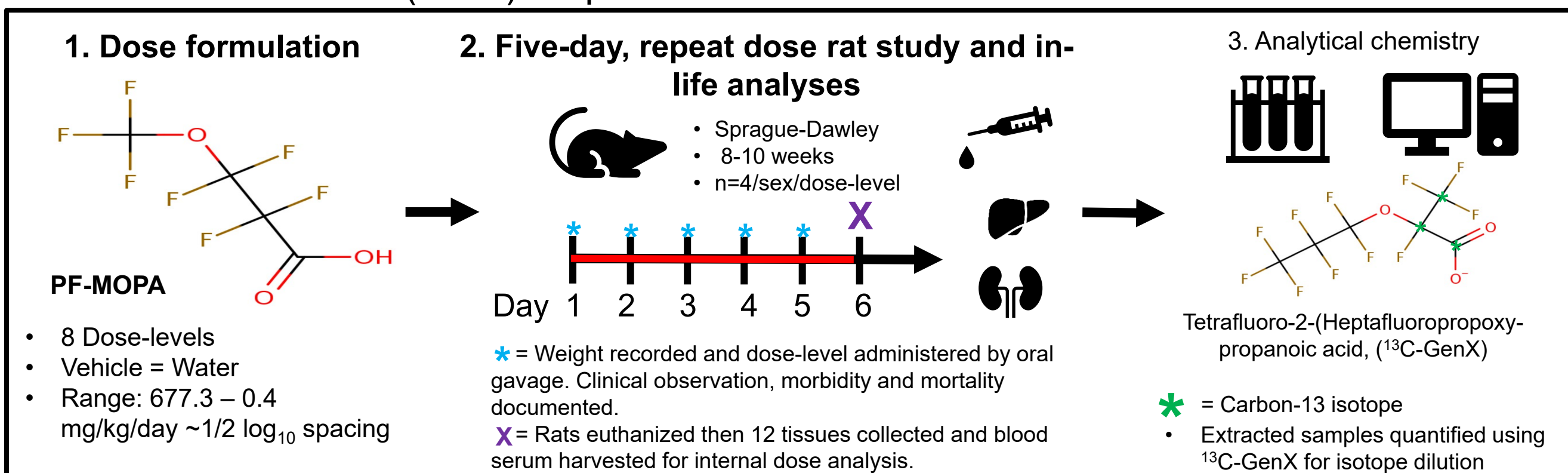


## Introduction

- Per- and polyfluoroalkyl substances (PFAS) are:
  - Industrial compounds that are ubiquitous, persistent environmental contaminants.
  - Numerous, with current estimates at 4700 and growing.
  - Lacking publicly available toxicological data for most compounds.
- Our goal is to develop a rapid assessment of potential toxicity when compared to the current 90-day and 2-year guideline bioassays.**
- Timely risk prioritization for data-poor PFAS will be enabled using**
  - Plasma concentration results, in-life observations (*Presented for perfluoro-3-methoxypropionic acid, PF-MOPA*)**, transcriptomics, thyroid hormone results, and benchmark (BMD) response.

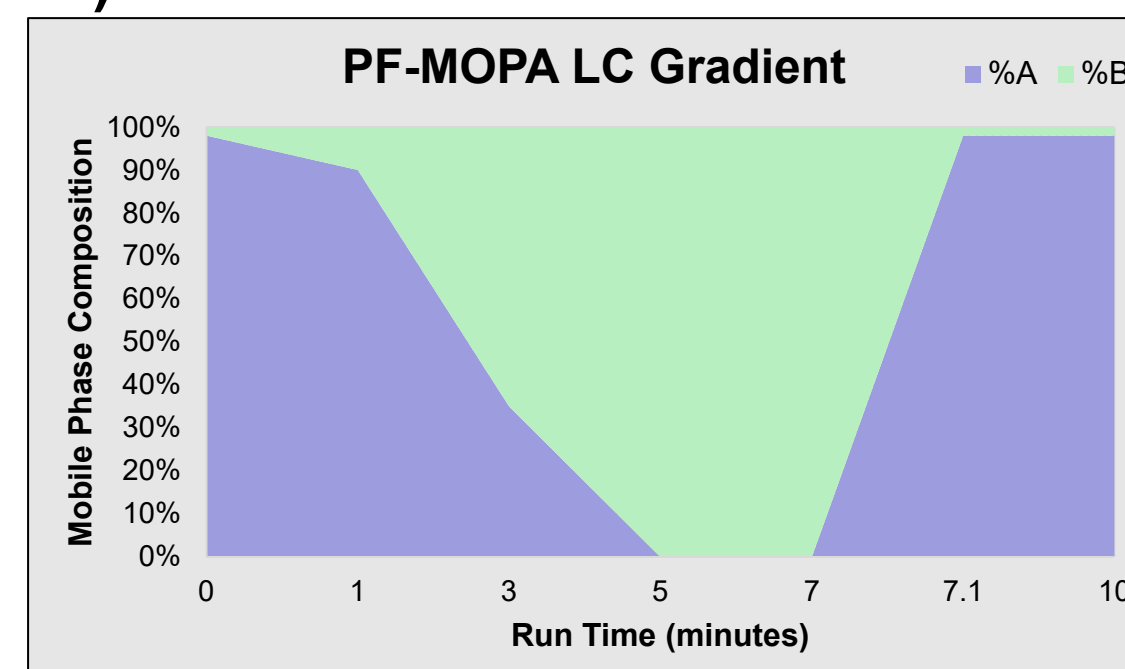


## Analytical Approach

- Plasma samples were extracted through protein precipitation using acetonitrile based upon their predicted PF-MOPA concentration.**
- Separation = Phenomenex (Torrance, CA) Kinetex XB-C18 (100 x 2.1 mm, 2.6 µm)
- Flow rate = 0.2 mL/min, injection volume = 5 µm.
  - Mobile Phase A: 95:5 H<sub>2</sub>O:MeOH, Mobile Phase B: 95:5 MeOH:H<sub>2</sub>O, both contain 4 mM ammonium formate
- LC/MS/MS performed using a Sciex (Framingham, MA) X500R QTOF
  - Negative ion, with electrospray ionization (ESI)**
  - Multiple reaction monitoring (MRM)**

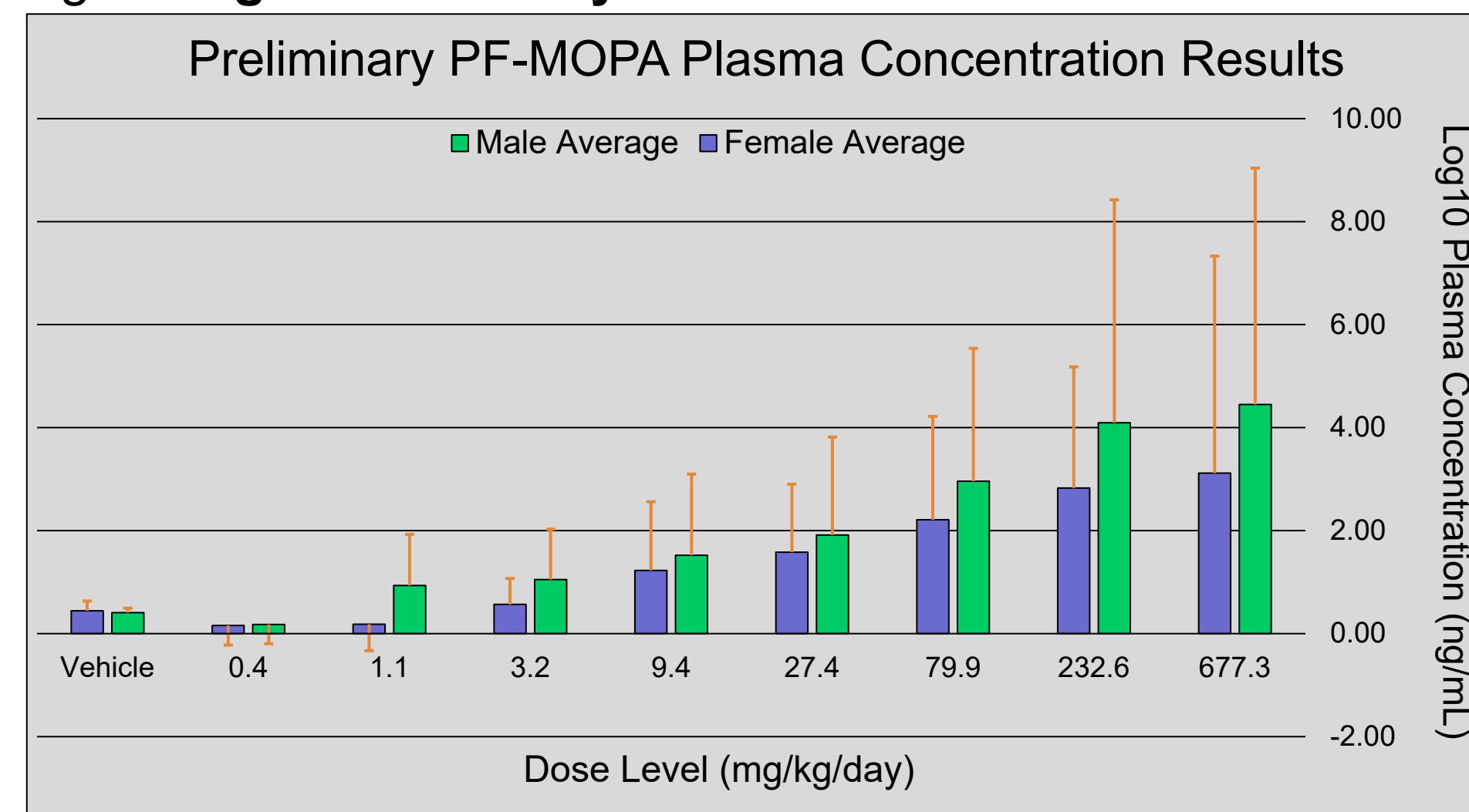
### MRM Fragments Used on Sciex X500 QTOF

Compound	Molecular Ion	Fragment Ion
PF-MOPA	228.97	84.9901
<sup>13</sup> C-GenX	331.98	286.9868



## Plasma Concentration Results

- All nine dose levels contained PF-MOPA above the limit of quantitation (1 ng PF-MOPA/mL plasma).**
- Female rat plasma had a 2-18 times lower concentration than male rat plasma for the highest 7 dose levels.**
- We observed large standard deviations across both sexes and all dose levels, suggesting **biological variability**.



## In-Life Observations

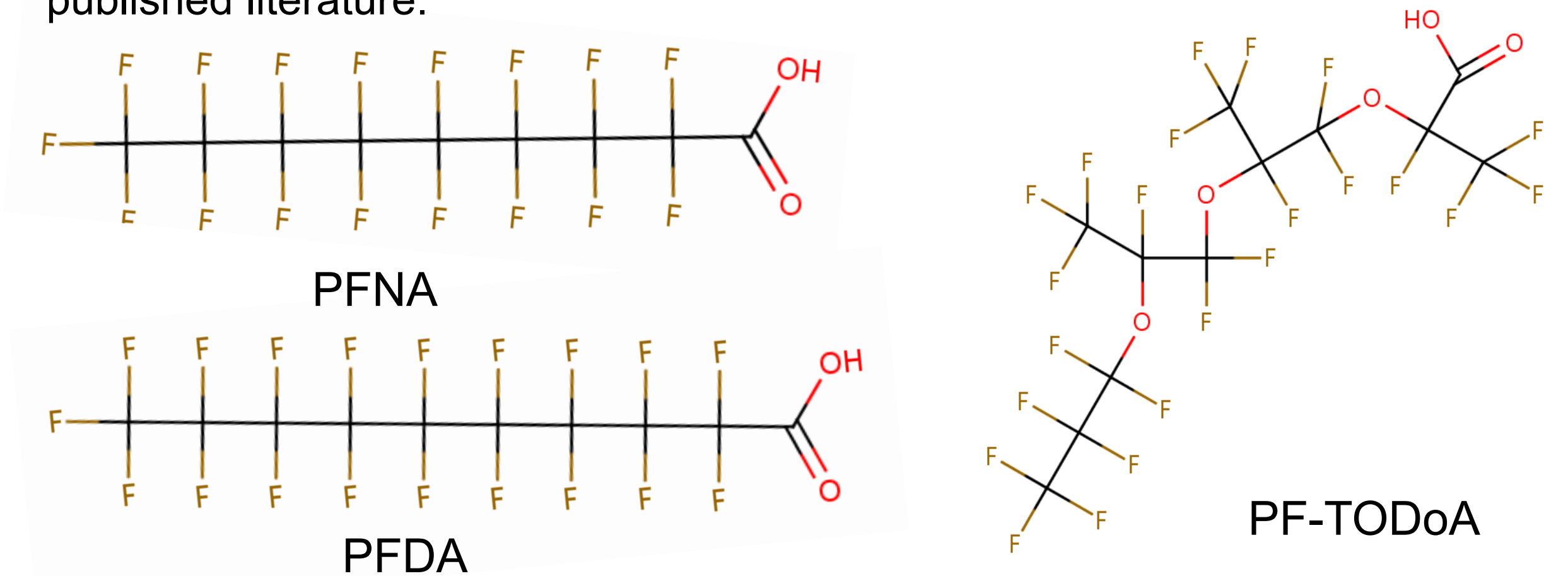
- Male and female rats showed weight gain at all except the highest dose level, at which point **weight losses** were observed for both sexes.

Weight Changes in Male and Female Sprague-Dawley Rats over 5-Day PF-MOPA Exposure		
Dose Level (mg/kg/day)	Male Avg. Weight Change (g)	Female Avg. Weight Change (g)
Vehicle	22.35	6.33
0.4	26.15	9.85
1.1	20.08	1.53
3.2	24.25	1.43
9.4	26.38	3.68
27.4	27.75	9.48
79.9	23.35	9.90
232.6	15.53	6.60
<b>677.3</b>	<b>-55.07</b>	<b>-12.70</b>

- Chronic toxicity signs observed in
  - Males: thin and rough coat; 1 fatality (677.3 mg/kg/day dose).
  - Females: thin and rough coat; piloerection; 1 fatality (677.3 mg/kg/day dose).

## Discussion and Conclusions

- The National Toxicology Program (NTP) ran 28-day studies for 7 PFAS chemicals over a range of concentrations.**<sup>1,2</sup>
  - An average decrease in body weight gain was observed for 5 of the PFAS.<sup>1,2</sup>
  - Two chemicals, perfluorononanoic acid (PFNA) and perfluorodecanoic acid (PFDA) saw a weight loss after at days 8 and 15 respectively.<sup>2</sup>
- The observed weight loss for PF-MOPA after 5 days suggests that it is potentially more acutely toxic than other PFAS.**
- A literature search showed no PFAS dosing studies that compared dosimetry between the sexes in blood or plasma.**
  - We observed a greater female rat plasma concentration in a perfluoro-(2,5,8-trimethyl-3,6,9-trioxadodecanoic) acid (PF-TODoA) 5-day dosing study (unpublished), the opposite trend of what we observed during this PF-MOPA dosing study.
  - Dosimetry in liver and kidney will be determined for data comparison to the published literature.



- Metabolomic, lipidomic, and transcriptomic data are currently being investigated for potential pathway changes. These could be better indicators of the onset of chronic toxicity.**

### References

- NTP Technical Report on the Toxicity Studies of Perfluoroalkyl Sulfonates (Perfluorobutane Sulfonic Acid, Perfluorohexane Sulfonate Potassium Salt, and Perfluorooctane Sulfonic Acid) Administered by Gavage to Sprague Dawley (Hsd: Sprague Dawley SD) rats – Toxicity Report 96. National Toxicology Program. Published August 2019.
- NTP Technical Report on the Toxicity Studies of Perfluoroalkyl Carboxylates (Perfluorohexanoic Acid, Perfluorooctanoic Acid, Perfluorononanoic Acid, and Perfluorodecanoic Acid) Administered by Gavage to Sprague Dawley (Hsd: Sprague Dawley SD) rats – Toxicity Report 97. National Toxicology Program. Published August 2019

See Poster  
3101/P205 for results  
from additional PFAS  
compounds