



# Ecological Toxicity Mapping of Per- and Polyfluoroalkyl Substances (PFAS) with ECOTOXicology Knowledgebase Protocols

Jennifer H. Olker  
Postdoctoral Researcher  
U.S. EPA ORD/CCTE/GLTED  
Duluth, MN

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# Conflict of Interest Statement

- I have no conflicts of interest to declare.

# Background

- Persistence and wide distribution of some PFAS in the environment
  - Detection of PFAS across the world in water and other media
  - Detection in tissue samples of invertebrates, fish, amphibians, birds, marine mammals, terrestrial mammals
- Potential to bioaccumulate
- Effects on ecological species
- Ecological toxicity information needed to inform risk assessment and management
  - Sensitive and susceptible species
  - Bioaccumulation
  - Benchmarks and thresholds for ecological toxicity

Across  
range of  
PFAS

# Objectives

- Identify and describe available empirical evidence for ecological effects of PFAS
- Identify potential ecological toxicity pathways

# Identifying Empirical Evidence: ECOTOX Knowledgebase

Curated database providing single chemical environmental toxicity data for aquatic life, terrestrial plants and wildlife

- Comprehensive literature searches
- Literature review
- Data extraction

ECOTOX Poster: Tues P767  
Demo @ EPA booth:  
Wed 2:30-3:30 pm

## ECOTOX Knowledgebase

[Home](#)[Search](#)[Explore](#)[Help](#)[Contact Us](#)

Data last updated

**Dec 12, 2019**

[See update totals](#)

Recent chemicals with full searches and coding completed

Endothall	Per- and Polyfluoroalkyl Su...	Tris(2-chloroethyl) phosphate
Glyphosate	Phosphoric acid, Triphenyl ...	Di-isobutyl phthalate
Fluometuron	Prothioconazole	Di-isodecyl phthalate
Fluoxastrobin	Tebuconazole	Di-isononyl phthalate
Napropamide	Tembotrione	Dicyclohexyl phthalate
Oxadiazon	Tetrabromobisphenol A	

Total in database


<b>11,822</b>	<b>13,039</b>
<b>Chemicals</b>	<b>Species</b>
<b>49,765</b>	<b>971,430</b>
<b>References</b>	<b>Results</b>

**WELCOME TO ECOTOX VERSION 5!**

Please click [here](#) to provide feedback so that we can continue to improve your experience.

### About ECOTOX

The ECOTOXicology knowledgebase (ECOTOX) is a comprehensive, publicly available knowledgebase providing single chemical environmental toxicity data on aquatic life, terrestrial plants and wildlife.



[Learn More](#)

**Disclaimer:** You should consult the original scientific paper to ensure an understanding of the context of the data retrieved from ECOTOX.

### Getting Started

- Use [Search](#) if you know exact parameters or search terms (chemical, species, etc.)
- Use [Explore](#) to see what data may be available in ECOTOX (including data plots)
- [ECOTOX Quick User Guide](#) (2 pp, 141 K)
- [ECOTOX User Guide](#) (84 pp, 1120 K)
- [ECOTOX Code Appendix \(PDF\)](#) (816 pp, 6868 K, [About PDF](#))

### Other Links

- [Limitations](#)
- [Frequent Questions](#)
- [Other Tools/Databases](#)
- [Recent Additions](#)

[Get Updates via Email](#)

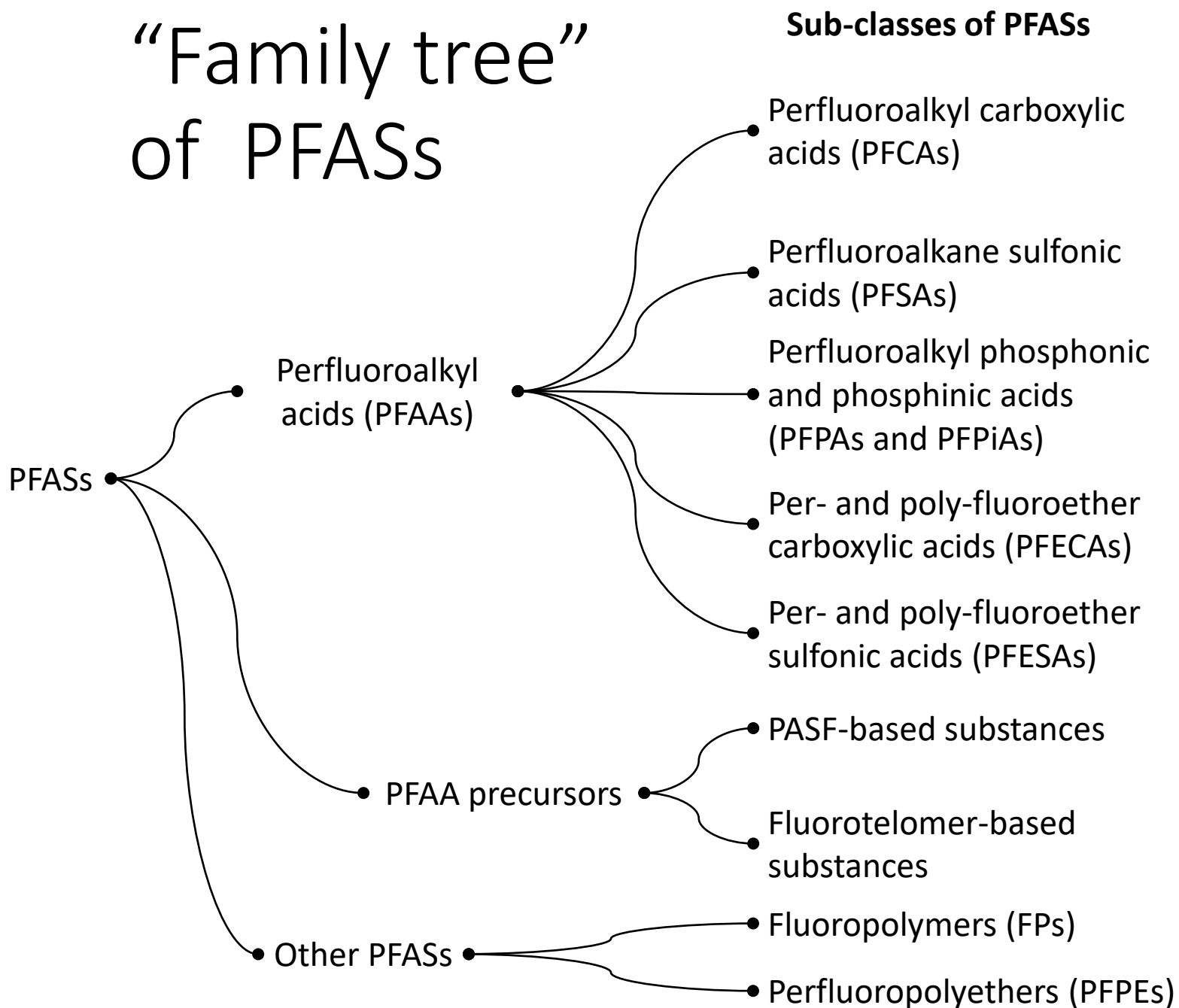
### Download

Download the entire database as an ASCII file via the button below.

[Download ASCII Data](#)

[www.epa.gov/ecotox](http://www.epa.gov/ecotox)

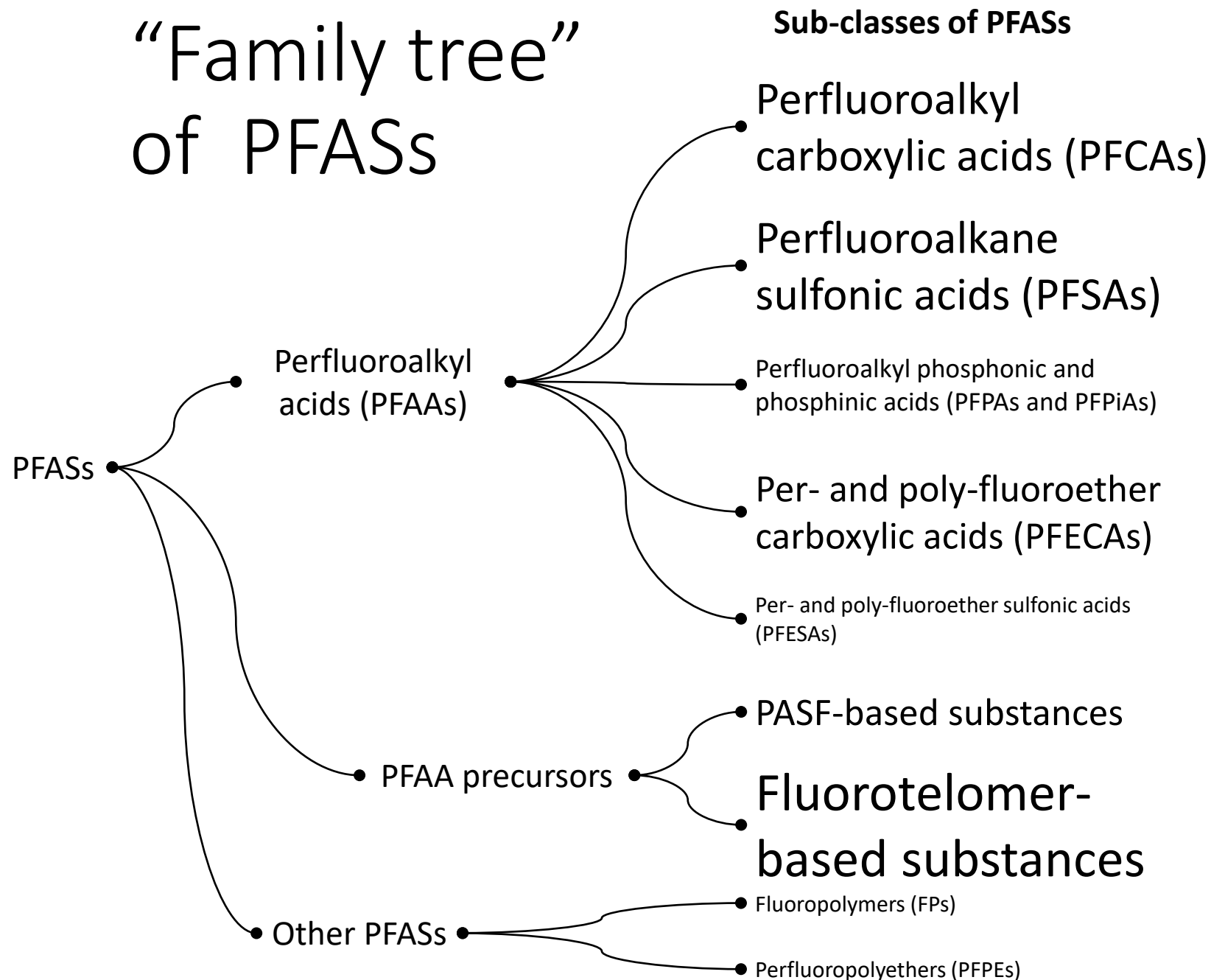
# “Family tree” of PFASs



## Literature Search Terms

- 322 chemical names with associated CASRNs
- General PFAS search terms (e.g., Dodecafluoro, Fluorotelomer, Nonafluoro, Pentafluoropropanoic, Perfluorobutanesulfon, Perfluoroheptanoate, Perfluorohexanoate, Perfluoropentyl)

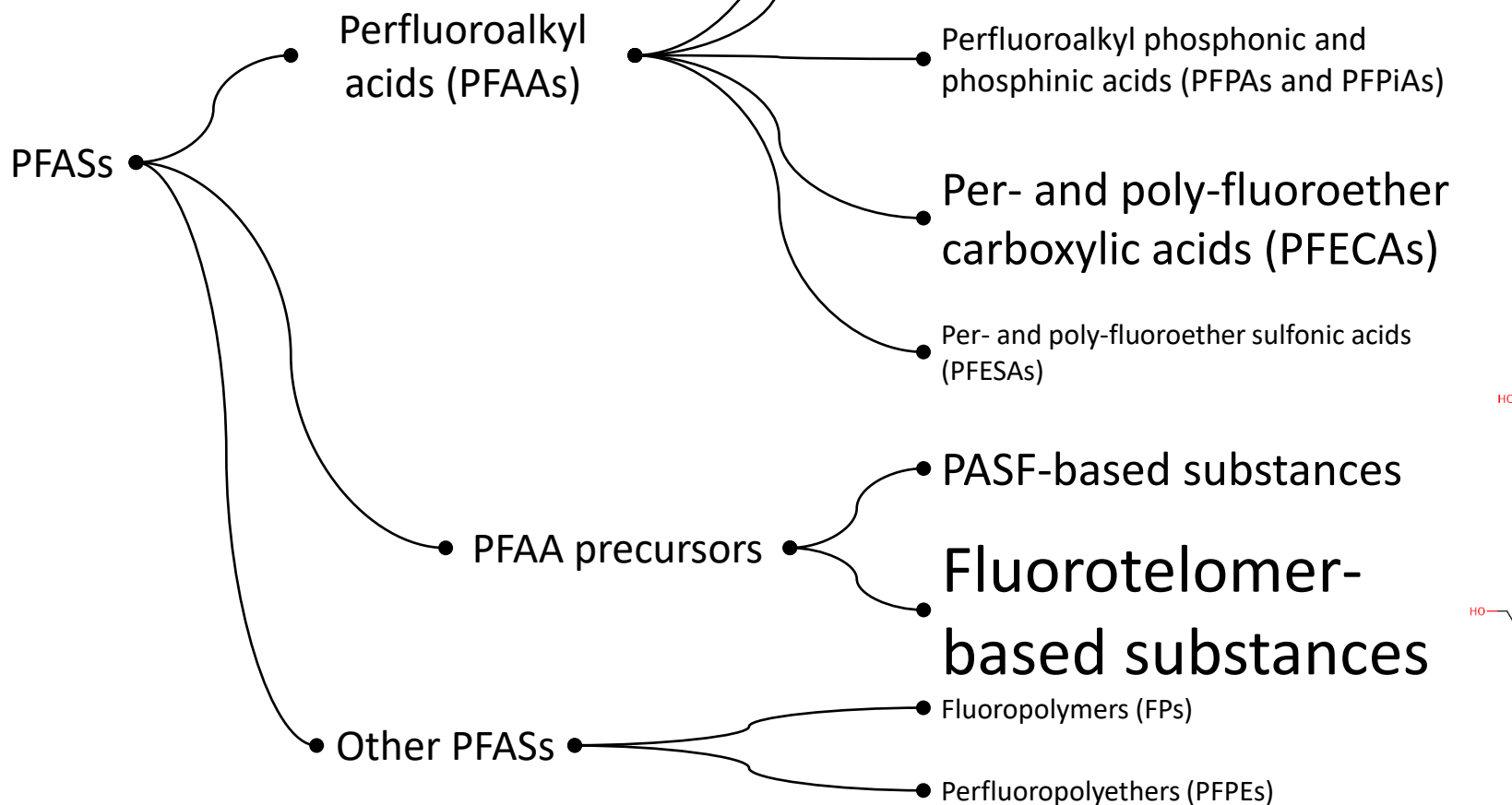
# “Family tree” of PFASs



## Literature Search Terms

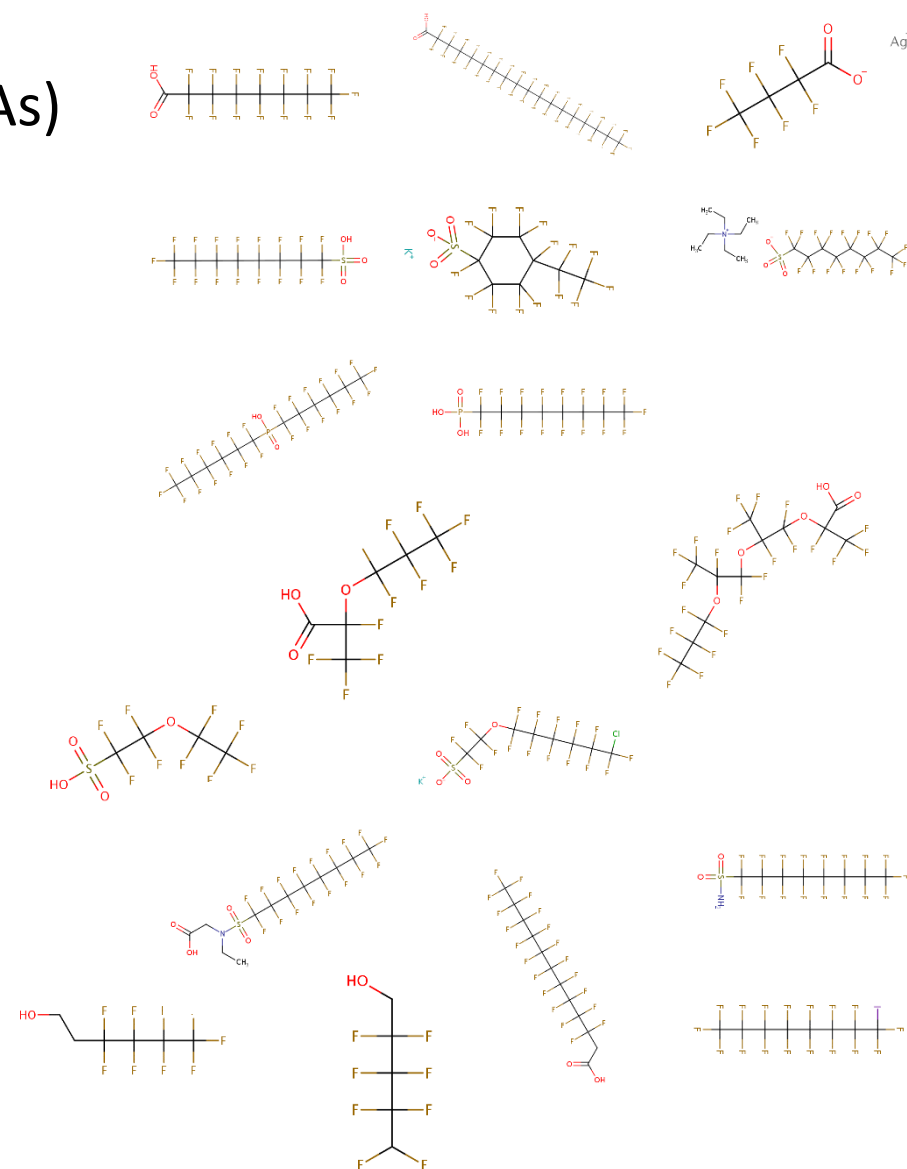
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# “Family tree” of PFASs



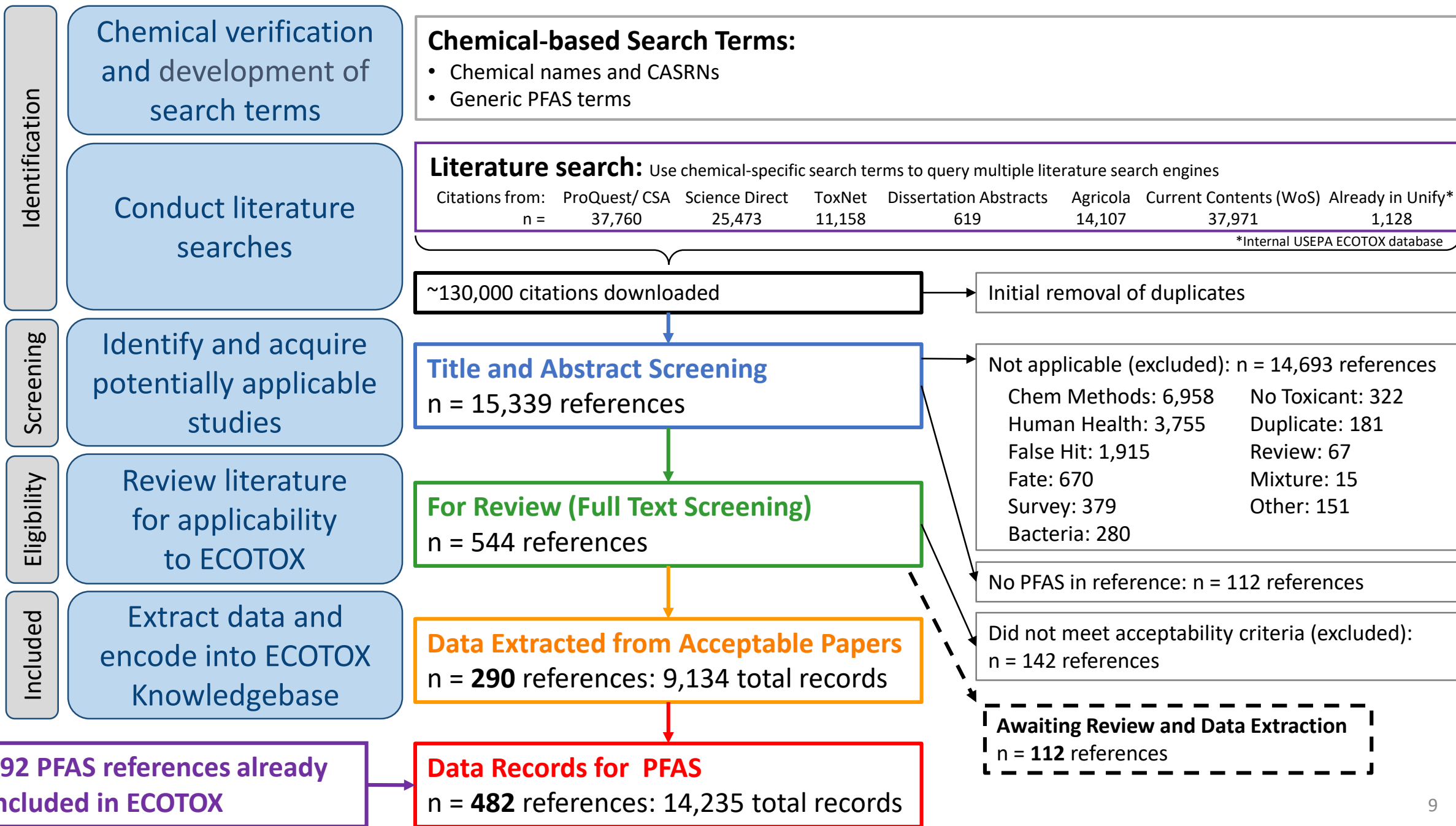
## Sub-classes of PFASs

## Literature Search Terms

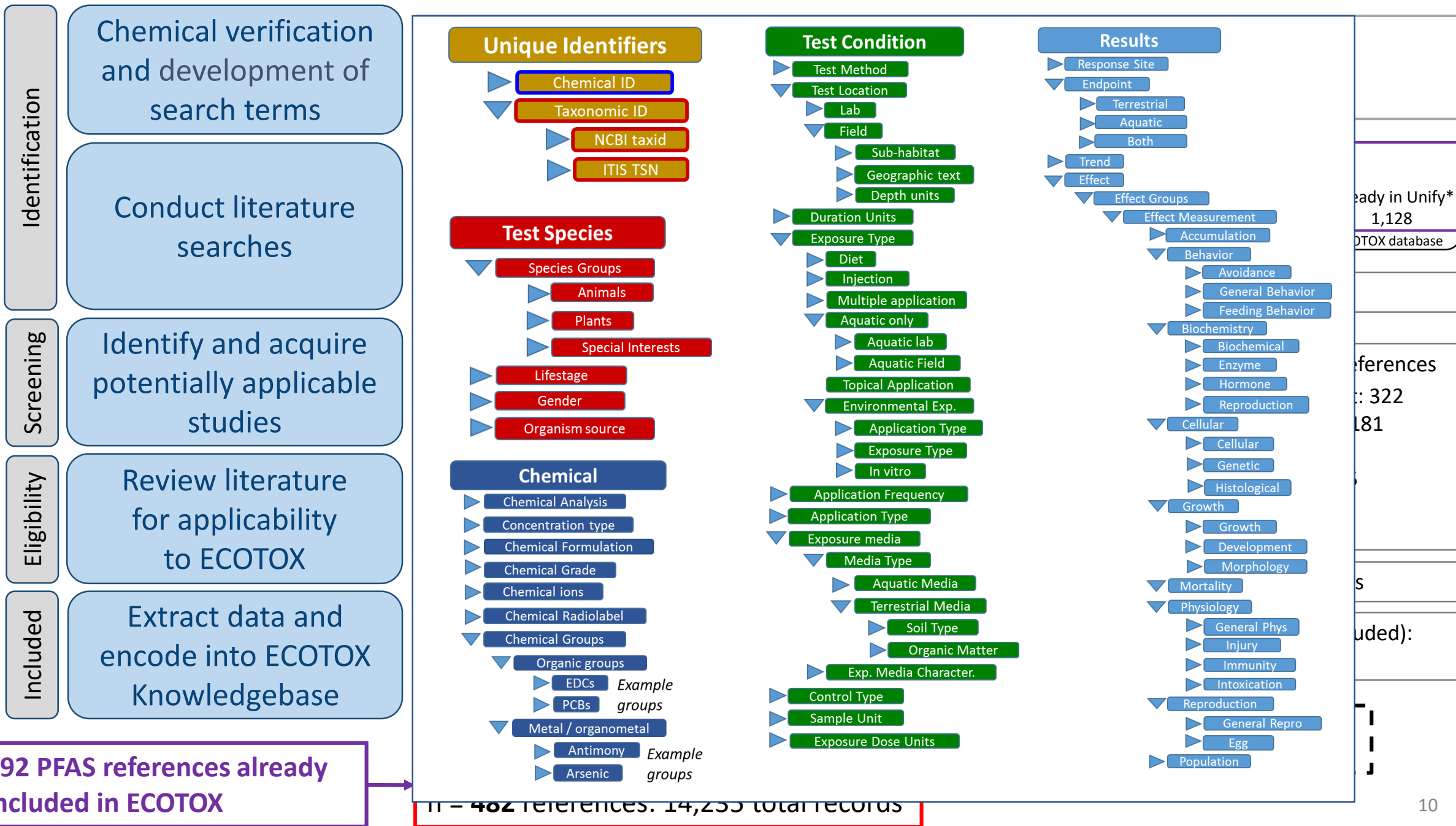




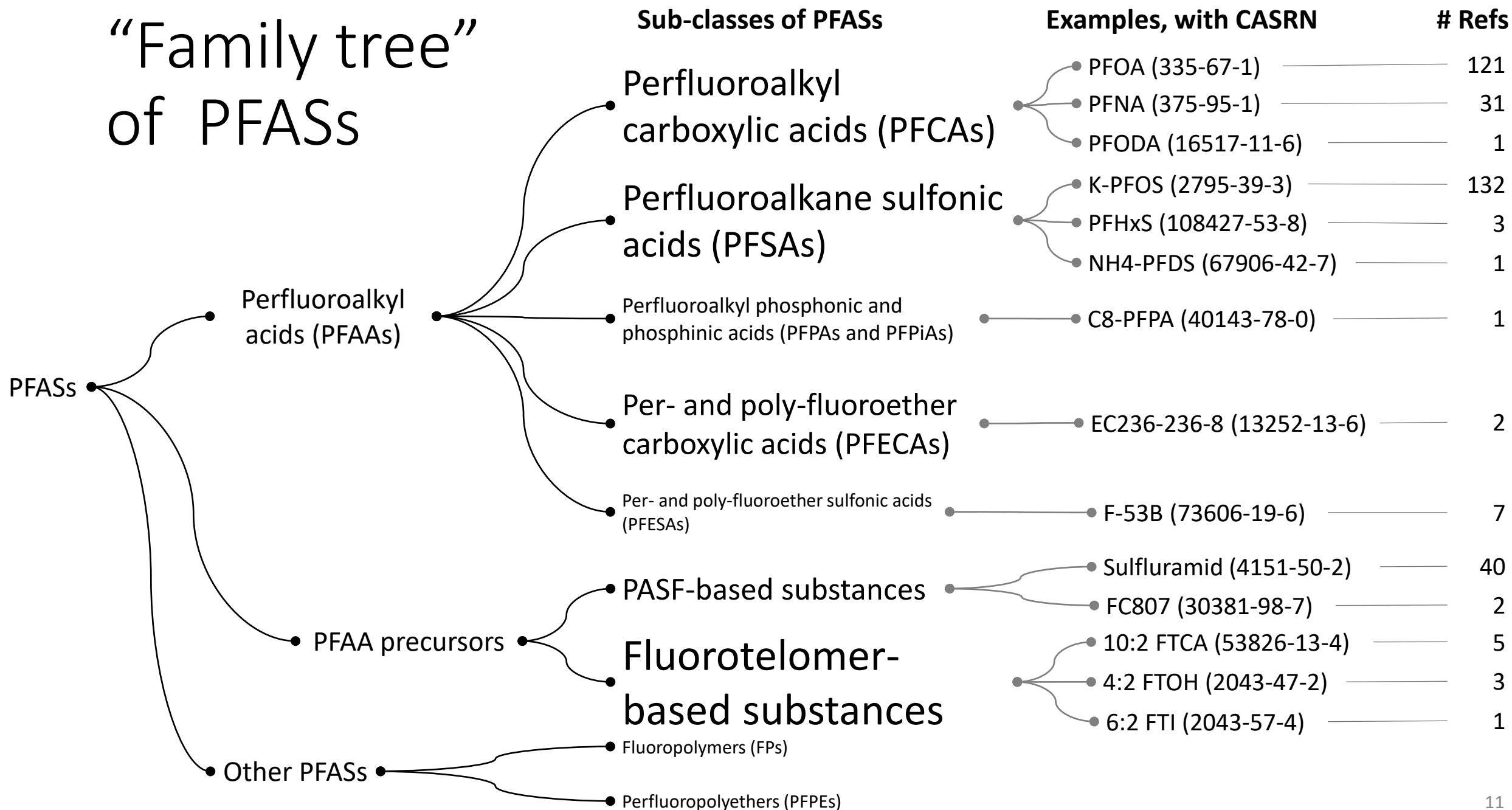
# ECOTOX Pipeline



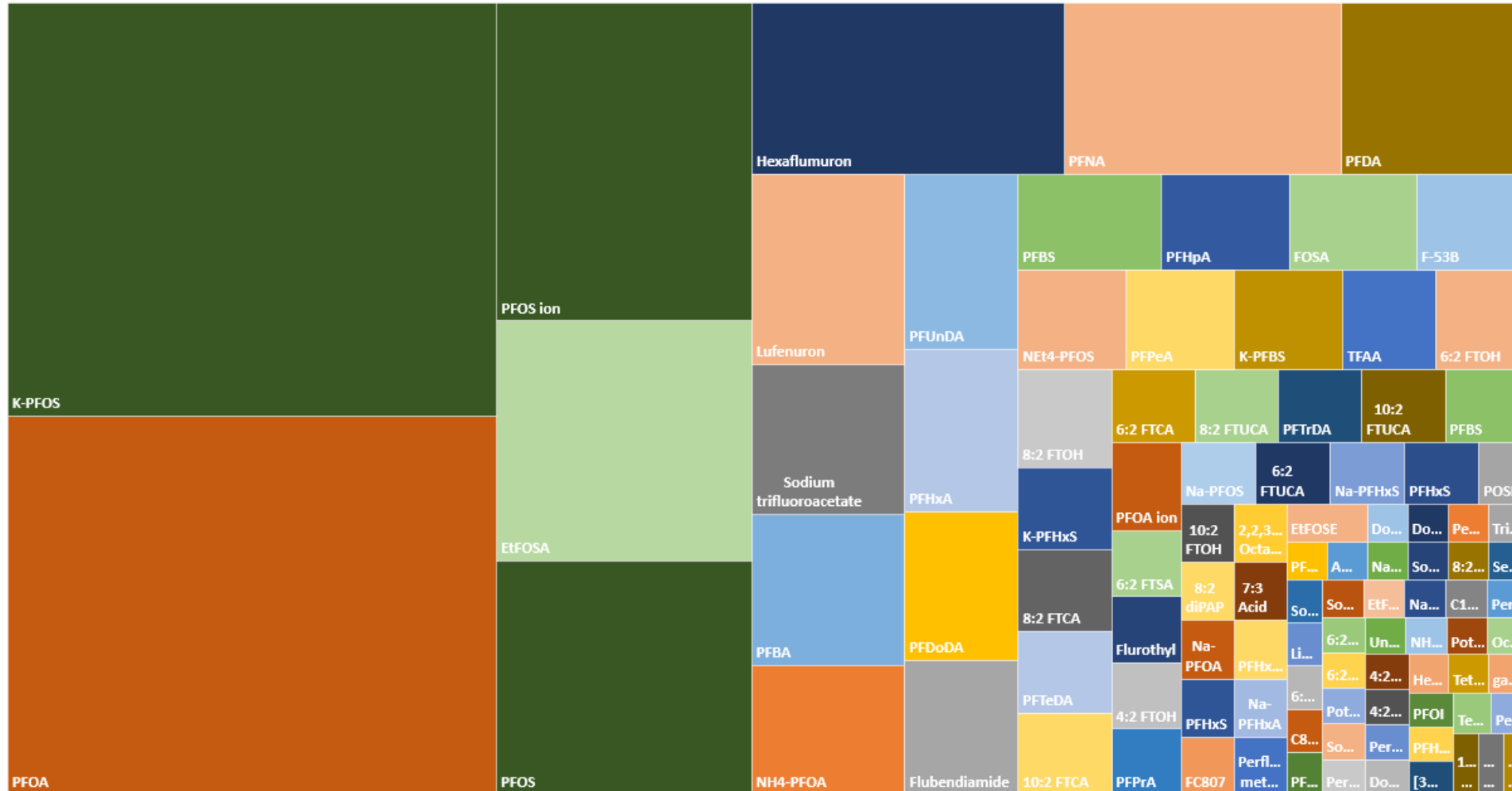
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# “Family tree” of PFASs

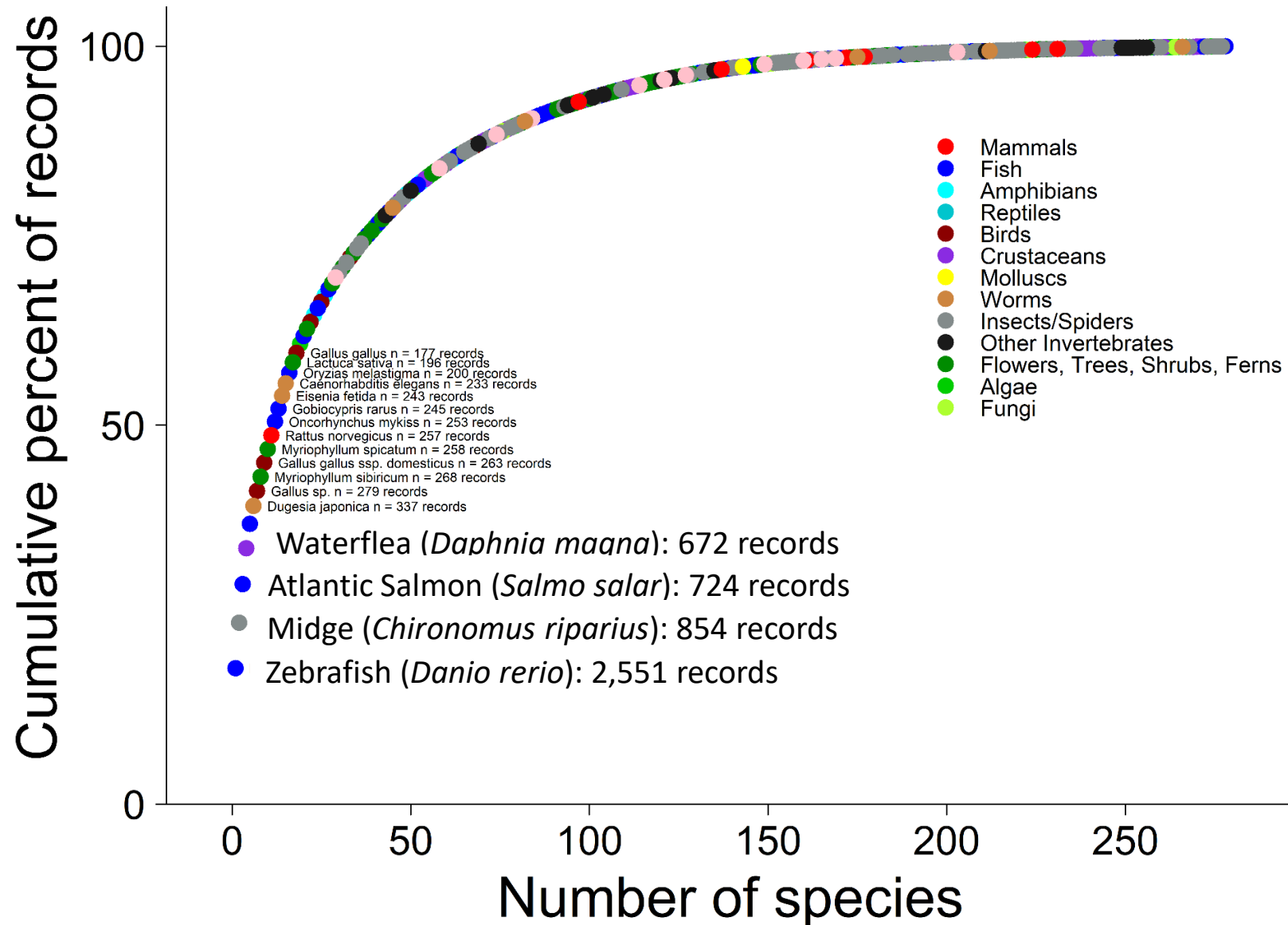


# 482 Publications, 100 PFAS with Ecological Toxicity Data



Box size represents # references that include relevant and acceptable ecological toxicity data

# PFAS Data for 278 Biological Species



# Diversity in Types of Effects



**PFAS records for Fish**

	Effect	# Records
Cellular Responses	Genetics	2,156
	Biochemistry	653
	Enzyme(s)	241
	Hormone(s)	214
	Cell(s)	63
Organ Responses	Histology	50
	Accumulation	236
	Immunological	2
	Physiology	126
Organism Responses	Injury	24
	Intoxication	2
	Development	70
	Growth	326
	Morphology	351
	Enzyme(s)	220
	Behavior	19
	Avoidance	2
	Feeding behavior	99
	Reproduction	468
	Mortality	5
	Population	55
	Multiple	55
	Total	5,382

Reproduction
Fecundity
Fertility
Fertilization
Gamete production
Hatch
Mean spawns per female
Motility
Number spawning
Pregnant, Paris or Gravid
Progeny counts/numbers
Spawning frequency
Sperm cell counts
Time to spawn
Velocity
Viability



# Ongoing Literature Search, Review, Data Extraction

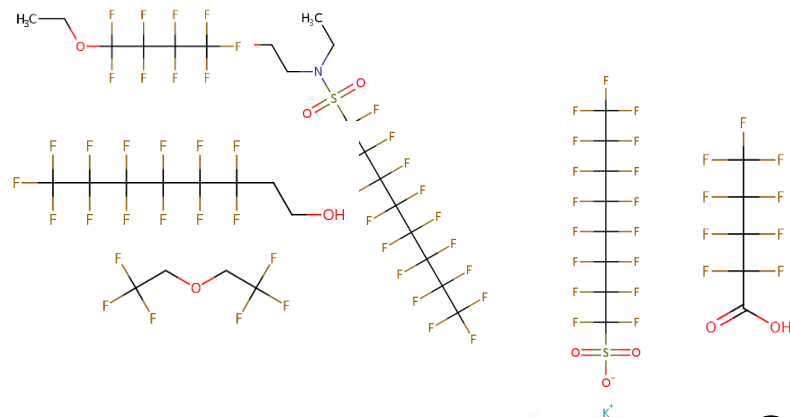
Updated list of >300 unique CASRN and associated chemical names

Conduct literature searches

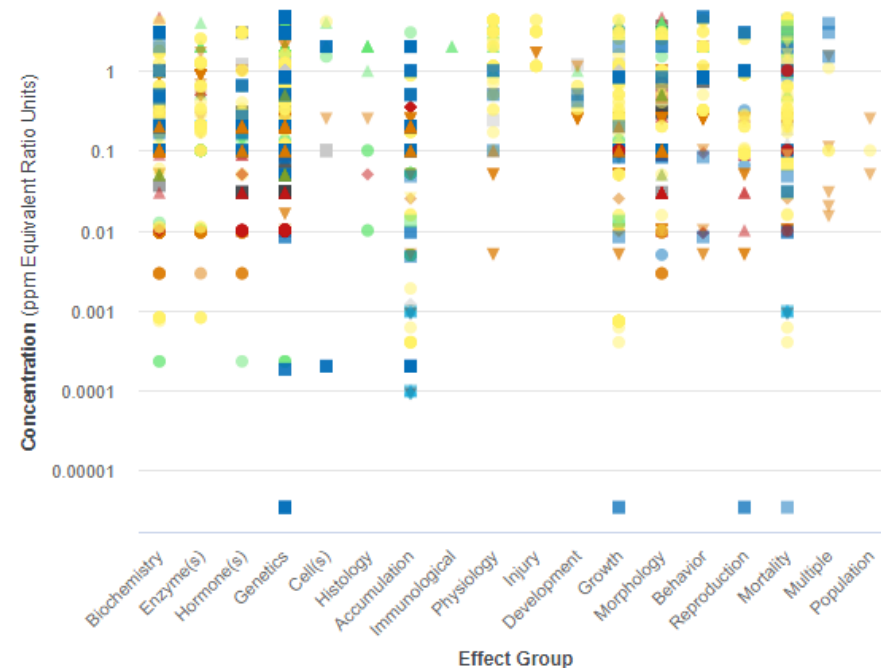
Identify and acquire potentially applicable studies

Review literature for applicability to ECOTOX

Extract data and encode into ECOTOX Knowledgebase



## Quarterly data releases to ECOTOX

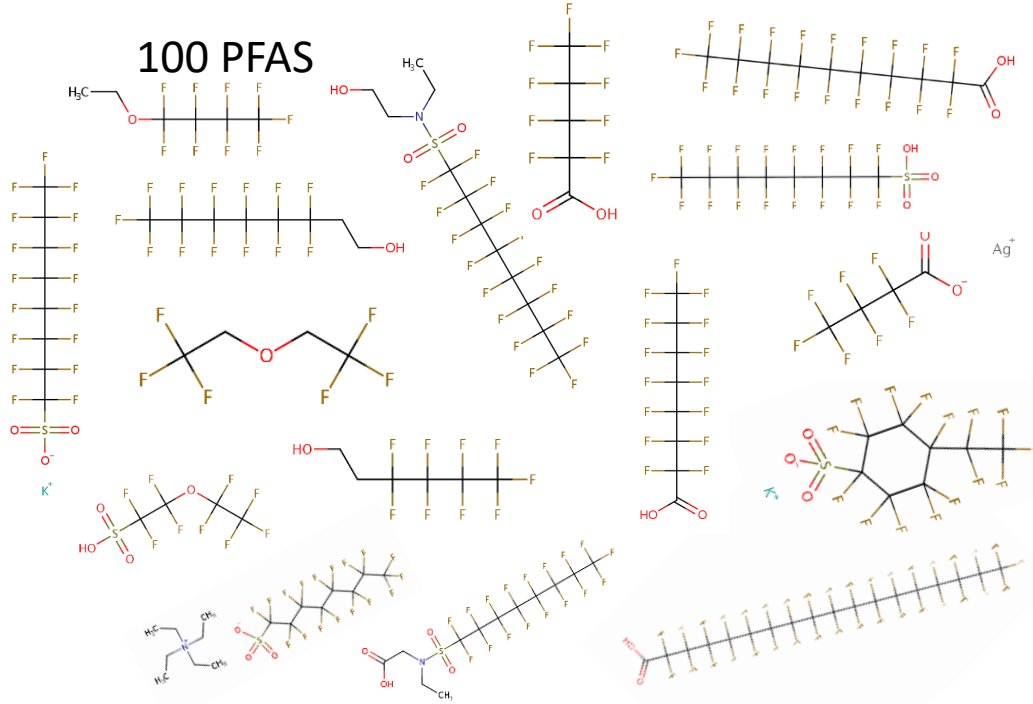


# Data Inventory → Summary/Synthesis

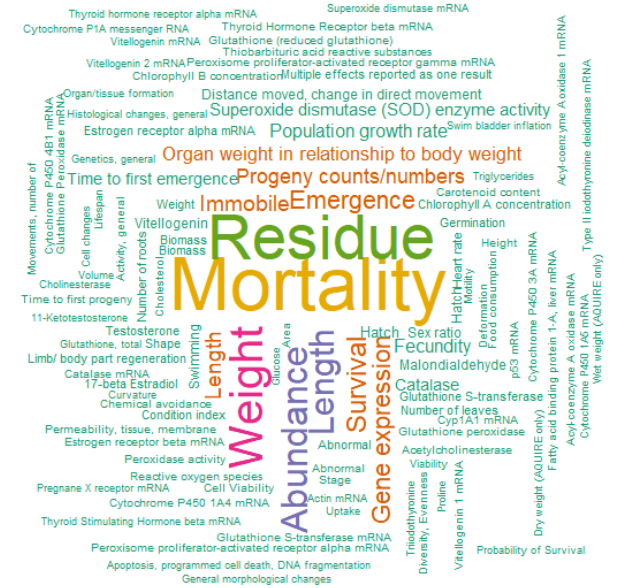
## 278 Biological Species



# 100 PFAS

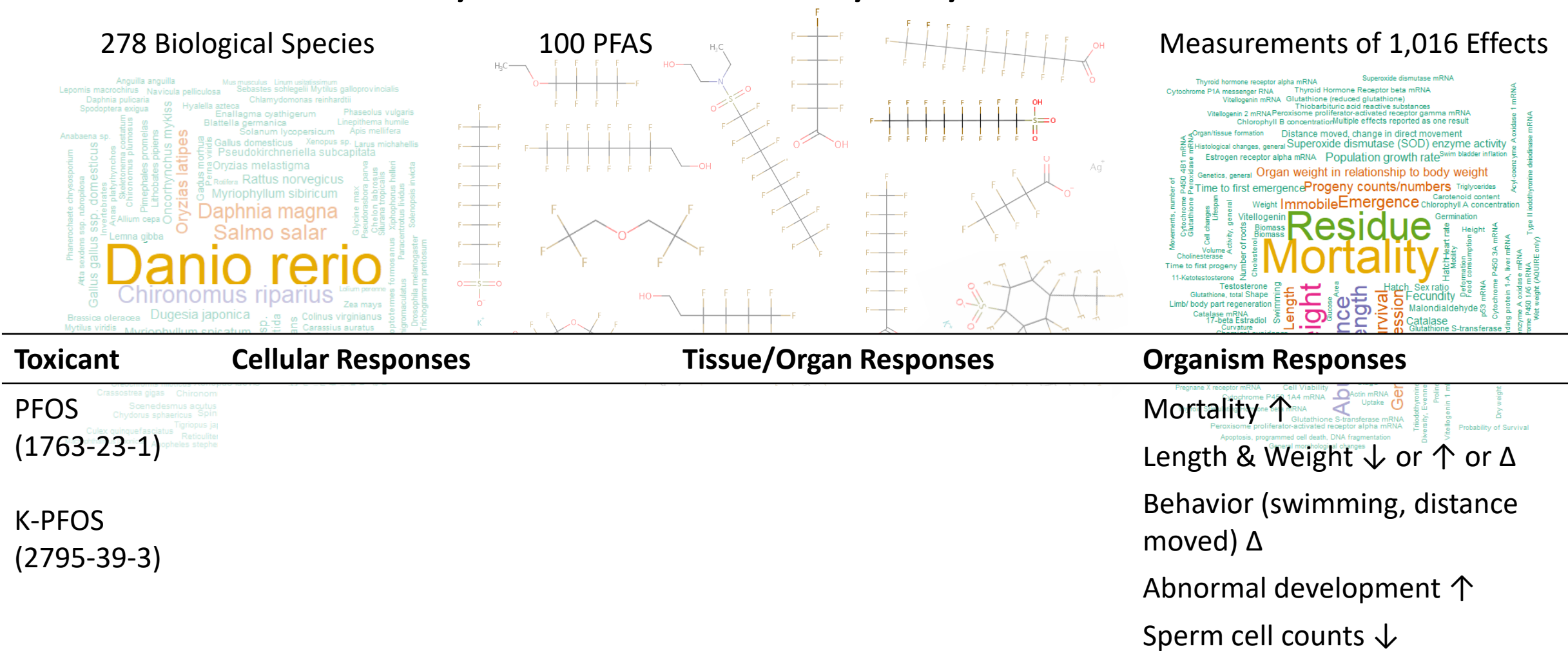


## Measurements of 1,016 Effects





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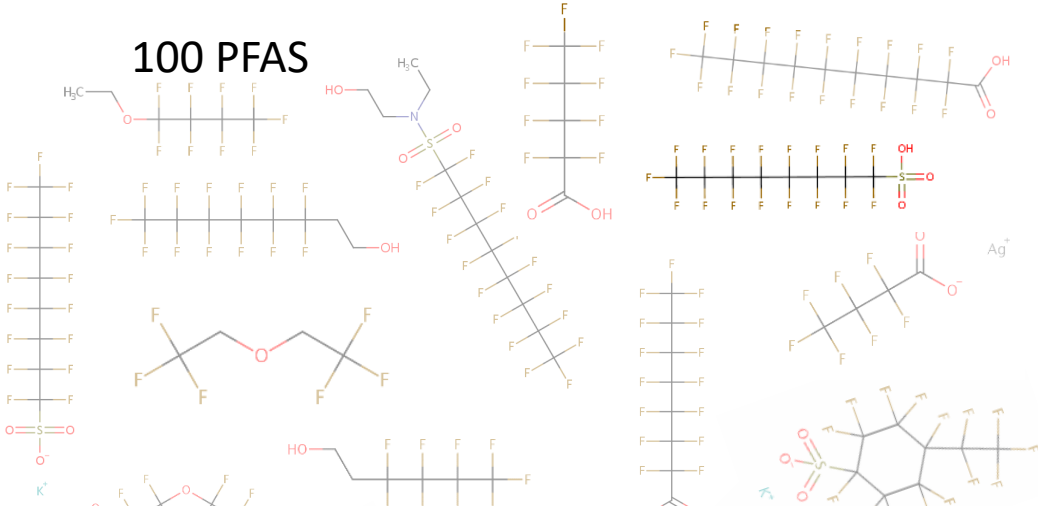


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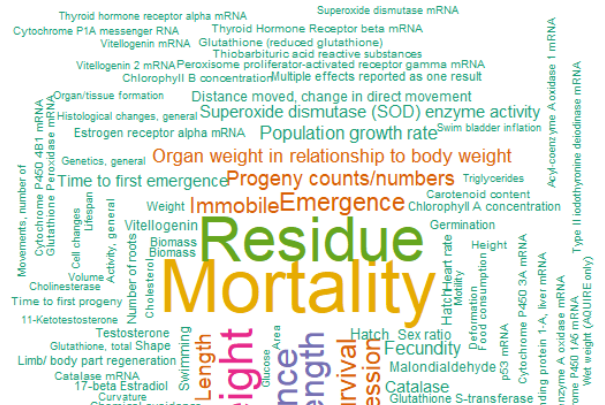
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100 PFAS



Measurements of 1,016 Effects

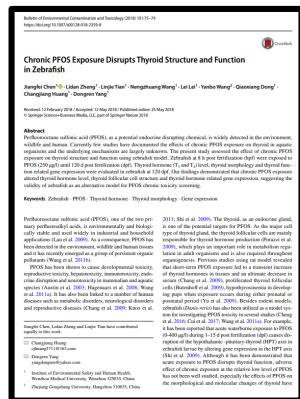


Toxicant	Cellular Responses	Tissue/Organ Responses	Organism Responses
PFOS (1763-23-1)	T4 & T3 ↓ Estrogen and 17-β Estradiol Δ	Heart rate Δ Swim bladder inflation Δ	Mortality ↑ Length & Weight ↓ or ↑ or Δ
K-PFOS (2795-39-3)	Vitellogenin Δ Acetylcholinesterase Δ Cholesterol & Lipids Δ Δ in expression of: PPAR-mediated genes (multiple) Thyroid-relevant genes (multiple)	Organ:Body weight Δ Vacuolization (Liver) Δ Accumulation: Residue, Uptake ↑	Behavior (swimming, distance moved) Δ Abnormal development ↑ Sperm cell counts ↓

# Identify Potential Toxicity Pathways

## Ontology-based semantic analysis

- Bridge the gap between the molecular/non-molecular phenotypes
- Lead to a better understanding of the underlying MOAs
- Allow comparisons across chemicals, both within and across species



➡  
*Data  
extraction*

ECOTOX



PFOS:

- decreased thyroid cell area
- Decreased T4
- Altered expression of 7 thyroid-related genes in larval zebrafish

➡  
*Annotate and  
convert to  
ontology classes*

*Assemble Chemical-Species  
Phenotypic Profiles*

PFOS on zebrafish - Ref#178023  
PFOS on zebrafish - Ref#175649  
PFOS on zebrafish - Ref#175223  
PFOS on zebrafish - Ref#175685  
...

*Compare to  
Phenotypic Profiles*

➡ Genes



➡ Pathways



➡ Diseases

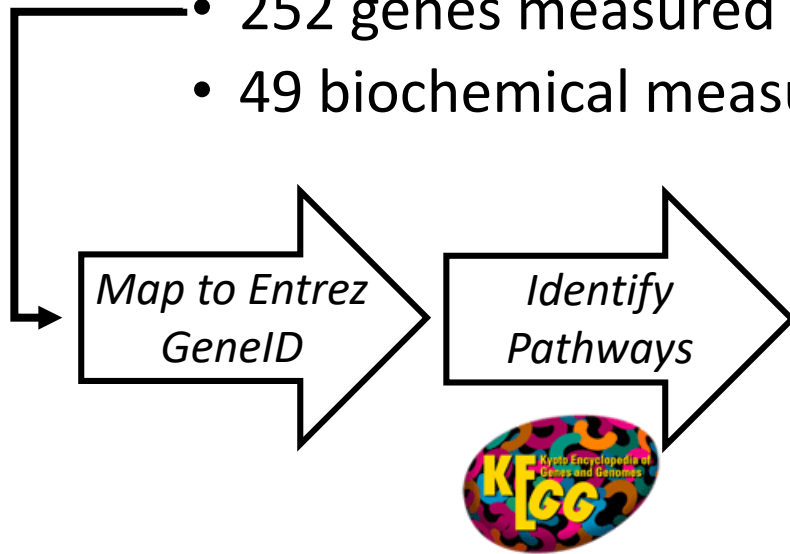


# Identify Potential Toxicity Pathways

- 40% of the effect measurements are biochemical or genetic effects

Zebrafish (*Danio rerio*) PFAS references include:

- 252 genes measured for changes in expression
- 49 biochemical measurements (e.g., proteins, enzymes, hormones)



## 73 Zebrafish Pathways Investigated

**Carbohydrate metabolism** (3): Glycolysis/Gluconeogenesis; Starch and sucrose metabolism

**Lipid metabolism** (5): Fatty acid elongation and degradation; Steroid hormone biosynthesis

**Energy metabolism** (1): Oxidative phosphorylation

**Immune system** (7): Toll-like receptor signaling pathway; NOD-like receptor signaling pathway

**Endocrine system** (6): PPAR signaling pathway; Insulin signaling pathway; Progesterone-mediated oocyte maturation

**Circulatory system** (2): Adrenergic signaling in cardiomyocytes; Vascular smooth muscle contraction

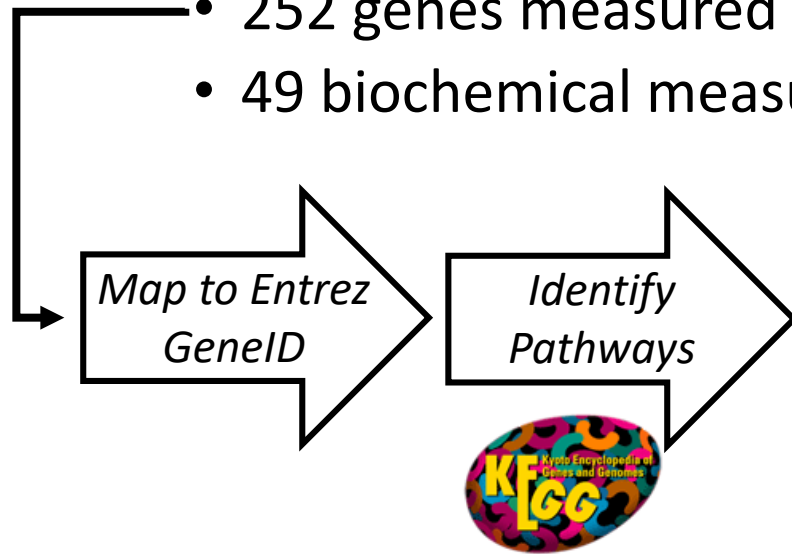
**Endocrine and metabolic disease** (1): AGE-RAGE signaling pathway in diabetic complications

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Genes with  
sig. change in  
transcription

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**Circulatory system** (2): Adrenergic signaling in cardiomyocytes; Vascular smooth muscle contraction

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# Summary

- Extent and distribution of literature of ecological toxicity of PFAS
  - Curated toxicity data for multiple applications
  - Identification of data gaps
- Literature identified for other areas of PFAS research
- Ontology-based semantic analysis could advance synthesis and interpretation
- Limitations:
  - Mixtures currently not included
  - Observational and (most) field data not represented here
  - Limited gene and pathway information for many ecological species



# Acknowledgements

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Thank you!

[olker.jennifer@epa.gov](mailto:olker.jennifer@epa.gov)

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\*Coauthors