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Accessing information for Per- & Polyfluoroalkyl Substances using the US EPA CompTox Chemistry Dashboard

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3) *NERL*
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5) *University of Luxembourg*

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

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ACS Fall Meeting, Boston

Abstract

- EPA's National Center for Computational Toxicology is developing automated workflows for curating large databases within the DSSTox project, and providing accurate linkages of data to chemical structures, exposure and hazard information. The data are made available via the EPA's CompTox Chemistry Dashboard (https://comptox.epa.gov/dashboard), a publicly accessible website providing access to data for ~760,000 chemical substances, the majority of these represented as chemical structures. The web application delivers a wide array of computed and measured physicochemical properties, *in vitro* high-throughput screening data and *in vivo* toxicity data, as well as integrated chemical linkages to a growing list of literature, toxicology, and analytical chemistry websites. In addition, several specific search types are in development to directly support the mass spectrometry non-targeted screening community, enabling cohesive workflows to support data generation for the detection and assessment of environmental exposures to chemicals contained within DSSTox. The application provides access to segregated lists of chemicals that are of specific interest to relevant stakeholders, including, for example, scientists interested in Per- & Polyfluoroalkyl Substances (PFAS). Added lists include those sourced from the European Union as well as developed in-house and now containing thousands of chemicals. A procured testing library of hundreds of PFAS chemicals annotated into chemical categories has been integrated into the dashboard with a number of resulting benefits: a searchable database of chemical properties, with hazard and exposure predictions, and links to the open literature. This presentation will provide an overview of the dashboard, the developing library of PFAS chemicals and associated categorization, and new physicochemical property and environmental fate and transport QSAR prediction models developed for these chemicals. The application of the dashboard to support mass spectrometry non-targeted analysis studies for the identification of PFAS chemicals will also be reviewed.

EPA activities around PFAS chemicals

https://www.epa.gov/pfas

EPA United States Environmental Protection Agency

Per- and Polyfluoroalkyl Substances (PFAS)

CONTACT US

SHARE

"The National Leadership Summit on PFAS provided an unprecedented opportunity for stakeholders to share vital information and best practices regarding PFAS." - *Former Administrator Pruitt*

- Community Events
- Infographic

Basic Information

- What are PFAS?
- Why are PFAS important?
- How people are exposed?

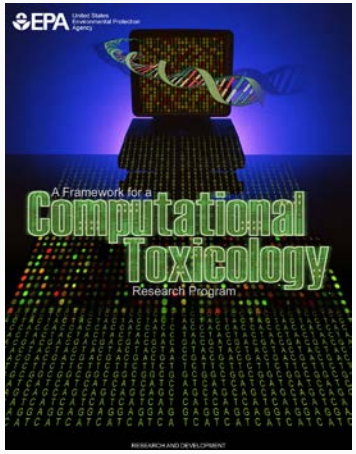
EPA Actions to Address PFAS

- EPA actions
- National leadership summit and engagement

Tools and Resources

- EPA data and tools
- State information
- Site-specific resources

National Center for Computational Toxicology



- National Center for Computational Toxicology established in 2005 to integrate:
  - High-throughput and high-content technologies
  - Modern molecular biology
  - Data mining and statistical modeling
  - Computational biology and chemistry
- Researching computational approaches to quickly evaluate the safety of chemicals for potential risk.
- Outputs: a lot of data, models, algorithms and software applications
- **How can these efforts support research into PFAS chemicals?**

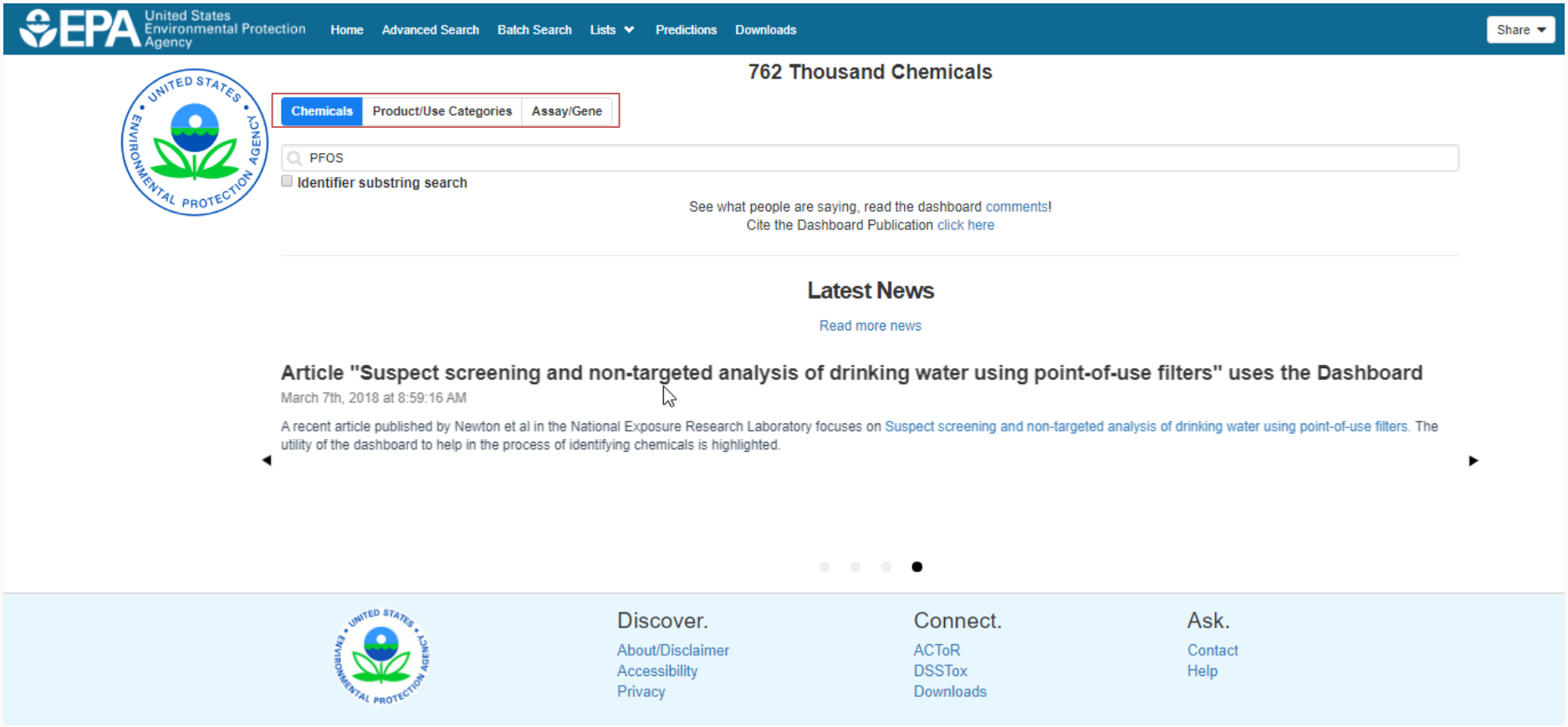
The CompTox Dashboard

- A **publicly accessible website** delivering access:
  - ~762,000 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
  - Real time prediction of physchem and toxicity endpoints

  - **Over 5,000 of the chemicals are classed as PFAS Chemicals**

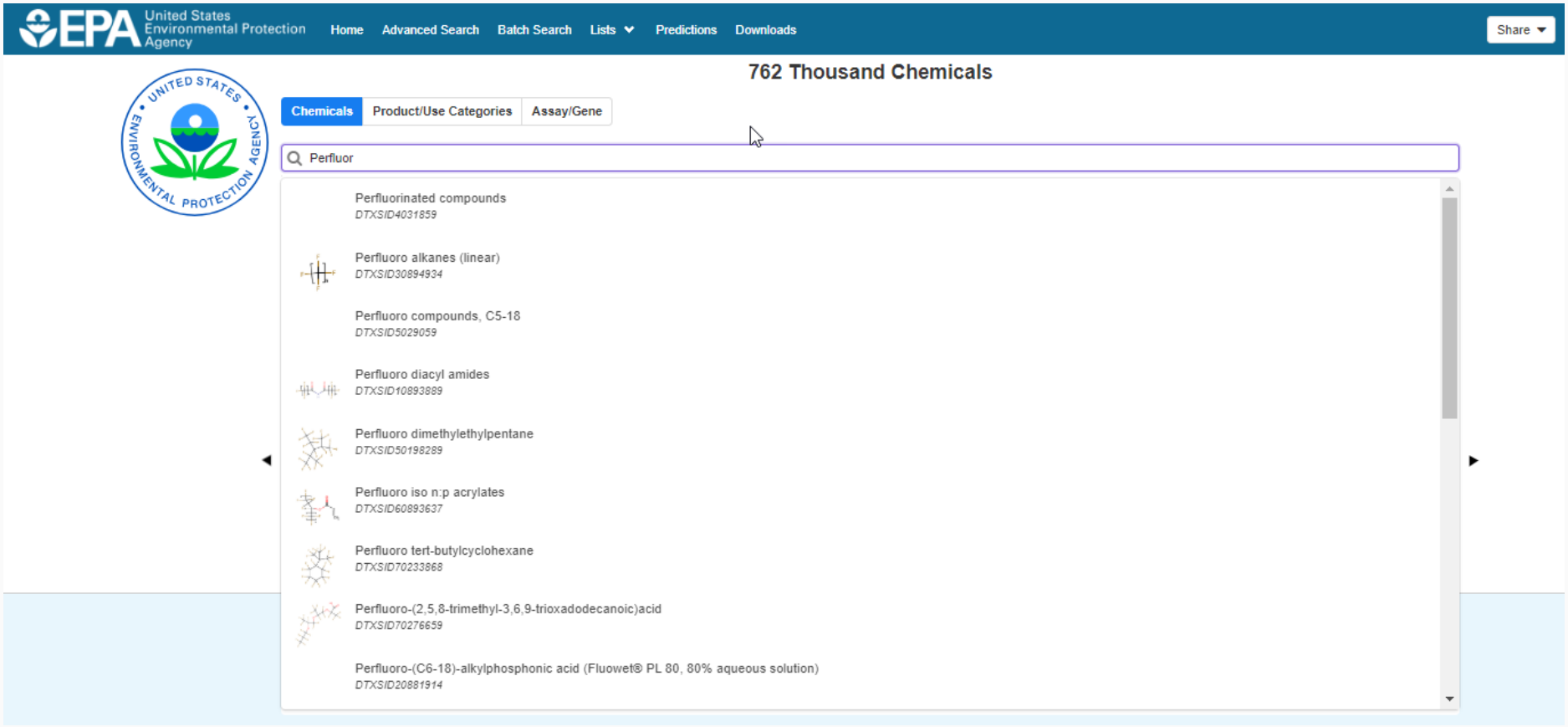
CompTox Dashboard

https://comptox.epa.gov/dashboard



CompTox Dashboard

https://comptox.epa.gov/dashboard



1 of ~762,000 Chemical Pages

EPA United States Environmental Protection Agency

EPA United States Environmental Protection Agency | Home | Advanced Search | Batch Search | Lists | Predictions | Downloads | Copy | Share | Submit Comment | Search all data

PFASEUOECD

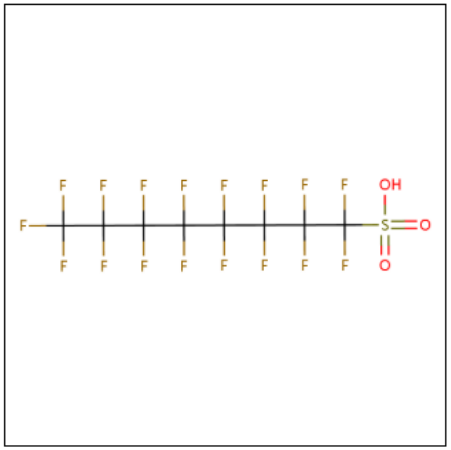
PFAS Listed in OECD Global Database

Perfluorooctanesulfonic acid

1763-23-1 | DTXSID3031864

Searched by DSSTox Substance Id.

- DETAILS
- EXECUTIVE SUMMARY
- PROPERTIES
- ENV. FATE/TRANSPORT
- HAZARD
- ADME
- EXPOSURE
- BIOACTIVITY
- SIMILAR COMPOUNDS
- GENRA (BETA)
- RELATED SUBSTANCES
- SYNONYMS
- LITERATURE
- LINKS
- COMMENTS



Wikipedia

Perfluorooctanesulfonic acid (conjugate base **perfluorooctanesulfonate**) (**PFOS**) is an anthropogenic fluorosurfactant and global pollutant. PFOS was the key ingredient in Scotchgard, a fabric protector made by 3M, and numerous stain repellents. It was added to Annex B of the Stockholm Convention on Persistent Organic Pollutants in May 2009. PFOS can be synthesized in industrial production or result from the degradation of precursors. PFOS levels that have been detected in wildlife

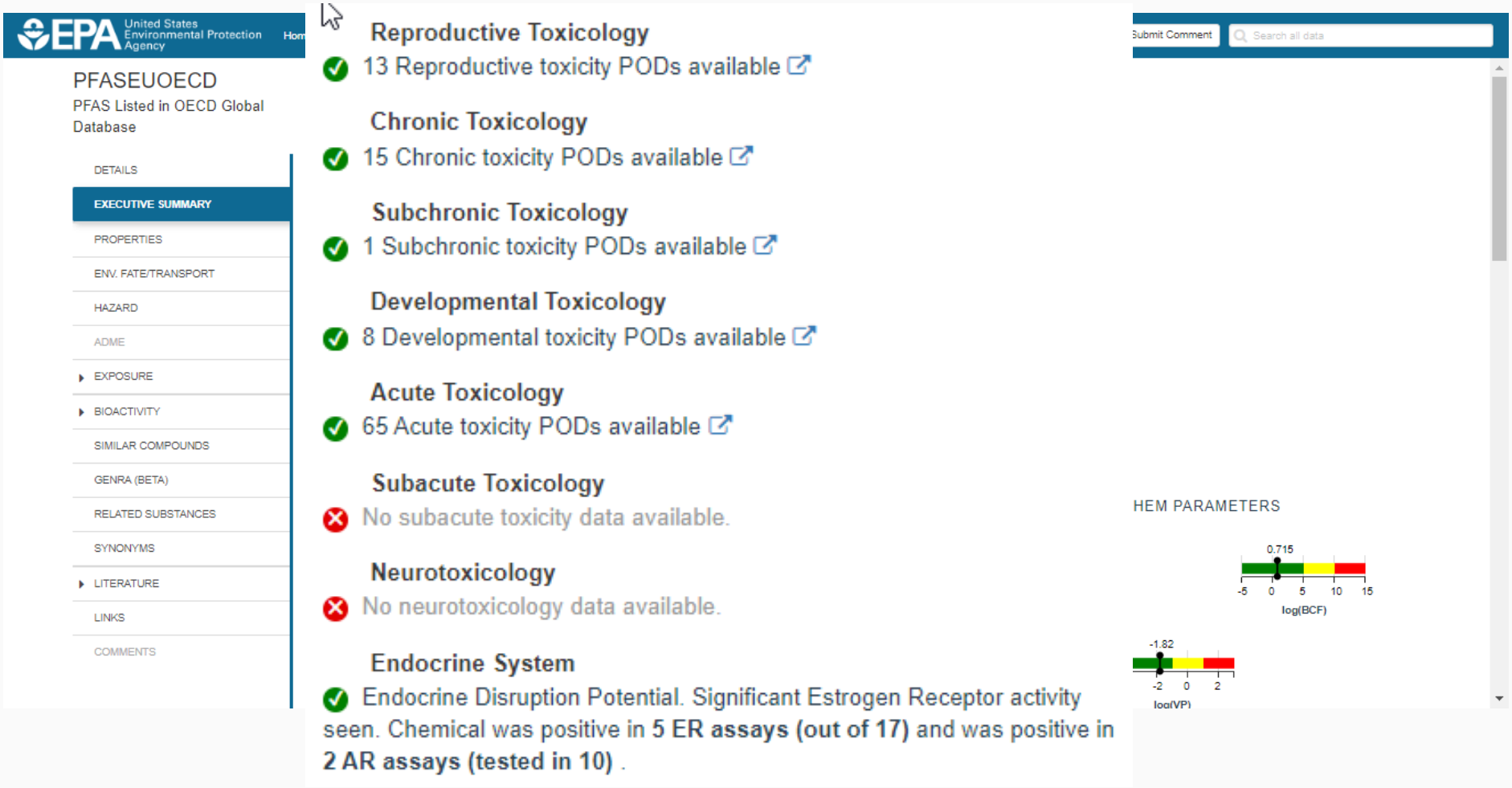
...

Read more

- Intrinsic Properties
- Structural Identifiers
- Linked Substances
- Presence in Lists
- Record Information
- Quality Control Notes

Discover | Connect | Ask

Executive Summary



Physicochemical properties

Property

Summary

- Summary
- LogP: Octanol-Water
- Melting Point
- Boiling Point
- Water Solubility
- Vapor Pressure
- Flash Point
- Surface Tension
- Index of Refraction
- Molar Refractivity
- Polarizability
- Density
- Molar Volume
- Thermal Conductivity
- Viscosity
- Henry's Law
- LogKoa: Octanol-Air

Summary

Search query

verage	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)

OPERA Predicted Properties

EPA United States Environmental Protection Agency

An automated curation procedure for addressing chemical errors and inconsistencies in public datasets used in QSAR modelling

K. Mansouri, C. M. Grulke, A. M. Richard, R. S. Judson & A. J. Williams

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An automate
datasets use
DOI: 10.108(

To link to th

Mansouri *et al. J Cheminform (2018) 10:10*
https://doi.org/10.1186/s13321-018-0263-1

Journal of Cheminformatics

RESEARCH ARTICLE Open Access

CrossMark

OPERA models for predicting physicochemical properties and environmental fate endpoints

Kamel Mansouri[1,2,3*], Chris M. Grulke[1], Richard S. Judson[1] and Antony J. Williams[1]

Detailed OPERA Prediction Reports

EPA United States Environmental Protection Agency

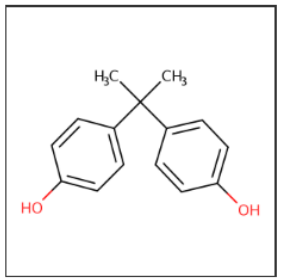
Source	Result	Calculation Details
Experimental Values		
PhysPropNCCT		
Predicted Values		
EPISUITE		
NICEATM		
ACD/Labs Conse		
ACD/Labs		
OPERA		

OPERA Models: LogP: Octanol-Water

Save PDF

Bisphenol A

80-05-7 | DTXSID7020182



Model Results

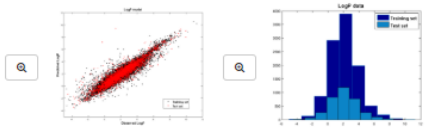
Predicted value: 3.35

Global applicability domain: Inside

Local applicability domain index: 0.88

Confidence level: 0.75

Model Performance

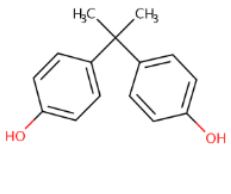


Weighted KNN model

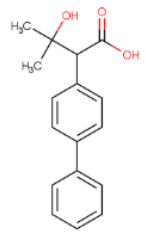
QMRF

5-fold CV (75%)		Training (75%)		Test (25%)	
Q2	RMSE	R2	RMSE	R2	RMSE
0.85	0.69	0.86	0.67	0.86	0.78

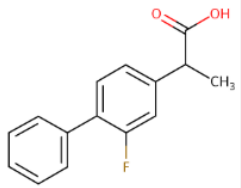
Nearest Neighbors from the Training Set



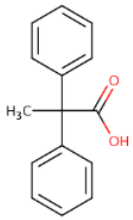
Bisphenol A
Measured: 3.32
Predicted: 3.35



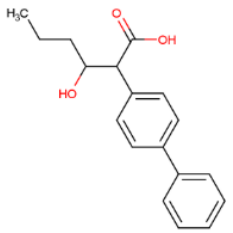
BUTANOIC ACID,2-(4-BIPHENYLYL)-3-HYDROX...
Measured: 3.25
Predicted: 3.45



Flurbiprofen
Measured: 4.16
Predicted: 3.83

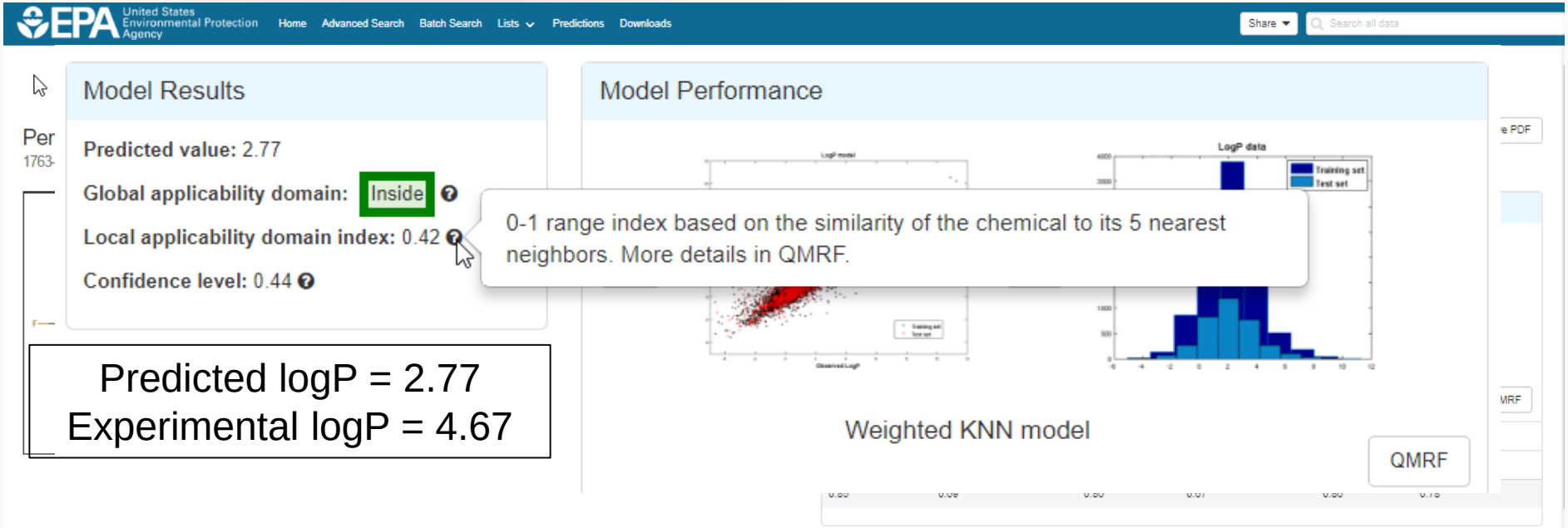


2,2-Diphenylpropionic acid
Measured: 2.69
Predicted: 2.93

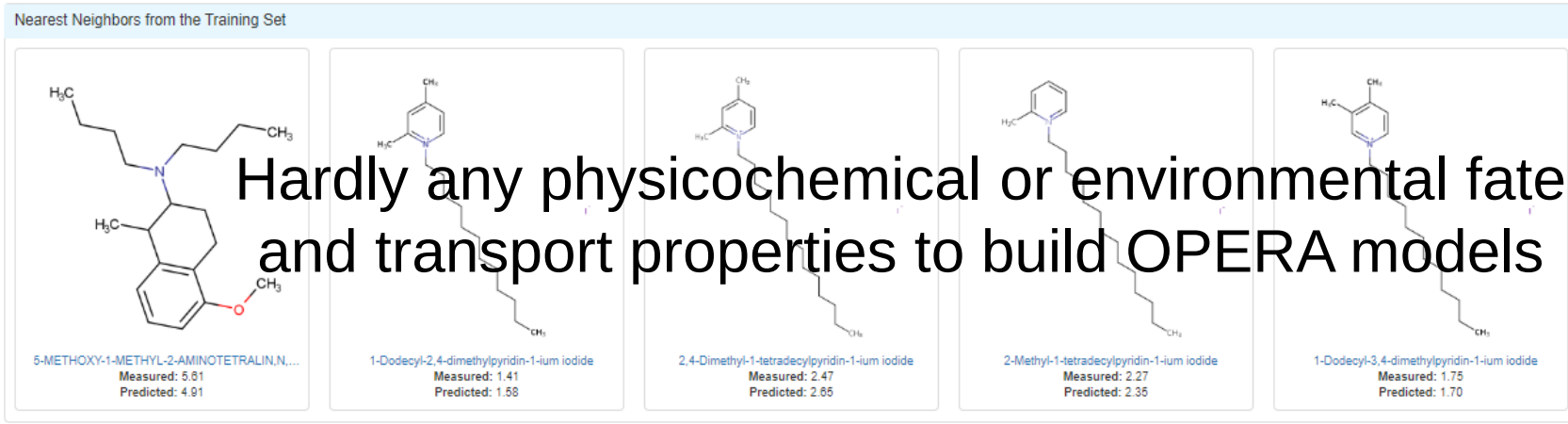


3-OH-2-(4-BIPHENYLYL)HEXANOIC ACID
Measured: 3.75
Predicted: 3.68

Not much data for PFAS - yet



Predicted logP = 2.77
Experimental logP = 4.67

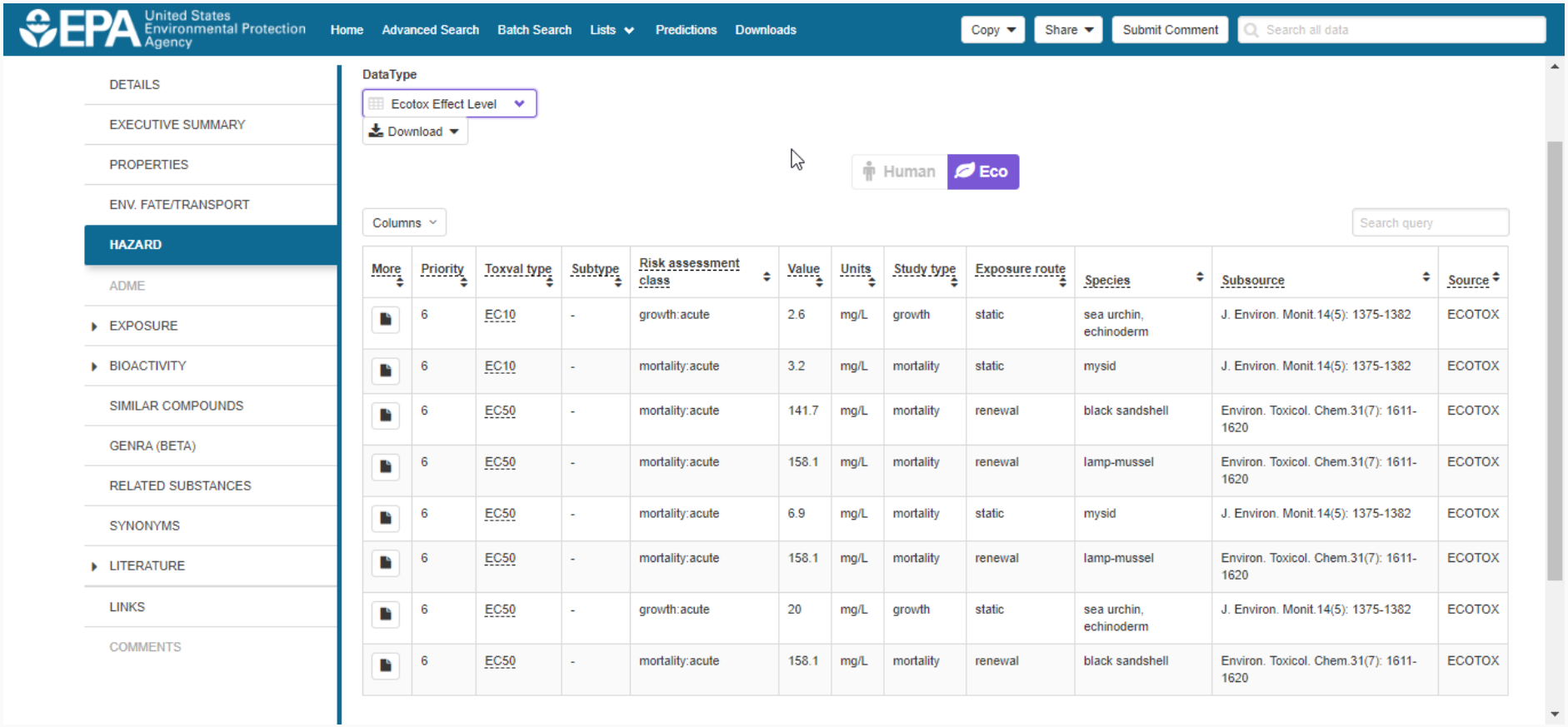


Hardly any physicochemical or environmental fate and transport properties to build OPERA models

Literature Data Extraction

- Physicochemical property and environmental fate and transport data has been extracted from the literature
- OPERA models will be rebuilt with these data for new predictions
- Data and predictions available Spring 2019

Hazard Data – Human and Eco

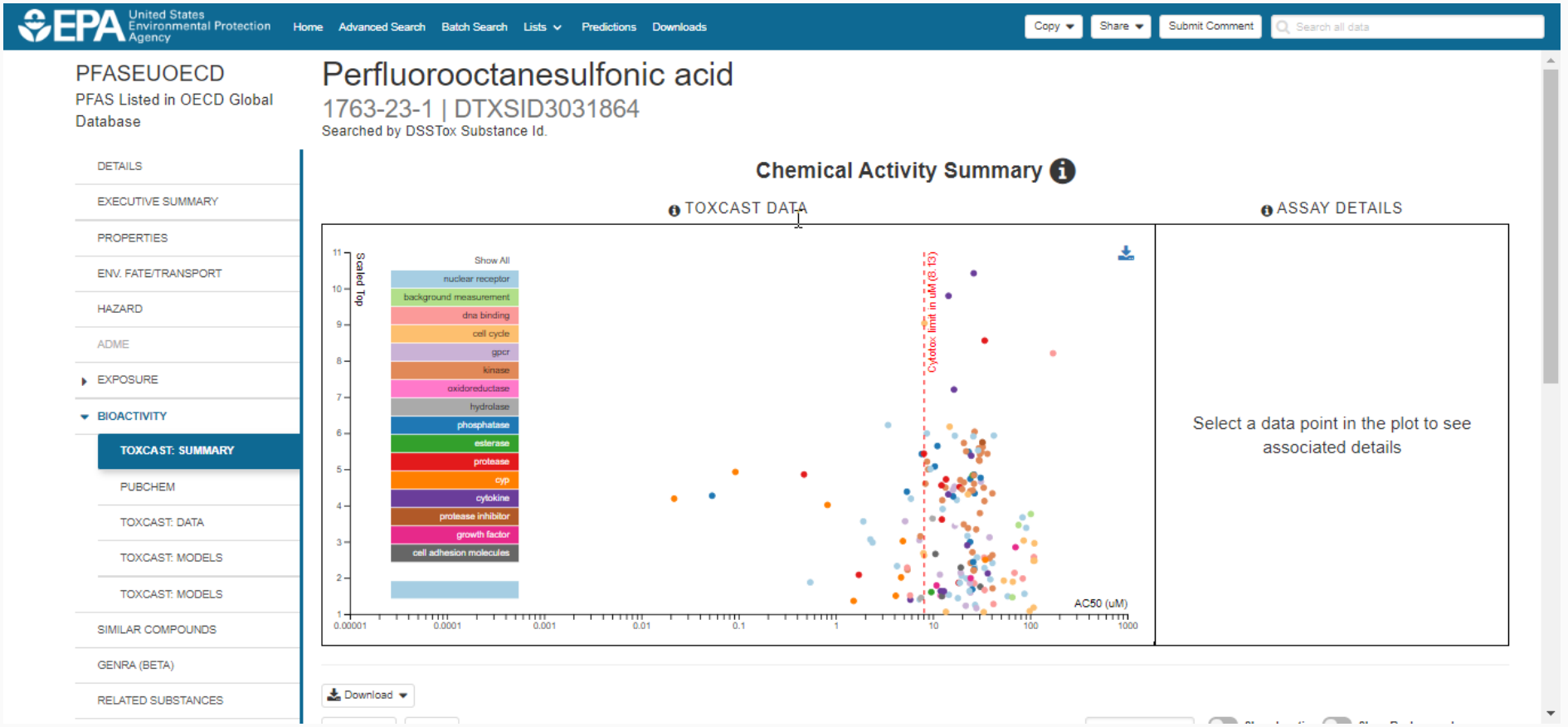


More	Priority	Toxval type	Subtype	Risk assessment class	Value	Units	Study type	Exposure route	Species	Subsource	Source
	6	EC10	-	growth:acute	2.6	mg/L	growth	static	sea urchin, echinoderm	J. Environ. Monit.14(5): 1375-1382	ECOTOX
	6	EC10	-	mortality:acute	3.2	mg/L	mortality	static	mysid	J. Environ. Monit.14(5): 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

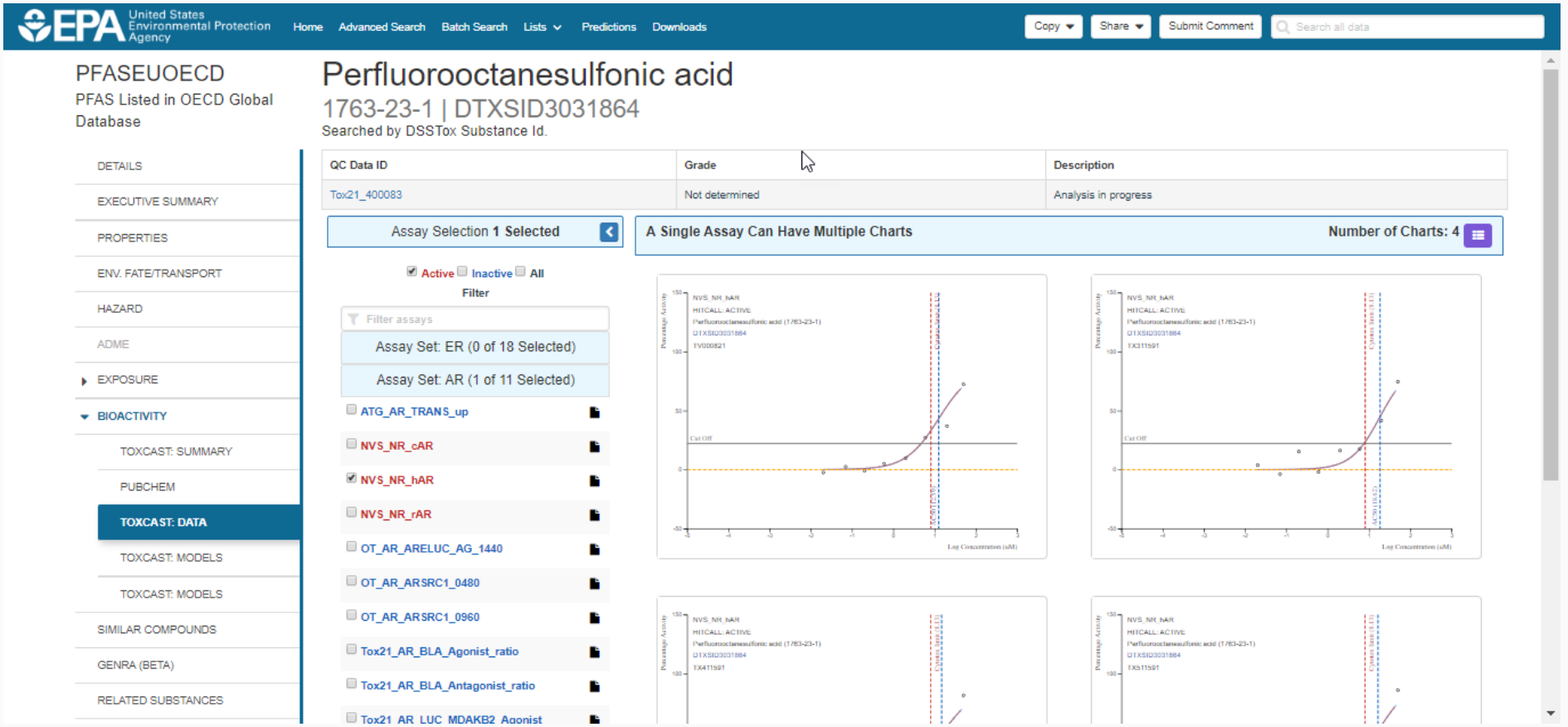
Hazard Data from “ToxVal_DB”

- ToxVal Database contains following data:
  - 30,050 chemicals
  - 772,721 toxicity values
  - 29 sources of data
  - 21,507 sub-sources
  - 4585 journals cited
  - 69,833 literature citations

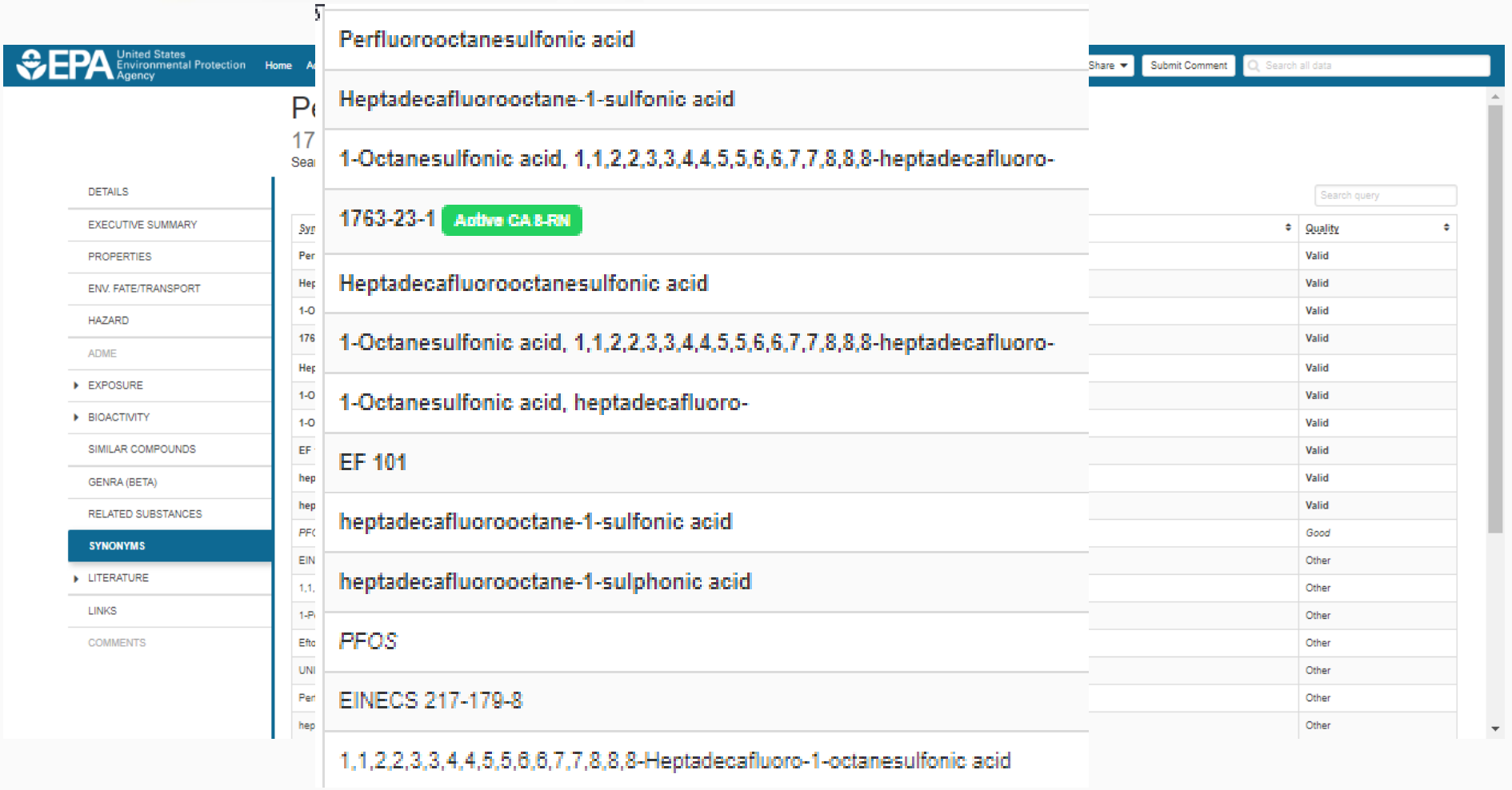
Bioactivity Data



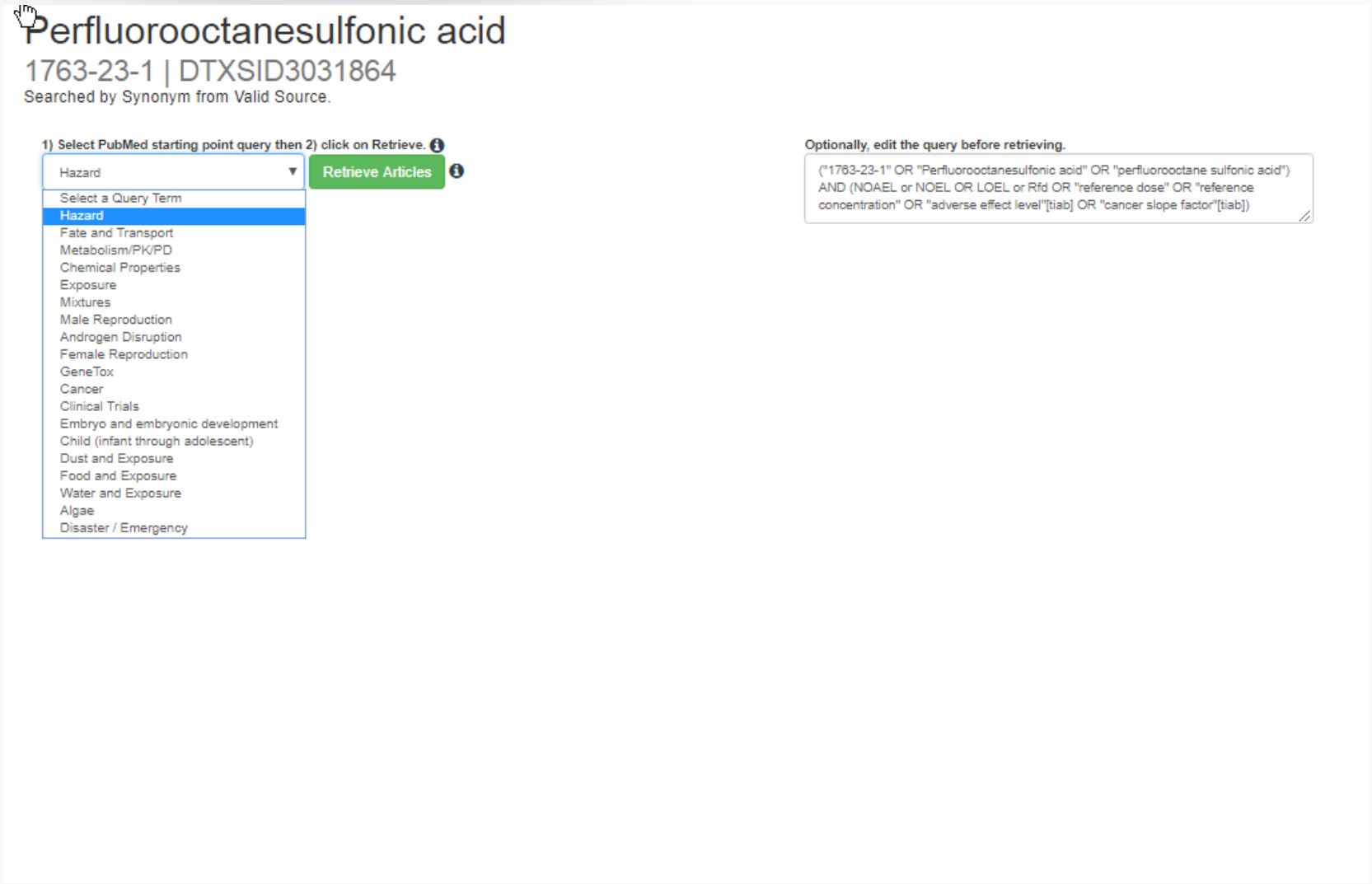
Boactivity Data



What is PFOS Called?



Literature Searching - PubMed



Literature Searching - PubMed

Perfluorooctanesulfonic acid

1763-23-1 | DTXSID3031864

Searched by Synonym from Valid Source.

1) Select PubMed starting point query then 2) click on Retrieve.

Hazard | Retrieve Articles

23 of 23 articles loaded...

Optionally, edit the query before retrieving.

("1763-23-1" OR "Perfluorooctanesulfonic acid" OR "perfluorooctane sulfonic acid") AND (NOAEL or NOEL OR LOEL or Rfd OR "reference dose" OR "reference concentration" OR "adverse effect level"[tiab] OR "cancer slope factor"[tiab])

To find articles quickly, enter terms to sift abstracts.

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PMID	Year	Title	Authors	Journal	Rev
29525662	2018	Modeling avian exposures to perfluoroalkyl substances in aquatic habitats...	Larson; Conder; Arblaster	Chemosphere	
28521193	2017	Issues raised by the reference doses for perfluorooctane sulfonate and pe...	Dong; Bahar; Jit; Kennedy; Priestly; Ng; Lamb; Liu; ...	Environment international	
24046276	2013	Dosimetric anchoring of in vivo and in vitro studies for perfluorooctanoate ...	Wambaugh; Setzer; Pitruzzello; Liu; Reif; Kleinstreu...	Toxicological sciences : an official journal of the Soc...	
22441698	2012	Perfluorooctane sulfonate increases β-oxidation of palmitic acid in chicke...	Nordén; Westman; Venizelos; Engwall	Environmental science and pollution research intern...	
21467747	2011	Induction of apoptosis and CYP4A1 expression in Sprague-Dawley rats e...	Kim; Jun Kwack; Sik Han; Seok Kang; Hee Kim; Yo...	The Journal of toxicological sciences	
21207445	2011	Aquatic predicted no-effect-concentration derivation for perfluorooctane s...	Qi; Wang; Mu; Wang	Environmental toxicology and chemistry	
20879709	2010	Distribution of perfluorooctane sulfonate and other perfluorochemicals in t...	Wang; Fu; Wang; Liang; Pan; Cai; Jiang	Environmental science & technology	
20709355	2010	Brominated flame retardants and perfluorinated compounds in indoor dust...	D'Hollander; Roosens; Covaci; Cornelis; Reynders; ...	Chemosphere	
19589327	2009	Perfluoroalkyl contaminants in an Arctic marine food web: trophic magnific...	Kelly; Ikonomou; Blair; Surridge; Hoover; Grace; Go...	Environmental science & technology	
19343326	2009	Chronic effects of perfluorooctanesulfonate exposure on immunotoxicity i...	Dong; Zhang; Zheng; Liu; Jin; He	Archives of toxicology	
19162172	2009	Gestational and lactational exposure to potassium perfluorooctanesulfona...	Butenhoff; Ehresman; Chang; Parker; Stump	Reproductive toxicology (Elmsford, N.Y.)	
19110351	2008	Behaviour of damselfly larvae (Enallagma cyathigerum) (Insecta, Odonata...	Van Gossum; Bots; Snijkers; Meyer; Van Wassenbe...	Environmental pollution (Barking, Essex : 1987)	

Literature Searching - PubMed

EPA United States Environmental Protection Agency

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23 of 23 articles loaded...

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("1763-23-1" OR "Perfluorooctanesulfonic acid" OR "perfluorooctane sulfonic acid") AND (NOAEL or NOEL OR LOEL or Rfd OR "reference dose" OR "reference concentration" OR "adverse effect level"[tiab] OR "cancer slope factor"[tiab])

To find articles quickly, enter terms to sift abstracts.

exposure | RfD | immunotox | | Clear Terms

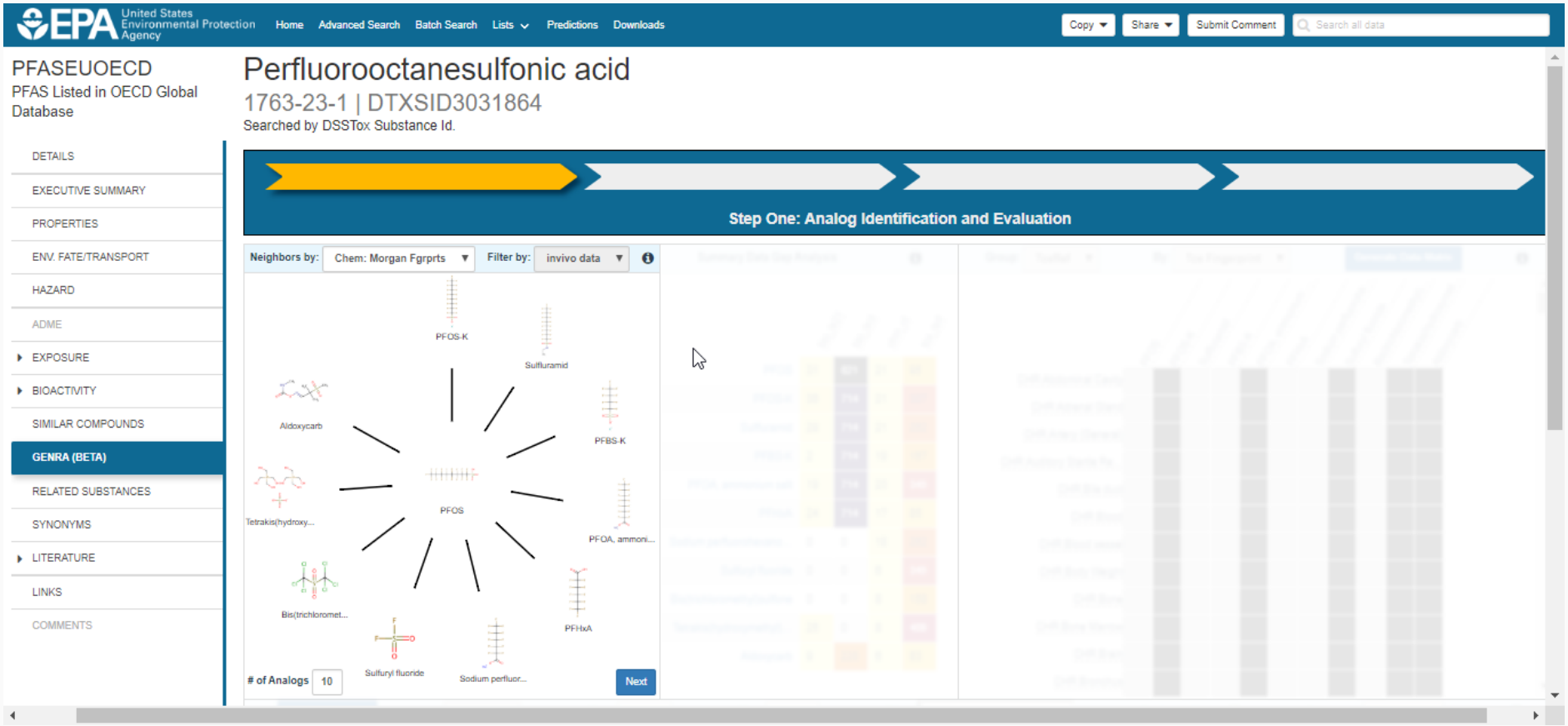
Download / Send to... | Download Sifter for Excel

exposure	RfD	immunotox	Total	PMID	Year	Title	Authors	Journal	Rev
8	0	0	8	29525662	2018	Modeling avian exposures to perfluoroalkyl substan...	Larson; Conder; Arblaster	Chemosphere	
2	5	1	8	28521193	2017	Issues raised by the reference doses for perfluoroo...	Dong; Bahar; Jit; Kennedy; Priestly; Ng; Lamb; Liu; ...	Environment international	
0	0	0	0	24046276	2013	Dosimetric anchoring of in vivo and in vitro studies f...	Wambaugh; Setzer; Pitruzzello; Liu; Reif; Kleinstreu...	Toxicological sciences : an official journal of the Soc...	
0	0	0	0	22441698	2012	Perfluorooctane sulfonate increases β-oxidation of ...	Nordén; Westman; Venizelos; Engwall	Environmental science and pollution research intern...	
0	0	0	0	21467747	2011	Induction of apoptosis and CYP4A1 expression in S...	Kim; Jun Kwack; Sik Han; Seok Kang; Hee Kim; Yo...	The Journal of toxicological sciences	
0	0	0	0	21207445	2011	Aquatic predicted no-effect-concentration derivation...	Qi; Wang; Mu; Wang	Environmental toxicology and chemistry	
0	0	0	0	20879709	2010	Distribution of perfluorooctane sulfonate and other p...	Wang; Fu; Wang; Liang; Pan; Cai; Jiang	Environmental science & technology	
1	0	0	1	20709355	2010	Brominated flame retardants and perfluorinated co...	D'Hollander; Roosens; Covaci; Cornelis; Reynders; ...	Chemosphere	
2	0	0	2	19569327	2009	Perfluoroalkyl contaminants in an Arctic marine food...	Kelly; Ikonomou; Blair; Surridge; Hoover; Grace; Go...	Environmental science & technology	
3	0	1	4	19343326	2009	Chronic effects of perfluorooctanesulfonate exposur...	Dong; Zhang; Zheng; Liu; Jin; He	Archives of toxicology	
3	0	0	3	19162172	2009	Gestational and lactational exposure to potassium p...	Butenhoff; Ehresman; Chang; Parker; Stump	Reproductive toxicology (Elmsford, N.Y.)	
2	0	0	2	19110351	2008	Behaviour of damselfly larvae (Enallagma cyathiger...	Van Gossum; Bots; Snijkers; Meyer; Van Wassenbe...	Environmental pollution (Barking, Essex : 1987)	

Issues raised by the reference doses for perfluorooctane sulfonate and perfluorooctanoic acid.

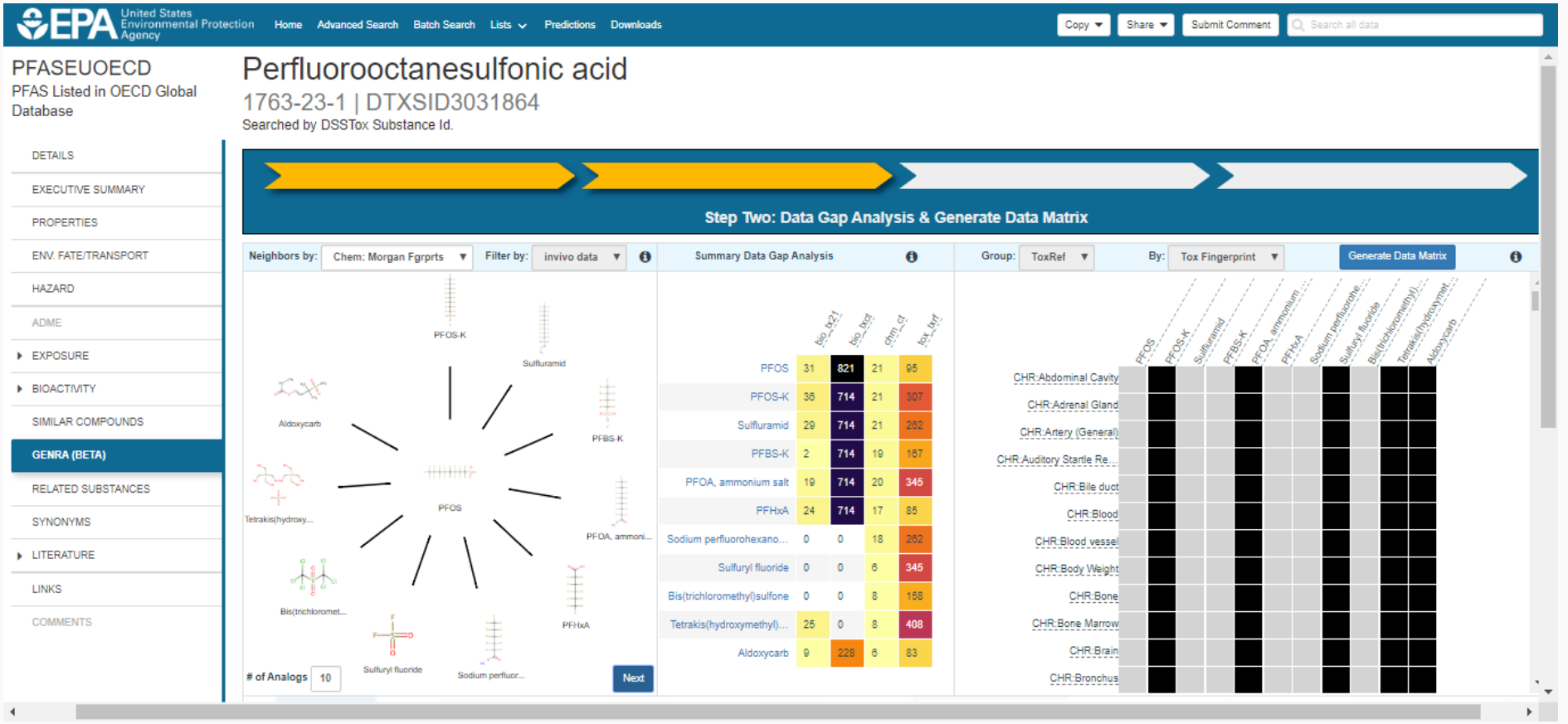
On 25th May 2016, the U.S. EPA released reference doses (RfDs) for Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA) of 20ng/kg/day, which were much more conservative than previous values. These RfDs rely on the choices of animal point of departure (PoD) and the toxicokinetics (TK) model. At this stage, considering that the human evidence is not strong enough for RfD determination, using animal data may be appropriate but with more uncertainties. In this article, the uncertainties concerning RfDs from the choices of PoD and TK models are addressed. Firstly, the candidate PoDs should include more critical endpoints (such as immunotoxicity), which may lead to lower RfDs. Secondly, the reliability of the adopted three-compartment TK model is compromised: the parameters are not non-biologically plausible; and this TK model was applied to simulate gestation and lactation exposures, while the two exposure scenarios were not actually included in the model structure.

Generalized Read-Across (GenRA)



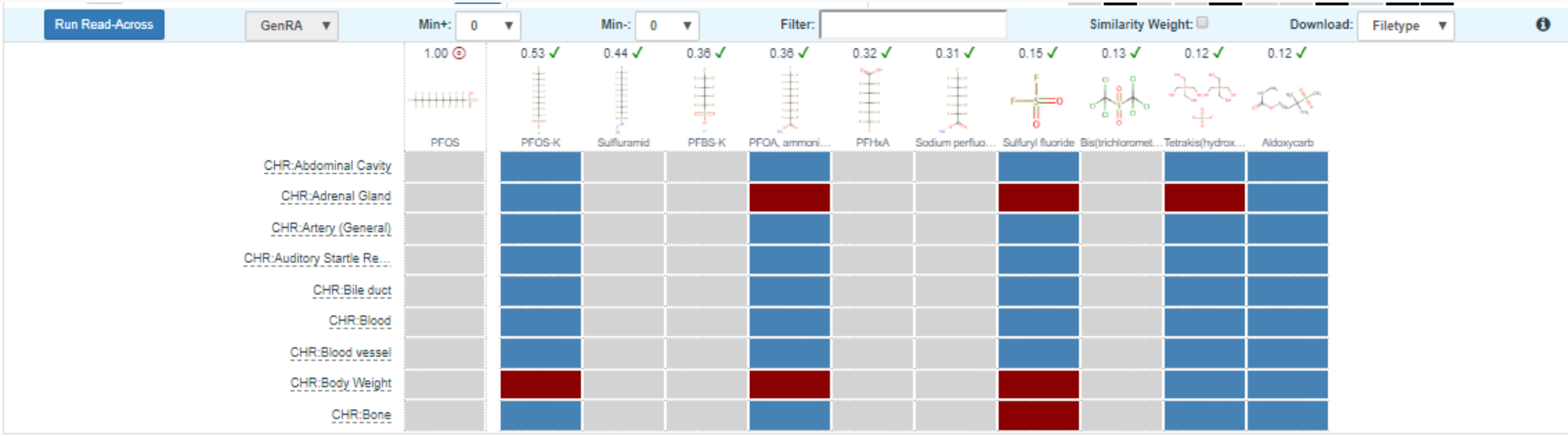
Select and Review Analogs

Generalized Read-Across (GenRA)



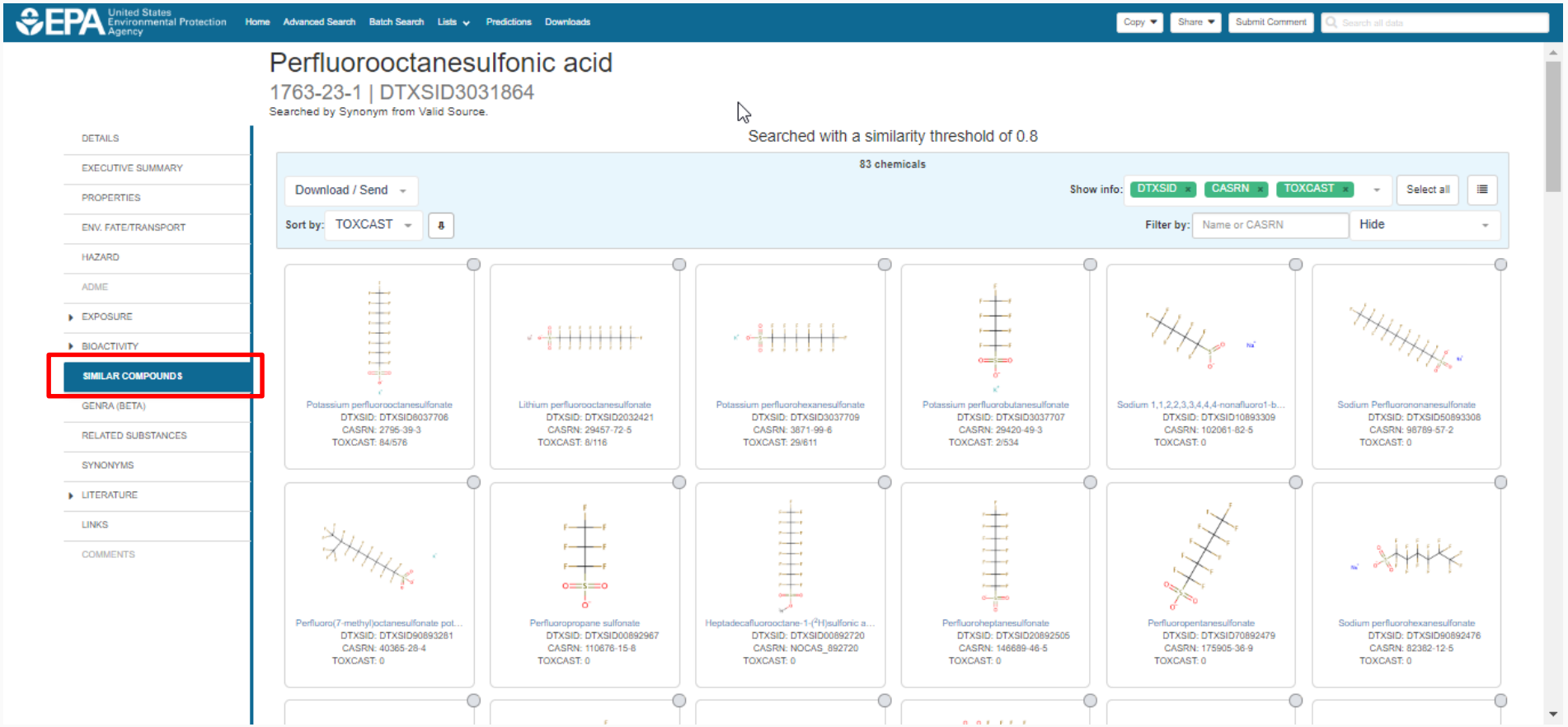
Select and Review Analogs	Review Available Data	Fingerprint indicating available data

Generalized Read-Across (GenRA)

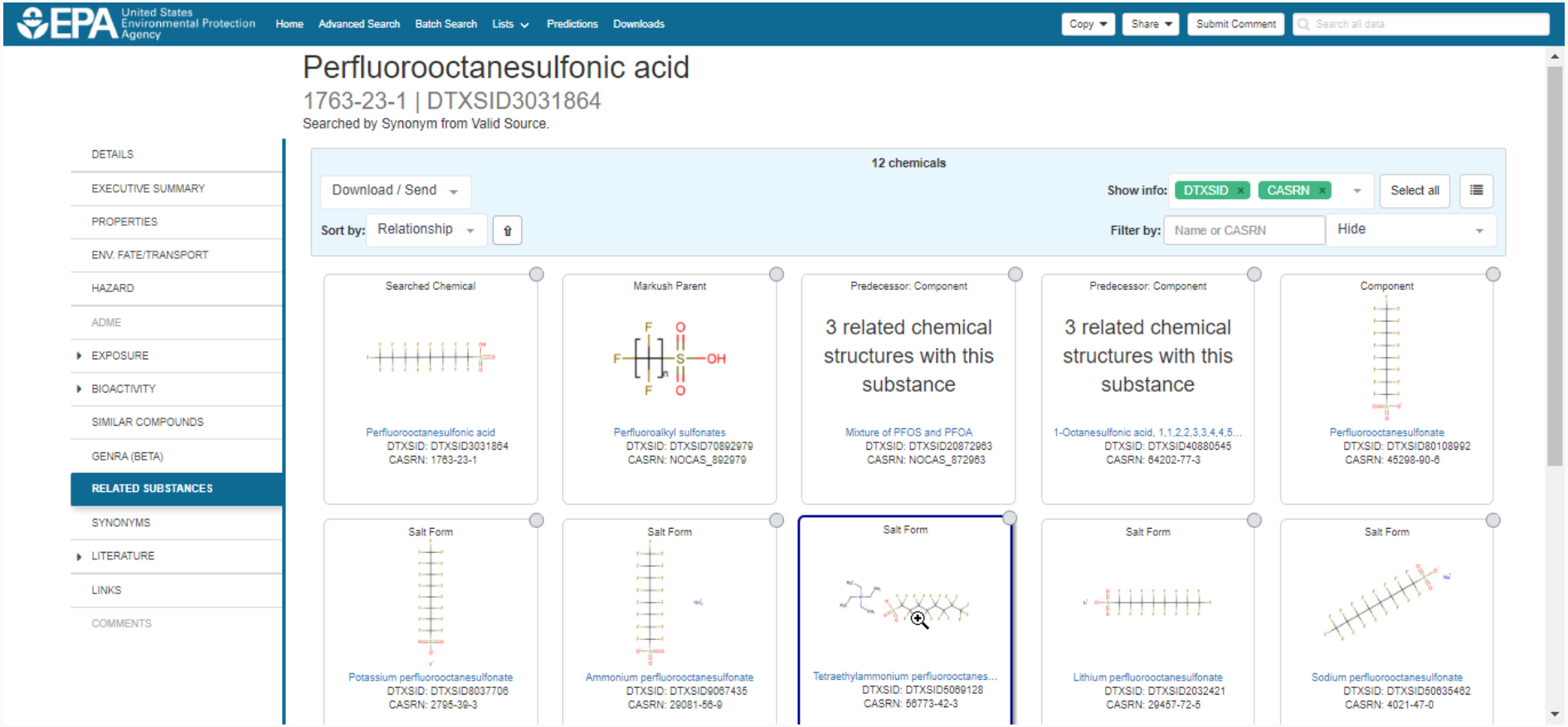


Red : Toxicity effects.
Blue: No Toxicity effects
Grey : Absence of data

Are there Similar Compounds?



Relationships in the data



7 salt forms of PFOS (and the ion)

Component

Perfluorooctanesulfonate
DTXSID: DTXSID80108992
CASRN: 45298-90-6

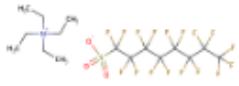
Salt Form

Potassium perfluorooctanesulfonate
DTXSID: DTXSID8037706
CASRN: 2795-39-3

Salt Form

Ammonium perfluorooctanesulfonate
DTXSID: DTXSID9067435
CASRN: 29081-56-9

Salt Form

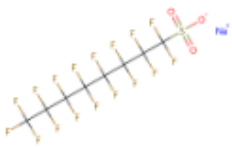


Tetraethylammonium perfluorooctanesu...
DTXSID: DTXSID5069128
CASRN: 56773-42-3

Salt Form

Lithium perfluorooctanesulfonate
DTXSID: DTXSID2032421
CASRN: 29457-72-5

Salt Form

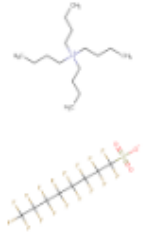


Sodium perfluorooctanesulfonate
DTXSID: DTXSID50635462
CASRN: 4021-47-0

Salt Form

Magnesium bis(heptadecafluorooctane...
DTXSID: DTXSID80881314
CASRN: 91036-71-4

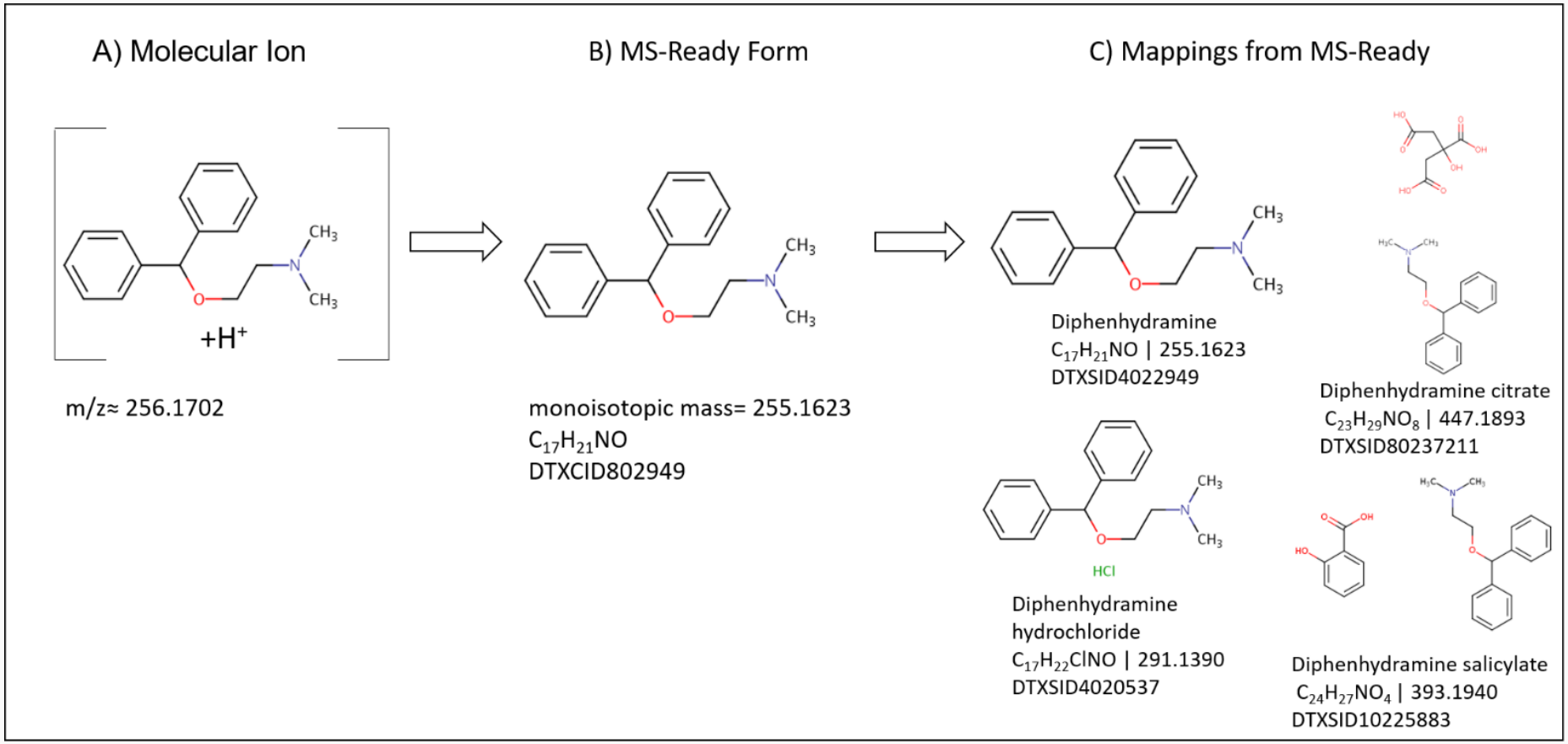
Salt Form



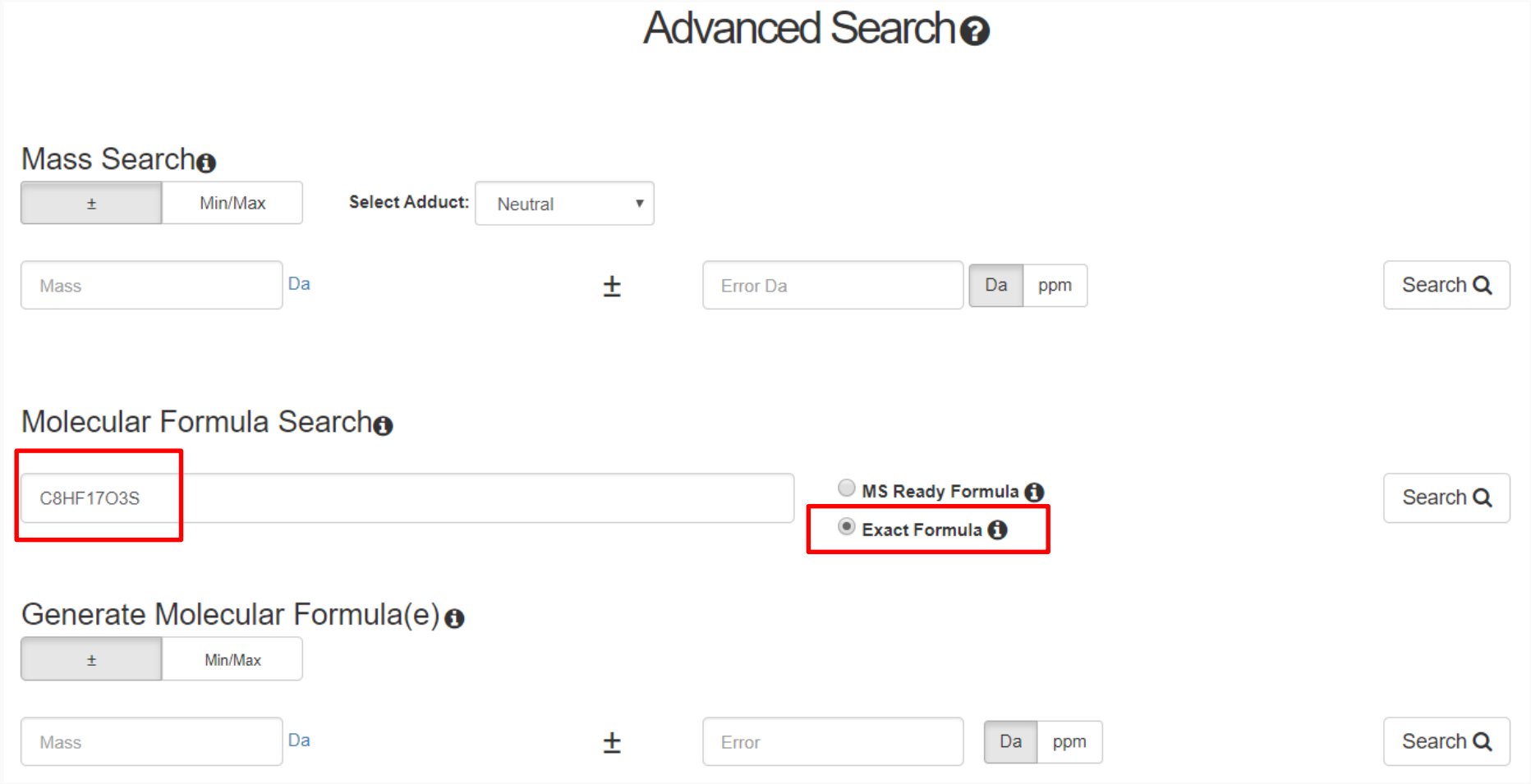
Tetrabutylammonium perfluorooctanesu...
DTXSID: DTXSID40584995
CASRN: 111873-33-7

Using data relationships

- We have purposely built relationships in the data. Specifically, “MS-Ready mappings”



Advanced Search
Supporting Target/Non-Target MS



2 Chemicals match the formula

Search Results

Searched by Exact Molecular Formula: C8HF17O3S.

2 of 2 chemicals visible

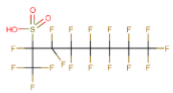
Download / Send

Show info: Data Picker | Select all

Sort by: DTXSID

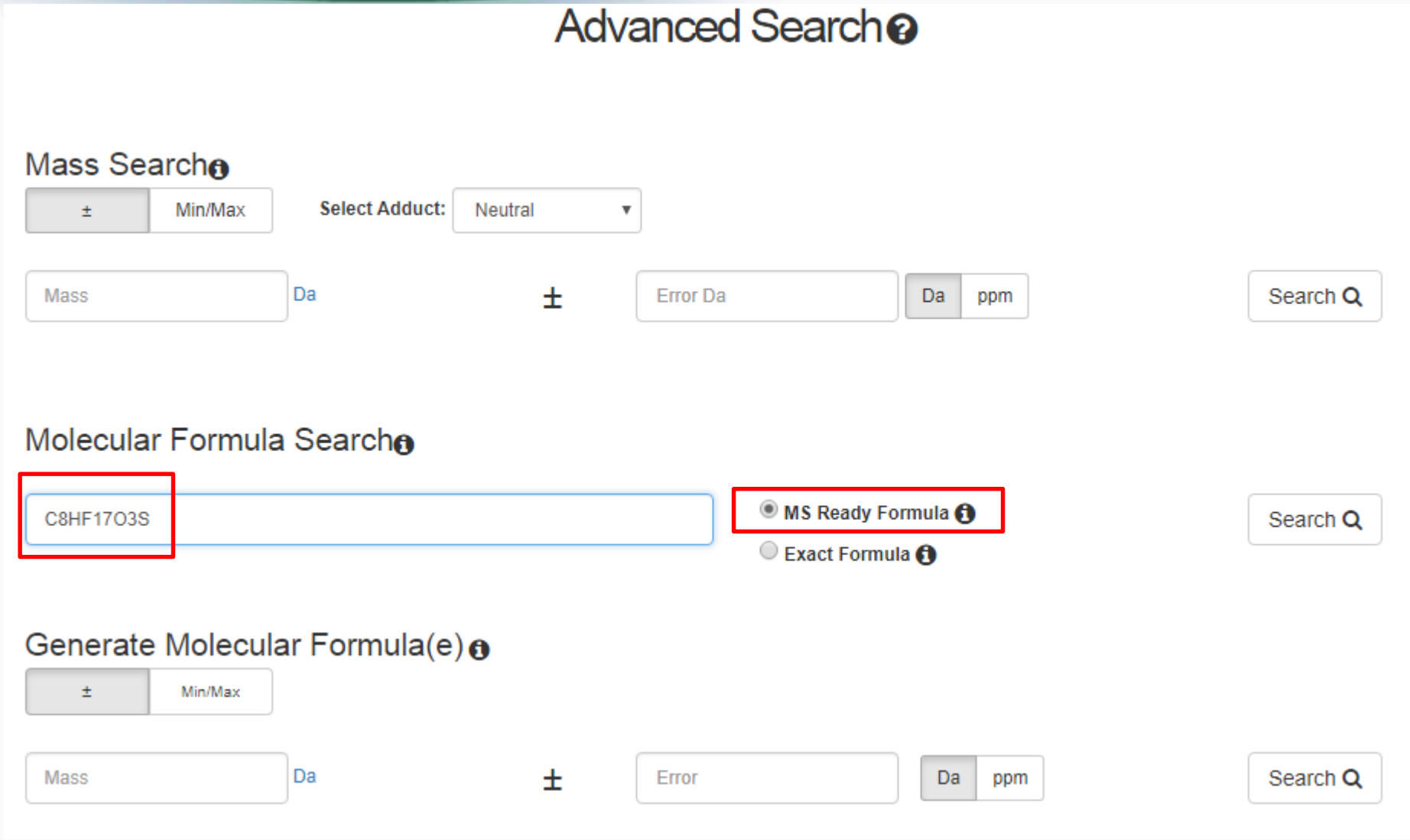
Filter by: Name or CASRN | Multicomponent Chemicals ×

Perfluorooctanesulfonic acid

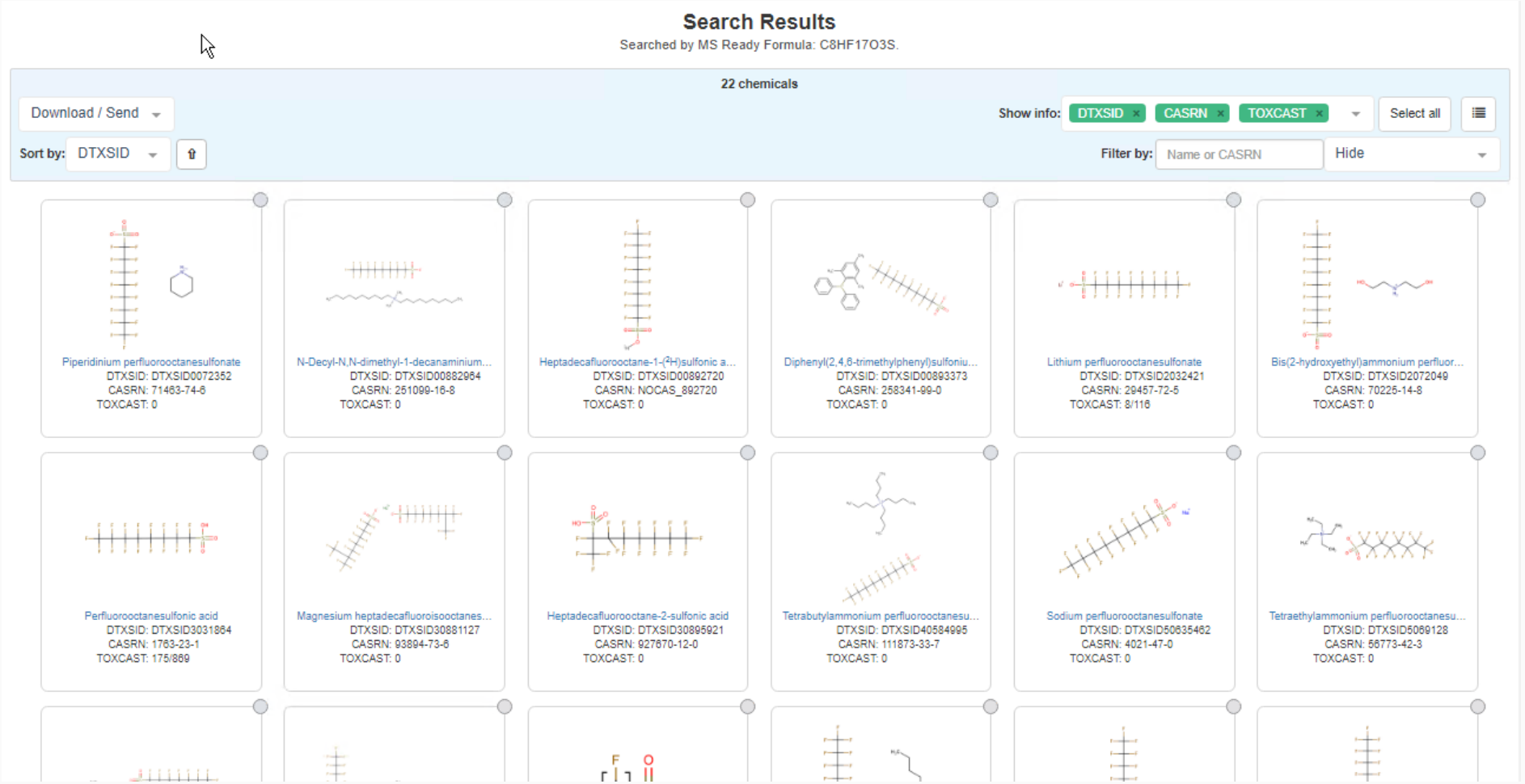


Heptadecafluorooctane-2-sulfonic acid

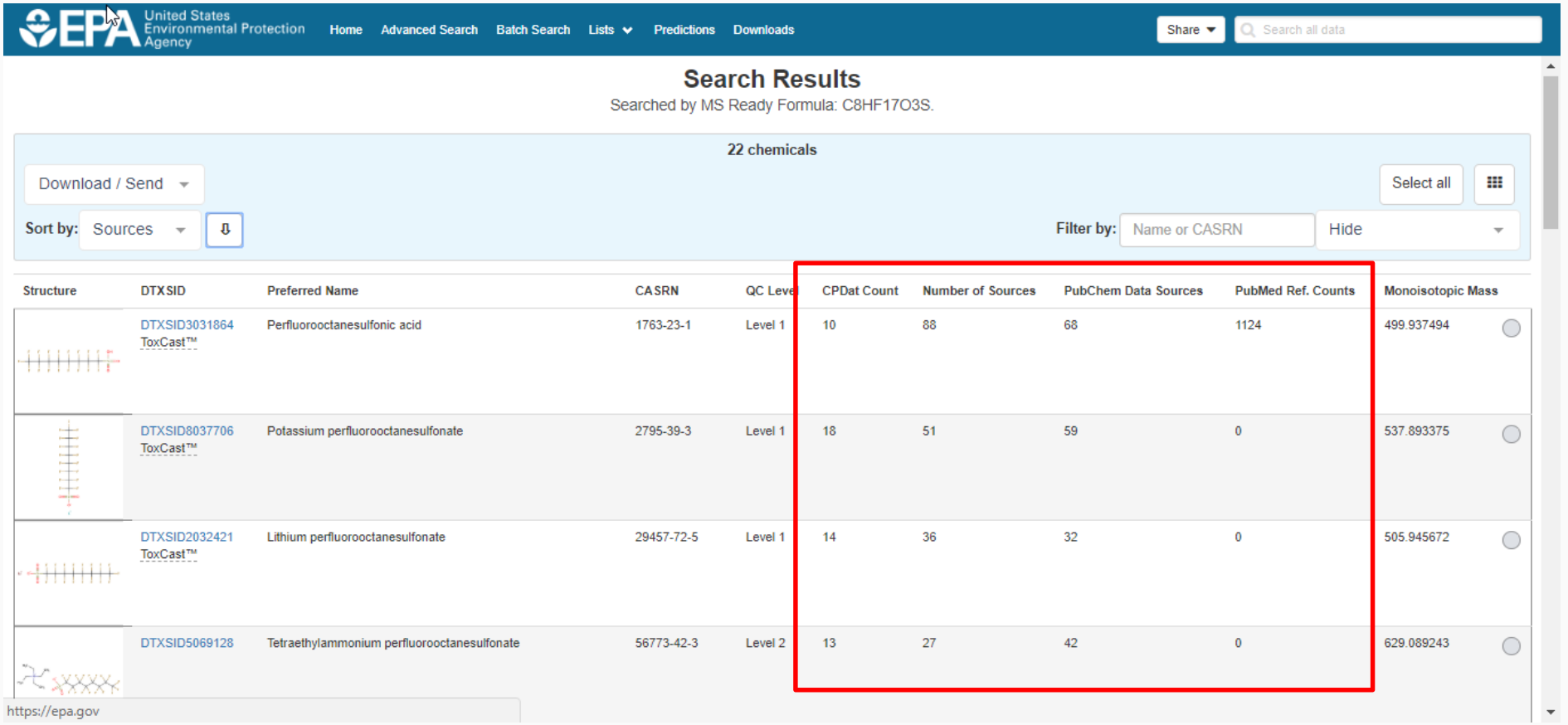
Advanced Search
Supporting Target/Non-Target MS



22 Chemicals match the formula



22 Chemicals match the formula



Suspect Screening and Non-Targeted Analysis Workflow

EPA United States Environmental Protection Agency

Suspect Screening

- Raw Samples
- Extracted Samples
- Raw Features
- "Molecular Features"
- DSSTox Chemical Database
- Matched Formulas
- Mapped Structures
- Prioritized Structures (using ToxPi)
- Confirmed Structures (using ToxCast standards)
- Predicted Concentrations

Non-Targeted Analysis

- Processed Features
- Prioritized Features
- Predicted Formulas
- Candidate Structures
- Sorted Structures
- Predicted Retention Times
- Predicted Mass Spectra
- Predicted/Observed Functional Use
- Predicted/Observed Media Occurrence
- Methodological Concordance
- Top Candidate Structure(s)

Color Key

Red = Analytical Chemistry

Blue = Data Processing & Analysis

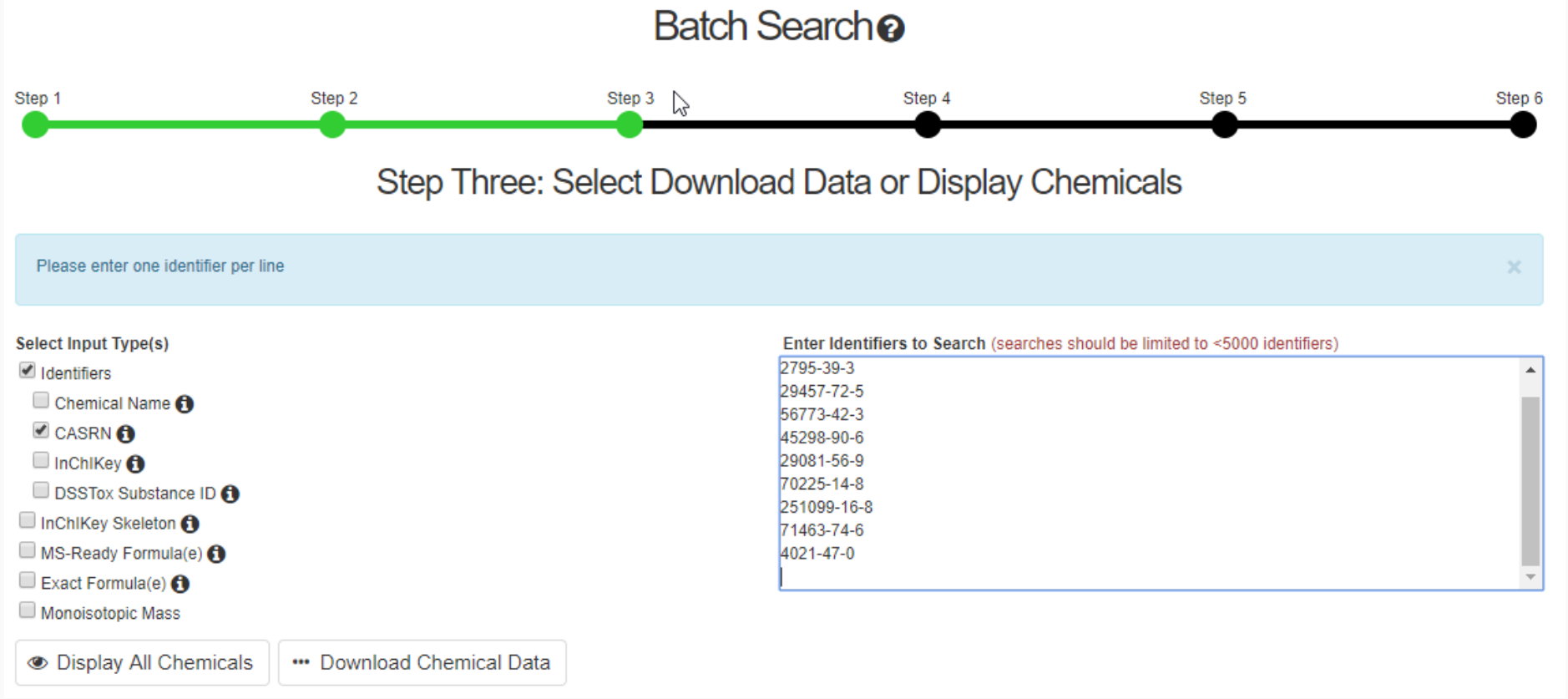
Purple = Mathematical & QSPR Modeling

Green = Informatics & Web Services

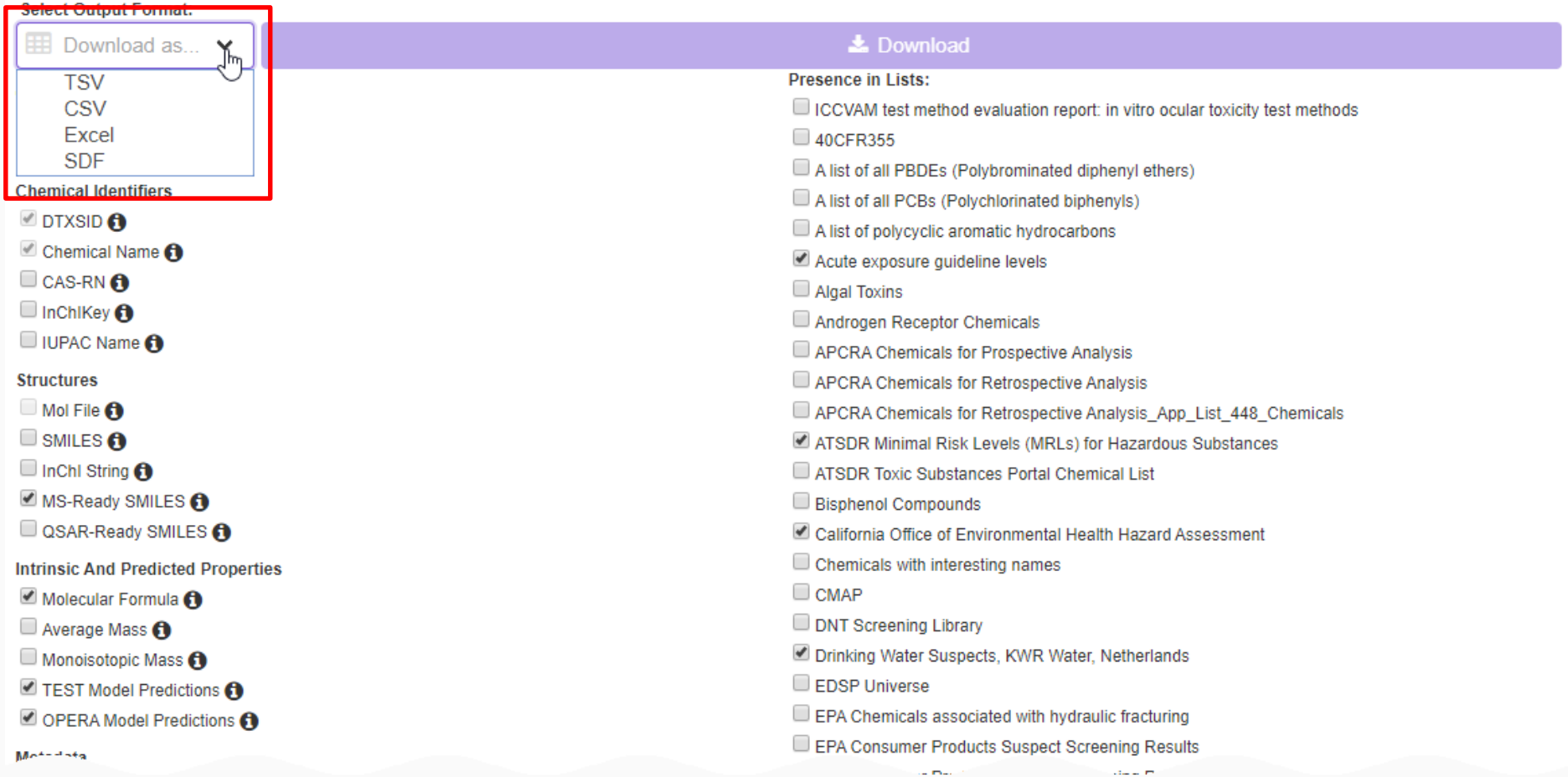
Content from J. Sobus, US-EPA-NERL

How to search 1000s of formulae?

Batch Searches



Batch Searches



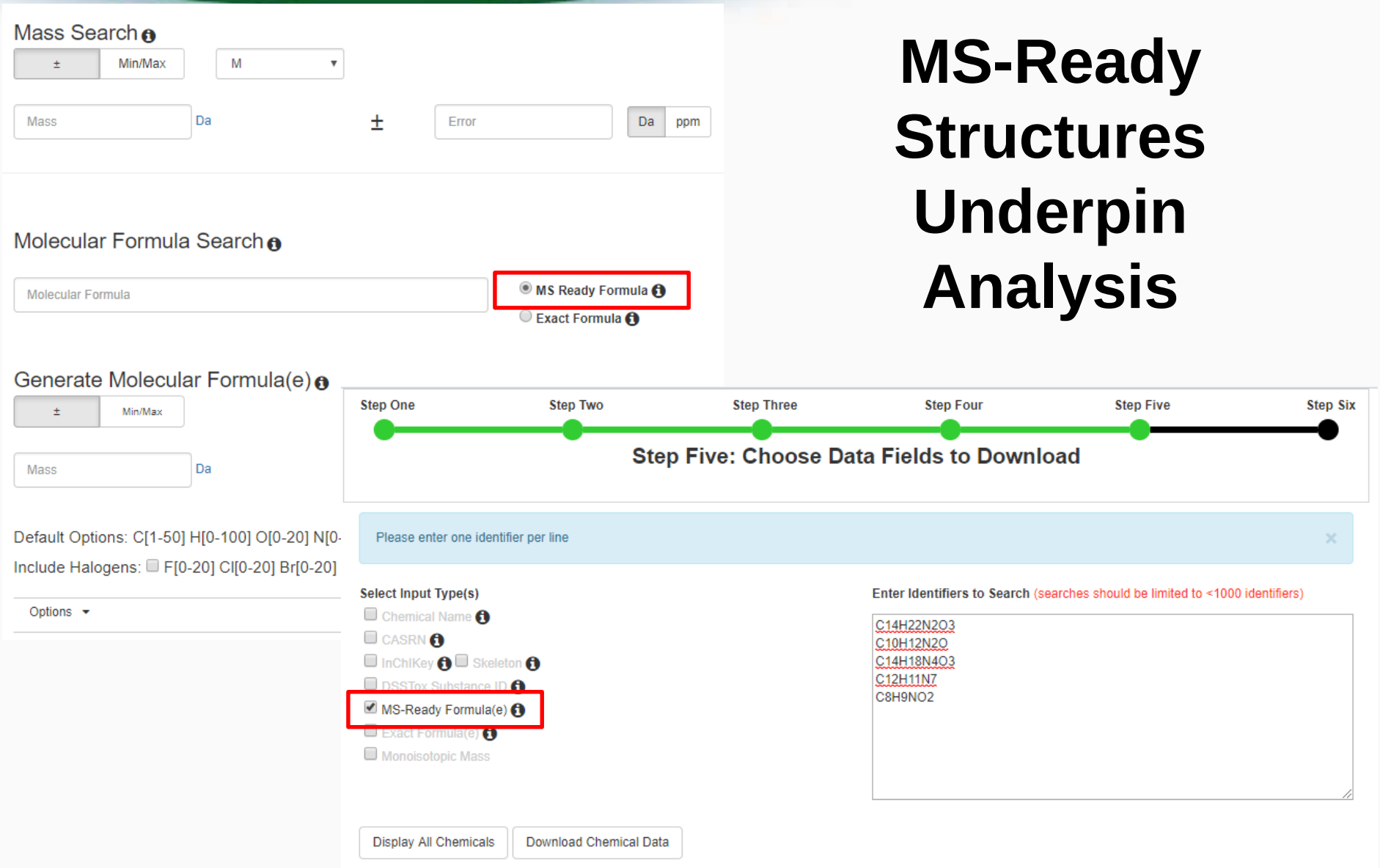
Surfacing Lists of Chemicals

- Specific subsets of chemicals, “lists”, can be displayed on the dashboard
- If there are chemicals that map together then these link to existing:
  - Property data
  - Hazard data
  - Exposure data
  - *In vitro* bioassay data
  - Documents and Literature

Batch Searches to Support MS-Analysis

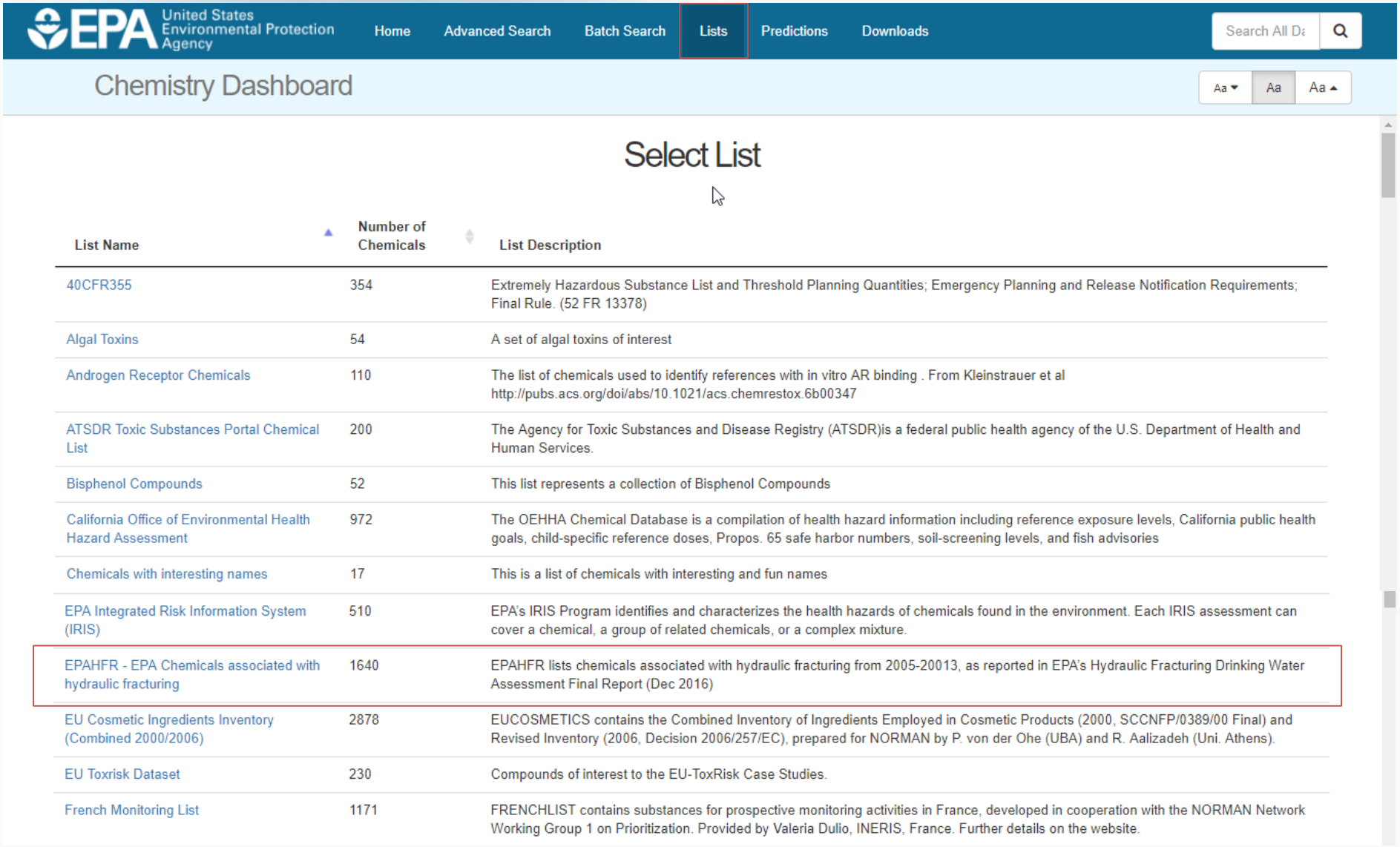
EPA United States Environmental Protection Agency

MS-Ready Structures Underpin Analysis



A List of Lists of Chemicals

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

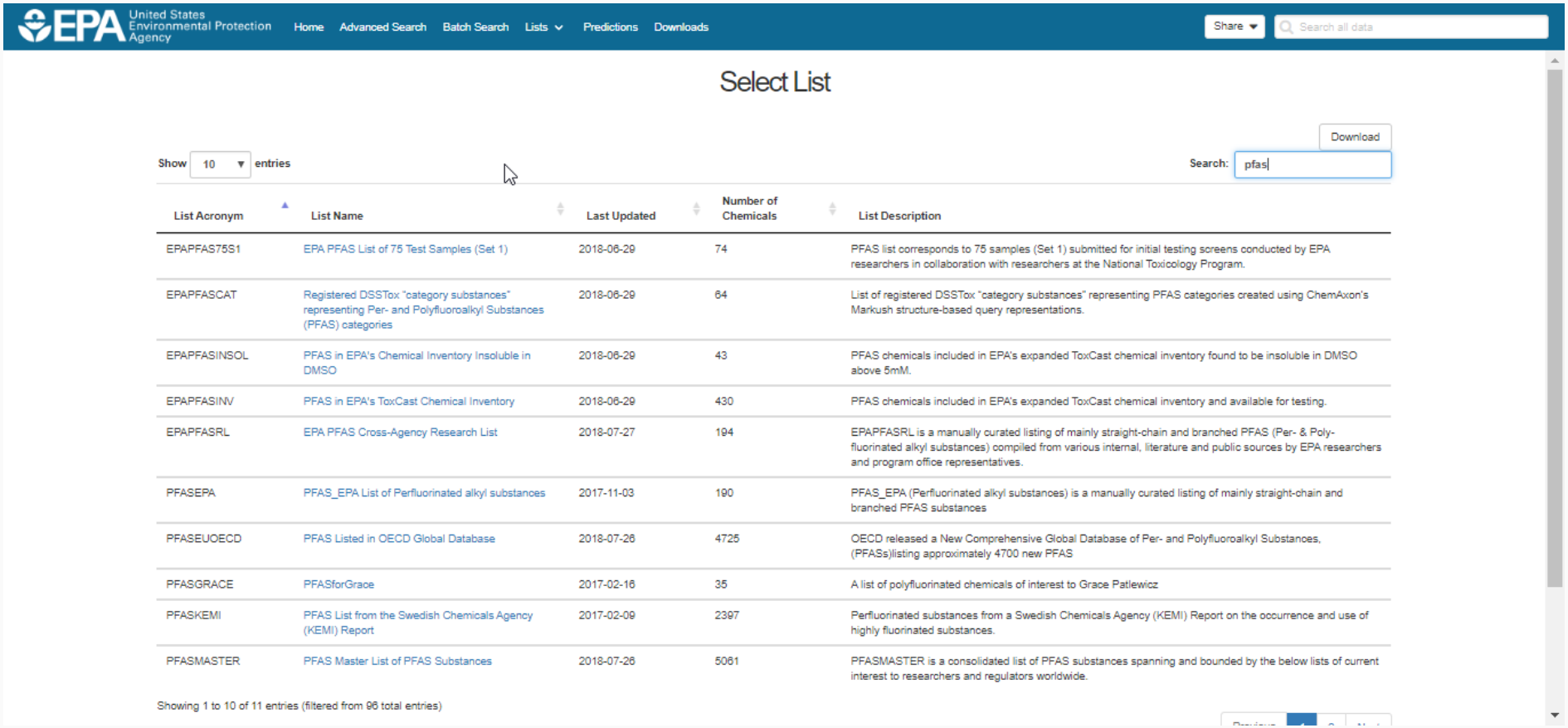


Select List

List Name	Number of Chemicals	List Description
40CFR355	354	Extremely Hazardous Substance List and Threshold Planning Quantities; Emergency Planning and Release Notification Requirements; Final Rule. (52 FR 13378)
Algal Toxins	54	A set of algal toxins of interest
Androgen Receptor Chemicals	110	The list of chemicals used to identify references with in vitro AR binding . From Kleinstrauer et al http://pubs.acs.org/doi/abs/10.1021/acs.chemrestox.6b00347
ATSDR Toxic Substances Portal Chemical List	200	The Agency for Toxic Substances and Disease Registry (ATSDR)is a federal public health agency of the U.S. Department of Health and Human Services.
Bisphenol Compounds	52	This list represents a collection of Bisphenol Compounds
California Office of Environmental Health Hazard Assessment	972	The OEHHA Chemical Database is a compilation of health hazard information including reference exposure levels, California public health goals, child-specific reference doses, Propos. 65 safe harbor numbers, soil-screening levels, and fish advisories
Chemicals with interesting names	17	This is a list of chemicals with interesting and fun names
EPA Integrated Risk Information System (IRIS)	510	EPA's IRIS Program identifies and characterizes the health hazards of chemicals found in the environment. Each IRIS assessment can cover a chemical, a group of related chemicals, or a complex mixture.
EPAHFR - EPA Chemicals associated with hydraulic fracturing	1640	EPAHFR lists chemicals associated with hydraulic fracturing from 2005-20013, as reported in EPA's Hydraulic Fracturing Drinking Water Assessment Final Report (Dec 2016)
EU Cosmetic Ingredients Inventory (Combined 2000/2006)	2878	EUCOSMETICS contains the Combined Inventory of Ingredients Employed in Cosmetic Products (2000, SCCNFP/0389/00 Final) and Revised Inventory (2006, Decision 2006/257/EC), prepared for NORMAN by P. von der Ohe (UBA) and R. Aalizadeh (Uni. Athens).
EU Toxrisk Dataset	230	Compounds of interest to the EU-ToxRisk Case Studies.
French Monitoring List	1171	FRENCHLIST contains substances for prospective monitoring activities in France, developed in cooperation with the NORMAN Network Working Group 1 on Prioritization. Provided by Valeria Dulio, INERIS, France. Further details on the website.

11 PFAS Lists

http://comptox-prod.epa.gov/dashboard/chemical_lists



List Acronym	List Name	Last Updated	Number of Chemicals	List Description
EPAPFAS75S1	EPA PFAS List of 75 Test Samples (Set 1)	2018-06-29	74	PFAS list corresponds to 75 samples (Set 1) submitted for initial testing screens conducted by EPA researchers in collaboration with researchers at the National Toxicology Program.
EPAPFASCAT	Registered DSSTox "category substances" representing Per- and Polyfluoroalkyl Substances (PFAS) categories	2018-06-29	64	List of registered DSSTox "category substances" representing PFAS categories created using ChemAxon's Markush structure-based query representations.
EPAPFASINSOL	PFAS in EPA's Chemical Inventory Insoluble in DMSO	2018-06-29	43	PFAS chemicals included in EPA's expanded ToxCast chemical inventory found to be insoluble in DMSO above 5mM.
EPAPFASINV	PFAS in EPA's ToxCast Chemical Inventory	2018-06-29	430	PFAS chemicals included in EPA's expanded ToxCast chemical inventory and available for testing.
EPAPFASRL	EPA PFAS Cross-Agency Research List	2018-07-27	194	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.
PFASEPA	PFAS_EPA List of Perfluorinated alkyl substances	2017-11-03	190	PFAS_EPA (Perfluorinated alkyl substances) is a manually curated listing of mainly straight-chain and branched PFAS substances
PFASEUOECD	PFAS Listed in OECD Global Database	2018-07-26	4725	OECD released a New Comprehensive Global Database of Per- and Polyfluoroalkyl Substances, (PFASs)listing approximately 4700 new PFAS
PFASGRACE	PFASforGrace	2017-02-16	35	A list of polyfluorinated chemicals of interest to Grace Patlewicz
PFASKEMI	PFAS List from the Swedish Chemicals Agency (KEMI) Report	2017-02-09	2397	Perfluorinated substances from a Swedish Chemicals Agency (KEMI) Report on the occurrence and use of highly fluorinated substances.
PFASMASTER	PFAS Master List of PFAS Substances	2018-07-26	5061	PFASMASTER is a consolidated list of PFAS substances spanning and bounded by the below lists of current interest to researchers and regulators worldwide.

Showing 1 to 10 of 11 entries (filtered from 96 total entries)

The OECD List of PFAS

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

EPA United States Environmental Protection Agency

The OECD releases a new list of PFASs

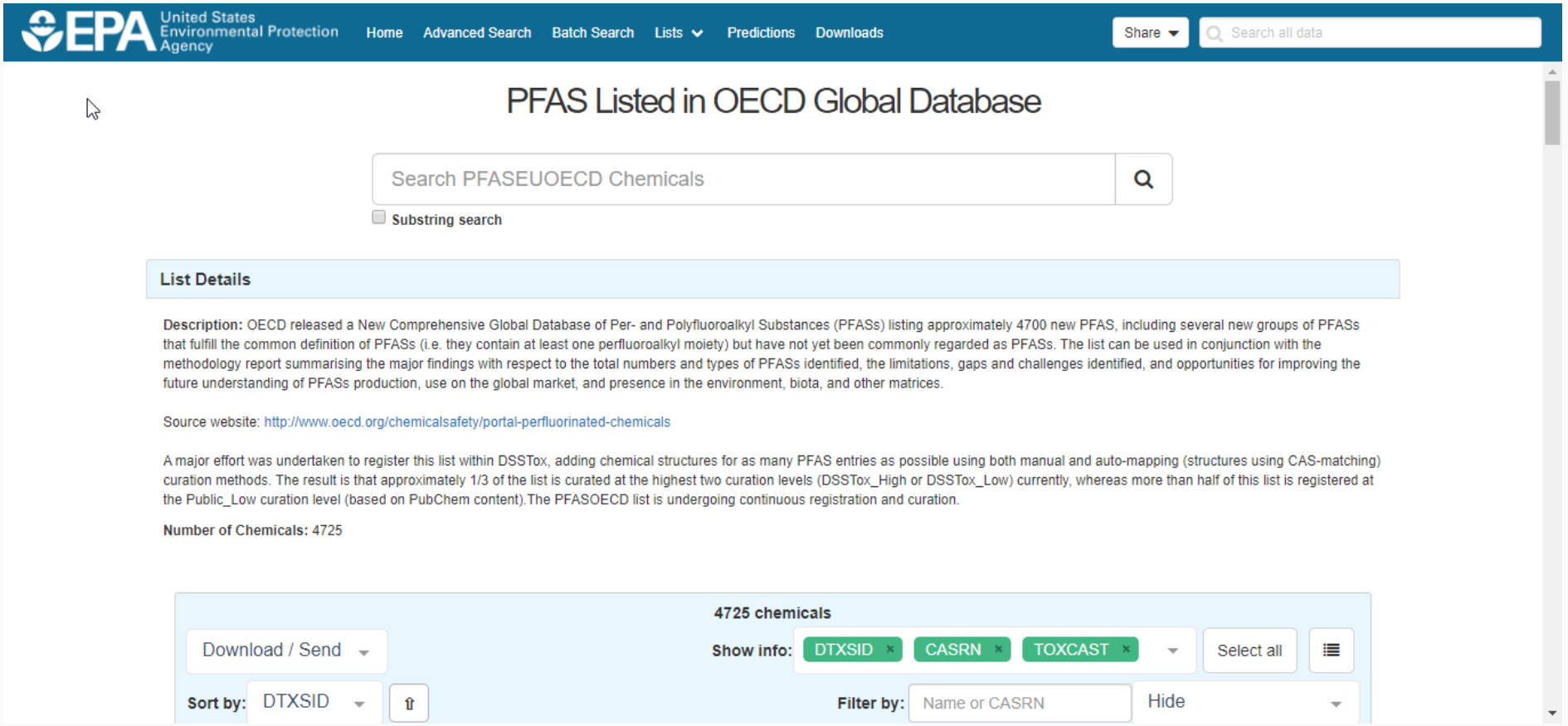
The OECD releases a new list of Per- and Polyfluoroalkyl Substances (PFASs) based on a comprehensive analysis of information available in the public domain. In total, 4730 PFAS-related CAS numbers have been identified and categorised in this study, including several new groups of PFASs that fulfil the 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/



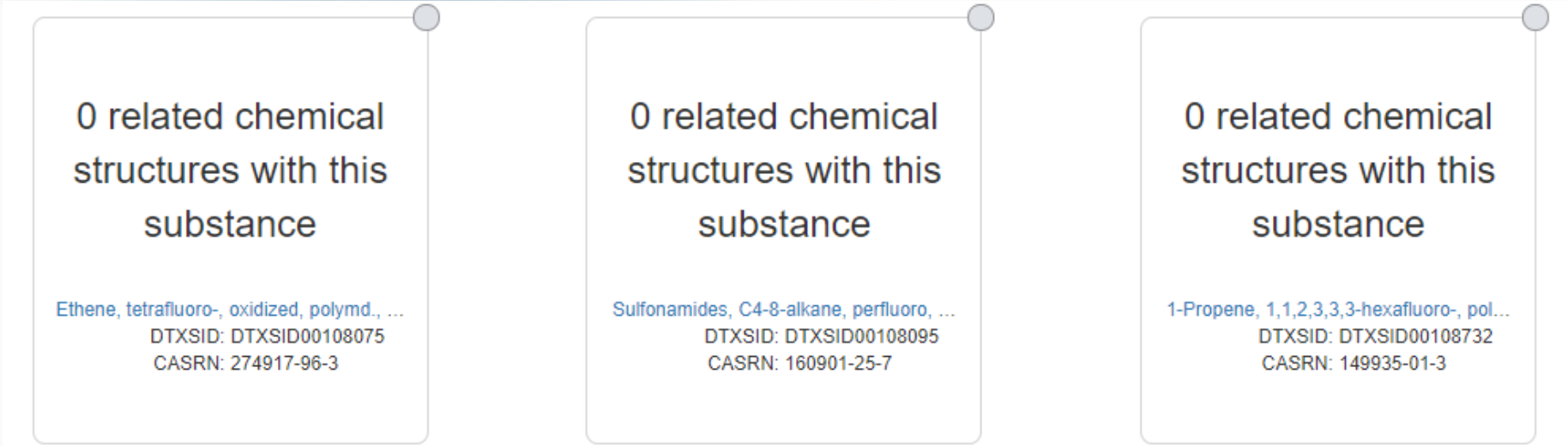
UVCB Chemicals

EPA United States Environmental Protection Agency

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.

Example PFAS-UVCBs

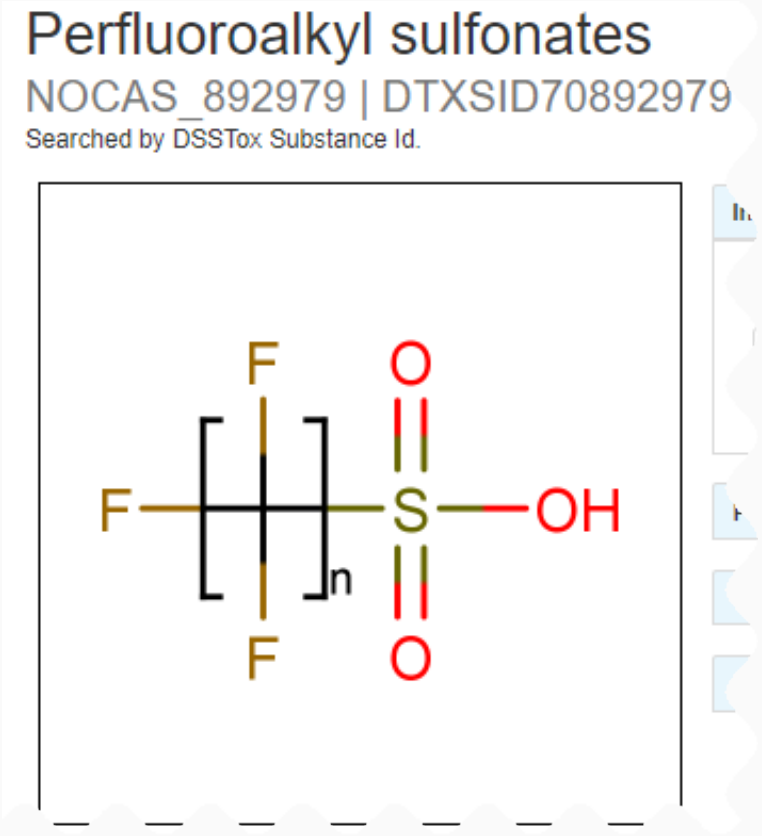


Ethene, tetrafluoro-, oxidized, polymd., reduced, decarboxylated, C6 fraction
274917-96-3 | DTXSID00108075

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

Markush Chemicals

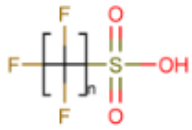
- PFOS is a member of linear perfluoroalkyl sulfonates



…and their Markush Children…

- Linear perfluoroalkyl sulfonates has children…

Searched Chemical



Perfluoroalkyl sulfonates
DTXSID: DTXSID70892979
CASRN: NOCAS_892979

Markush Child

Perfluorobutanesulfonic acid
DTXSID: DTXSID5030030
CASRN: 375-73-5

Markush Child

Perfluorooctanesulfonic acid
DTXSID: DTXSID3031864
CASRN: 1763-23-1

Markush Child

Perfluorodecanesulfonic acid
DTXSID: DTXSID3040148
CASRN: 335-77-3

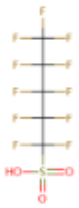
Markush Child

Perfluorohexanesulfonic acid
DTXSID: DTXSID7040150
CASRN: 355-46-4

Markush Child

Perfluoroheptanesulfonic acid
DTXSID: DTXSID8059920
CASRN: 375-92-8

Markush Child



Perfluoropentanesulfonic acid
DTXSID: DTXSID8062600
CASRN: 2706-91-4

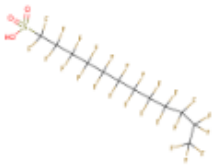
Markush Child

Perfluorononanesulfonic acid
DTXSID: DTXSID8071356
CASRN: 68259-12-1

Markush Child

Perfluoropropanesulfonic acid
DTXSID: DTXSID30870531
CASRN: 423-41-6

Markush Child



Perfluorododecanesulfonic acid (PFDOS)
DTXSID: DTXSID20873011
CASRN: 79780-39-5

PFAS Categories in Development

Registered DSSTox "category substances" representing Per- and Polyfluoroalkyl Substances (PFAS) categories

Search EPAPFASCAT Chemicals

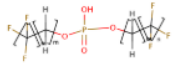
Substring search

List Details

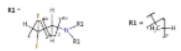
Description: List of registered DSSTox "category substances" representing Per- and Polyfluoroalkyl Substances (PFAS) categories created using ChemAxon's Markush structure-based query representations. Markush categories can be broad and inclusive of more specific categories, or can represent a unique category not overlapping with other registered categories. Each PFAS category registered with a unique DTXSID is considered a generalized substance or "parent ID" that can be associated with one or many "child IDs" (i.e. many parent-child mappings) within the full DSSTox database. These category DTXSIDs can be used to search and retrieve all currently registered DSSTox substances within the category group, and offer an objective, transparent and reproducible structure-based means of defining a category of chemicals. This list and the corresponding category mappings is undergoing continuous curation and expansion.

Number of Chemicals: 64

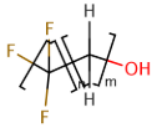
PFAS Categories in Development


Fluorotelomer (linear) phosphate esters...

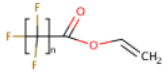

Fluorotelomer (linear) n:2 amines (prim...


Fluorotelomer (linear) amines (tertiary) (...

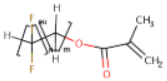

Perfluoroalkyl (linear) carboxylic acids


Fluorotelomer (linear) alcohols

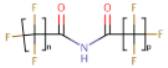

Fluorotelomer (linear) carboxylic acids

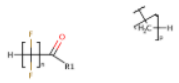

Perfluoroalkyl esters (vinyl)

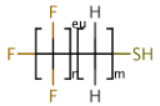

Perfluoroalkyl acyl fluorides

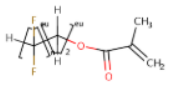

Fluorotelomer (linear) methacrylates (-...

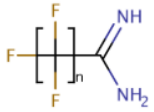

Perfluoroalkyl (linear) amides (primary)

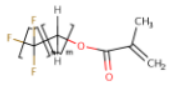

Perfluoro diacyl amides

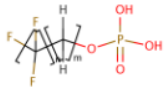

Polyfluoroalkyl (linear) (-CF2H) alkyl (lin...

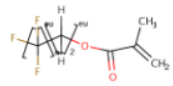

Fluorotelomer (linear) thiols


Fluorotelomer (linear) n:2 methacrylate...


Perfluoroalkyl amidines

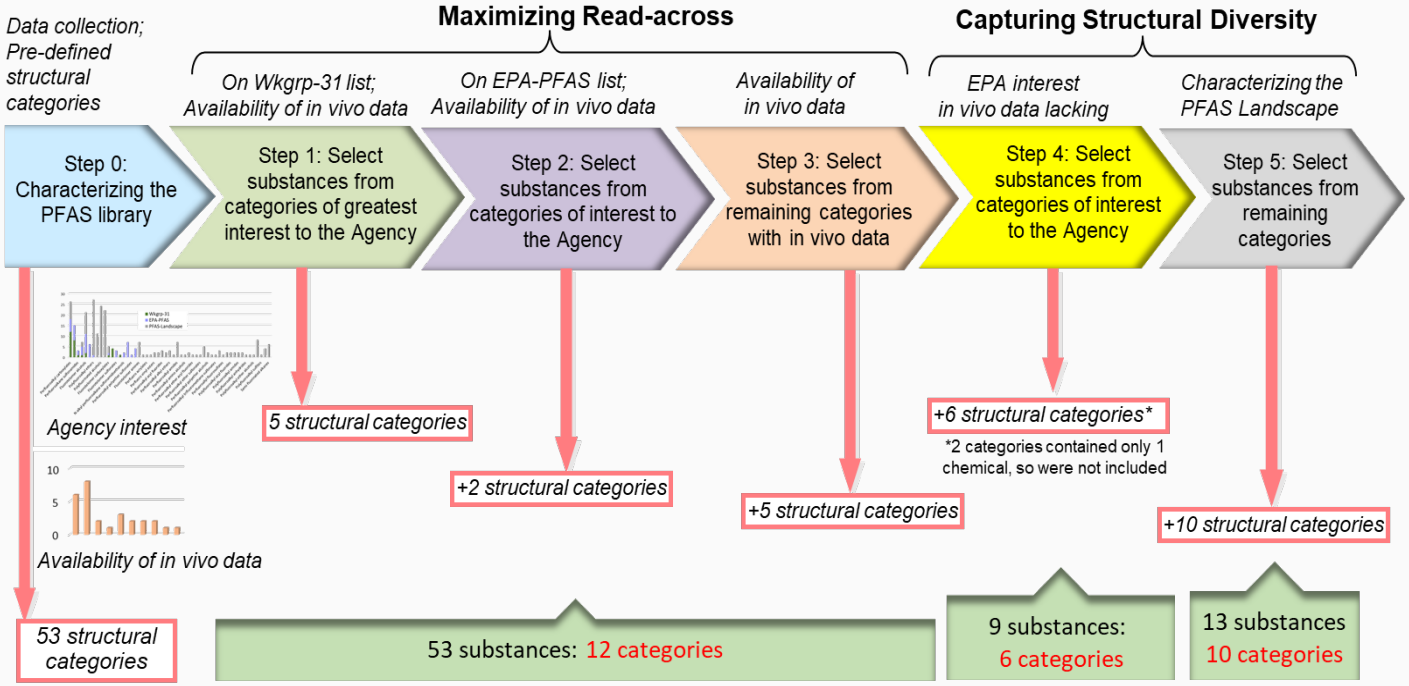

Fluorotelomer (linear) n:2 methacrylates


Fluorotelomer (linear) phosphate esters...


Fluorotelomer (linear) methacrylates

Work in progress

- Development of a high-throughput screening library and collection of physical samples (~400)
- 75 PFAS chemicals for screening based on categories, diversity, exposure considerations, procurability and testability, availability of existing toxicity data



Supporting future work

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

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- 1. Mobility: A wide and dynamic distribution of short chain PFAS due to their high polarity, persistency and volatility. (**OPERA 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**)

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Conclusions

- The CompTox 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
  - Physical library of ~400 chemicals has been acquired
  - High-throughput screening of ~75 chemicals
  - Classification approaches and Markush representations

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