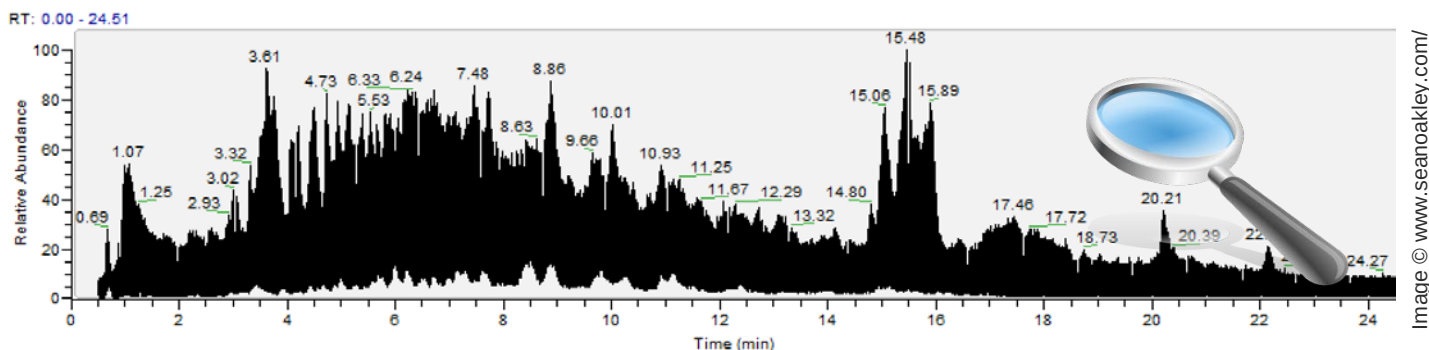


Community Resources Connecting Chemistry and Toxicity Knowledge to Environmental Observations



Emma L. Schymanski
Luxembourg Centre for Systems Biomedicine (LCSB),
University of Luxembourg
Email: emma.schymanski@uni.lu

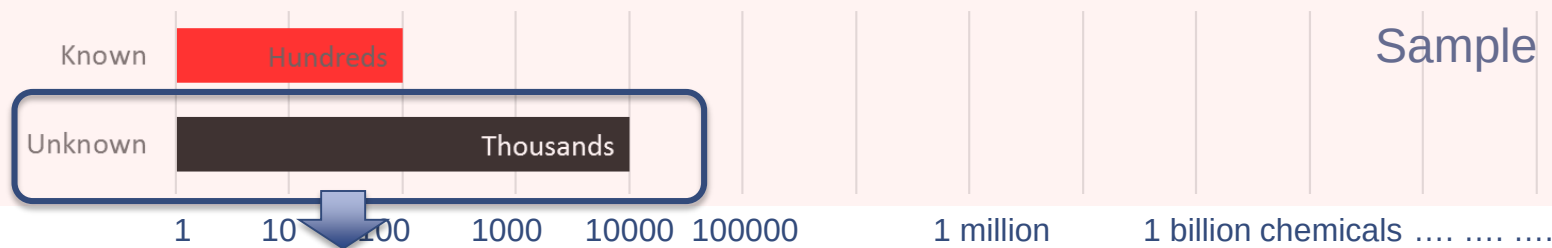
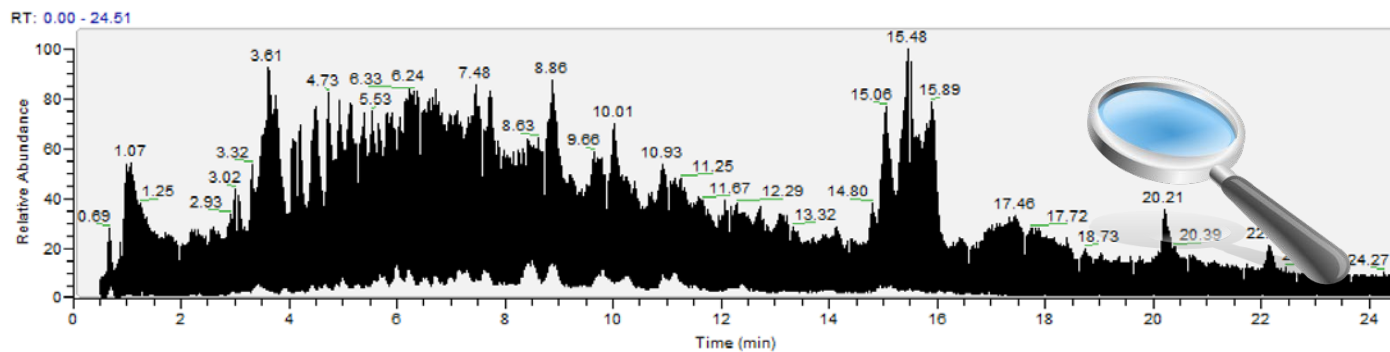
Antony J. Williams
National Centre for Computational Toxicity (NCCT),
US Environmental Protection Agency (US EPA), NC, USA

(European) Environmental Community (subset!)



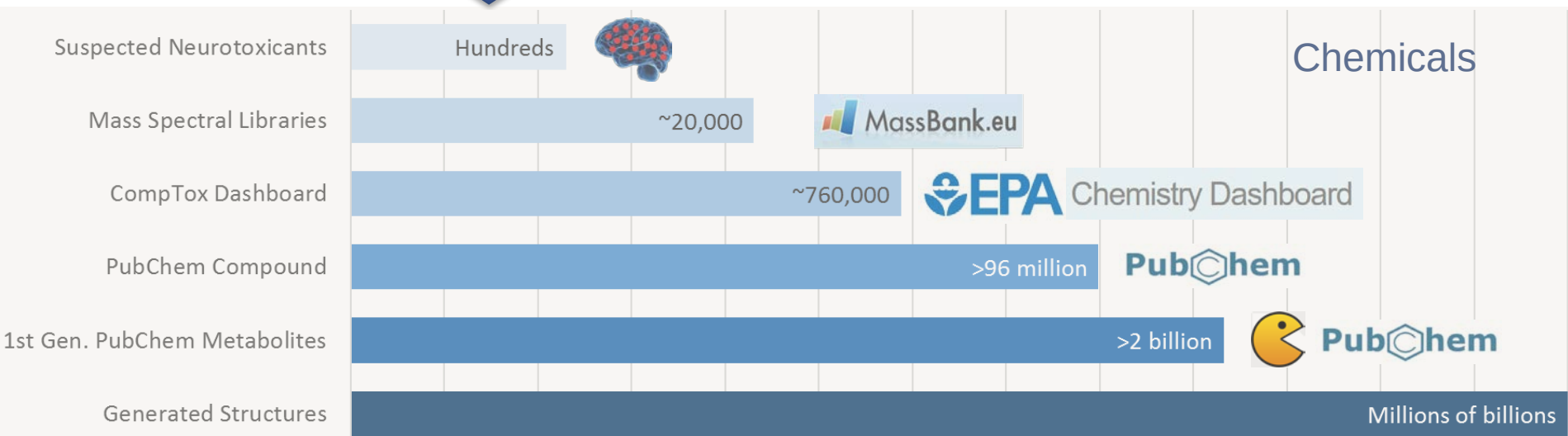
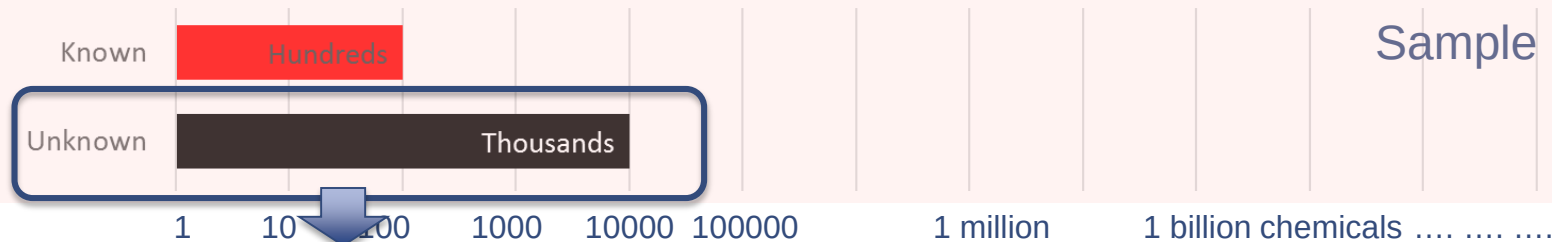
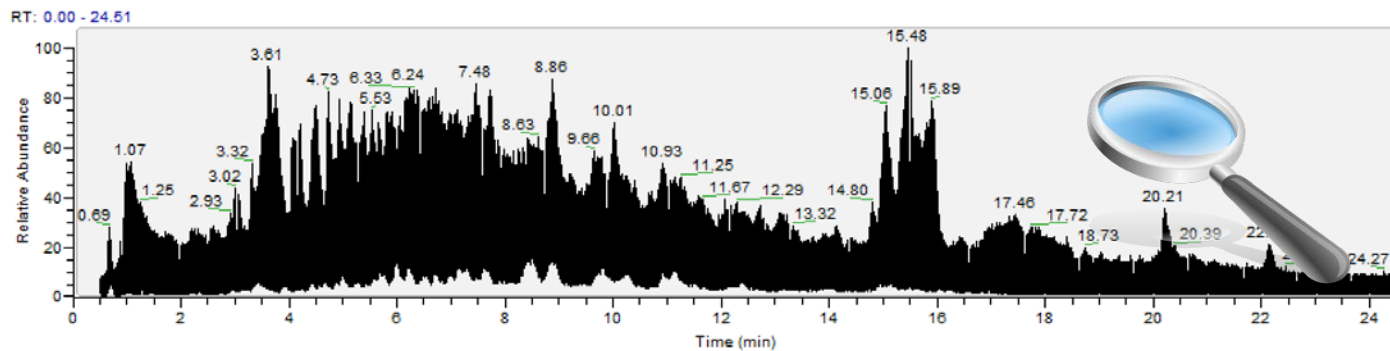
Our (Community) Challenge: Identifying Chemicals

High resolution
mass spectrometry



Our (Community) Challenge: Identifying Chemicals

High resolution
mass spectrometry
AND connecting
chemical knowledge

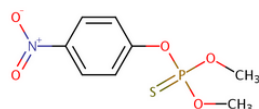


Chemistry Dashboard | HUMANNEUROTOX

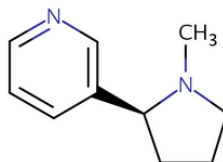
Description: A set of chemicals listed as neurotoxicants in the article "Developmental Neurotoxicity of Industrial Chemicals" by Grandjean and Landrigan, *The Lancet*, Volume 368, No. 9553, p2167–2178, 16 December 2006 ([https://doi.org/10.1016/S0140-6736\(06\)69665-7](https://doi.org/10.1016/S0140-6736(06)69665-7)). The authors list 5 of these chemicals additionally as developmental neurotoxins (arsenic and arsenic compounds; lead and lead compounds; methylmercury, toluene; polychlorinated biphenyls).

Number of Chemicals: 190

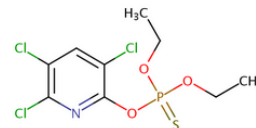
https://comptox.epa.gov/dashboard/chemical_lists/humanneurotox



Methyl parathion
298-00-0



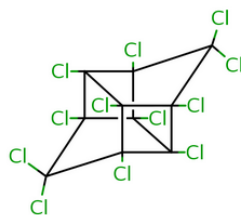
Nicotine
54-11-5



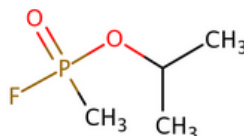
Chlorpyrifos
2921-88-2



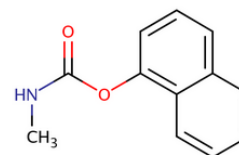
Isolane
119-38-0



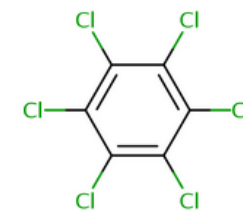
Mirex
2385-85-5



Sarin
107-44-8



Carbaryl
63-25-2



Hexachlorobenzene
118-74-1

>46,000 spectra

32 contributors



MassBank ID:

Go

European MassBank (NORMAN MassBank)

 Quick Search

[illegible]

➡ Peak Search

The screenshot shows the PubChem search results for the query "2,3,4,5-tetrahydro-2H-pyridine". The interface includes a search bar at the top with the query text. Below the search bar, there are tabs for "Search by" (Structure, Name, Molecular Formula) and "Filter by" (Molecular Weight, Molecular Weight Range, Molecular Weight Range, Molecular Weight Range). The search results are displayed in a table with columns for "Rank", "Name", "Molecular Weight", "Molecular Weight Range", and "Molecular Weight Range". The first result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The second result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The third result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The fourth result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The fifth result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The sixth result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The seventh result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The eighth result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The ninth result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12. The tenth result is "2,3,4,5-tetrahydro-2H-pyridine" with a molecular weight of 106.12.

[➔ Record Index](#)

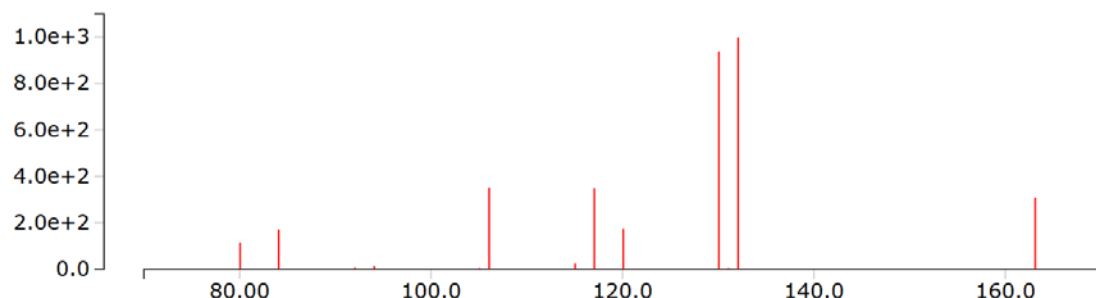


MassBank Record: EQ300804

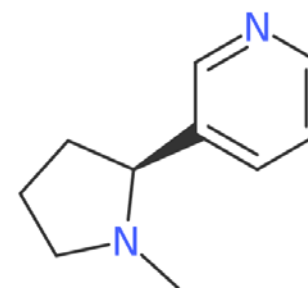
[Home](#) |
 [Quick Search](#) |
 [Peak Search](#) |
 [Record Index](#) |
 [Statistics](#) |
 [Imprint/Data privacy](#)
 MassBank ID:

Nicotine; LC-ESI-QFT; MS2; CE: 60; R=35000; [M+H]⁺

Mass Spectrum



Chemical Structure



Options
• Labels

PK\$NUM_PEAK: 24
 PK\$PEAK: m/z int. rel.int.
 70.065 454569.9 3
 78.0334 160392.5 1
 80.0494 14365987.5 115
 82.065 352108.2 2
 84.0807 21553065.2 172
 91.0541 243012.2 1
 92.0494 1173136.6 9
 93.0571 190301.4 1
 94.065 1842197.3 14
 103.054 194746.7 1
 105.0698 991130.4 7
 106.065 43816128.6 351
 110.0598 348436.9 2
 115.0541 3367681.5 27
 117.0571 43503063 349
 118.0649 392125 3
 119.0726 230767.3 1
 120.0806 21877380.1 175
 130.065 116905175 937
 131.073 880898.8 7
 132.0806 124509966.1 999
 134.0962 389380.4 3
 146.0961 136376.5 1
 163.1227 38578752.8 309
 //

ACCESSION: EQ300804

RECORD_TITLE: Nicotine; LC-ESI-QFT; MS2; CE: 60; R=35000; [M+H]⁺

DATE: 2015.08.25

AUTHORS: Beck B, Stravs M, Schvmanski E, Singer H, Department of Environmental Chemistrv, Eawag

LICENSE: [CC BY](#)

COPYRIGHT: Copy: CH\$NAME: Nicotine

PUBLICATION: CH\$NAME: 3-[(2S)-1-methylpyrrolidin-2-yl]pyridine

COMMENT: CONFID: CH\$NAME: 3-[(2S)-1-methyl-2-pyrrolidinyl]pyridine

COMMENT: EAWAG: CH\$COMPOUND_CLASS: N/A; Environmental Standard

CH\$FORMULA: [C10H14N2](#)

CH\$EXACT_MASS: 162.11570

CH\$SMILES: [n1cc\(ccc1\)\[C@H\]2N](#)

CH\$IUPAC: InChI=1S/C10H14N2,

CH\$LINK: CAS [54-11-5](#)

CH\$LINK: CHEBI [17688](#)

CH\$LINK: HMDB [HMDB01934](#)

CH\$LINK: KEGG [C00745](#)

CH\$LINK: PUBCHEM [CID:89594](#)

CH\$LINK: INCHIKEY [SNICXCGAK](#)

CH\$LINK: CHEMSPIDER [80863](#)

AC\$INSTRUMENT: Q Exactive Orbitrap Thermo Scientific

AC\$INSTRUMENT_TYPE: LC-ESI-QFT

AC\$MASS_SPECTROMETRY: MS_TYPE MS2

AC\$MASS_SPECTROMETRY: IONIZATION ESI

AC\$MASS_SPECTROMETRY: ION_MODE POSITIVE

AC\$MASS_SPECTROMETRY: FRAGMENTATION_MODE HCD

AC\$MASS_SPECTROMETRY: COLLISION_ENERGY 60 (nominal)

AC\$MASS_SPECTROMETRY: RESOLUTION 35000

AC\$CHROMATOGRAPHY: COLUMN_NAME XBridge C18 3.5um, 2.1x50mm, Waters

AC\$CHROMATOGRAPHY: FLOW_GRADIENT 90/10 at 0 min, 50/50 at 4 min, 5/95 at 17 min

AC\$CHROMATOGRAPHY: FLOW_RATE 200 ul/min

AC\$CHROMATOGRAPHY: RETENTION_TIME 0.9 min

AC\$CHROMATOGRAPHY: SOLVENT A water with 0.1% formic acid

AC\$CHROMATOGRAPHY: SOLVENT B methanol with 0.1% formic acid

CompTox Chemistry Dashboard

<https://comptox.epa.gov/dashboard/>



Home

Advanced Search

Batch Search

Lists

Predictions

Downloads

Chemistry Dashboard

Aa ▼

761 Thousand Chemicals



nicotine

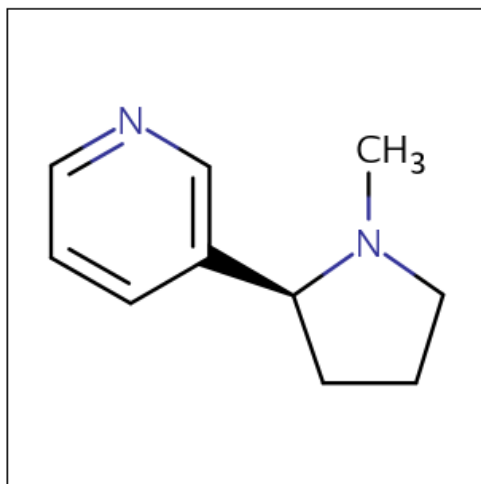


☐ Identifier substring search

Nicotine

54-11-5 | DTXSID1020930

Searched by Approved Name.



Wikipedia

Nicotine is a potent parasympathomimetic stimulant and an alkaloid found in the nightshade family of plants. Nicotine acts as an agonist at most nicotinic acetylcholine receptors (nAChRs), except at two nicotinic receptor subunits (nAChRα9 and nAChRα10) where it acts as a receptor antagonist. Nicotine is found in the leaves of *Nicotiana rustica*, in concentrations of 2–14%; in the tobacco plant, *Nicotiana tabacum*; in *Duboisia hopwoodii*; and in *Asclepias syriaca*...

[Read more](#)

Intrinsic Properties

Structural Identifiers

Linked Substances

Presence in Lists

Record Information

Quality Control Notes

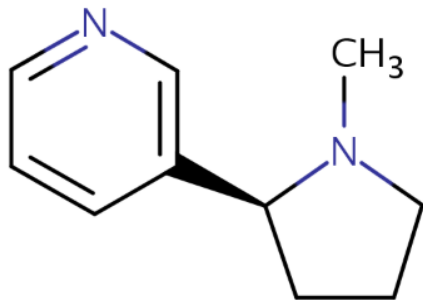
CompTox Chemistry Dashboard – Presence in Lists

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

Nicotine

54-11-5 | DTXSID1020930

Searched by Approved Name.



Wikipedia

Intrinsic Properties

Structural Identifiers

Linked Substances

Presence in Lists

Federal

TOX21SL: Tox21 Screening Library

NIOSH Skin Notation Profiles

NIOSH International Chemical Safety Cards

NIOSH Pocket Guide to Chemical Hazards

NIOSH IDLH Values

TOXCAST - EPA ToxCast Screening Library

US State

California Office of Environmental Health Hazard Assessment

International

GENRA

Grace Patlewicz's Chemicals of Interest

Superfund Chemicals

REACH Dossier Chemicals

KEMI List of Substances on the Market

Other

DNT Screening Library

MassBank Reference Spectra Collection

NORMAN Collaborative Trial 2015 Targets and Suspects

STOFF-IDENT Database of Water-Relevant Substances

National Environmental Methods Index

EDSP Universe

40CFR355

TSCAACTIVE

CompTox Chemistry Dashboard – Additional Data

<https://comptox.epa.gov/dashboard/>

Nicotine

54-11-5 | DTXSID1020930

Searched by Approved Name.

DataType

Point of Departure

Download



Human



Eco

Columns

10

Search query

	More	Priority	Toxval type	Subtype	Risk assessment class	Value	Units	Study type	Exposure route	Species	Subsource	Source
ADME		7	LEL	systemic	developmental neurotoxicity	2.9	mg/kg-day	developmental neurotoxicity	oral	rat	open_lit	ToxRefDB
EXPOSURE		7	LEL	developmental	developmental	2.9	mg/kg-day	developmental neurotoxicity	oral	rat	open_lit	ToxRefDB
BIOACTIVITY		7	LEL	systemic	developmental	12	mg/kg-day	developmental	oral	mouse	open_lit	ToxRefDB
GENRA		7	LEL	systemic	developmental neurotoxicity	0.5	mg/kg-day	developmental neurotoxicity	direct	mouse	open_lit	ToxRefDB
SIMILAR COMPOUNDS		7	LEL	developmental	developmental	12	mg/kg-day	developmental	oral	mouse	open_lit	ToxRefDB
RELATED SUBSTANCES		7	LEL	developmental	developmental	0.5	mg/kg-day	developmental neurotoxicity	direct	mouse	open_lit	ToxRefDB
SYNONYMS		7	LEL	reproductive	reproductive	2.9	mg/kg-day	developmental neurotoxicity	oral	rat	open_lit	ToxRefDB
LITERATURE		7	LEL	reproductive	reproductive	12	mg/kg-day	developmental	oral	mouse	open_lit	ToxRefDB
LINKS		7	LOAEL	systemic	developmental neurotoxicity	4.4	mg/kg-day	developmental neurotoxicity	oral	rat	open_lit	ToxRefDB
COMMENTS		7	LOAEL	reproductive	reproductive	4.4	mg/kg-day	developmental neurotoxicity	oral	rat	open_lit	ToxRefDB

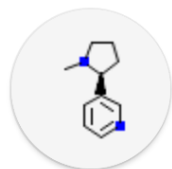
<< < 1 2 3 4 > >>

Showing 1 to 10 of 32 records

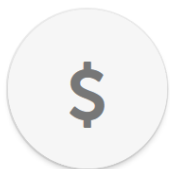


Nicotine

► Cite this Record



STRUCTURE



VENDORS



DRUG INFO



PHARMACOLOGY



LITERATURE



PATENTS



BIOACTIVITIES

PubChem CID: 89594

Chemical Names: Nicotine; L-Nicotine; 54-11-5; (-)-Nicotine; (S)-Nicotine; Habitrol [More...](#)

Molecular Formula: $C_{10}H_{14}N_2$

Molecular Weight: 162.236 g/mol

InChI Key: SNICXCGAKADSCV-JTQLQIEISA-N

Connecting Resources in MetFrag



<https://msbi.ipb-halle.de/MetFragBeta/>



MetFrag

In silico fragmentation for computer assisted identification of metabolite mass spectra

Database Settings

Database: Include references: ☒ Parent Ion:

Neutral Mass: Search ppm:

Formula:

Identifiers:

Candidate Filter & Score Settings

Fragmentation Settings & Processing

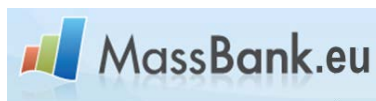
Mzppm:

Mzabs:

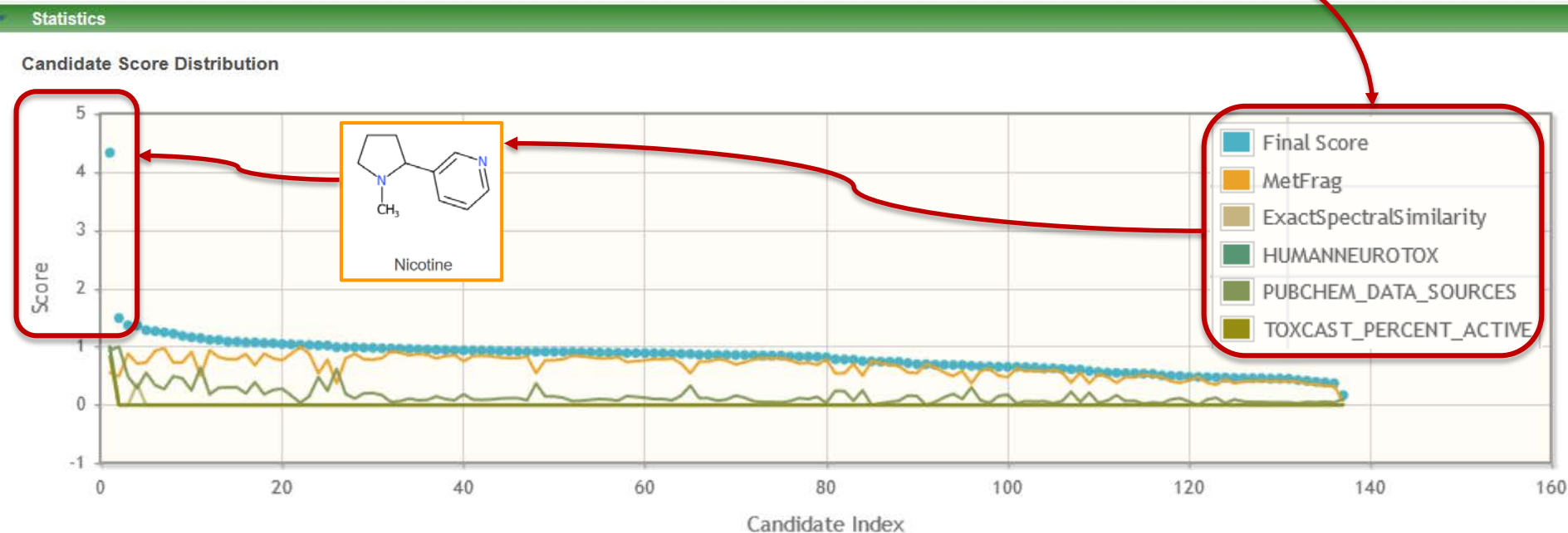
MS/MS Peak list

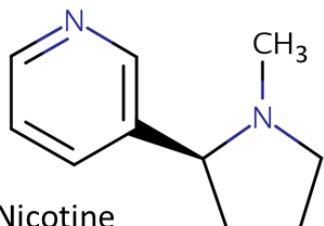
```
70.065 454569.9 3
78.0334 160392.5 1
80.0494 14365987.5
...
```

Connecting Resources in MetFrag



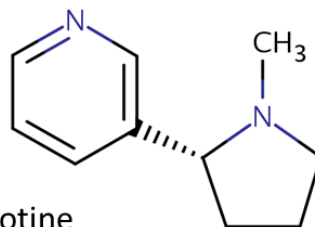
Combined evidence clearly highlights **potential neurotoxicant** among chemical candidates





Nicotine

CN1CCC[C@H]1C1=CN=CC=C1
 DTXSID1020930 | SNICXCGAKADSCV
 54-11-5 | **162.1157** | 0.929 | **72**
 Tox: **yes** | Expo: **yes** | Bioassay: **yes**



D-Nicotine

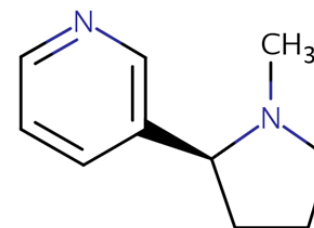
CN1CCC[C@@H]1C1=CN=CC=C1
 DTXSID0046351 | SNICXCGAKADSCV
 25162-00-9 | **162.1157** | 0.929 | **20**
 Tox: **no** | Expo: **yes** | Bioassay: **yes**

LEGEND: Name, SMILES

DTXSID | InChIKey 1st Block

CAS | **Monoiso.** Mass | logP | **Sources**

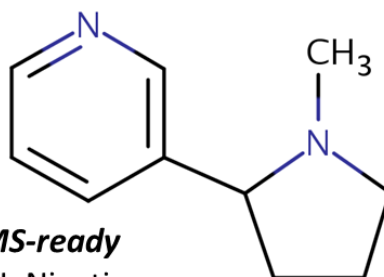
Data on: **Toxicity** | **Exposure** | **Bioassays**



HCl

Nicotine hydrochloride

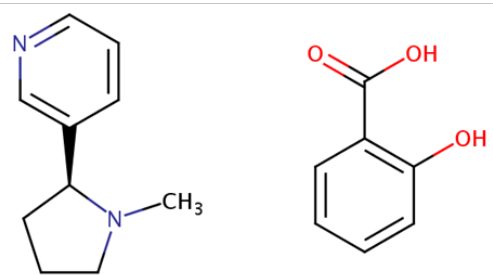
Cl.CN1CCC[C@H]1C1=CN=CC=C1
 DTXSID6020931 | HDJBTCAJIMNXEW
 2820-51-1 | **198.0924** | 0.929 | **9**
 Tox: **no** | Expo: **yes** | Bioassay: **yes**



MS-ready

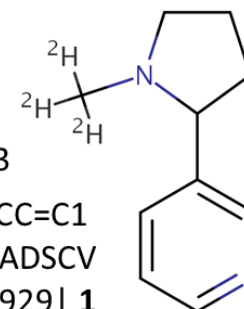
DL-Nicotine

CN1CCCC1C1=CN=CC=C1
 DTXSID3048154 | SNICXCGAKADSCV
 22083-74-5 | **162.1157** | 0.953 | **9**
 Tox: **yes** | Expo: **no** | Bioassay: **yes**



Benzoic acid, 2-hydroxy-, compd. with
 3-[(2S)-1-methyl-2-pyrrolidinyl]pyridine (1:1)

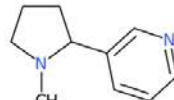
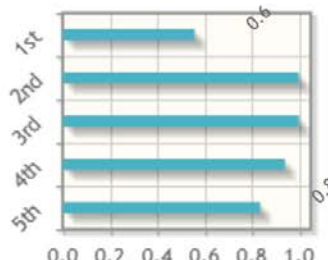
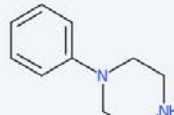
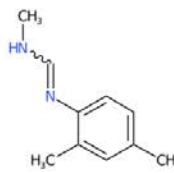
OC(=O)C1=CC(=O)C=CC=C1.CN1CCC[C@H]1C1=CN=CC=C1
 DTXSID5075319 | AIBWPBUAKCMKNS
 29790-52-1 | **300.1474** | 0.929 | **6**
 Tox: **no** | Expo: **yes** | Bioassay: **no**



DL-Nicotine-d3

[2H]C([2H])([2H])N1CCCC1C1=CN=CC=C1
 DTXSID80442666 | SNICXCGAKADSCV
 69980-24-1 | **165.1345** | 0.929 | **1**
 Tox: **no** | Expo: **no** | Bioassay: **no**

Connecting Resources in MetFrag

#	Molecule	Identifier	Mass	Formula	Normalized Scores	FinalScore	Details
1	 Nicotine	DTXSID1020930 DTXSID8021725 DTXSID3048154 DTXSID0046351 DTXSID6020931 DTXSID00657553 DTXSID5075319 InChIKeyBlock1 = SNICXCGAKADSCV	162.11576	C ₁₀ H ₁₄ N ₂		4.3349	Peaks: 18 / 23 Fragments Scores Download
2	 Phenylpiperazine	DTXSID40176612 DTXSID40193102 DTXSID90216632 DTXSID50291046 DTXSID00293111 DTXSID50296613 InChIKeyBlock1 = YZTJYBJCZXZGCT	162.11576	C ₁₂ H ₁₄ N ₂			
3	 N'-(2,4-Dimethylphenyl)-N-methylformamidin e	DTXSID1037696 DTXSID10199510 InChIKeyBlock1 = JIIOLEGNERQDIP	162.11576	C ₁₂ H ₁₄ N ₂			

LEGEND: Name, SMILES
DTXSID | InChIKey 1st Block
CAS | Monoiso. Mass | logP | Sources
Data on: Toxicity | Exposure | Bioassays

Nicotine
CN1CCC[C@H]1C1=CN=CC=C1
 DTXSID0046351 | SNICXCGAKADSCV
 25162-00-9 | **162.1157** | 0.929 | **20**
 Tox: **no** | Expo: **yes** | Bioassay: **yes**

D-Nicotine
CN1CCC[C@@H]1C1=CN=CC=C1
 DTXSID0046351 | SNICXCGAKADSCV
 25162-00-9 | **162.1157** | 0.929 | **20**
 Tox: **no** | Expo: **yes** | Bioassay: **yes**

Nicotine hydrochloride
Cl.CN1CCC[C@H]1C1=CN=CC=C1
 DTXSID6020931 | HDJBTCAJIMNXEW
 2820-51-1 | **198.0924** | 0.929 | **9**
 Tox: **no** | Expo: **yes** | Bioassay: **yes**

MS-ready DL-Nicotine
CN1CCCC1C1=CN=CC=C1
 DTXSID3048154 | SNICXCGAKADSCV
 22083-74-5 | **162.1157** | 0.953 | **9**
 Tox: **yes** | Expo: **no** | Bioassay: **yes**

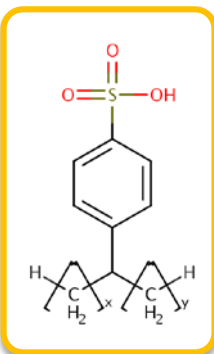
Benzoic acid, 2-hydroxy-, compd. with 3-[(2S)-1-methyl-2-pyrrolidinyl]pyridine (1:1)
OC(=O)C1=C(O)C=CC=C1.CN1CCC[C@H]1C1=CN=CC=C1
 DTXSID5075319 | AIBWBPBUAKCMKNS
 29790-52-1 | **300.1474** | 0.929 | **6**
 Tox: **no** | Expo: **yes** | Bioassay: **no**

DL-Nicotine-d3
[2H]C([2H])([2H])N1CCCC1C1=CN=CC=C1
 DTXSID80442666 | SNICXCGAKADSCV
 69980-24-1 | **165.1345** | 0.929 | **1**
 Tox: **no** | Expo: **no** | Bioassay: **no**

Connecting and Enhancing Open Resources

- Sharing knowledge is a win-win situation

2014



MassBank.eu

norman
suspects

EPA
Chemistry
Dashboard

2015: found in waters across Europe



2016: 1 datapoint cross-annotates 3072 in GNPS

Hits in GNPS Massive datasets:

Surfactants: <http://goo.gl/7sY9Pf>

2017: Early-Warning System is born

normanews

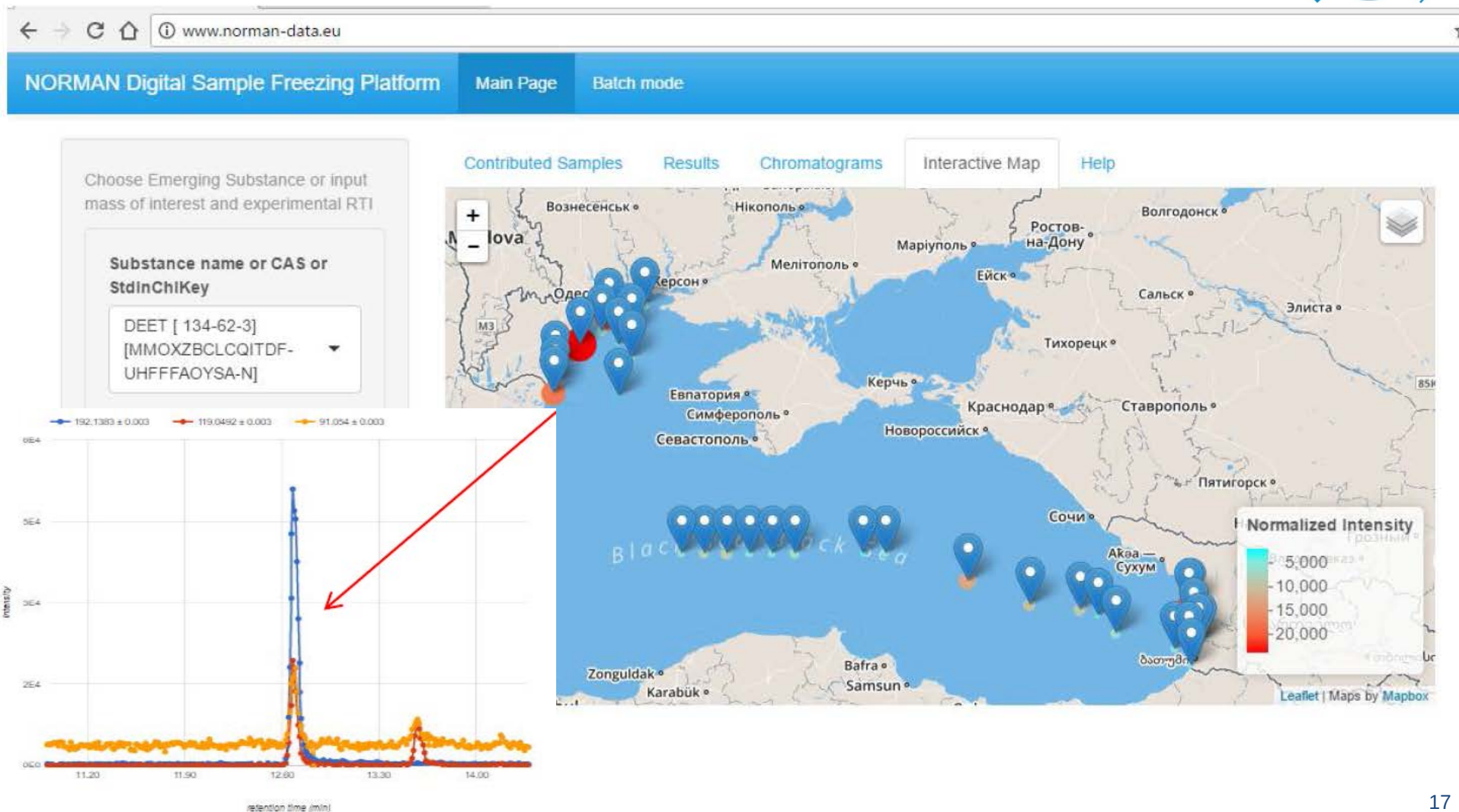
2018: Highlighted in



CHEMISTRY
Early warning about
emerging contaminants



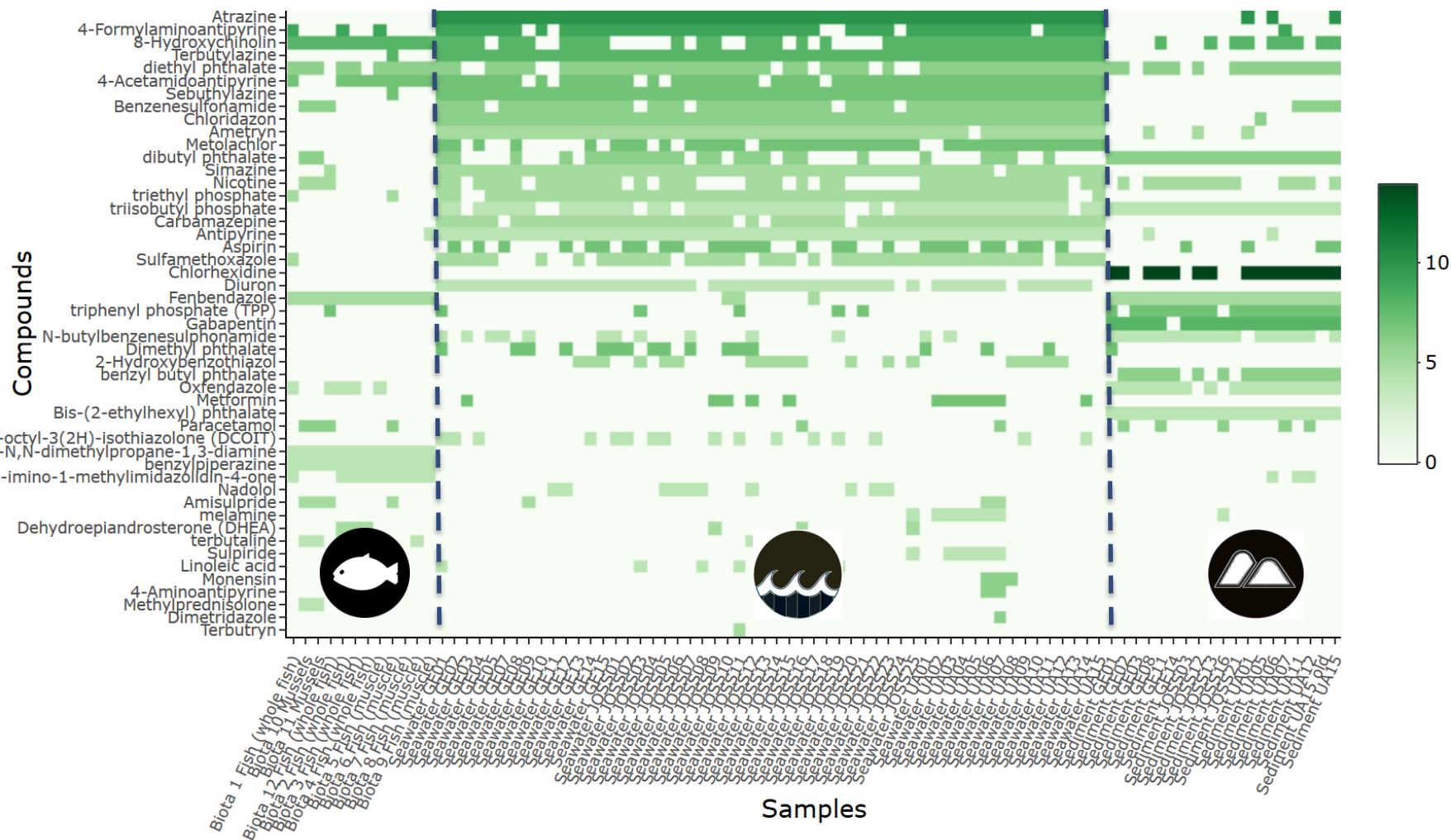
“Live” retrospective screening of known and unknown chemicals in European samples (various matrices)



Retrospective screening of REACH chemicals in Black Sea samples (various matrices)

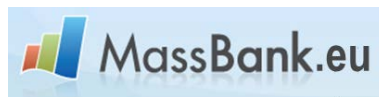
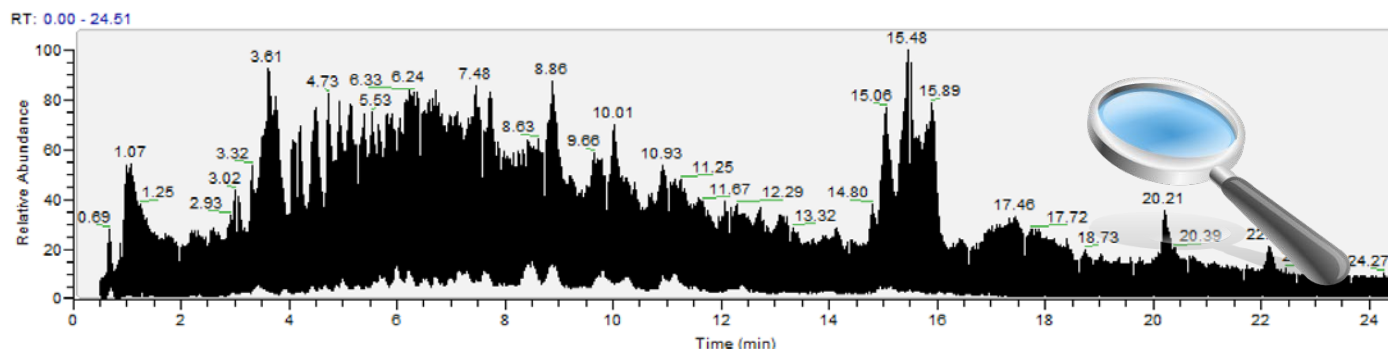


Occurrence Results



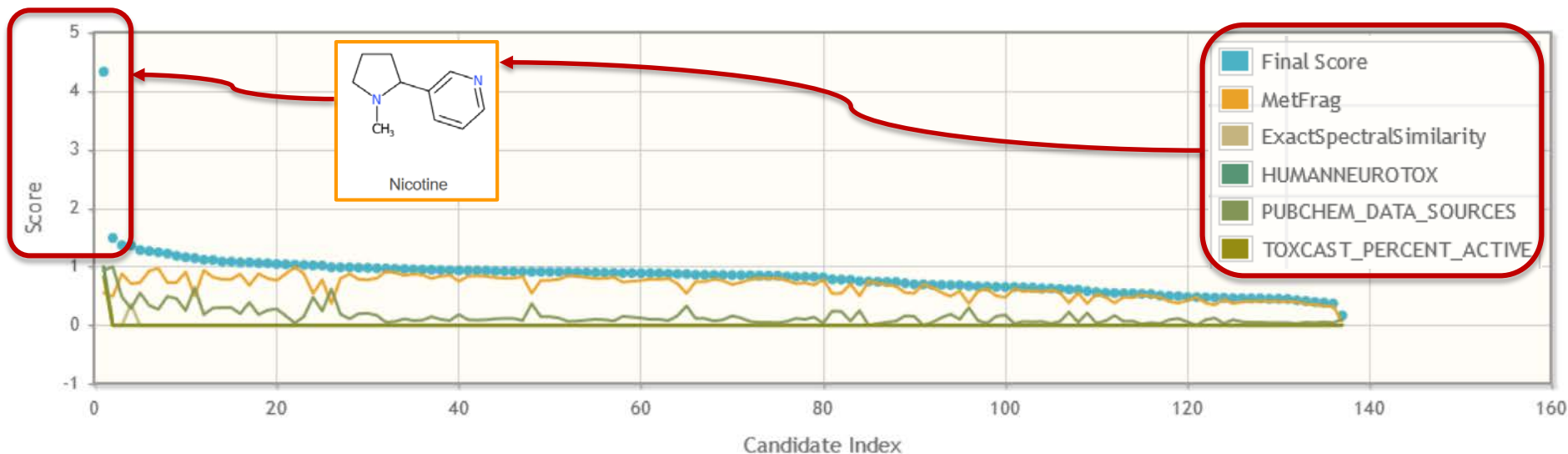
Community Challenges ... and Solutions

High resolution
mass spectrometry
AND connecting
chemical knowledge



Statistics

Candidate Score Distribution





Thank you

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MassBank consortium

