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PFAS Chemistry: Range, Complexity, Groupings, and the CompTox Chemicals Dashboard

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

September 2020

The Science of PFAS, Virtual Conference

CompTox Chemicals Dashboard

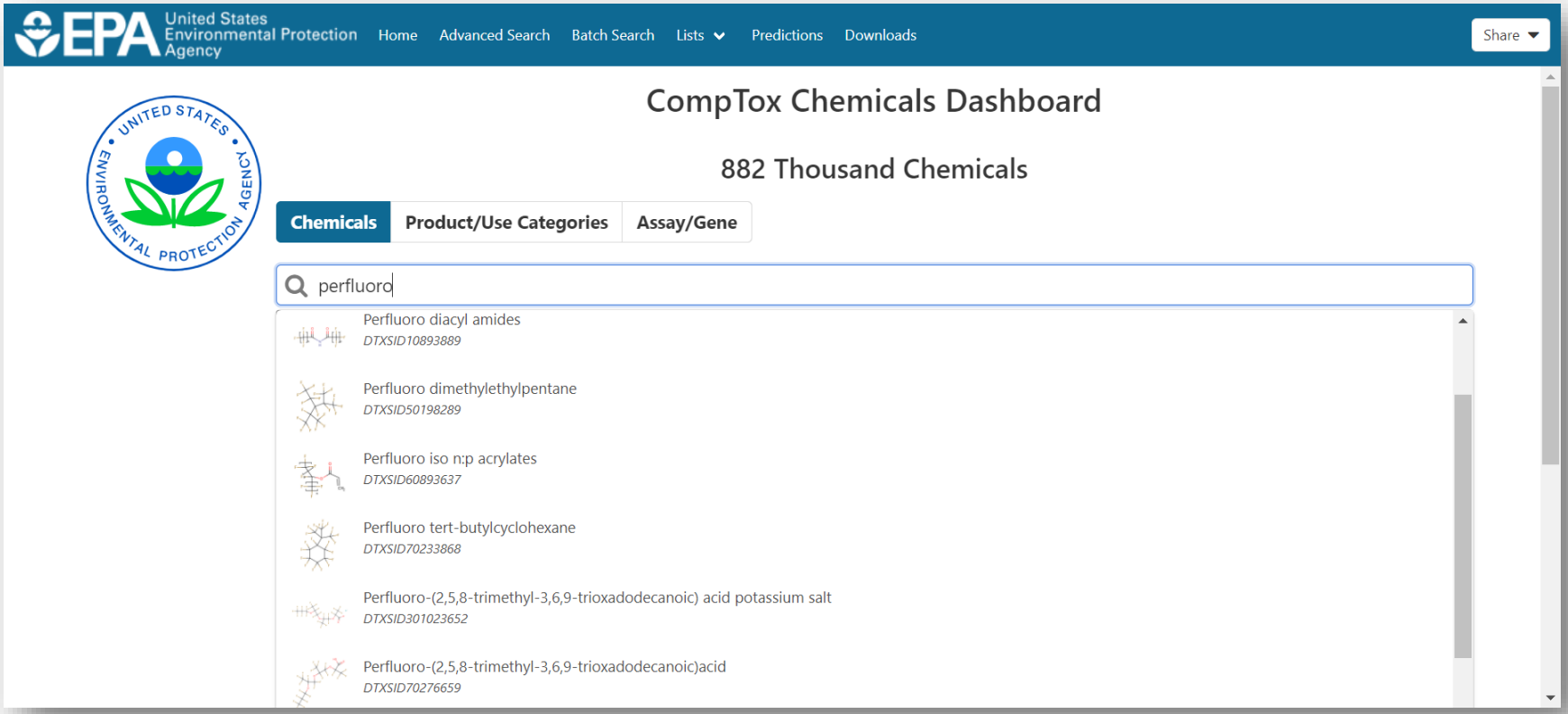
- A **publicly accessible website** delivering access:
  - ~882,000 chemicals with related property data
  - Experimental and predicted physicochemical property data
  - Experimental Human and Ecological hazard data
  - Integration to “biological assay data” for 1000s of chemicals
  - Information regarding consumer products containing chemicals
  - Links to other agency websites and public data resources
  - “Literature” searches for chemicals using public resources
  - “Batch searching” for thousands of chemicals

  - **Over 10,000 of the chemicals are classed as PFAS Chemicals**

CompTox Chemicals Dashboard

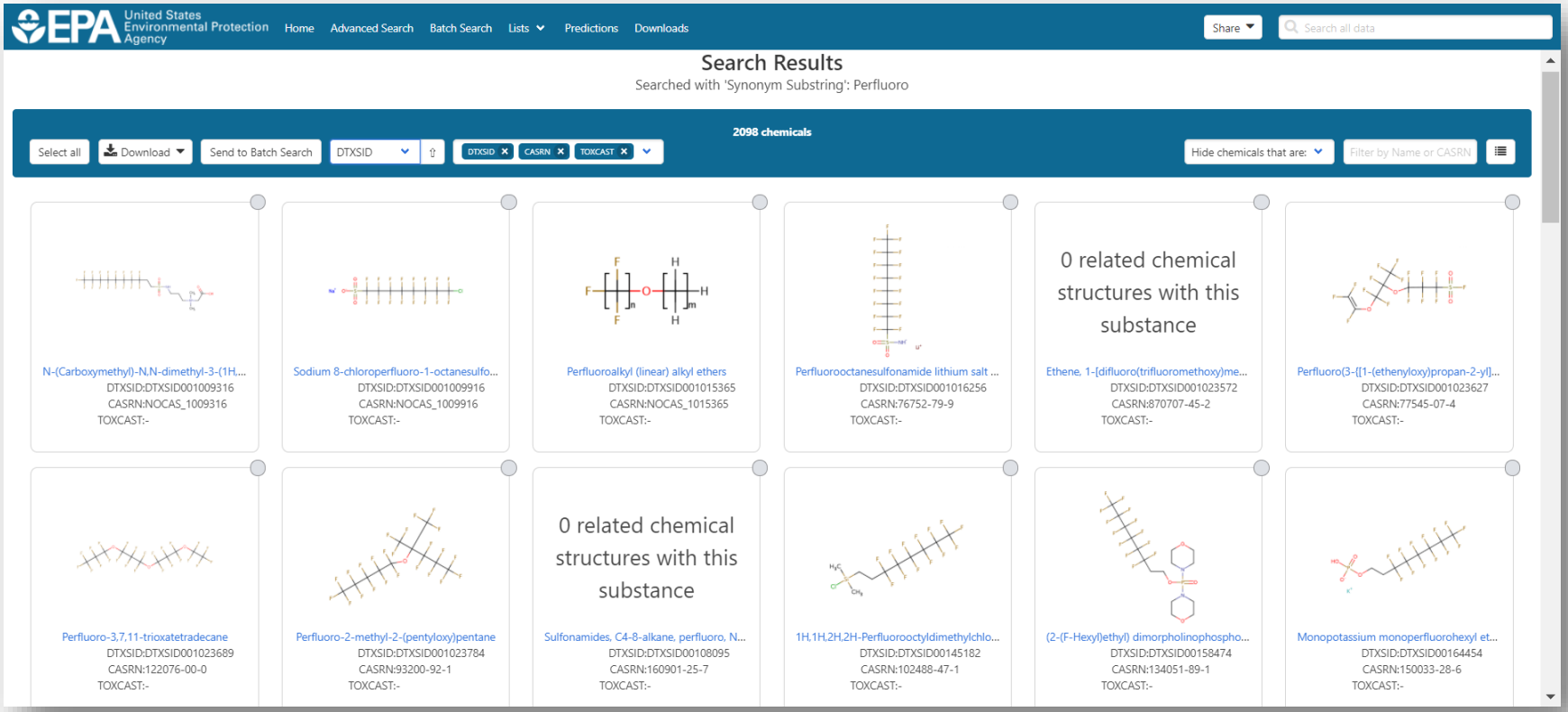
https://comptox.epa.gov/dashboard

- Searching – CAS Numbers, systematic names and synonyms, structures (as InChIs)

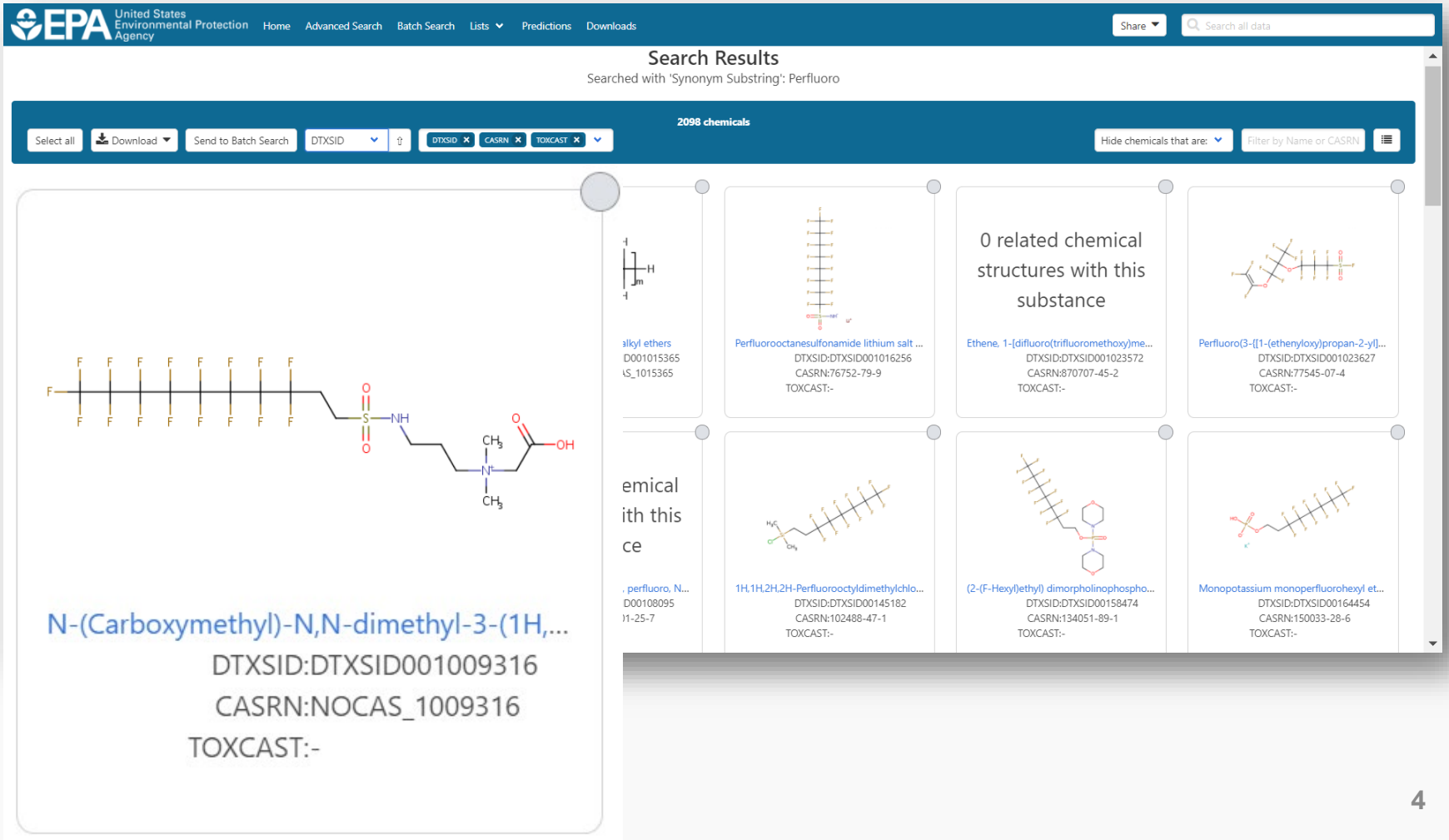


Substring search “perfluoro”

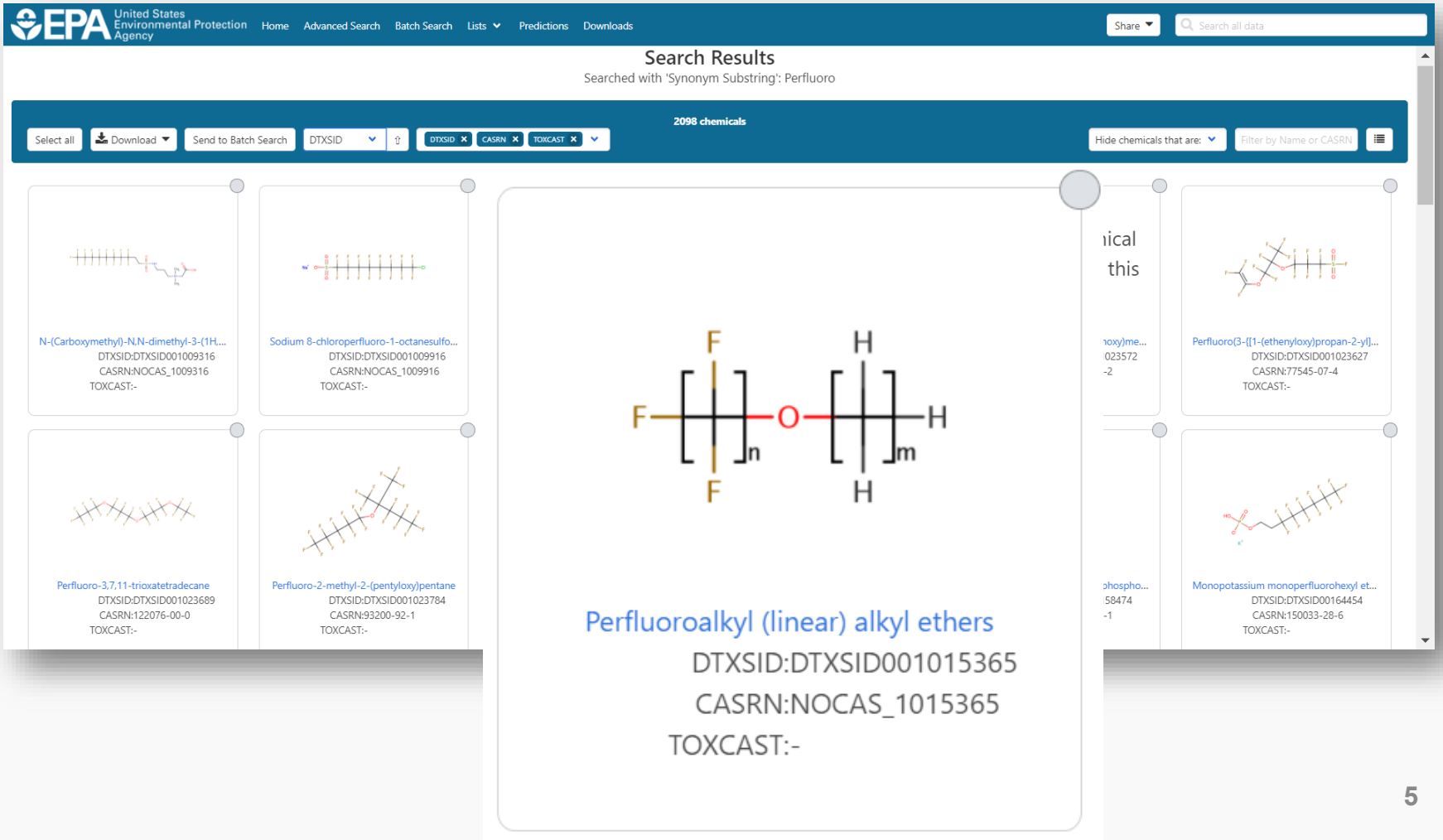
- Substring search ~2000 chemicals



Substring search “perfluoro”
“Explicit” structures

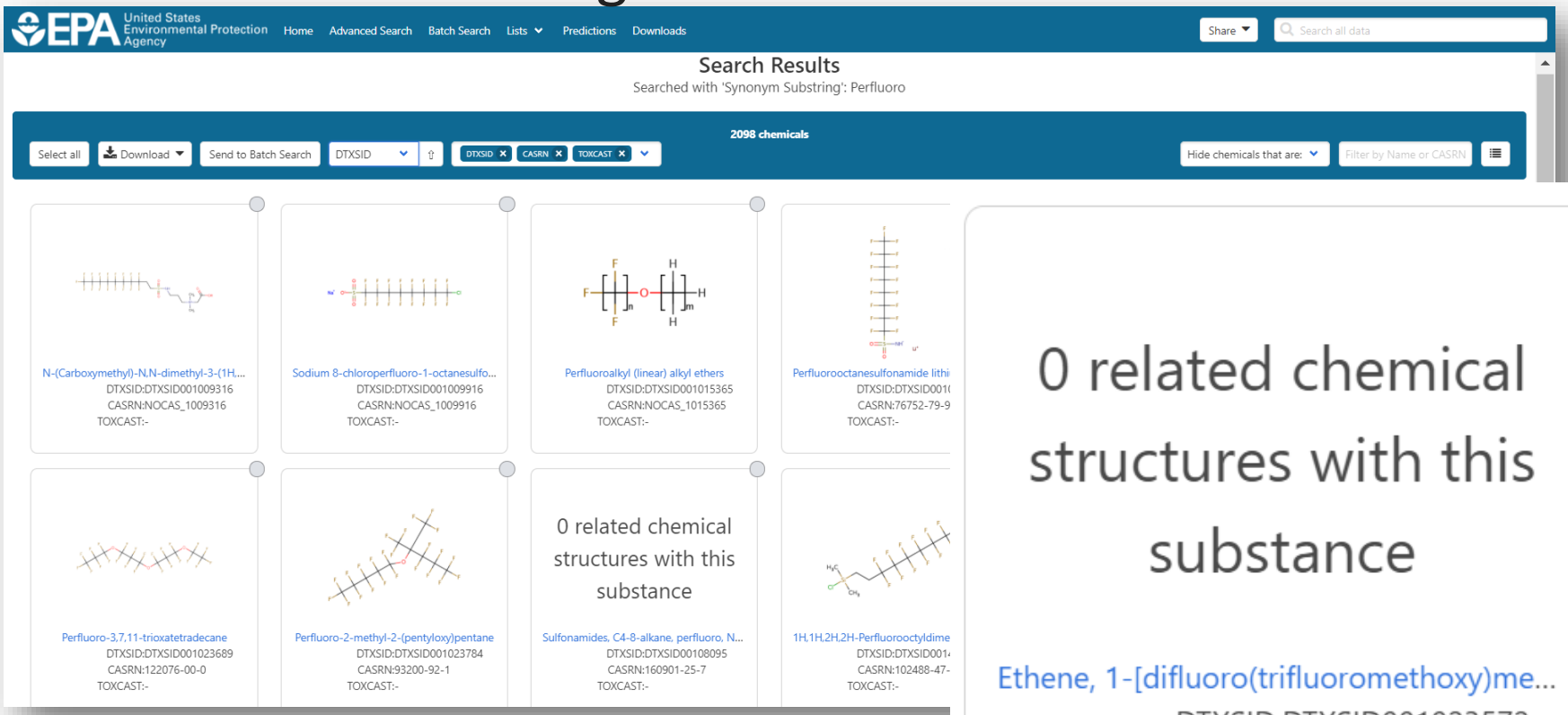


Substring search “perfluoro” “Markush” representations

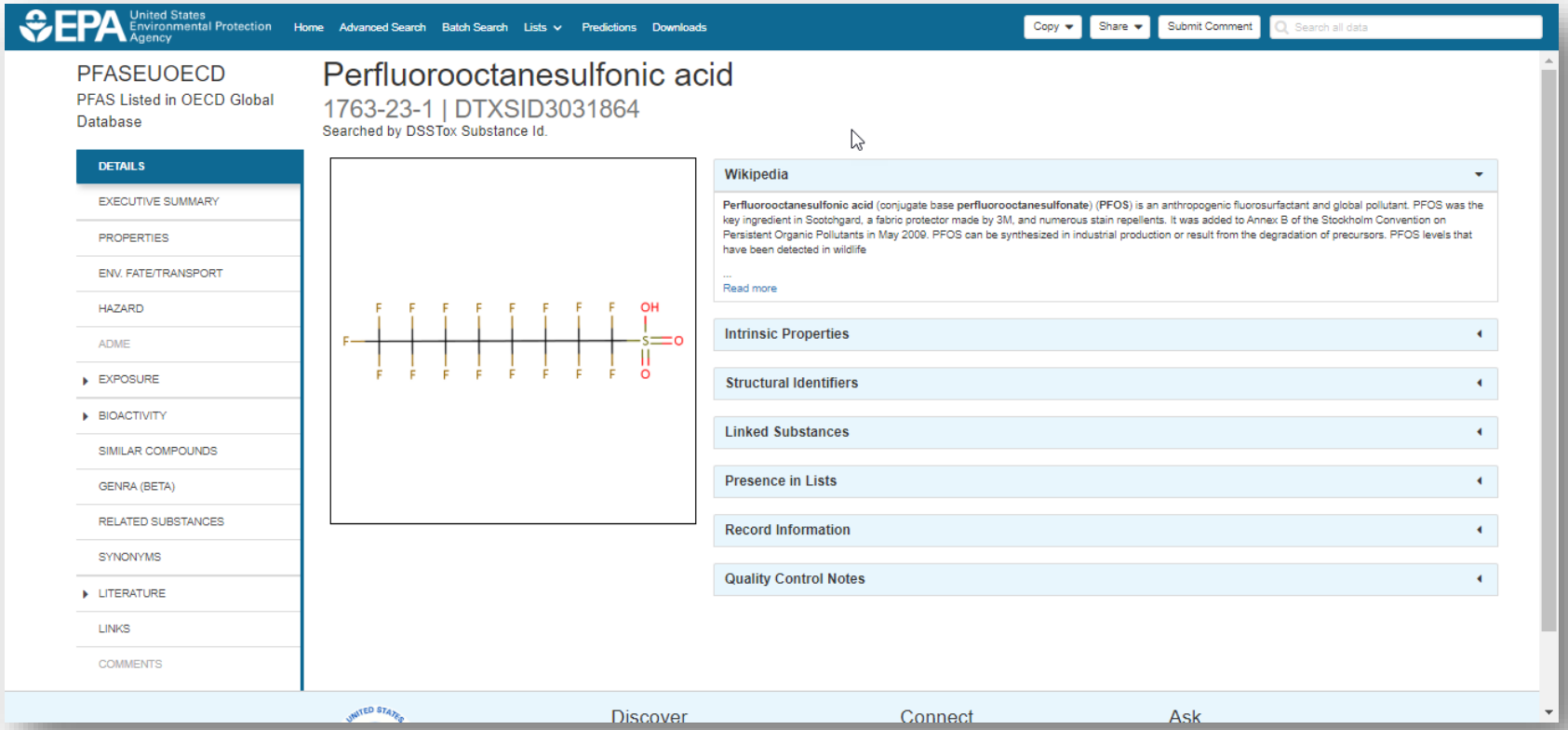


Substring search “perfluoro” “UVCB” chemicals

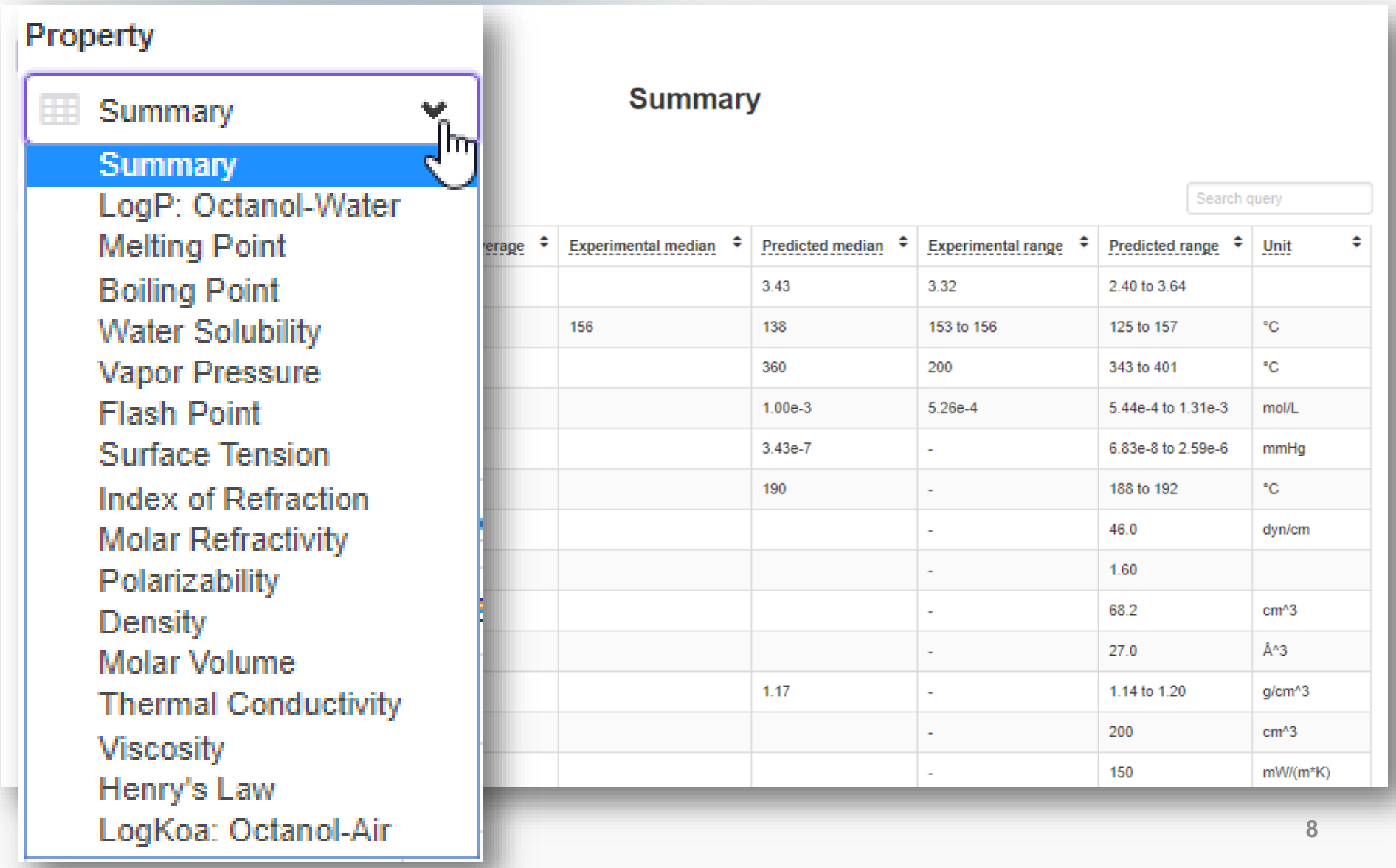
- Unknown or Variable Composition, Complex Reaction Products and Biological Materials



1 of ~882,000 Chemical Pages

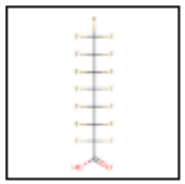


Physicochemical properties



erage	Experimental median	Predicted median	Experimental range	Predicted range	Unit
		3.43	3.32	2.40 to 3.64	
	156	138	153 to 156	125 to 157	°C
		360	200	343 to 401	°C
		1.00e-3	5.26e-4	5.44e-4 to 1.31e-3	mol/L
		3.43e-7	-	6.83e-8 to 2.59e-6	mmHg
		190	-	188 to 192	°C
			-	46.0	dyn/cm
			-	1.60	
			-	68.2	cm^3
			-	27.0	Å^3
		1.17	-	1.14 to 1.20	g/cm^3
			-	200	cm^3
			-	150	mW/(m*K)

Experimental Data



Perfluorooctanoic acid

335-67-1 | DTXSID8031865

Searched by Synonym from Valid Source.

Property

Water Solubility

Water Solubility

Download Summary

Type	Average	Median	Range
Experimental	1.56e-2	1.56e-2	8.21e-3 to 2.29e-2
Predicted	1.01e-2	6.38e-5	6.27e-8 to 4.01e-2

Experimental

Download Experimental Data

Source	Result	Experimental Details
3M_PFOA_Sheet	8.21e-3	
ATSDR_Perfluoroalkyl_Cheminfo	2.29e-2	
Danish_EPA_PFOA_Report_2005	2.29e-2	
Danish_EPA_SCPFAS_Report_2015	8.21e-3	

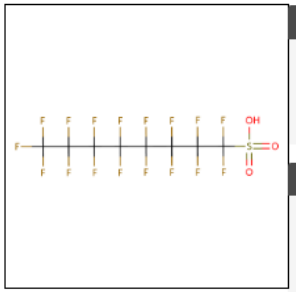
Detailed QSAR Prediction Reports

OPERA Models: Vapor Pressure

Perfluorooctanesulfonic acid

1763-23-1 | DTXSID3031864

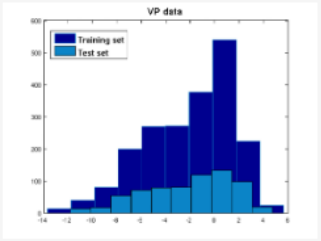
Print PDF

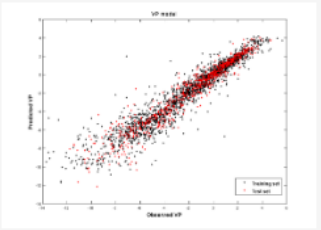


Model Results

Predicted value: 1.49e-2 mmHg
Global applicability domain: Outside
Local applicability domain index: 0.338
Confidence level: 0.286

Model Performance





QMRF

Weighted KNN model

5-fold CV (75%)		Training (75%)		Test (25%)	
Q2	RMSE	R2	RMSE	R2	RMSE
0.910	1.08	0.910	1.08	0.920	1.00

Nearest Neighbors from the Training Set

N-Ethylperfluorooctanesulfonamide
Measured:4.27957e-7
Predicted: 0.00000157466

Perfluorooctanesulfonamide
Measured:0.248028
Predicted: 0.181011

Perfluorooctanoic acid
Measured:0.525049
Predicted: 0.339896

Perfluoroheptanoic acid
Measured:0.133015
Predicted: 0.127572

Training sets enhanced QSAR

Environmental Toxicology and Chemistry—Volume 39, Number 4—pp. 775–786, 2020
Received: 8 October 2019 | Revised: 30 October 2019 | Accepted: 3 February 2020

Environmental Chemistry

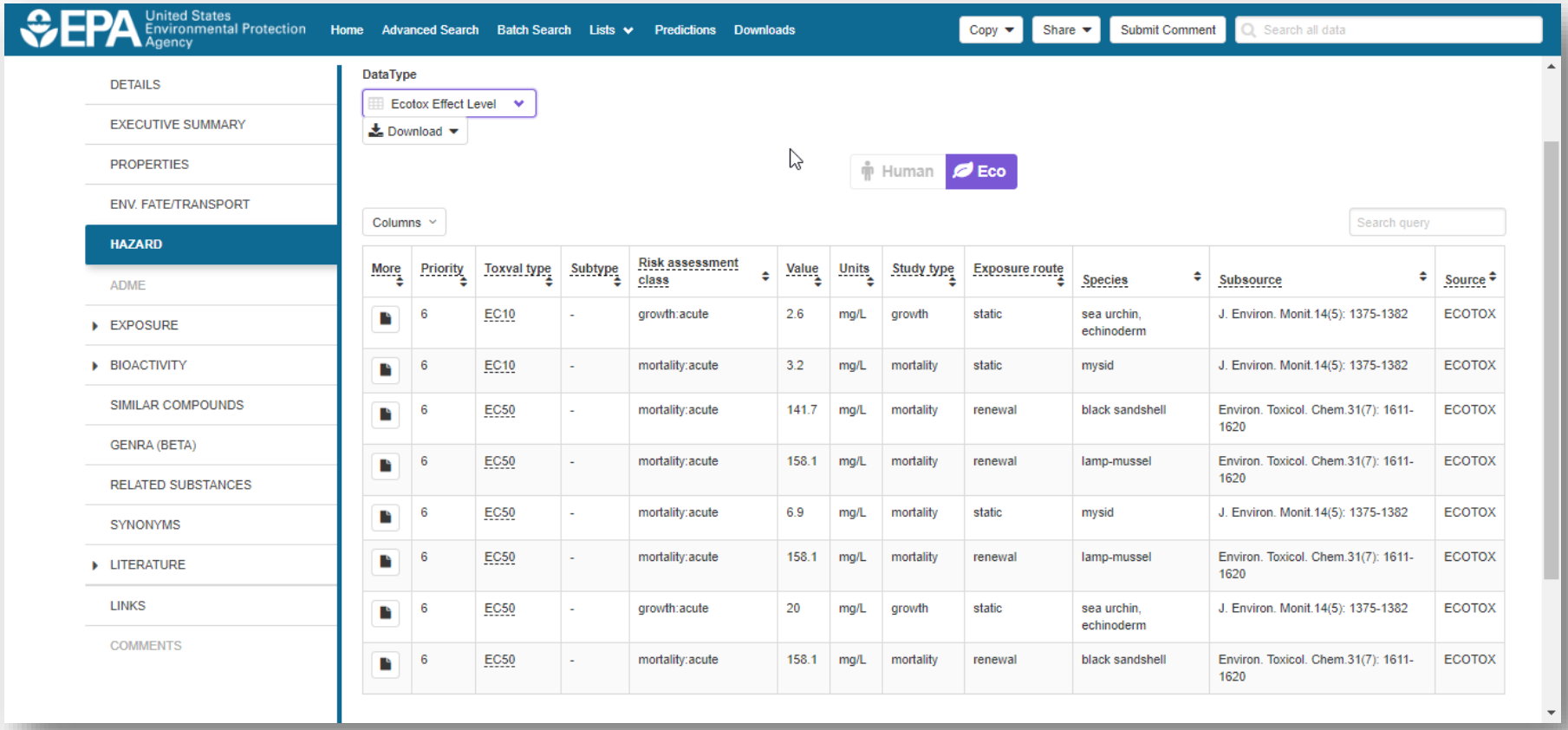
Property Estimation of Per- and Polyfluoroalkyl Substances: A Comparative Assessment of Estimation Methods

Alina Lampic and J. Mark Parnis*

Chemical Properties Research Group (Canadian Environmental Modelling Centre), Department of Chemistry, Trent University, Peterborough, Ontario, Canada

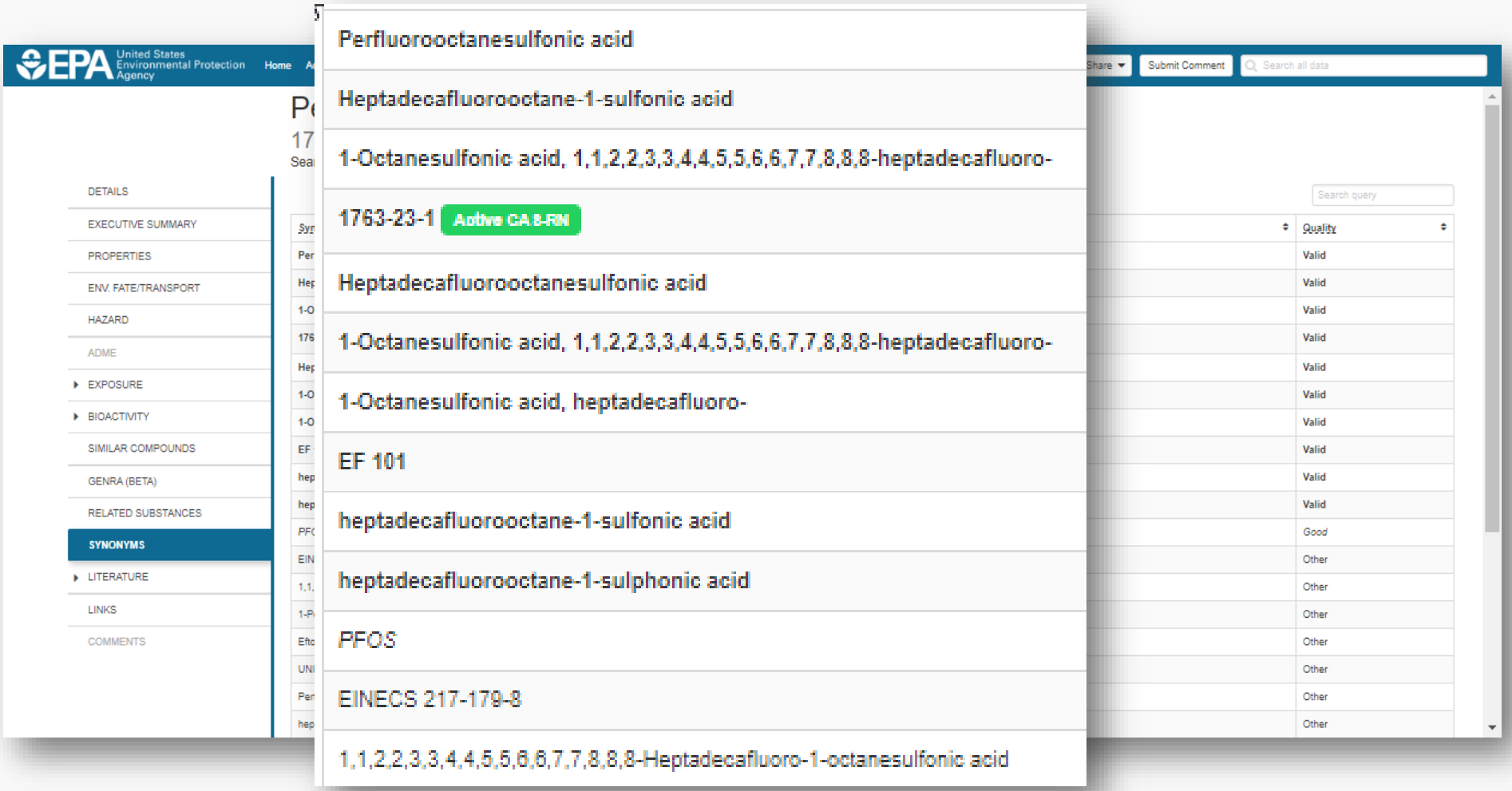
- Comparison of COSMOtherm, EPI Suite ACD/Labs, TEST and OPERA
- OPERA **best performance**: Vapor Pressure, Solubility, Octanol-water partitioning, Octanol-Air partitioning, Soil-Adsorption coefficient

Hazard Data – Human and Eco



More	Priority	Toxval type	Subtype	Risk assessment class	Value	Units	Study type	Exposure route	Species	Subsource	Source
	6	EC10	-	growth:acute	2.6	mg/L	growth	static	sea urchin, echinoderm	J. Environ. Monit.14(5): 1375-1382	ECOTOX
	6	EC10	-	mortality:acute	3.2	mg/L	mortality	static	mysid	J. Environ. Monit.14(5): 1375-1382	ECOTOX
	6	EC50	-	mortality:acute	141.7	mg/L	mortality	renewal	black sandshell	Environ. Toxicol. Chem.31(7): 1611-1620	ECOTOX
	6	EC50	-	mortality:acute	158.1	mg/L	mortality	renewal	lamp-mussel	Environ. Toxicol. Chem.31(7): 1611-1620	ECOTOX
	6	EC50	-	mortality:acute	6.9	mg/L	mortality	static	mysid	J. Environ. Monit.14(5): 1375-1382	ECOTOX
	6	EC50	-	mortality:acute	158.1	mg/L	mortality	renewal	lamp-mussel	Environ. Toxicol. Chem.31(7): 1611-1620	ECOTOX
	6	EC50	-	growth:acute	20	mg/L	growth	static	sea urchin, echinoderm	J. Environ. Monit.14(5): 1375-1382	ECOTOX
	6	EC50	-	mortality:acute	158.1	mg/L	mortality	renewal	black sandshell	Environ. Toxicol. Chem.31(7): 1611-1620	ECOTOX

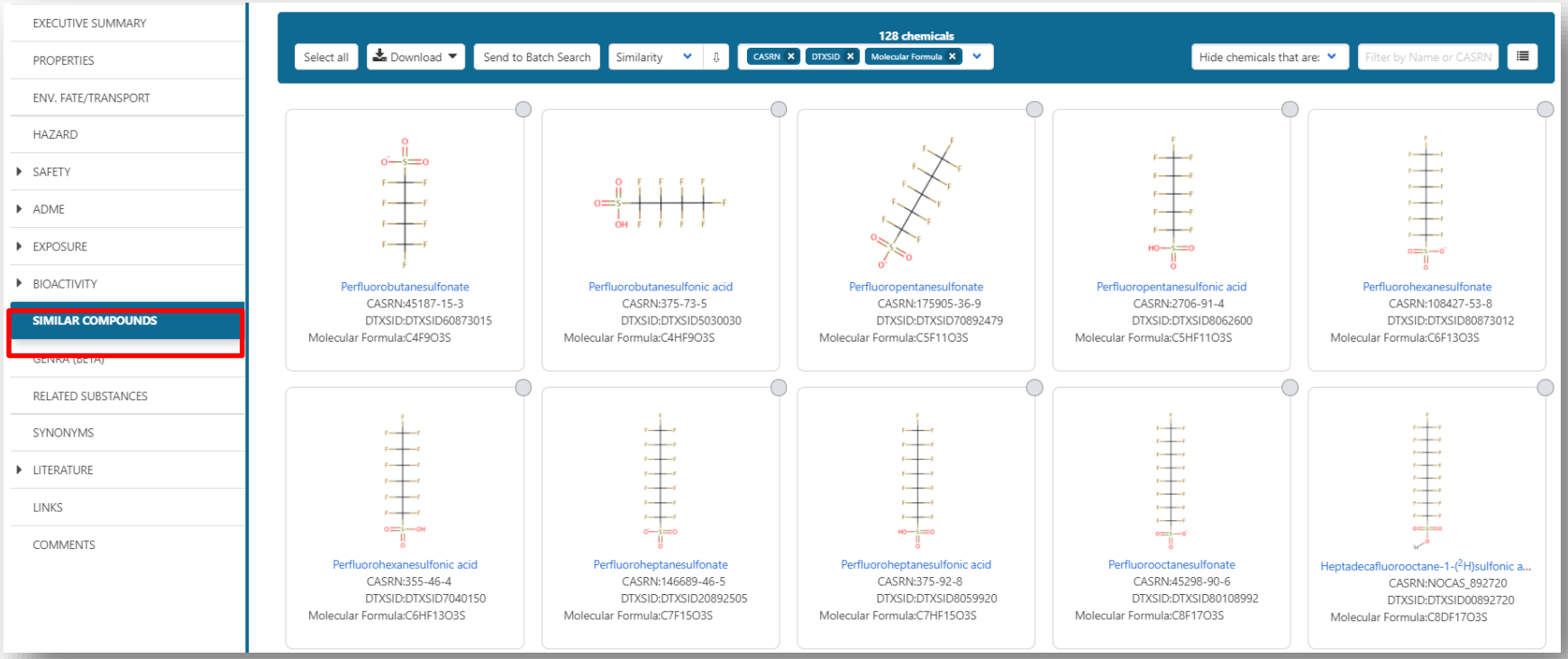
What is PFOS Called? Synonyms, CASRNs and more



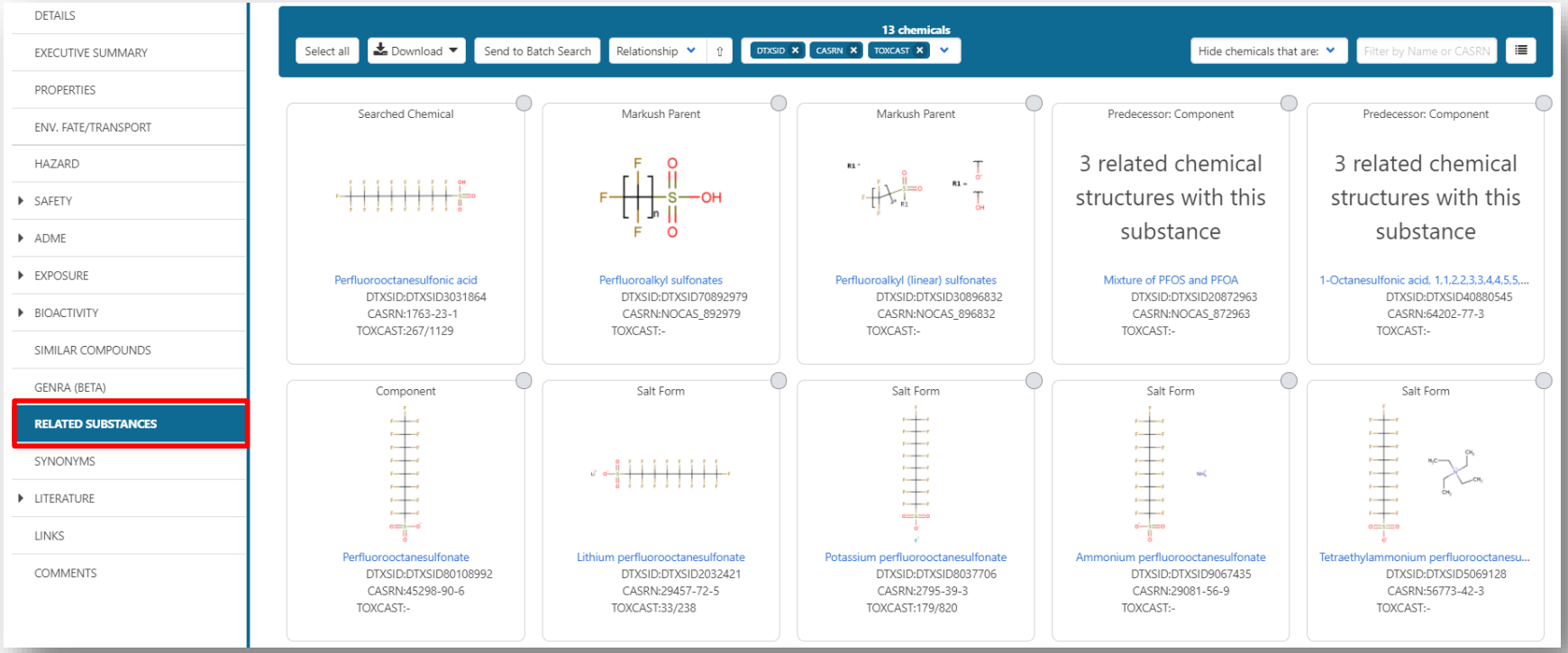
Substance Relationship Mappings

- Similar compounds - based on structure “fingerprints”
- Structure mappings - between parent and salts, multicomponent chemicals, isotopomers
- Related substances – monomer to polymer, parent to transformation products

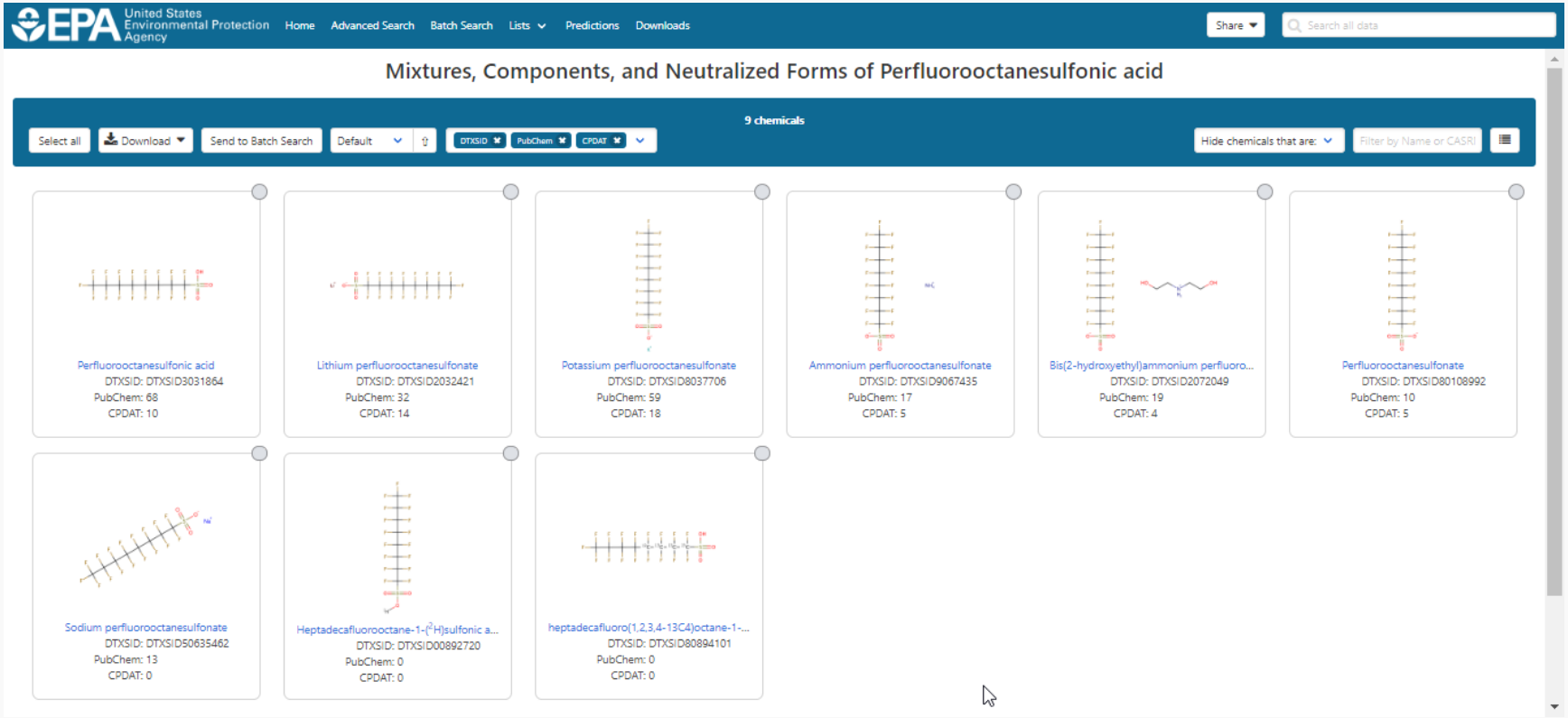
Are there Similar Compounds?
128 chemicals >0.8 match factor



Relationships in the data



9 salt forms of PFOS (and the ion)



CHEMICAL LISTS OF PFAS

A List of Lists of Chemicals

https://comptox.epa.gov/dashboard/chemical_lists

Download | Columns | 10 | PFAS | Copy Filtered Lists URL

List Acronym	List Name	Last Updated	Number of Chemicals	List Description
PFASSTRUCT	PFAS|EPA: PFAS structures in DSSTox (update August 2020)	2020-09-04	8163	List of all structures contained in DSSTox bounded by multiple substructure filters used to identify PFAS (per- and polyfluorinated substances)
PFASMASTER	PFAS Master List of PFAS Substances	2018-06-29	5070	PFASMASTER is a consolidated list of PFAS substances spanning and bounded by the below lists of current interest to researchers and regulators worldwide.
PFASOECD	PFAS: Listed in OECD Global Database	2018-05-16	4729	OECD released a New Comprehensive Global Database of Per- and Polyfluoroalkyl Substances, (PFASs) listing more than 4700 new PFAS
PFASOECDNA	NORMAN: List of PFAS from the OECD Curated by Nikiforos Alygizakis	2019-05-03	3213	List of PFAS released by the OECD, provided by Zhanyun Wang, curated and mapped to structures by Nikiforos Alygizakis
PFASKEMI	PFAS: List from the Swedish Chemicals Agency (KEMI) Report	2017-02-09	2416	Perfluorinated substances from a Swedish Chemicals Agency (KEMI) Report on the occurrence and use of highly fluorinated substances.
PFASDEV1	PFAS|EPA PFAS chemicals without explicit structures	2020-08-29	1097	List of PFAS chemicals without explicit structures - polymers and other UVCB chemicals
PFASTRIER	PFAS Community-Compiled List (Trier et al., 2015)	2017-07-16	597	PFASTRIER community-compiled public listing of PFAS (Trier et al, 2015)
EPAPFASINV	PFAS|EPA: ToxCast Chemical Inventory	2018-06-29	430	PFAS chemicals included in EPA's expanded ToxCast chemical inventory and available for testing.
PFASNORDIC	PFAS: Nordic PFAS Report 2019	2020-01-31	386	List of PFAS cited in the Nordic Working Paper on Per- and polyfluoroalkylether substances:identity, production and use (2020)
EPAPFASRL	PFAS|EPA: Cross-Agency Research List	2017-11-16	199	EPAPFASRL is a manually curated listing of mainly straight-chain and branched PFAS (Per- & Poly-fluorinated alkyl substances) compiled from various internal, literature and public sources by EPA researchers and program office representatives.

<< < 1 2 3 > >>

Showing 1 to 10 of 28 records

Chemical Lists

- Assembled chemical lists give access to curated data
  - Names and synonyms
  - Physicochemical/Fate and Transport data
  - Toxicity data
  - Relationships in the data
  - Regulatory lists

The OECD List of PFAS

http://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/

The OECD releases a new list of PFASs

The OECD releases a new list of Per- and Polyfluoroalkyl Substances (PFASs) based on a comprehensive analysis of information available in the public domain. In total, 4730 PFAS-related CAS numbers have been identified and categorised in this study, including several new groups of PFASs that fulfil the common definition of PFASs (i.e. they contain at least one perfluoroalkyl moiety) but have not yet been commonly regarded as PFASs.

This work has been conducted under the OECD/UN Environment Global PFC Group in support of the Strategic Approach to International Chemicals Management (SAICM) and shifting to safer alternatives for PFASs.

The New Comprehensive Global Database of Per- and Polyfluoroalkyl Substances (PFASs) comes with a methodology report also detailing the major findings with respect to the total numbers and types of PFASs identified, the limitations, gaps and challenges identified in the development of the new list, and opportunities for improving the future understanding of PFASs production, use on the global market, and presence in the environment, biota, and other matrices.

The OECD List of PFAS

http://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/

EPA United States Environmental Protection Agency

PFAS: Listed in OECD Global Database

Search PFASOECD Chemicals

Identifier substring search

List Details

Description: OECD released a New Comprehensive Global Database of Per- and Polyfluoroalkyl Substances (PFASs) listing more than 4700 new PFAS, including several new groups of PFASs that fulfill the common definition of PFASs (i.e. they contain at least one perfluoroalkyl moiety) but have not yet been commonly regarded as PFASs. The list can be used in conjunction with the methodology report summarising the major findings with respect to the total numbers and types of PFASs identified, the limitations, gaps and challenges identified, and opportunities for improving the future understanding of PFASs production, use on the global market, and presence in the environment, biota, and other matrices.

Source website: http://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals

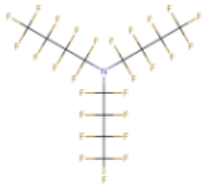
A major effort was undertaken to register this list within DSSTox, adding chemical structures for as many PFAS entries as possible using both manual and auto-mapping (structures using CAS-matching) curation methods. The result is that approximately 1/3 of the list is curated at the highest two curation levels (DSSTox_High or DSSTox_Low) currently, whereas more than half of this list is registered at the Public_Low curation level (based on PubChem content).The PFASOECD list is undergoing continuous registration and curation.

Number of Chemicals: 4729

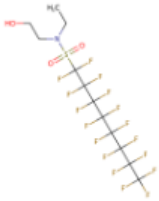
4729 chemicals

Select all | Download | Send to Batch Search | Default | DTXSID | PubChem | CPDAT | Hide chemicals that are: | Filter by Name or CASRN

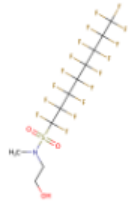
Perfluorooctanesulfonyl fluoride
DTXSID: DTXSID5027140
PubChem: 71
CPDAT: 6



Perfluorotributylamine
DTXSID: DTXSID0027141
PubChem: 71
CPDAT: 0



N-Ethyl-N-(2-hydroxyethyl)perfluorooct...
DTXSID: DTXSID6027426
PubChem: 54
CPDAT: 3



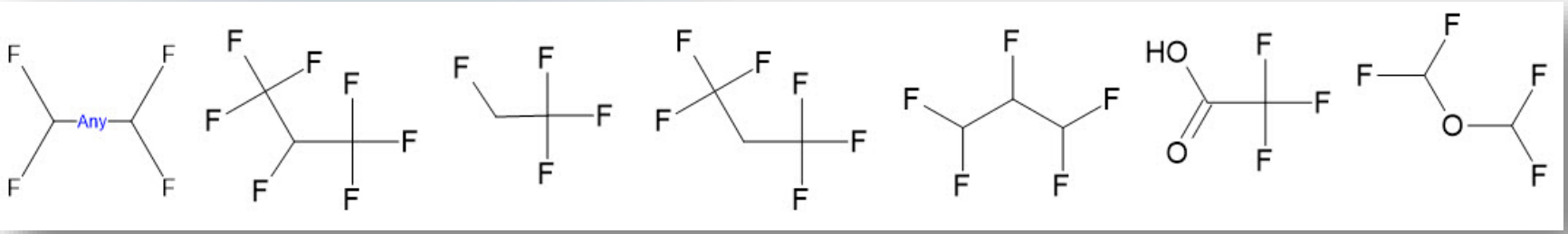
N-Methyl-N-(2-hydroxyethyl)perfluoroo...
DTXSID: DTXSID7027831
PubChem: 24
CPDAT: 16

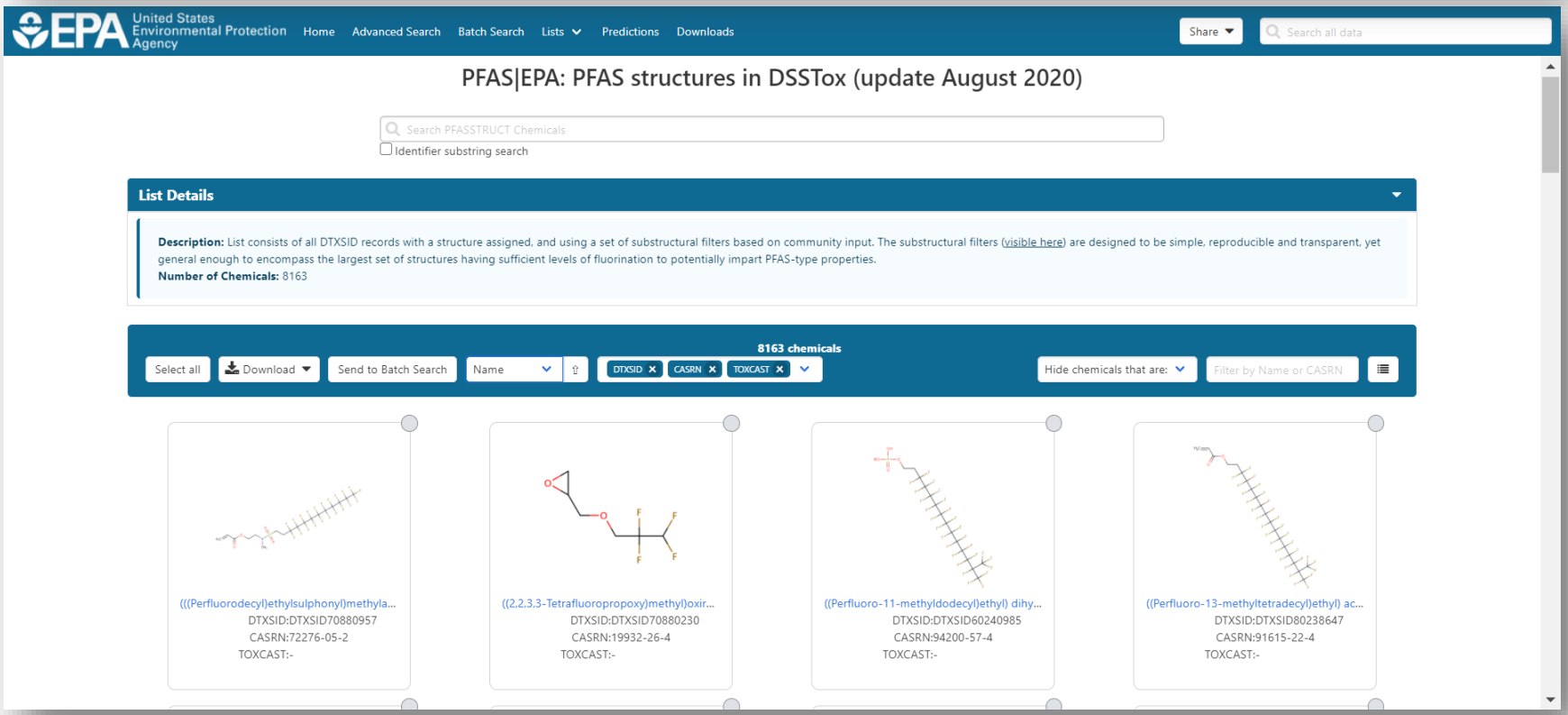
0 related chemical structures with this

Building a “Master PFAS List”

- What is a PFAS? Different definitions from different groups and publications.
- Difficult to get to a consistent definition
- We have taken an iterative approach
  - Substances with specific substructural elements as chemical “structures”

PFAS Structure List (8163)





Building a “Master PFAS List”

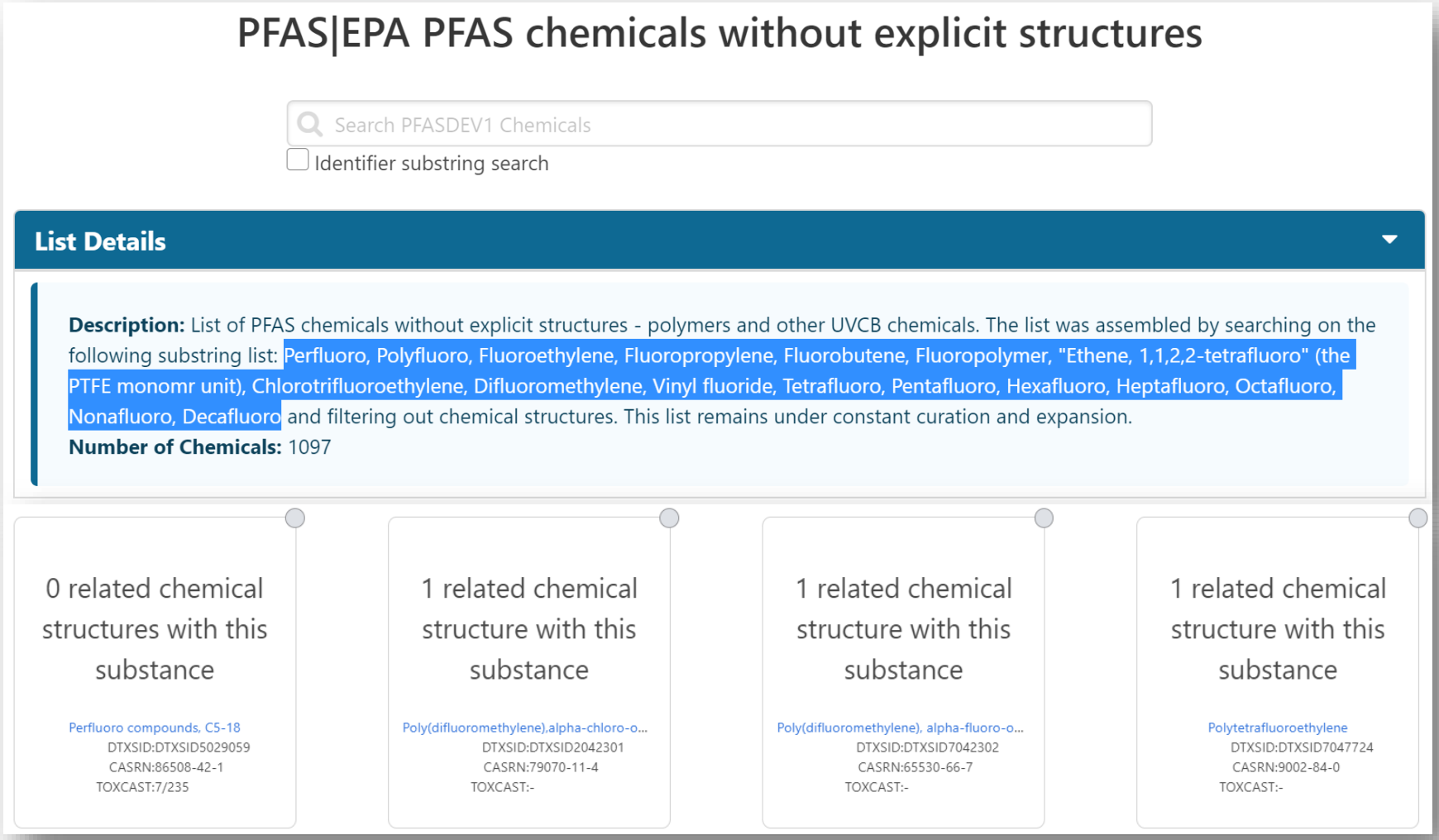
- What is a PFAS? Different definitions from different groups and publications.
- Difficult to get to a consistent definition
- We have taken an iterative approach
  - Substances with specific substructural elements as chemical “structures”
  - Substances with specific “substrings” to represent PFAS elements in UVCB chemicals

UVCB Chemicals

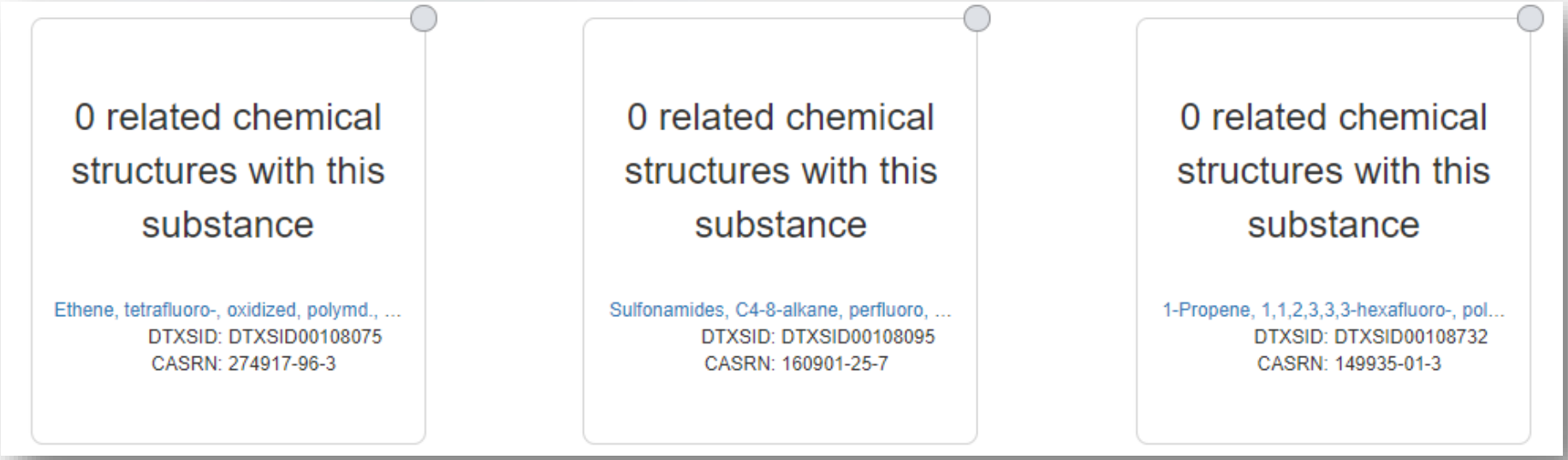
Chemical Substances of Unknown or Variable Composition, Complex Reaction Products and Biological Materials (UVCB Substance) on the TSCA Inventory

This paper is a compendium of information related to the broad class of chemical substances referred to as UVCBs for the Toxic Substances Control Act (TSCA) Chemical Substance Inventory. These chemical substances cannot be represented by unique structures and molecular formulas.

PFAS “UVCB Chemicals”



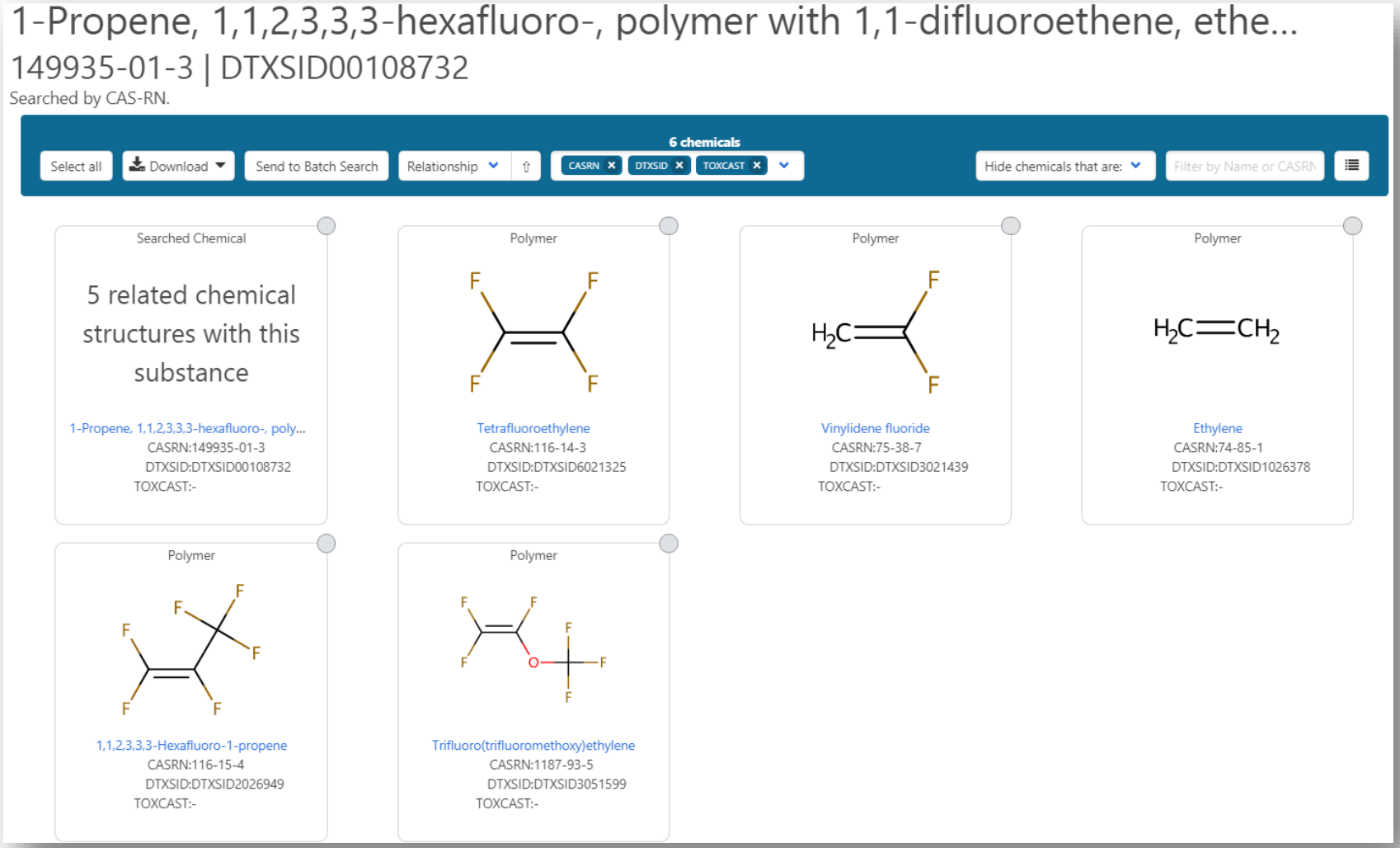
Example PFAS-UVCBs



Ethene, tetrafluoro-, oxidized, polymd., reduced, decarboxylated, C6 fraction
274917-96-3 | DTXSID00108075

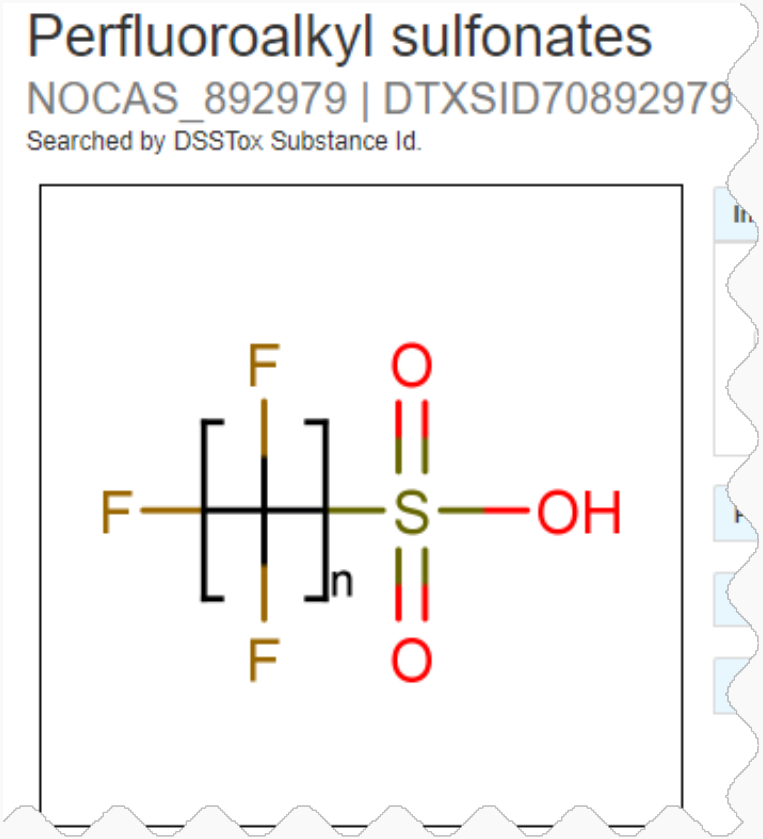
1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethene, ethene, 1,1,2,2-tetrafluoroethene and 1,1,2-trifluoro-2-(trifluoromethoxy)ethene
149935-01-3 | DTXSID00108732

1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethene, ethene, 1,1,2,2-tetrafluoroethene and 1,1,2-trifluoro-2-(trifluoromethoxy)ethene



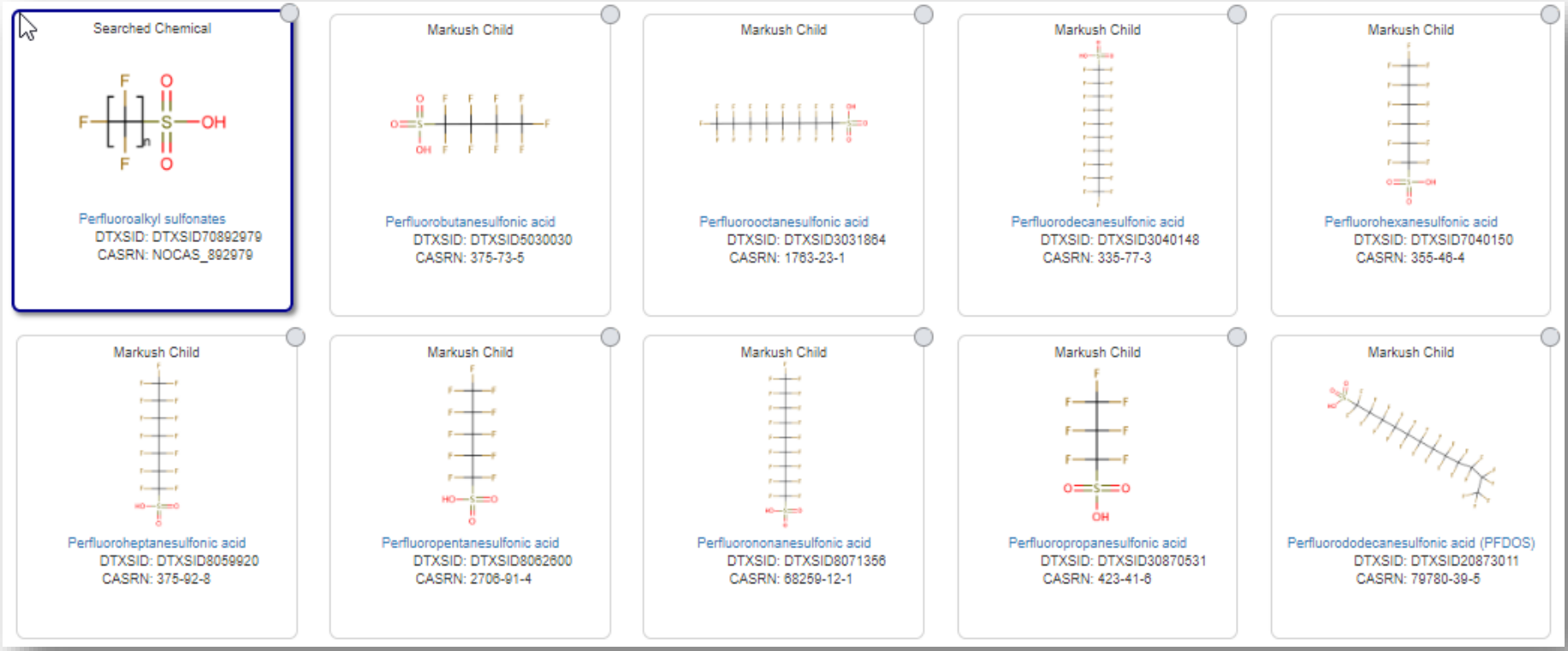
“Markush” Chemical Categories

- PFOS is a linear perfluoroalkyl sulfonate

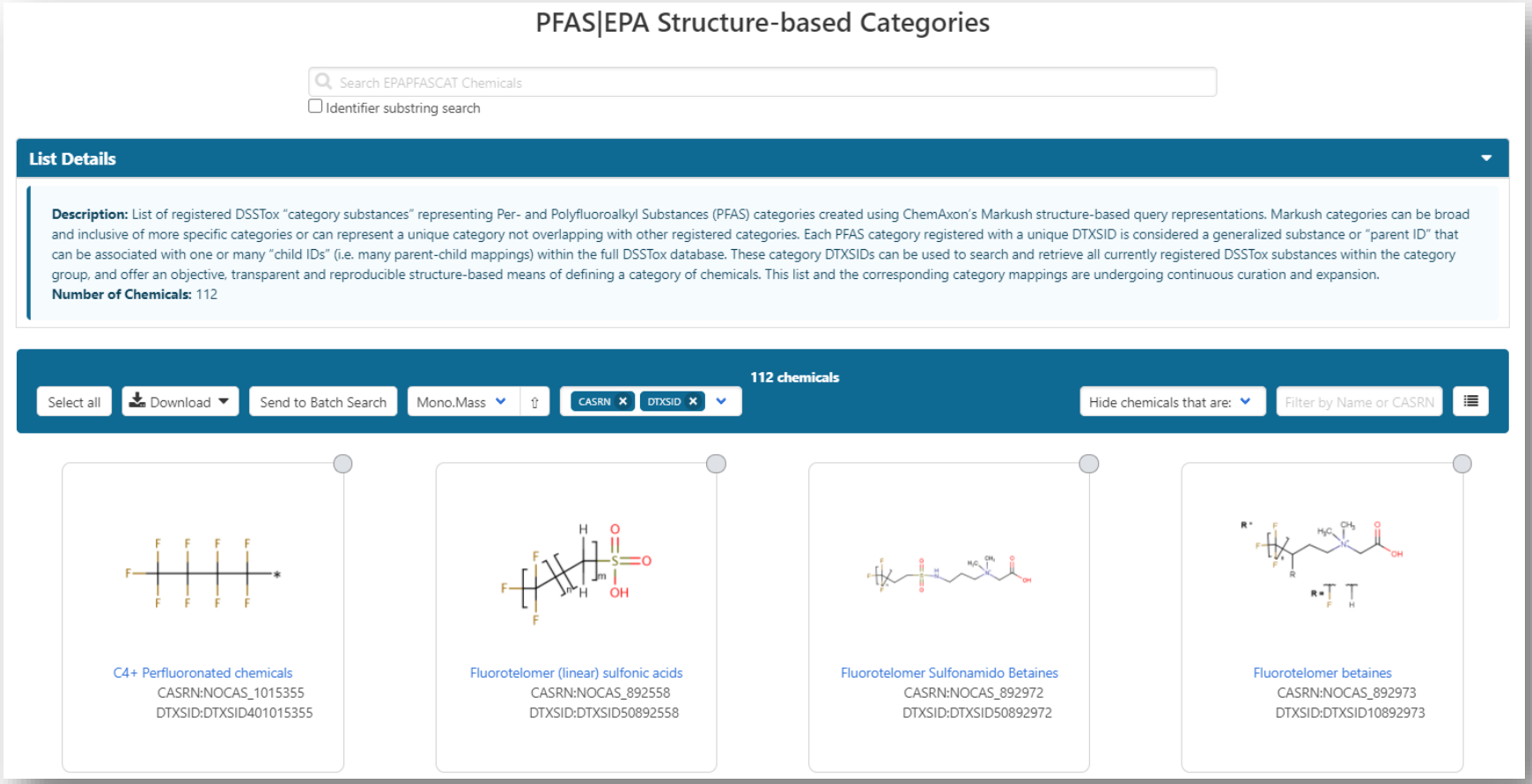


…and their Markush Children…

- Linear perfluoroalkyl sulfonates has children…



PFAS Categories in Development



PFAS Categories in Development (112 categories so far…)

Vol. 127, No. 1 | Brief Communication

A Chemical Category-Based Prioritization Approach for Selecting 75 Per- and Polyfluoroalkyl Substances (PFAS) for Tiered Toxicity and Toxicokinetic Testing

Grace Patlewicz, Ann M. Richard, Antony J. Williams, Christopher M. Grulke, Reeder Sams, Jason Lambert, Pamela D. Noyes, Michael J. DeVito, Ronald N. Hines, Mark Strynar, Annette Guiseppi-Elie, and Russell S. Thomas

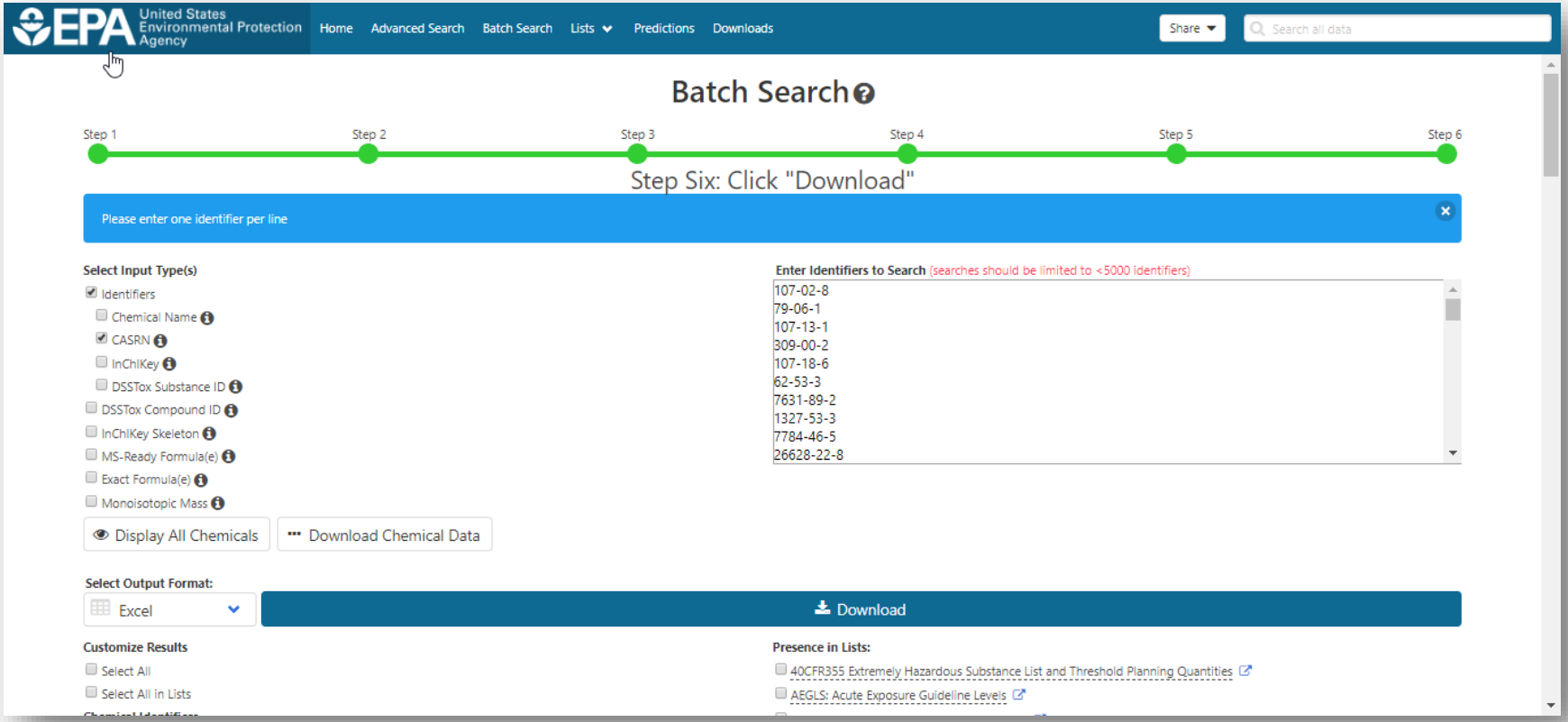
Published: 11 January 2019 | CID: 014501 | https://doi.org/10.1289/EHP4555 | **Cited by:** 17

BATCH SEARCHING

Batch Search

- Search ***thousands*** of chemicals based on CASRN, names and identifiers
- Harvest *en masse* the data available for single chemicals – properties, tox data, chemical relationships, category mappings, presence in lists

Batch Searches



SUPPORTING MASS SPECTROMETRY

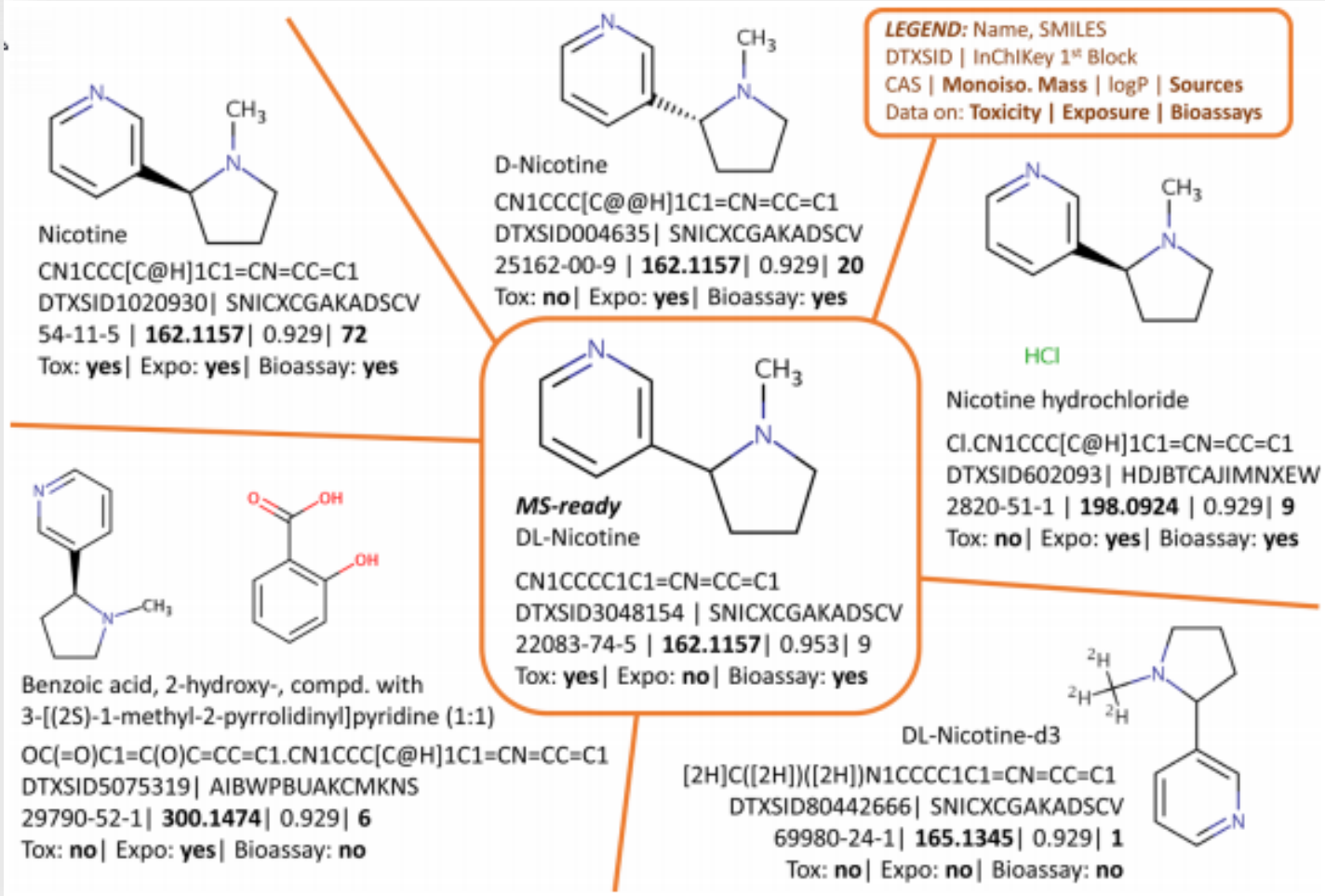
Environmental Science & Technology

Viewpoint

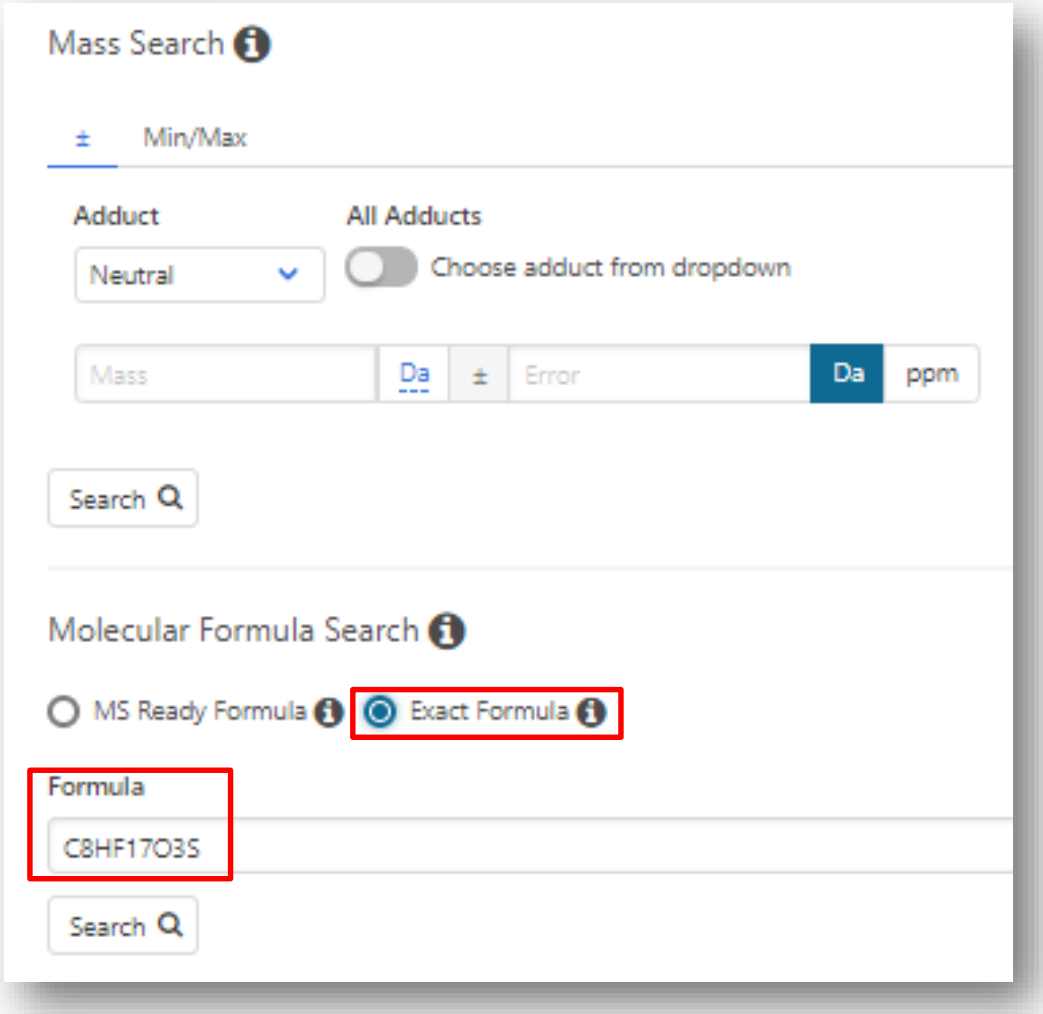
pubs.acs.org/est

Open Science for Identifying "Known Unknown" Chemicals

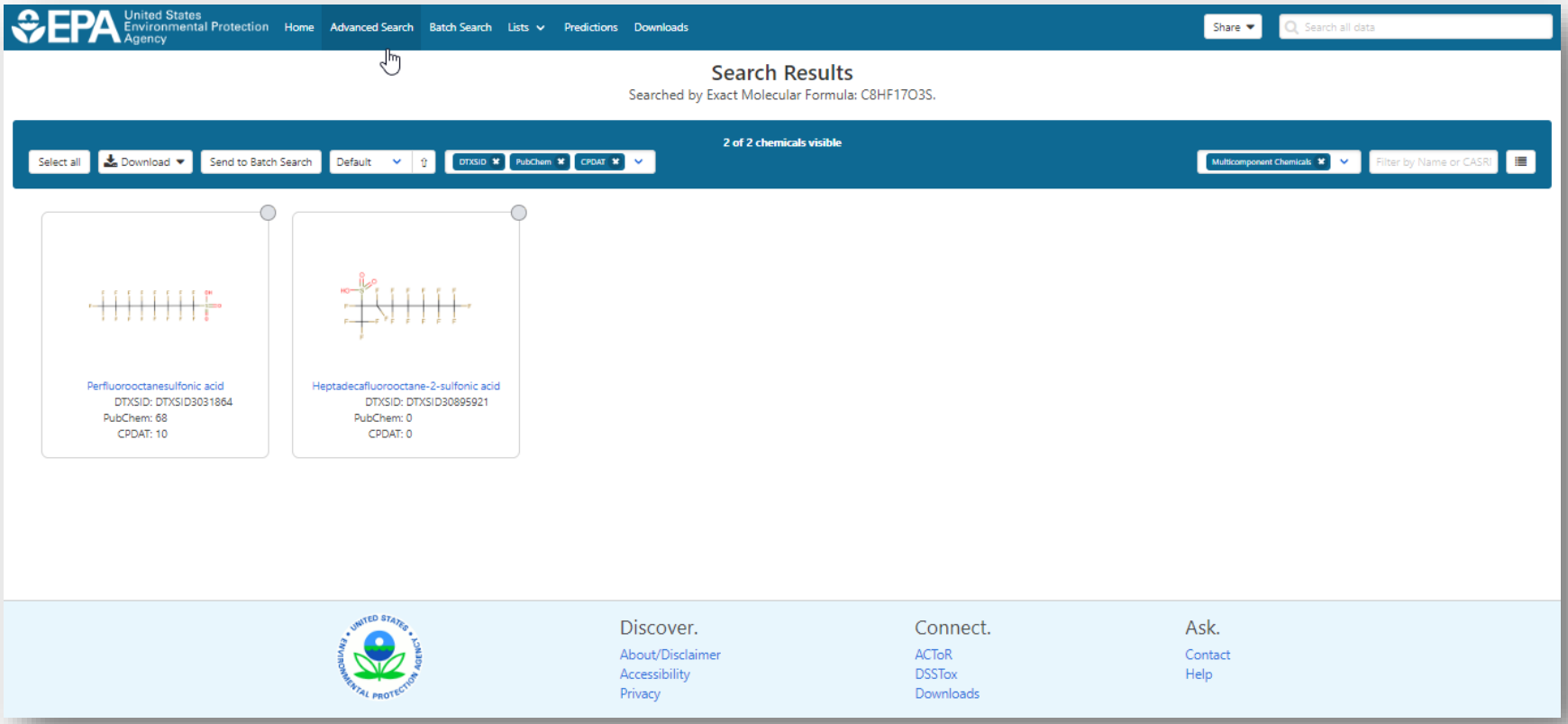
Emma L. Schymanski*,† and Antony J. Williams*,‡



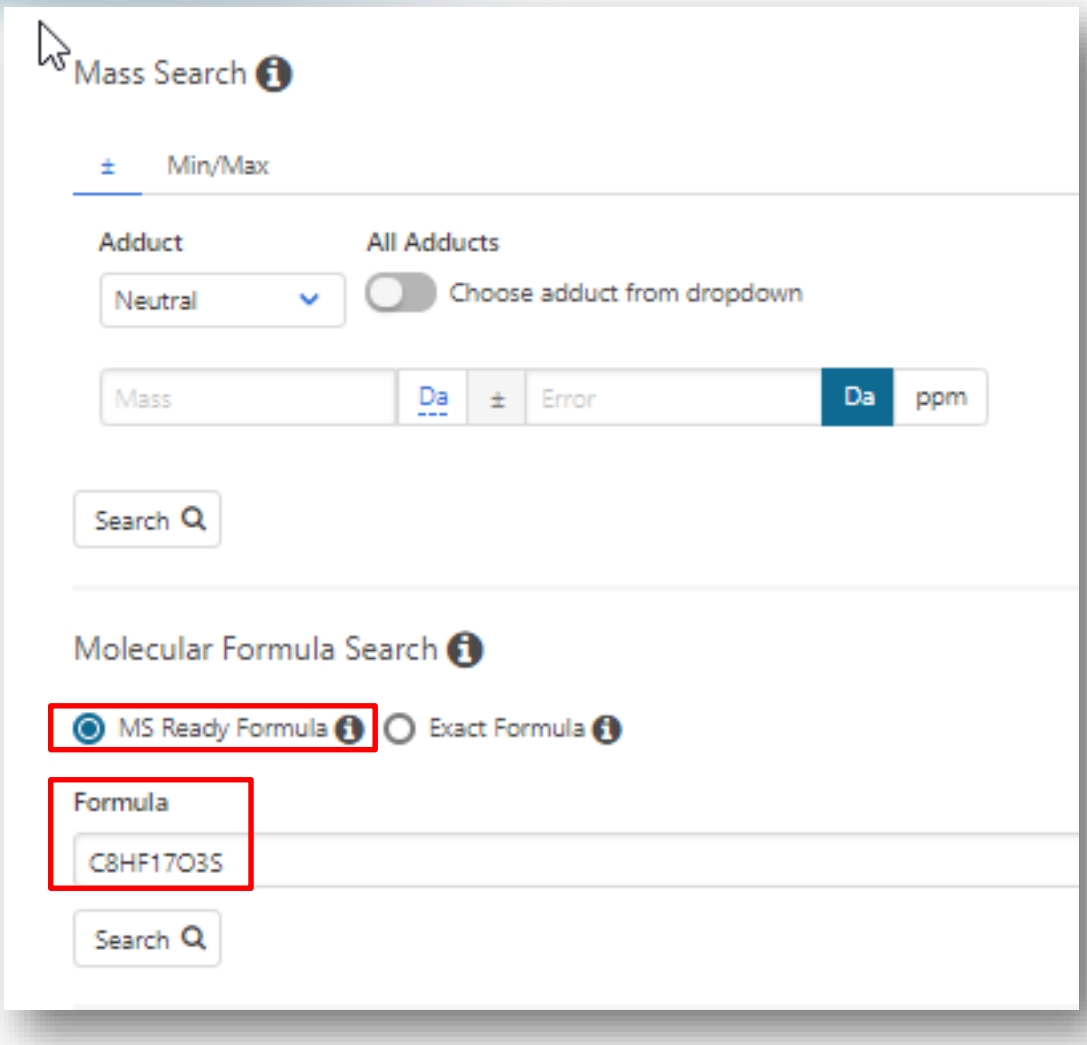
Advanced Search
Supporting Target/Non-Target MS



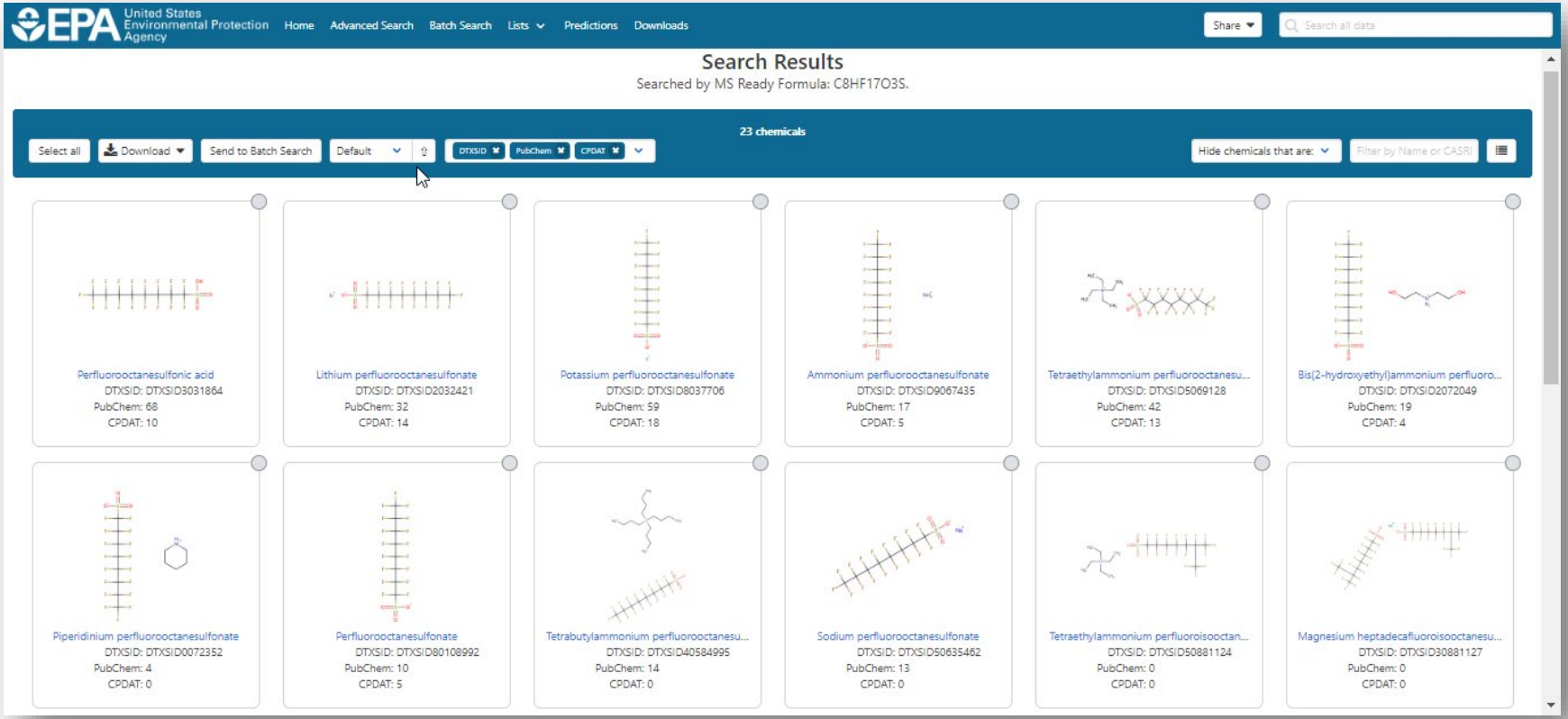
2 Chemicals match the formula



Advanced Search
Supporting Target/Non-Target MS



23 Chemicals match the formula



Supporting future work

Four Chemical Trends Will Shape the Next Decade's Directions in Perfluoroalkyl and Polyfluoroalkyl Substances Research

Matthias Kotthoff and Mark Bücking*

Department Environmental and Food Analysis, Fraunhofer Institute for Molecular Biology and Applied Ecology, Schmallenberg, Germany

- 1. Mobility: A wide and dynamic distribution of short chain PFAS due to their high polarity, persistency and volatility. (**QSAR Predictions**)
- 2. Substitution of regulated substances: The ban or restrictions of individual molecules will lead to a replacement with substitutes of similar concern. (**Database content and Markush Enumeration**)
- 3. Increase in structural diversity of existing PFAS molecules: Introduction of e.g., hydrogens and chlorine atoms instead of fluorine, as well as branching and cross-linking lead to a high versatility of unknown target molecules. (**Database content**)
- 4. Unknown "Dark Matter": The amount, identity, formation pathways, and transformation dynamics of polymers and PFAS precursors are largely unknown. (**Working with agency analytical scientists and collaborators to link and host data**)

Front Chem. 2018; 6: 103.

Conclusions

- CompTox Chemicals Dashboard supports PFAS research at EPA in numerous ways
  - Delivery of curated lists of PFAS chemicals (growing)
  - Flexible search capabilities – support for Mass Spec
  - Relationships in the data enrich navigation between chemicals

- Ongoing research efforts for PFAS chemicals
  - Continue harvesting physicochemical & fate and transport data
  - Classification approaches and Markush representations
  - Expand available toxicity data and integration to systematic review data as it becomes available

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- *An enormous team of contributors from CCTE, especially the IT software development team*
- *Our curation team for their care and focus on data quality*

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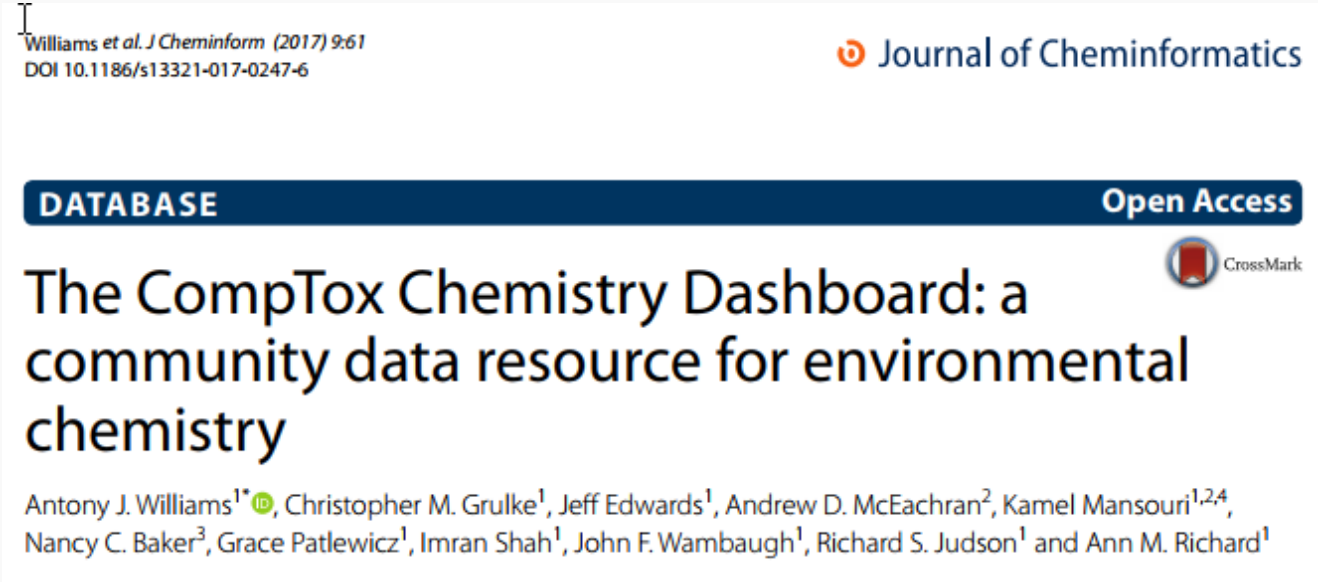

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Journal of Cheminformatics

DATABASE Open Access

The CompTox Chemistry Dashboard: a community data resource for environmental chemistry

Antony J. Williams[1*], Christopher M. Grulke[1], Jeff Edwards[1], Andrew D. McEachran[2], Kamel Mansouri[1,2,4], Nancy C. Baker[3], Grace Patlewicz[1], Imran Shah[1], John F. Wambaugh[1], Richard S. Judson[1] and Ann M. Richard[1]

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