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

The US-EPA CompTox Chemicals Dashboard to support Mass Spectrometry

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Center for Computational Toxicology and Exposure, US-EPA, RTP, NC

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

Agilent

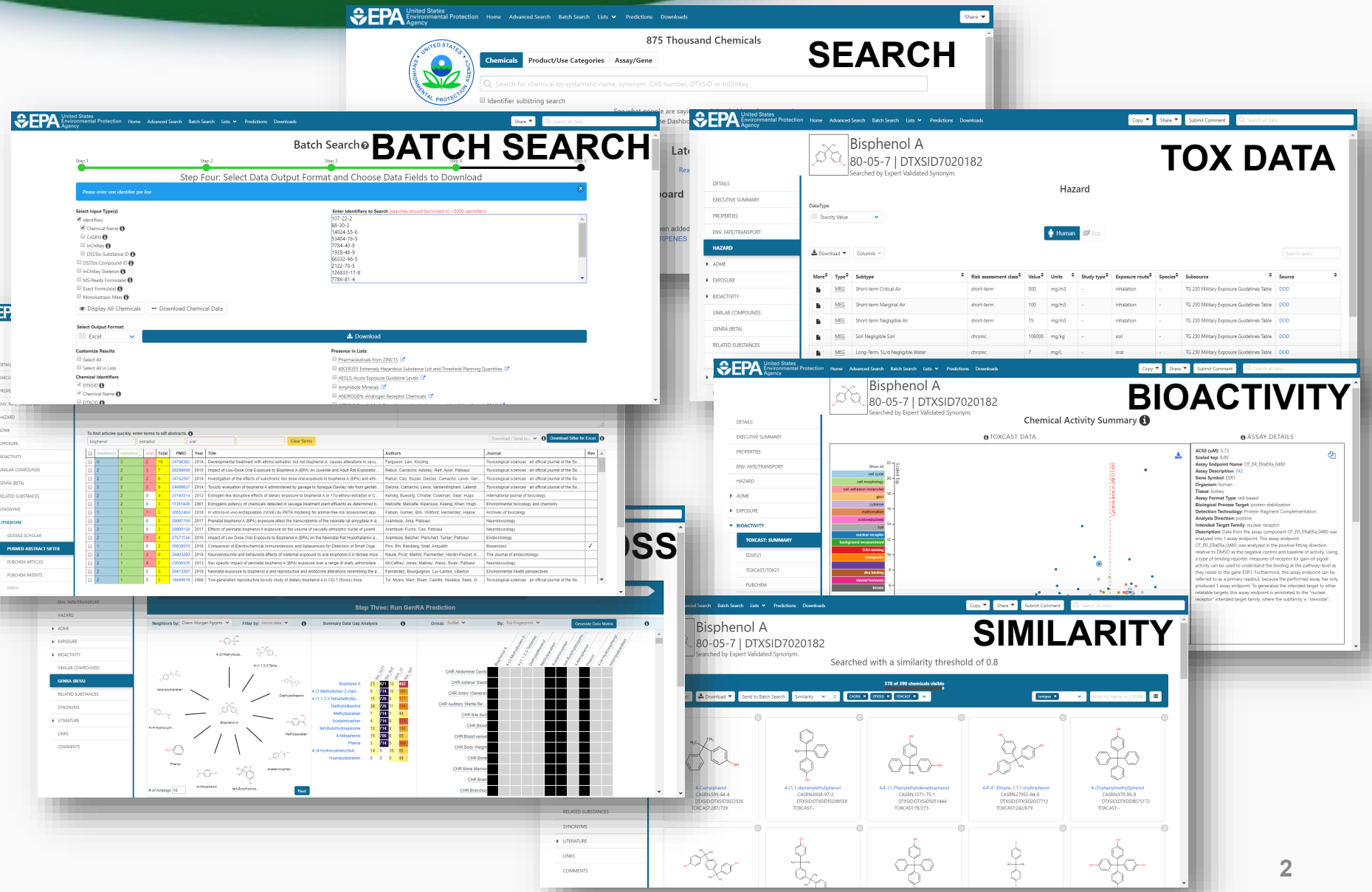
February 5th 2021

Outline

- Quick overview of the dashboard
- Specific data of interest to this audience (it's not just Computational Toxicology)
- Support for Mass Spectrometry
- Data ***quality*** in the public domain
- Work in progress – prototypes

CompTox Chemicals Dashboard

https://comptox.epa.gov/dashboard



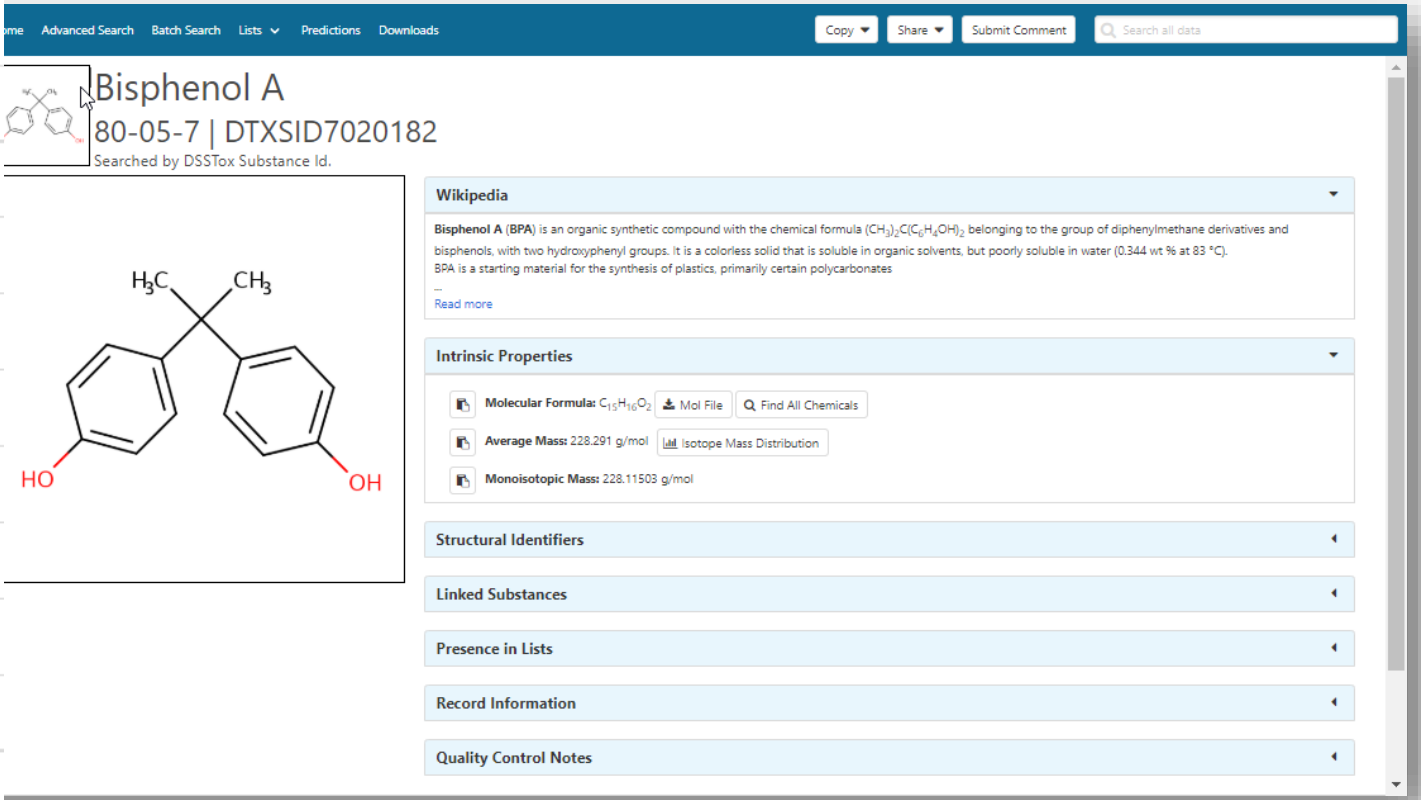
EPA United States Environmental Protection Agency

LIVE DEMO

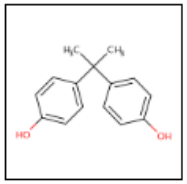
Detailed Chemical Pages

EPA United States Environmental Protection Agency

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



Properties, Fate and Transport



Bisphenol A

80-05-7 | DTXSID7020182

Searched by DSSTox Substance Id.

Property

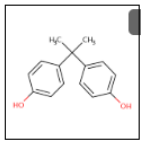
Summary

Summary

Download Columns

Property	Experimental average	Predicted average	Experimental median	Predicted median
LogKow: Octanol-Water	3.32 (1)	3.30		3.39
Melting Point	155 (7)	140	156	144
Boiling Point	200 (1)	360		355
Water Solubility	8.55e-4 (3)	8.78e-4	5.26e-4	7.56e-4
Vapor Pressure	-	6.83e-7		1.51e-7
Flash Point	-	190		190
Surface Tension	-	46.0		
Index of Refraction	-	1.60		
Molar Refractivity	-	68.2		

Hazard



Bisphenol A

80-05-7 | DTXSID7020182

Searched by Expert Validated Synonym.

Hazard

DataType

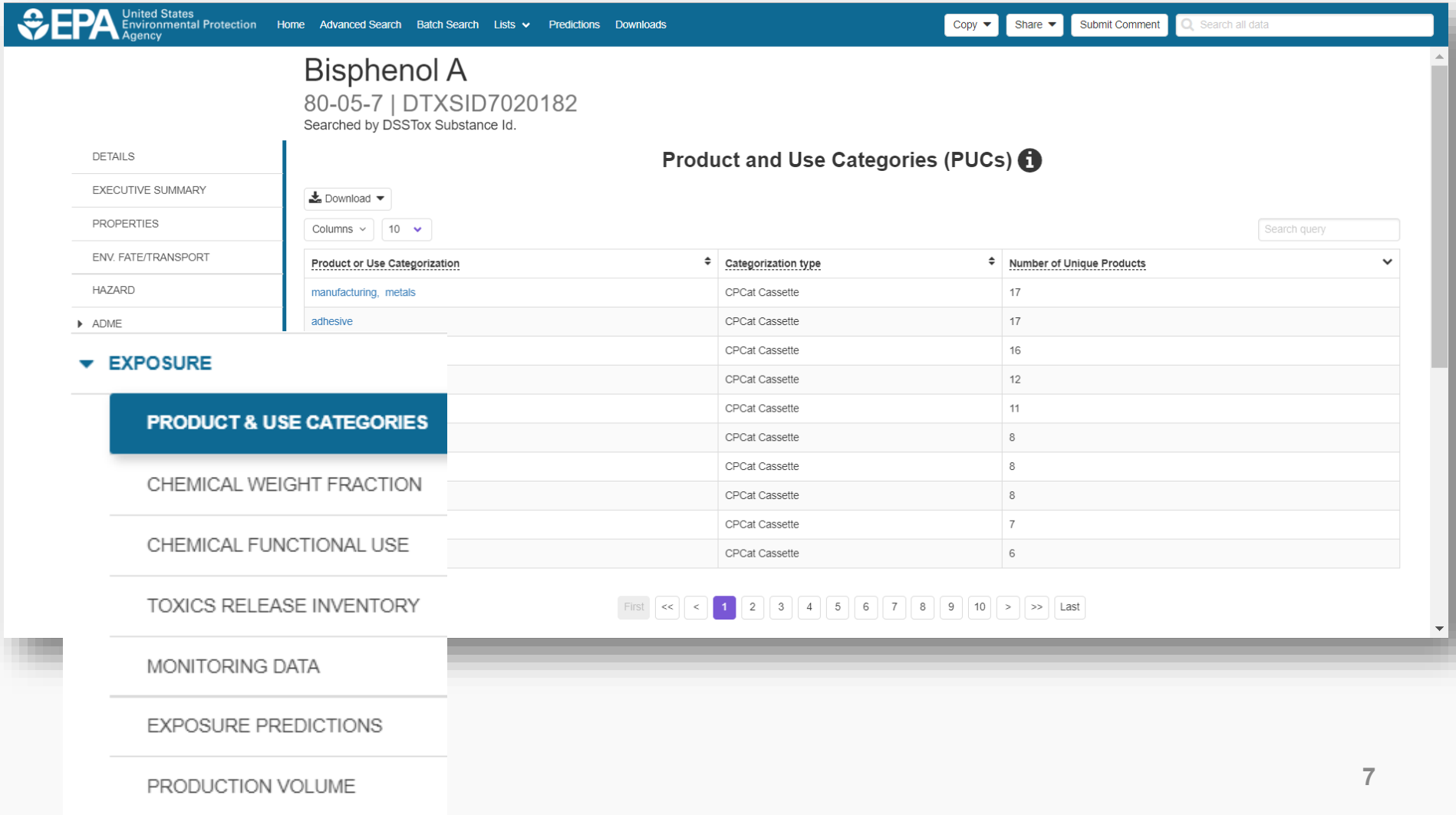
Point of Departure

Human | Eco

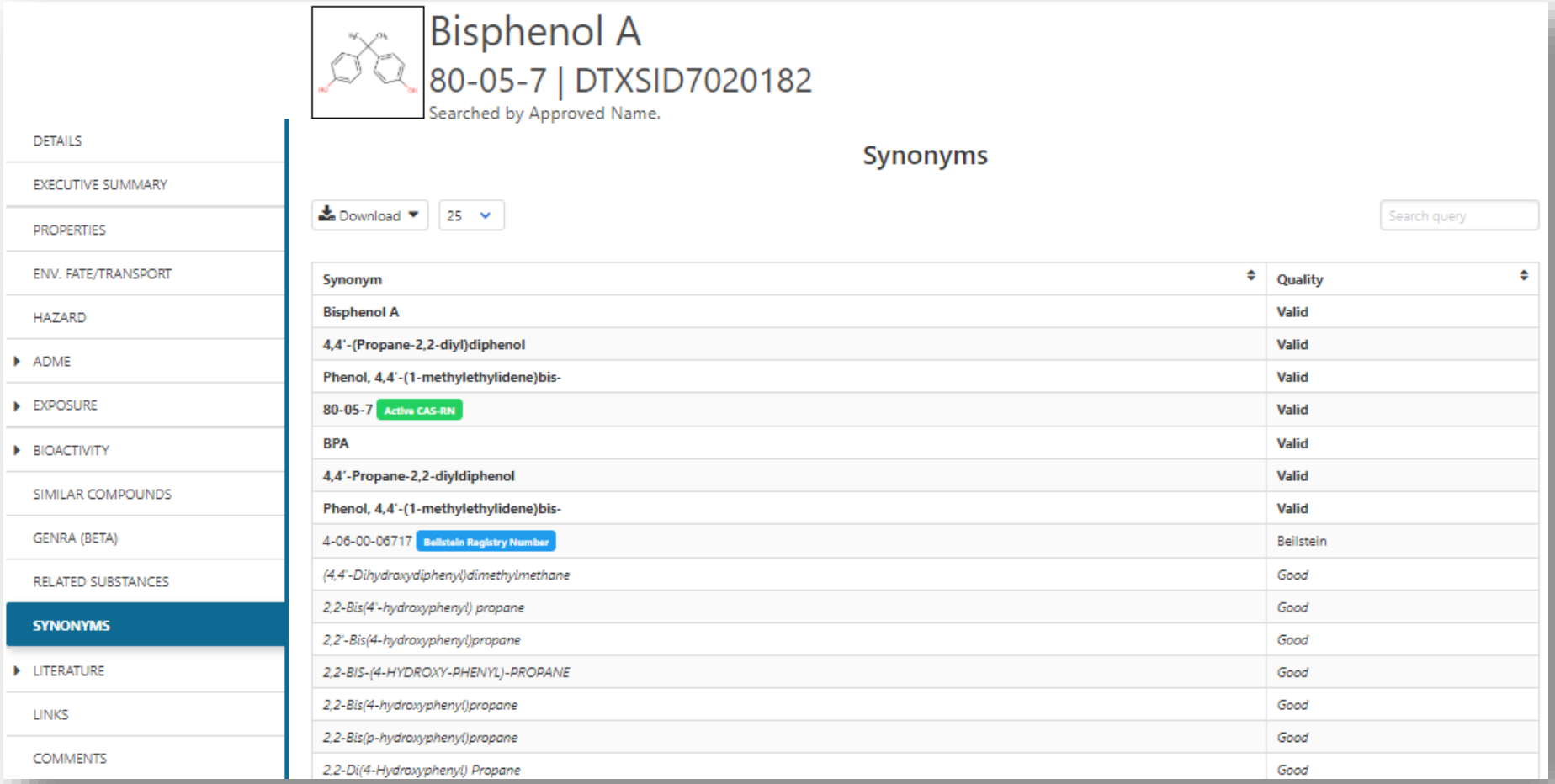
Download | Columns | 10 | Search query

More	Priority	Type	Subtype	Risk assessment class	Value	Units	Study type	Exposure route	Species	Subsource	Source
	4	NOAEL	-	developmental neurotoxicity	0.015	mg/kg-day	developmental neurotoxicity	oral	rat	EPA ORD	ToxRefDB
	4	NEL	-	developmental neurotoxicity	0.015	mg/kg-day	developmental neurotoxicity	oral	rat	EPA ORD	ToxRefDB
	4	LOAEL	-	developmental neurotoxicity	0.015	mg/kg-day	developmental neurotoxicity	oral	rat	EPA ORD	ToxRefDB
	4	LEL	-	developmental neurotoxicity	0.015	mg/kg-day	developmental neurotoxicity	oral	rat	EPA ORD	ToxRefDB
	4	NEL	-	developmental neurotoxicity	0.03	mg/kg-day	developmental neurotoxicity	oral	mouse	EPA ORD	ToxRefDB
	4	LEL	-	developmental neurotoxicity	0.03	mg/kg-day	developmental neurotoxicity	oral	mouse	EPA ORD	ToxRefDB
	4	NEL	-	developmental neurotoxicity	0.04	mg/kg-day	developmental neurotoxicity	oral	rat	EPA ORD	ToxRefDB
	4	LEL	-	developmental neurotoxicity	0.04	mg/kg-day	developmental neurotoxicity	oral	rat	EPA ORD	ToxRefDB

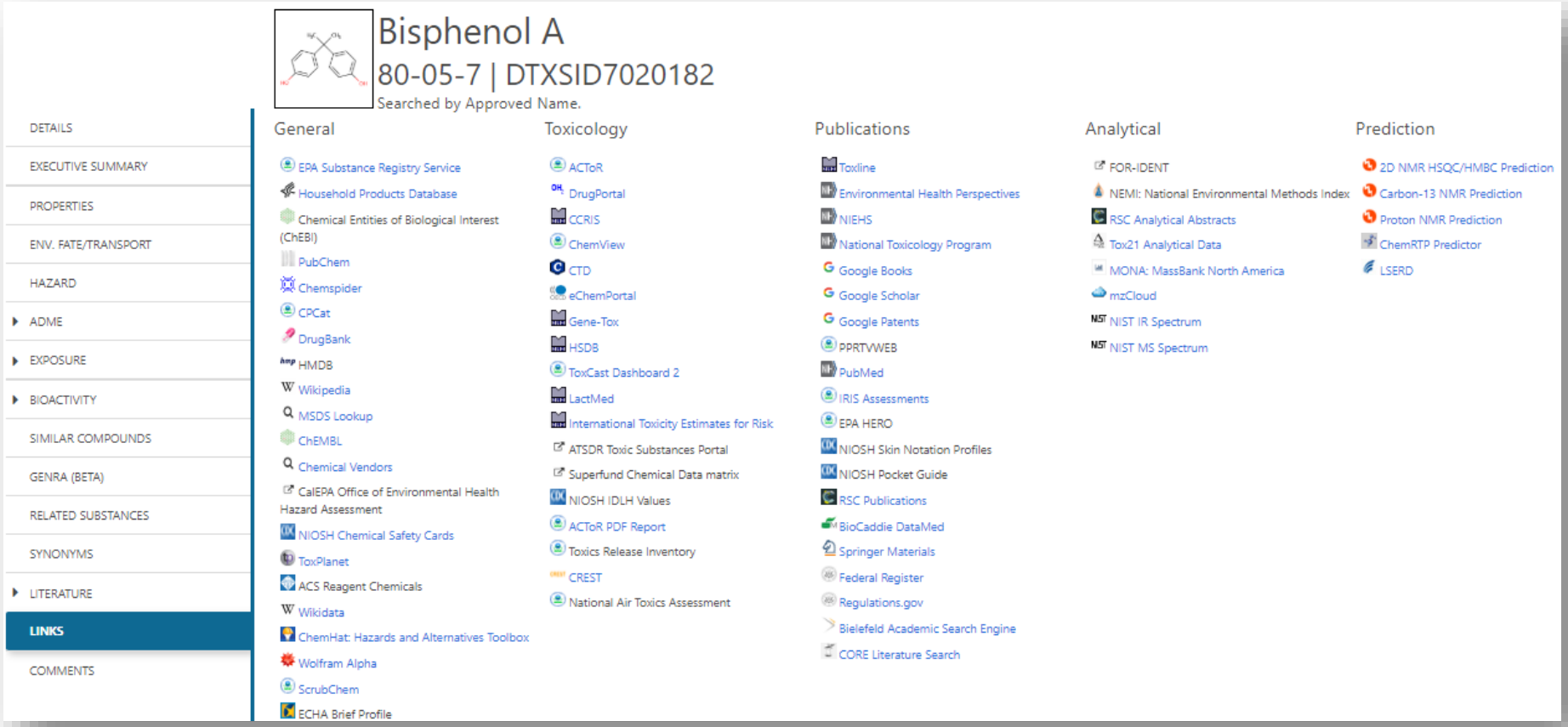
Sources of Exposure to Chemicals



Identifiers to Support Searches



Link Access


Bisphenol A
80-05-7 | DTXSID7020182
Searched by Approved Name.
DETAILS
EXECUTIVE SUMMARY
PROPERTIES
ENV. FATE/TRANSPORT
HAZARD
ADME
EXPOSURE
BIOACTIVITY
SIMILAR COMPOUNDS
GENRA (BETA)
RELATED SUBSTANCES
SYNONYMS
LITERATURE
LINKS
COMMENTS
General
EPA Substance Registry Service
Household Products Database
Chemical Entities of Biological Interest (ChEBI)
PubChem
Chemspider
CPCat
DrugBank
HMDB
Wikipedia
MSDS Lookup
ChEMBL
Chemical Vendors
CalEPA Office of Environmental Health Hazard Assessment
NIOSH Chemical Safety Cards
ToxPlanet
ACS Reagent Chemicals
Wikidata
ChemHat: Hazards and Alternatives Toolbox
Wolfram Alpha
ScrubChem
ECHA Brief Profile
Toxicology
ACToR
DrugPortal
CCRIS
ChemView
CTD
eChemPortal
Gene-Tox
HSDB
ToxCast Dashboard 2
LactMed
International Toxicity Estimates for Risk
ATSDR Toxic Substances Portal
Superfund Chemical Data matrix
NIOSH IDLH Values
ACToR PDF Report
Toxics Release Inventory
CREST
National Air Toxics Assessment
Publications
Toxline
Environmental Health Perspectives
NIEHS
National Toxicology Program
Google Books
Google Scholar
Google Patents
PPRTVWEB
PubMed
IRIS Assessments
EPA HERO
NIOSH Skin Notation Profiles
NIOSH Pocket Guide
RSC Publications
BioCaddie DataMed
Springer Materials
Federal Register
Regulations.gov
Bielefeld Academic Search Engine
CORE Literature Search
Analytical
FOR-IDENT
NEMI: National Environmental Methods Index
RSC Analytical Abstracts
Tox21 Analytical Data
MONA: MassBank North America
mzCloud
NIST IR Spectrum
NIST MS Spectrum
Prediction
2D NMR HSQC/HMBC Prediction
Carbon-13 NMR Prediction
Proton NMR Prediction
ChemRTP Predictor
LSERD

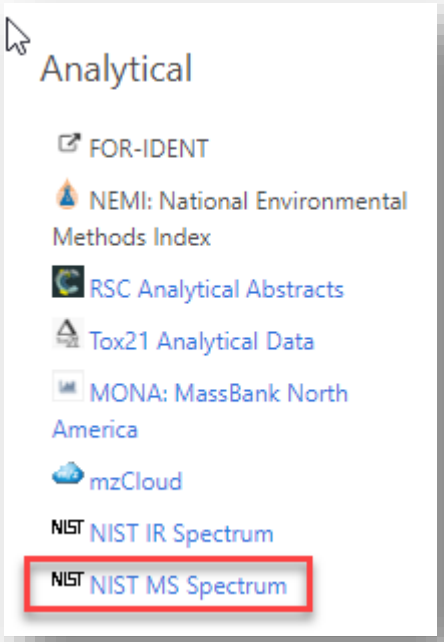
Mass Spec Links

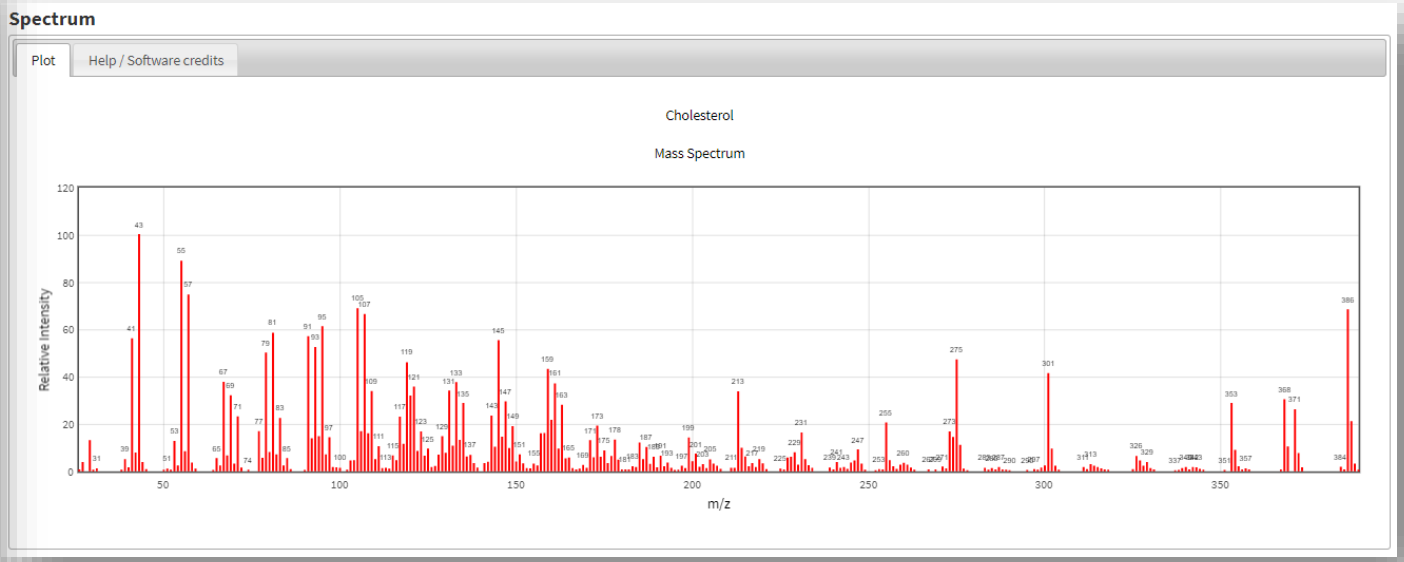
Analytical

- 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

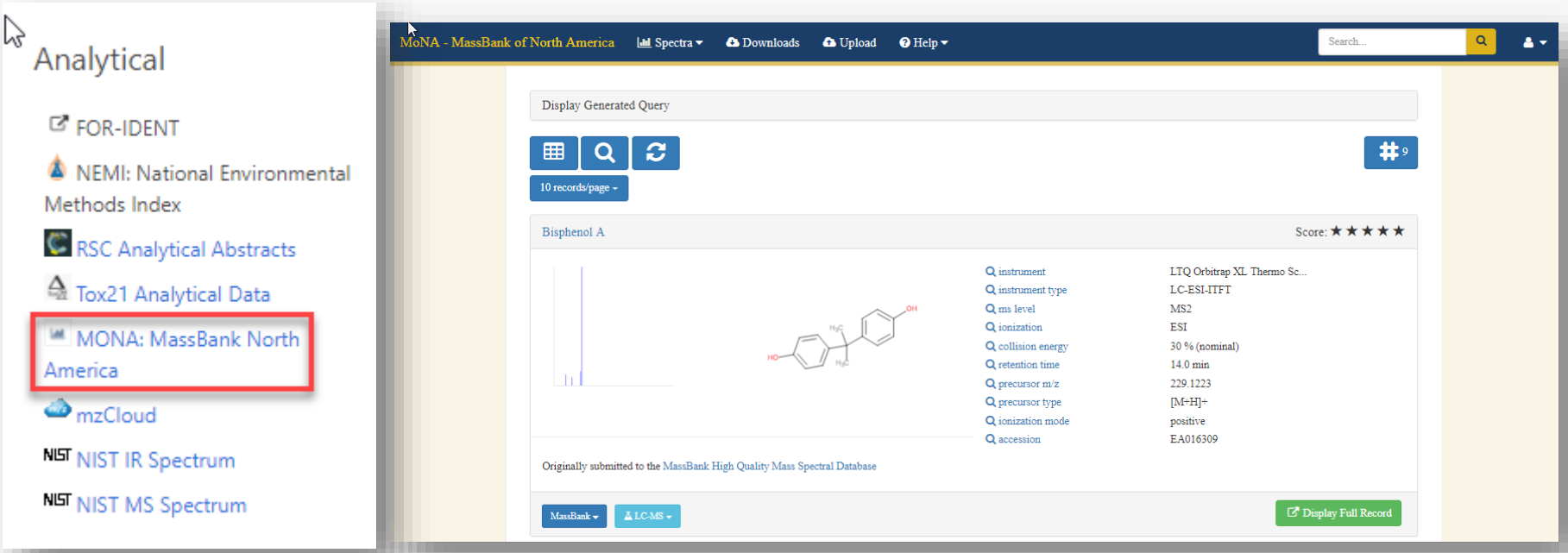
NIST WebBook
https://webbook.nist.gov/chemistry/

EPA United States Environmental Protection Agency





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



Batch Searching

Aggregate data for a list of chemicals

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]

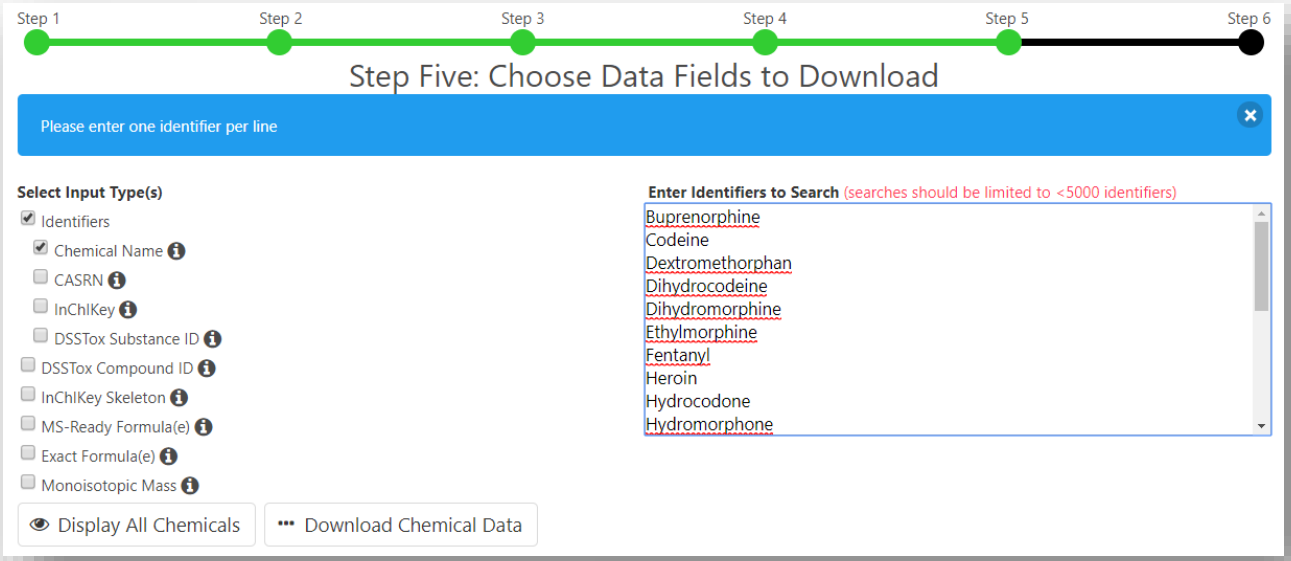
Show more

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

Get rights and content

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

Add Other Data of Interest

Chemical Identifiers

- [x] DTXSID
- [x] Chemical Name
- [ ] DTXCID
- [x] CAS-RN
- [x] InChIKey
- [ ] IUPAC Name

Structures

- [ ] Mol File
- [ ] SMILES
- [ ] InChI String
- [x] MS-Ready SMILES
- [ ] QSAR-Ready SMILES

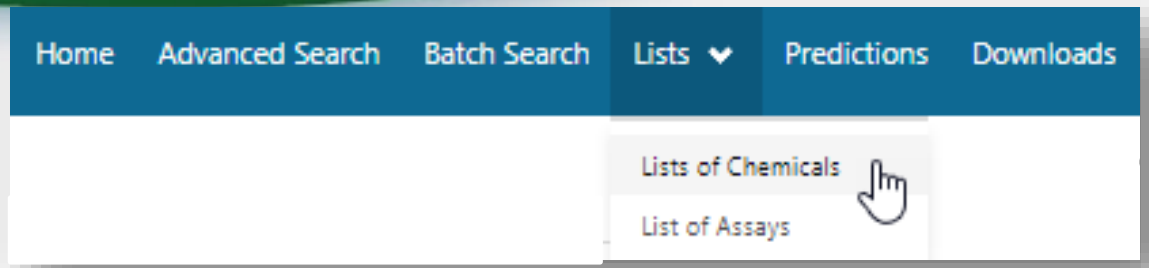
Intrinsic And Predicted Properties

- [x] Molecular Formula
- [ ] Average Mass
- [x] Monoisotopic Mass
- [ ] TEST Model Predictions
- [ ] OPERA Model Predictions

INPUT	DTXSID	CASRN	MOLECULAR_F	MONOISOTOPIC	MS_READY_SMI
Buprenorph	DTXSID202	52485-79-7	C29H41NO4	467.3035588	[H]C12CC3=C4C(
Codeine	DTXSID202	76-57-3	C18H21NO3	299.1521435	[H]C12CC3=C4C(
Dextrometh	DTXSID302	125-71-3	C18H25NO	271.1936144	[H]C12CC3=C(C=
Dihydrocod	DTXSID502	125-28-0	C18H23NO3	301.1677936	[H]C12CC3=C4C(
Dihydromor	DTXSID704	509-60-4	C17H21NO3	287.1521435	[H]C12CC3=C4C(
Ethylmorph	DTXSID104	76-58-4	C19H23NO3	313.1677936	[H]C12CC3=C4C(
Fentanyl	DTXSID902	437-38-7	C22H28N2O	336.2201635	CCC(=O)N(C1CC
Heroin	DTXSID604	561-27-3	C21H23NO5	369.1576228	[H]C12CC3=C4C(
Hydrocodor	DTXSID802	125-29-1	C18H21NO3	299.1521435	[H]C12CC3=C4C(
Hydromorph	DTXSID802	466-99-9	C17H19NO3	285.1364935	[H]C12CC3=C4C(
Ketamine	DTXSID802	6740-88-1	C13H16ClNO	237.0920418	CNC1(CCCCC1=(
Meperidine	DTXSID902	57-42-1	C15H21NO2	247.1572289	CCOC(=O)C1(CC
Methadone	DTXSID702	76-99-3	C21H27NO	309.2092645	CCC(=O)C(CC(C)
Morphine	DTXSID902	57-27-2	C17H19NO3	285.1364935	[H]C12CC3=C4C(
Morphinone	DTXSID501	467-02-7	C17H17NO3	283.1208434	[H]C12CC3=C4C(
Naloxone	DTXSID802	465-65-6	C19H21NO4	327.1470582	[H]C12CC3=C4C(
Naltriben	-	-	-	-	-
Oxycodone	DTXSID502	76-42-6	C18H21NO4	315.1470582	[H]C12CC3=C4C(
Oxymorpho	DTXSID502	76-41-5	C17H19NO4	301.1314081	[H]C12CC3=C4C(
Propoxyphe	DTXSID102	469-62-5	C22H29NO2	339.2198292	CCC(=O)OC(CC1
Sufentanil	DTXSID602	56030-54-7	C22H30N2O2S	386.2027994	CCC(=O)N(C1=C
Tramadol	DTXSID908	27203-92-5	C16H25NO2	263.188529	COC1=CC=CC(=

Chemical Lists of Interest…

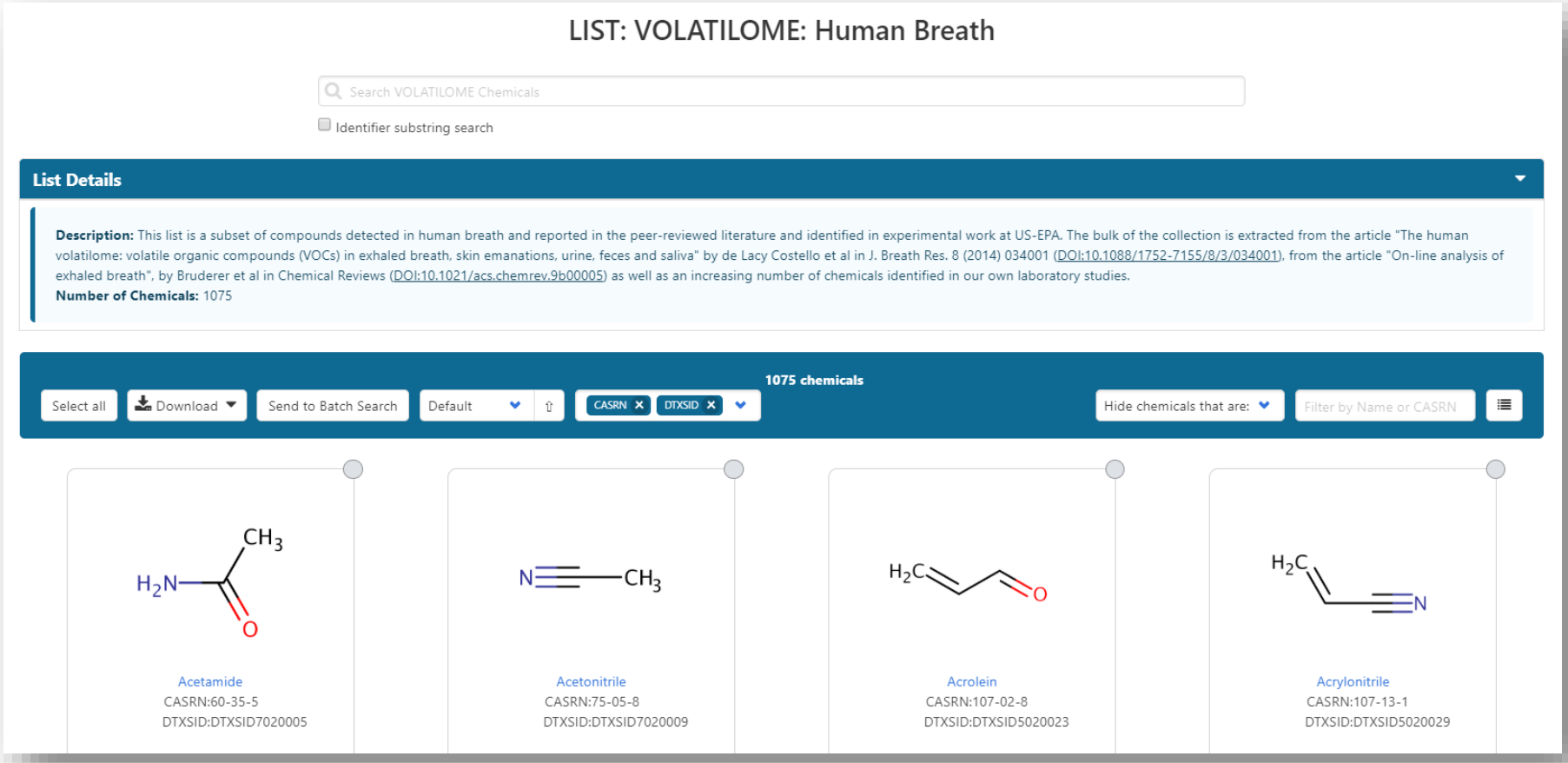
290 Chemical Lists (and growing)



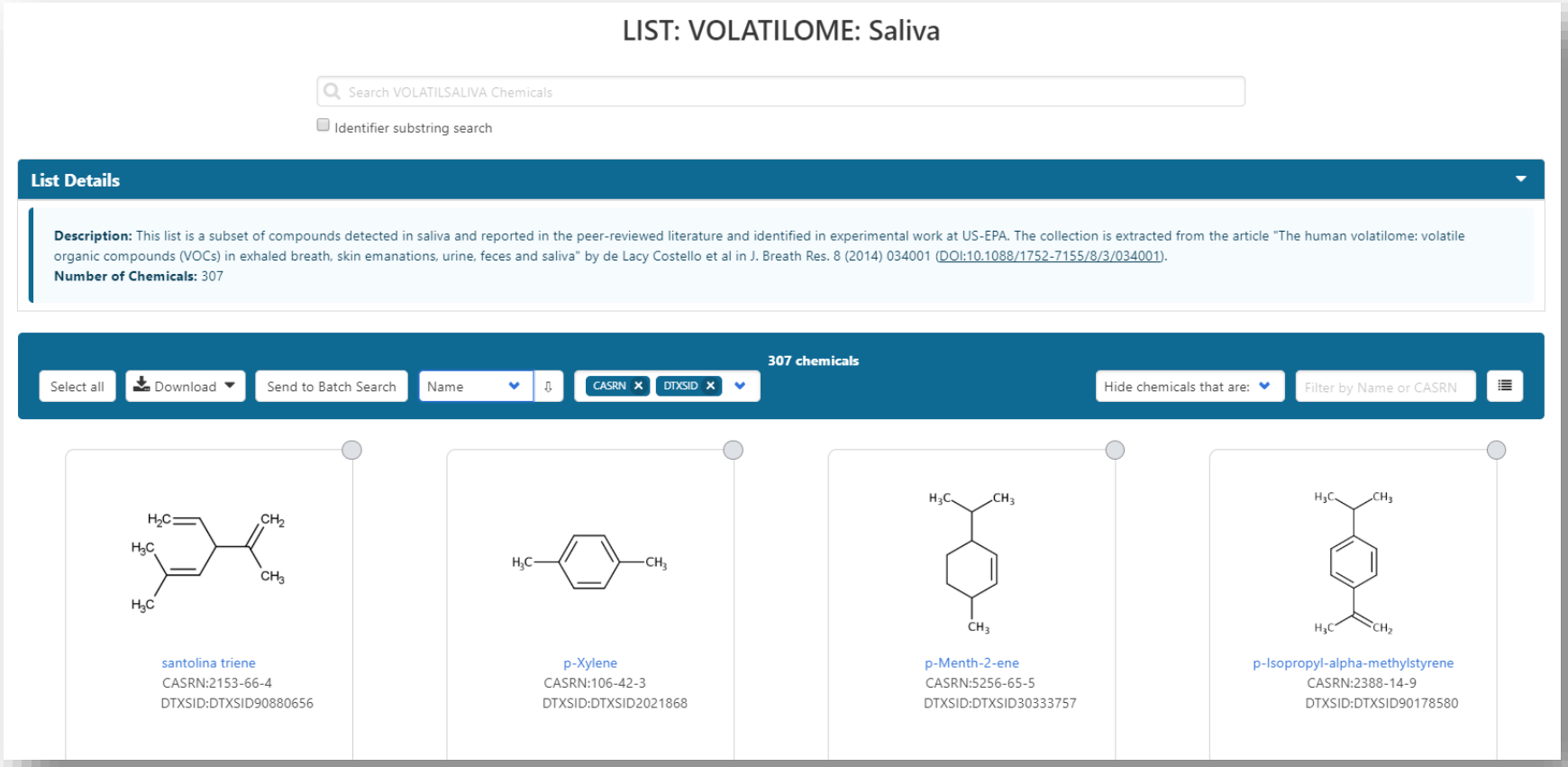
Download | Columns | mass | Copy Filtered Lists URL

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

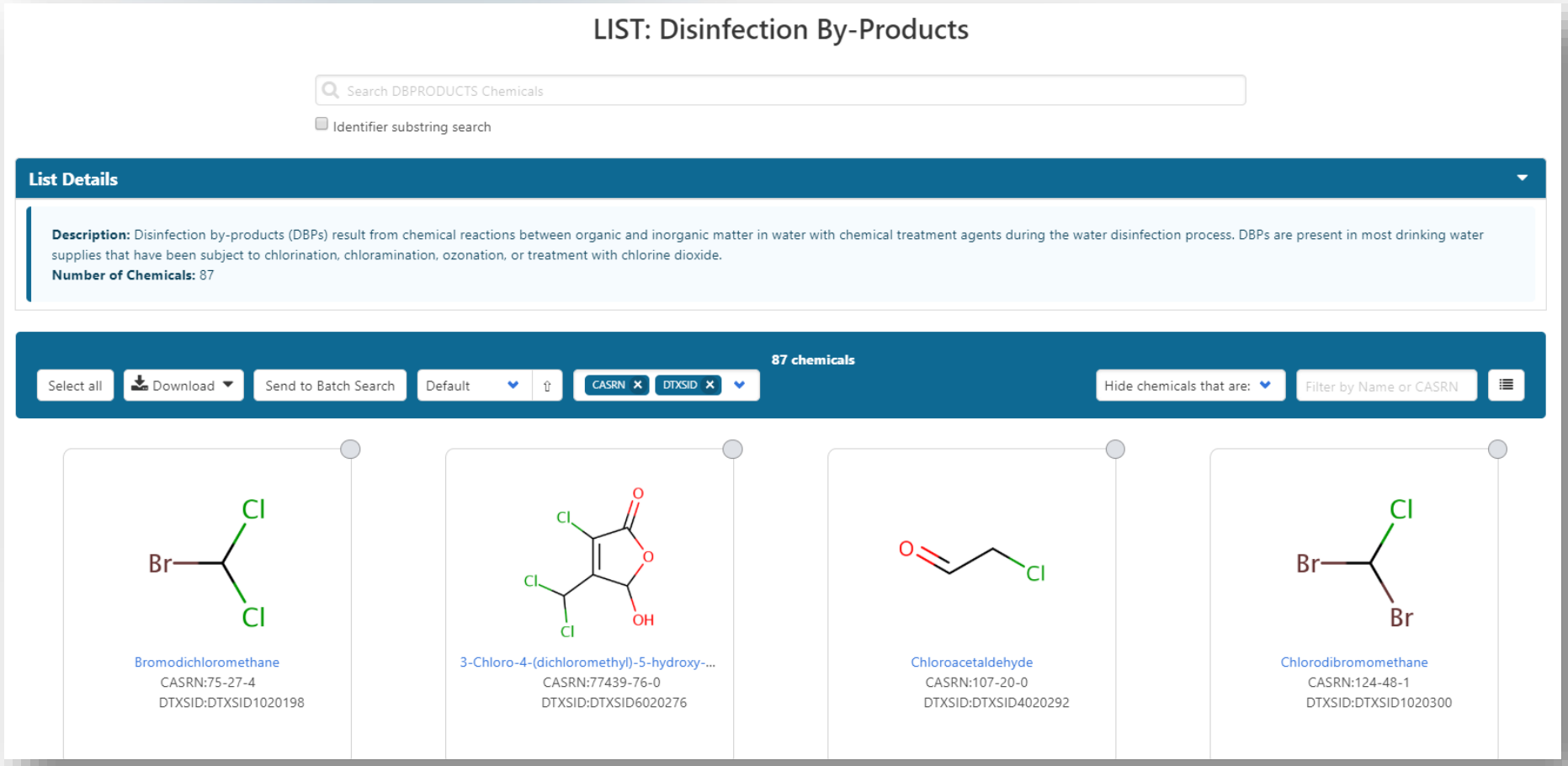
“Volatilome” Human Breath



“Volatilome” Saliva



Disinfection By-Products



Tire Crumb Rubber (298)

EPA United States Environmental Protection Agency

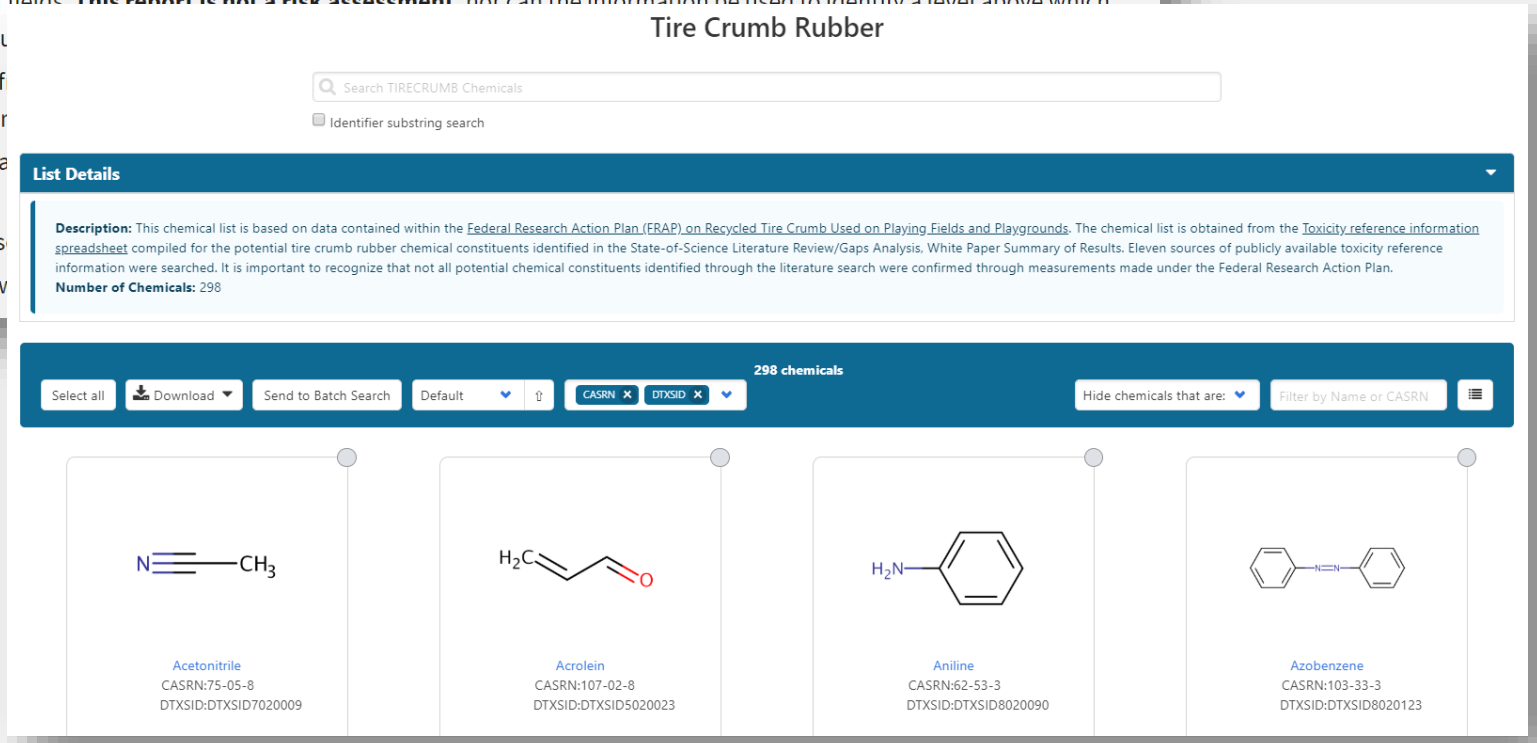
Related Topics: Safer Chemicals Research

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



Terpenes in Vape (37)

EPA United States Environmental Protection Agency

LIST: Terpenes in vape

Search VAPETERPENES Chemicals

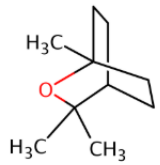
Identifier substring search

List Details

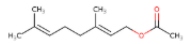
Description: Terpenes are organic compounds found in the marijuana plant that give strains their distinct aromatic and flavor profiles. They are now being isolated and concentrated into oils for individual vaping.
Number of Chemicals: 37

37 chemicals

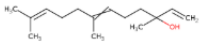
Select all | Download | Send to Batch Search | Default | CASRN | DTXSID | Hide chemicals that are: | Filter by Name or CASRN



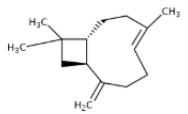
1,8-Cineol
CASRN:470-82-6
DTXSID:DTXSID4020616



Geranyl acetate
CASRN:105-87-3
DTXSID:DTXSID0020654



Nerolidol
CASRN:7212-44-4
DTXSID:DTXSID3022247



beta-Caryophyllene
CASRN:87-44-5
DTXSID:DTXSID8024739

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

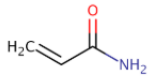
*Note that Appendix H chemical listings in Tables H-2 and H-4 were mapped to current DSSTox content, which has undergone additional curation since the publication of the original EPA HF Report (Dec 2016). In the few cases where a Chemical Name and CASRN from the original report map to distinct substances (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

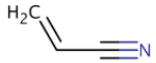
1640 chemicals

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

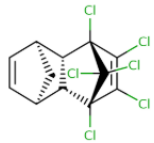
Acrolein
CASRN:107-02-8
DTXSID:DTXSID5020023



Acrylamide
CASRN:79-06-1
DTXSID:DTXSID5020027

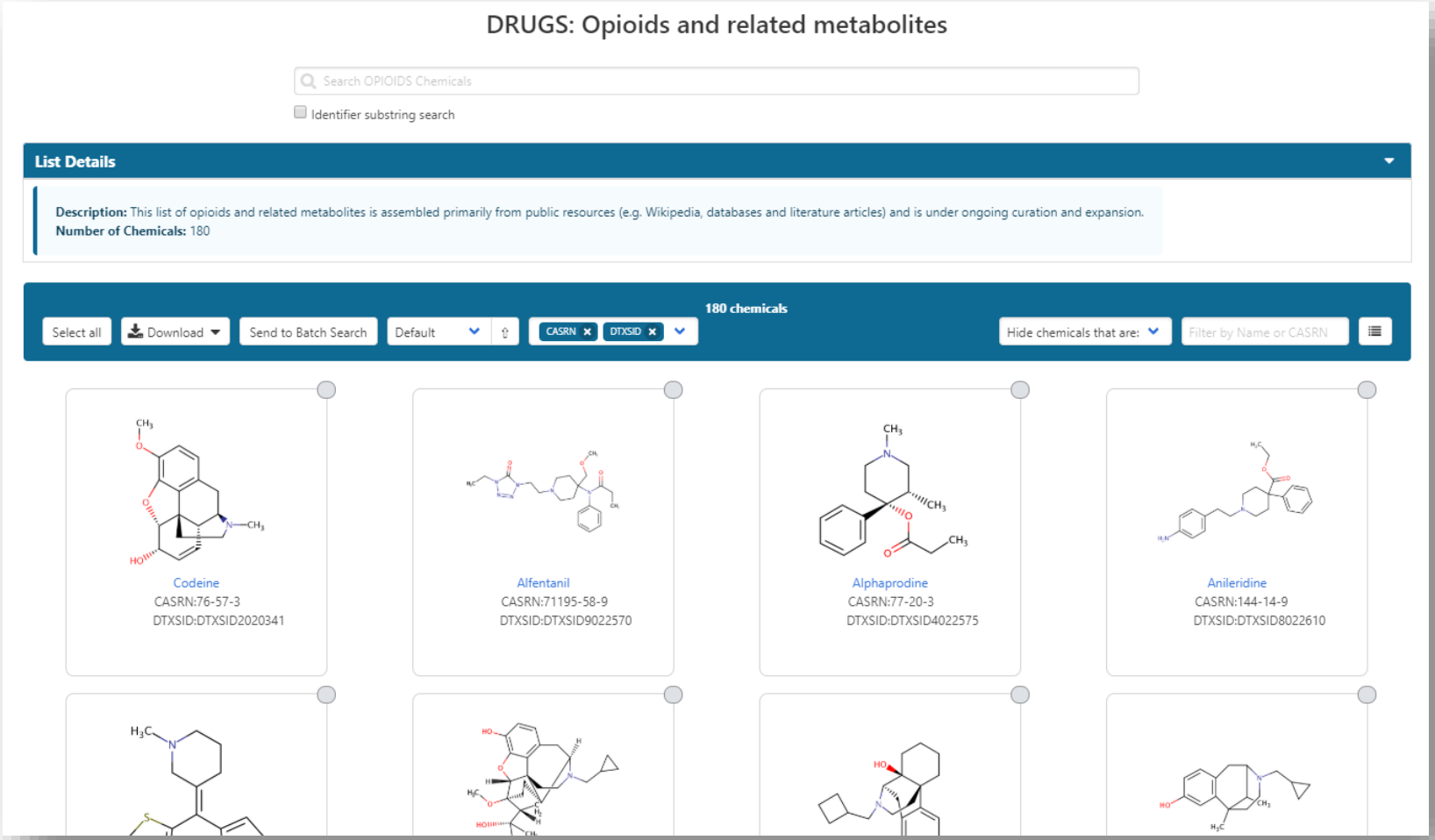


Acrylonitrile
CASRN:107-13-1
DTXSID:DTXSID5020029



Aldrin
CASRN:309-00-2
DTXSID:DTXSID8020040

Opioids and Metabolites (160)



Mycotoxins

EPA United States Environmental Protection Agency

MASSPECDB: Mycotoxins from MassBank.EU

Search MYCOTOXINS Chemicals

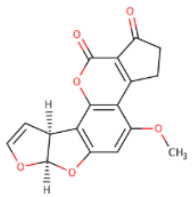
Identifier substring search

List Details

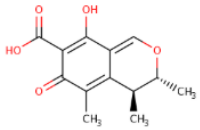
Description: This is a set of mycotoxins, initiated by the contribution of spectra of 90 mycotoxins to MassBank.EU by Justin Renaud and colleagues from Agriculture and Agri-Food Canada, Government of Canada. This list is also a part of the MASSBANKREF list and the NORMAN Suspect Exchange and will be expanded as new contributions arrive.
Number of Chemicals: 88

88 chemicals

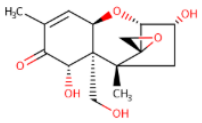
Select all | Download | Send to Batch Search | Default | CASRN | DTXSID | Hide chemicals that are: | Filter by Name or CASRN



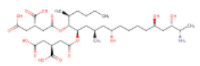
Aflatoxin B1
CASRN:1162-65-8
DTXSID:DTXSID9020035



Citrinin
CASRN:518-75-2
DTXSID:DTXSID8020333

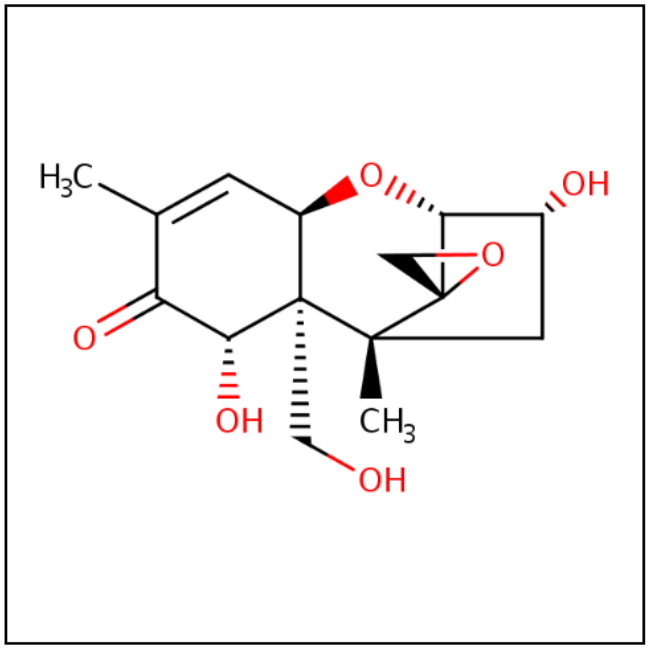


Vomitoxin
CASRN:51481-10-8
DTXSID:DTXSID3020382



Fumonisin B1
CASRN:116355-83-0
DTXSID:DTXSID6020644

Vomitoxin



Structural Identifiers

IUPAC Name: (3alpha,7alpha)-3,7,15-Trihydroxy-12,13-epoxytrichothec-9-en-8-one

SMILES: CC1=C[C@H]2O[C@@H]3[C@H](O)C[C@@](C)([C@]33CO3)[C@@]2(CO)[C

InChI String: InChI=1S/C15H20O6/c1-7-3-9-14(5-16,11(19)10(7)18)13(2)4-8(17)12(2

2H3/t8-,9-,11-,12-,13-,14-,15+/m1/s1

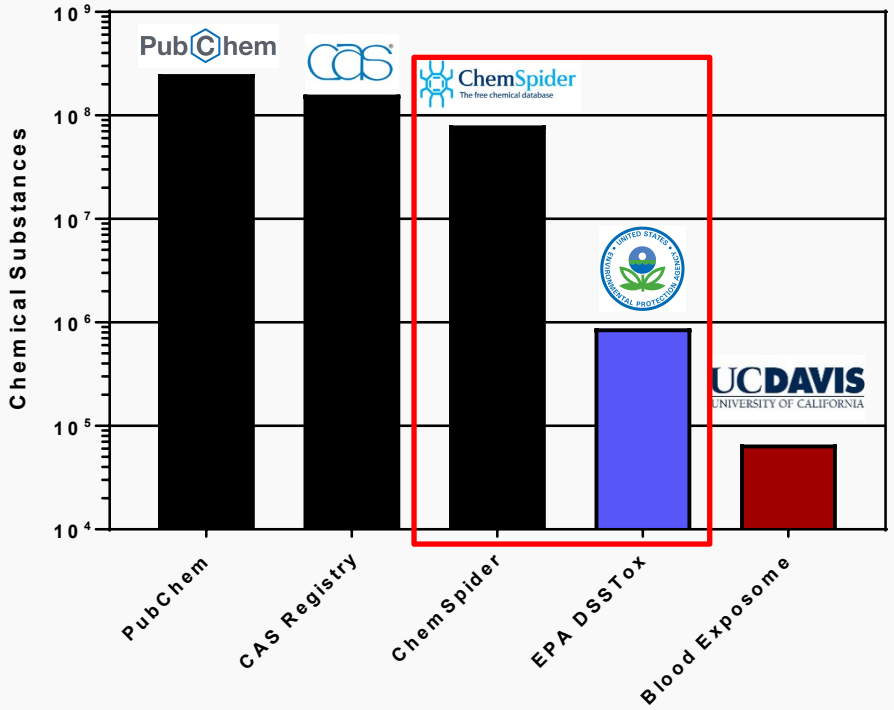
InChIKey: LINOMUASTDIRTM-QGRHZQQGSA-N

Search Google for: Structural Skeleton | Full Structure

Copy All

BIG databases are GREAT!

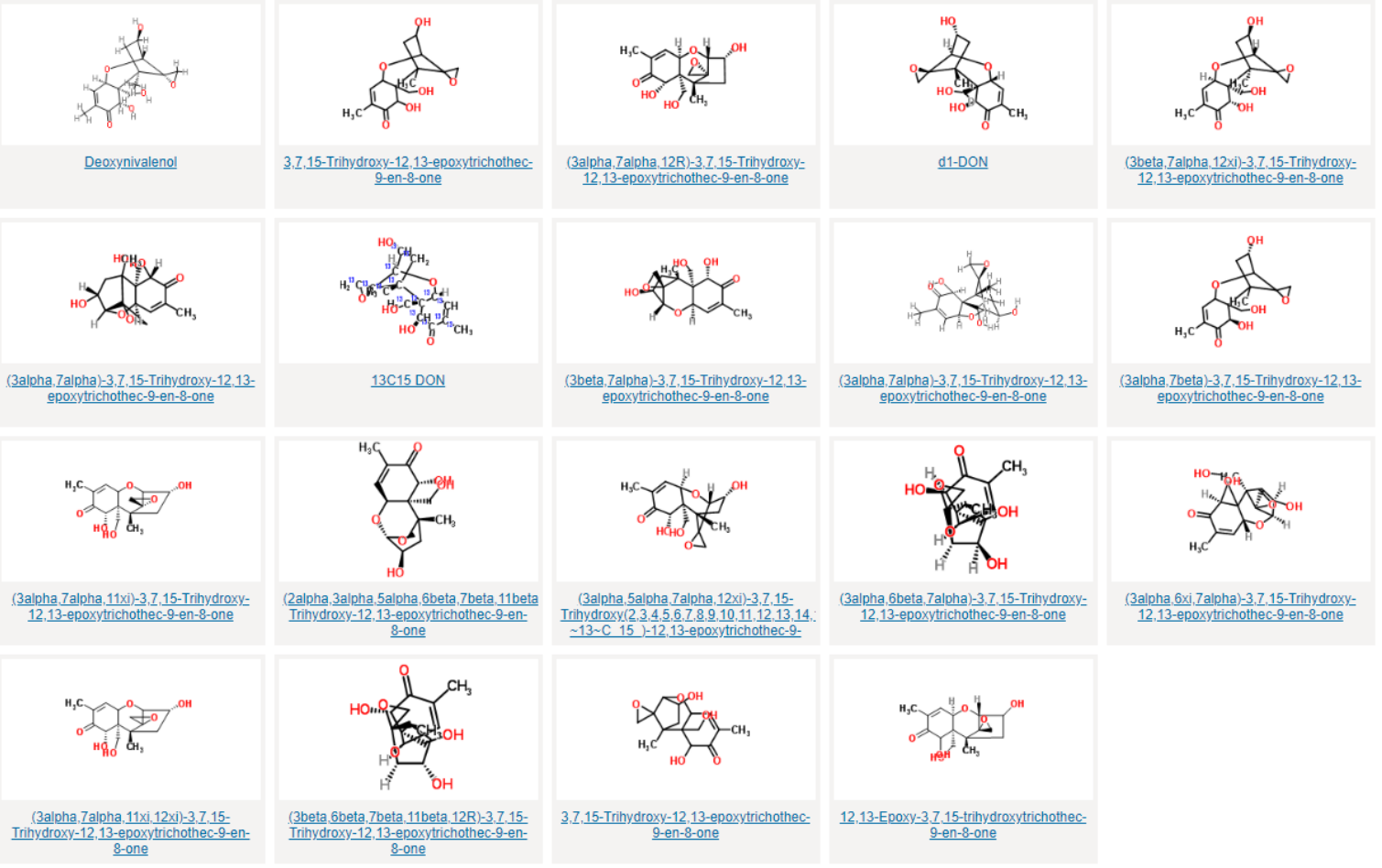
- Thanks to all of the public database efforts
- So much benefit from what's been done
- There are hundreds of them at this point…



Vomitoxin - ChemSpider

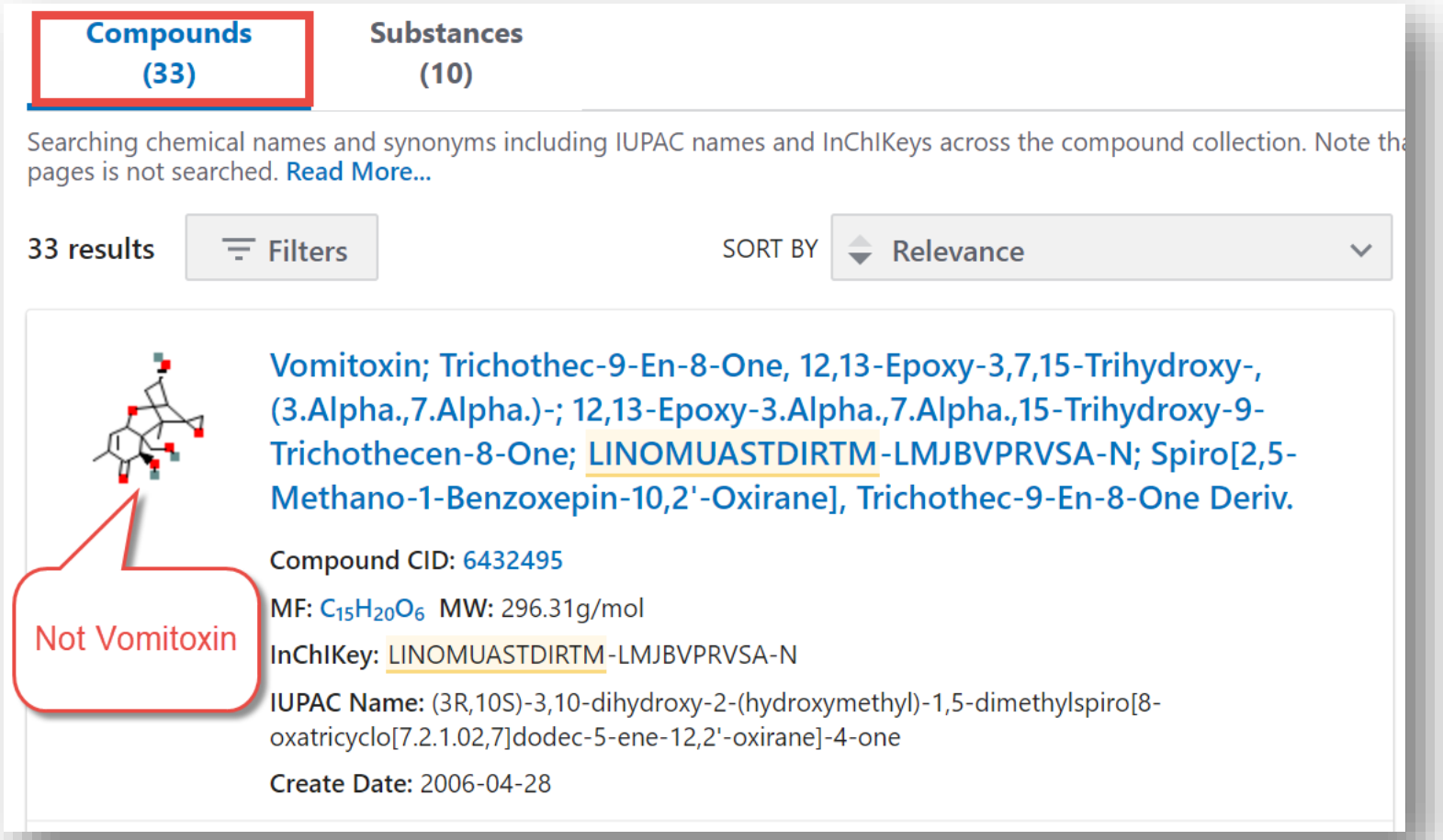
- 19 “Vomitoxins” – 3 isotopically labeled

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



Vomitoxin – PubChem

- 33 unique InChI Keys



PubChem – “virtual chemistry”

- Other databases grow quickly…a lot of “virtual chemistry” and “make on demand” compounds. Vomitoxin has 7 ZINC stereoforms.

PUBCHEM_CID	Compound_Name	Compound_Synonym	InChIKey
98043267	(1R,2S,3R,7R,9S,10R,12S)	ZINC100006545	LINOMUASTDIRTM-DOZBXCHUSA-N
98051113	(1R,2R,3S,7S,9S,10R,12S)	ZINC100066010	LINOMUASTDIRTM-KCWNRFLPSA-N
100853641	(1R,2R,3S,7S,9S,10R,12R)	ZINC229762267	LINOMUASTDIRTM-OMTHLLQNSA-N
98043268	(1R,2S,3R,7S,9S,10R,12S)	ZINC100006546	LINOMUASTDIRTM-UBTIPYQWSA-N
95566296	(1R,2S,3R,7R,9R,10R,12S)	ZINC71789640	LINOMUASTDIRTM-WYQUPHEGSA-N
100853642	(1R,2R,3S,7R,9S,10R,12R)	ZINC229762273	LINOMUASTDIRTM-XFRIDARHSA-N
95566297	(1R,2S,3R,7S,9R,10R,12S)	ZINC71789642	LINOMUASTDIRTM-XGQZSAOASA-N

- The Dashboard database grows slowly (next release is +20k chemicals in 6 months)

ChemSpider – lots of virtuals???

- 52 million chemicals from one vendor

Data Sources

Data Source	Count	Date Created	Last Updated
Aurora Fine Chemicals	51885566	13/04/2009	09/01/2020
Chemspace	14283313	30/11/2016	04/12/2018
AKos	12326374	15/04/2008	09/10/2017
Mcule	9299739	21/01/2014	26/10/2018
Molport	8200357	09/02/2010	09/01/2020
Enamine	3056649	15/04/2008	15/10/2019

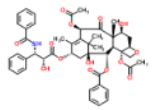
Taxol: 79 Results

EPA United States Environmental Protection Agency

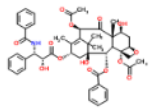
Found 79 results

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

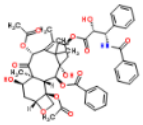
First | < | > | Last



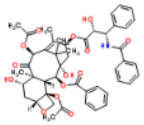
paclitaxel



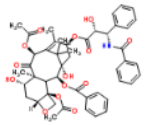
(2alpha,3xi,5beta,7beta,10beta,13alpha)-4 Diacetoxy-13-{[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-



(2alpha,5beta,7alpha,10beta,13alpha)-4,1 Diacetoxy-13-{[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-



(5beta,7beta,10alpha,13alpha)-4,10-bis(acetyloxy)-13-{[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-



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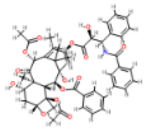
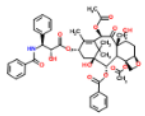
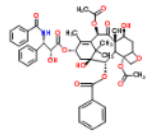


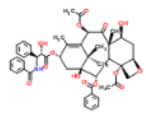
NSC-LSC-1



(2alpha,3xi,5beta,7alpha,10beta,13alpha)-Diacetoxy-13-{[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-



(2alpha,3xi,7beta,10beta,13alpha)-4,10-Diacetoxy-13-{[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-



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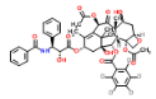

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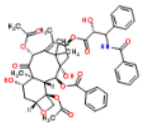

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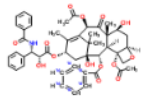

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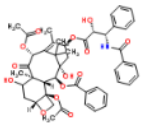

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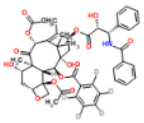
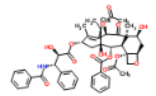
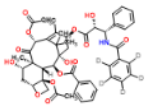


(2alpha,5beta,7beta,10beta,13alpha)-4,10 Diacetoxy-13-{[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-



(2alpha,5beta,7beta,8alpha,10beta,13alph Diacetoxy-13-{[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-



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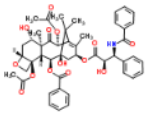

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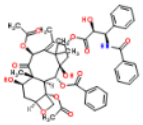
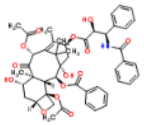


(1beta,2beta,3beta,4alpha,5alpha,7alpha,1 Diacetoxy-13-{[(2S,3R)-3-(benzoylamino)-2-hydroxy-3-



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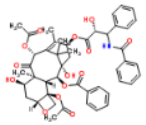
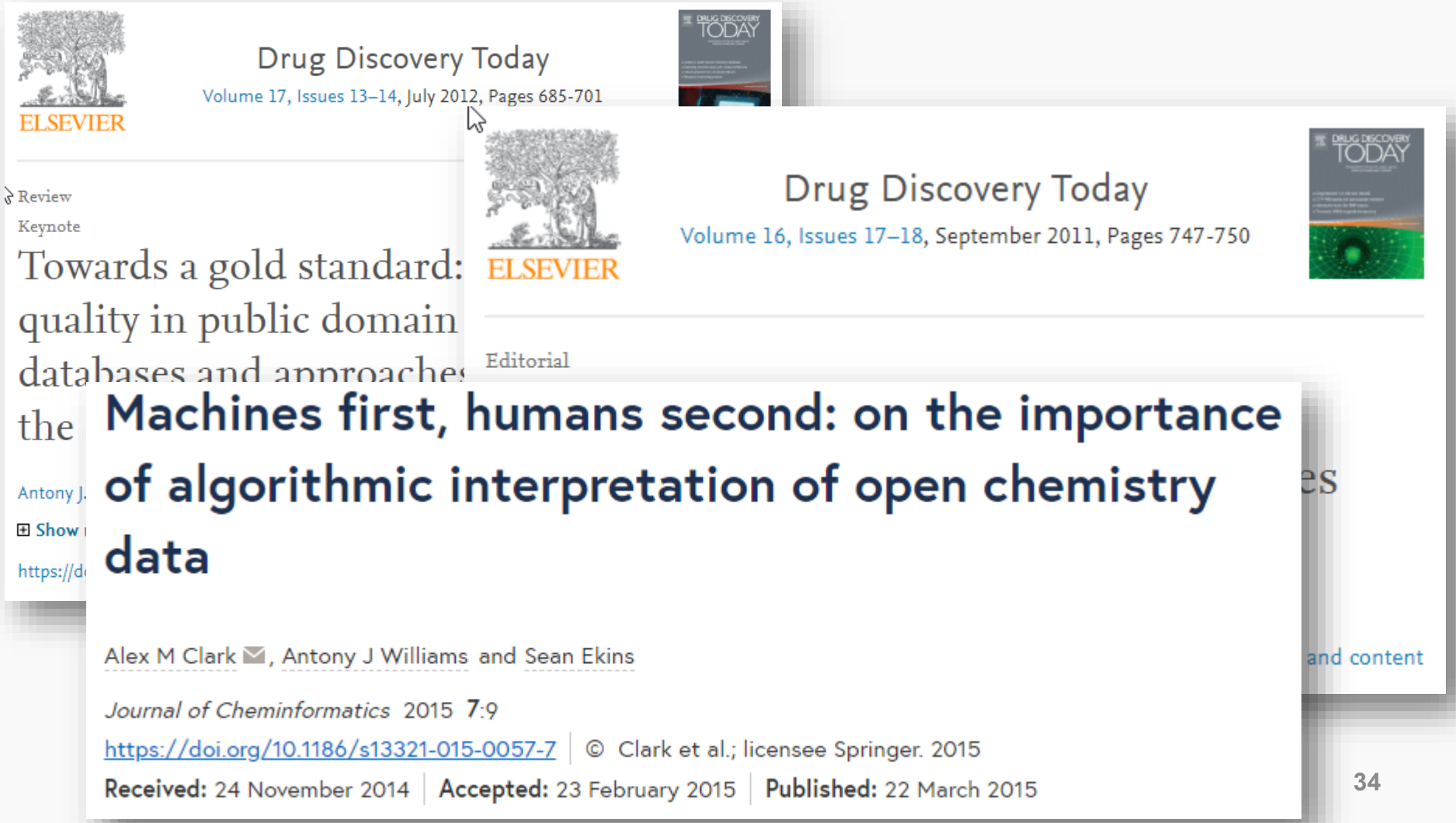


(2alpha,5beta,7alpha,10beta,13alpha)-4,1 Diacetoxy-13-{[(2R)-3-(benzoylamino)-2-hydroxy-3-phenylpropanoyl]oxy}-1,7-

Data Quality is important

- Data quality in free web-based databases!



Drug Discovery Today
Volume 17, Issues 13–14, July 2012, Pages 685-701
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Keynote
Towards a gold standard:
quality in public domain
databases and approaches
the
Antony J.
Show
https://d

Drug Discovery Today
Volume 16, Issues 17–18, September 2011, Pages 747-750
ELSEVIER
Editorial

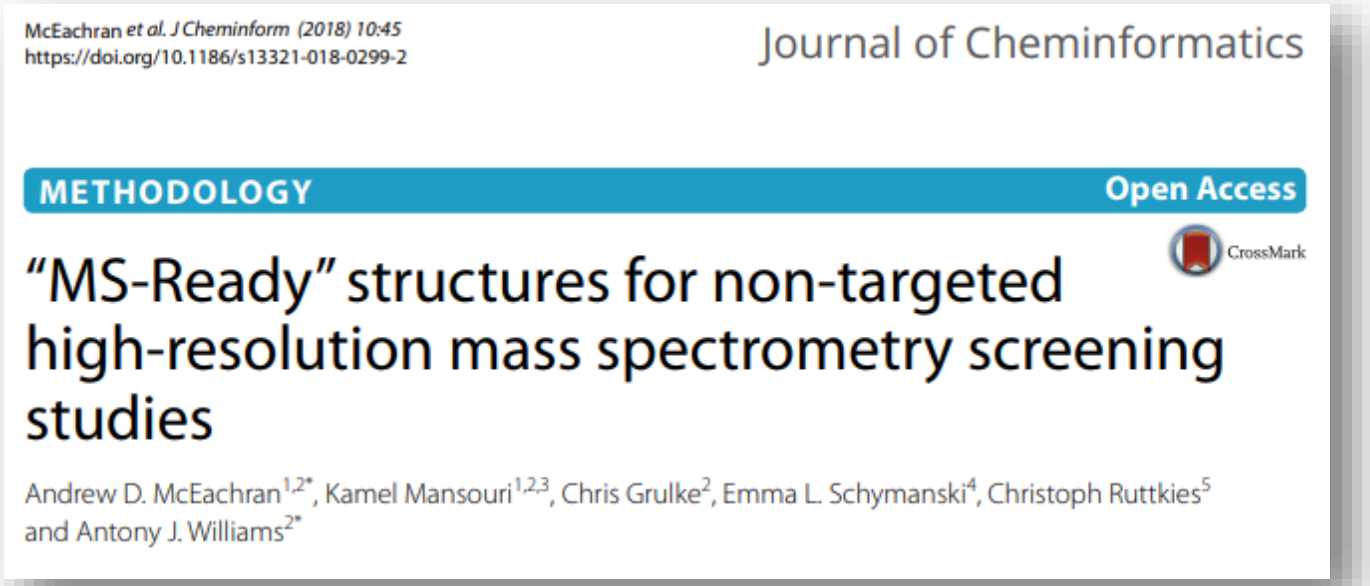
Machines first, humans second: on the importance of algorithmic interpretation of open chemistry data

Alex M Clark, Antony J Williams and Sean Ekins

Journal of Cheminformatics 2015 **7**:9
https://doi.org/10.1186/s13321-015-0057-7 | © Clark et al.; licensee Springer. 2015
Received: 24 November 2014 | **Accepted:** 23 February 2015 | **Published:** 22 March 2015

es
and content

"MS-ready" structures



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

Journal of Cheminformatics

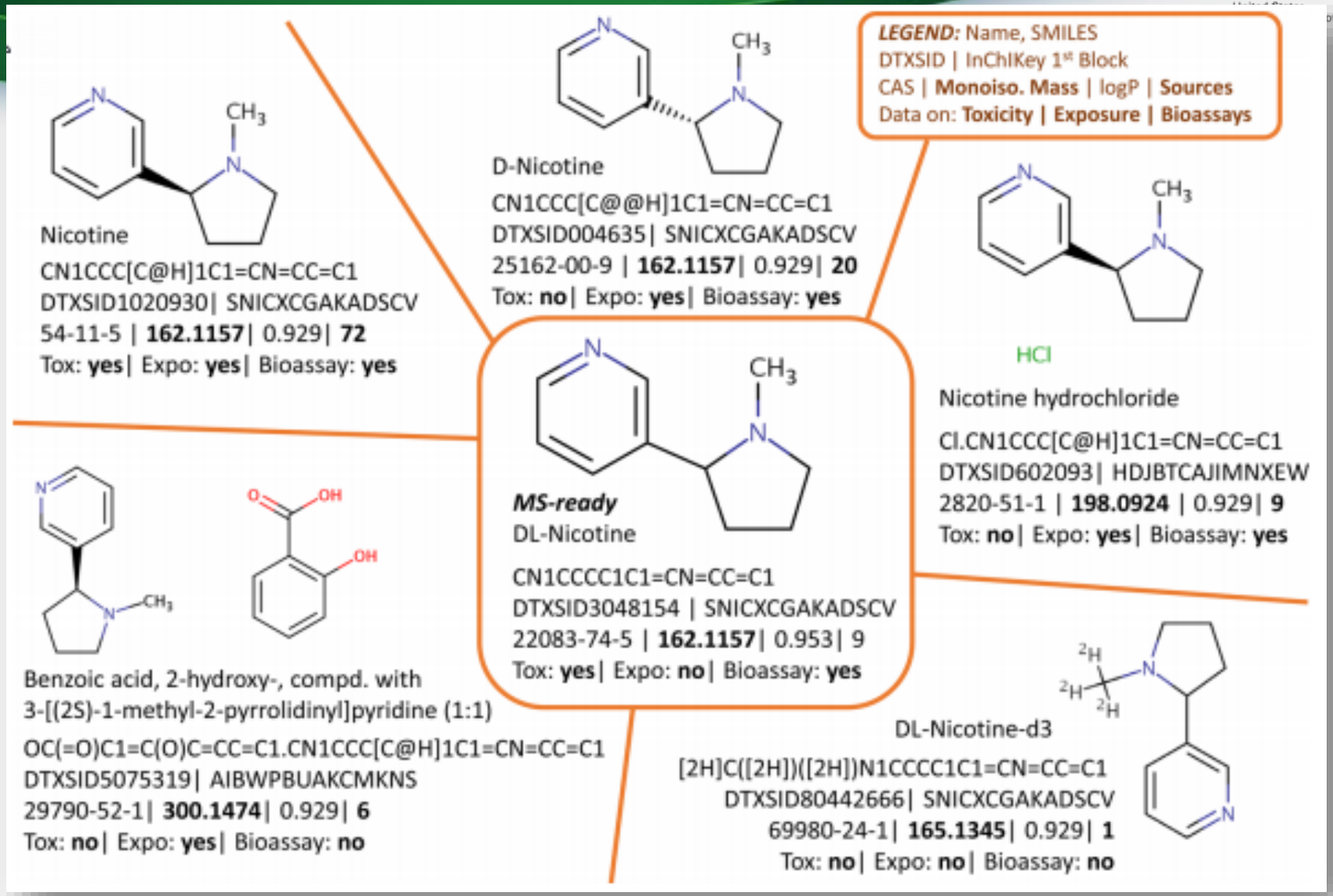
METHODOLOGY Open Access

"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*]

Overview of MS-Ready Structures

- All structure-based chemical substances are algorithmically processed to
  - Split multicomponent chemicals into individual structures
  - Desalt and neutralize individual structures
  - Remove stereochemical bonds from all chemicals
- MS-Ready structures are then mapped to original substances to provide a path between chemicals detected by mass spectrometry to original substances

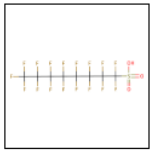


Environmental Science & Technology
Viewpoint
pubs.acs.org/est

Open Science for Identifying "Known Unknown" Chemicals

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

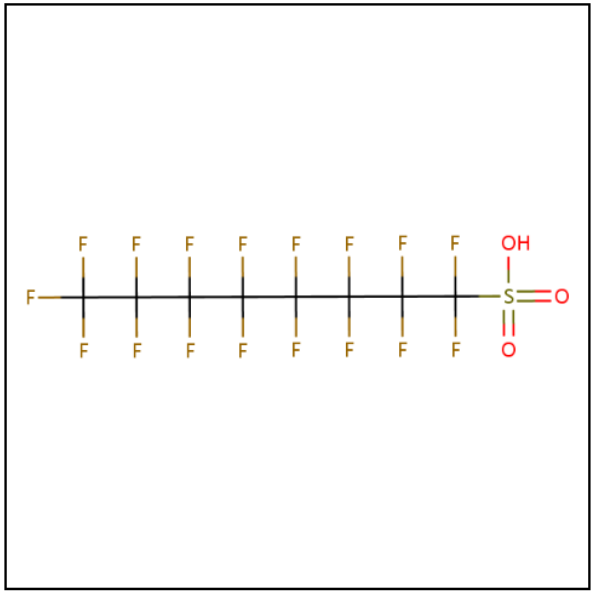
MS-Ready Mappings from Details Page



Perfluorooctanesulfonic acid

1763-23-1 | DTXSID3031864

Searched by Synonym from Valid Source.



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

Quality Control Notes

Intrinsic Properties

Structural Identifiers

Linked Substances

Same Connectivity: 4 records (based on first layer of InChI)

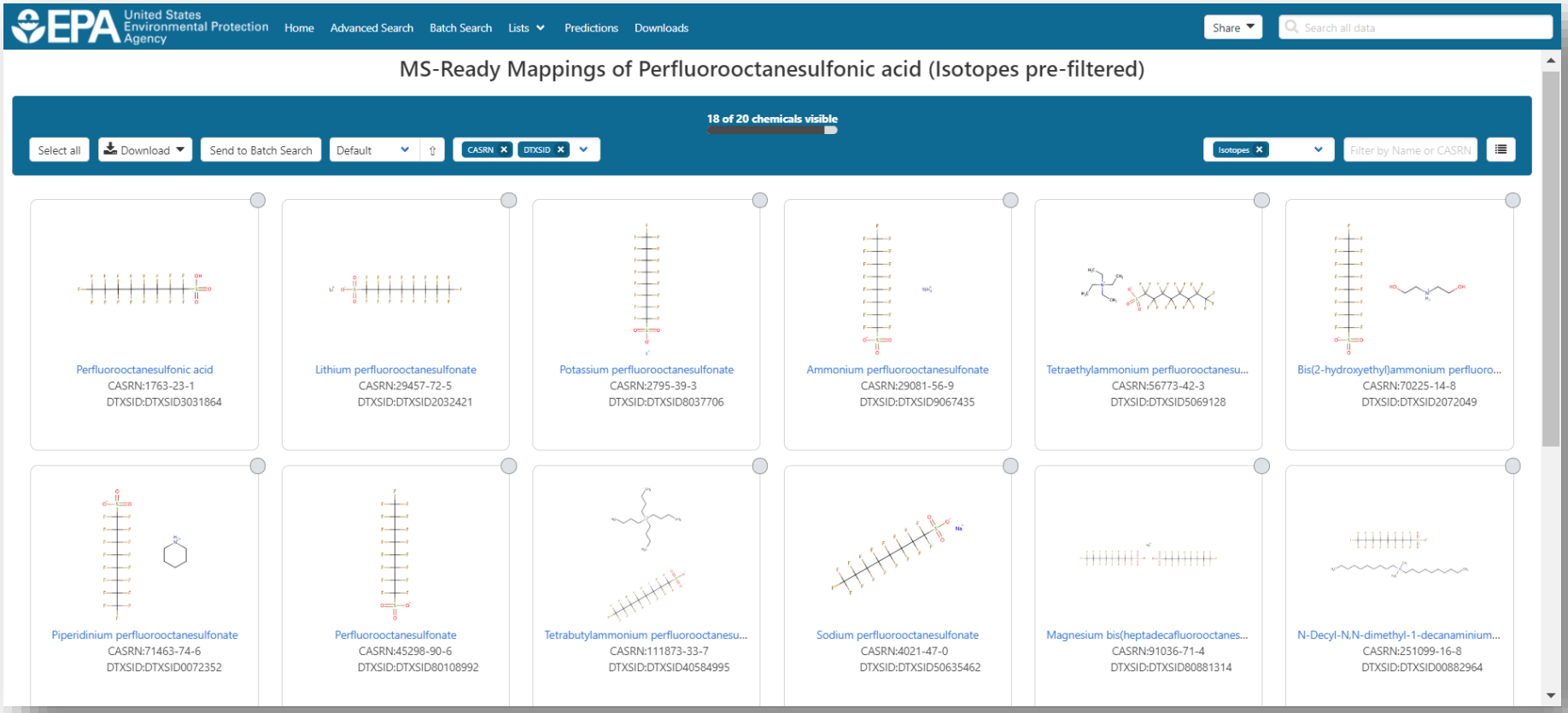
Mixtures, Components and Neutralized Forms: 9 records (based on QSAR ready mappings and with the compound as a component of a mixture)

MS-Ready Mappings: DTXCID1011864: 18 records;

Similar Compounds: 83 records (based on Tanimoto coefficient >0.8)

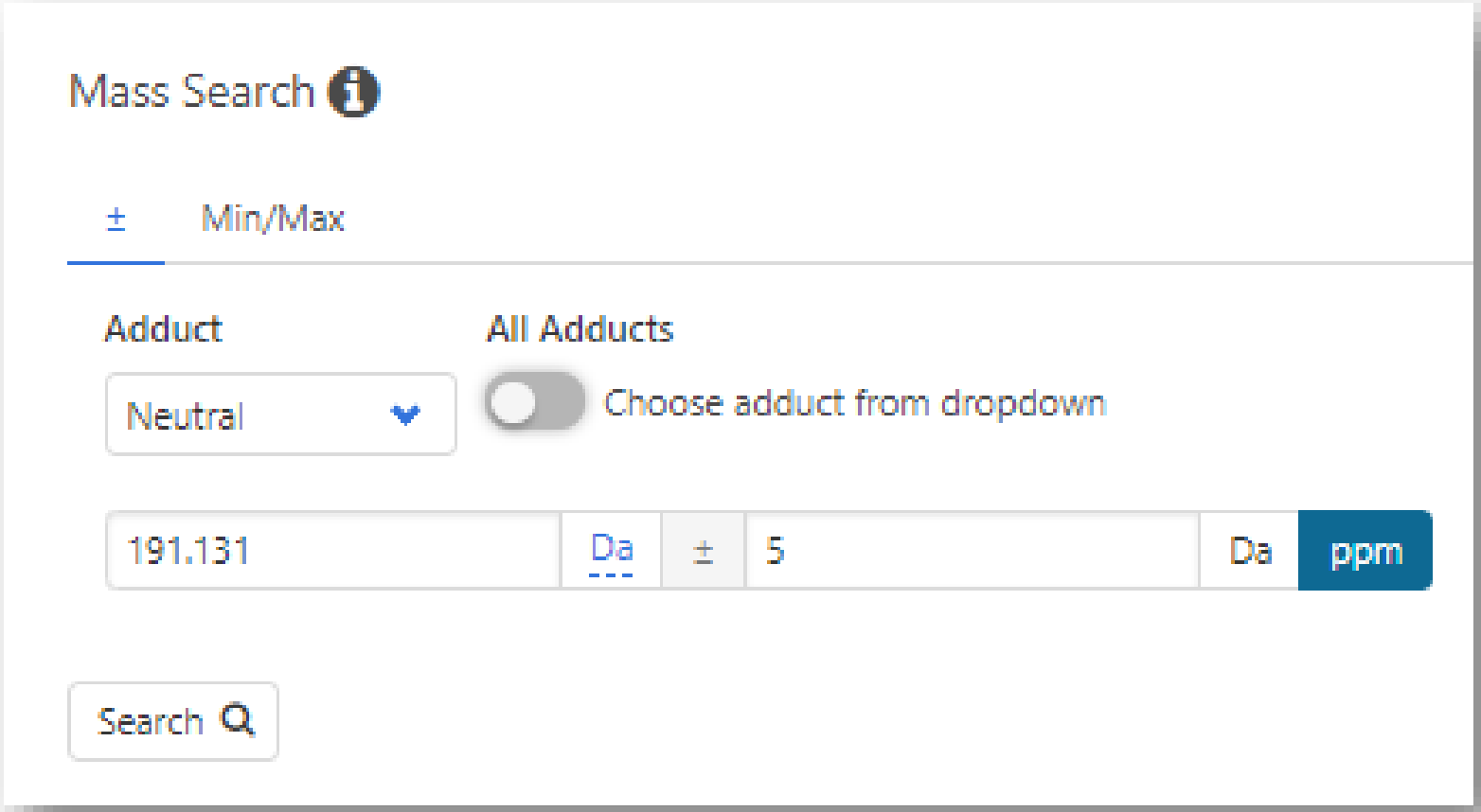
ed_search/index

MS-Ready Mappings Set of 20 substances for “PFOS”

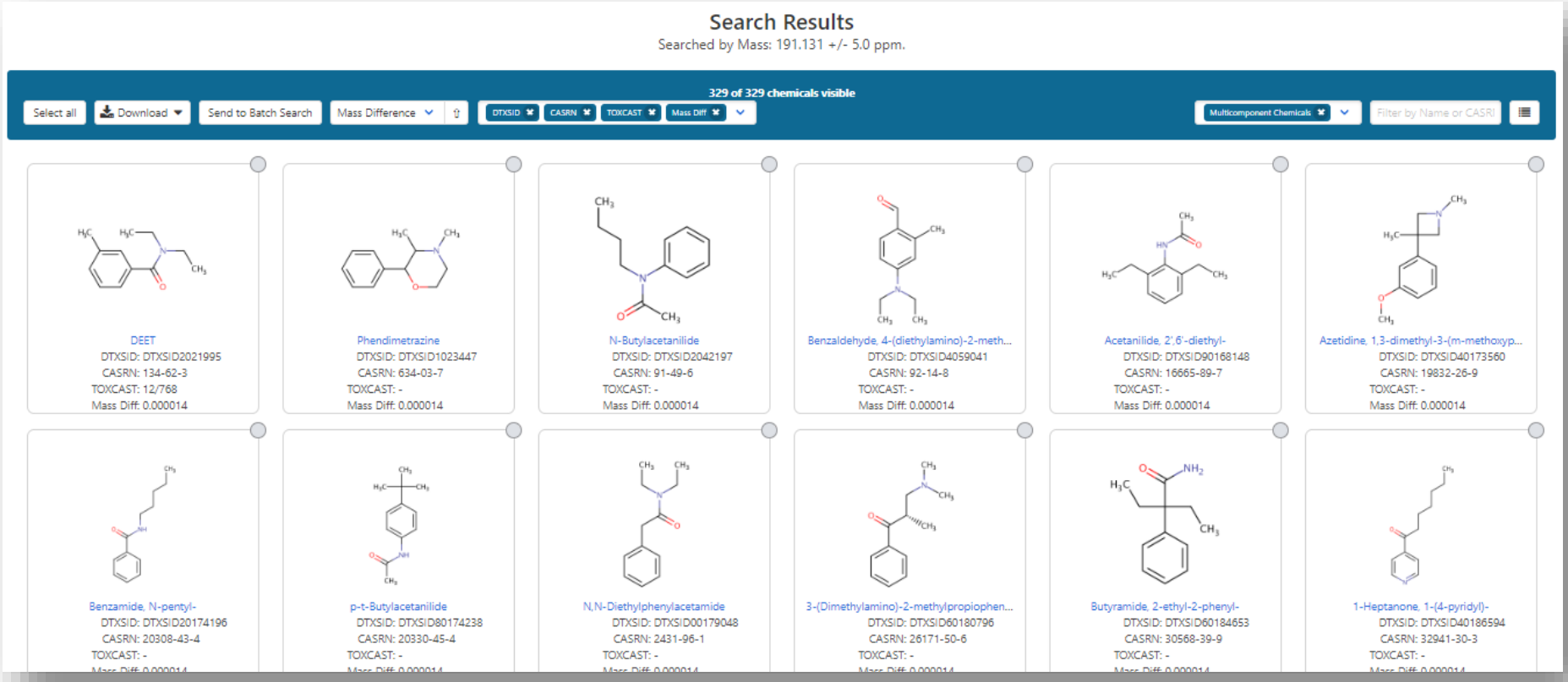


Mass and Formula Searching

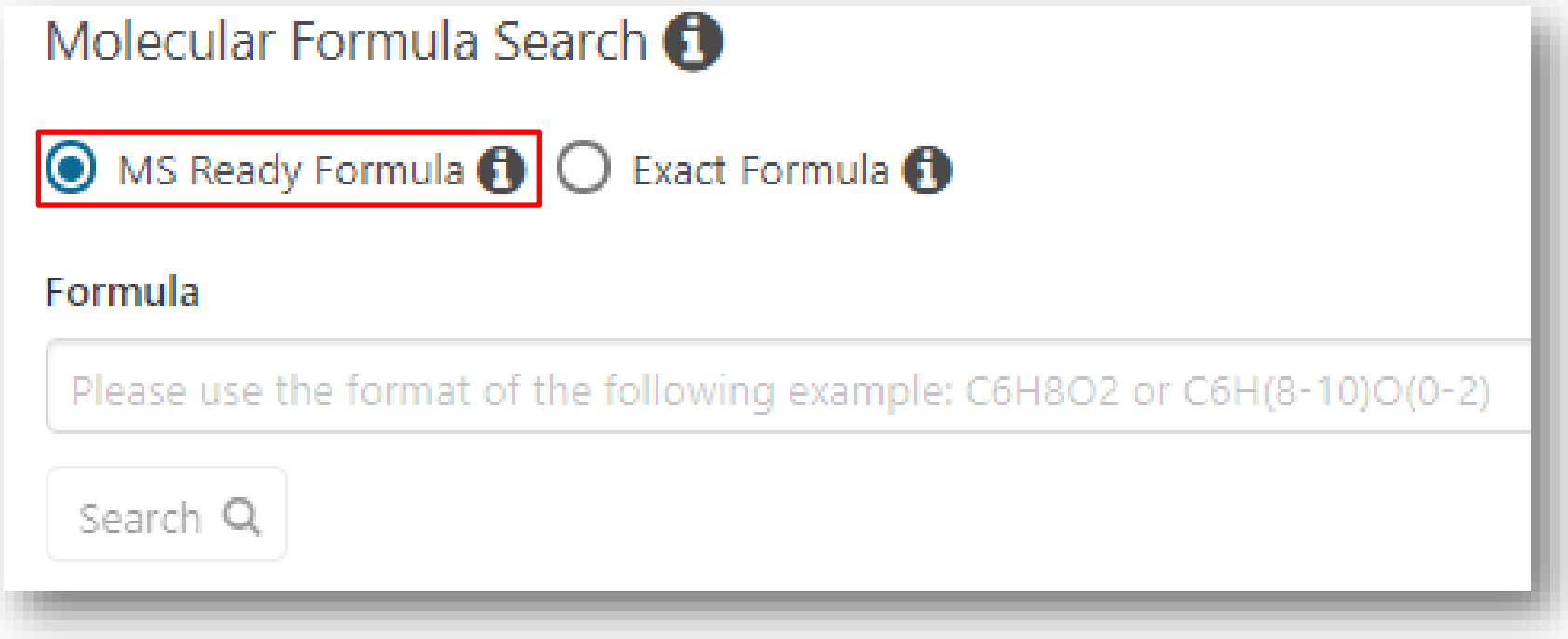
Advanced Searches
Mass Search



Advanced Searches
Mass Search

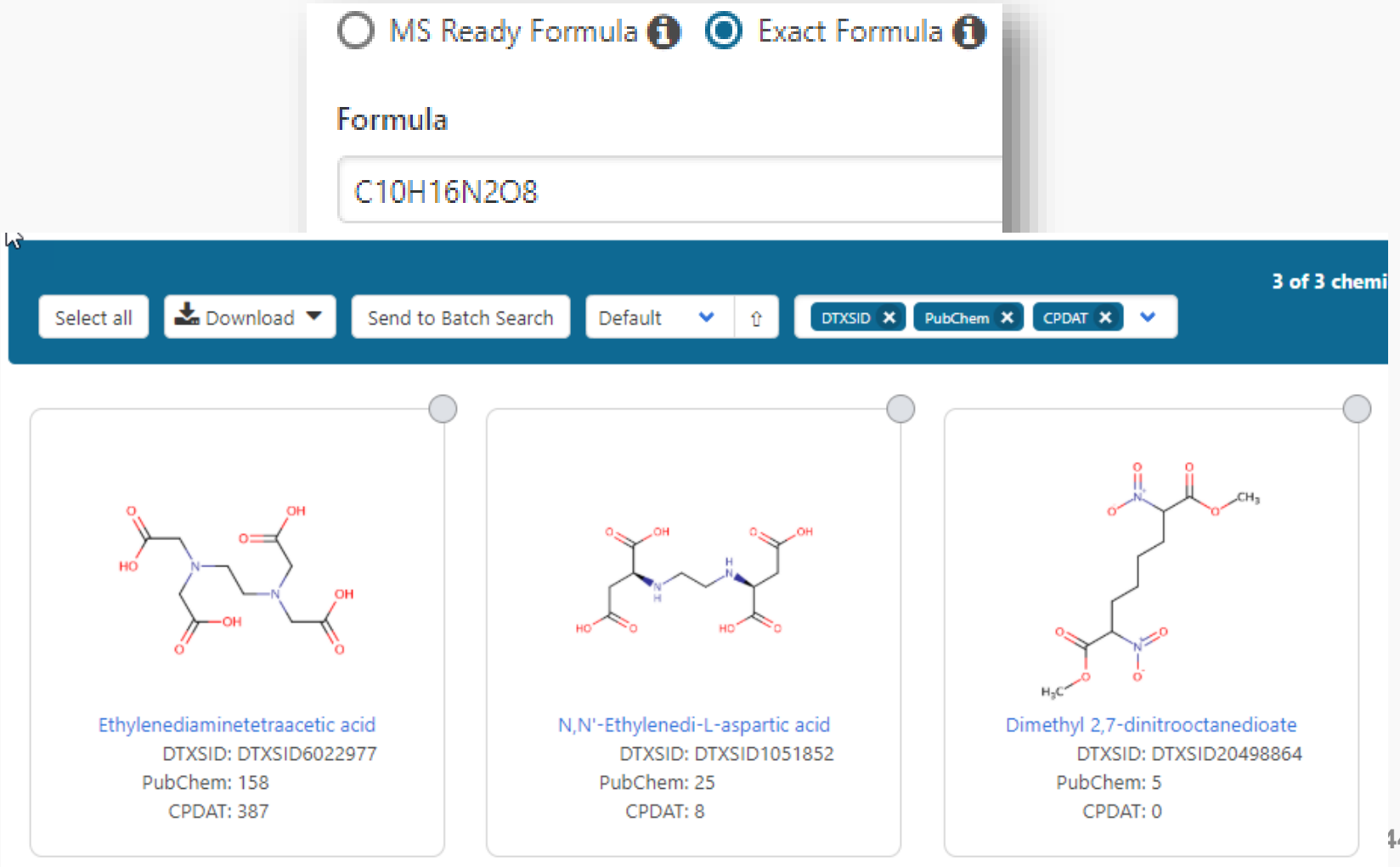


MS-Ready Structures for **Formula Search**



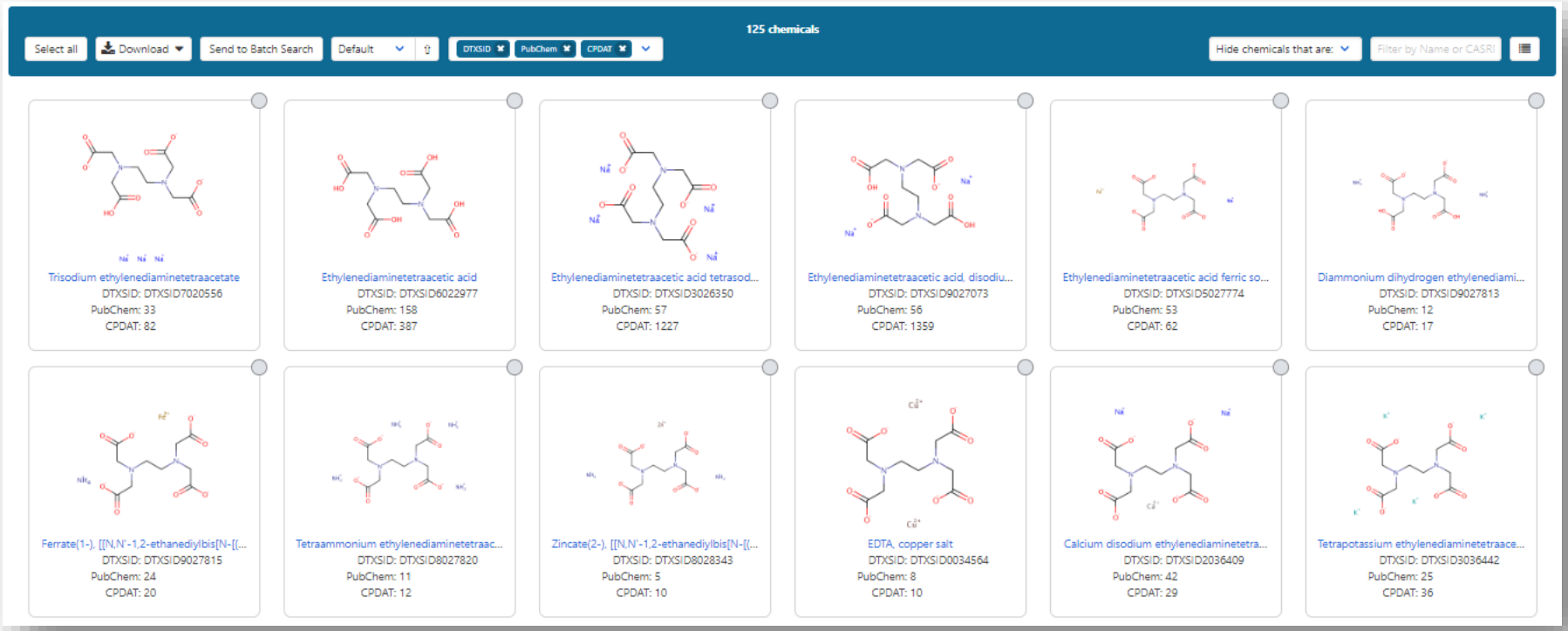
MS-Ready Mappings

- **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**

- Multiple components, stereo, isotopes and charge all collapsed and mapped through MS-Ready

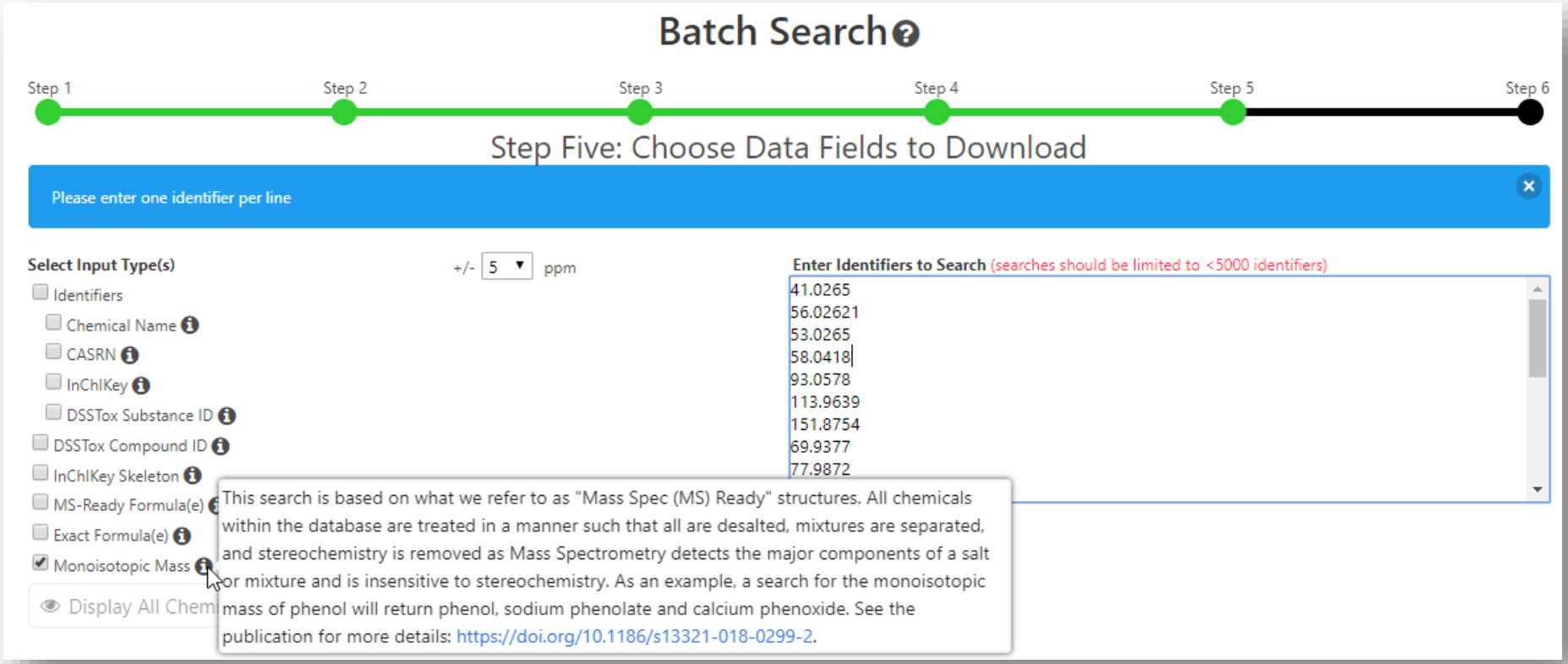
Batch Searching mass and formula

Batch Searching

- Singleton searches are useful but we work with **thousands** of masses and 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

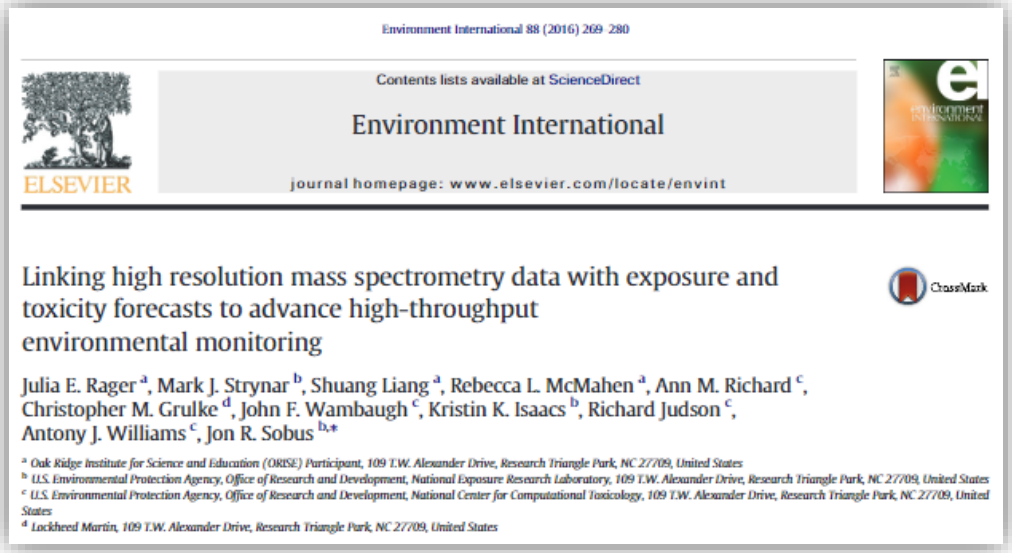
Batch Search in specific lists

EPA United States Environmental Protection Agency

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

Benefits of bringing it all together

- The true dashboard benefit is integration
- Rank potential candidates for toxicity using available data – hazard, exposure, *in vitro*



Environment International 88 (2016) 269–280

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Linking high resolution mass spectrometry data with exposure and toxicity forecasts to advance high-throughput environmental monitoring

Julia E. Rager [a], Mark J. Strynar [b], Shuang Liang [a], Rebecca L. McMahen [a], Ann M. Richard [c], Christopher M. Grulke [d], John F. Wambaugh [c], Kristin K. Isaacs [b], Richard Judson [c], Antony J. Williams [c], Jon R. Sobus [b,*]

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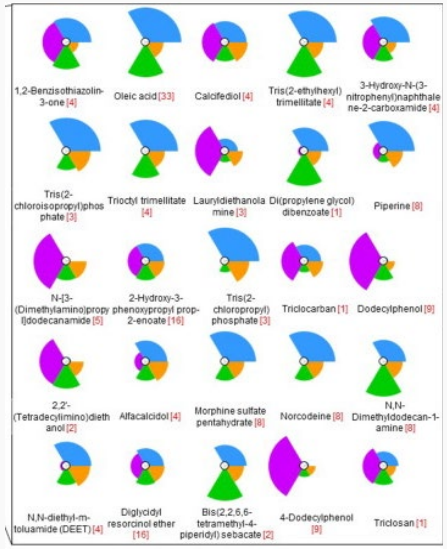


EPA United States Environmental Protection Agency

Candidate ranking using metadata

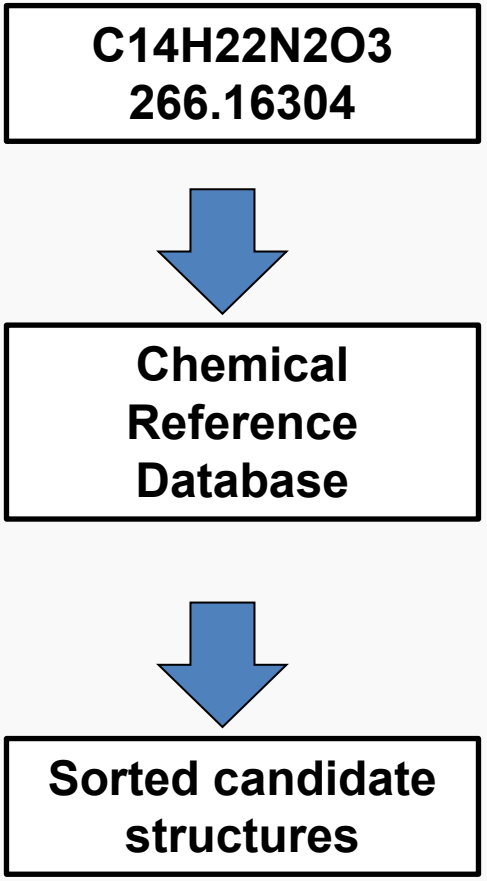
J. Am. Soc. Mass Spectrom. (2012) 23:179–185
DOI: 10.1007/s13361-011-0265-y

RESEARCH ARTICLE

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

Data Source Ranking of "*known unknowns*"

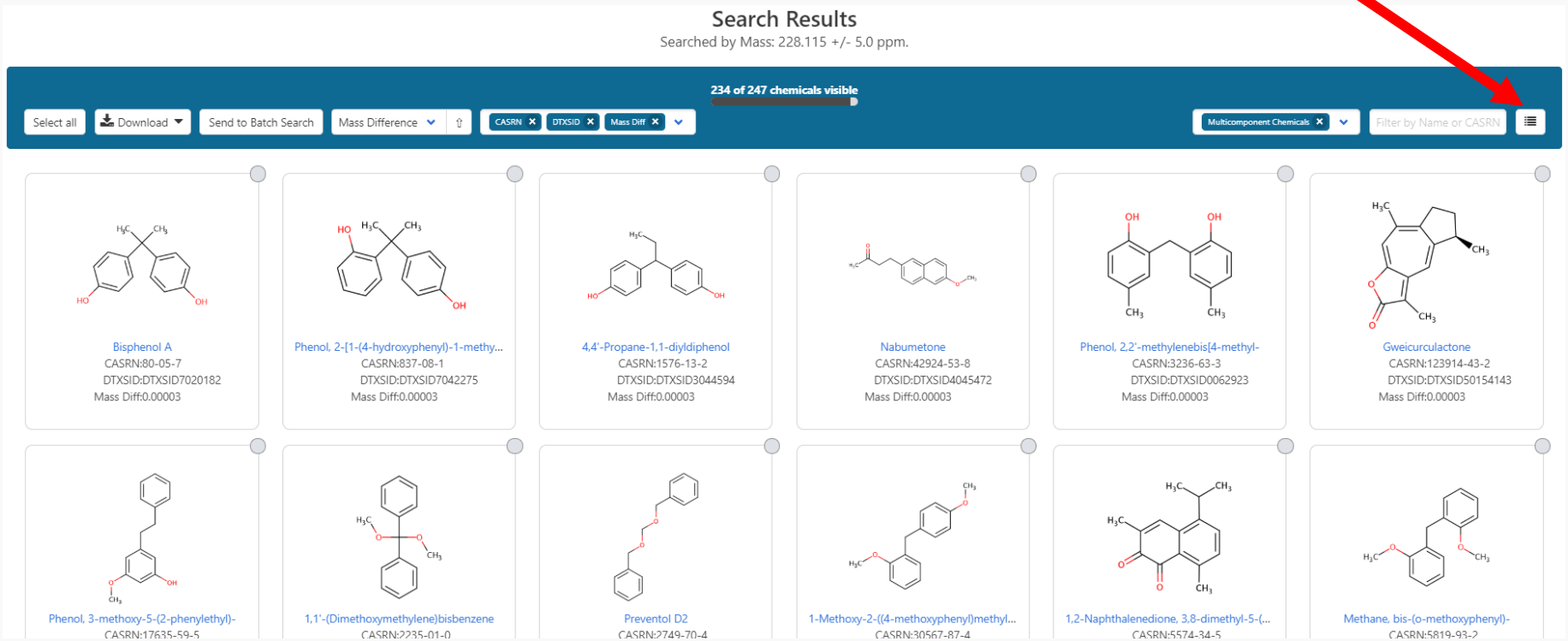
- A mass and/or formula search is for an ***unknown*** chemical but it is a ***known*** chemical contained within a reference database
- **Most likely** candidate chemicals have the **most** associated data sources, **most** associated literature articles or both



Data Streams for Ranking

- CompTox Dashboard Data Sources
- PubChem Data Source Count
- PubMed.gov Reference Count
- Toxcast *in* vitro bioactivity
- Presence in CPDat database
- OPERA PhysChem Properties
- Other possibilities – predicted media occurrence, frequency of InChIs online

Search 228.115 +/- 5.0 ppm
234 single component chemicals



Search 228.115 +/- 5.0 ppm
234 single component chemicals

CASRN	QC Level	CPDat Count	Number of Sources	PubChem Data Sources	PubMed Ref. Counts
80-05-7	Level 1	326	170	161	3850
42924-53-8	Level 2	14	45	138	342
87619-52-1	Level 5	0	2		0
87607-32-7	Level 5	0	2		0

The original ChemSpider work

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			

Is a bigger database better?

- ChemSpider was 26 million chemicals for the original work
- Much BIGGER today
- Is bigger better??
- Are there other metadata to use for ranking?

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]

- When dashboard contained 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			

EXACTLY THE SAME DATASET

How did performance compare?

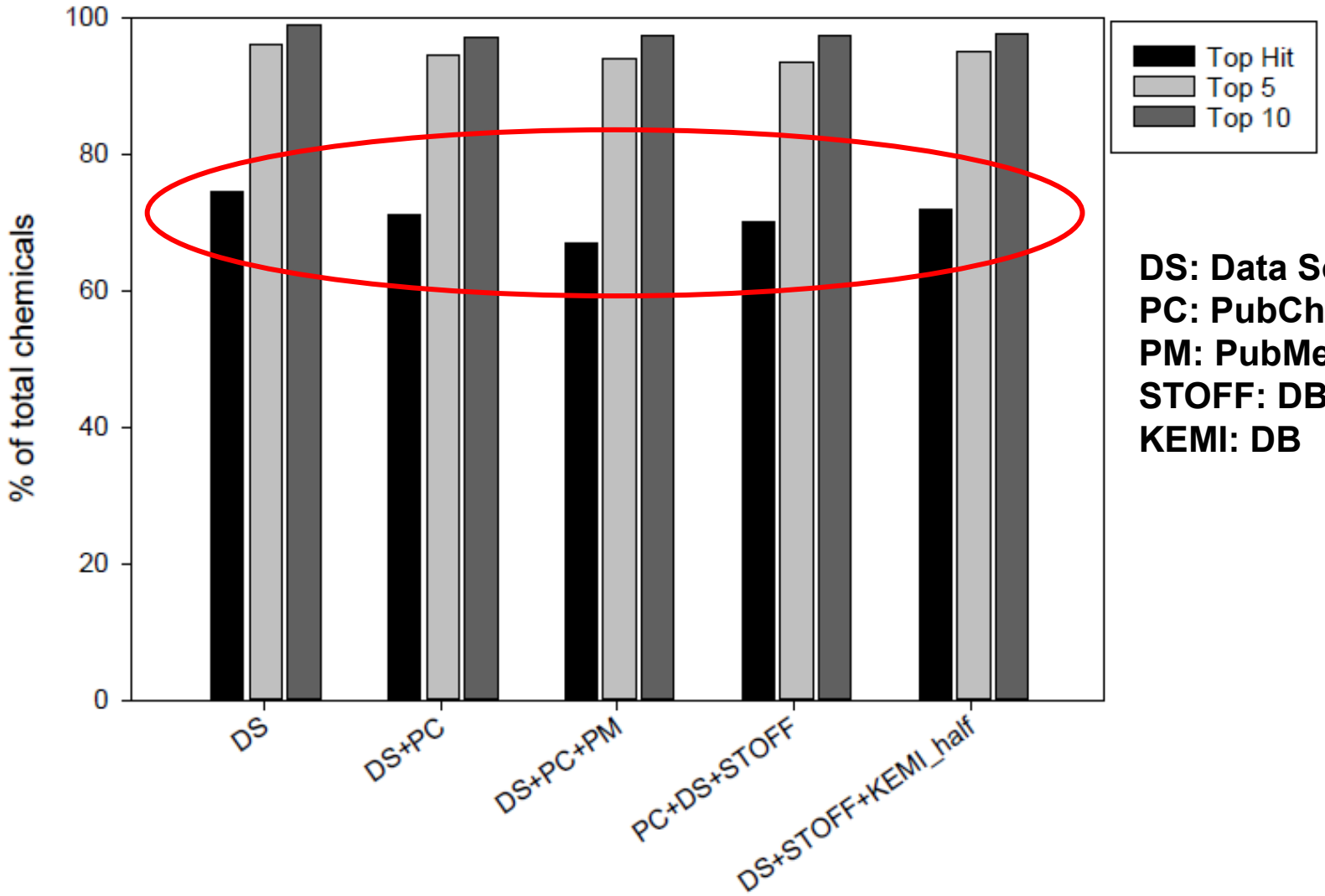
	Mass-based searching		Formula-based searching	
	Dashboard	ChemSpider	Dashboard	ChemSpider
Average rank position	1.3	2.2[a]	1.2	1.4
Percent in #1 position	85%	70%	88%	80%

[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 for both Mass and Formula Ranking

Identification ranks for **1783 chemicals** using multiple data streams

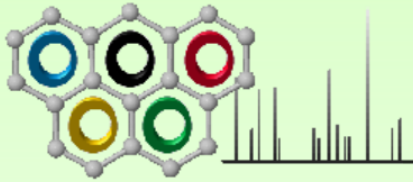
Data Sources alone rank ~75% of the chemicals as Top Hit



DS: Data Sources
PC: PubChem
PM: PubMed
STOFF: DB
KEMI: DB

CASMI

EPA United States Environmental Protection Agency



CASMI 2017

CASMI 2017
- Important Dates
- Contest Rules
- Challenge Data
- Solutions
- Preliminary results
- Results
- About the Team

CASMI 2016

CASMI 2014

CASMI 2013

CASMI 2012

Critical Assessment of Small Molecule Identification

The experimental and computational mass spectrometry communities are invited to participate in the fifth round of an open contest on the identification of small molecules from mass spectrometry data.

This year the contest will test the applicability of MS and MS/MS on natural products chemistry identifications. With 45 (Category 1) and up to 243 (Categories 2&3) natural products challenges - including a few tricky ones - there's something for everyone!

CASMI 2017 is organised by Dr. Dejan Nikolic (University of Illinois at Chicago, USA), Dr. Nir Shahaf (Weizmann Institute of Science, Israel), Dr. Emma Schymanski (Eawag, Switzerland) and Dr. Steffen Neumann (IPB Halle, Germany).

Mailing lists

CASMI

metabolites

MDPI

Article

Revisiting Five Years of CASMI Contests with EPA Identification Tools

Table 2. Percentage of the total number of compounds from each CASMI contest year that were ranked in the top 5 by Competitive Fragmentation Modeling for Metabolite Identification (CFM-ID) only and by the summation of CFM-ID and DSSTox Data Source Counts (DS), alongside the percentage in the top 5 reported by the contest years' winning entry. Complete ranking results are provided in Supplemental File S1.

CASMI Year	CFM-ID Only	CFM-ID + DS	Winners' Results [1]	Total in DB/Total in Dataset [2]
2012	36%	64%	36%	14/14
2013	81%	88%	88%	16/16
2014	57%	76%	71%	42/42
2016-training	63%	96%		312/312
2016-challenge	66%	94%	81%	208/208
2017	59%	53%	74% [3]	227/243

Work in Progress

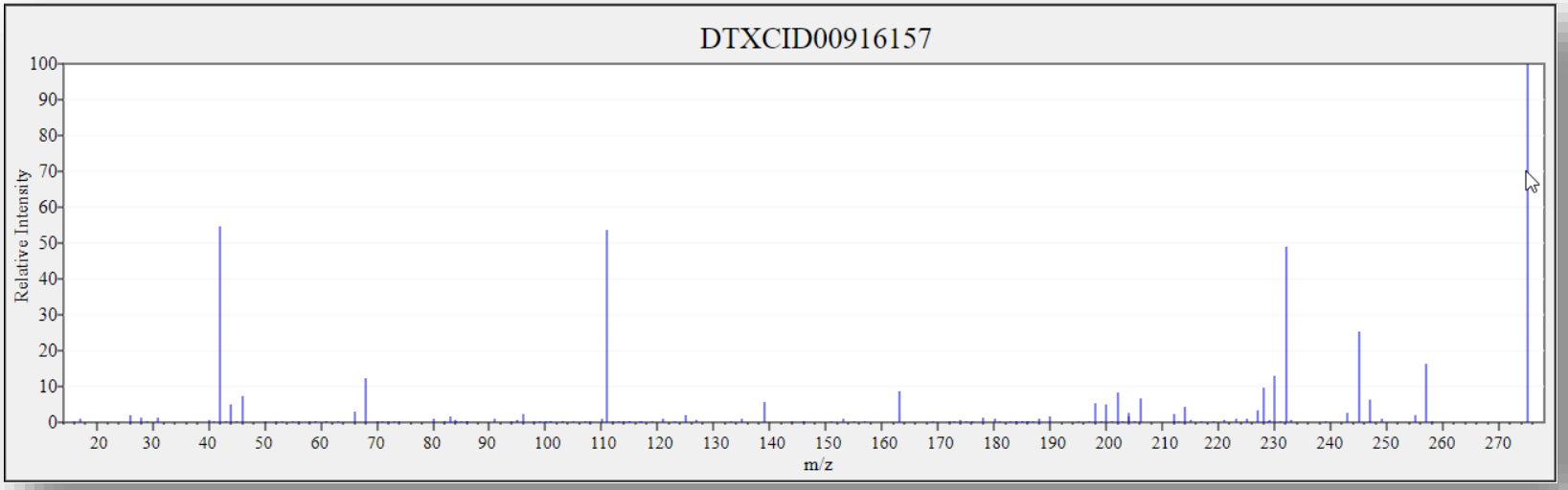
Prototype Work in Progress

- CFM-ID
  - Viewing and Downloading pre-predicted spectra
  - Search spectra against the database
- Structure/substructure/similarity search
- Access to API and web services
- Integration to EPA “Chemical Transformation Simulator”

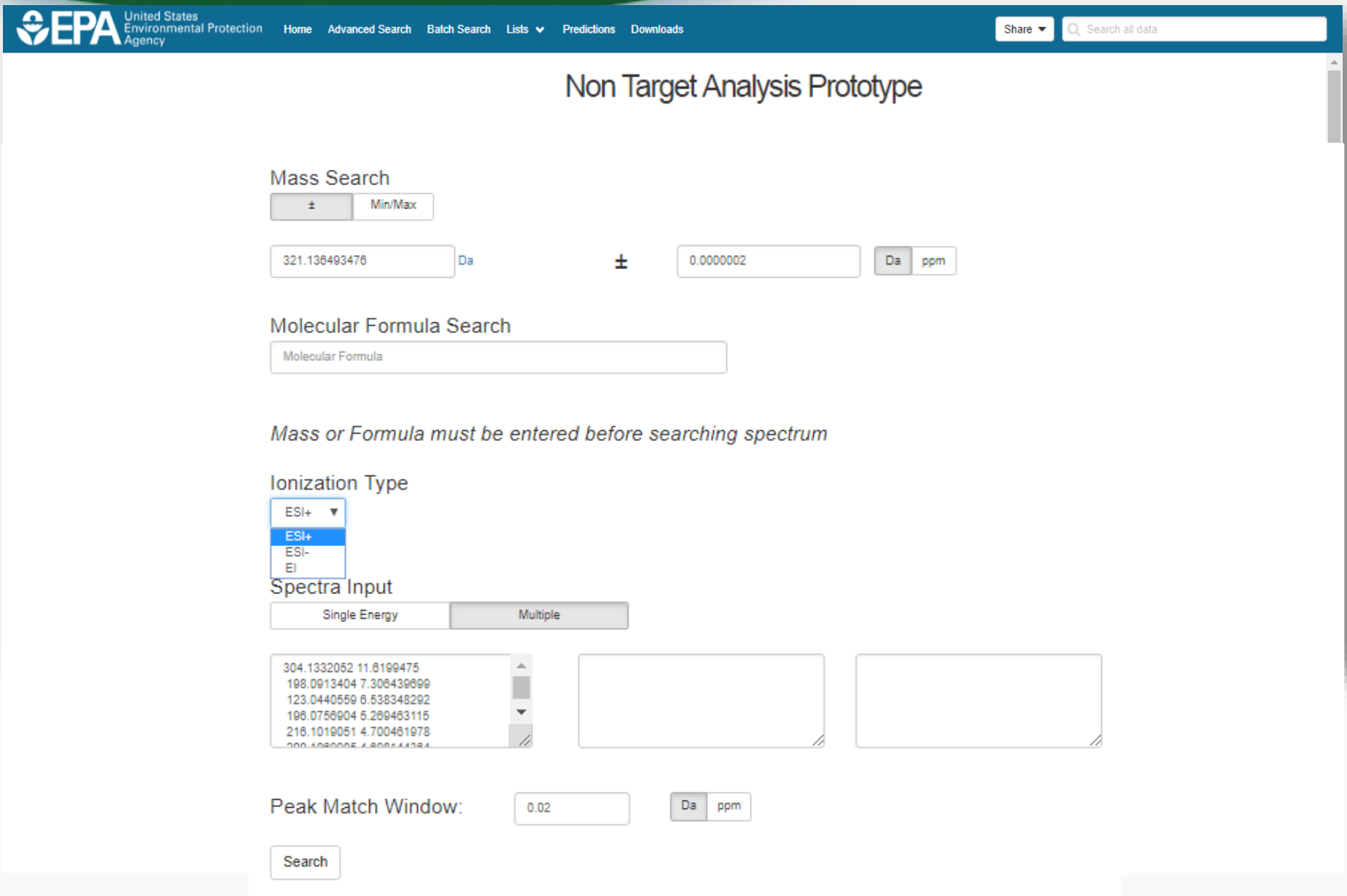
Predicted Mass Spectra

http://cfmid.wishartlab.com/

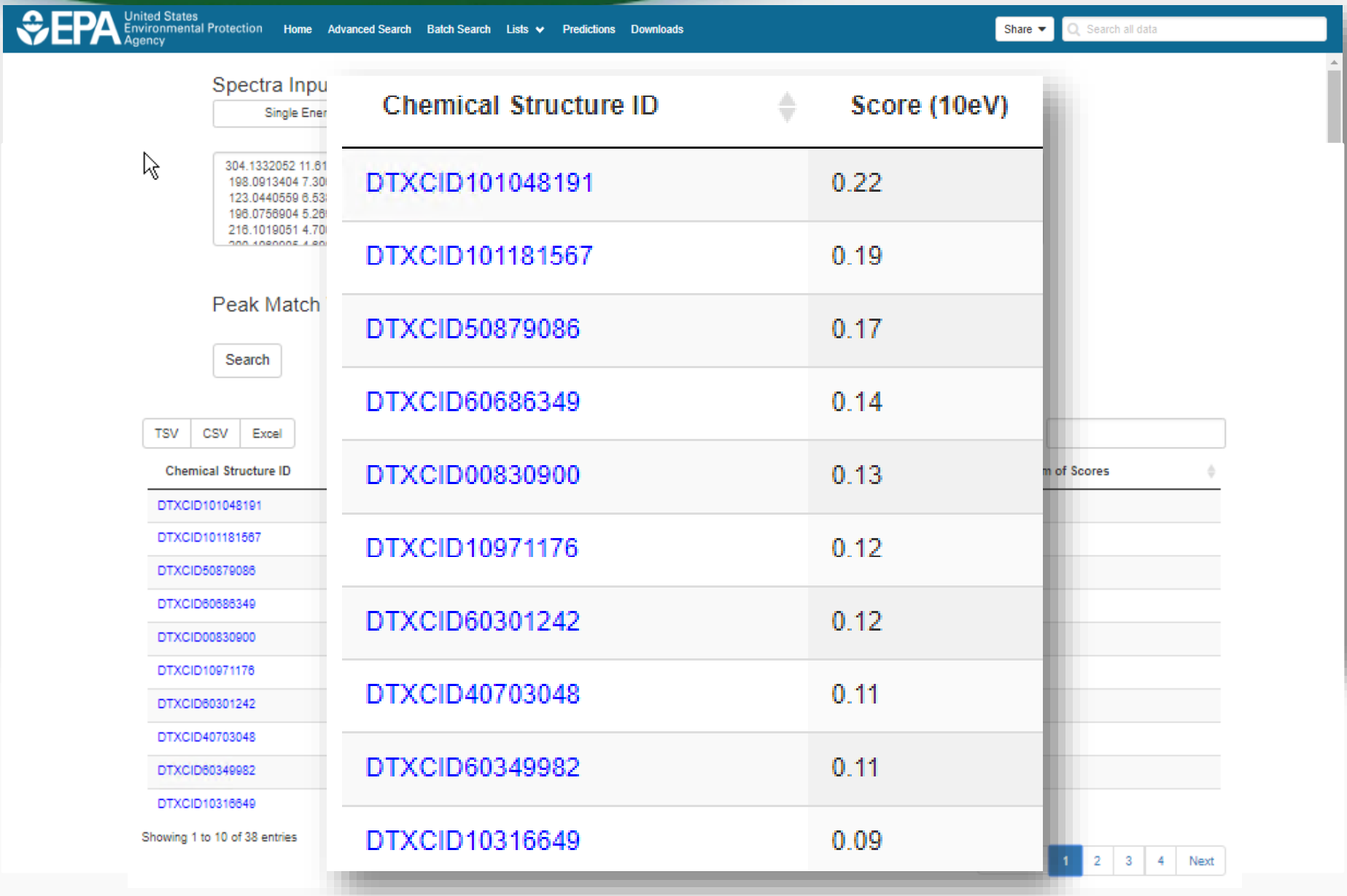
- MS/MS spectra prediction for ESI+, ESI-, and EI
- Predictions generated and stored for >800,000 structures, to be accessible via Dashboard



Search Expt. vs. Predicted Spectra

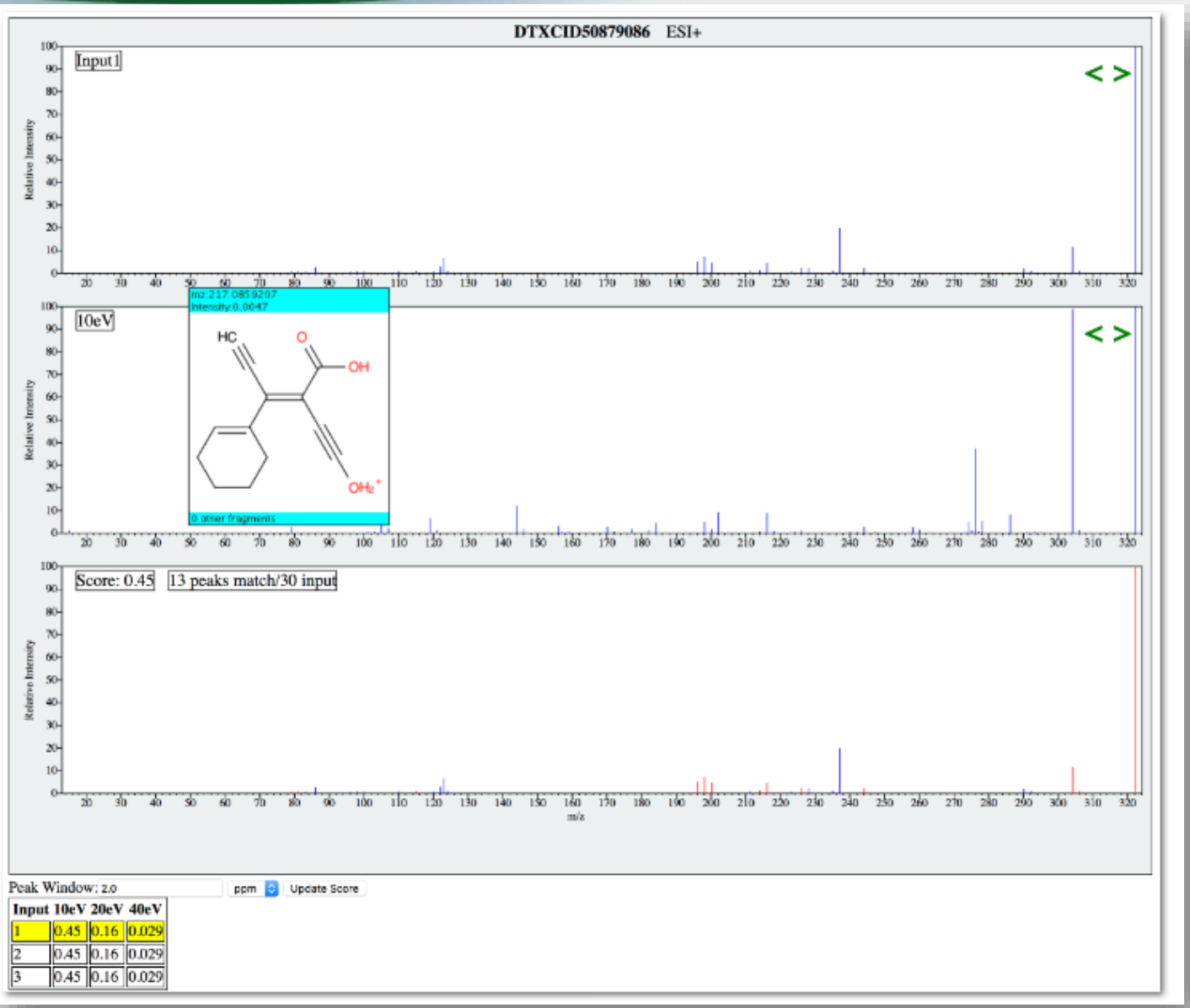


Search Expt. vs. Predicted Spectra



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



Published: Alex Chao et al

Analytical and Bioanalytical Chemistry

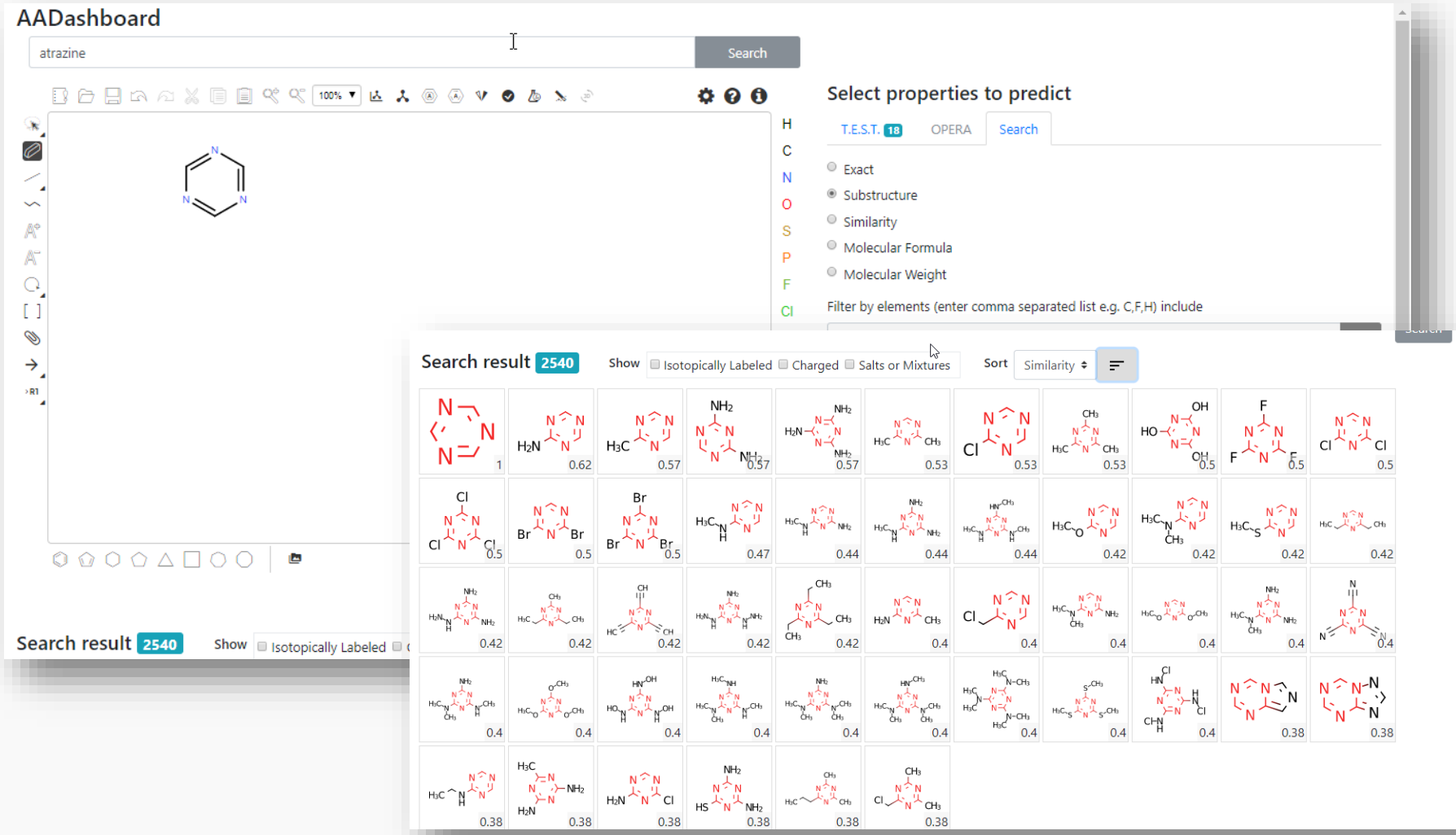
RESEARCH PAPER

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

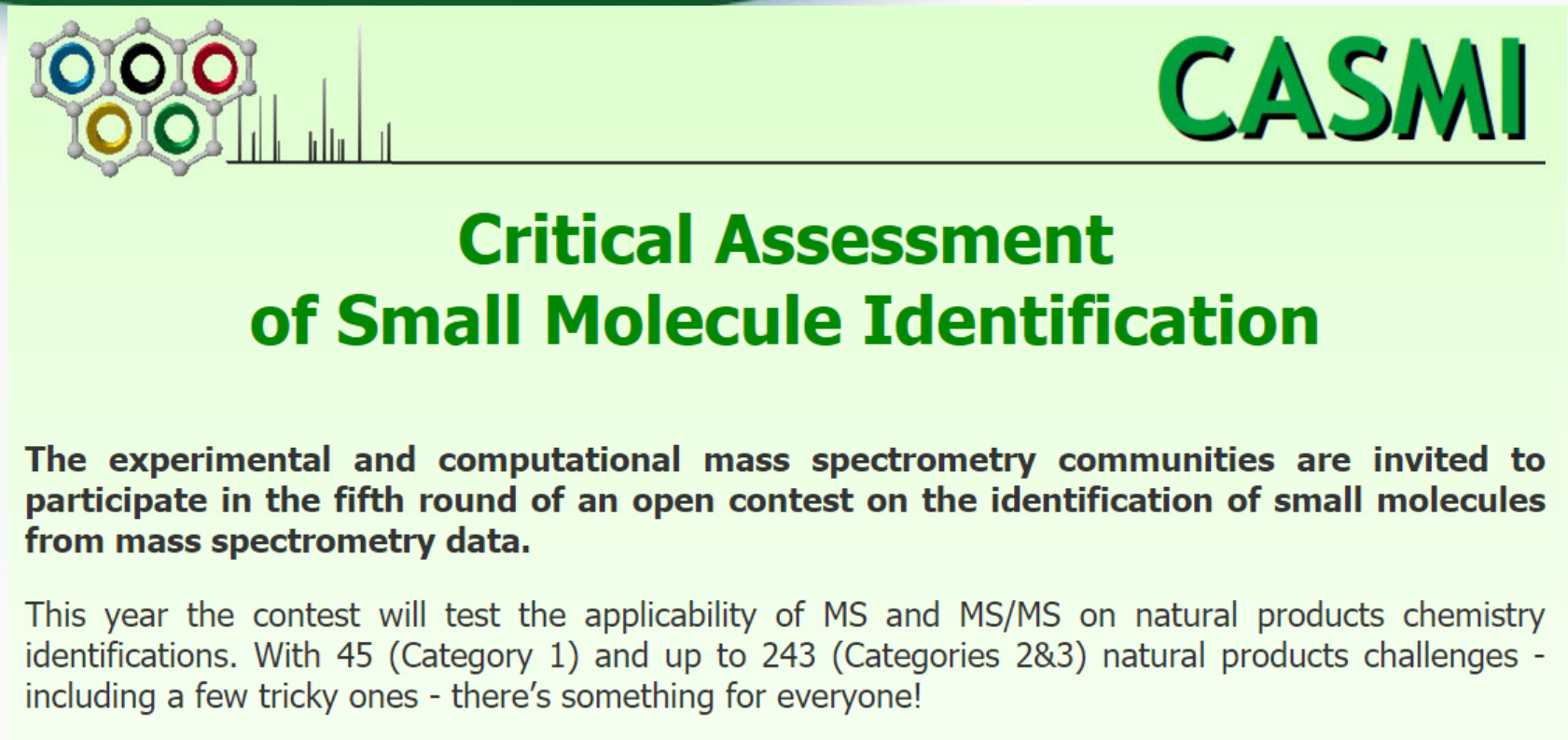
Alex Chao [1,2] · Hussein Al-Ghoul [1,2] · Andrew D. McEachran [1,3] · Ilya Balabin [4] · Tom Transue [4] · Tommy Cathey [4] · Jarod N. Grossman [2,3] · Randolph Singh [1,5] · Elin M. Ulrich [2] · Antony J. Williams [6] · Jon R. Sobus [2]

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

Prototype Development



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.

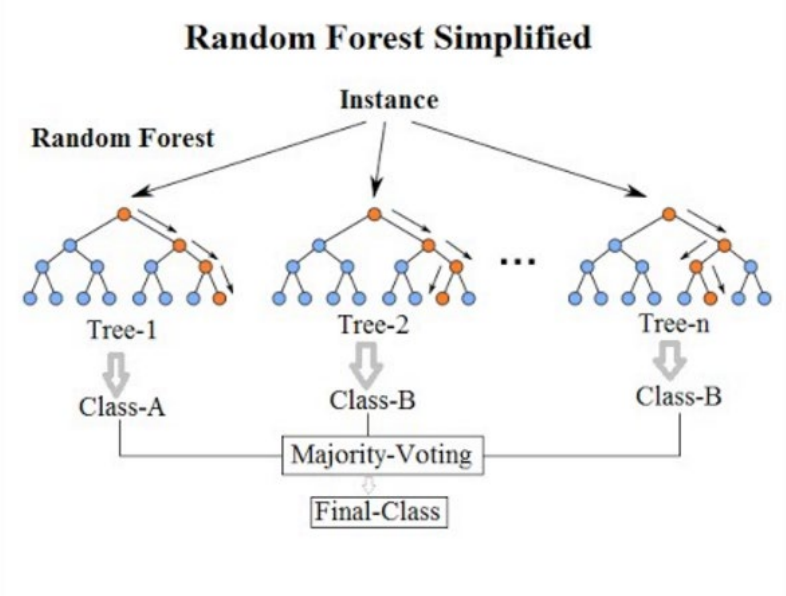
Metabolites **2020**, *10*(6), 260; https://doi.org/10.3390/metabo10060260

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

Method Amenability Prediction
Charlie Lowe

Why?

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



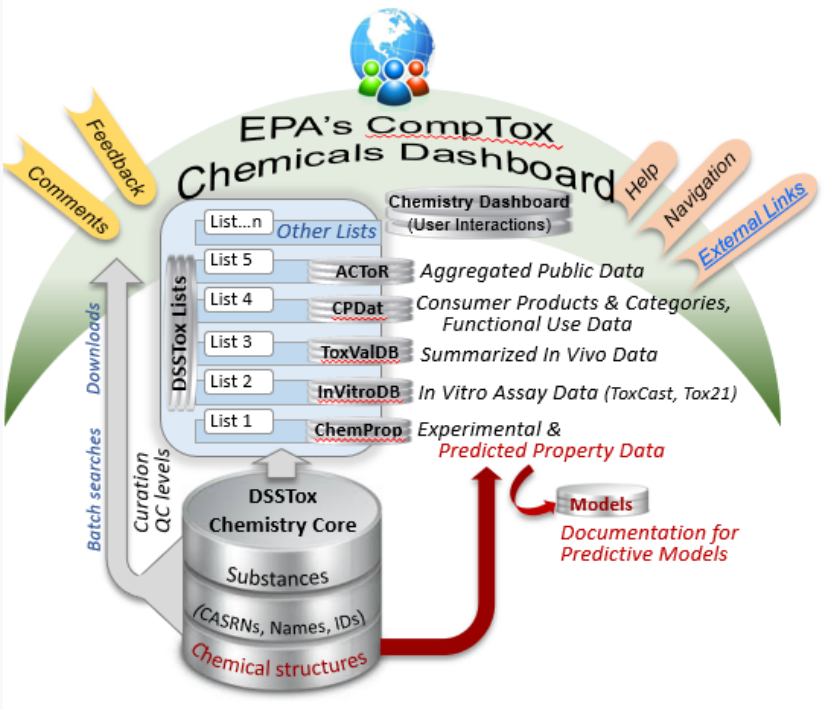
Ongoing Work

- 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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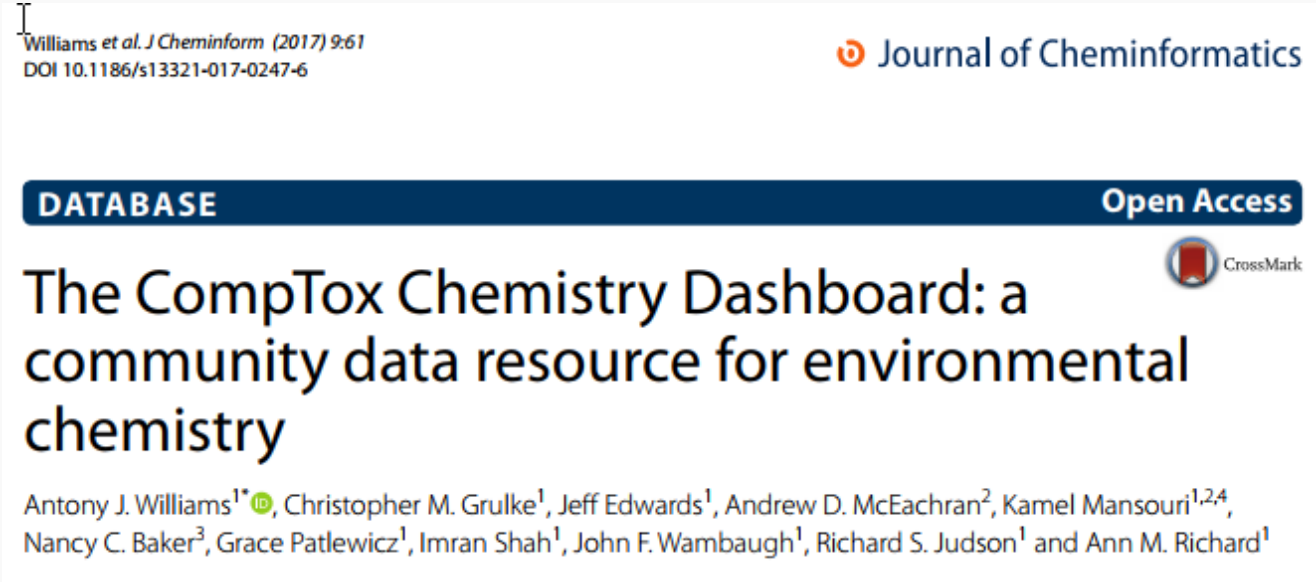

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The CompTox Chemistry Dashboard: a community data resource for environmental chemistry

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