Biopartitioning of PFAS: Case examples & discussion starter

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PFAS TSCA Workshop (Virtual Presentation)

Session 2: Testing Overview

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The John Edward Porter Neuroscience Research Center

National Institutes of Health

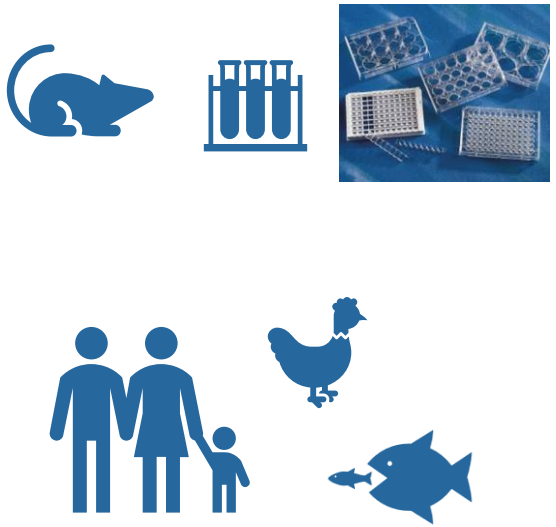
Bethesda, MD

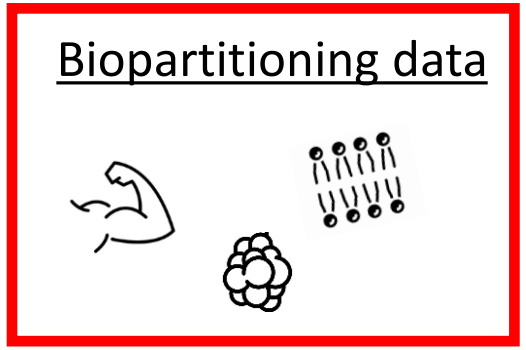
Arnot Research & Consulting

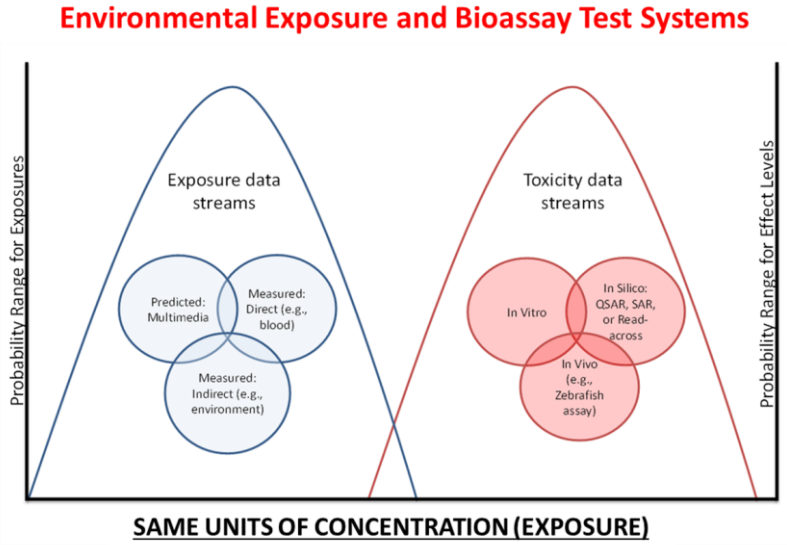
UNIVERSITY OF TORONTO

Physical-(Bio)Chemical Properties: Biopartitioning

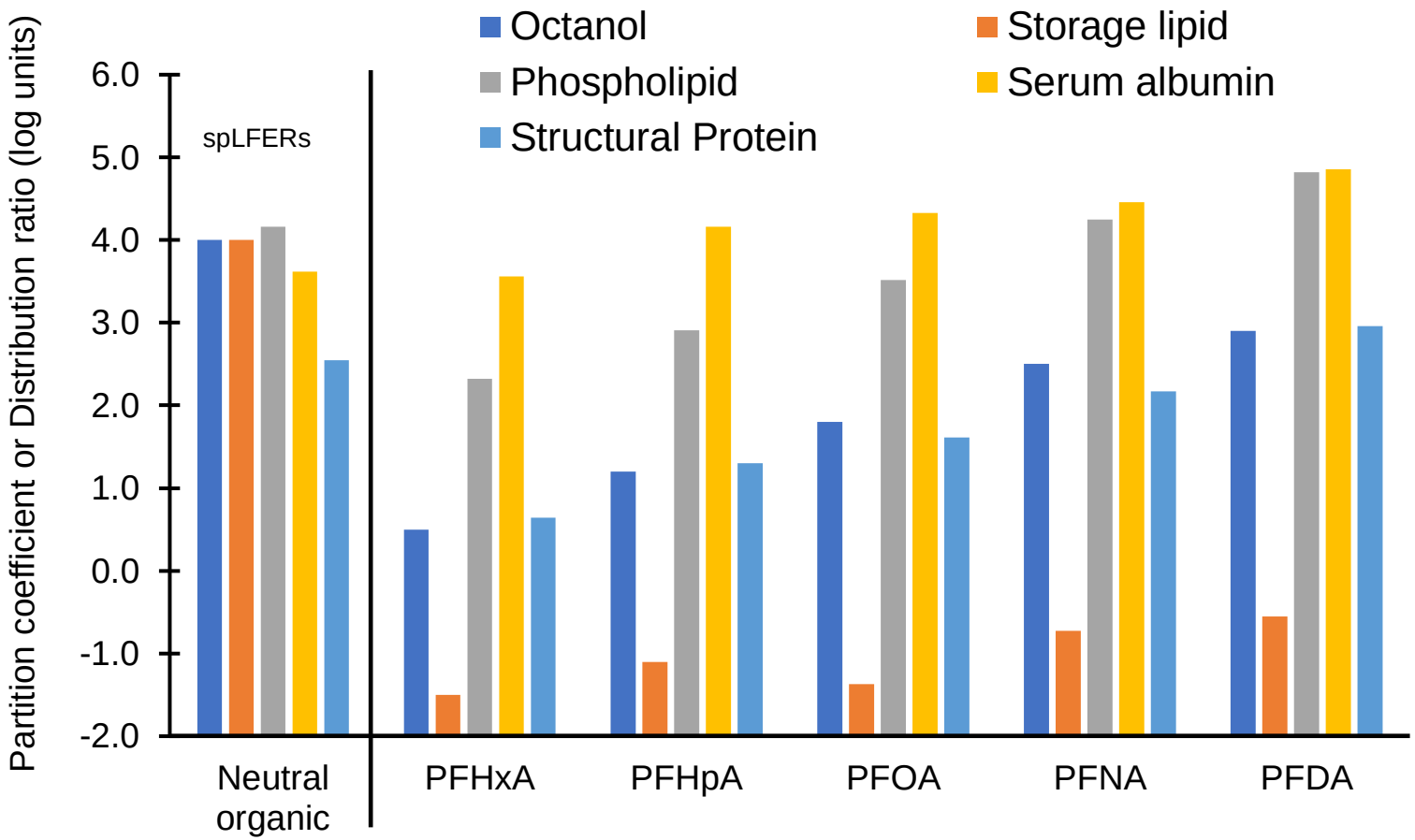
- **Know your chemical properties; Know your system, e.g., know TK & appropriately interpret TD**
- What is biopartitioning and why reliable information for PFAS biopartitioning is important?
  - Understanding and quantifying chemical distribution in in vitro and in vivo systems
  - In Vitro-In Vivo Extrapolation (IVIVE) models
  - Forward and reverse TK models (internal – external exposures): exposure and risk estimation
  - Bioaccumulation (B): hazard assessment
- The **assumption** of using octanol as a surrogate for biopartitioning works very well for many neutral hydrophobic organic chemicals; it is not appropriate for many PFAS (i.e., perfluorinated acids and bases, ?)







Physical-(Bio)Chemical Properties: Biopartitioning



spLFERs (neutral): Endo et al. 2010 doi.org/10.1021/es200855w;
Endo et al. 2011 doi.org/10.1021/tx200431b

Octanol-water (PFCAs): Jing et al. 2009 doi.org/10.1021/ja807961s

Biopartitioning (PFCAs): Allendorf et al. 2021 doi.org/10.1002/etc.4954

B & TK: in vivo

2012

2024

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USE OF THE BIOACCUMULATION FACTOR TO SCREEN CHEMICALS FOR BIOACCUMULATION POTENTIAL

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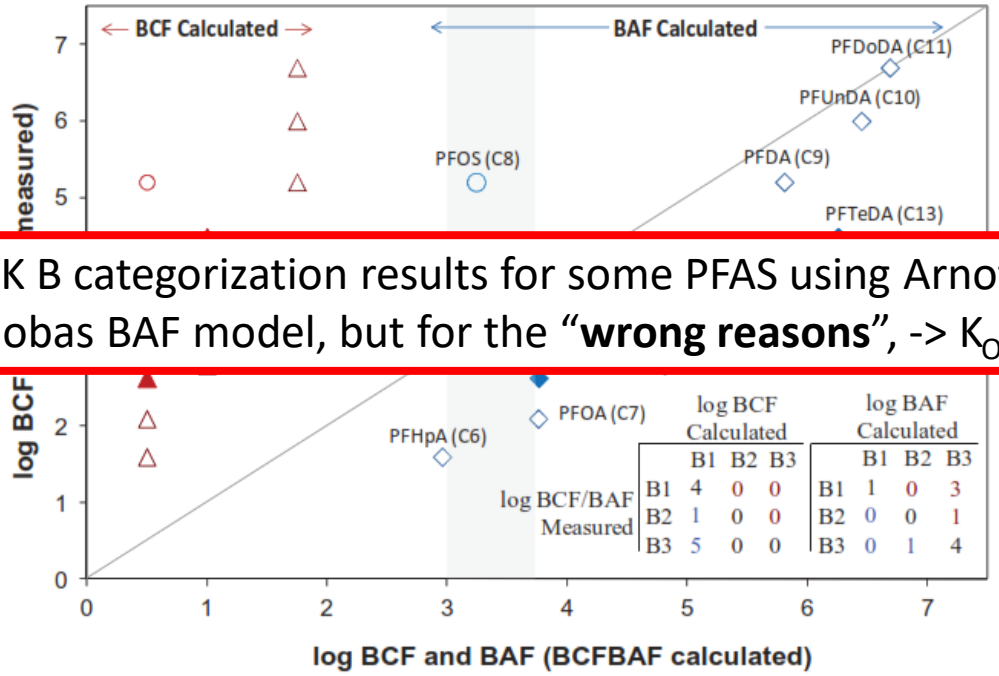
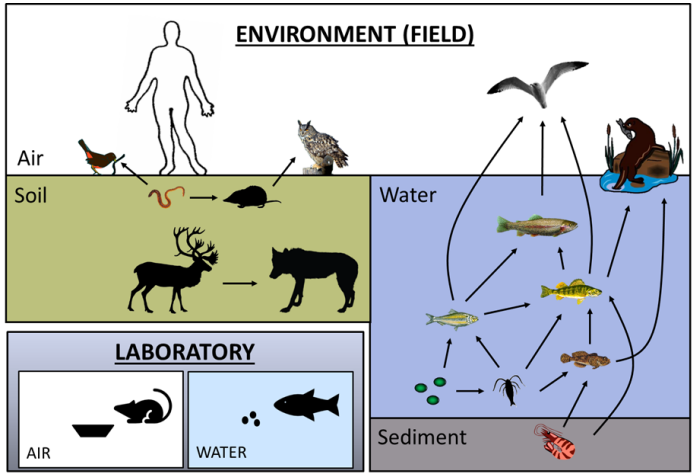
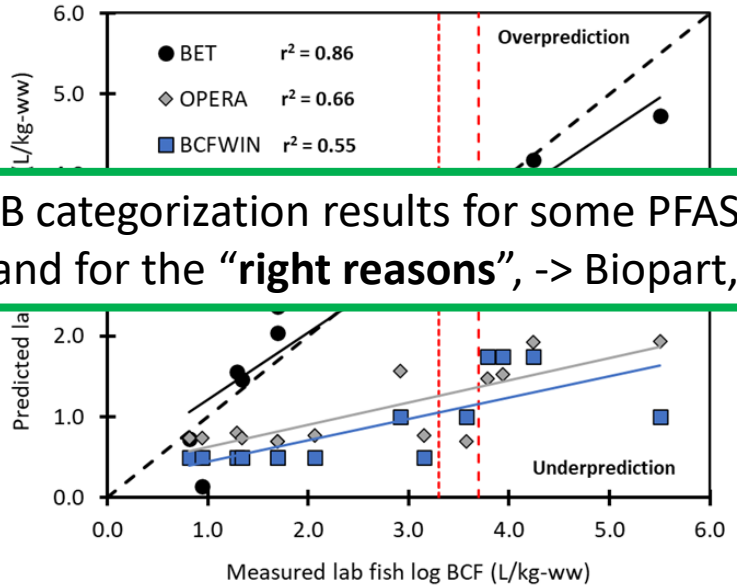


OK B categorization results for some PFAS using Arnot & Gobas BAF model, but for the "**wrong reasons**", -> $K_{OW,N}$

Bioaccumulation Estimation Tool (BET) in EAS-E Suite

EAS-E SUITE
EXPOSURE AND SAFETY ESTIMATION (EAS-E) SUITE



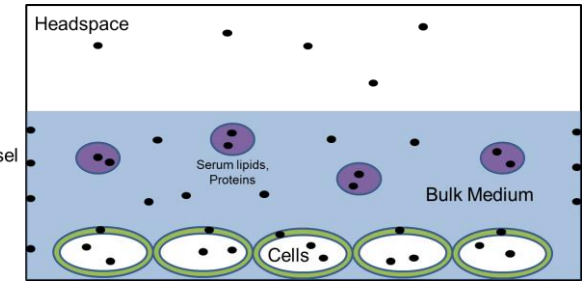


Better B categorization results for some PFAS using BET, and for the "**right reasons**", -> Biopart, pKa

EXPOSURE AND SAFETY ESTIMATION (EAS-E) SUITE

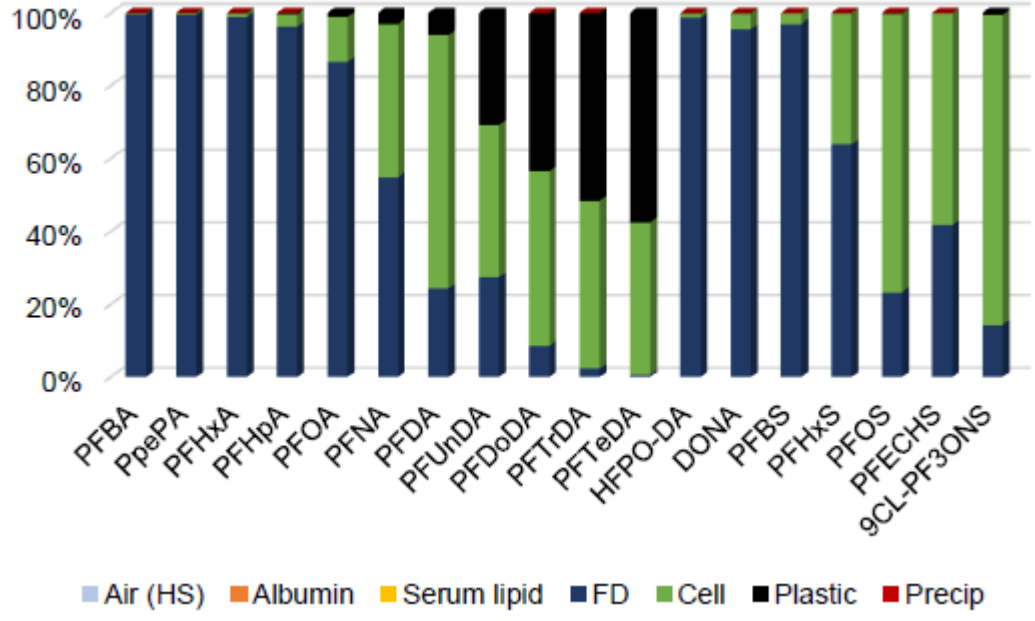
Health Canada

In Vitro Mass Balance: Disposition

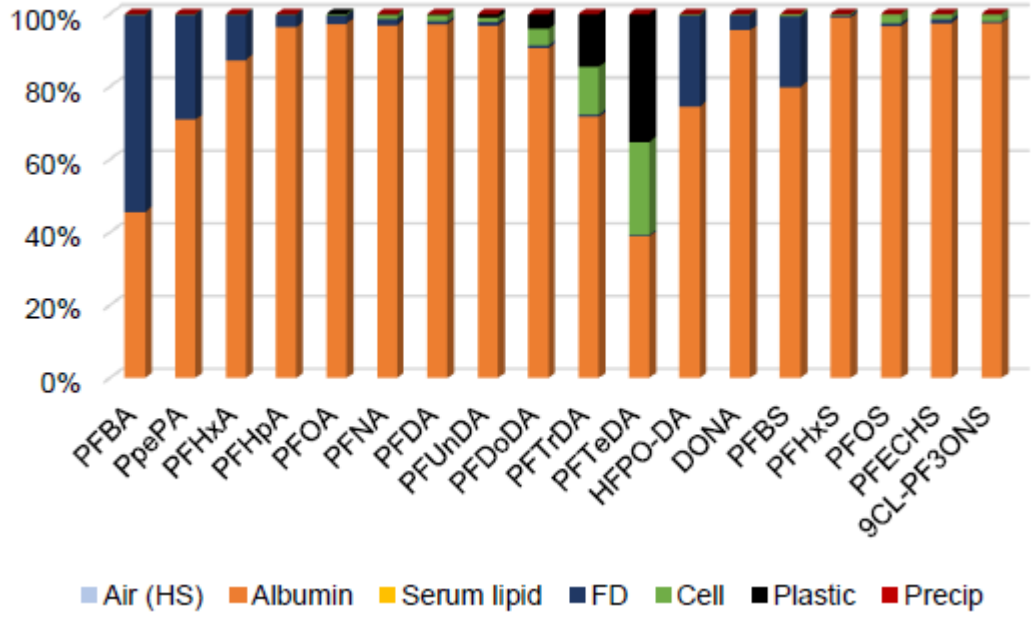


Illustrative applications to **ionizable PFAS**

FBS = 0%



FBS = 10%



KEY TAKEAWAY: The presence/absence of FBS can have a large influence on the in vitro disposition of **ionizable PFAS** (PFAAs & alternatives)

Armitage et al., 2022

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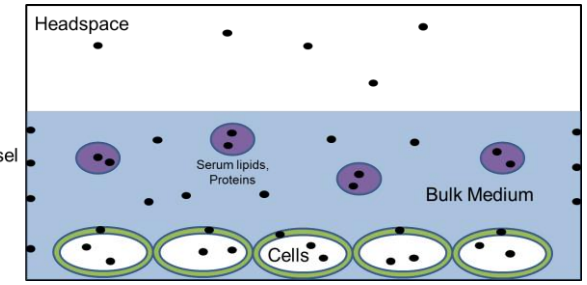
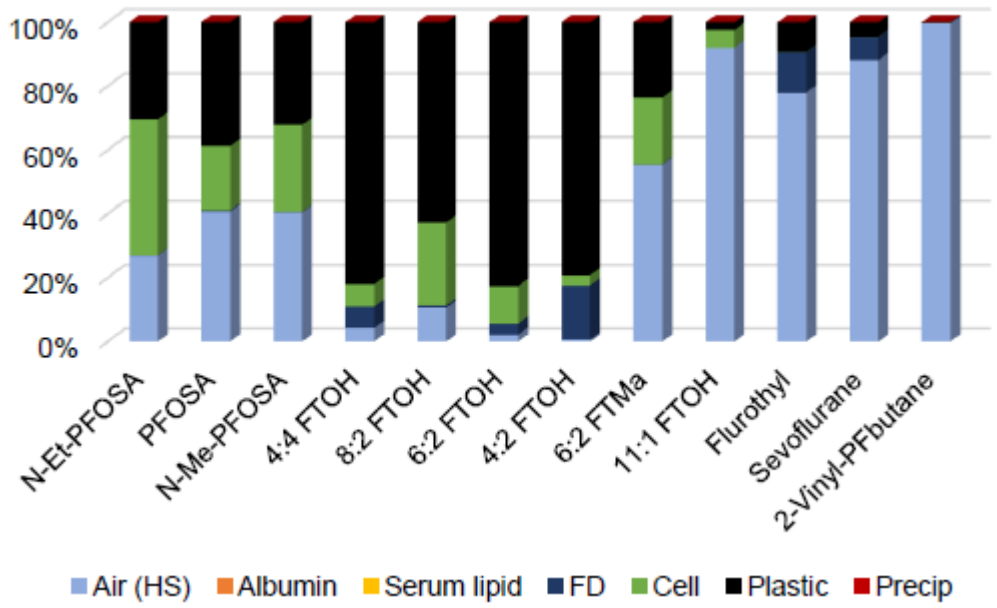
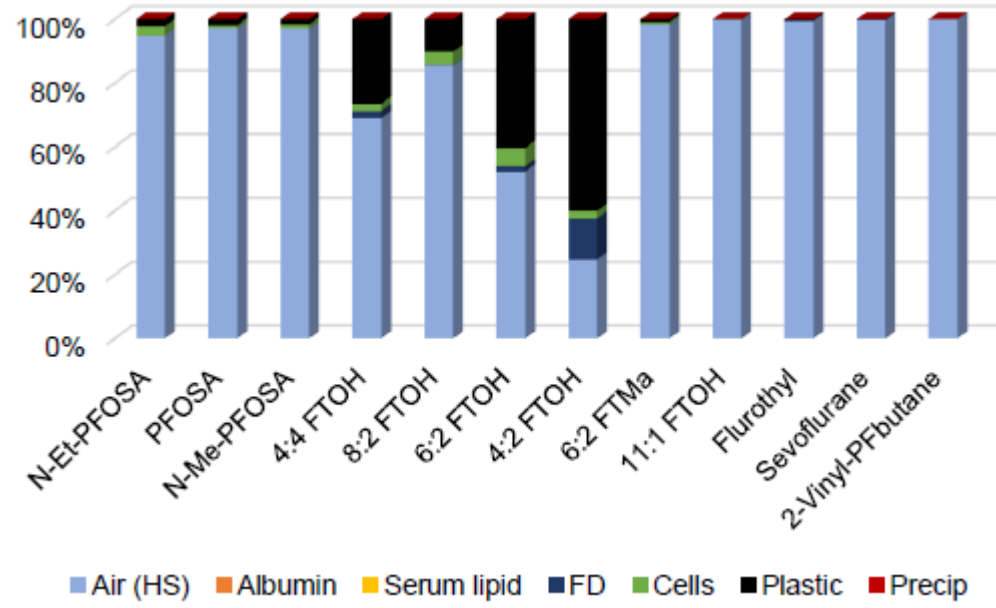


Illustrative applications to **neutral PFAS**

Headspace = “sealed”



Headspace = “leaky (50x)”



KEY TAKEAWAY: Mass transport out of the test system (“sealed” or “leaky”) can have a large influence on the in vitro disposition of **neutral PFAS**

Armitage et al., 2022

Systematic approach to testing & assessment, e.g.:

Summary of 12,034 PFAS EPA MasterList	
Total	12034
With defined formula & reported MW	10770
Min MW	53.0
Median	407.0
Average	464.8
Max MW	3476.6
Number with less than 20% of MW as F	94
Number with less than 35% of MW as F	1468
Number with less than 50% of MW as F	4799
Number with greater than 50% of MW as F	5971
Number with greater than 70% of MW as F	874
Chemical	**F % of MW**
PFOA (335-67-1)	68.8
PFOS (1763-23-1)	64.6

Develop standardized test guidelines for biopartitioning measurements (build from Droge, Goss, others)

↓

Select representative highly fluorinated PFAS from OECD categories for biopartitioning measurements

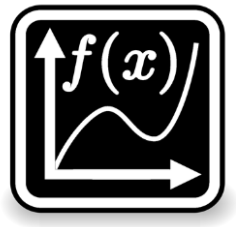
↓

OECD: 173 Structural Categories for PFAS, e.g.,

102: perfluoroalkyl carboxylic acids (PFCAs), their salts and esters
202: perfluoroalkane sulfonic acids (PFSAs), their salts and esters
402.03: n:2 fluorotelomer alcohols (n:2 FTOHs) / thiols
402.07: n:2 fluorotelomer sulfonic acids (n:2 FTSAs)

↓

High quality data to develop OECD validated QSARs



OECD Integrated Approach to Testing and Assessment (IATA) ??
Initial discussions with Canada and UK

Recommendations

- **Know your chemical properties** with some confidence ideally **before doing bioassays** (in vitro, in vivo)
- Prioritize testing for **PFAS with unique properties** (**e.g., EPA priority lists 1 and 2**, *not 13,000*!)
- **Short-term:** EPA review papers and consult with recognized experts in the field of biopartitioning measurement and prediction (e.g., Goss, Droge, Fischer, Escher, Endo, Brown) for testing guidance (i.e., potential pitfalls) before sending out testing orders to CROs with limited experience in biopartitioning for PFAS
- **Mid-term:** Develop OECD standardized testing guidelines and IATA for biopartitioning (e.g., discussions with UK EA, ECCC/HC)
- **Same general issues** relating to the partitioning and sorption of **SOME PFAS** to environmental phases, i.e., measuring K_{OC} is not relevant for many PFAS, numerous publications on this topic as well….