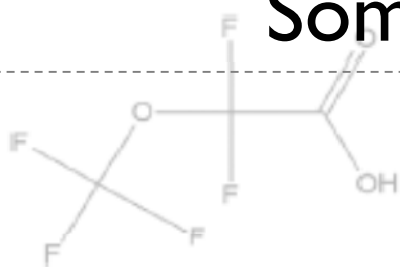
Analogous to flu shot.

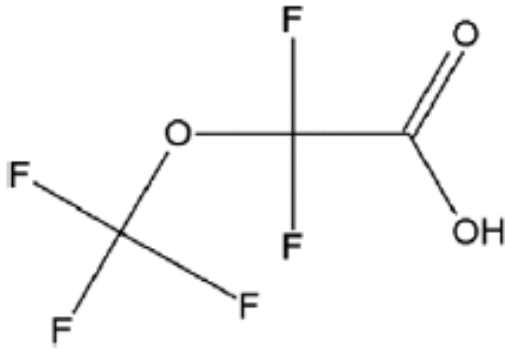
Study end at day 31. Evaluation of organ weights, numbers of cells in immune organs, strength of antibody response, and other data.

Basic measures of **toxicity**.



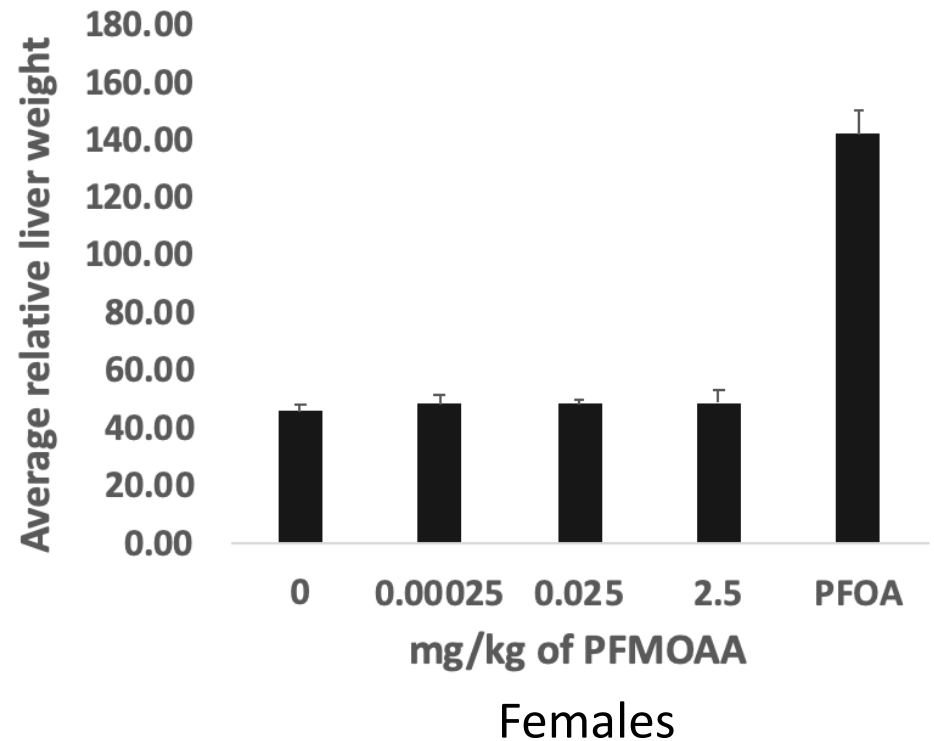
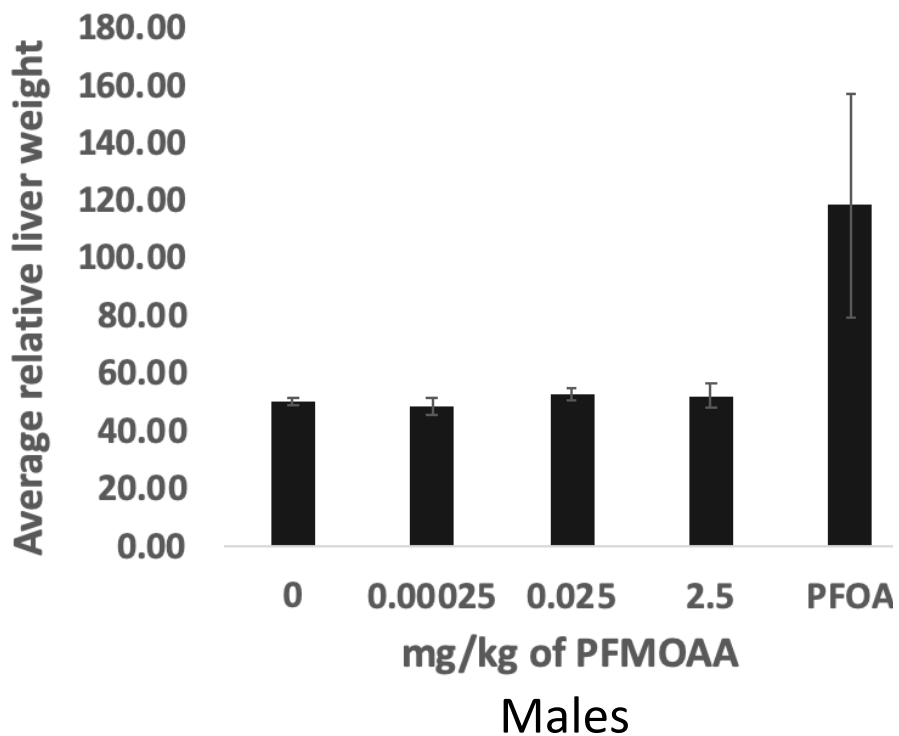
Some of our experimental findings.

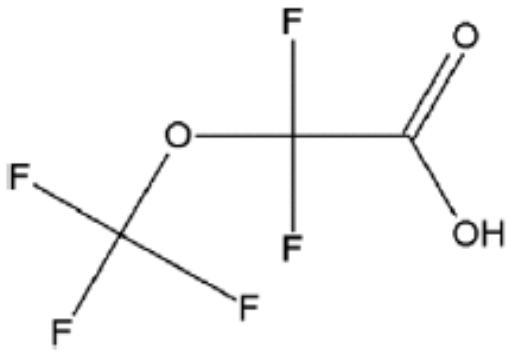




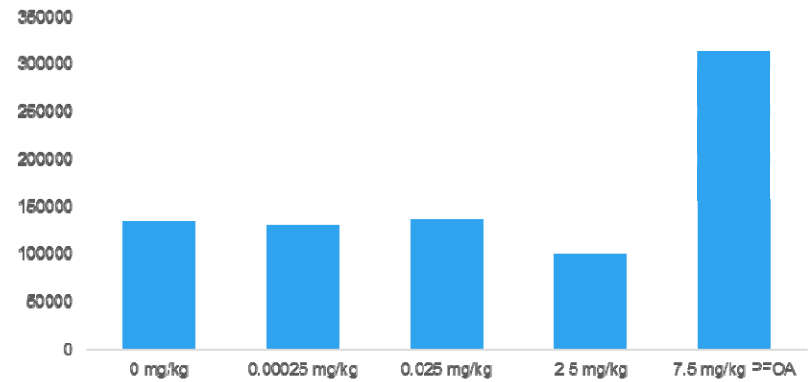
PFMOAA - $C_3HF_5O_3$ perfluoro-2-methoxyacetic acid (mono-ether carboxylic acid)

Dominant PFEA detected in Cape Fear River of North Carolina in 2018 at 35,000 ng/L (Hopkins et al., 2018).

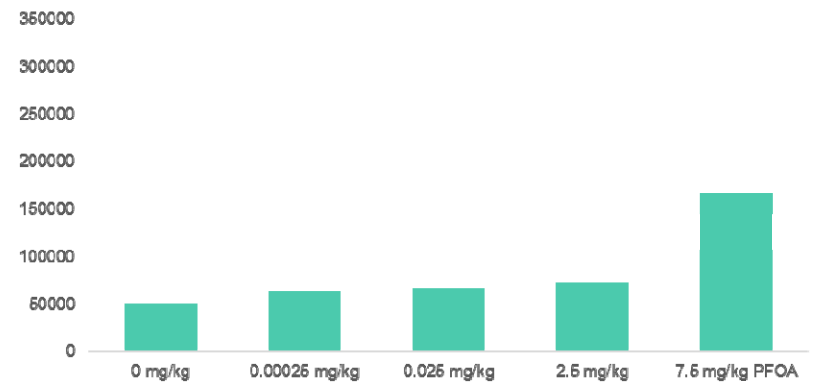




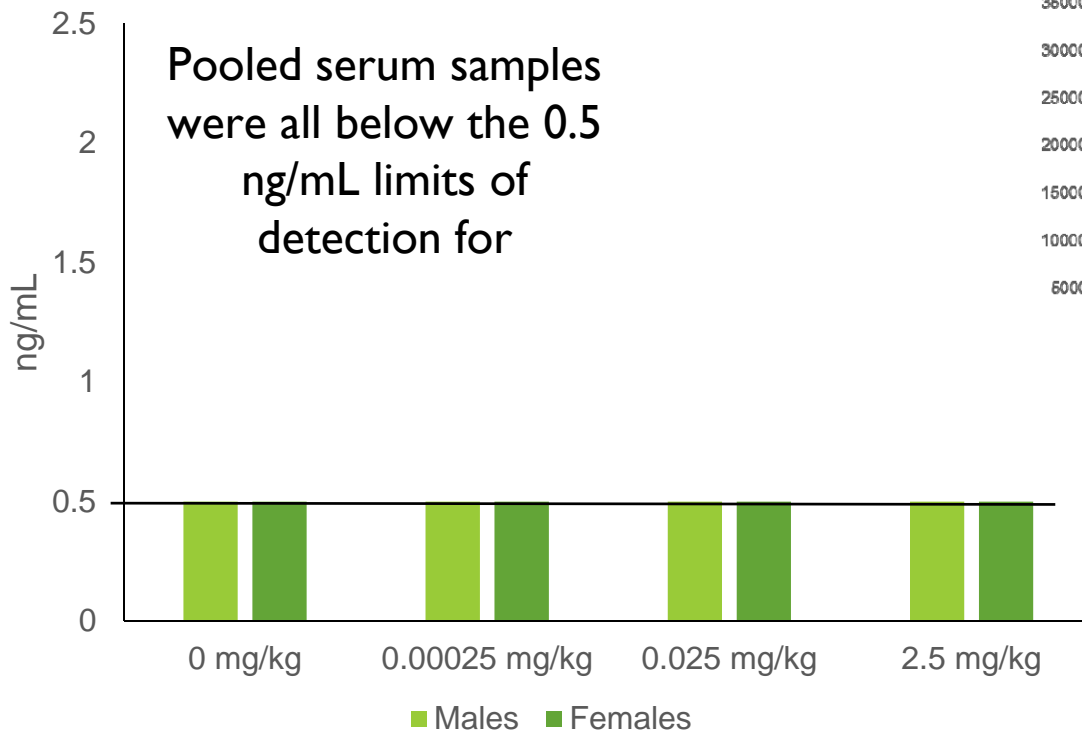
Male Peroxisomal Enzyme Activity (nmole/min/mg of liver)

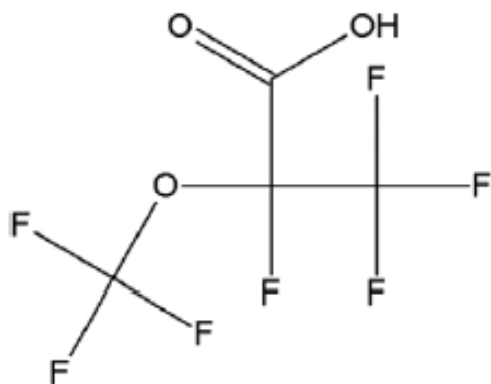


Female Peroxisomal Enzyme Activity (nmole/min/mg of liver)



Peroxisome proliferation was not statistically elevated relative to controls for PFMOAA.

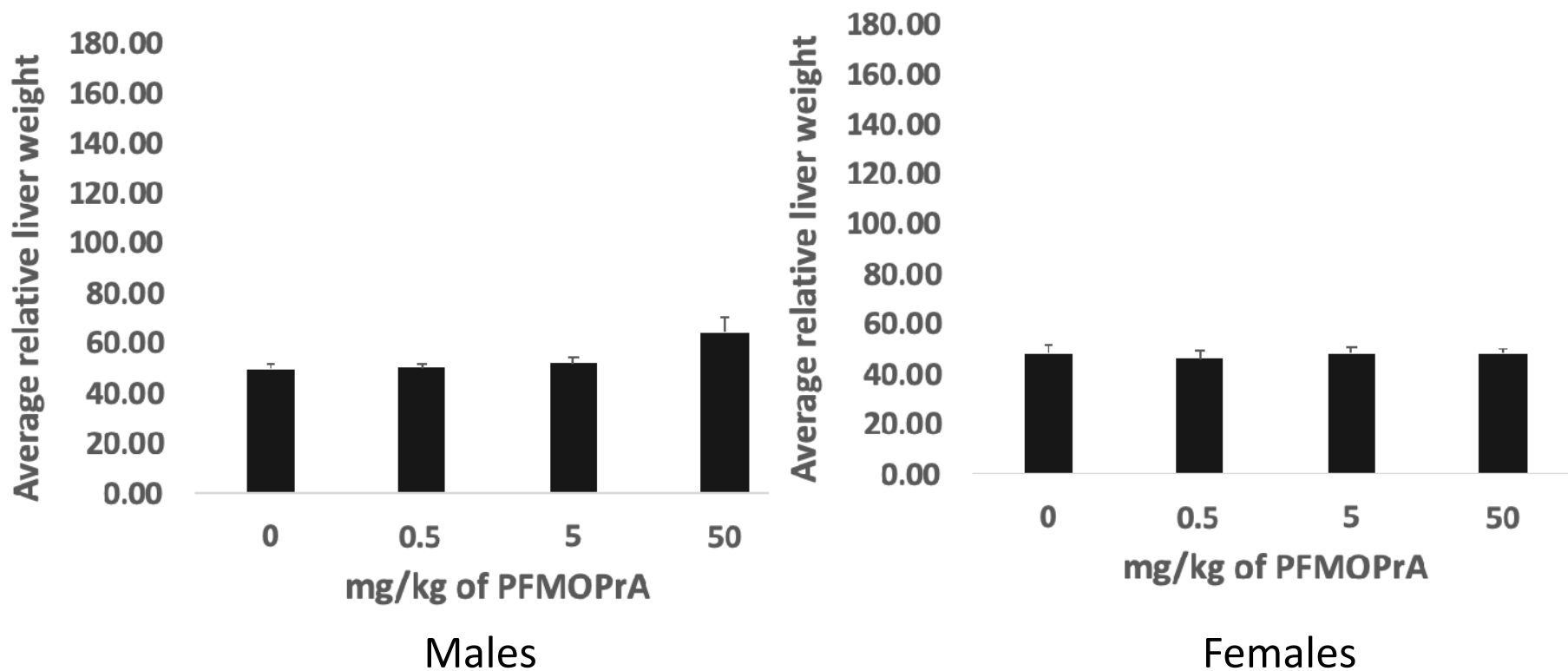


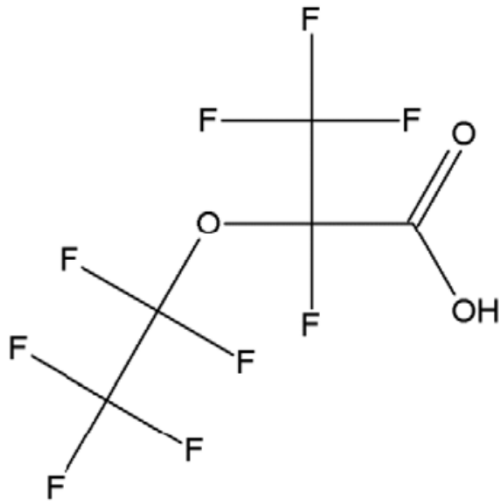


PFMOPrA - C₄HF₇O₃

Perfluoro-2-methoxypropanoic acid
(mono-ether carboxylic acid)

A PFEA detected in Cape Fear River of North Carolina in 2018 (Hopkins et al., 2018).

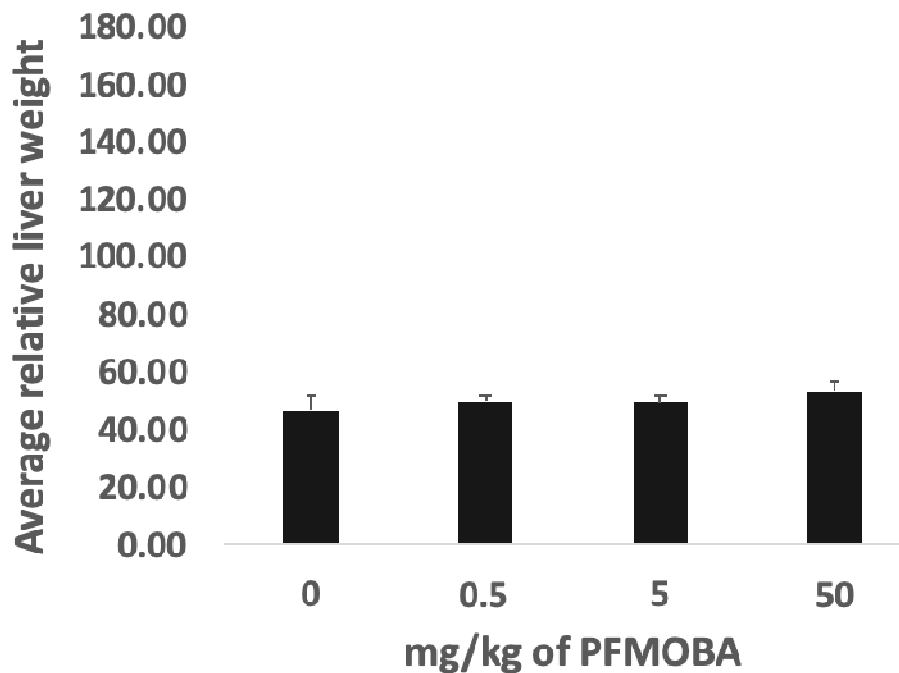




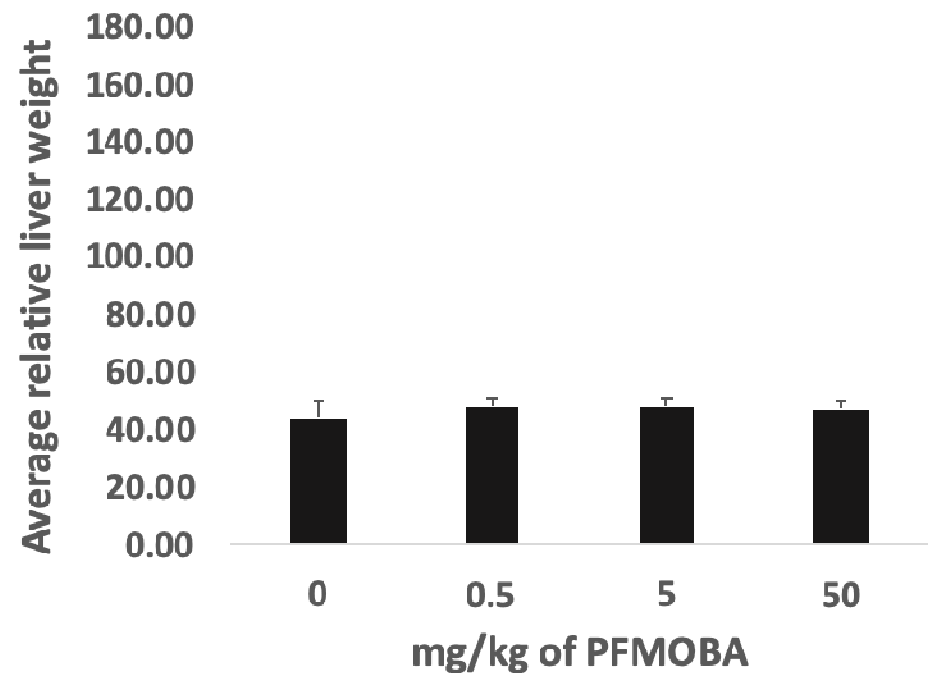
PFMOBA – C₅HF₉O₃

Perfluoro-4-methoxybutanoic acid
(mono-ether carboxylic acid)

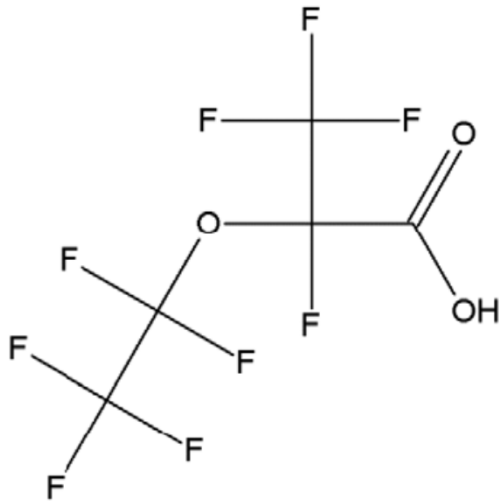
A PFEA detected in Cape Fear River of North Carolina in 2018 (Hopkins et al., 2018).



Males



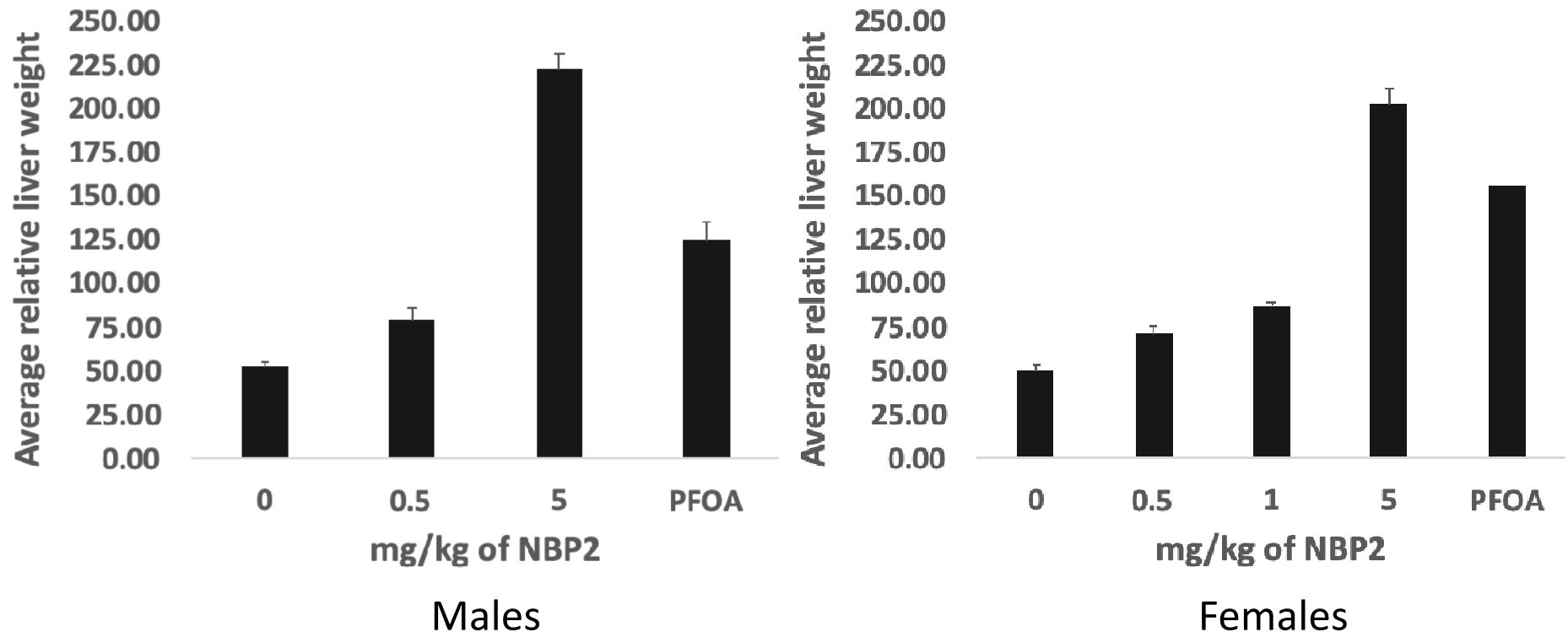
Females



Nafion By-product 2 – C₅HF₉O₃

Perfluoro-4-methoxybutanoic acid
(mono-ether carboxylic acid)

A PFEA detected in Cape Fear River of North Carolina in 2018 (Hopkins et al., 2018).



Thank you to:
NC General Assembly,
NC Policy Collaboratory,
PFAS Testing Network,
members of the DeWitt lab, and
you for listening.

I welcome your questions.