http://www.orcid.org/0000-0002-2668-4821

Structure identification approaches using the EPA CompTox Chemicals Dashboard to support mass spectrometry analyses

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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

August 2021

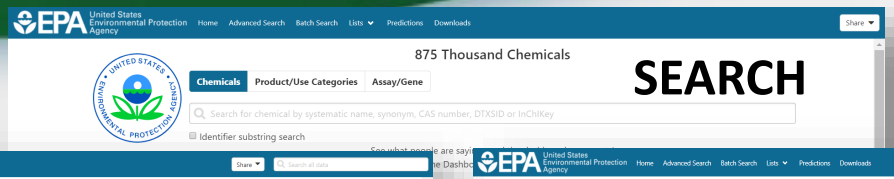
ACS Fall Meeting, Atlanta

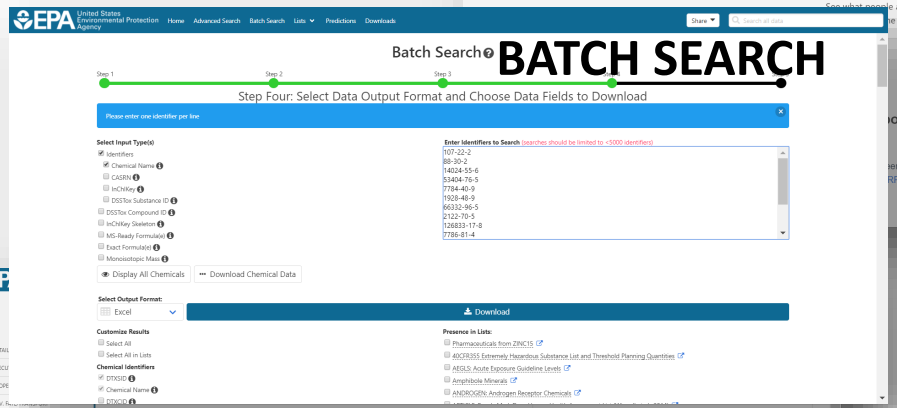
EPA's CompTox Chemicals Dashboard

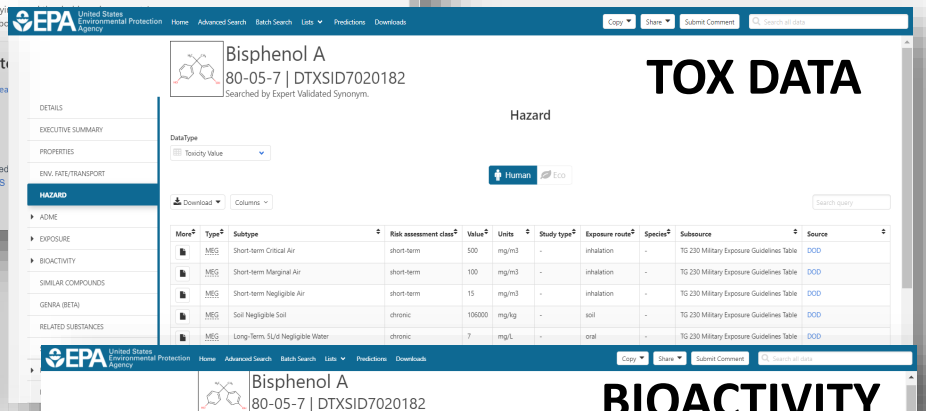
A publicly accessible website delivering:

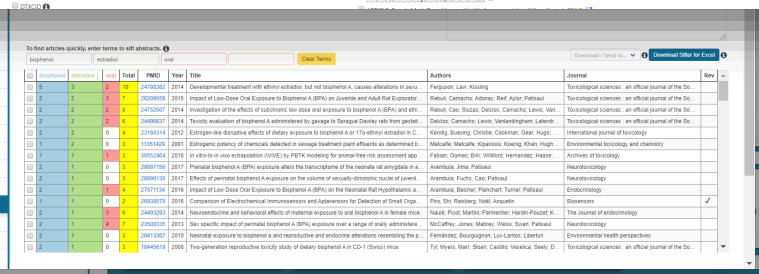
- ~883,000 chemicals with related property data
- Experimental and predicted physicochemical property data
- Integration to "biological assay data" for 1000's of chemicals
- Information regarding consumer products containing chemicals
- Links to other agency websites and public data resources
- "Literature" searches for chemicals using public resources
- "Batch searching" for thousands of chemicals
- Downloadable Open Data for reuse and repurposing

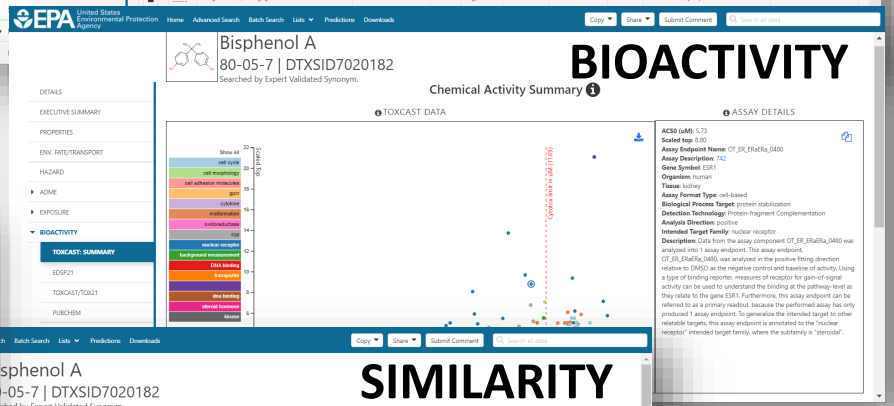
A single app integrating…

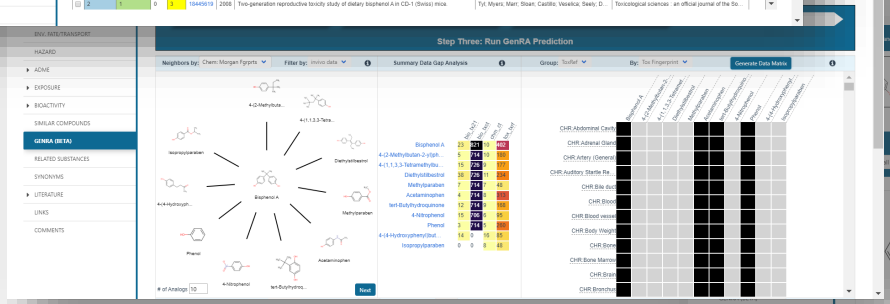


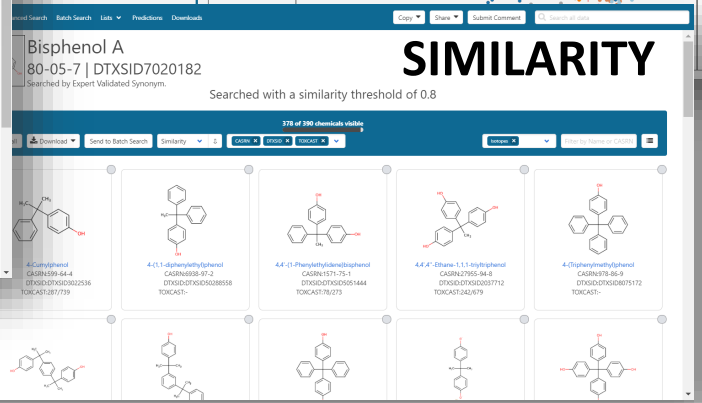






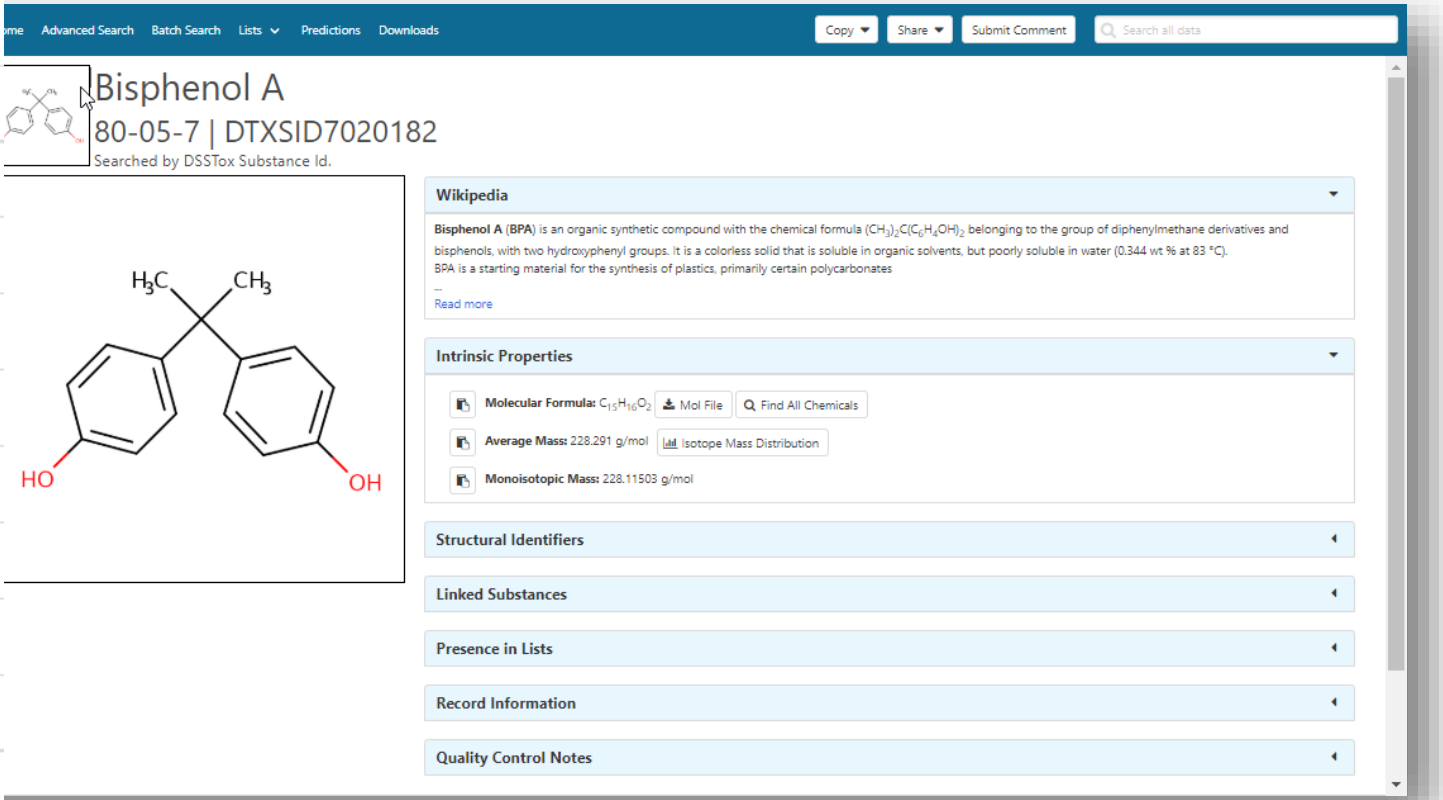




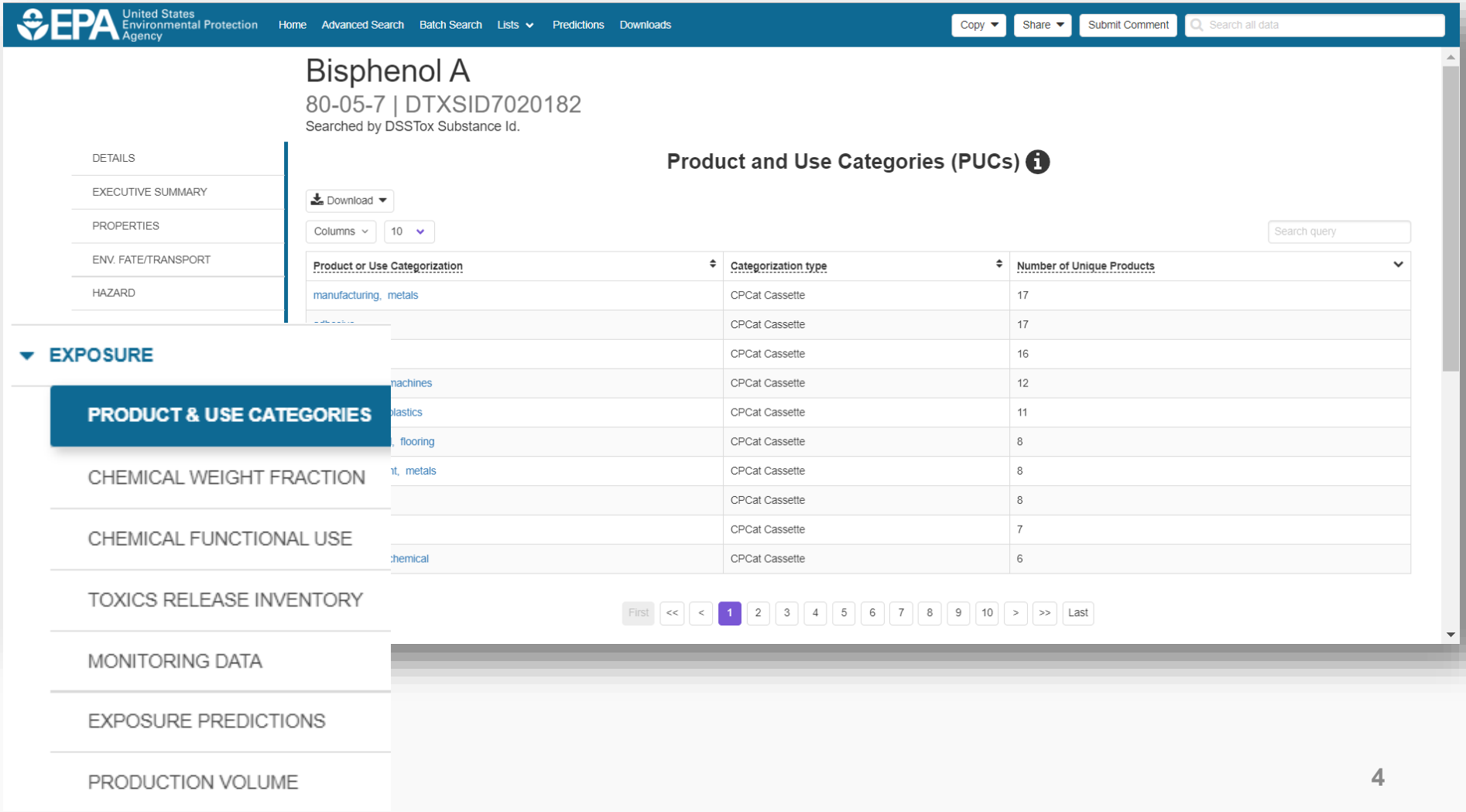


Detailed Chemical Pages

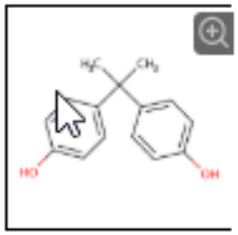
- DETAILS
- EXECUTIVE SUMMARY
- PROPERTIES
- ENV. FATE/TRANSPORT
- HAZARD
- ADME
- EXPOSURE
- BIOACTIVITY
- SIMILAR COMPOUNDS
- GENRA (BETA)
- RELATED SUBSTANCES
- SYNONYMS
- LITERATURE
- LINKS
- COMMENTS



Sources of Exposure to Chemicals



Physicochemical properties and environmental fate and transport



Bisphenol A

80-05-7 | DTXSID7020182

Searched by DSSTox Substance Id.

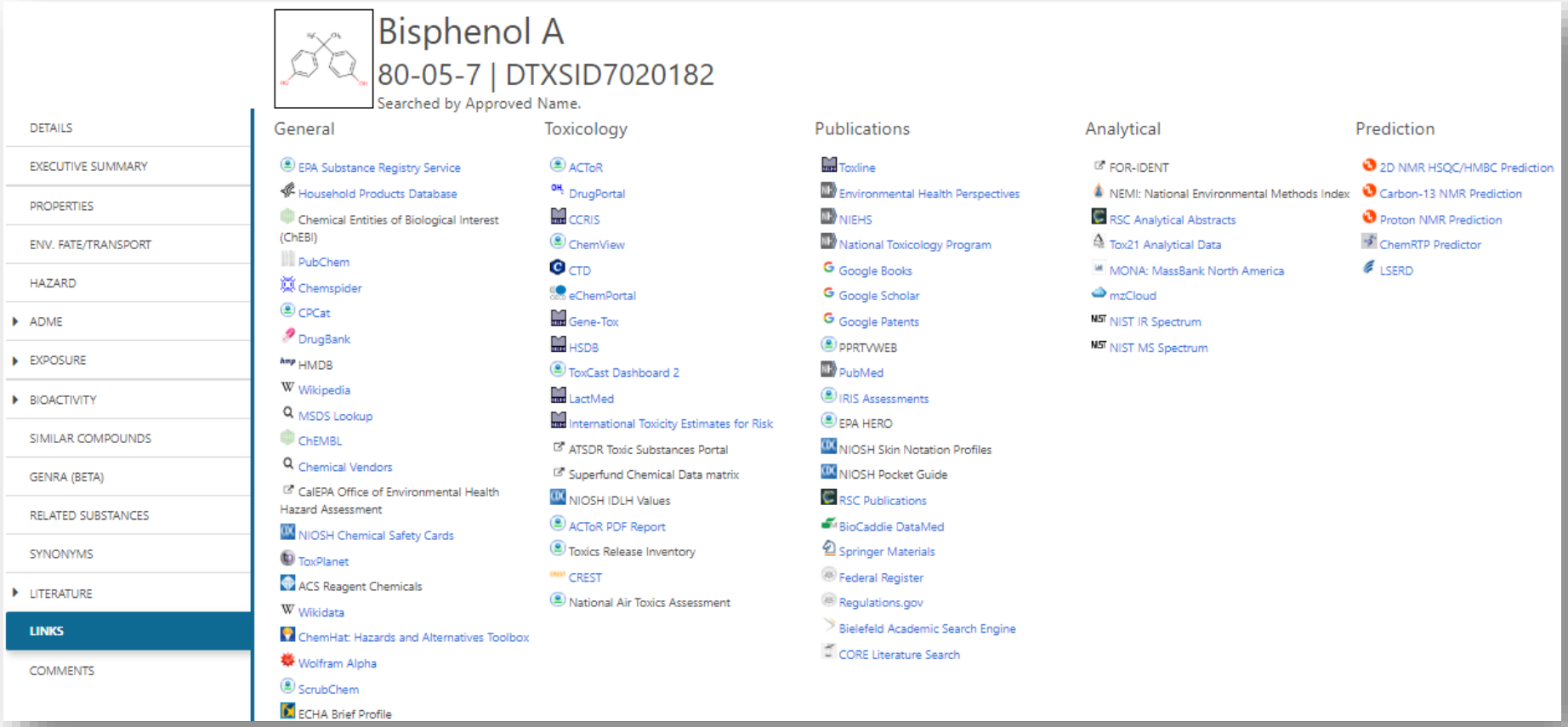
Property

Summary

Download Columns

Property	Experimental average	Predicted average
LogP: Octanol-Water	3.32 (1)	3.29
Melting Point	155 (7)	139
Boiling Point	200 (1)	363
Water Solubility	5.26e-4 (1)	9.62e-4
Vapor Pressure	-	8.37e-7
Flash Point	-	190

Link farm to public resources

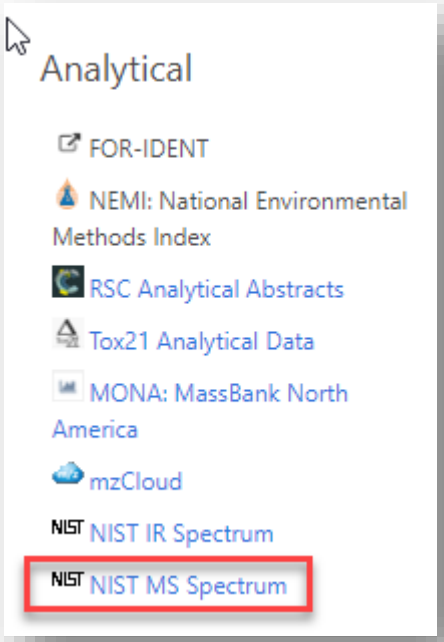


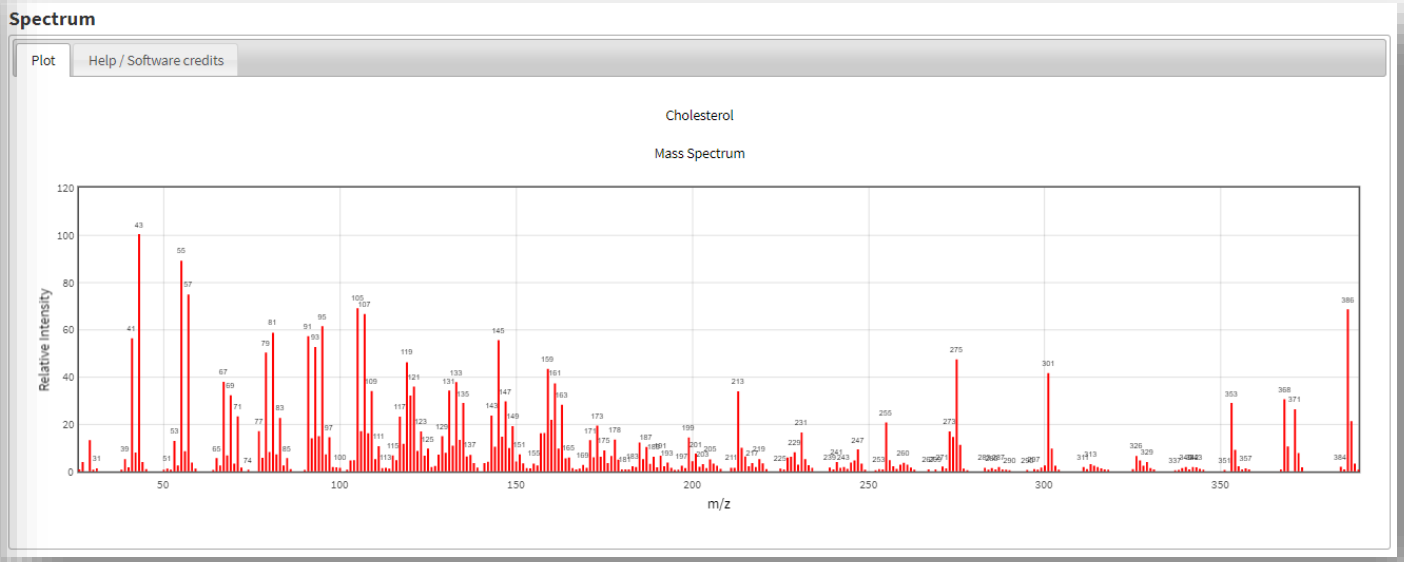
Mass Spec Links

Analytical

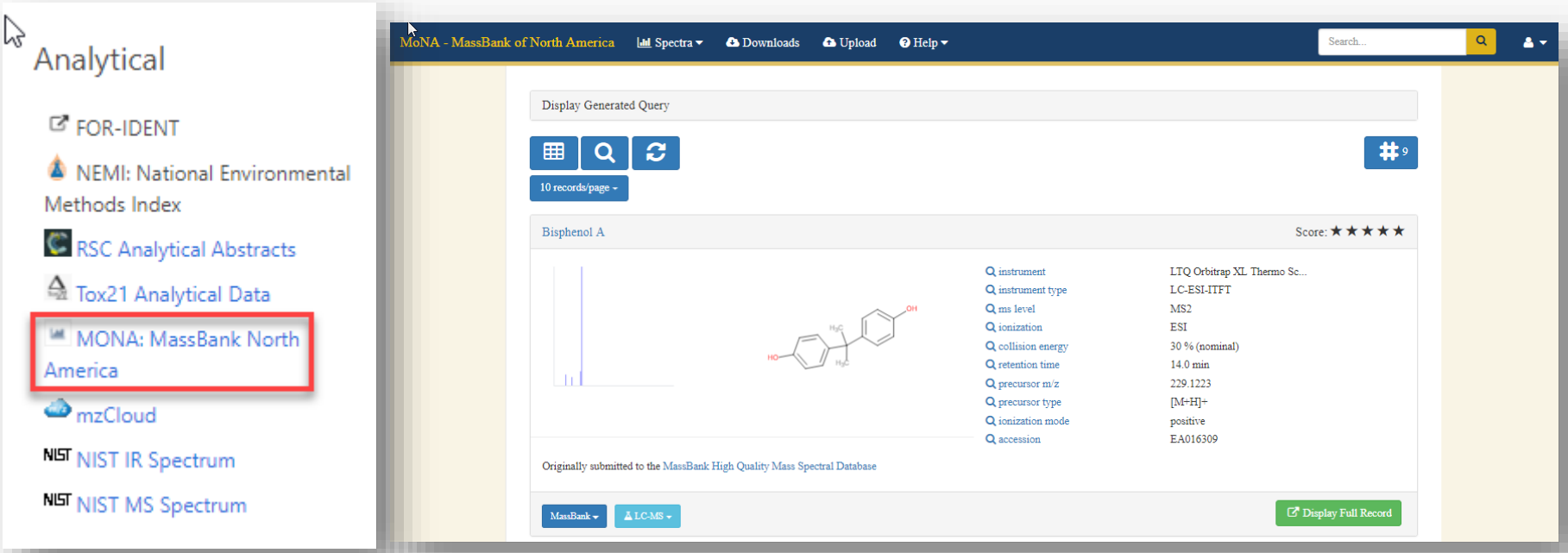
- RSC Analytical Abstracts
- Tox21 Analytical Data
- MONA: MassBank North America
- mzCloud
- NIST IR Spectrum
- NIST MS Spectrum
- MassBank
- NEMI: National Environmental Methods Index
- NIST Antoine Constants
- IR Spectra on PubChem
- NIST Kovats Index values

NIST WebBook
https://webbook.nist.gov/chemistry/



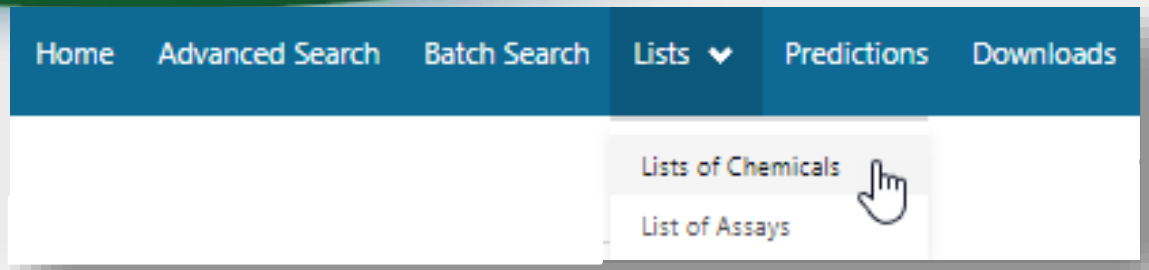


MassBank of North America
https://mona.fiehnlab.ucdavis.edu



Chemical lists

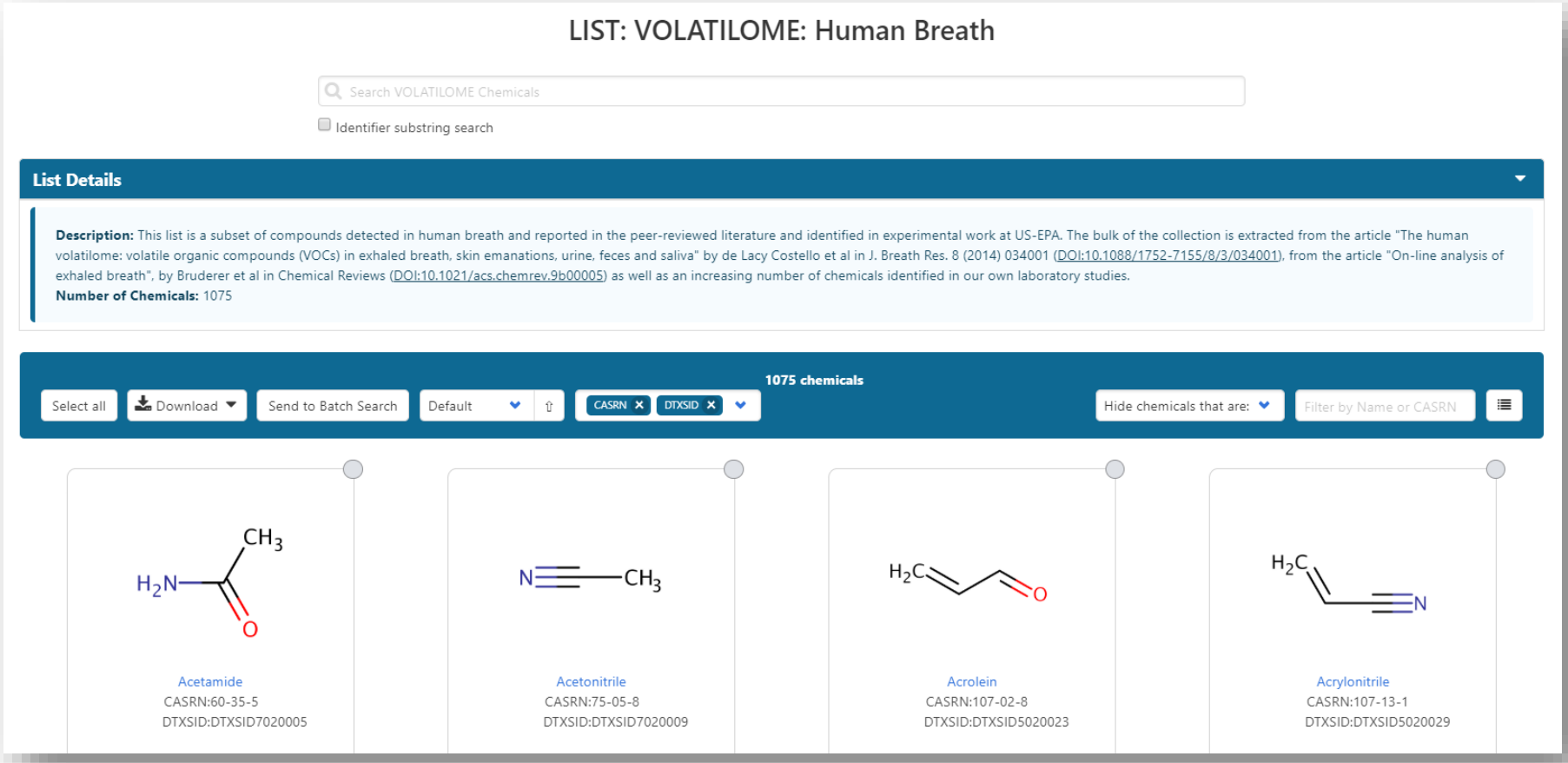
>300 Chemical Lists (and growing)



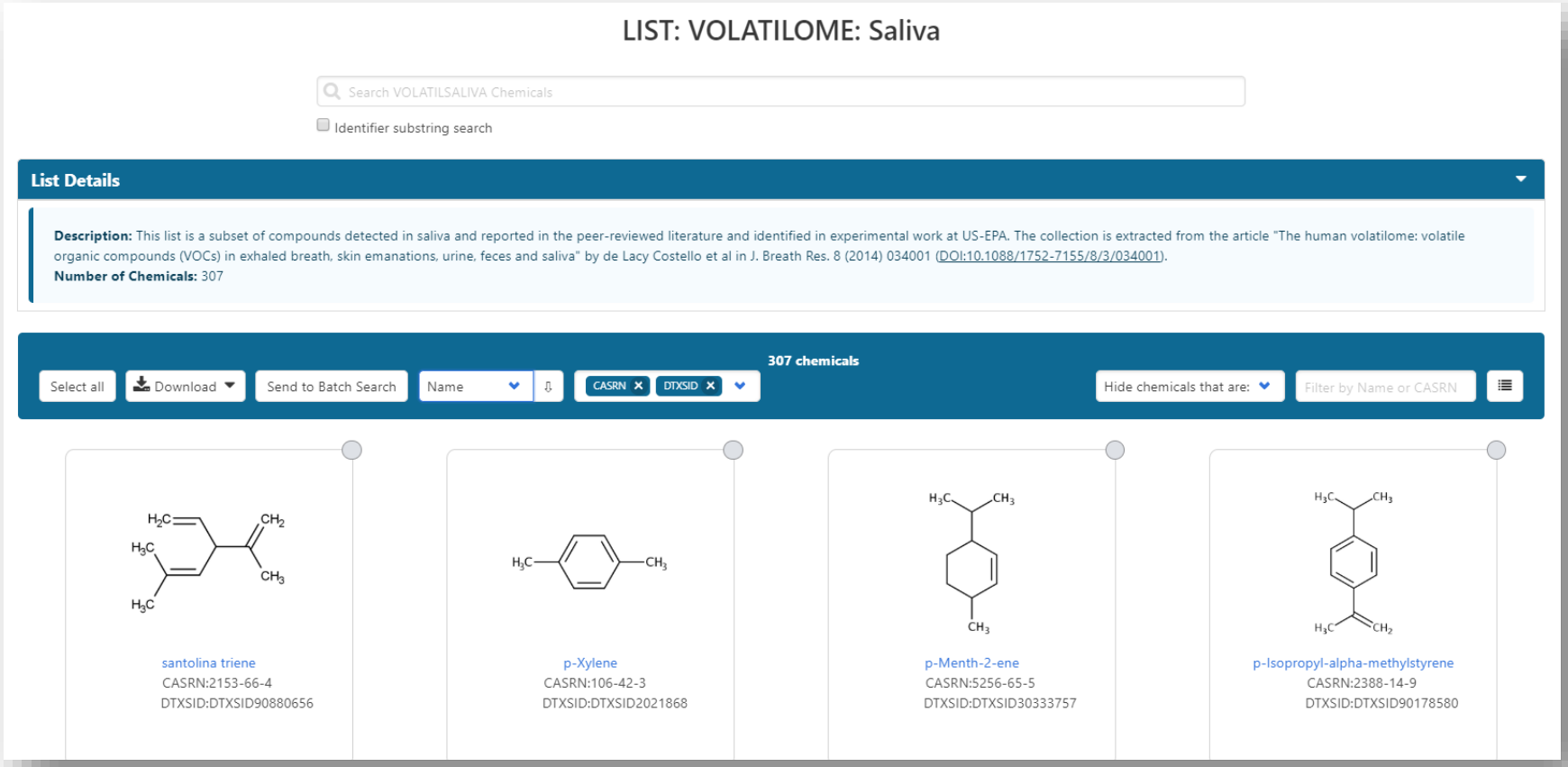
Download | Columns | mass | Copy Filtered Lists URL

List Acronym	List Name	Last Updated	Number of Chemicals	List Description
HDXEXCH	MASSPECDB: Hydrogen Deuterium Exchange Standard Set - Under HDX Conditions	2018-11-07	592	Observed species (deuterated and undeuterated) from the HDXNOEX list under hydrogen deuterium exchange conditions (Ruttkies, Schymanski et al. in prep.)
HDXNOEX	MASSPECDB: Hydrogen Deuterium Exchange Standard Set - No Exchange	2018-11-07	765	Environmental standard set used to investigate hydrogen deuterium exchange in small molecule high resolution mass spectrometry (Ruttkies, Schymanski et al. in prep.)
MASSBANKEUSP	MASSPECDB: MassBank.EU Collection: Special Cases	2017-07-16	263	The MassBank.EU list contains curated chemicals (Schymanski/Williams) associated with the literature/tentative/unknown/SI spectra available on MassBank.EU that are not available as part of the full MassBank collection of reference standard spectra.
MASSBANKREF	MASSPECDB: MassBank Reference Spectra Collection	2017-07-13	1267	This MassBank list contains chemicals associated with the full MassBank collection of reference standard spectra available on MassBank.EU, MassBank.JP and MassBank of North America as well as the Open Data collection, curated by Williams/Schymanski.
MYCOTOXINS	MASSPECDB: Mycotoxins from MassBank.EU	2017-08-02	88	This is a set of mycotoxins, initiated by the contribution of spectra of 90 mycotoxins to MassBank.EU by Justin Renaud and colleagues from Agriculture and Agri-Food Canada, Government of Canada

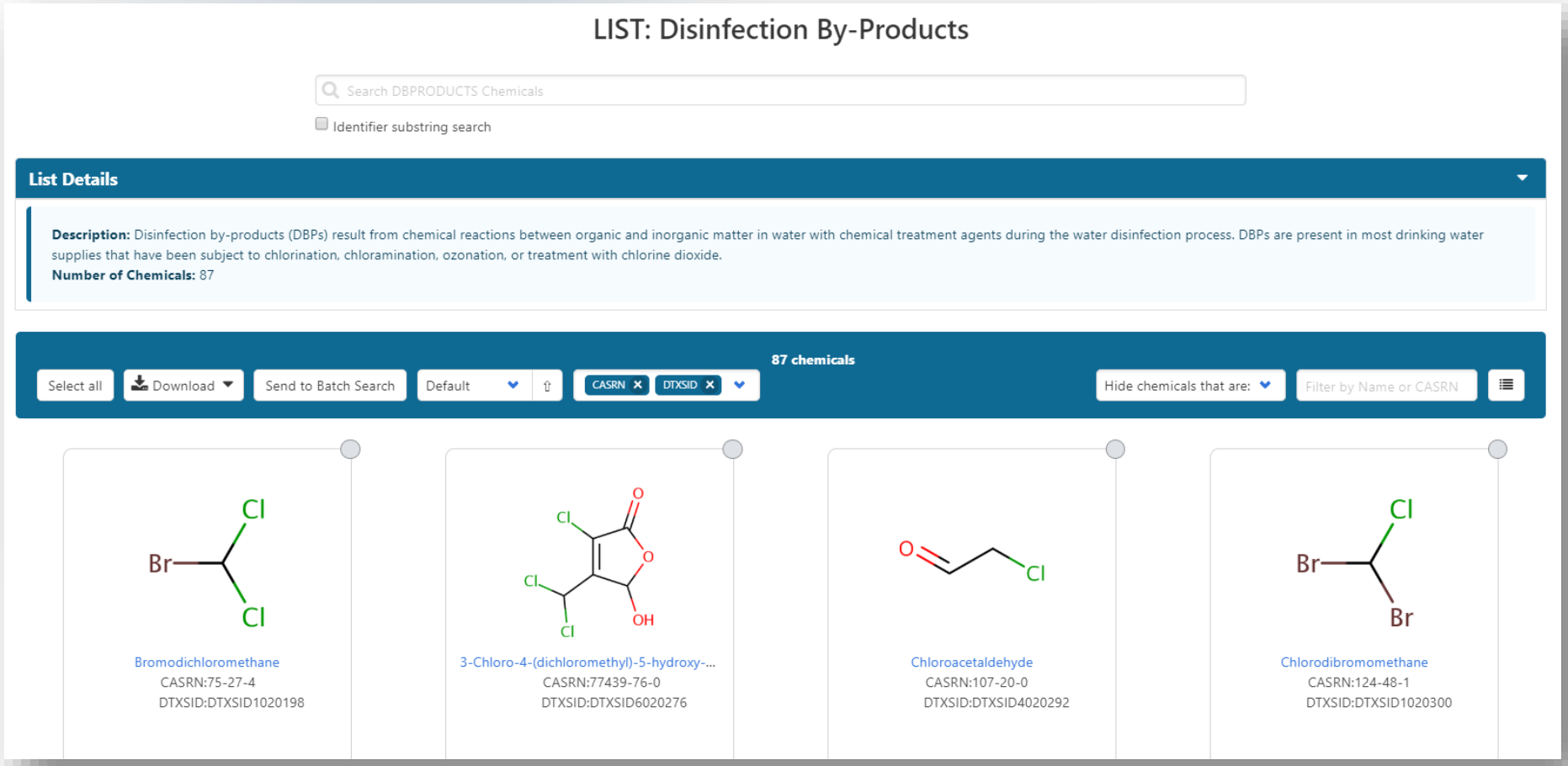
“Volatilome” Human Breath



“Volatilome” Saliva



Disinfection By-Products



Tire Crumb Rubber (298)

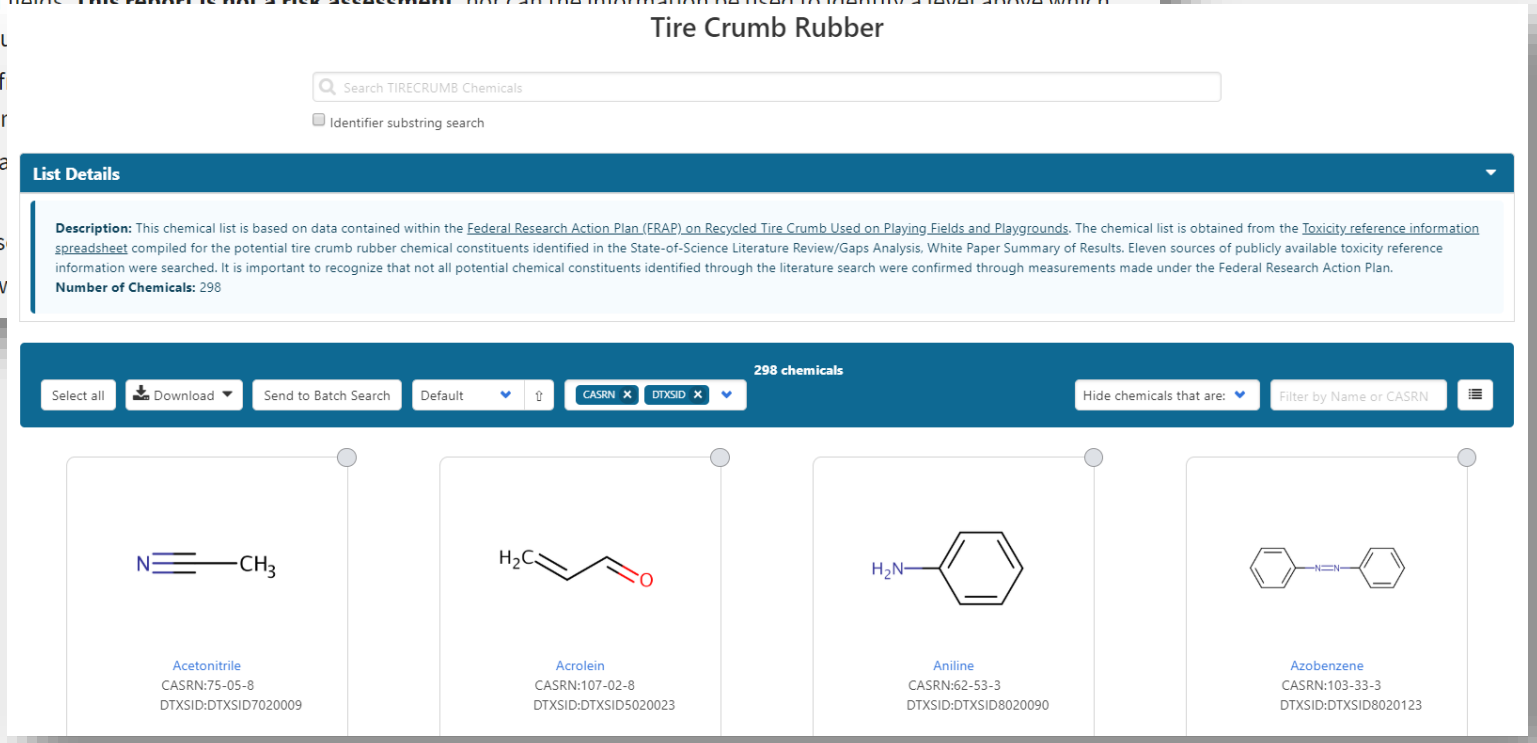
Related Topics: Safer Chemicals Research

CONTACT US SHARE

July 2019 Report: Tire Crumb Rubber Characterization

Key Takeaways:

- EPA is releasing a new report that addresses exposure (that is, chemicals and how people come in contact with these) to tire crumb rubber on synthetic turf fields. **This report is not a risk assessment**, nor can the information be used to identify a level above which health effects could occu
- In general, the findings f human exposure appear
- Only Part 1 is being relea assessment.
- Part 1 of this report pres
- The scope of this study w



Hydraulic Fracturing (1640)

EPA United States Environmental Protection Agency

Contact Us

EPA's Study of Hydraulic Fracturing and Its Potential Impact on Drinking Water Resources

- Hydraulic Fracturing Study Home
- **Final Assessment**
- EPA Published Research
- Fact Sheets
- Questions & Answers about the final assessment
- Multi-agency collaboration on unconventional oil and gas research
- EPA Hydraulic Fracturing - Agency Main Page

Hydraulic Fracturing For Oil And Gas: Impacts From The Hydraulic

WATER|EPA; Chemicals associated with hydraulic fracturing

Search EPAHFR Chemicals

Identifier substring search

List Details

Description: Chemicals used in hydraulic fracturing fluids and/or identified in produced water from 2005-2013, corresponding to chemicals listed in Appendix H of EPA's Hydraulic Fracking Drinking Water Assessment Final Report (Dec 2016). Citation: U.S. EPA, Hydraulic Fracturing for Oil and Gas: Impacts from the Hydraulic Fracturing Water Cycle on Drinking Water Resources in the United States (Final Report). U.S. Environmental Protection Agency, Washington, D.C. EPA/600/R-16/236F, 2016. https://www.epa.gov/hfstudy

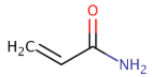
*Note that Appendix H chemical listings in Tables H-2 and H-4 were mapped to current DSSTox content, which has undergone additional curation since the publication of the original EPA HF Report (Dec 2016). In the few cases where a Chemical Name and CASRN from the original report map to distinct substances (as of Jan 2018), both were included in the current EPAHFR chemical listing for completeness; additionally, 34 previously unmapped chemicals in Table H-5 are now registered in DSSTox (all but 2 assigned CASRN) and, thus, have been added to the current EPAHFR listing.

Number of Chemicals: 1640

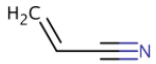
1640 chemicals

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

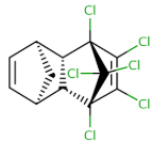
Acrolein
CASRN:107-02-8
DTXSID:DTXSID5020023



Acrylamide
CASRN:79-06-1
DTXSID:DTXSID5020027

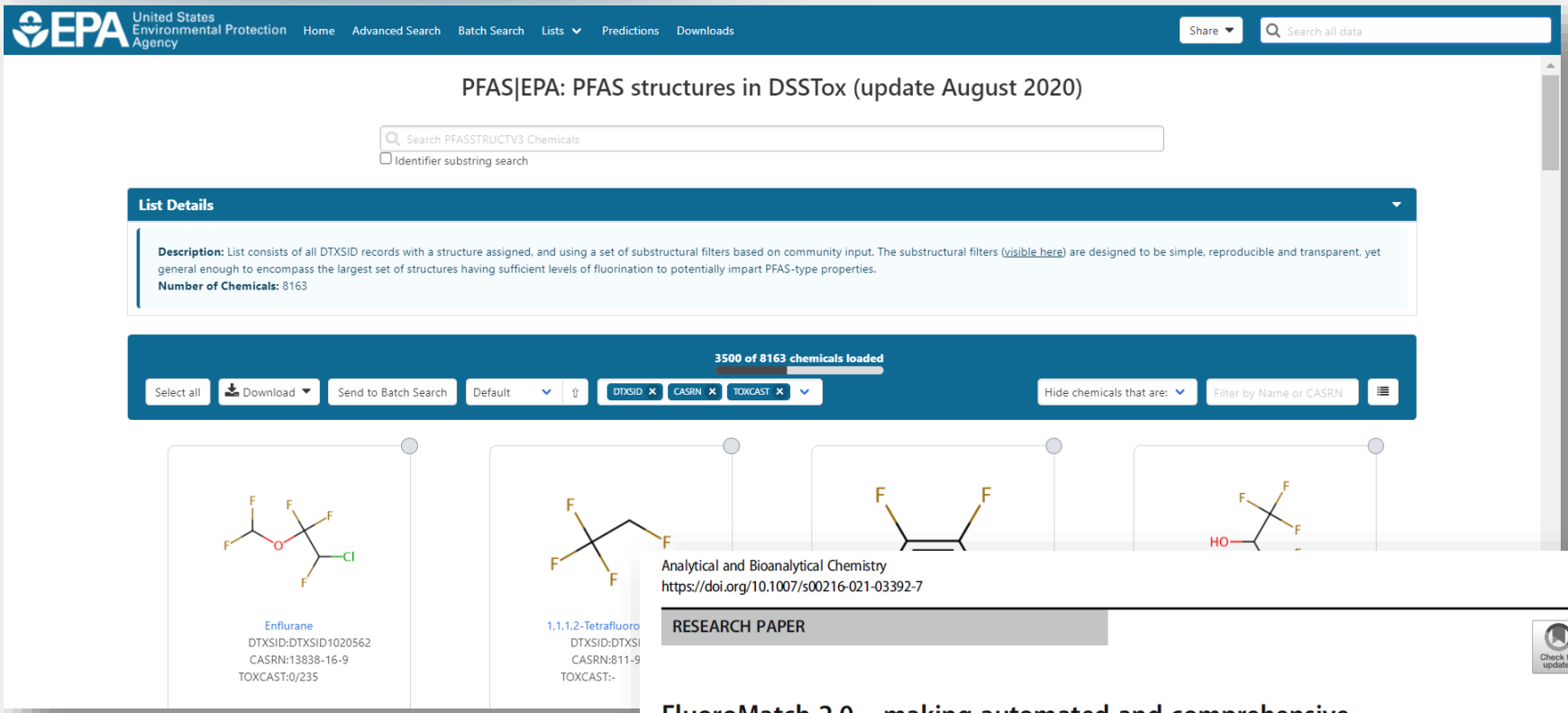


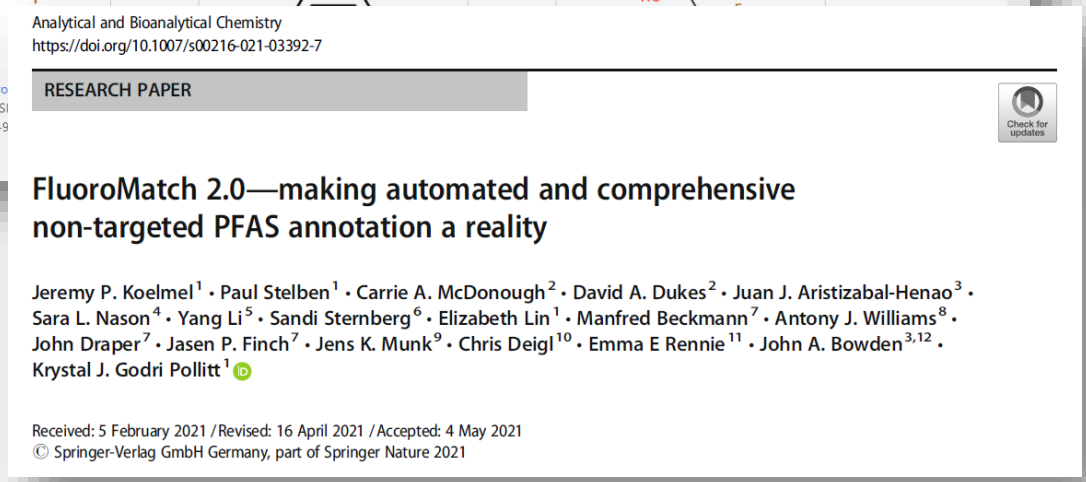
Acrylonitrile
CASRN:107-13-1
DTXSID:DTXSID5020029



Aldrin
CASRN:309-00-2
DTXSID:DTXSID8020040

PFAS Lists


United States Environmental Protection Agency
Home
Advanced Search
Batch Search
Lists
Predictions
Downloads
Share
Search all data
PFAS|EPA: PFAS structures in DSSTox (update August 2020)
Search PFASSTRUCTV3 Chemicals
Identifier substring search
List Details
Description: List consists of all DTXSID records with a structure assigned, and using a set of substructural filters based on community input. The substructural filters (visible here) are designed to be simple, reproducible and transparent, yet general enough to encompass the largest set of structures having sufficient levels of fluorination to potentially impart PFAS-type properties.
Number of Chemicals: 8163
3500 of 8163 chemicals loaded
Select all
Download
Send to Batch Search
Default
DTXSID
CASRN
TOXCAST
Hide chemicals that are:
Filter by Name or CASRN
Enflurane
DTXSID:DTXSID1020562
CASRN:13838-16-9
TOXCAST:0/235
1,1,1,2-Tetrafluoro
DTXSID:DTXSI
CASRN:811-9
TOXCAST:-


Analytical and Bioanalytical Chemistry
https://doi.org/10.1007/s00216-021-03392-7
RESEARCH PAPER
Check for updates
FluoroMatch 2.0—making automated and comprehensive non-targeted PFAS annotation a reality
Jeremy P. Koelmel[1] · Paul Stelben[1] · Carrie A. McDonough[2] · David A. Dukes[2] · Juan J. Aristizabal-Henao[3] · Sara L. Nason[4] · Yang Li[5] · Sandi Sternberg[6] · Elizabeth Lin[1] · Manfred Beckmann[7] · Antony J. Williams[8] · John Draper[7] · Jasen P. Finch[7] · Jens K. Munk[9] · Chris Deigl[10] · Emma E Rennie[11] · John A. Bowden[3,12] · Krystal J. Godri Pollitt[1]
Received: 5 February 2021 / Revised: 16 April 2021 / Accepted: 4 May 2021
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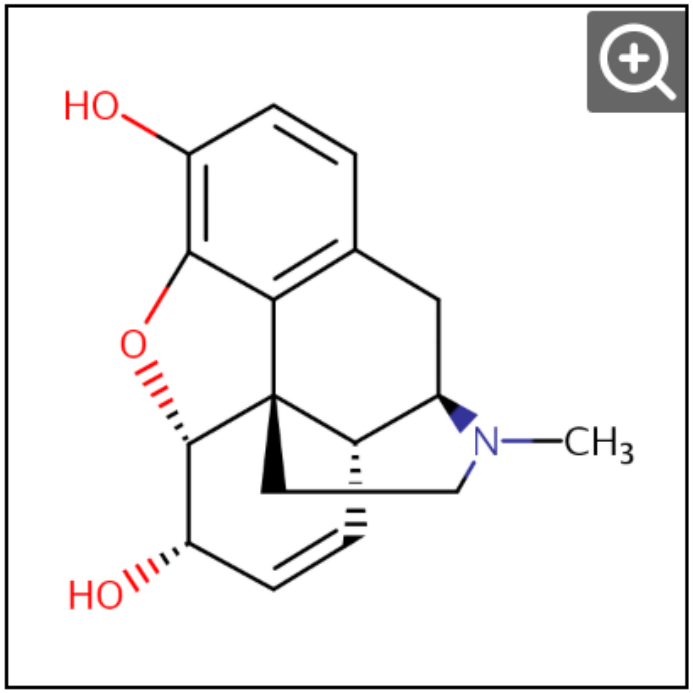
Related Searches to Support Mass Spectrometry

Find me “related structures” Formula-Based Search



Wikipedia

Morphine is a pain medication of the opiate family which is found naturally in a number of plants and animals. It acts directly on the central nervous system (CNS) to decrease the feeling of pain. It can be taken for both acute pain and chronic pain. It is frequently used for pain from myocardial infarction and during labor. It can be given by mouth, by injection into a muscle, by injection under the skin, intravenously, injection into the space around the

...

Read more

Intrinsic Properties

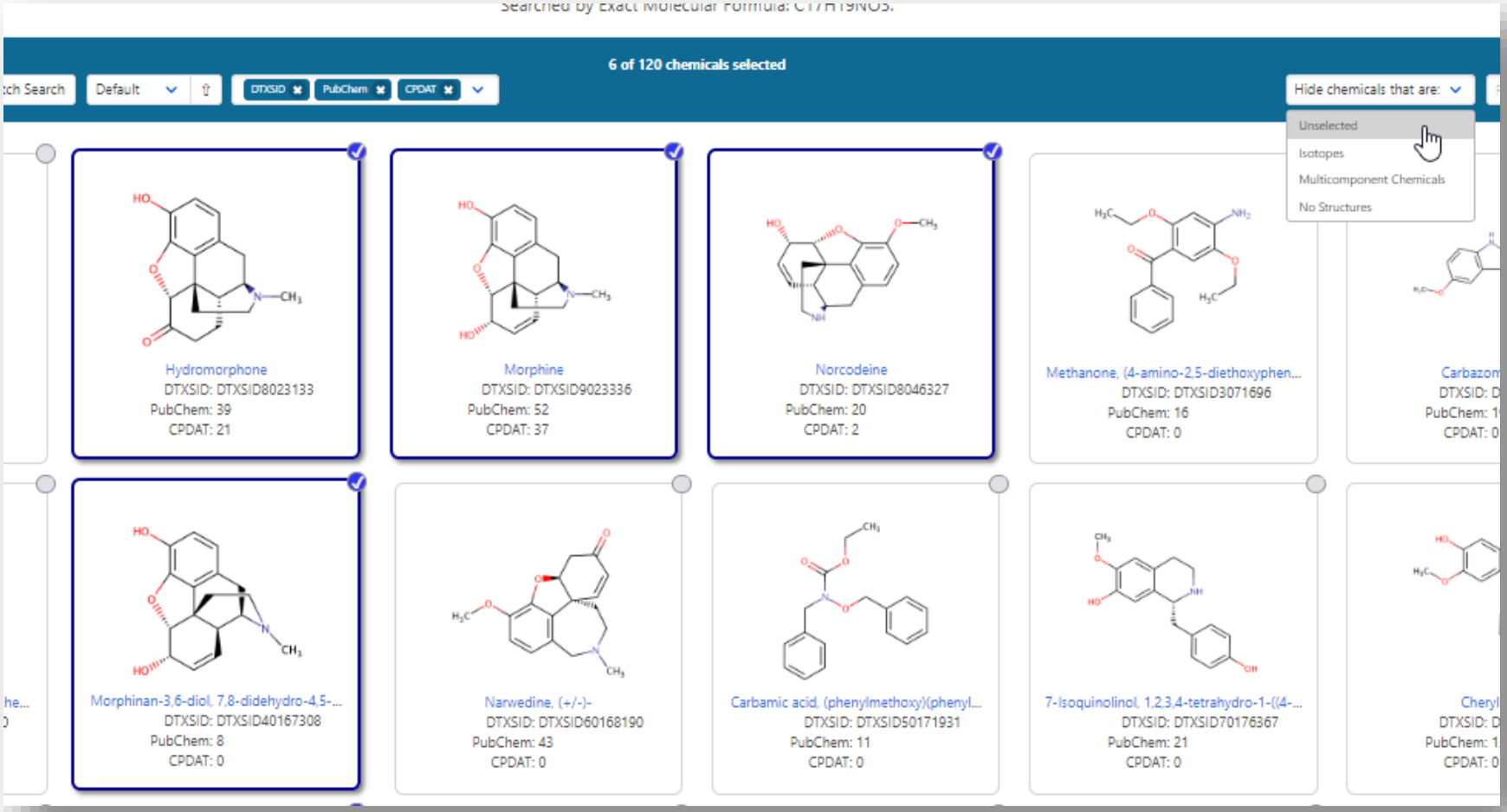
Molecular Formula: $C_{17}H_{19}NO_3$ Mol File Find All Chemicals

Average Mass: 285.343 g/mol Isotope Mass Distribution

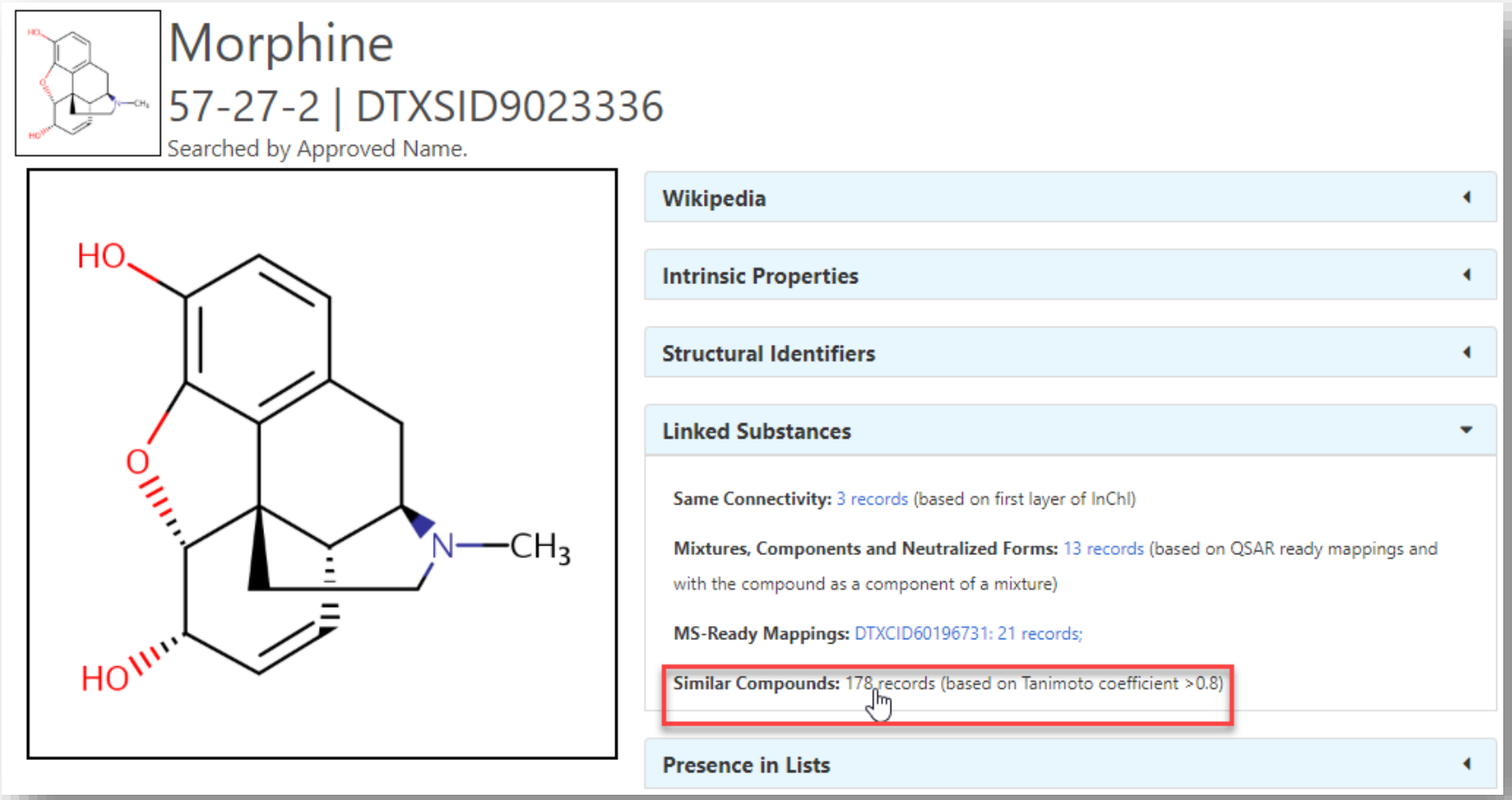
Monoisotopic Mass: 285.136493 g/mol

Structural Identifiers

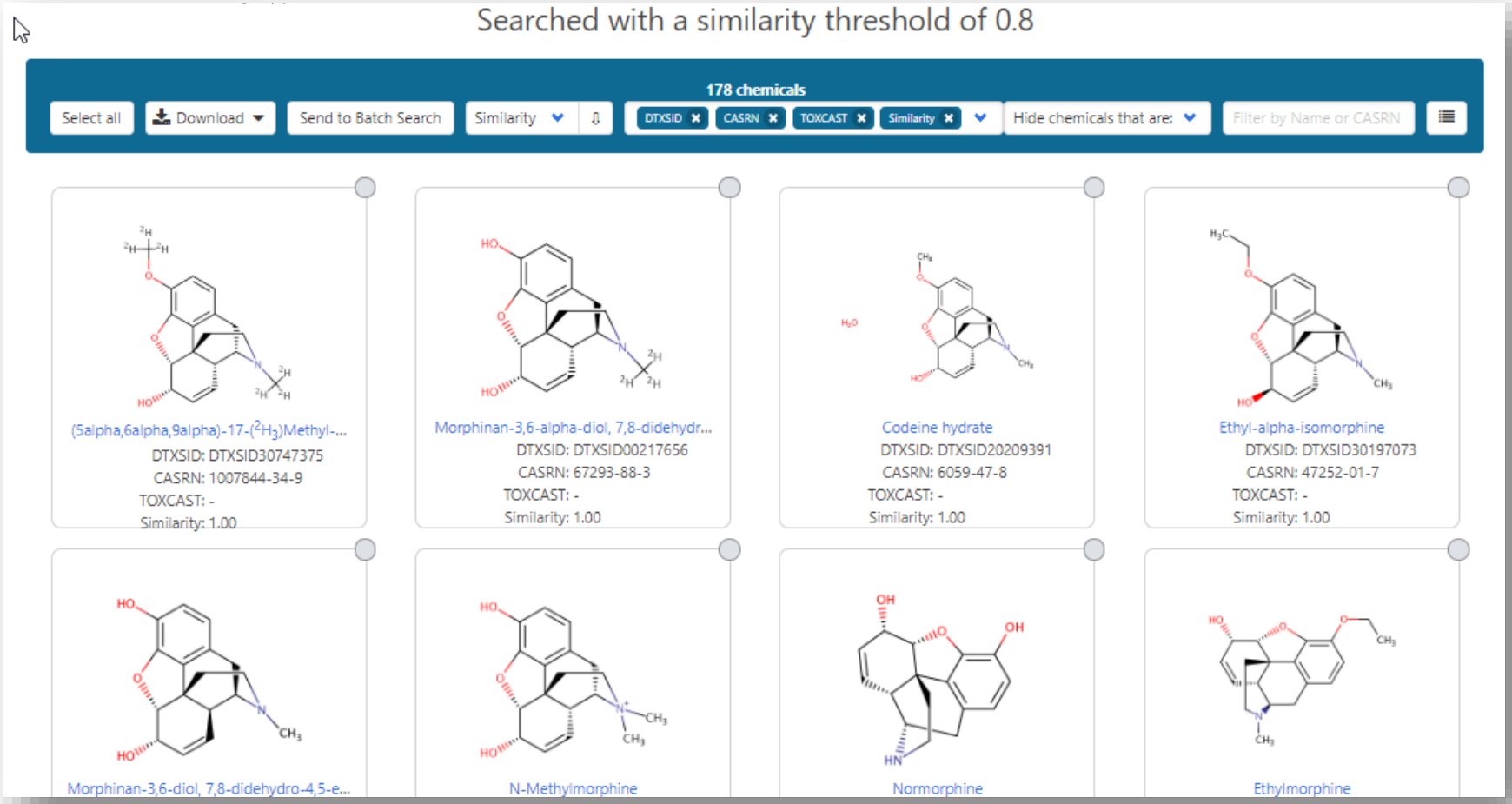
Select Chemicals of Interest



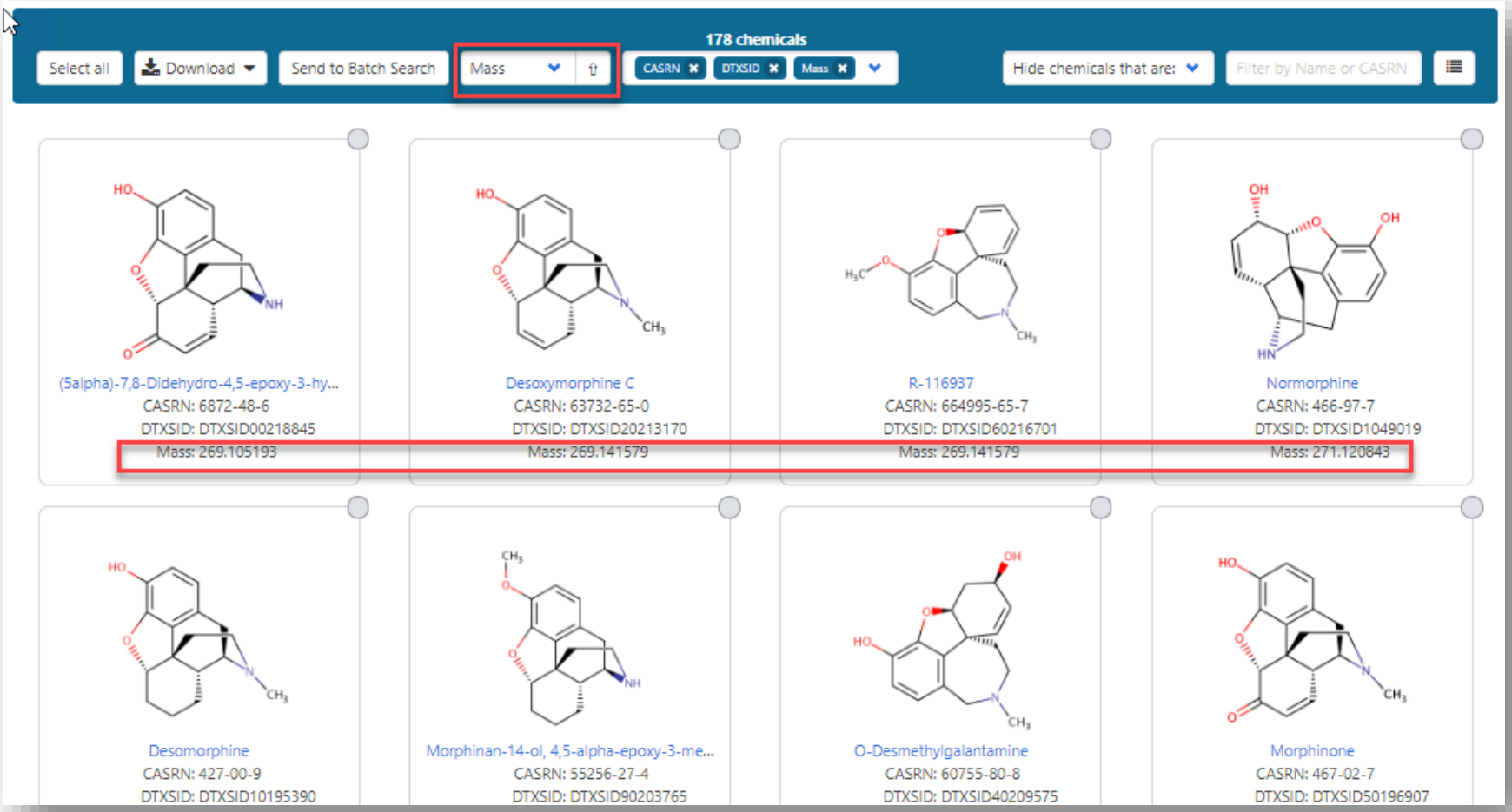
Find me “related structures” Based on Structure Similarity



Find me “related structures” Based on Structure Similarity

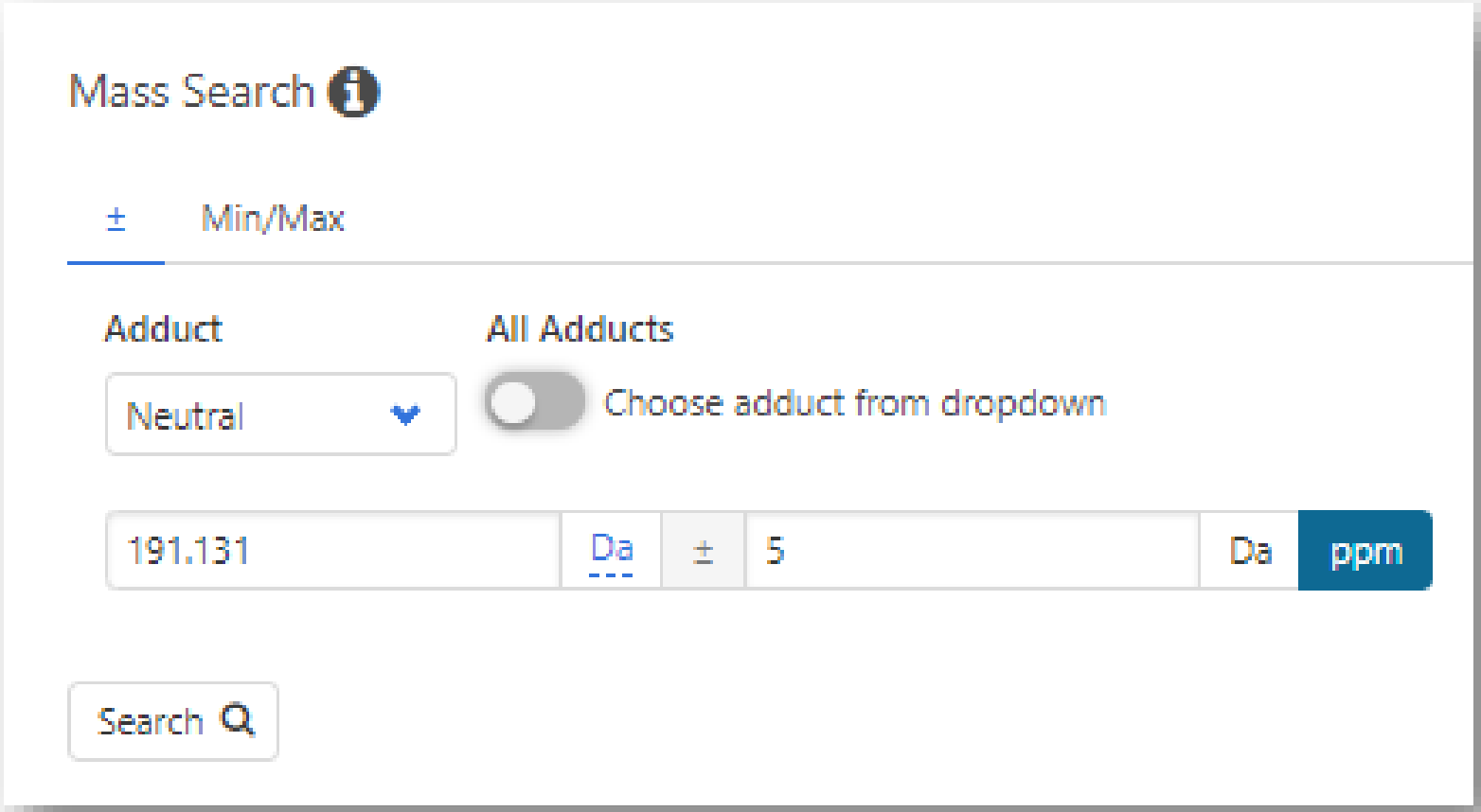


Find me “related structures”
Structure Similarity – sort on mass

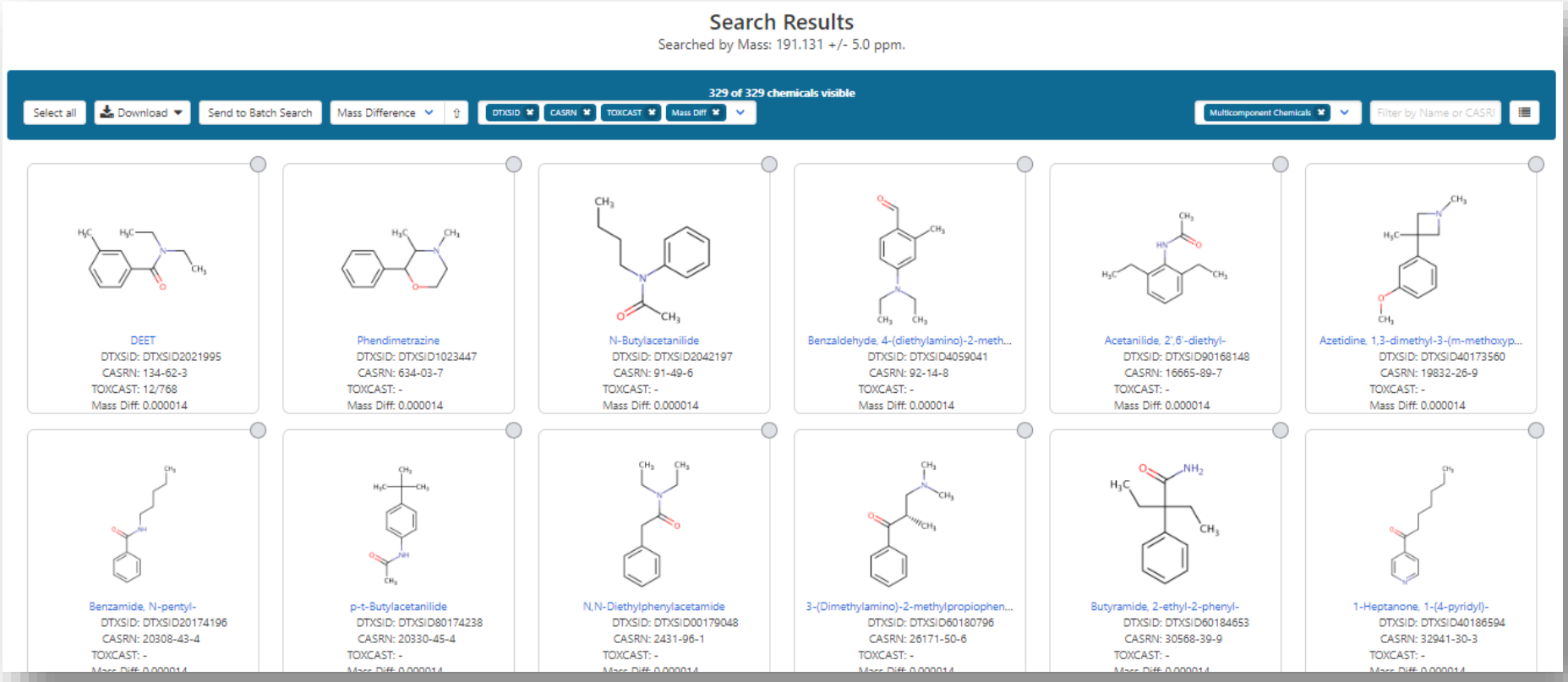


Mass & Formula Searching

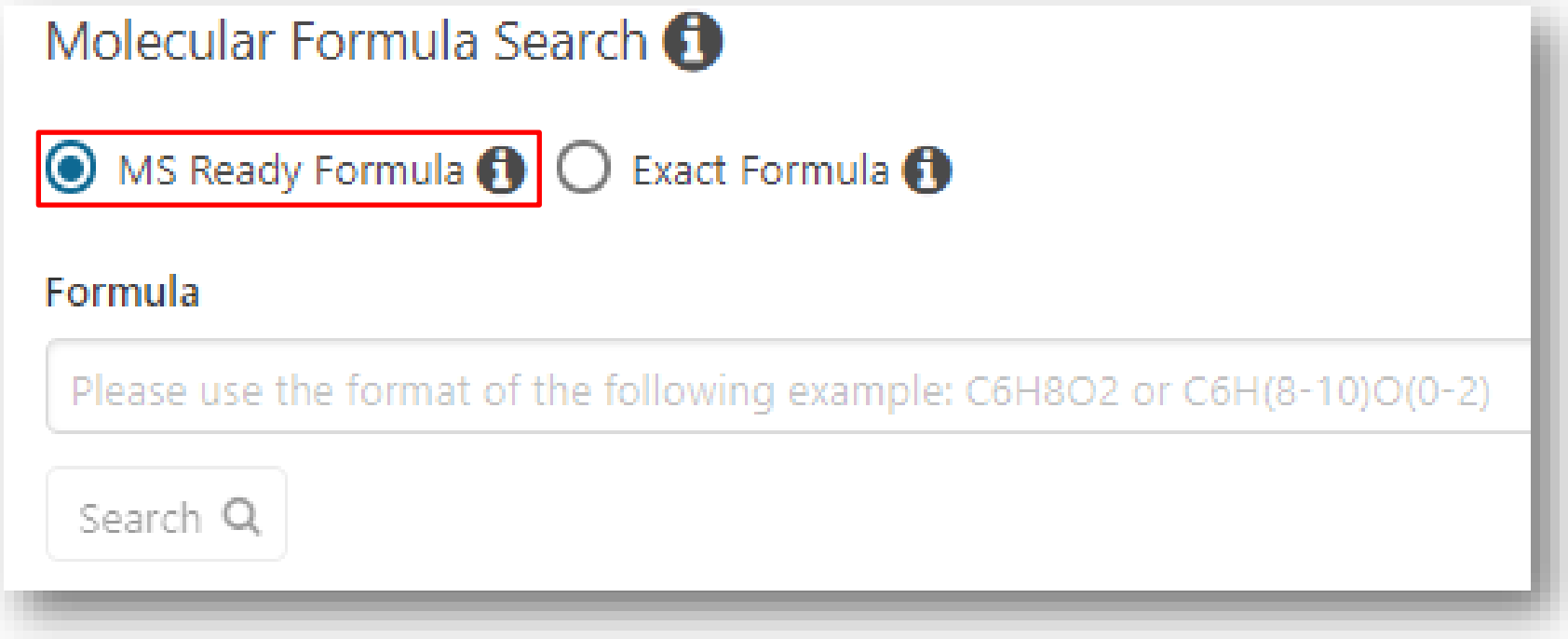
Advanced Searches
Mass Search



Advanced Searches
Mass Search



MS-Ready Structures for **Formula Search**



“MS-Ready Structures”

https://doi.org/10.1186/s13321-018-0299-2

McEachran *et al. J Cheminform (2018) 10:45*
https://doi.org/10.1186/s13321-018-0299-2

Journal of Cheminformatics

METHODOLOGY

Open Access

“MS-Ready” structures for non-targeted high-resolution mass spectrometry screening studies

Andrew D. McEachran[1,2*], Kamel Mansouri[1,2,3], Chris Grulke[2], Emma L. Schymanski[4], Christoph Ruttkies[5] and Antony J. Williams[2*]

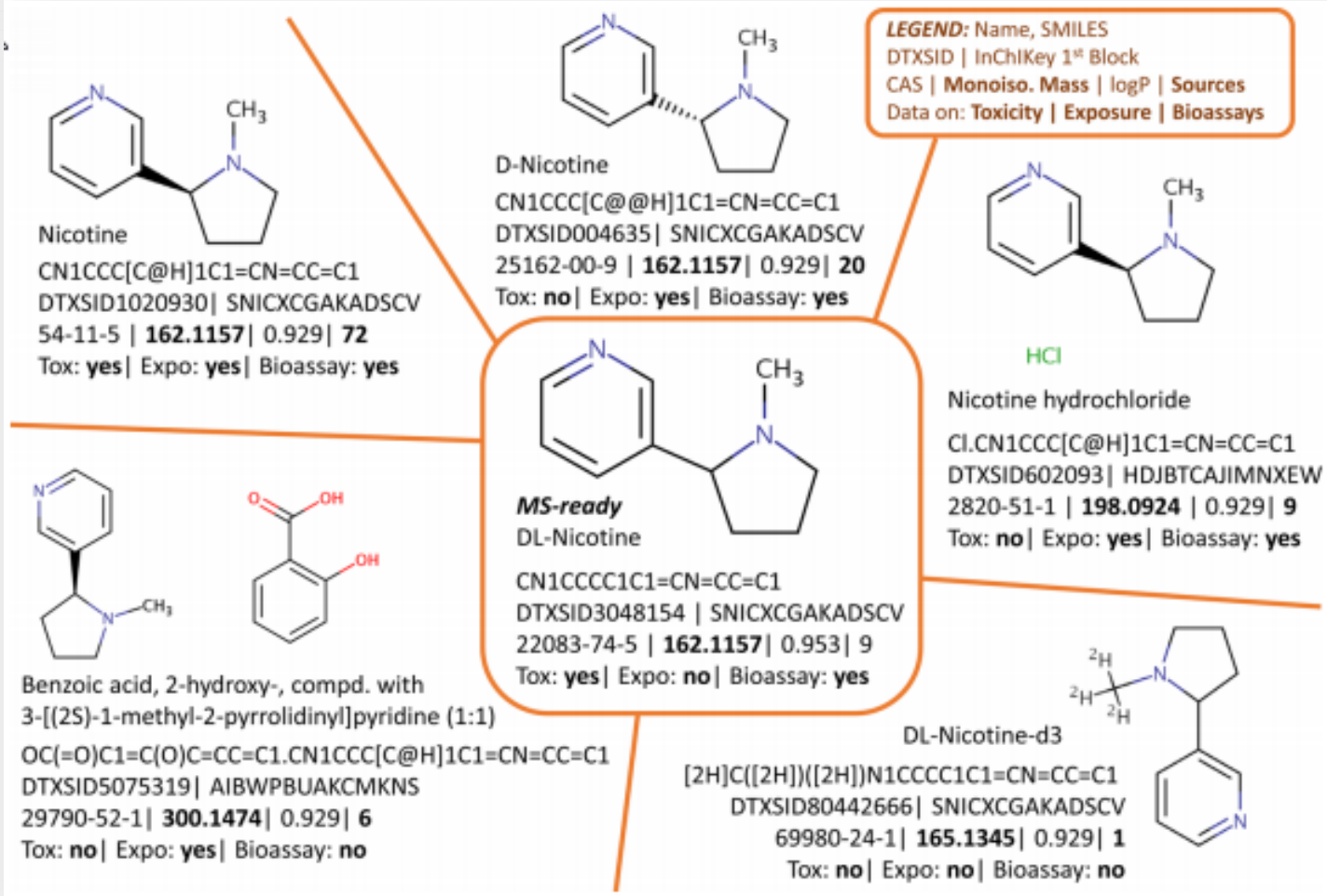
Environmental Science & Technology

Viewpoint

pubs.acs.org/est

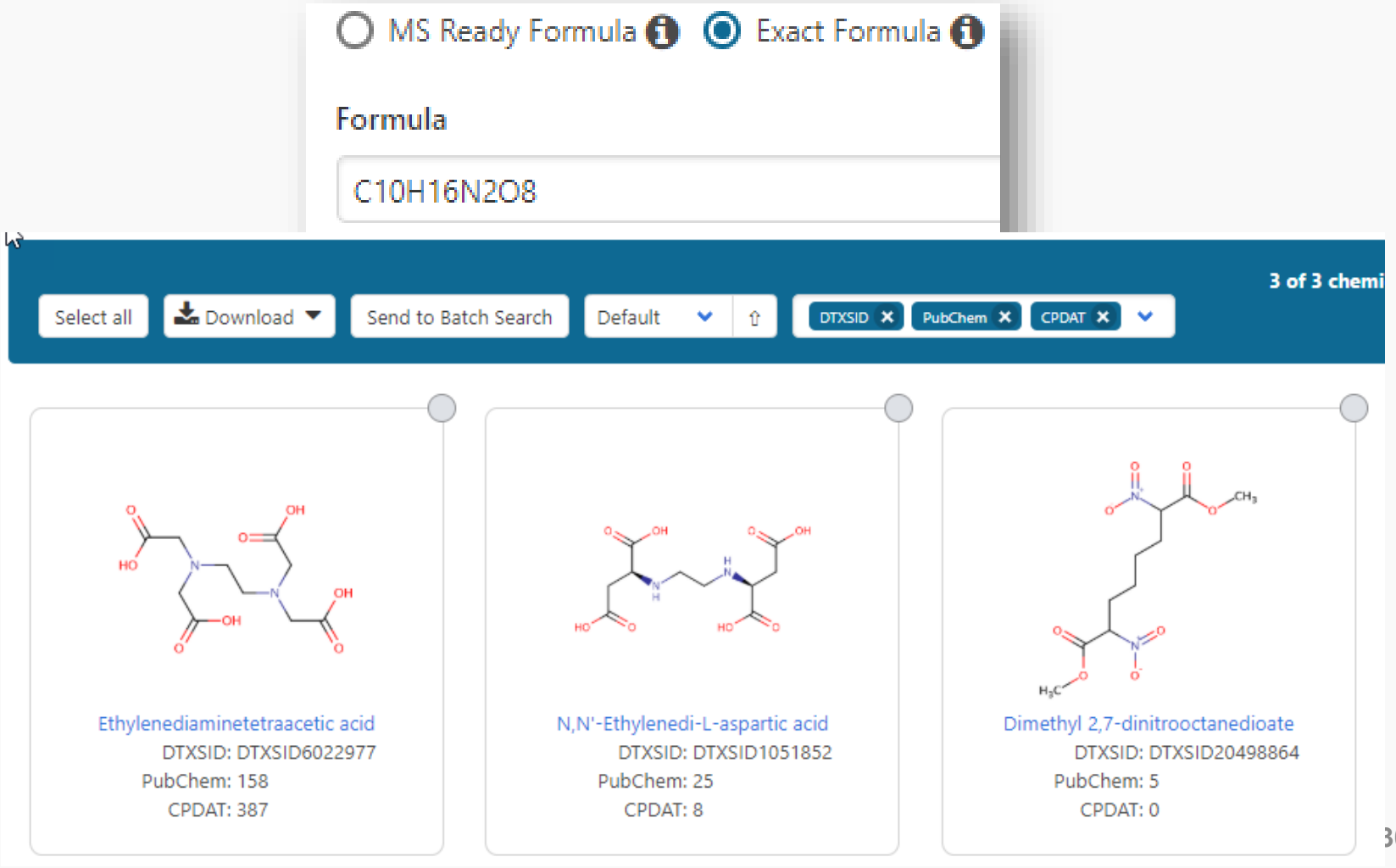
Open Science for Identifying "Known Unknown" Chemicals

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



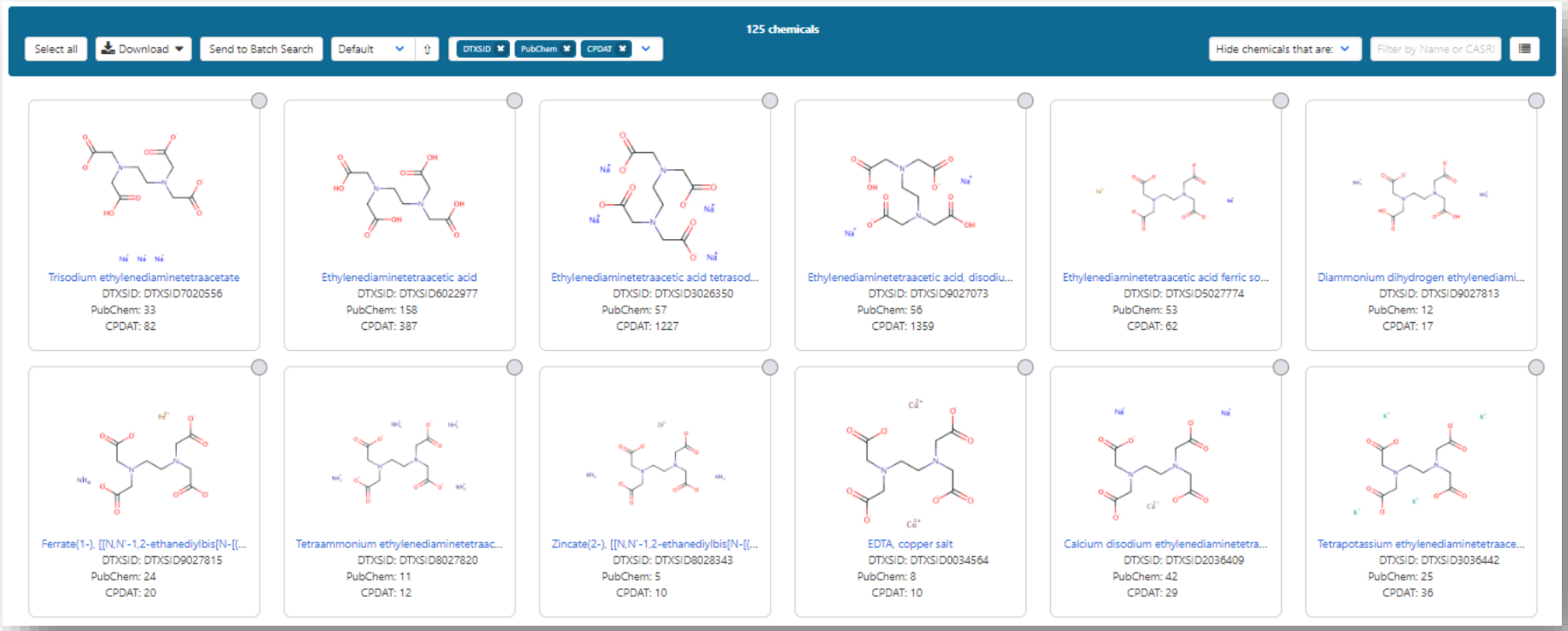
MS-Ready Mappings

- **EXACT Formula**: C10H16N2O8: 3 Hits



MS-Ready Mappings

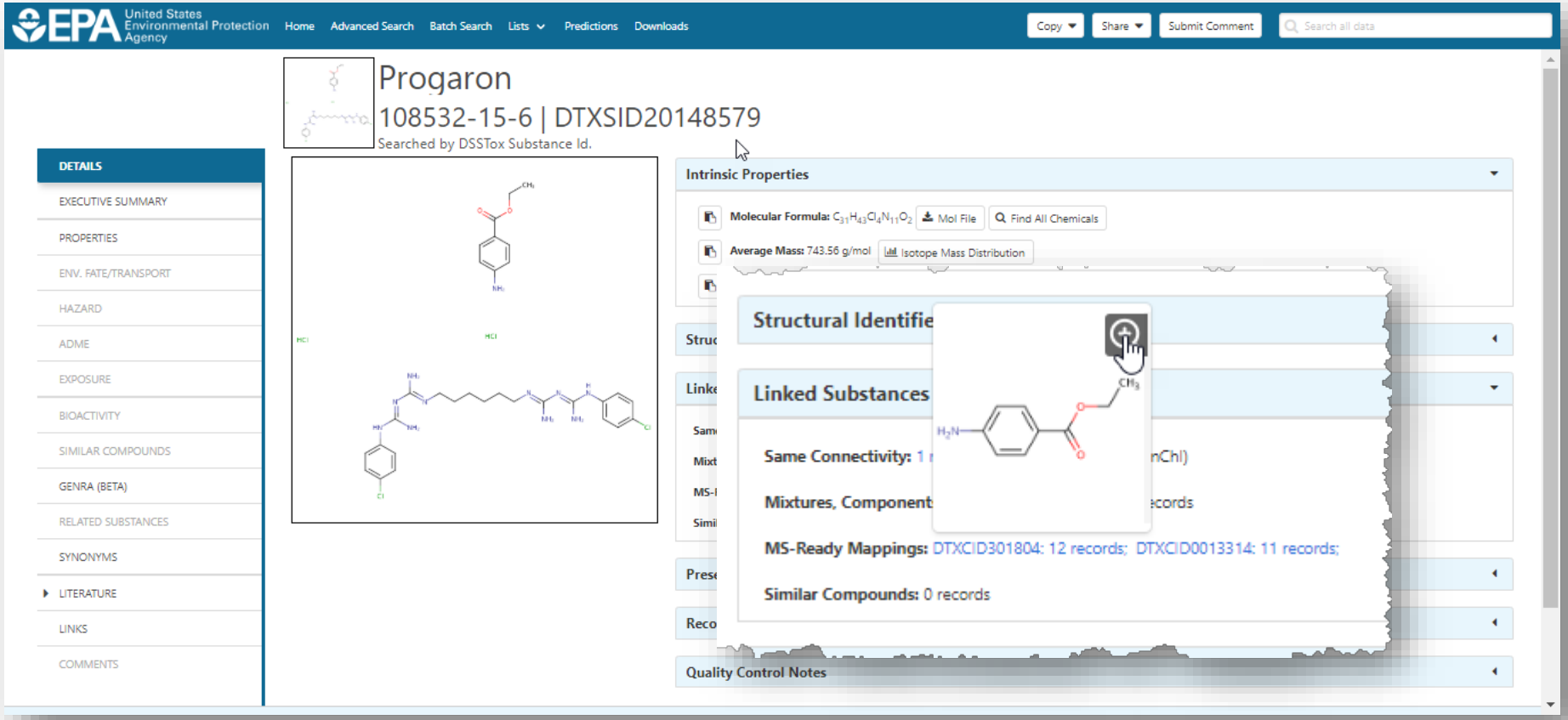
- **Same** Input Formula: C10H16N2O8
- **MS Ready Formula** Search: **125** Chemicals



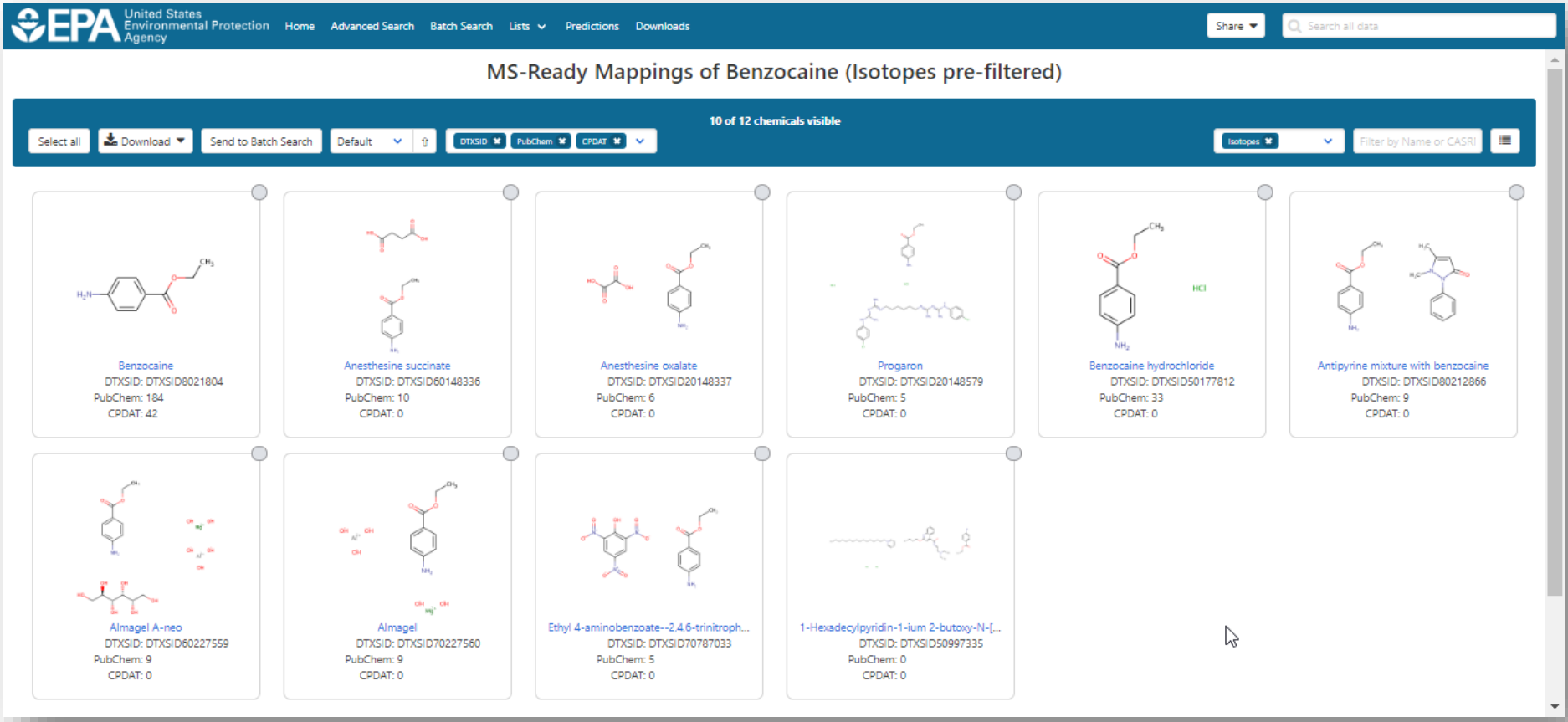
MS-Ready Mappings

- 125 chemicals returned in total
  - 8 of the 125 are **single component** chemicals
  - 3 of the 8 are **isotope-labeled**
  - 3 are **neutral compounds** and 2 are **charged**

MS-Ready Mappings



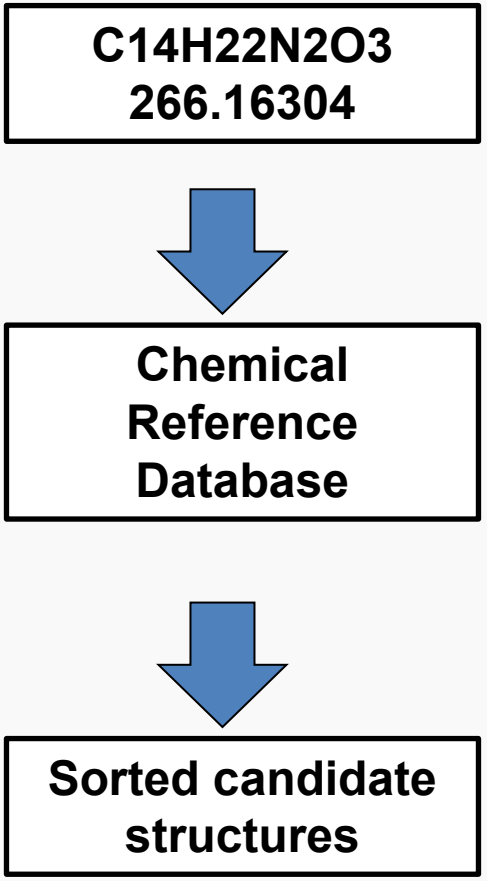
MS-Ready Mappings Set



Candidate ranking

Data Source Ranking of "known unknowns"

- Mass and/or formula is for an unknown chemical but contained within a reference database
- Most likely candidate chemicals have the most associated data sources, most associated lit. articles or both



Is a bigger database better?

J. Am. Soc. Mass Spectrom. (2012) 23:179–185
DOI: 10.1007/s13361-011-0265-y

RESEARCH ARTICLE

Identification of "Known Unknowns" Utilizing Accurate Mass Data and ChemSpider

- ChemSpider was 26 million chemicals then
- Much BIGGER today
- Is bigger better??

110 Million
chemical structures

Using Metadata for Ranking

- Use available metadata to rank candidates
  - Associated data sources
    - Associated lists in the underlying database
    - Associated data sources in PubChem
    - Specific types (e.g. water, surfactants, pesticides etc.)
  - Number of associated literature articles (Pubmed)
  - **Chemicals in the environment** – the number of products/categories containing the chemical is a very important source of data

Comparing Search Performance

Anal Bioanal Chem (2017) 409:1729–1735
DOI 10.1007/s00216-016-0139-z

RAPID COMMUNICATION

Identifying known unknowns using the US EPA's CompTox Chemistry Dashboard

Andrew D. McEachran[1] · Jon R. Sobus[2] · Antony J. Williams[3]

- Dashboard content *was* 720k chemicals
- Only 3% of ChemSpider size
- What was the comparison in performance?

SAME dataset for comparison

Compound class	Number in class	Average rank	Number of compounds in each position rank-ordered				
			#1	#2	#3	#4	#5+
Pharmaceutical drug	72	1.4	55	9	6	2	
Industrial chemicals	42	5.5	28	6	3		5
Personal care products	8	6.1	3	1			4
Steroid hormones	7	1.0	7				
Perfluorochemicals	6	1.2	5	1			
Pesticides	12	2.3	6	2	3		1
Veterinary drugs	3	1.3	2	1			
Dyes	2	1.0	2				
Food product/natural compounds	4	3.8	2			1	1
Illicit drugs	2	2.0	1		1		
Misc. molecules	3 [a]	1.3	2	1			

How did performance compare?

	Mass-based searching		Formula-based searching	
	Dashboard	ChemSpider	Dashboard	ChemSpider
Average rank position	1.3	2.2[a]	1.2	1.4
Percent in #1 position	85%	70%	88%	80%

[a] Average rank in ChemSpider shown here does not include an outlier where the rank was 201, when added the average rank position is 3.5

For the same 162 chemicals, Dashboard outperforms ChemSpider

How did performance compare?

Summary statistics and rank-ordered position in the CompTox Chemistry Dashboard and ChemSpider of the 89 compound subset from the Little et al. [7] study

		Average rank	Number in each position rank-ordered				
		(±SD)	#1	#2	#3	#4	#5+
Mass-based	Dashboard	1.2 ± 0.7	77[a]	5	3	3	
	ChemSpider	2.2 ± 6.1[b]	68	8	7	1	5
Formula-based	Dashboard	1.1 ± 0.4	78[a]	8	2		
	ChemSpider	1.3 ± 1.0	77	8	2	1	2

[a]One chemical (tephrosin) not present in the Dashboard

Will the correct Microcystin LR Stand Up? ChemSpider Skeleton Search

Matches any text strings used to describe a molecule.

ZYZCGGRZINLQBL

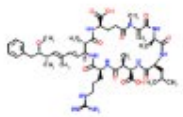
Systematic Name, Synonym, Trade Name, Registry Number, SMILES, InChI or CSID

FILTER

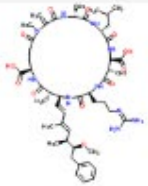
Search Hits Limit: 100

Found 9 results

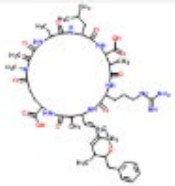
Search term: **ZYZCGGRZINLQBL** (Found by InChIKey (skeleton match))



Cyanoginosin

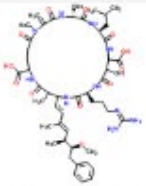


MCYST-LR

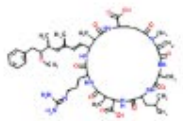


15-(3-Carbamimidamidopropyl)-8-isobutyl-18-[(1E,3E)-6-methoxy-3,5-dimethyl-7-phenyl-1,3-heptadien-1-

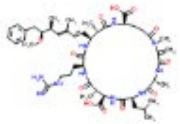
(5R,8S,11R,12S,15S,18R,19S,22R)-15-(3-Carbamimidamidopropyl)-8-isobutyl-18-[(1E,3E,5S,6S)-6-methoxy-3,5-



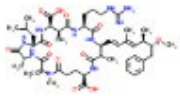
(5R,8S,15S)-15-(3-[(Diaminomethylene)amino]propyl)-8-isobutyl-18-[(1E,3E,5S,6S)-6-methoxy-



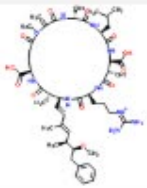
15-(3-[(Diaminomethylene)amino]propyl)-8-isobutyl-18-(6-methoxy-3,5-dimethyl-7-



(5R,8S,11R,12S,15S,18S,19S,22R)-15-(3-Carbamimidamidopropyl)-8-isobutyl-18-[(1E,5S,6S)-6-methoxy-3,5-dimethyl-

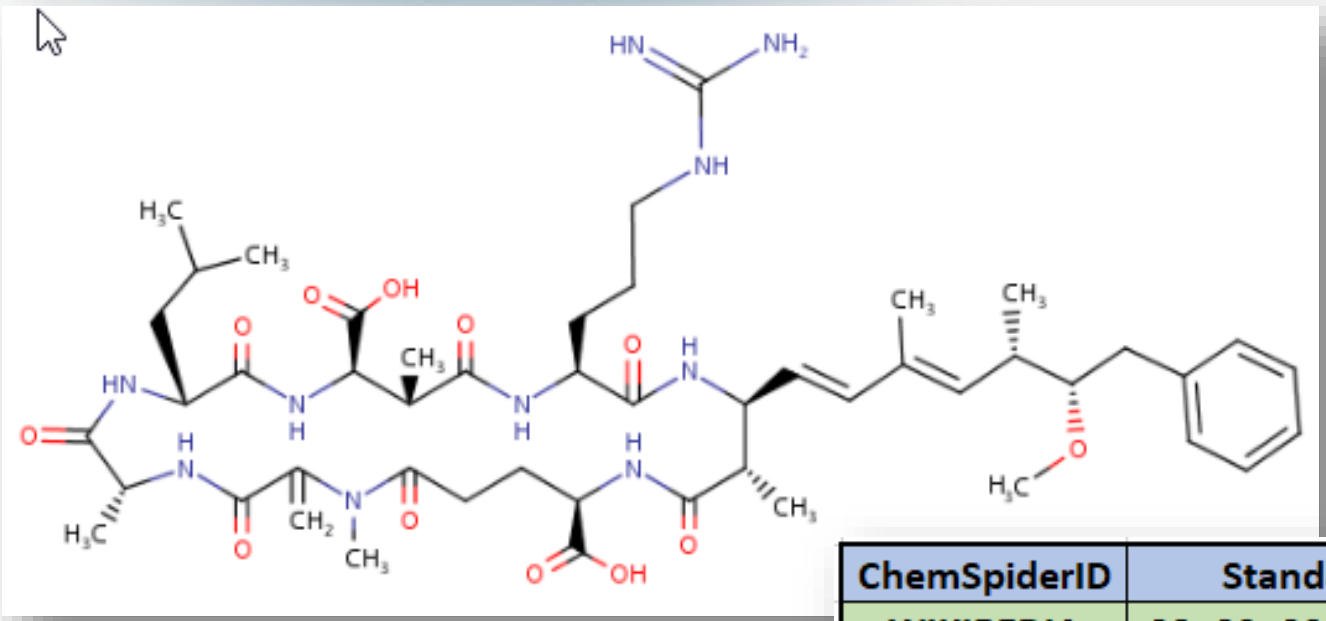


(5R,8R,11R,12S,15S,18S,22R)-15-(3-Carbamimidamidopropyl)-8-isobutyl-18-[(1E,3E,5R,6R)-6-methoxy-3,5-dimethyl-



Diamino-N-(3-{(5R,8S,11R,12S,15S,18S,19S,22R)-11,22-dicarboxy-8-isobutyl-18-

Comparing ChemSpider Structures

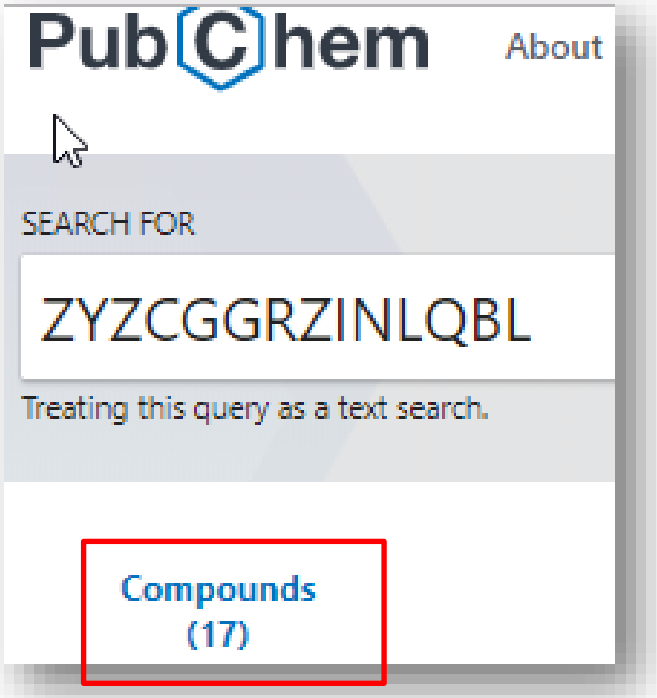


ChemSpiderID	Standard InChIKey Stereolayer
WIKIPEDIA	t28-,29-,30-,31+,34-,35-,36+,37+,38-,40+
CompTox	t28-,29-,30-,31+,34-,35-,36+,37+,38-,40+
4941647	t28-,29-,30-,31+,34-,35-,36+,37+,38-,40+
393078	t28-,29-,30-,31+,34-,35-,36+,**37-**,38-,40+
57618348	t28-,29-,30-,31+,34-,35-,36+,**37-**,38-,40+
29342071	t28-,29-,30-,31+,**34+**,35-,36+,**37-**,38-,40+
7987594	t28-,**29?**,**30?**,31+,**34?**,35-,**36?**,**37-**,38-,**40?**
22900854	t28-,**29?**,**30+**,**31-**,**34+**,**35+**,**36-**,**37-**,38-,**40-**
19692240	NONE
2831283	NONE

Comparing ChemSpider Structures

ChemSpiderID	InChIKey	# Stereocenters	# Different
WIKIPEDIA	ZYZCGGRZINLQBL-JCGNTXOTSA-N	10/10	0
CompTox	ZYZCGGRZINLQBL-JCGNTXOTSA-N	10/10	0
4941647	ZYZCGGRZINLQBL-JCGNTXOTSA-N	10/10	0
393078	ZYZCGGRZINLQBL-GWRQVWKTSA-N	10/10	1
57618348	ZYZCGGRZINLQBL-UPPCHHEJSA-N	10/10	1
29342071	ZYZCGGRZINLQBL-IIJTUTQBSA-N	10/10	2
7987594	ZYZCGGRZINLQBL-BESLYTPASA-N	5/10	6
22900854	ZYZCGGRZINLQBL-QAXSDTKVSA-N	9/10	8
19692240	ZYZCGGRZINLQBL-ORZJCNCZSA-N	0/10	10
2831283	ZYZCGGRZINLQBL-UHFFFAOYSA-N	0/10	10

Other Searches



UniChem

Show All entries

CMR. Query InChI...	src_id	Source	src_compound_id
...matches...	1	ChEMBL	CHEMBL444092
...matches...	4	Guide to Pharmacology	4735
...matches...	6	KEGG Ligand	C05371
...matches...	7	ChEBI	6925
...matches...	9	ZINC	ZINC000169715525
...matches...	9	ZINC	ZINC000255288110
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...matches...	9	ZINC	ZINC000255288112
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...matches...	10	eMolecules	26754757
...matches...	10	eMolecules	31239828
...matches...	11	IBM Patent System	DA3C2F25F29692734272194ED0E2C009
...matches...	14	FDA SRS	EQ8332842Y

Batch Searches

List of Opioids – Presence in Lists?

Trends in Environmental Analytical Chemistry

Volume 20, October 2018, e00059

Opioid occurrence in environmental water samples—A review

Marina Celia Campos-Mañas [a], Imma Ferrer [b], E.Michael Thurman [b], Ana Agüera [a]

Show more

https://doi.org/10.1016/j.teac.2018.e00059

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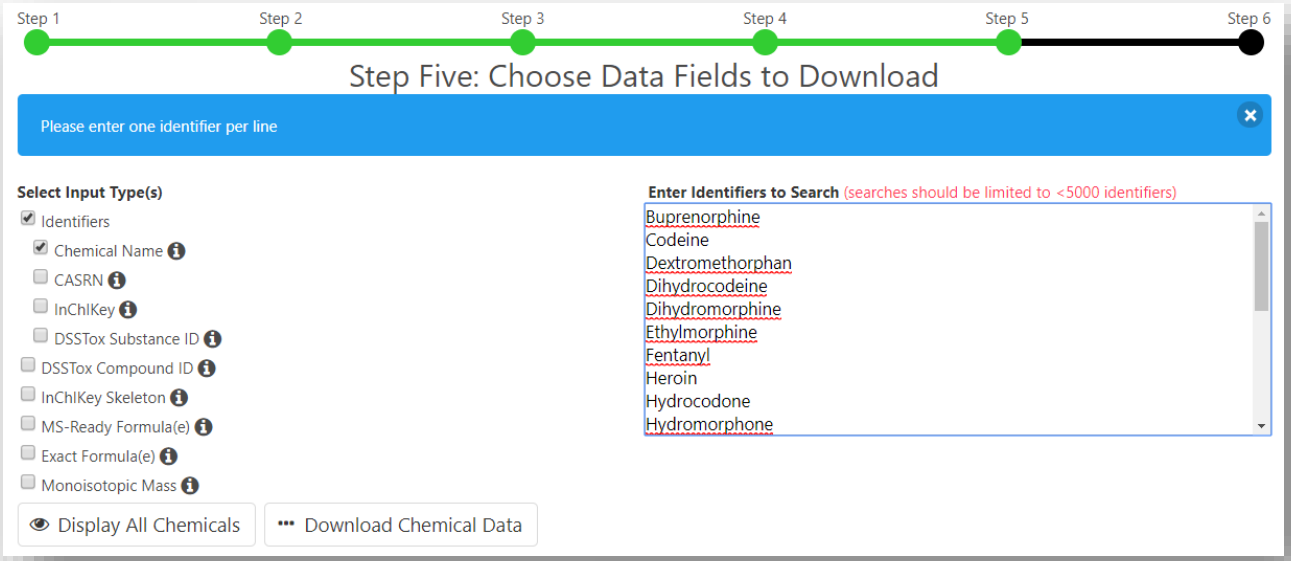
Batch Search Names

Buprenorphine
Codeine
Dextromethorphan
Dihydrocodeine
Dihydromorphine
Ethylmorphine
Fentanyl
Heroin
Hydrocodone
Hydromorphone
Ketamine
Meperidine
Methadone
Morphine
Morphinone
Naloxone
Naltriben
Oxycodone
Oxymorphone
Propoxyphene
Sufentanil
Tramadol



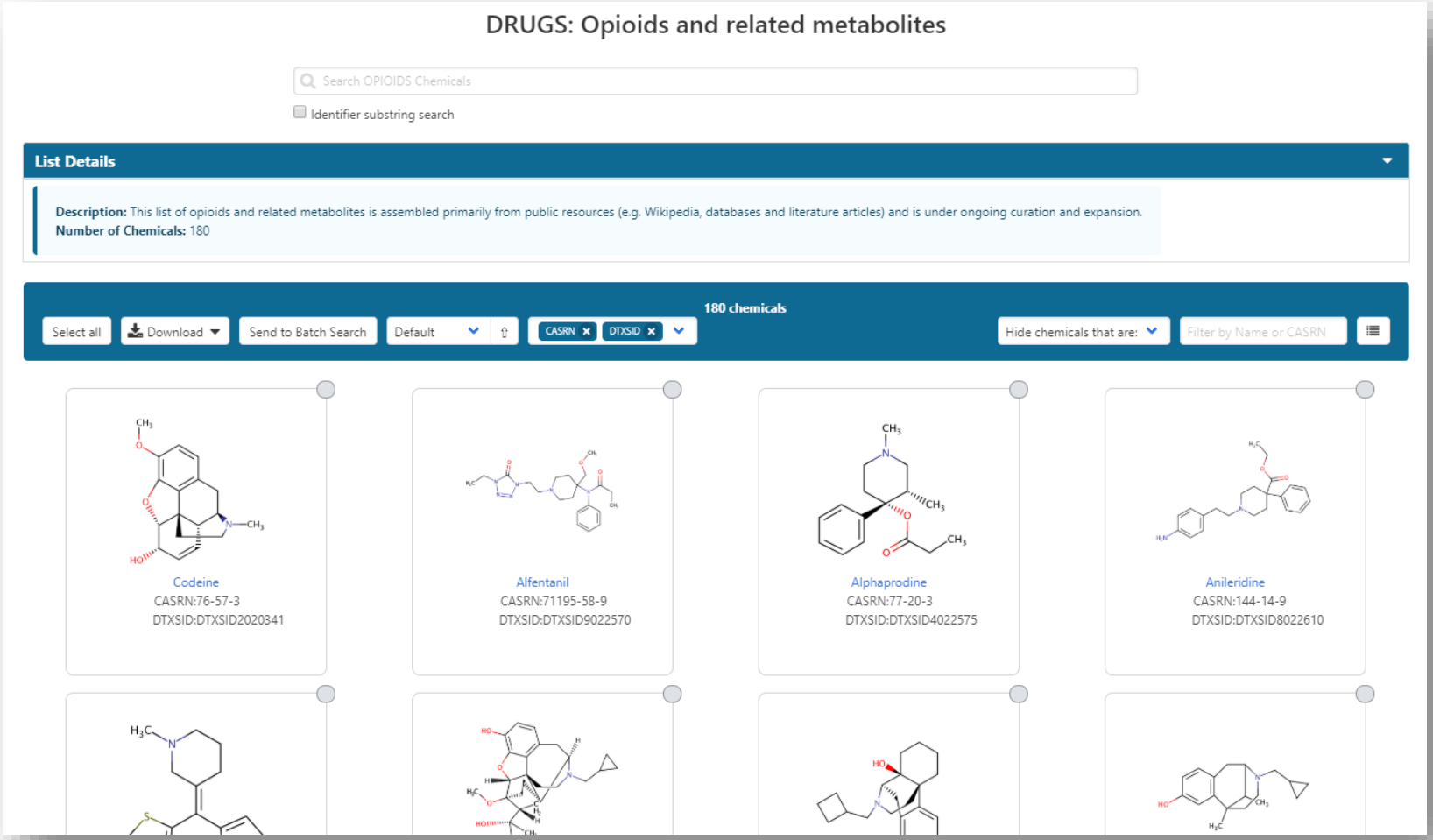
Excel Download

INPUT	FOUND_BY	DTXSID
Buprenorphine	Approved Name	DTXSID2022705
Codeine	Approved Name	DTXSID2020341
Dextromethorphan	Approved Name	DTXSID3022908
Dihydrocodeine	Approved Name	DTXSID5022936
Dihydromorphine	Approved Name	DTXSID7048908
Ethylmorphine	Approved Name	DTXSID1046760
Fentanyl	Approved Name	DTXSID9023049
Heroin	Synonym	DTXSID6046761
Hydrocodone	Approved Name	DTXSID8023131
Hydromorphone	Approved Name	DTXSID8023133
Ketamine	Approved Name	DTXSID8023187
Meperidine	Approved Name	DTXSID9023253
Methadone	Approved Name	DTXSID7023273
Morphine	Approved Name	DTXSID9023336

Batch Search in specific lists

INPUT	DTXSID	MASSBANKREF	NEMILIST	WRTMSD	NORMANPRI	SUSDAT
Buprenorph	DTXSID202	-	-	Y	-	Y
Codeine	DTXSID202	Y	Y	Y	Y	Y
Dextrometh	DTXSID302	Y	Y	Y	-	Y
Dihydrocod	DTXSID502	Y	-	Y	Y	Y
Dihydromor	DTXSID704	-	-	-	-	Y
Ethylmorph	DTXSID104	-	-	Y	-	Y
Fentanyl	DTXSID902	Y	-	Y	-	Y
Heroin	DTXSID604	Y	-	Y	Y	Y
Hydrocodor	DTXSID802	Y	Y	Y	Y	Y
Hydromorpl	DTXSID802	-	-	Y	-	Y
Ketamine	DTXSID802	Y	-	Y	-	Y
Meperidine	DTXSID902	Y	-	Y	-	Y
Methadone	DTXSID702	Y	Y	Y	-	Y
Morphine	DTXSID902	Y	Y	Y	Y	Y
Morphinone	DTXSID501	-	-	-	-	Y
Naloxone	DTXSID802	-	-	Y	-	Y
Naltriben	-	-	-	-	-	-
Oxycodone	DTXSID502	Y	Y	Y	Y	Y
Oxymorpho	DTXSID502	-	-	Y	-	Y
Propoxyphe	DTXSID102	Y	Y	Y	-	Y
Sufentanil	DTXSID602	-	-	Y	-	Y
Tramadol	DTXSID908	Y	Y	Y	Y	Y

Opioids and Metabolites (160)

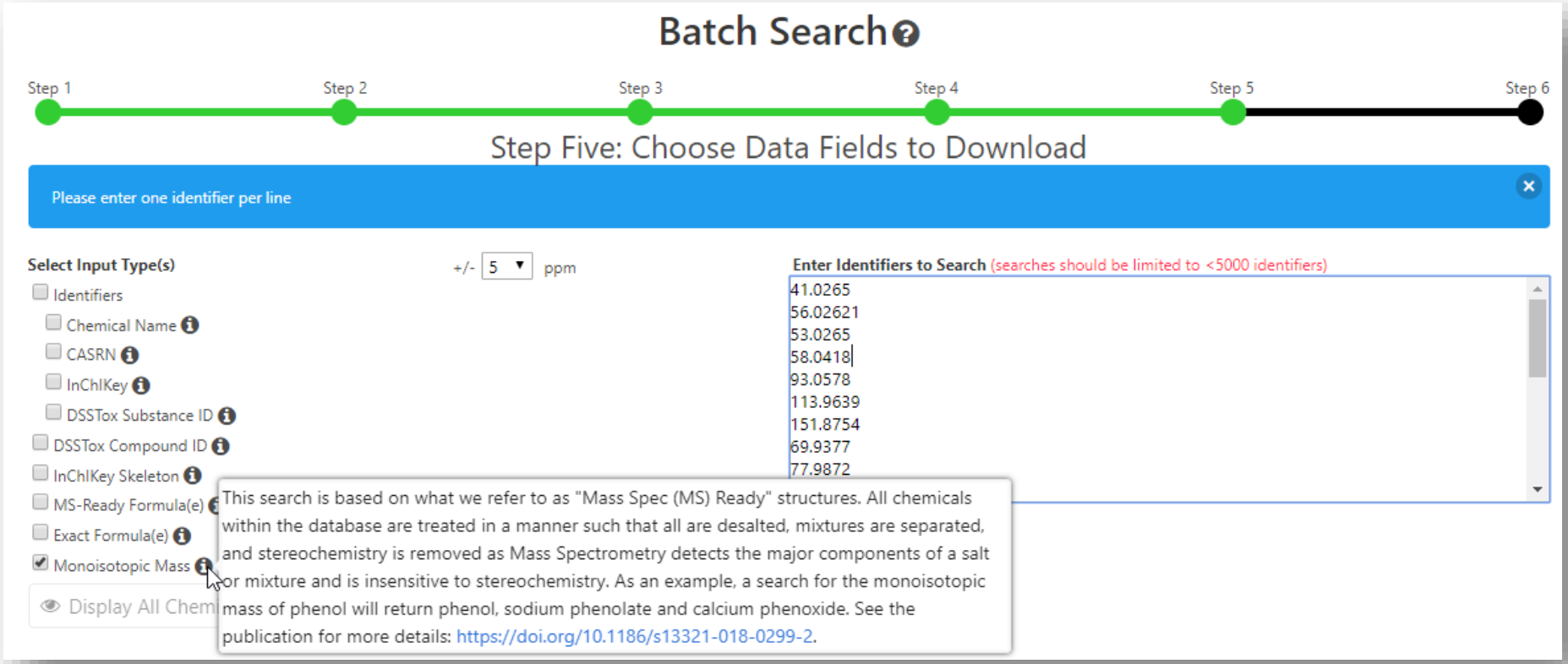


Batch Searching

- We work with **thousands** of masses/formulae!

- Typical questions
  - What is the list of chemicals for the formula $C_xH_yO_z$
  - What is the list of chemicals for a mass +/- error
  - Can I get chemical lists in Excel files? In SDF files?
  - Can I include properties in the download file?

Batch Searching Formula/Mass



Searching batches using MS-Ready Formula (or mass) searching

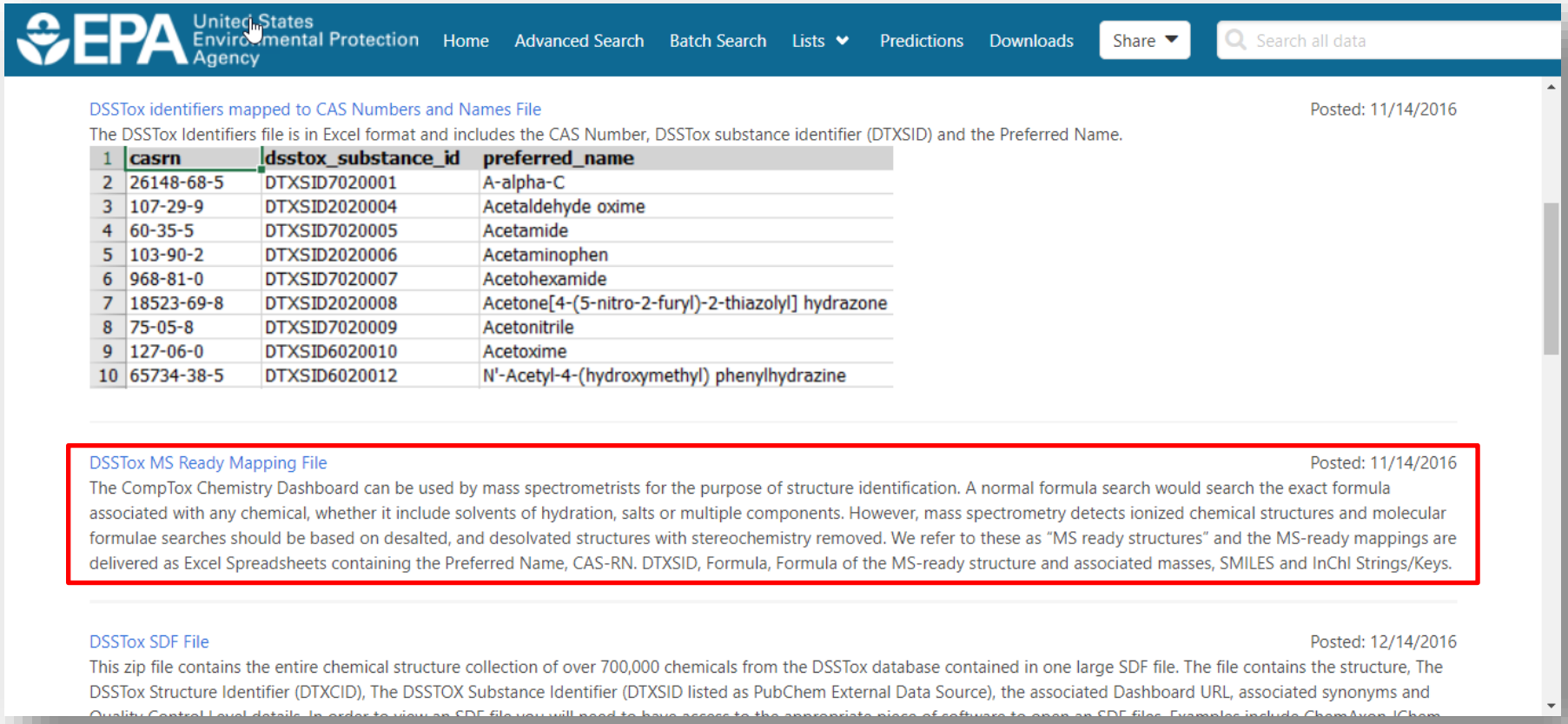
EPA United States Environmental Protection Agency

	A	B	C	D	E	F	G
1	INPUT	DTXSID	CASRN	PREFERRED NAME	MOL FORMULA	MONOISOTOPIC MASS	DATA SOURCES
2	C14H22N2O3	DTXSID2022628	29122-68-7	Atenolol	C14H22N2O3	266.163042576	46
3	C14H22N2O3	DTXSID0021179	6673-35-4	Practolol	C14H22N2O3	266.163042576	32
4	C14H22N2O3	DTXSID4048854	841-73-6	Bucolome	C14H22N2O3	266.163042576	20
5	C14H22N2O3	DTXSID1045407	13171-25-0	Trimetazidine dihydrochloride	C14H24Cl2N2O3	338.116398	19
6	C14H22N2O3	DTXSID0045753	56715-13-0	R-(+)-Atenolol	C14H22N2O3	266.163042576	19
7	C14H22N2O3	DTXSID2048531	5011-34-7	Trimetazidine	C14H22N2O3	266.163042576	14
8	C14H22N2O3	DTXSID10239405	93379-54-5	Esatenolol	C14H22N2O3	266.163042576	12
9	C14H22N2O3	DTXSID50200634	52662-27-8	N-(2-Diethylaminoethyl)-2-(4-hydroxyphenoxy)acetamide	C14H22N2O3	266.163042576	7
10	C14H22N2O3	DTXSID4020111	51706-40-2	dl-Atenolol hydrochloride	C14H23ClN2O3	302.1397203	6
11	C14H22N2O3	DTXSID1068693	51963-82-7	Benzenamine, 2,5-diethoxy-4-(4-morpholinyl)-	C14H22N2O3	266.163042576	5
12	C18H34N2O6S	DTXSID3023215	154-21-2	Lincomycin	C18H34N2O6S	406.213757997	35
13	C18H34N2O6S	DTXSID7047803	859-18-7	Lincomycin hydrochloride	C18H35ClN2O6S	442.1904357	22
14	C18H34N2O6S	DTXSID20849438	1398534-62-7	PUBCHEM_71432748	C18H35ClN2O6S	442.1904357	1
15	C10H12N2O	DTXSID1047576	486-56-6	Cotinine	C10H12N2O	176.094963014	40
16	C10H12N2O	DTXSID8075330	50-67-9	Serotonin	C10H12N2O	176.094963014	22
17	C10H12N2O	DTXSID8044412	2654-57-1	4-Methyl-1-phenylpyrazolidin-3-one	C10H12N2O	176.094963014	18
18	C10H12N2O	DTXSID80165186	153-98-0	Serotonin hydrochloride	C10H13ClN2O	212.0716407	11
19	C10H12N2O	DTXSID2048870	29493-77-4	(4R,5S)-4-methyl-5-phenyl-4,5-dihydro-1,3-oxazol-2-amine	C10H12N2O	176.094963014	10
20	C10H12N2O	DTXSID10196105	443-31-2	6-Hydroxytryptamine	C10H12N2O	176.094963014	9
21	C10H12N2O	DTXSID90185693	31822-84-1	1,4,5,6-Tetrahydro-5-phenoxypyrimidine	C10H12N2O	176.094963014	7
22	C10H12N2O	DTXSID40178777	2403-66-9	2-Benzimidazolepropanol	C10H12N2O	176.094963014	7
23	C10H12N2O	DTXSID80157026	13140-86-8	N-Cyclopropyl-N'-phenylurea	C10H12N2O	176.094963014	6
24	C10H12N2O	DTXSID30205607	570-14-9	4-Hydroxytryptamine	C10H12N2O	176.094963014	6
25	C14H18N4O3	DTXSID5023900	17804-35-2	Benomyl	C14H18N4O3	290.137890456	68
26	C14H18N4O3	DTXSID3023712	738-70-5	Trimethoprim	C14H18N4O3	290.137890456	51
27	C14H18N4O3	DTXSID40209671	60834-30-2	Trimethoprim hydrochloride	C14H19ClN4O3	326.1145682	8
28	C14H18N4O3	DTXSID70204210	55687-49-5	Benzenemethanol, 4-((2,4-diamino-5-pyrimidinyl)methyl)-2,	C14H18N4O3	290.137890456	5
29	C14H18N4O3	DTXSID20152671	120075-57-2	6-Methoxy-4-(3-(N,N-dimethylamino)propylamino)-5,8-quina	C14H18N4O3	290.137890456	4
30	C14H18N4O3	DTXSID30213742	63931-79-3	1H-1,2,4-Benzotriazepine-3-carboxylic acid, 4,5-dihydro-4-	C14H18N4O3	290.137890456	3
31	C14H18N4O3	DTXSID30219608	69449-07-6	2,4-Pyrimidinediamine, 5-((3,4,5-trimethoxyphenyl)methyl)-	C14H20N4O4	308.14845514	3
32	C14H18N4O3	DTXSID20241155	94232-27-6	L-Aspartic acid, compound with 5-((3,4,5-trimethoxyphenyl	C18H25N5O7	423.175398165	3
33	C14H18N4O3	DTXSID80241156	94232-28-7	L-Glutamic acid, compound with 5-((3,4,5-trimethoxypheny	C19H27N5O7	437.191048229	3
34	C14H18N4O3	DTXSID20143781	101204-93-7	1H-Pyrido(2,3-e)-1,4-diazepine-2,3,5-trione, 4-(2-(diethylam	C14H18N4O3	290.137890456	3
35	C12H11N7	DTXSID6021373	396-01-0	Triamterene	C12H11N7	253.107593382	52
36	C12H11N7	DTXSID00204465	5587-93-9	Ampyrimine	C12H11N7	253.107593382	7
37	C12H11N7	DTXSID5064621	7300-26-7	Benzenamine, 4-azido-N-(4-azidophenyl)-	C12H9N7	251.091943318	4
38	C12H11N7	DTXSID00848025	90293-82-6	Sulfuric acid--6-phenylpteridine-2,4,7-triamine (1/1)	C12H13N7O4S	351.074973101	1
39	C12H11N7	DTXSID50575293	92310-83-3	(1E)-N-Phenyl-1,2-bis(1H-1,2,4-triazol-1-yl)ethan-1-imine	C12H11N7	253.107593382	1
40	C8H9NO2	DTXSID2020006	103-90-2	Acetaminophen	C8H9NO2	151.063328534	75
41	C8H9NO2	DTXSID6026567	134-20-3	Methyl 2-aminobenzoate	C8H9NO2	151.063328534	60

Benefits of Open Data

API services and Open Data

- Available API and web services
- Open Data available for download



	casrn	dsstox_substance_id	preferred_name
2	26148-68-5	DTXSID7020001	A-alpha-C
3	107-29-9	DTXSID2020004	Acetaldehyde oxime
4	60-35-5	DTXSID7020005	Acetamide
5	103-90-2	DTXSID2020006	Acetaminophen
6	968-81-0	DTXSID7020007	Acetohexamide
7	18523-69-8	DTXSID2020008	Acetone[4-(5-nitro-2-furyl)-2-thiazolyl] hydrazone
8	75-05-8	DTXSID7020009	Acetonitrile
9	127-06-0	DTXSID6020010	Acetoxime
10	65734-38-5	DTXSID6020012	N'-Acetyl-4-(hydroxymethyl) phenylhydrazine

Web Services
https://actorws.epa.gov/actorws/

- Dozens of web services to provide access to data
- Data in UI, JSON and XML format

https://actorws.epa.gov/actorws/dsstox/v02/msready?identifier=80-05-7
https://actorws.epa.gov/actorws/dsstox/v02/msready.json?identifier=80-05-7
https://actorws.epa.gov/actorws/dsstox/v02/msready.xml?identifier=80-05-7

https://actorws.epa.gov/actorws/dsstox/v02/msready?identifier=DTXCID60513
https://actorws.epa.gov/actorws/dsstox/v02/msready.json?identifier=DTXCID60513
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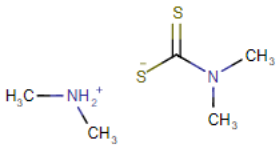
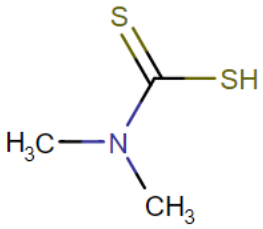
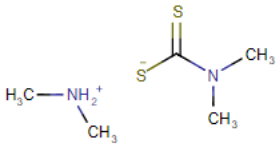
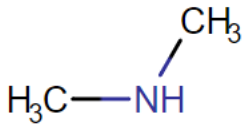
https://actorws.epa.gov/actorws/dsstox/v02/msready?identifier=UVOFGKIRTCCNKG-UHFFFAOYSA-N
https://actorws.epa.gov/actorws/dsstox/v02/msready.json?identifier=UVOFGKIRTCCNKG-UHFFFAOYSA-N
https://actorws.epa.gov/actorws/dsstox/v02/msready.xml?identifier=UVOFGKIRTCCNKG-UHFFFAOYSA-N

Example: InChIKey to DTXCIDs

https://actorws.epa.gov/actorws/dsstox/v02/msready?identifier=UVOFGKIRTCCNKG-UHFFFAOYSA-N

Image	DTXCID	Smiles	Image	MsReady DTXCID	MsReady SMILES
	DTXCID60513	C[NH2+]C.CN(C)C([S-])=S		DTXCID0023797	CN(C)C(S)=S
	DTXCID60513	C[NH2+]C.CN(C)C([S-])=S		DTXCID704057	CNC

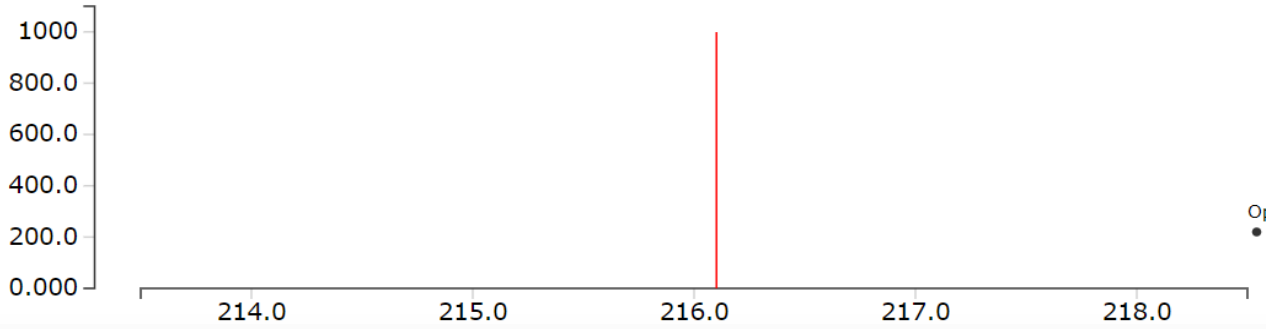
MassBank mapping to Dashboard

MassBank Record: EA028808

Home | Search | Record Index | Data Privacy | Imprint | MassBank ID: Go

Atrazine; LC-ESI-ITFT; MS2; CE: 15%; R=15000; [M+H]+

Mass Spectrum



Options
• Labels

Chemical Structure

CH$NAME: Atrazine
CH$NAME: 6-chloro-N-ethyl-N'-isopropyl-1,3,5-triazine-2,4-diamine
CH$NAME: 6-chloranyl-N4-ethyl-N2-propan-2-yl-1,3,5-triazine-2,4-diamine
CH$COMPOUND_CLASS: N/A; Environmental Standard
CH$FORMULA: C8H14ClN5
CH$EXACT_MASS: 215.0932
CH$SMILES: c1(nc(nc(n1)Cl)NCC)NC(C)C
CH$IUPAC: InChI=1S/C8H14ClN5/c1-4-10-7-12-6(9)13-8(14-7)11-5(2)3/h5H,4H2,1-3H3,(H2,10,11,12,13,14)
CH$LINK: CAS 1912-24-9
CH$LINK: CHEBI 15930
CH$LINK: KEGG C06551
CH$LINK: PUBCHEM CID:2256
CH$LINK: INCHIKEY MXWJVTOOROXGIU-UHFFFAOYSA-N
CH$LINK: CHEMSPIDER 2169
CH$LINK: COMPTOX DTXSID9020112

NORMAN Suspect List Exchange

https://www.norman-network.com/?q=node/236

NORMAN

Network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances

Wastewater Suspect List based on Swedish Product Data	Wastewater Suspect List **Original File with Mapped DTXSIDs** (12/02/2019)	KEMIWWSUS **InChIKeys** (12/02/2019)	A prioritized list of 1,123 substances relevant for wastewater based on Swedish product registry data, including scores. Provided by Stellan Fischer, KEMI.
Algal toxins list from CompTox	ALGALTOX **XLSX**, **CSV** (14/02/2019) CompTox **ALGALTOX List**	ALGALTOX **InChIKeys** (14/02/2019)	List of algal toxins (generated during blooms) from the CompTox Chemicals Dashboard.
CCL 4 Chemical Candidate List	CCL4 **XLSX**, **CSV** (14/02/2019) CompTox **CCL4 List**	CCL4 **InChIKeys** (14/02/2019)	Contaminants that are not (yet) regulated in the USA but are known or anticipated to occur in public water systems; from CompTox.
Hydrogen Deuterium Exchange (HDX) Standard Set	HDXNOEX **XLSX**, **CSV** (14/02/2019) CompTox **HDXNOEX List** CompTox **HDXEXCH List**	HDXNOEX **InChIKeys** (14/02/2019)	Environmental standard set used to investigate hydrogen deuterium exchange in small molecule HRMS (Ruttkies et al. submitted). **HDXEXCH** list also contains observed deuterated species.
Neurotoxicants Collection from Public Resources	NEUROTOXINS **XLSX**, **CSV** (14/02/2019) CompTox **NEUROTOXINS List**	NEUROTOXINS **InChIKeys** (14/02/2019)	A list of neurotoxicants compiled from public resources, details on CompTox and Schymanski *et al.* (submitted).
Statins Collection from Public Resources	STATINS **XLSX**, **CSV** (14/02/2019) CompTox **STATINS List**	STATINS **InChIKeys** (14/02/2019)	A list of statins (lipid-lowering medications) compiled from public resources, details on CompTox.
Synthetic Cannabinoids and Psychoactive Compounds	SYNTHCANNAB **XLSX**, **CSV** (14/02/2019) CompTox **SYNTHCANNAB List**	SYNTHCANNAB **InChIKeys** (14/02/2019)	A list of synthetic cannabinoids and psychoactive compounds assembled from public resources, from CompTox.

Integration to MetFrag in place

https://jcheminf.biomedcentral.com/articles/10.1186/s13321-018-0299-2

Work in Progress

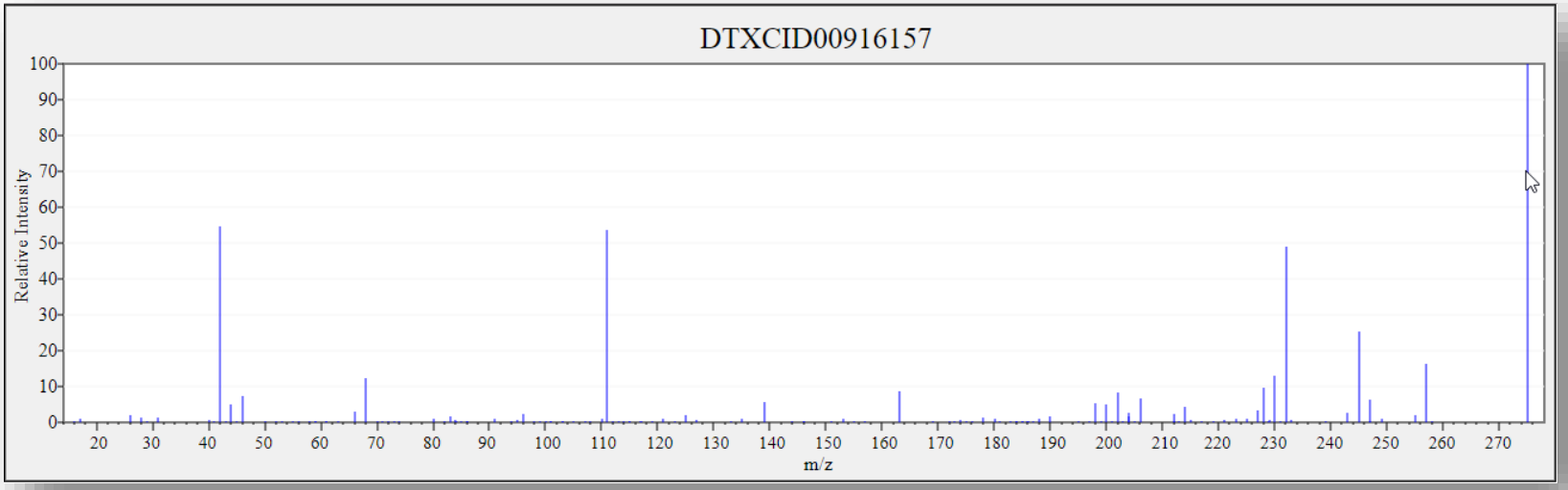
Prototype Work in Progress

- CFM-ID
  - Viewing and Downloading pre-predicted spectra
  - Search spectra against the database
- Structure/substructure/similarity search
- The EPA NTA WebApp
- Access to API and web services

Predicted Mass Spectra

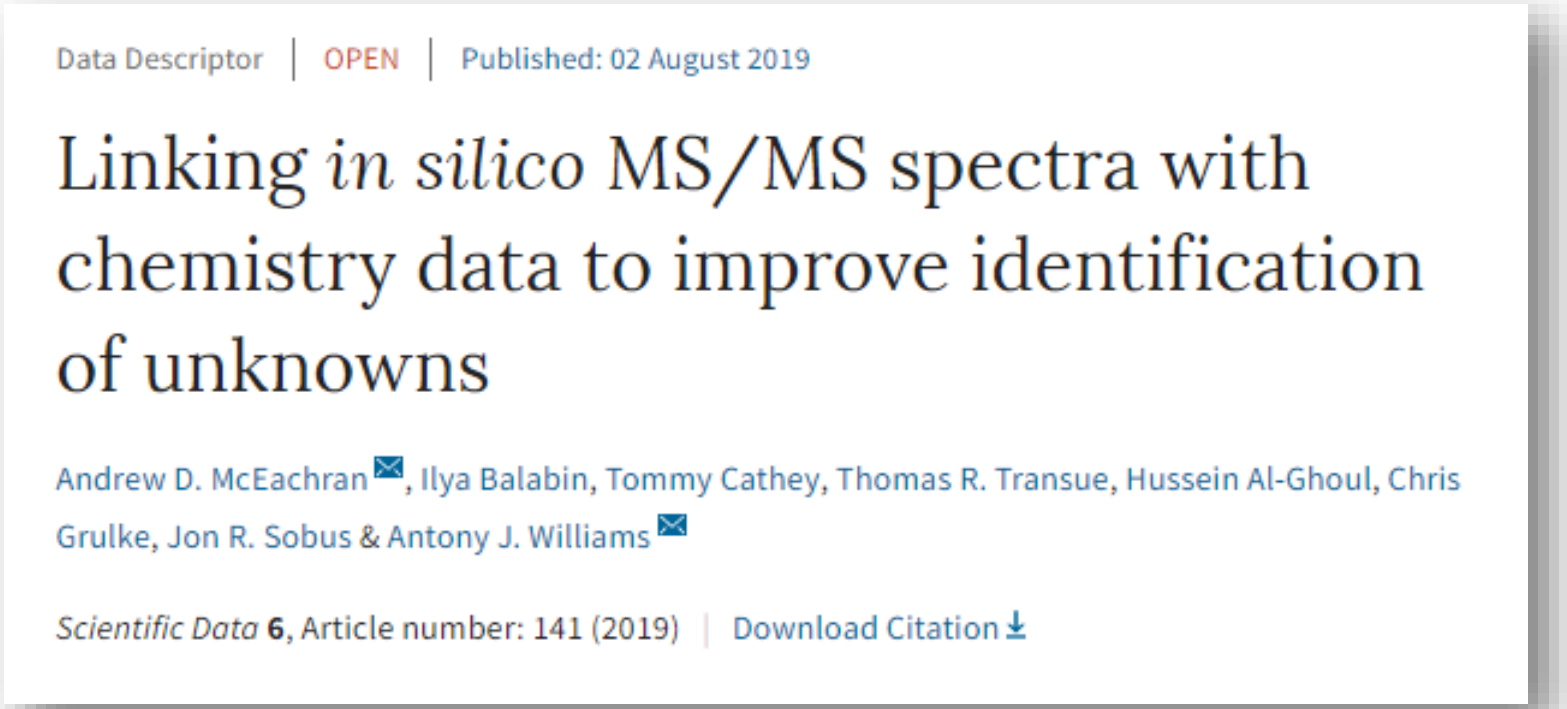
http://cfmid.wishartlab.com/

- MS/MS spectra prediction for ESI+, ESI-, and EI
- Predictions generated and stored for >800,000 structures, to be accessible via Dashboard



CFM-ID Predicted Library Available

- Predictions generated and stored for >800,000 structures
- Python code to score experimental vs predicted spectra
- Cosine dot product match score calculation



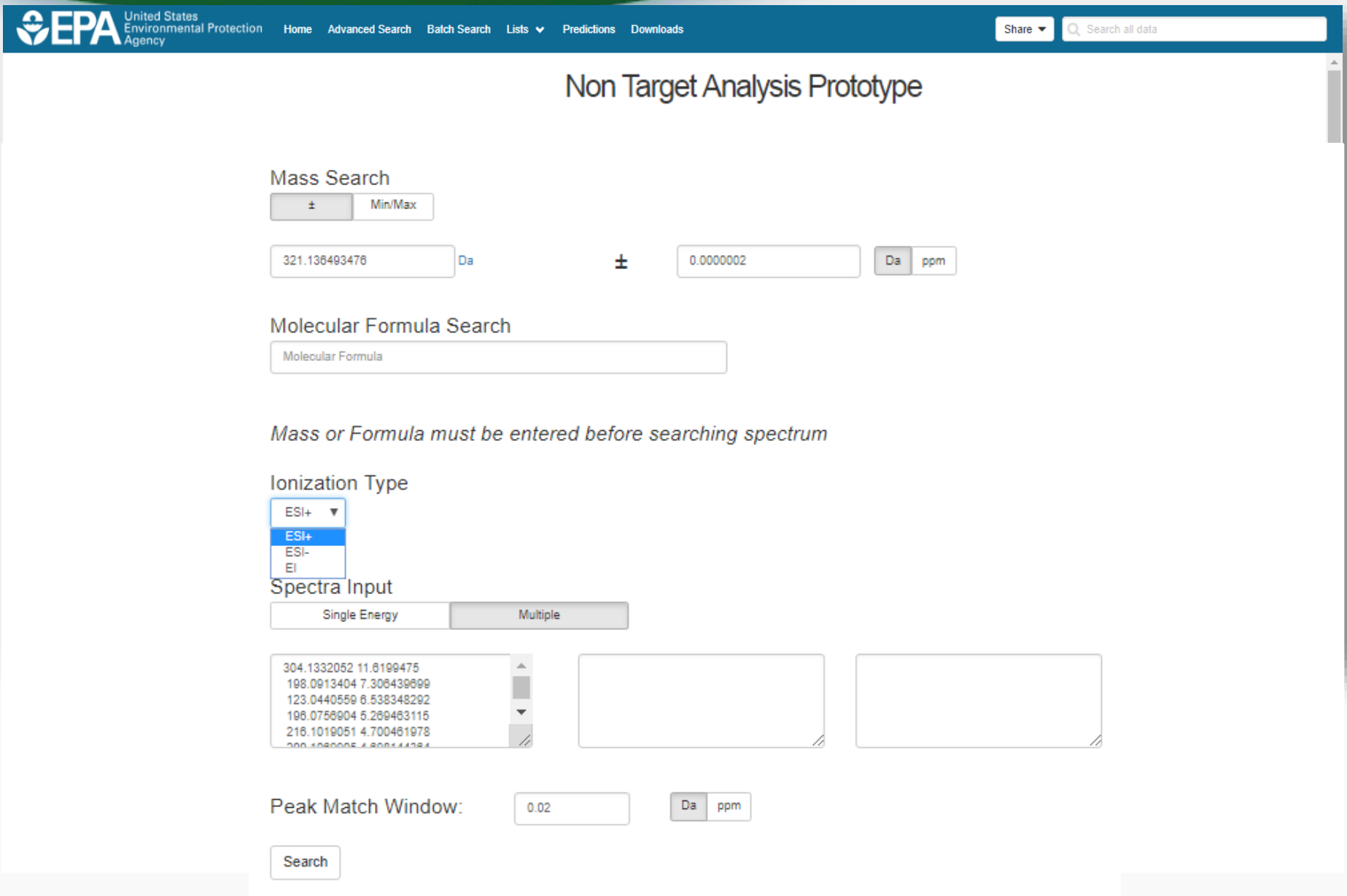
Data Descriptor | OPEN | Published: 02 August 2019

Linking *in silico* MS/MS spectra with chemistry data to improve identification of unknowns

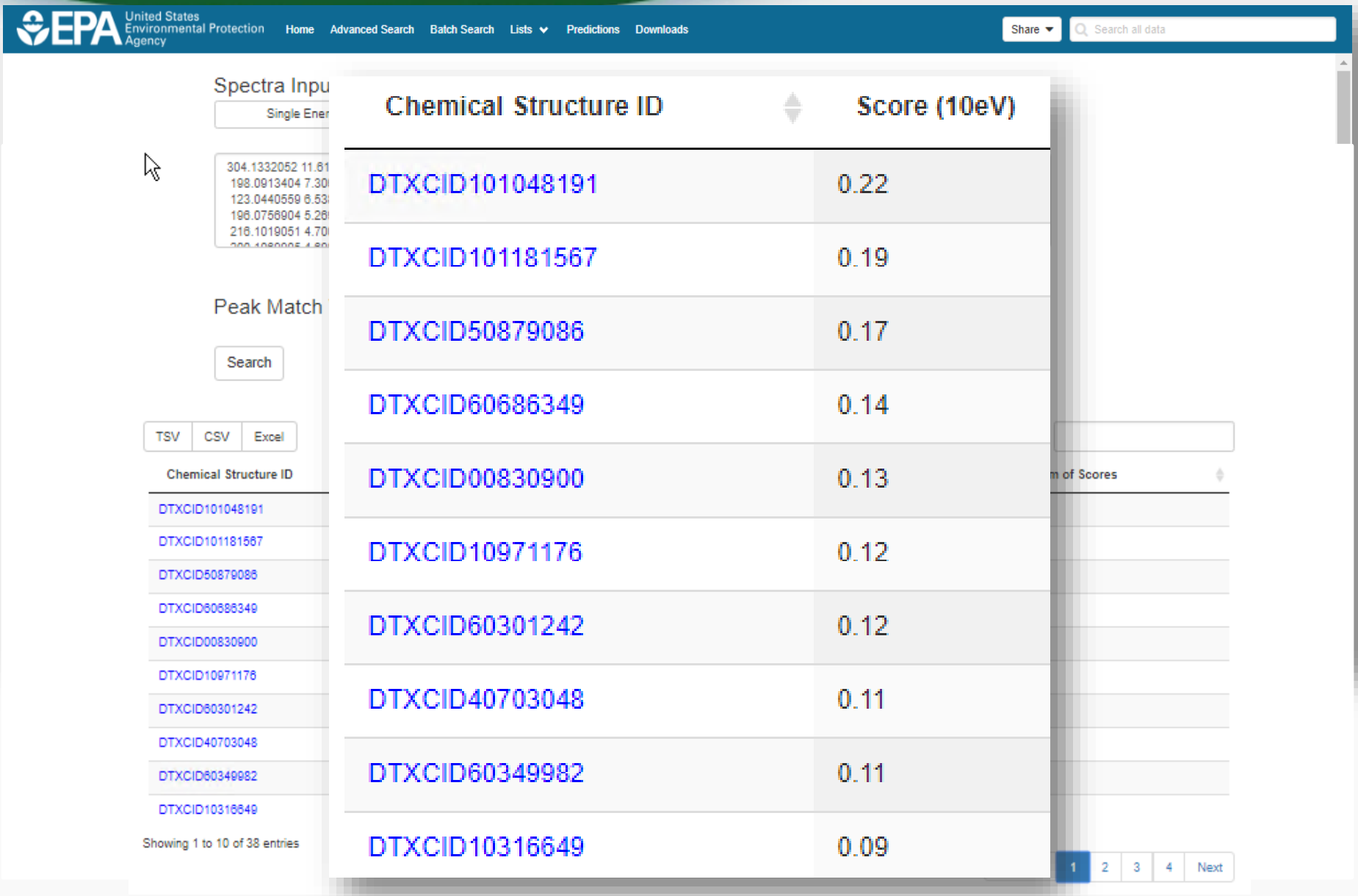
Andrew D. McEachran, Ilya Balabin, Tommy Cathey, Thomas R. Transue, Hussein Al-Ghoul, Chris Grulke, Jon R. Sobus & Antony J. Williams

Scientific Data **6**, Article number: 141 (2019) | Download Citation

Search Expt. vs. Predicted Spectra

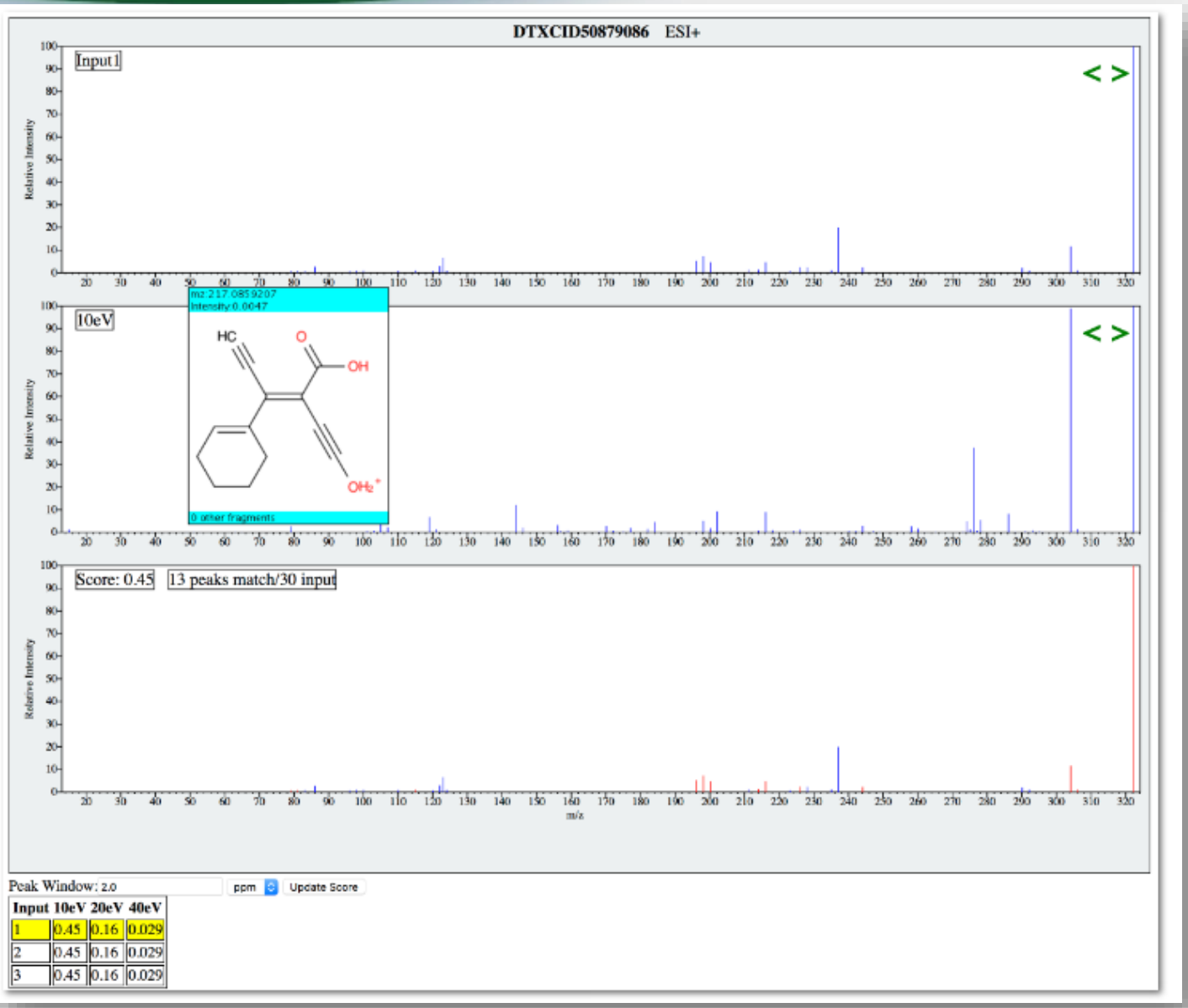


Search Expt. vs. Predicted Spectra

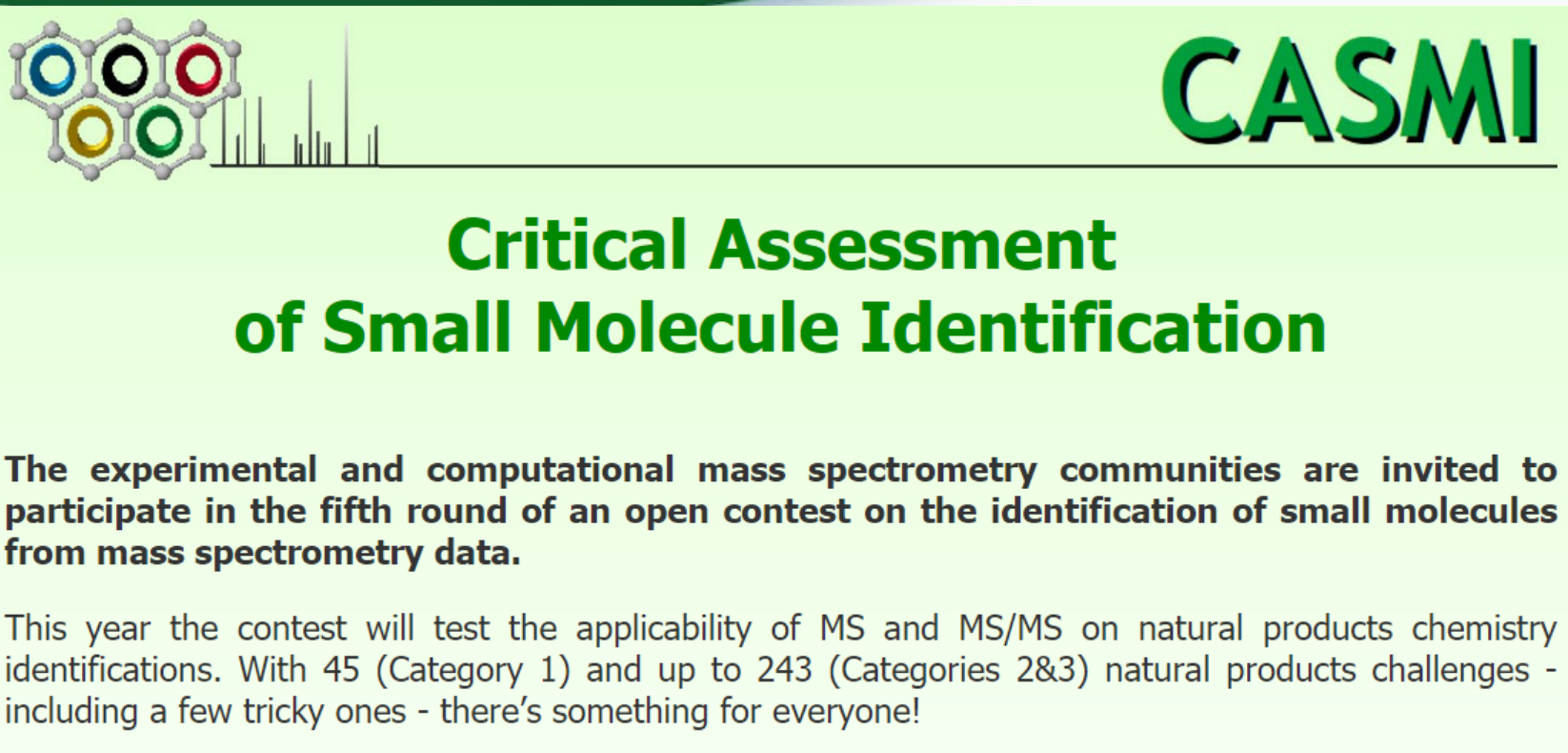


Chemical Structure ID	Score (10eV)
DTXCID101048191	0.22
DTXCID101181567	0.19
DTXCID50879086	0.17
DTXCID60686349	0.14
DTXCID00830900	0.13
DTXCID10971176	0.12
DTXCID60301242	0.12
DTXCID40703048	0.11
DTXCID60349982	0.11
DTXCID10316649	0.09

Spectral Viewer Comparison



CASMI 2012-2017 revisited



- Application of metadata candidate ranking and CFM-ID to all five years of CASMI data

Open Access Article

Revisiting Five Years of CASMI Contests with EPA Identification Tools

by Andrew D. McEachran [1,*], Alex Chao [1], Hussein Al-Ghoul [1], Charles Lowe [2], Christopher Grulke [2], Jon R. Sobus [2] and Antony J. Williams [2,*]

[1] Oak Ridge Institute for Science and Education (ORISE) Participant, 109 T.W. Alexander Drive, Research Triangle Park, NC 27709, USA

[2] Center for Computational Toxicology and Exposure, Office of Research and Development, U.S. Environmental Protection Agency, 109 T.W. Alexander Drive, Research Triangle Park, NC 27709, USA

[*] Authors to whom correspondence should be addressed.

Metabolites **2020**, *10*(6), 260; https://doi.org/10.3390/metabo10060260

Received: 3 May 2020 / Revised: 3 June 2020 / Accepted: 17 June 2020 / Published: 23 June 2020

Published: Alex Chao et al

Analytical and Bioanalytical Chemistry

RESEARCH PAPER

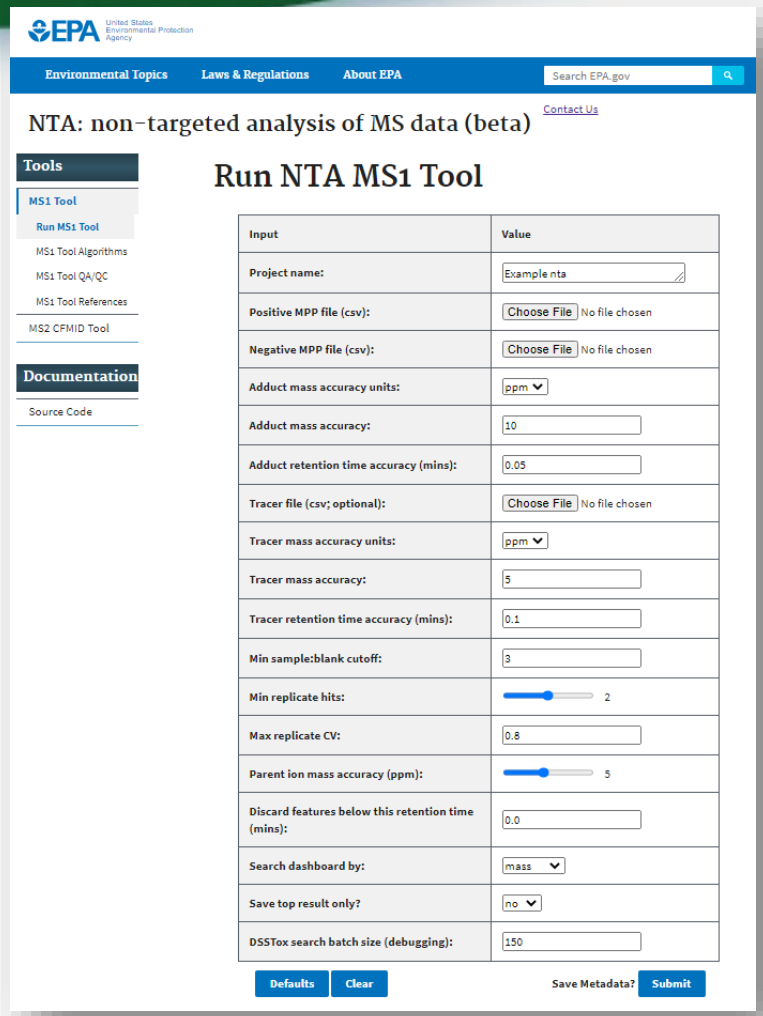
In silico MS/MS spectra for identifying unknowns: a critical examination using CFM-ID algorithms and ENTACT mixture samples

Alex Chao [1,2] · Hussein Al-Ghoul [1,2] · Andrew D. McEachran [1,3] · Ilya Balabin [4] · Tom Transue [4] · Tommy Cathey [4] · Jarod N. Grossman [2,3] · Randolph Singh [1,5] · Elin M. Ulrich [2] · Antony J. Williams [6] · Jon R. Sobus [2]

Received: 4 October 2019 / Revised: 27 November 2019 / Accepted: 11 December 2019

NTA WebApp Development

NTA WebApp: Input Page



Jeff Minucci

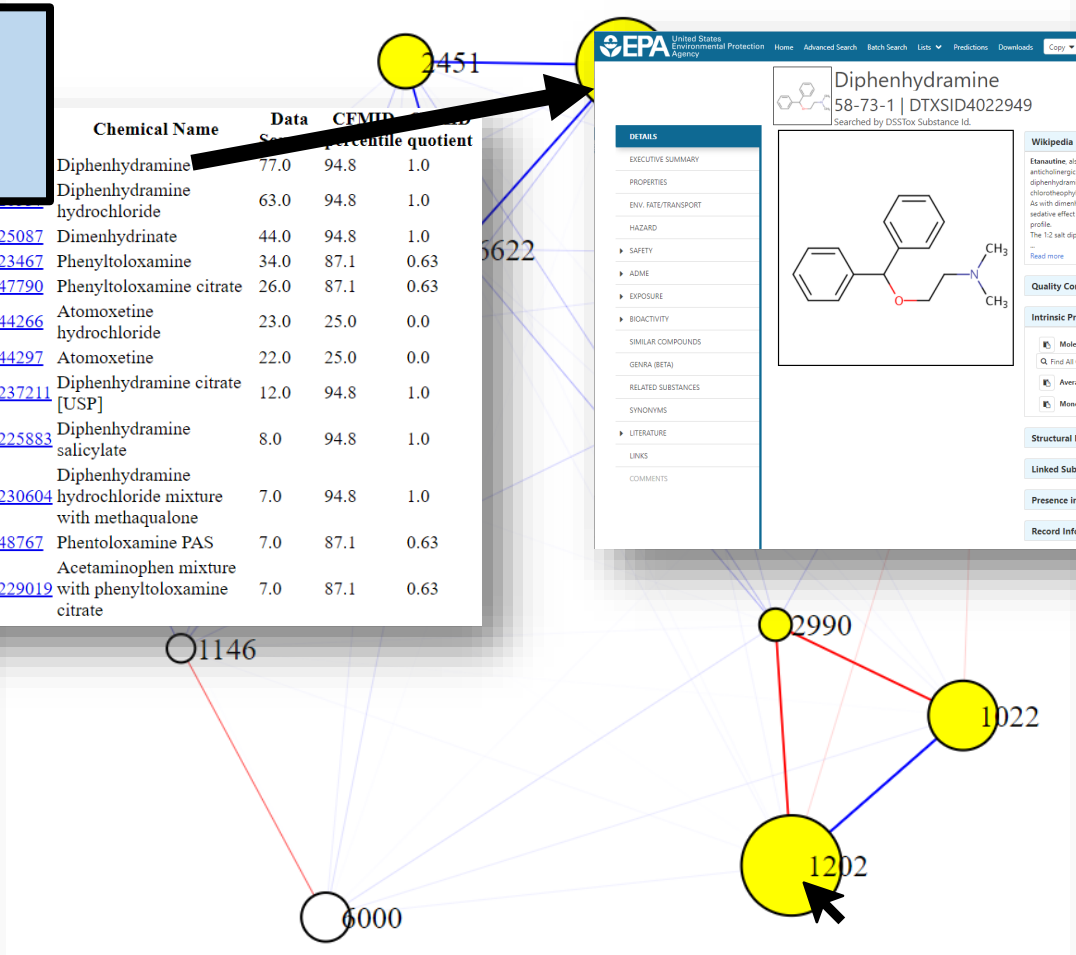
NTA data input files

Parameters for NTA clean-up / database searching

Visualizations of Data – Cluster 1

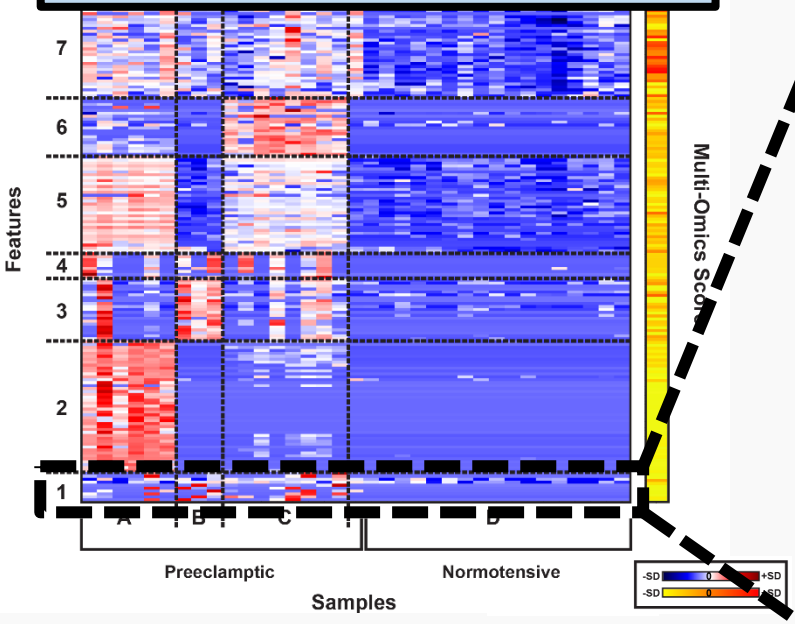
Chemical Candidate Information

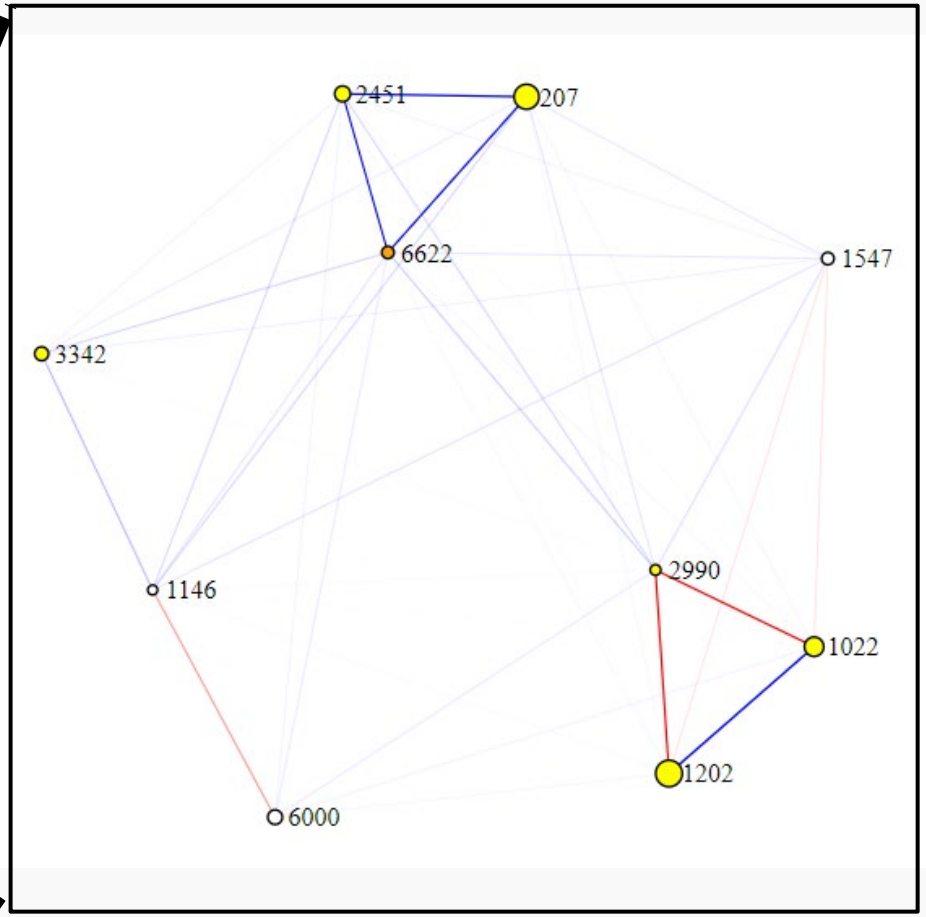
Chemical Name	Data Score	CEMPD percentile	quotient
Diphenhydramine	77.0	94.8	1.0
Diphenhydramine hydrochloride	63.0	94.8	1.0
DTXSID9025087 Dimenhydrinate	44.0	94.8	1.0
DTXSID9023467 Phenyltoloxamine	34.0	87.1	0.63
DTXSID5047790 Phenyltoloxamine citrate	26.0	87.1	0.63
DTXSID2044266 Atomoxetine hydrochloride	23.0	25.0	0.0
DTXSID9044297 Atomoxetine	22.0	25.0	0.0
DTXSID80237211 Diphenhydramine citrate [USP]	12.0	94.8	1.0
DTXSID10225883 Diphenhydramine salicylate	8.0	94.8	1.0
DTXSID60230604 Diphenhydramine hydrochloride mixture with methaqualone	7.0	94.8	1.0
DTXSID0048767 Phentoloxamine PAS	7.0	87.1	0.63
DTXSID20229019 Acetaminophen mixture with phenyltoloxamine citrate	7.0	87.1	0.63



Patterns of Cluster Results

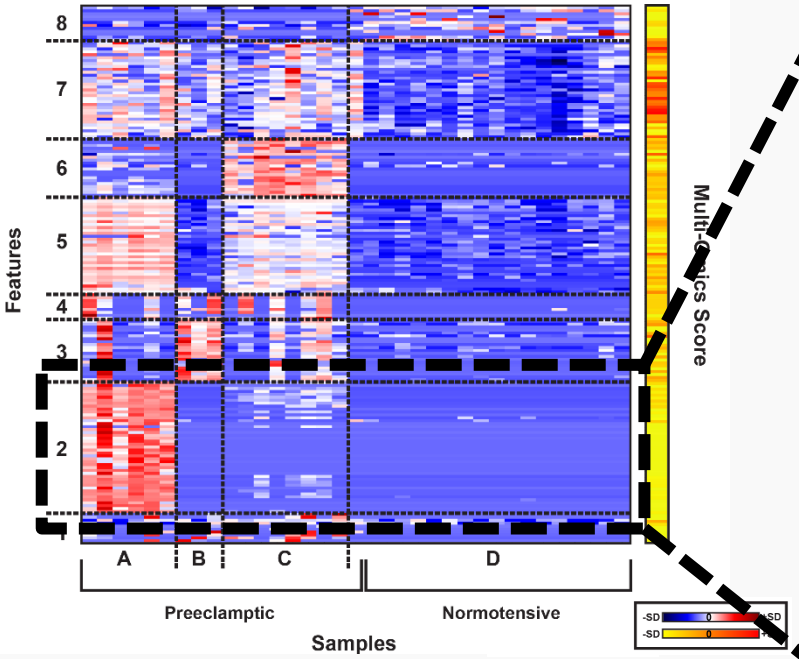
Cluster 1: Primarily drugs (e.g. diphenhydramine, labetalol, clindamycin)

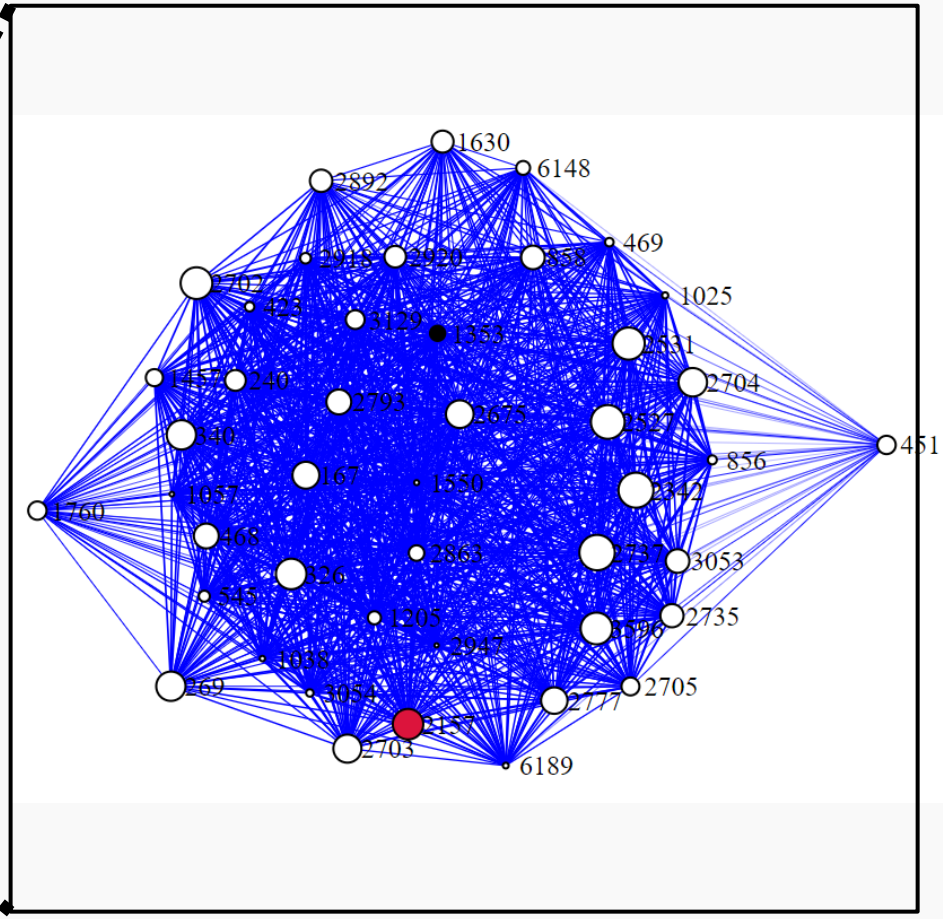




Patterns of Cluster Results

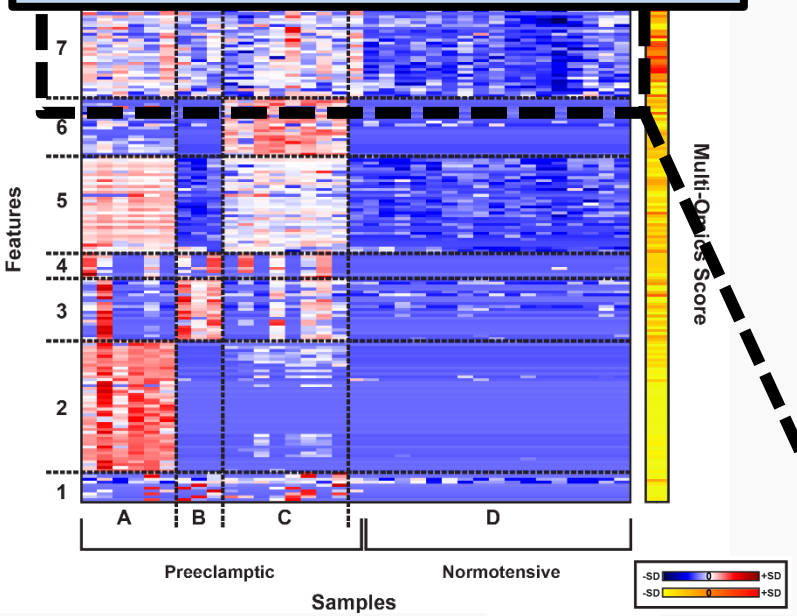
Cluster 2: Likely xenobiotics (ethanolamides)

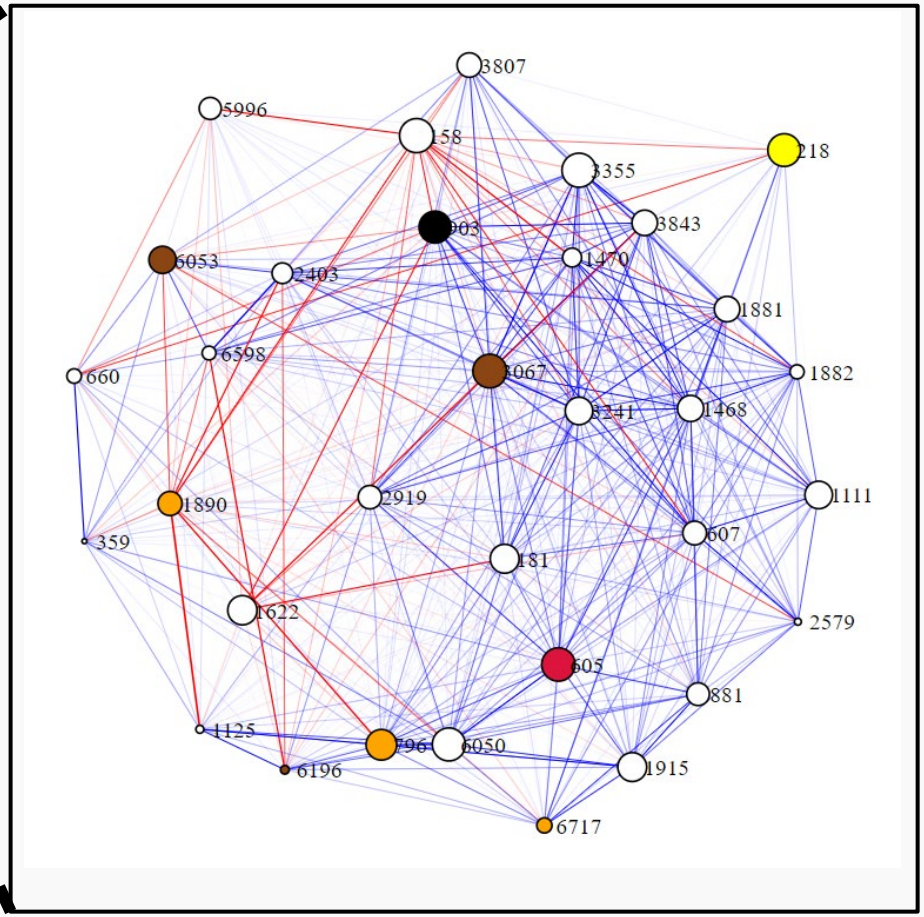




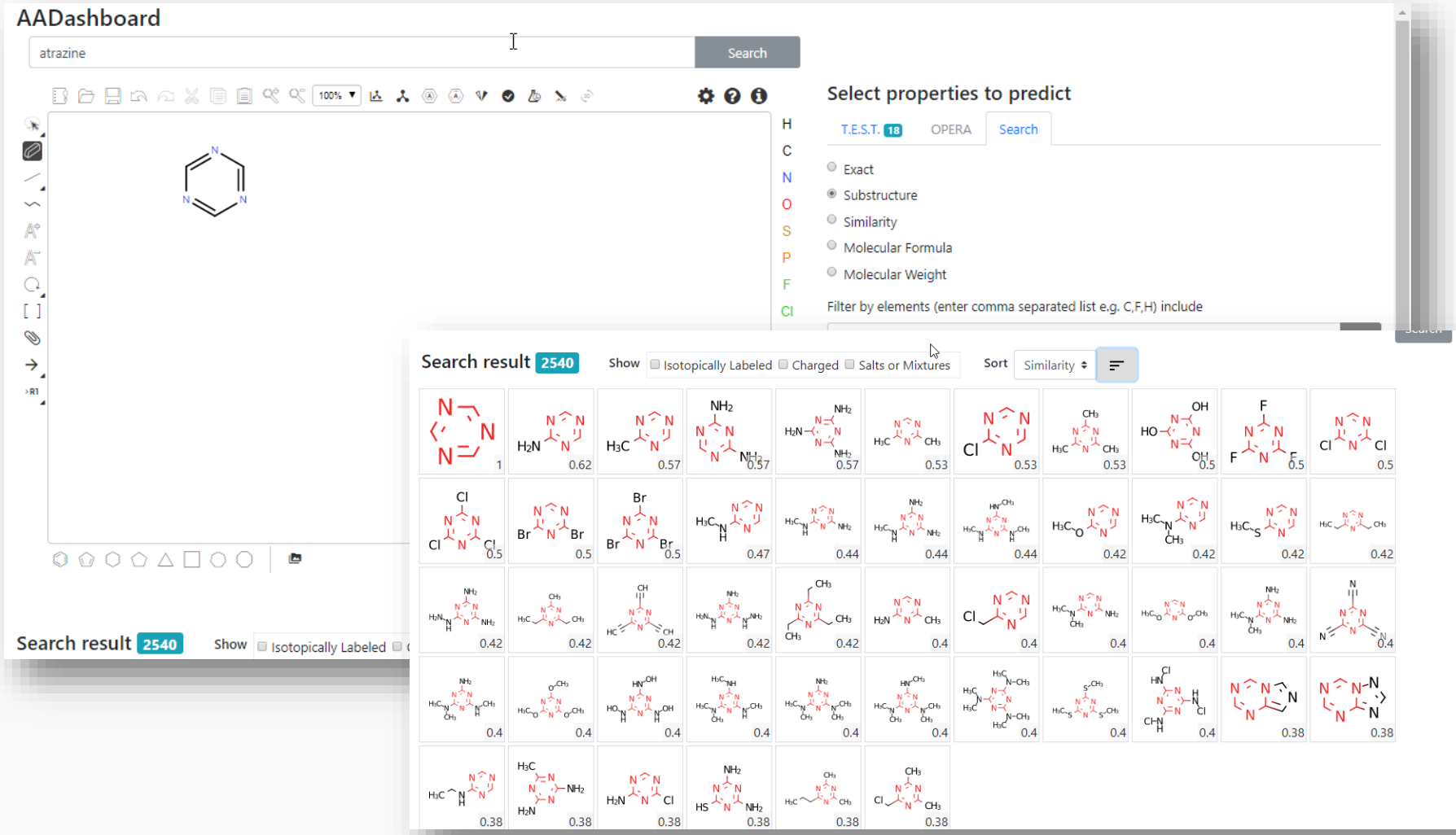
Patterns of Cluster Results

Cluster 7: Mostly human metabolism chemicals (acyl carnitines, amino acids, peptides)





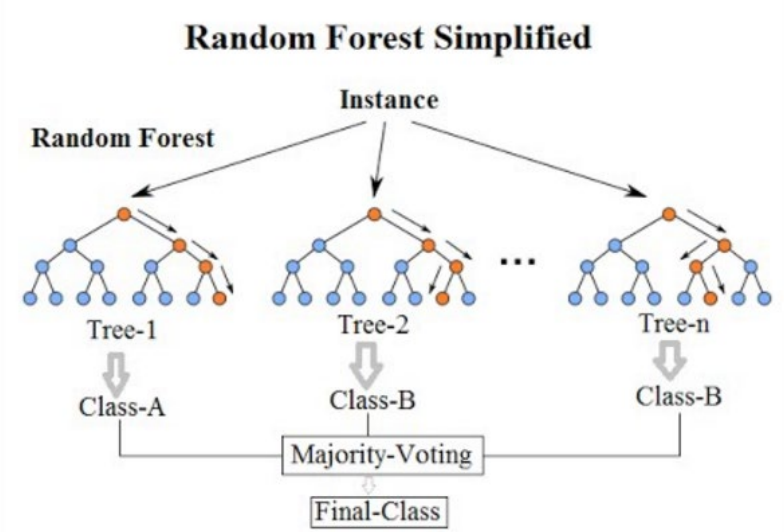
Prototype Development



Method Amenability Prediction
Charlie Lowe

Why?

- Chromatography-mass spectrometry can be LC or GC
- Which phase is more appropriate for which chemicals?

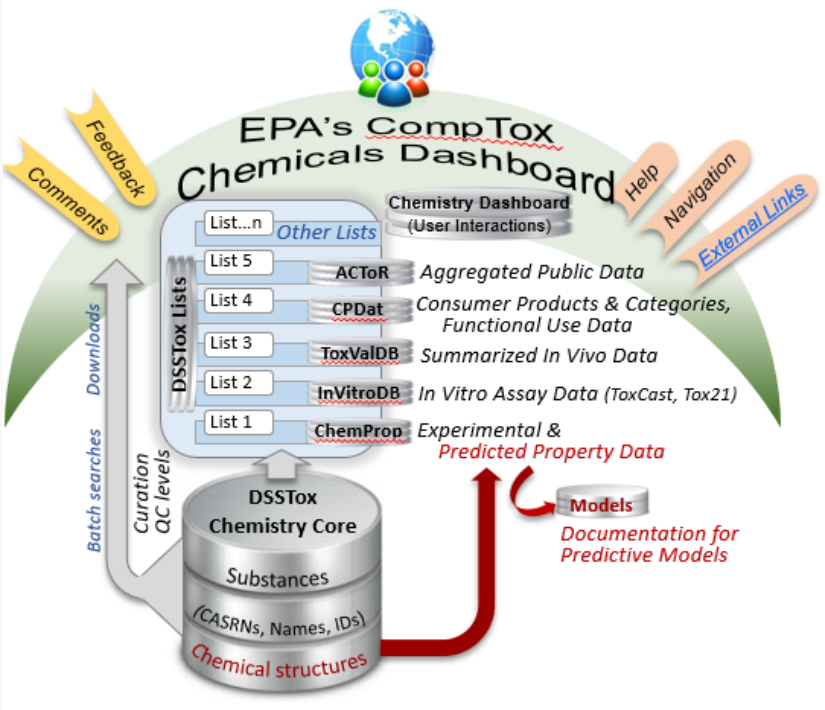


Ongoing Work

- Data sources to date
  - **Massbank of North America**
    - 9,275 chemicals for non-derivatized GC
    - 846 chemicals for derivatized GC
    - 816 chemicals for APCI+
    - 454 chemicals for APCI-
    - 4,907 chemicals for ESI+
    - 3,430 chemicals for ESI-
  - **EPA Non-targeted Analysis Collaborative Trial (ENTACT)**
    - 886 chemicals for non-derivatized GC
    - 44 chemicals for derivatized GC
    - 774 chemicals for APCI+
    - 431 chemicals for APCI-
    - 1,113 chemicals for ESI+
    - 648 chemicals for ESI-

Conclusion

- Dashboard access to data for ~883,000 chemicals MS-Ready data facilitates structure identification
- Related metadata facilitates candidate ranking
- Relationship mappings and chemical lists of great utility
- Curation and mutual sharing of chemical lists is important (e.g. NORMAN)



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- *NCCT IT development team*
- *Tommy Cathey, ACTOR Web Services*
- *Nancy Baker, Abstract Sifter*
- *Todd Martin & Valery Tkachenko, WebTEST*
- *Kathie Dionisio & Kristin Isaacs, CPDat*
- *Thanks to Emma Schymanski, University of Luxembourg, for coordinating all efforts with the NORMAN Network for curation of lists on the Suspect Exchange*

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National Center for Computational Toxicology

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RETURN TO ISSUE | < PREV **SUSTAINABLE SYSTEMS** NEXT >

Chemical Characterization of Recycled Consumer Products Using Suspect Screening Analysis

Charles N. Lowe, Katherine A. Phillips, Kristin A. Favela, Alice Y. Yau, John F. Wambaugh, Jon R. Sobus, Antony J. Williams, Ashley J. Pfirrman, and Kristin K. Isaacs*

Cite this: *Environ. Sci. Technol.* 2021, 55, 16, 11375−11387

Publication Date: August 4, 2021

https://doi.org/10.1021/acs.est.1c01907

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