Ecological Toxicity of Per- and Polyfluoroalkyl Substances (PFAS): Data Identification, Curation, and Distribution using ECOTOXicology Knowledgebase Protocols

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

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The views expressed in this presentation are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA.

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

Houde *et al*. 2006 *Environ. Sci. Technol.* 40:3463-3473
McCarthy *et al*. 2017 *Curr. Pollution Rep.* 3:289-301

Goals

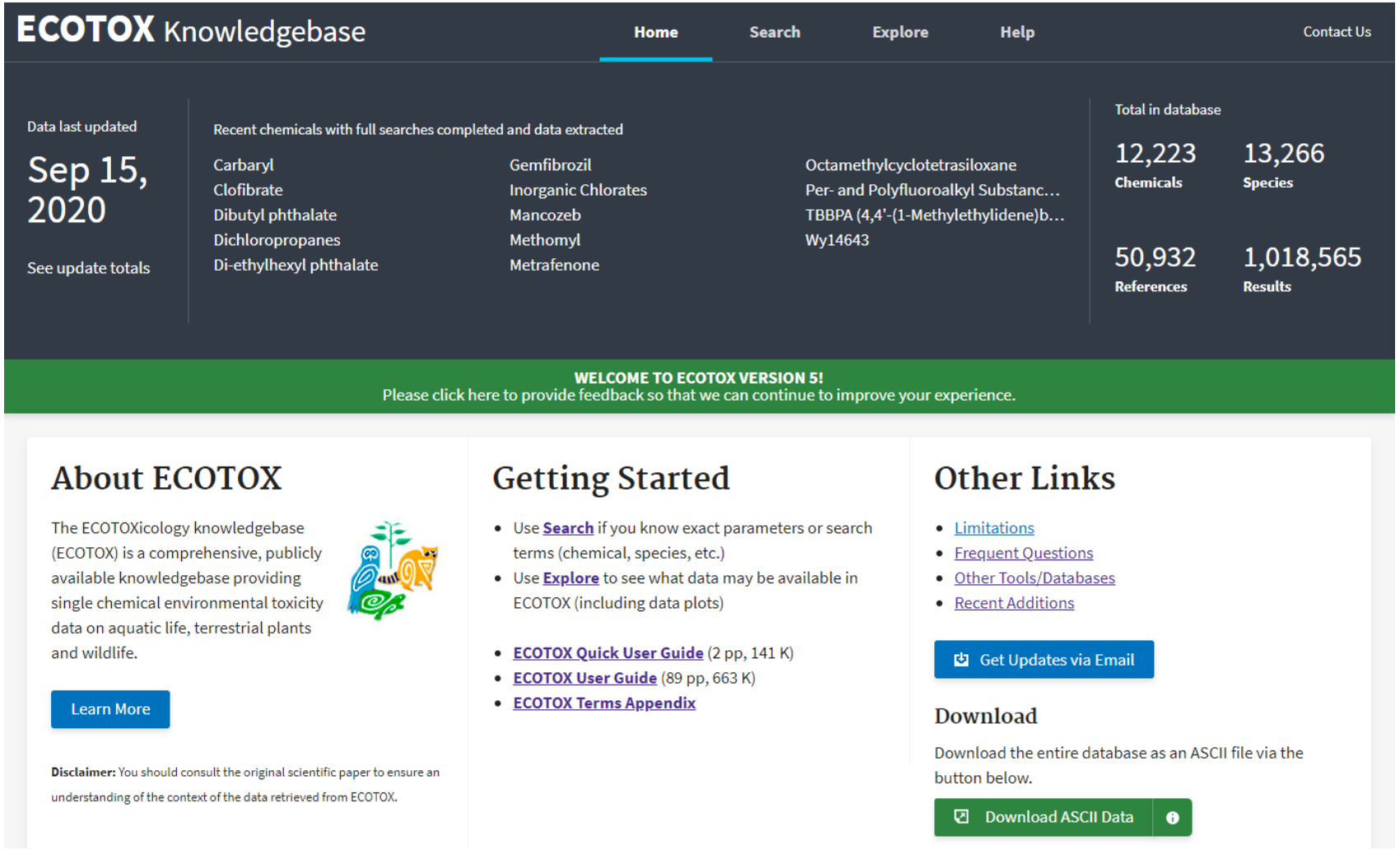
- Comprehensively and systematically assessable available evidence for ecological effects of PFAS
- Characterize the extent, distribution, and types of evidence for PFAS ecotoxicity
  - Data gaps
  - Susceptible species
  - Target endpoints

Identifying Empirical Evidence: ECOTOX Knowledgebase

www.epa.gov/ecotox

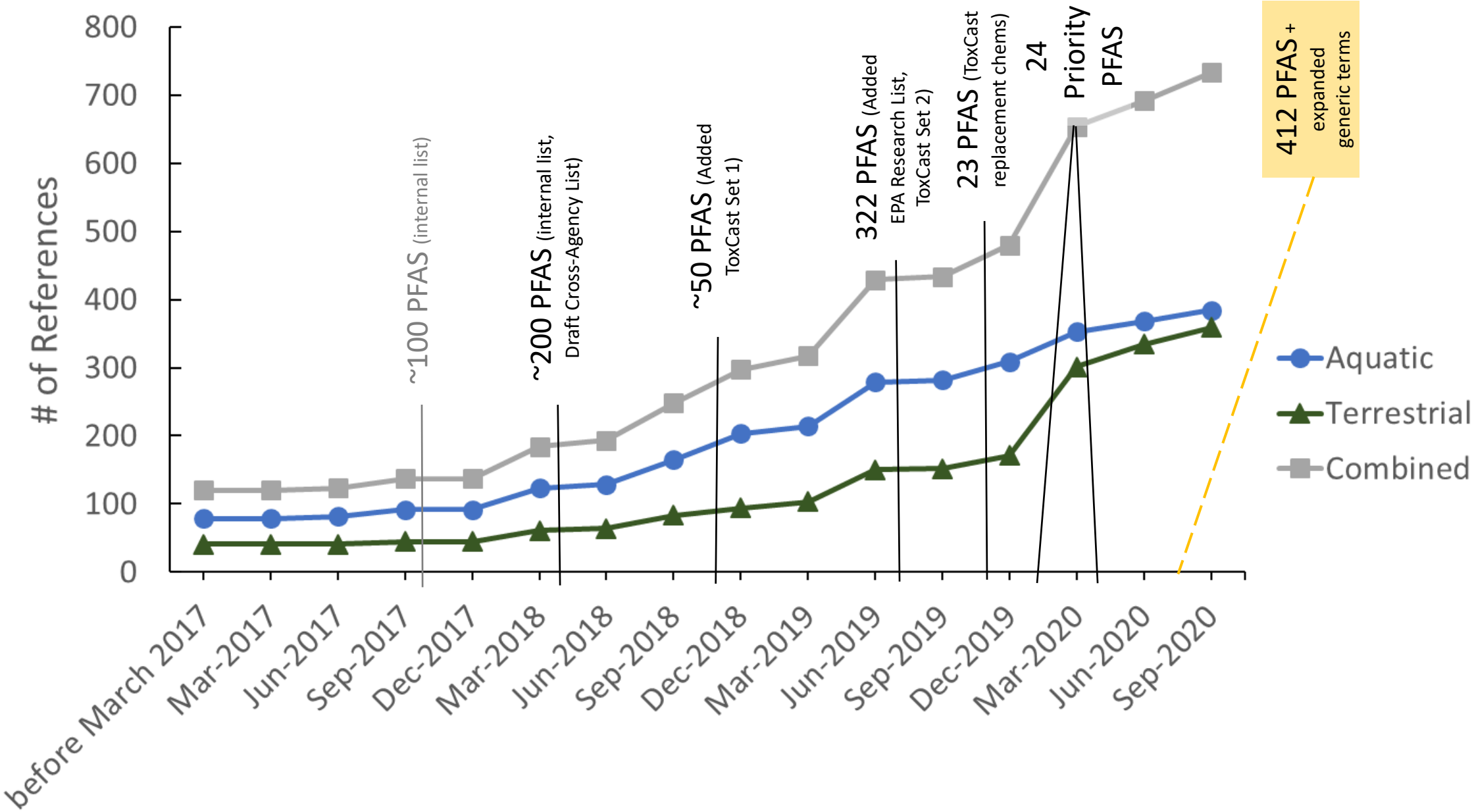
Curated database providing single chemical environmental toxicity data for aquatic life, terrestrial plants and wildlife

- Comprehensive literature searches
- Literature review
- Data extraction



ECOTOX presentations/posters
D. Hoff ID: 5.17.01
C. Elonen ID: 5.17.09

PFAS Searches and References with Curated Data



ECOTOX Pipeline

Identification

- Chemical verification and development of search terms
- Conduct literature searches

Screening

- Identify and acquire potentially applicable studies

Eligibility

- Review literature for applicability to ECOTOX

Included

- Extract data into ECOTOX Knowledgebase

Chemical-based Search Terms:

- >300 Chemical names and CASRNs
- Generic PFAS terms

Literature search: Use chemical-specific search terms to query multiple literature search engines

Citations from:	ProQuest/ CSA	Science Direct	ToxNet/ ToxLine	Dissertation Abstracts	Agricola	Web of Science	Already in Unify*
n =	45,950	28,759	18,635	643	16,813	6,639	3,921

*Internal USEPA ECOTOX database

~164,000 citations downloaded → Initial removal of duplicates

Title and Abstract Screening
n ~19,500 references

→ Not applicable (excluded):
n = 18,814 references

- Chem Methods
- Human Healt
- Fate
- Survey
- Bacteria
- False Hit
- No Toxicant
- Review
- Mixture
- Other

For Review (Full Text Screening)
n ~ 720 references

→ No PFAS in reference:
n ~ 85 references

→ Did not meet acceptability criteria (excluded):
n ~ 75 references

Data Extracted from Acceptable Papers
n ~ **540** references: 15,650 total records

→ **Awaiting Review and Data Extraction**
n = **~20** references

192 PFAS references already included in ECOTOX → **Data Records for PFAS**
n = **733** references: 20,615 total records

ECOTOX Pipeline

Identification
- Chemical verification and development of search terms
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Eligibility
- Review literature for applicability to ECOTOX

Included
- Extract data into ECOTOX Knowledgebase

192 PFAS references already included in ECOTOX

Unique Identifiers
- Chemical ID
- Taxonomic ID
  - NCBI taxid
  - ITIS TSN

Test Species
- Species Groups
  - Animals
  - Plants
  - Special Interests
- Lifestage
- Gender
- Organism source

Chemical
- Chemical Analysis
- Concentration type
- Chemical Formulation
- Chemical Grade
- Chemical ions
- Chemical Radiolabel
- Chemical Groups
  - Organic groups
    - EDCs
    - PCBs
    - *Example groups*
  - Metal / organometal
    - Antimony
    - Arsenic
    - *Example groups*

Test Condition
- Test Method
- Test Location
  - Lab
  - Field
    - Sub-habitat
    - Geographic text
    - Depth units
- Duration Units
- Exposure Type
  - Diet
  - Injection
  - Multiple application
  - Aquatic only
    - Aquatic lab
    - Aquatic Field
  - Topical Application
  - Environmental Exp.
    - Application Type
    - Exposure Type
    - In vitro
- Application Frequency
- Application Type
- Exposure media
  - Media Type
    - Aquatic Media
    - Terrestrial Media
      - Soil Type
      - Organic Matter
  - Exp. Media Character.
- Control Type
- Sample Unit
- Exposure Dose Units

Results
- Response Site
- Endpoint
  - Terrestrial
  - Aquatic
  - Both
- Trend
- Effect
  - Effect Groups
    - Effect Measurement
      - Accumulation
      - Behavior
        - Avoidance
        - General Behavior
        - Feeding Behavior
      - Biochemistry
        - Biochemical
        - Enzyme
        - Hormone
        - Reproduction
      - Cellular
        - Cellular
        - Genetic
        - Histological
      - Growth
        - Growth
        - Development
        - Morphology
      - Mortality
      - Physiology
        - General Phys
        - Injury
        - Immunity
        - Intoxication
      - Reproduction
        - General Repro
        - Egg
      - Population

"Family tree" of PFASs

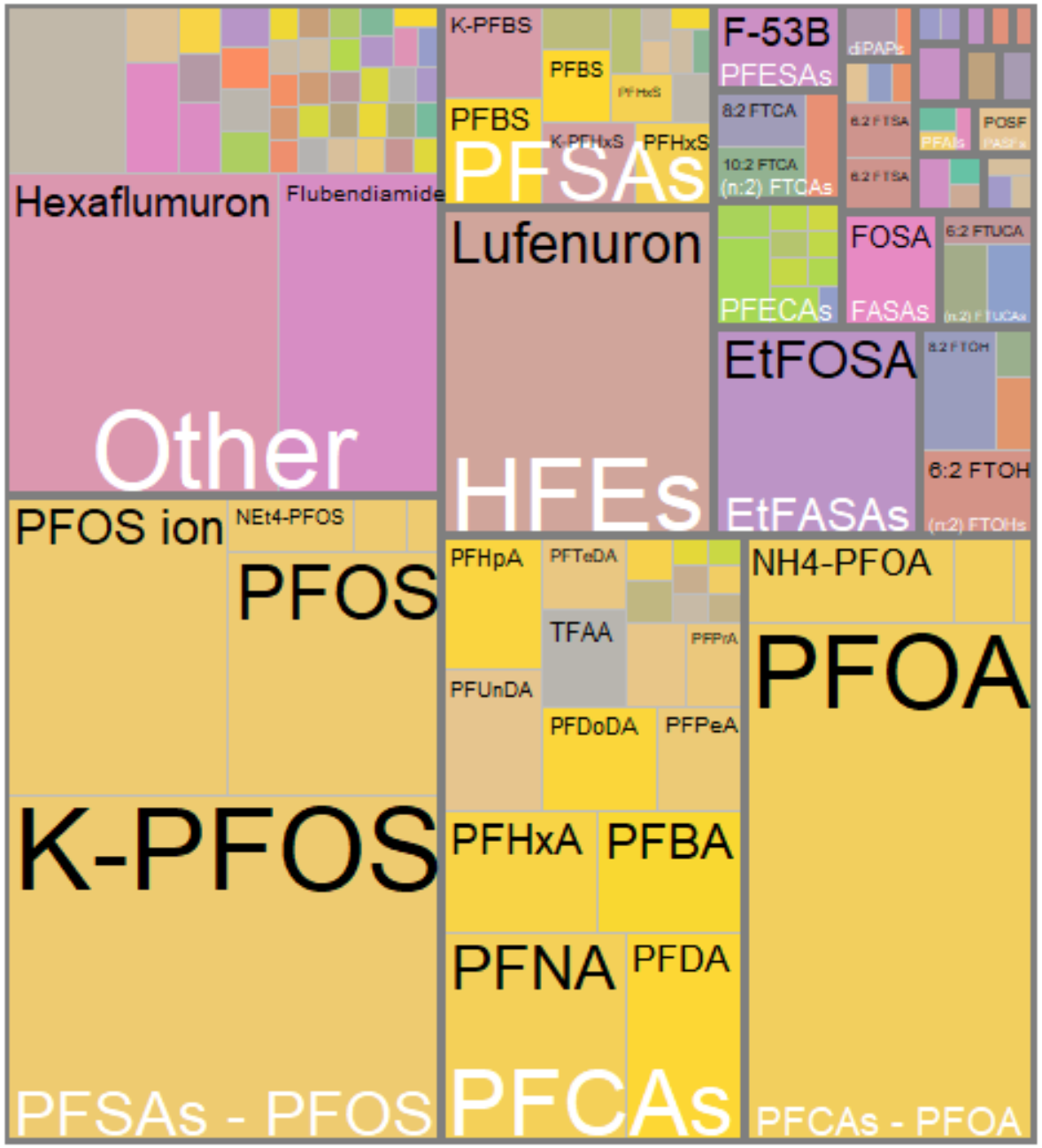
Sub-classes of PFASs	Examples, with CASRN	# Refs
PFASs → Perfluoroalkyl acids (PFAAs) → **Perfluoroalkyl carboxylic acids (PFCAs)**	PFOA (335-67-1)	151
	PFNA (375-95-1)	38
	PFODA (16517-11-6)	1
Perfluoroalkane sulfonic acids (PFSAs)	K-PFOS (2795-39-3)	152
	PFHxS (108427-53-8)	7
	NH4-PFDS (67906-42-7)	2
Perfluoroalkyl phosphonic and phosphinic acids (PFPAs and PFPiAs)	C8-PFPA (40143-78-0)	1
Per- and poly-fluoroether carboxylic acids (PFECAs)	EC236-236-8 (13252-13-6)	5
Per- and poly-fluoroether sulfonic acids (PFESAs)	F-53B (73606-19-6)	11
PFAA precursors → PASF-based substances	Sulfluramid (4151-50-2)	43
	FC807 (30381-98-7)	2
Fluorotelomer-based substances	10:2 FTCA (53826-13-4)	5
	4:2 FTOH (2043-47-2)	3
	6:2 FTI (2043-57-4)	1
Other PFASs → Fluoropolymers (FPs)		
Other PFASs → Perfluoropolyethers (PFPEs)		

OECD 2018 ENV/JM/MONO(2018)7
Wang et al. 2017 *Environ. Sci. Technol.* 51:2508-2518

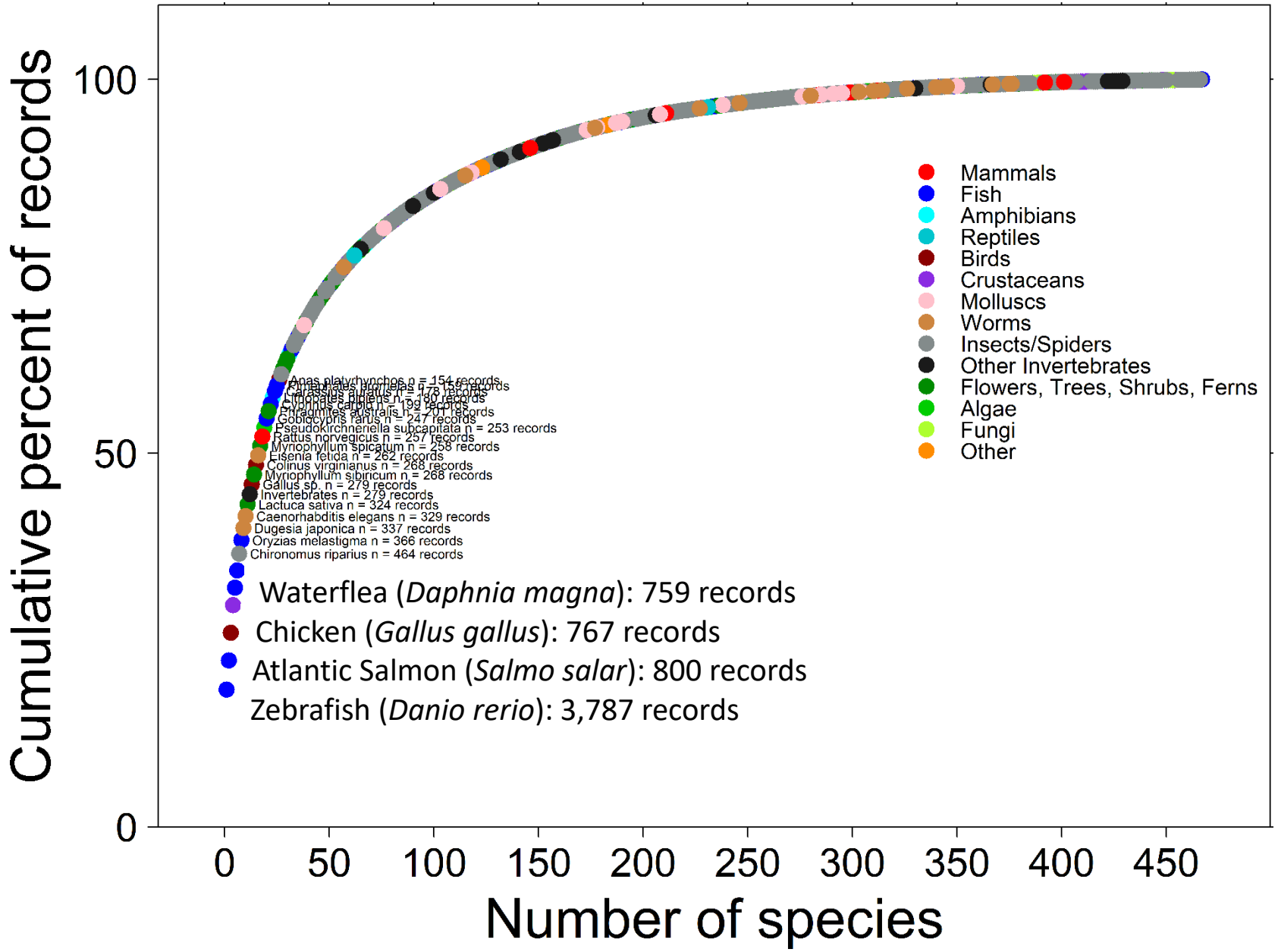
733 Publications

134 PFAS with Ecological Toxicity Data

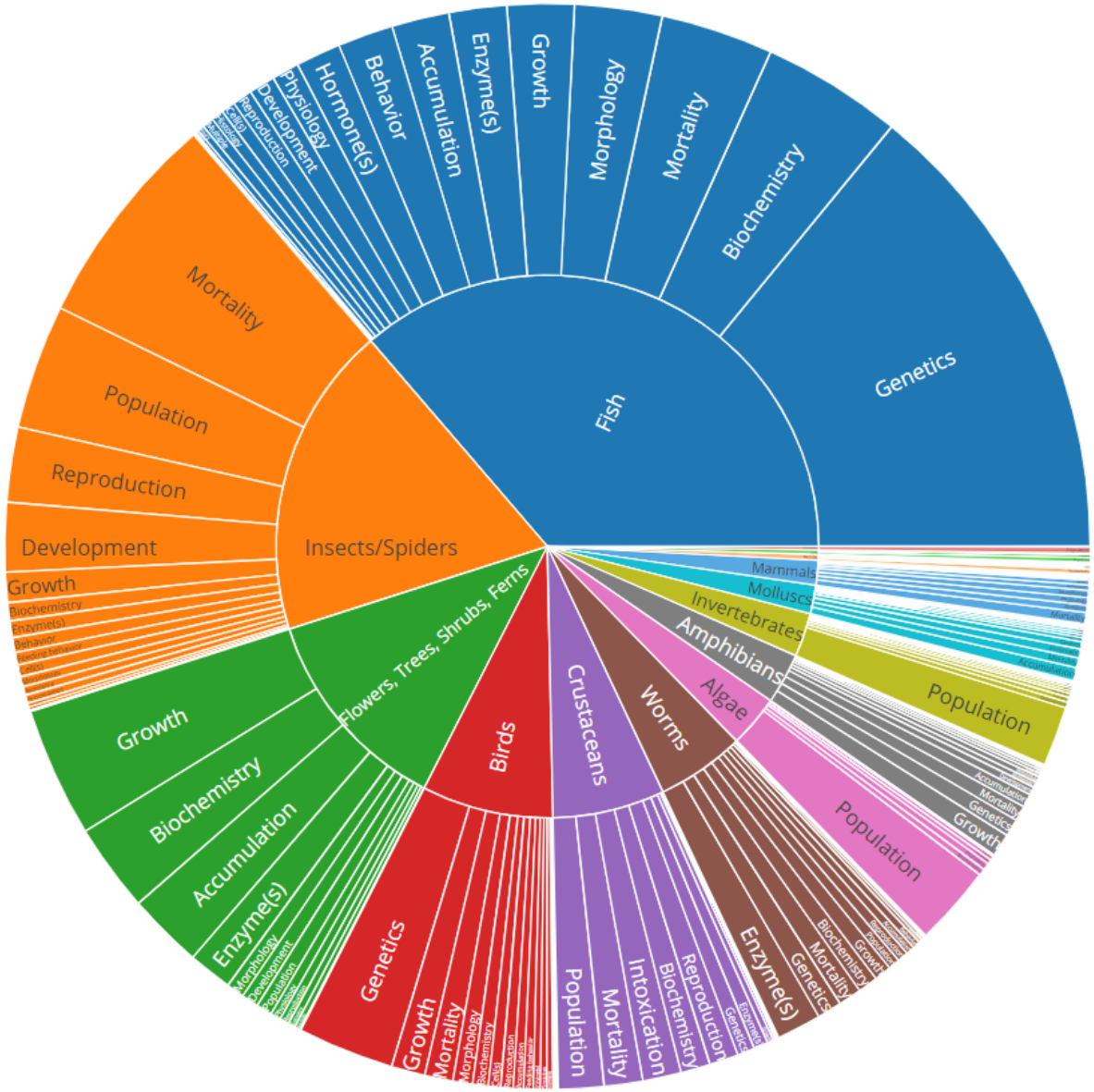
- Box size represents # of references for each chemical



PFAS Data for 467 Biological Species



Diversity in Types of Effects



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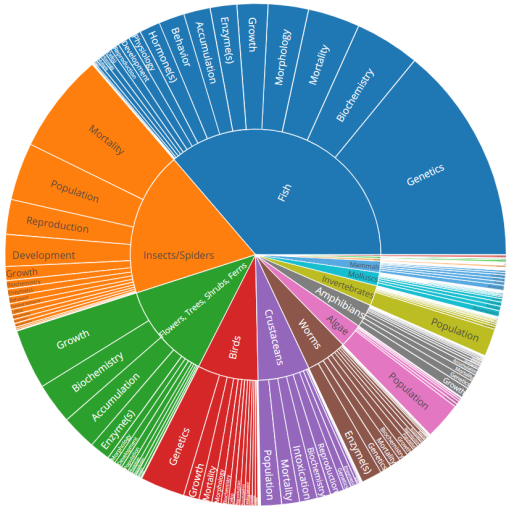
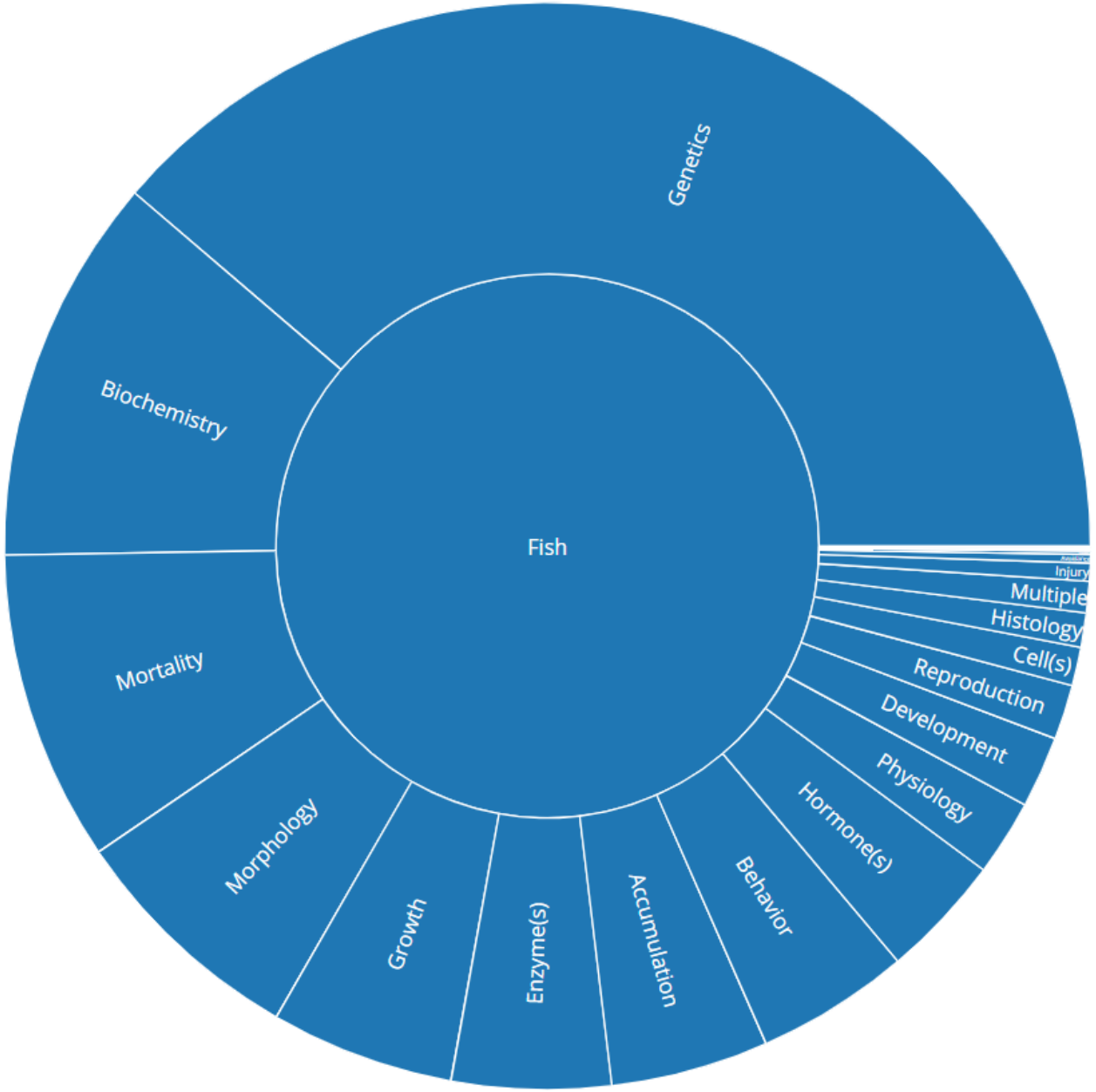
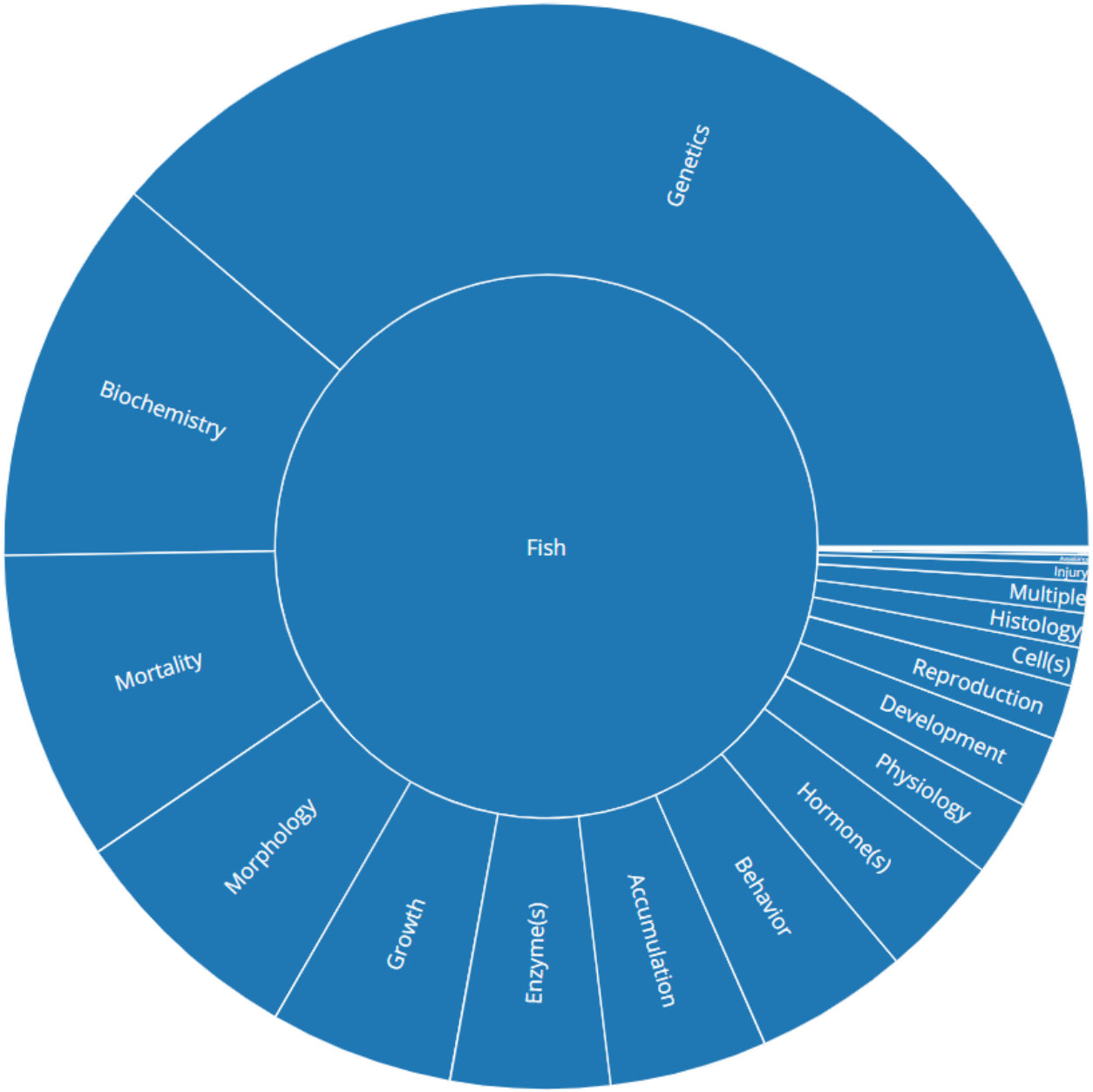




PFAS records for Fish

	Effect	# Records
Cellular Responses	Genetics	2,900
	Biochemistry	862
	Enzyme(s)	355
	Hormone(s)	275
	Cell(s)	86
Organ Responses	Histology	76
	Accumulation	352
	Immunological	3
	Physiology	169
Organism Responses	Injury	40
	Intoxication	4
	Development	160
	Growth	410
	Morphology	536
	Behavior	342
	Avoidance	19
	Feeding behavi	4
	Reproduction	122
	Mortality	692
Population Responses	Population	7
Other	Multiple	70
	Total	**7,484**

Diversity in Types of Effects



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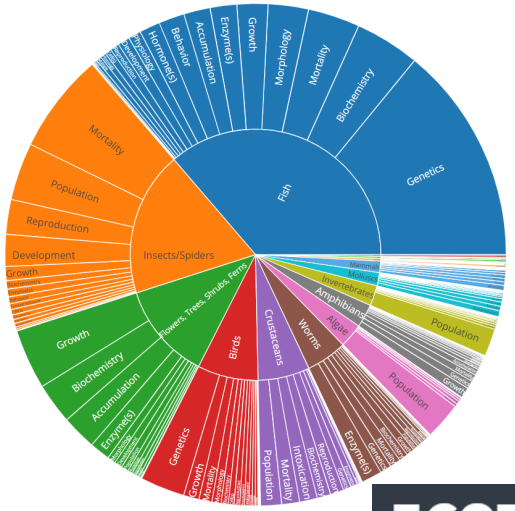
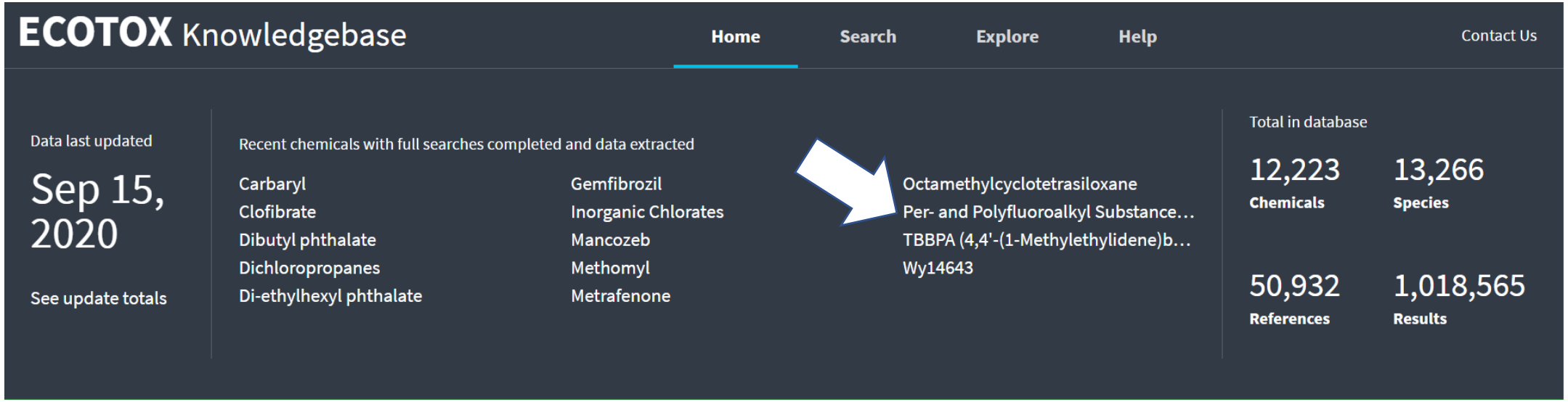
Reproduction
Fecundity
Fertility
Fertilization
Gamete production
Hatch
Mean spawns per female
Motility
Number spawning
Pregnant, Paris or Gravid
Progeny counts/numbers
Spawning frequency
Sperm cell counts
Time to spawn
Velocity
Viability

Providing Ecological Toxicity Data

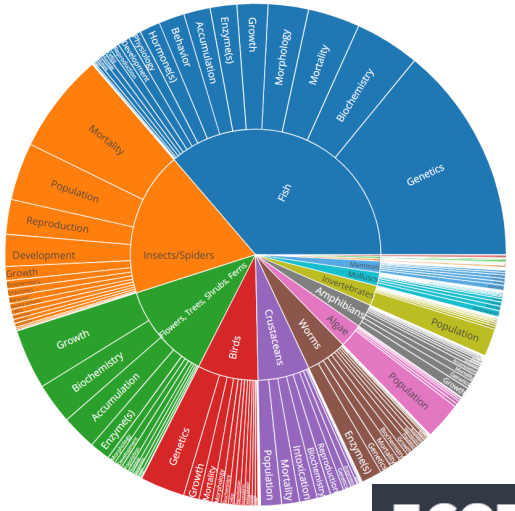


EPA Researchers
EPA ERA Forum
DoD Tri-Services ERA Work Group
and others

www.epa.gov/ecotox



Providing Ecological Toxicity Data



EPA Researchers
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and others

www.epa.gov/ecotox

ECOTOX Knowledgebase

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Data last updated

Sep 15, 2020

See update totals

Recent chemicals with full searches completed and data extracted

Carbaryl
Clofibrate
Dibutyl phthalate
Dichloropropanes
Di-ethylhexyl phthalate
Gemfibrozil
Inorganic Chlorates
Mancozeb
Methomyl
Metrafenone
Octamethylcyclotetrasiloxane
Per- and Polyfluoroalkyl Substance…

Total in database

12,223 **Chemicals**

13,266 **Species**

Environmental Toxicology and Chemistry

Invited Presentation
G. Ankley Monday 11/16

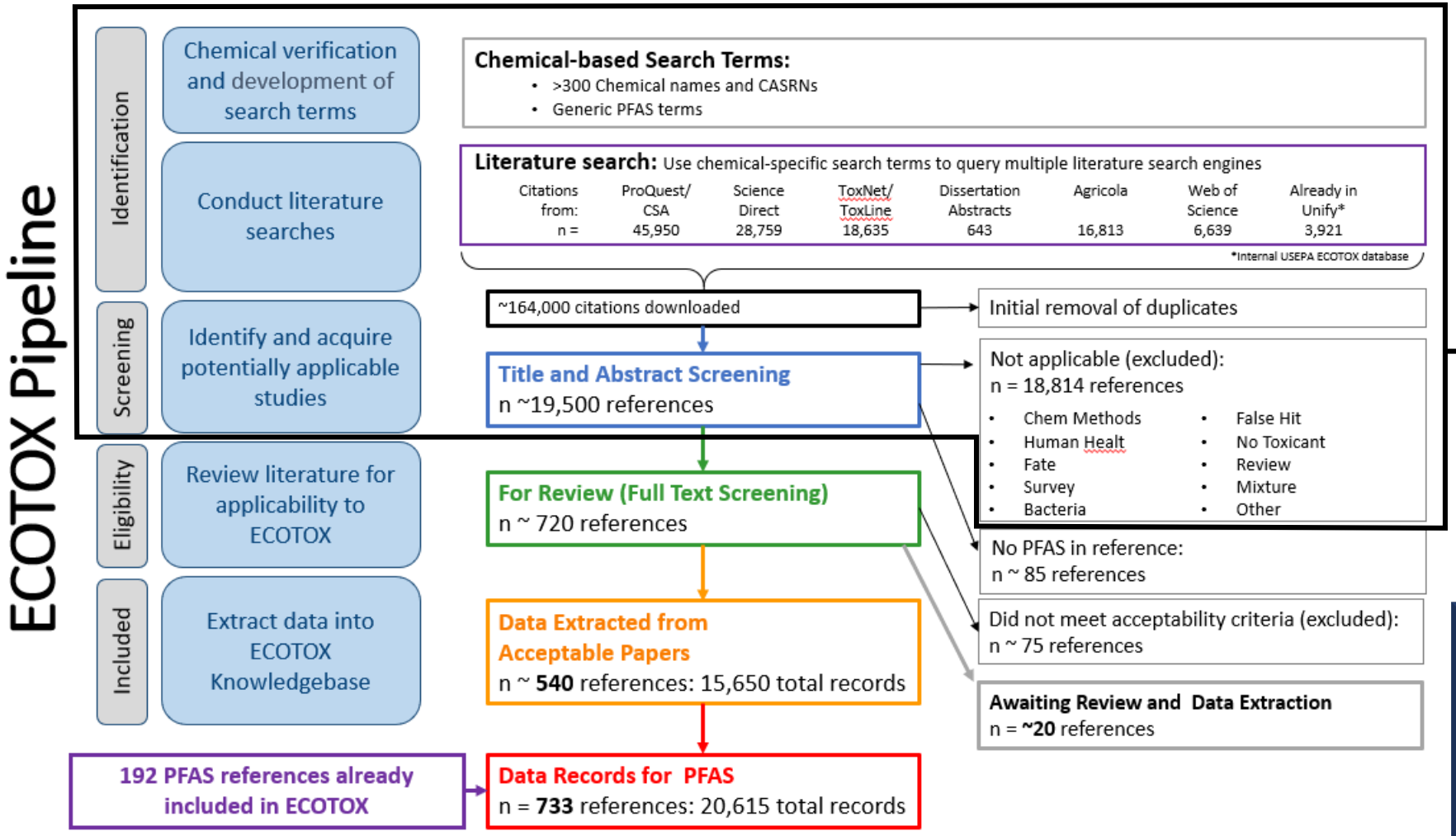
Critical Review | Open Access

Assessing the Ecological Risks of Per- and Polyfluoroalkyl Substances: Current State-of-the Science and a Proposed Path Forward

Gerald T. Ankley, Philippa Cureton, Robert A. Hoke, Magali Houde, Anupama Kumar, Jessy Kurias, Roman Lanno, Chris McCarthy, John Newsted, Christopher J. Salice … See all authors

First published: 08 September 2020 | https://doi.org/10.1002/etc.4869

Providing Literature Search Results



Human Health
Fate and Transport
Bioaccumulation
Field Surveys
Mixtures

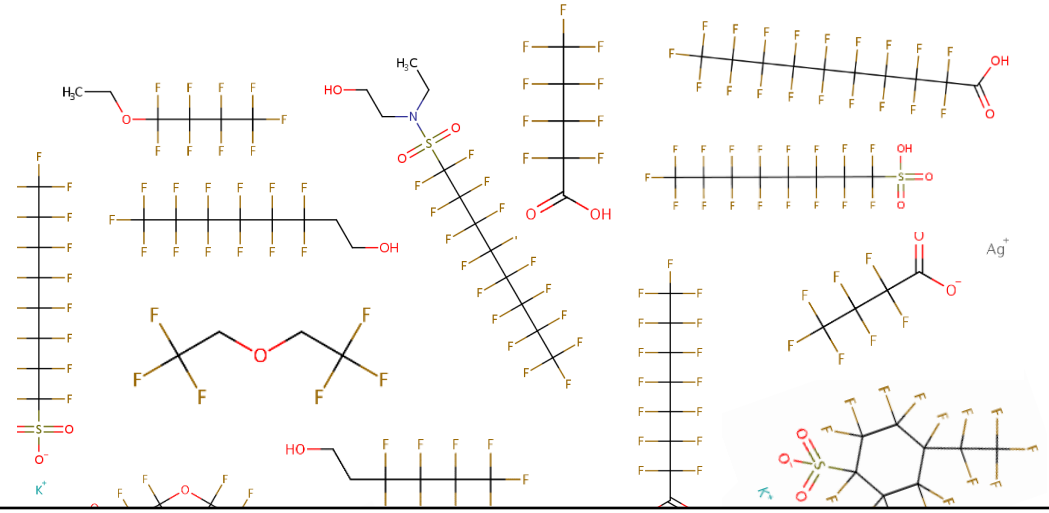
Literature Review of PFAS Bioaccumulation Data: BCFs and BAFs

L. Burkhard *In Review*

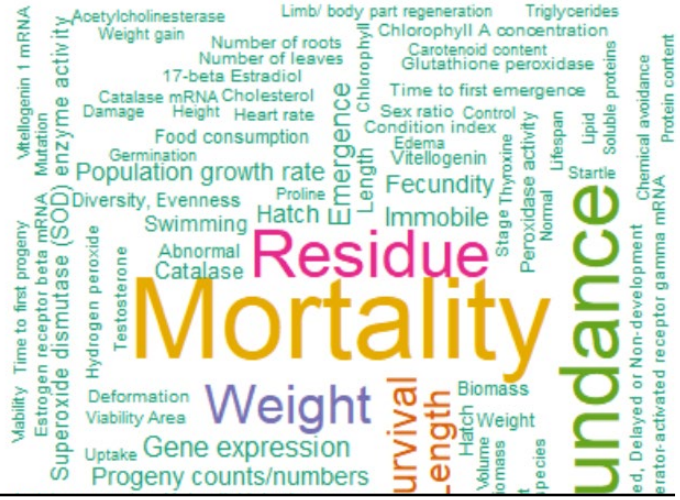
Data Inventory → Summary/Synthesis

467 Biological Species

134 PFAS



Measurements of 1,302 Effects

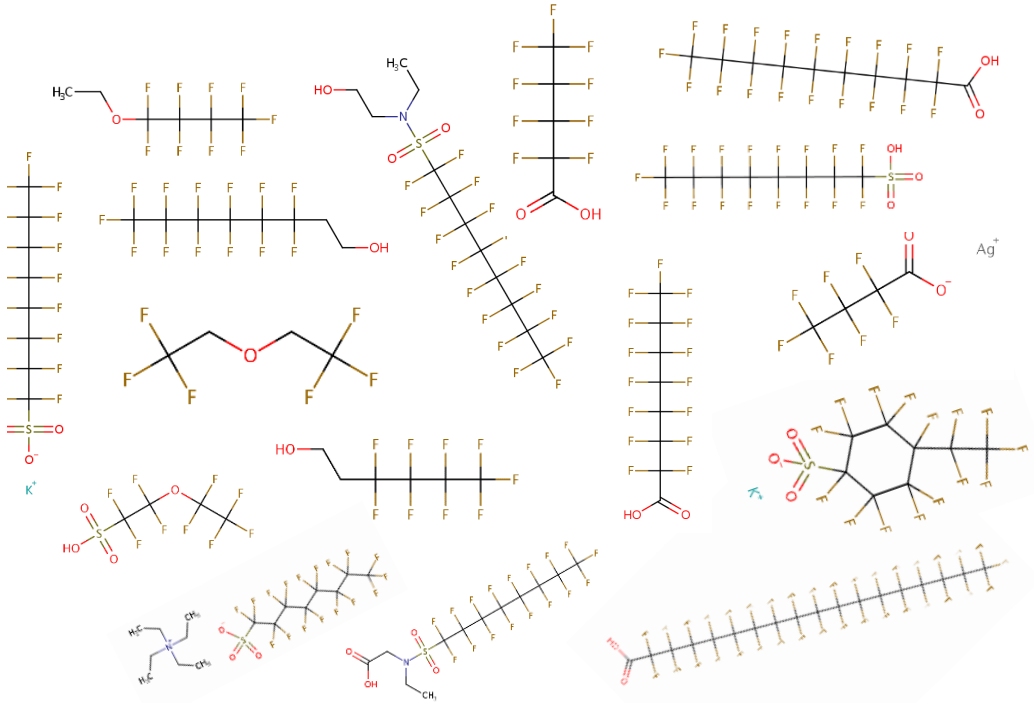


Toxicant	Cellular Responses	Tissue/Organ Responses	Organism Responses
PFOS (1763-23-1) K-PFOS (2795-39-3)	T4 & T3 ↓ Estrogen and 17-β Estradiol Δ Vitellogenin Δ Acetylcholinesterase Δ Cholesterol & Lipids Δ <u>Δ in expression of</u>: PPAR-mediated genes (multiple) Thyroid-relevant genes (multiple) …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

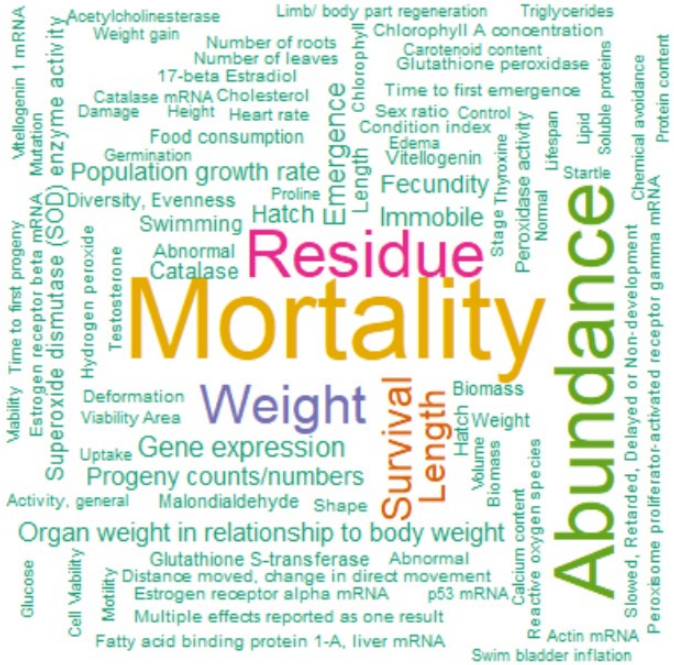
Data Inventory → Summary/Synthesis

467 Biological Species

134 PFAS



Measurements of 1,302 Effects



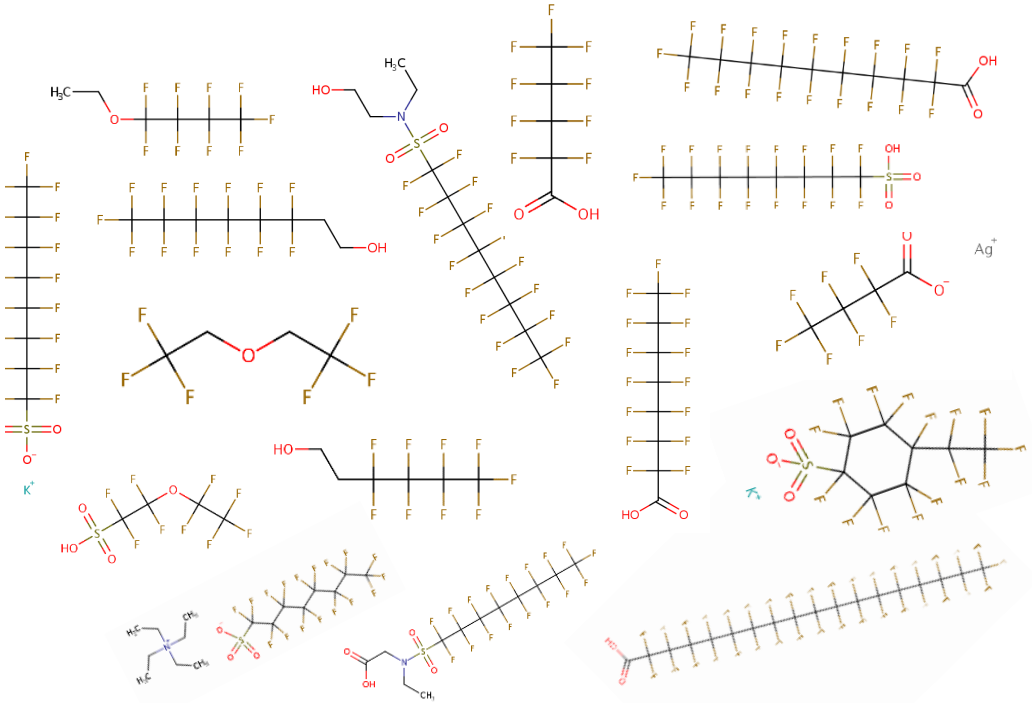
Unique Identifiers, Controlled Vocabularies, & Ontologies

Species	NCBI TaxID
Zebrafish (*Danio rerio*)	7955
Atlantic Salmon (*Salmo salar*)	8030
Chicken (*Gallus gallus*)	9031
Water Flea (*Daphnia magna*)	35525

Data Inventory → Summary/Synthesis

467 Biological Species

134 PFAS



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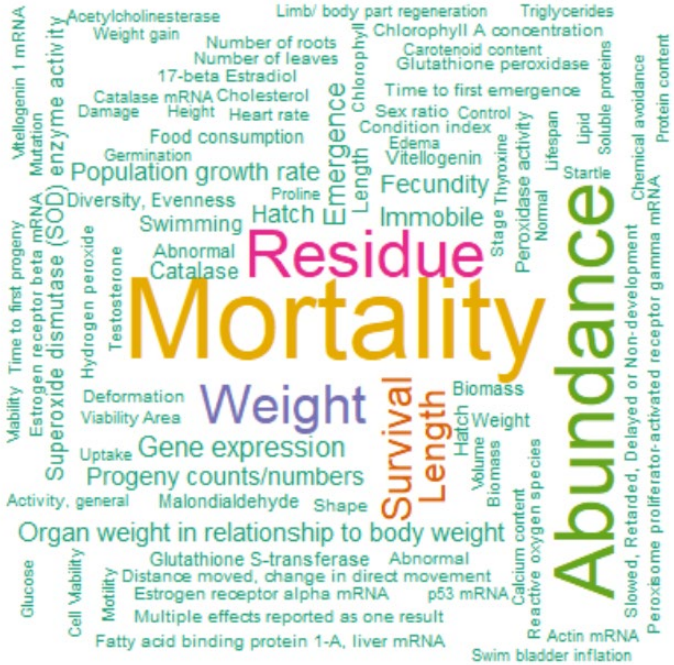


Unique Identifiers, Controlled Vocabularies, & Ontologies

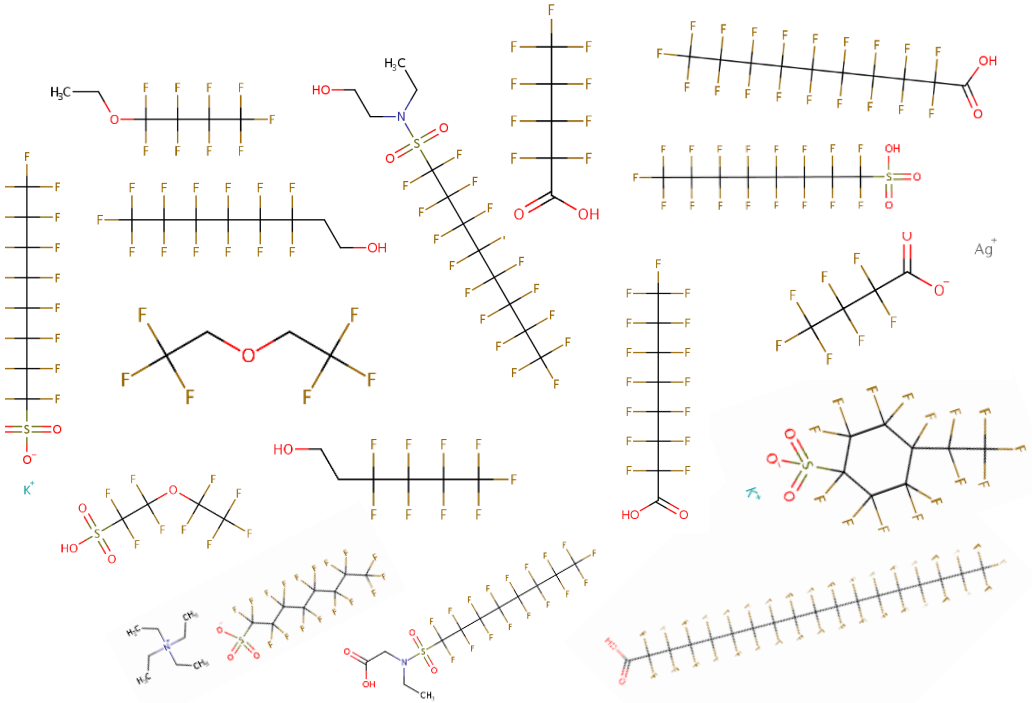
Species:
- **Taxonomy**
- **NCBI TaxID**

Toxicants	CASRN	DSSTOX Substance ID
PFOS	1763-23-1	DTXSID3031864
K-PFOS	2795-39-3	DTXSID8037706
PFOA	335-67-1	DTXSID8031865
PFHxS	355-46-4	DTXSID7040150
GenX	62037-80-3	DTXSID40108559

Data Inventory → Summary/Synthesis

467 Biological Species

134 PFAS



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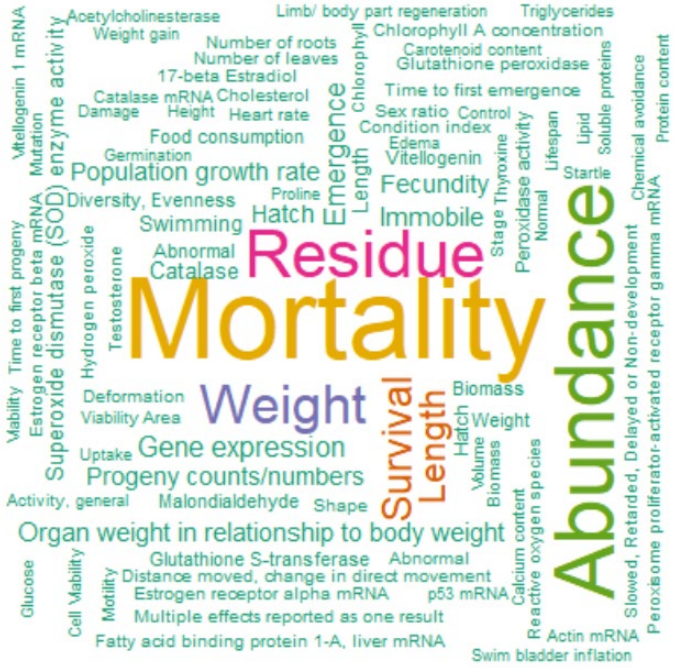


Unique Identifiers, Controlled Vocabularies, & Ontologies

Species:
- **Taxonomy**
- **NCBI TaxID**

Toxicants
- **CASRN**
- **DTXSID**

Effect	Mapping
PPARalpha b mRNA	NCBI-GENEID:557714
Cholesterol	CHEBI:16113
Thyroxine	CHEBI:30660
Activity, general	XCO:0000001
Survival	MESH:Q000401

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
- Mapping to controlled vocabularies and ontologies will 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

Ongoing Literature Search, Review, Data Extraction

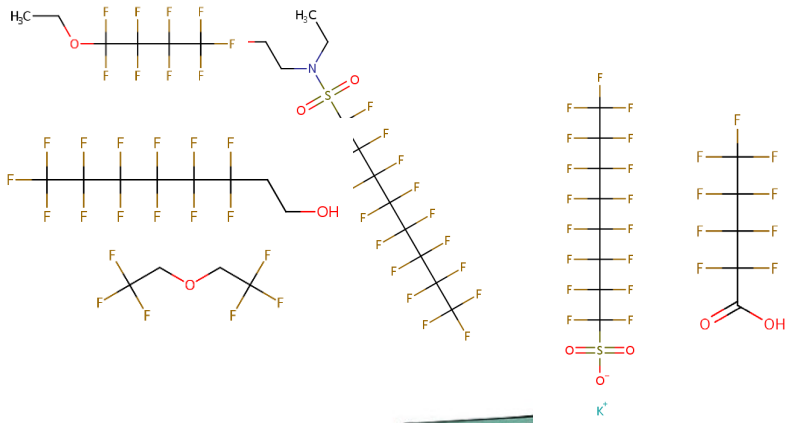
Updated list of >400 unique CASRNs and associated chemical names

Conduct literature searches

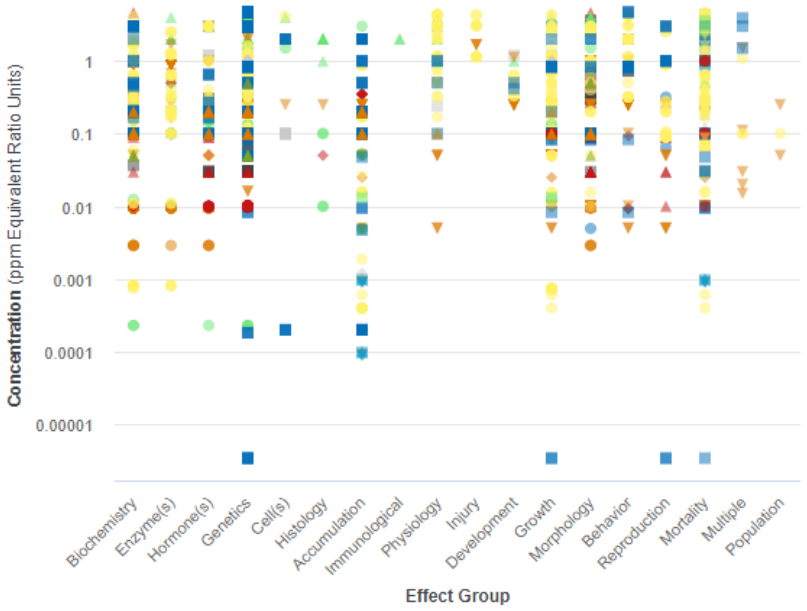
Identify and acquire potentially applicable studies

Review literature for applicability to ECOTOX

Extract data and encode into ECOTOX Knowledgebase



Quarterly data releases to ECOTOX



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Data last updated

Sep 15, 2020

See update totals

Recent chemicals with full searches completed and data extracted

Carbaryl
Clofibrate
Dibutyl phthalate
Dichloropropanes
Di-ethylhexyl phthalate
Gemfibrozil
Inorganic Chlorates
Mancozeb
Methomyl
Metrafenone
Octamethylcyclotetrasiloxane
* Per- and Polyfluoroalkyl Substance…
TBBPA (4,4'-(1-Methylethylidene)b…
Wy14643

Total in database

12,223 **Chemicals**

13,266 **Species**

50,932 **References**

1,018,565 **Results**

Contact Us About the ECOTOX Knowledgebase

EPA welcomes your comments on this version of ECOTOX. We are specifically interested in feedback from users about the new functionality and usability. What, if any, issues did you experience? Please be as specific as possible in your comments. If you or your team would like training on how to use and find information in ECOTOX, please indicate that in the Feedback box below.

For technical questions about the scientific information and data interpretation, you may use the comment form below, or the contact information in the right-side bar, to contact the ECOTOX Support Staff.

Demonstrations and training available

Get Updates via Email

Telephone: 218-529-5225
Fax: 218-529-5003
E-mail: ecotox.support@epa.gov

Mailing address:
ECOTOX Support
Great Lakes Toxicology Ecology Division
6201 Congdon Boulevard
Duluth, MN 55804

Acknowledgements

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Anne Pilli*

Brian Kinziger

SpecPro Professional Services

Gregory Elonen*

Dan Peterson

*Coauthors

Thank you!

olker.jennifer@epa.gov