http://orcid.org/0000-0003-1423-330X

United States Environmental Protection Agency

EA 504: Non-targeted Environmental Analysis

Andrew D. McEachran

7/13/2017

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

Office of Research and Development
National Center for Computational Toxicology, RTP, NC

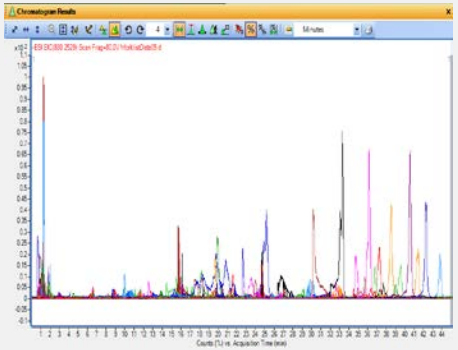
EPA United States Environmental Protection Agency

Comparing Analysis Approaches

- Targeted Analysis:
  - We know exactly what we're looking for
  - 10s – 100s of chemicals

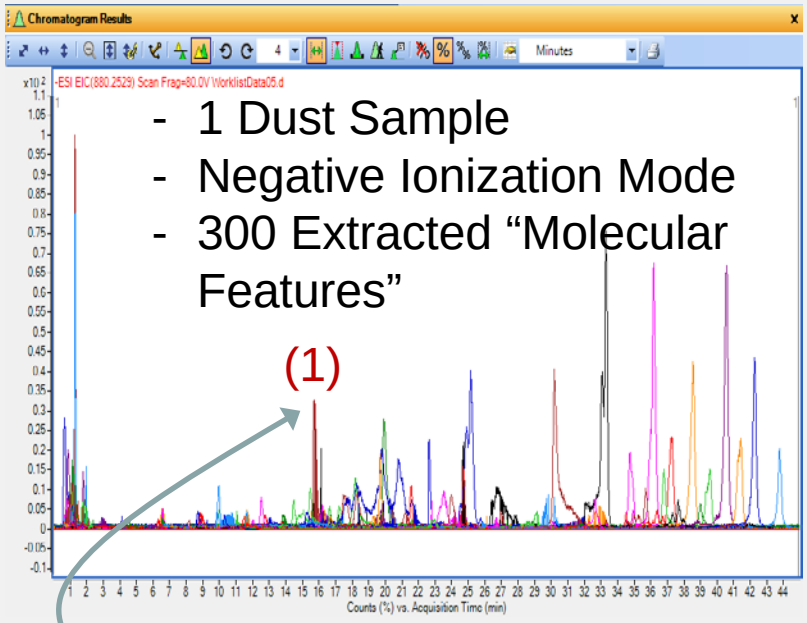
- Suspect Screening Analysis (SSA):
  - We have chemicals of interest
  - 100s – 1,000s of chemicals

- Non-Targeted Analysis (NTA):
  - We have no preconceived lists
  - 1,000s – 10,000s of chemicals
  - In dust, soil, food, air, water, products- potential exposure source for plants, animals, and humans



Slide from Sobus, Williams

General Goals of SSA/NTA



- 1 Dust Sample
- Negative Ionization Mode
- 300 Extracted "Molecular Features"

(1)

1) Prioritize "Molecular Features"

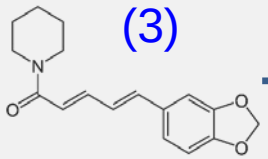
2) Correctly assign formulas

3) Correctly assign structures

4) Determine chemical sources

5) Predict chemical concentrations

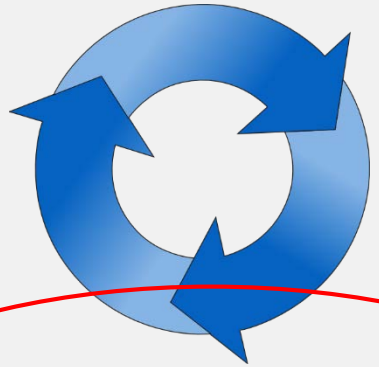
EXPOSURE

(2) C17H19NO3 → (3)  → (4)  → (5) 12 µg/g

EPA United States Environmental Protection Agency

The General Approach

Analytical Instruments



Comp. Tools & Workflows

FOR IDENT

Xcms Online

MetFrag

Databases

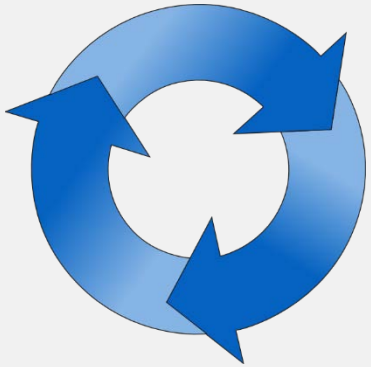
ChemSpider
Search and share chemistry

PubChem

MassBank

The General Approach

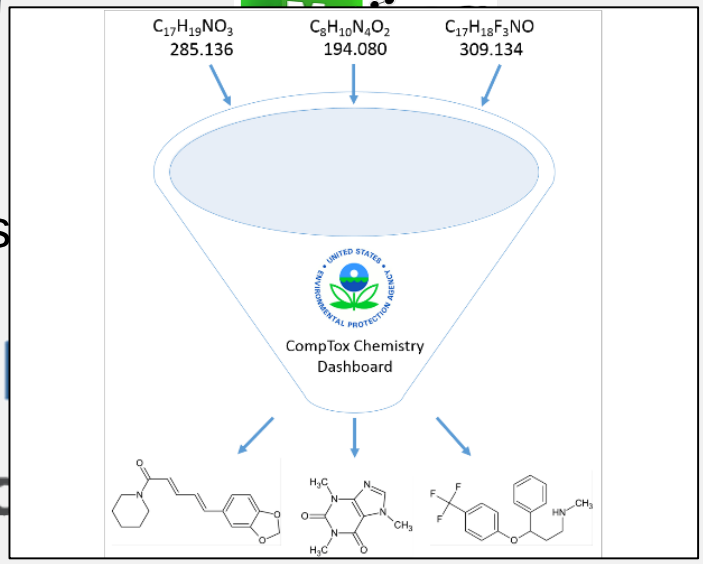
Analytical Instruments



Comp. Tools & Workflows

FOR IDENT

Xcms Online



Databases

ChemSpider
Search and share chemistry

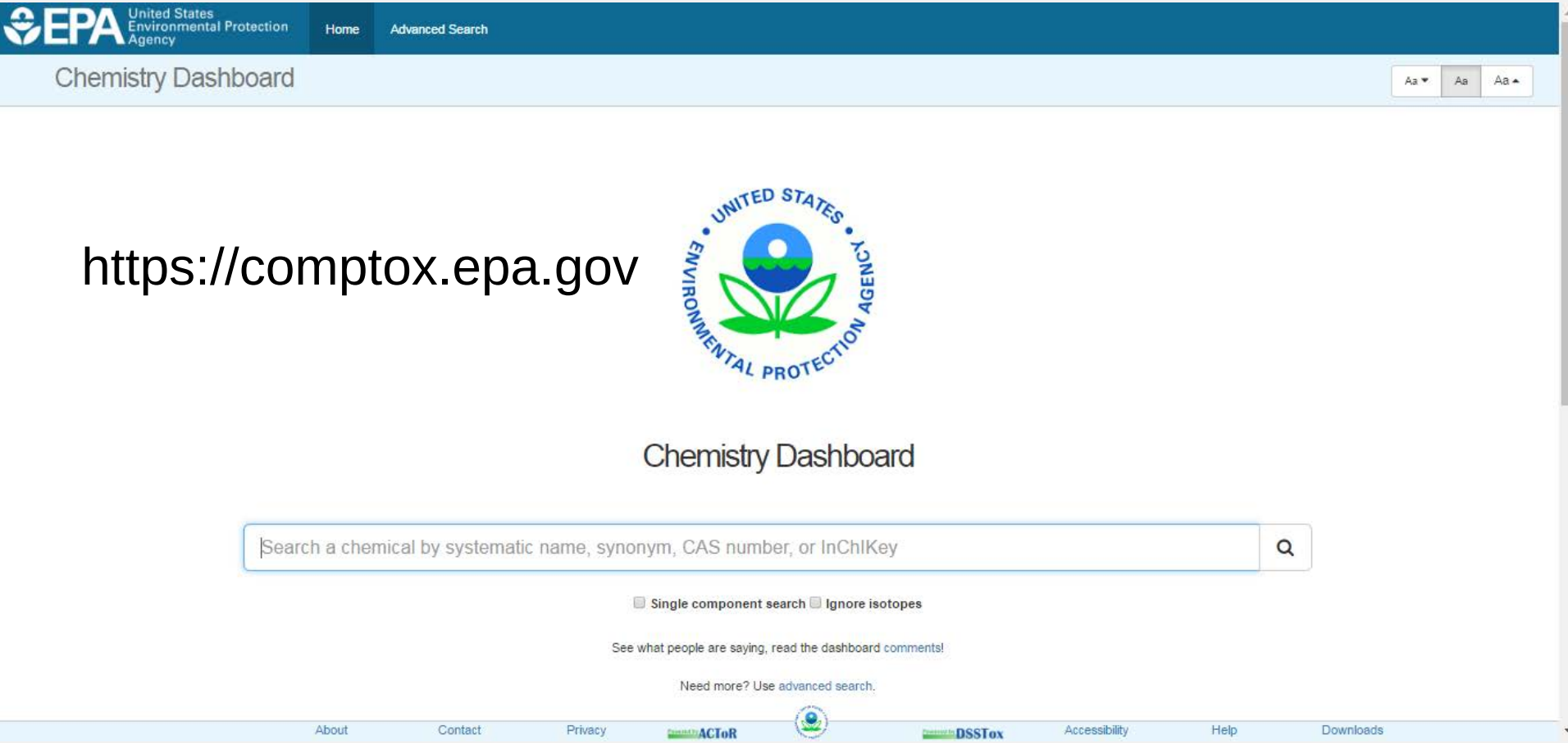
Pu

MassBa

EPA United States Environmental Protection Agency

CompTox Chemistry Dashboard

https://comptox.epa.gov



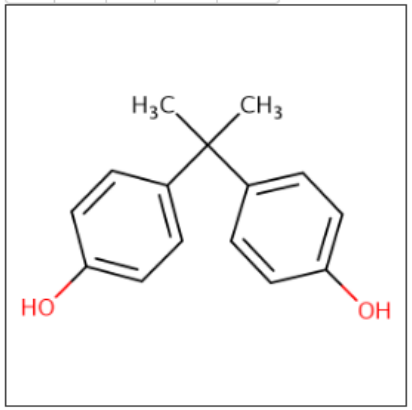
EPA United States Environmental Protection Agency

CompTox Chemistry Dashboard

Bisphenol A

80-05-7 | DTXSID7020182

Searched by Expert Validated Synonym: Found 1 result for 'bpa'.



Wikipedia

Bisphenol A (BPA) is an organic synthetic compound with the chemical formula (CH3)2C(C6H4OH)2 belonging to the group of diphenylmethane derivatives and bisphenols, with two hydroxyphenyl groups. It is a colorless solid that is soluble in organic solvents, but poorly soluble in water. It has been in commercial use since 1957. BPA is employed to make certain plastics and epoxy resins. BPA-based plastic is clear and tough... Read more

- Intrinsic Properties
- Structural Identifiers
- Related Compounds (Beta)
- Presence in Lists
- Record Information

EPA United States Environmental Protection Agency

CompTox Chemistry Dashboard

Bisphenol A

80-05-7 | DTXSID7020182

Searched by Expert Validated Synonym: Found 1 result for 'bpa'.

Chemical Properties | Env. Fate/Transport | Synonyms | External Links | Toxicity Values (Beta) | Exposure | Bioassays | Similar Molecules (Beta) | Literature | Comments

Summary

- LogP: Octanol-Water
- Water Solubility
- Density
- Melting Point
- Boiling Point
- Surface Tension
- Vapor Pressure
- LogKoa: Octanol-Air
- Henry's Law
- Index of Refraction

Download as: TSV | Excel | SDF

Property	Average		Median		Range		Unit
	Experimental	Predicted	Experimental	Predicted	Experimental	Predicted	
LogP: Octanol-Water	3.32 (1)	3.24 (4)	3.32 to 3.32	3.24	3.32	2.40 to 3.73	-
Water Solubility	5.26e-04 (1)	1.58e-03 (4)	5.26e-04 to 5.26e-04	1.58e-03	5.26e-04	5.70e-04 to 3.68e-03	mol/L
Density	-	1.14 (1)	-	1.14	-	-	g/cm^3
Melting Point	155 (7)	144 (3)	153 to 158	144	153 to 158	132 to 157	°C
Boiling Point	200 (1)	349 (3)	200 to 200	349	200	334 to 364	°C
Surface Tension	-	46.0 (1)	-	46.0	-	-	dyn/cm
Vapor Pressure	-	2.52e-07 (3)	-	2.52e-07	-	7.01e-08 to 5.34e-07	mmHg
LogKoa: Octanol-Air	-	8.38 (1)	-	8.38	-	-	-
Henry's Law	-	6.96e-07 (1)	-	6.96e-07	-	-	atm-m3/mole
Index of Refraction	-	1.60 (1)	-	1.60	-	-	-
Molar Refractivity	-	68.2 (1)	-	68.2	-	-	cm^3
pKa Acidic Apparent	-	10.3 (1)	-	10.3	-	-	-
Molar Volume	-	200 (1)	-	200	-	-	cm^3

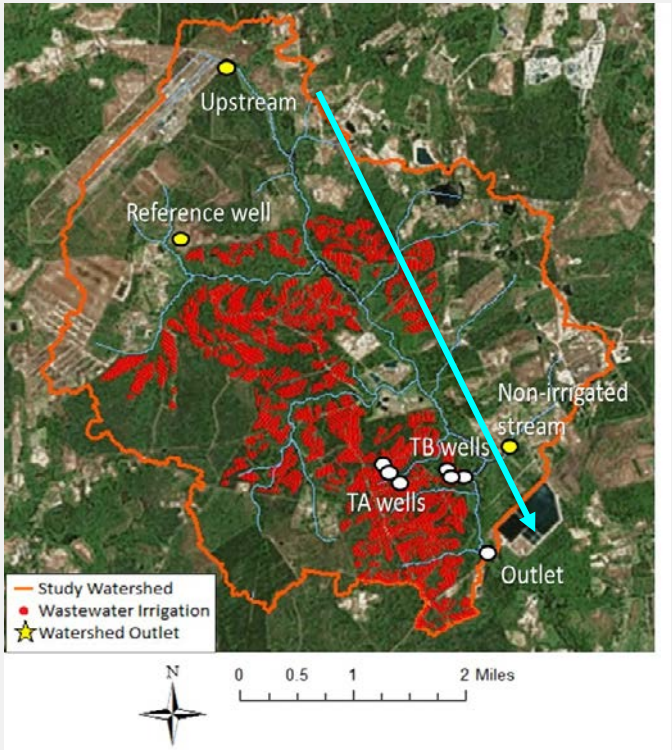
EPA United States Environmental Protection Agency

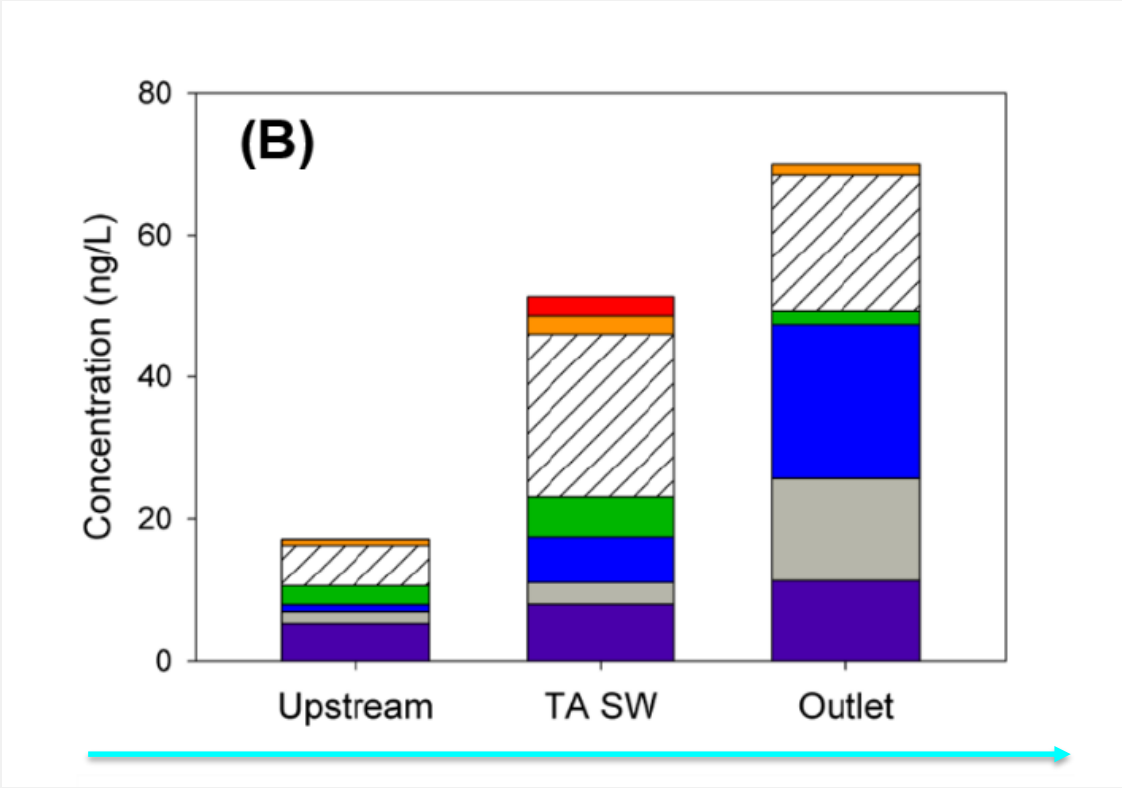
Application to environmental samples

Forested wastewater land application

"Pharmaceutical and Personal Care Product (PPCP) Occurrence, Distribution, and Export at a Forest-Water Reuse System." 2016. Dissertation, NC State Univ.

Do Forest Water Reuse Systems Export PPCPs?





	Mean Log Kow
Plasticizer	3.32
Hormones	3.32
Prescription/OTC Drugs	2.61
NSAIDs	2.21
Antibiotics/Antimicrobials	1.94
Cotinine	0.07
Caffeine+metabolite	-0.07

Surface water flow direction

McEachran *et al.*, 2017.
10.1016/j.scitotenv.2016.12.185

Conventional wastewater treatment

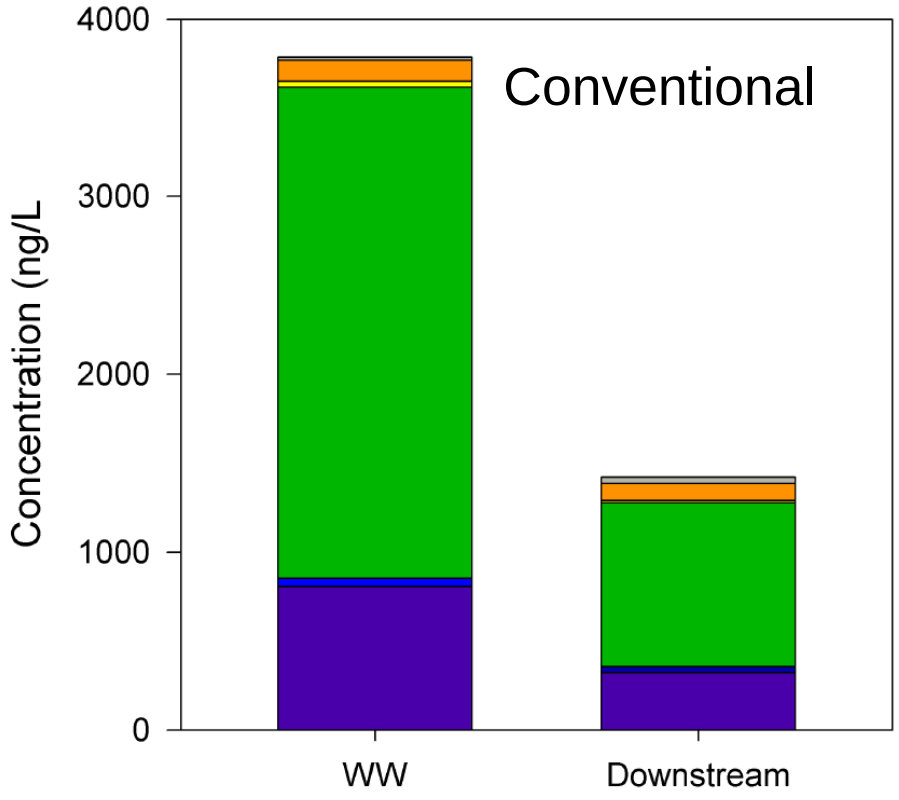
- 6.5 MGD average treatment
- Tertiary treatment with UV disinfection
- Discharge of treated effluent →
- More urbanized area

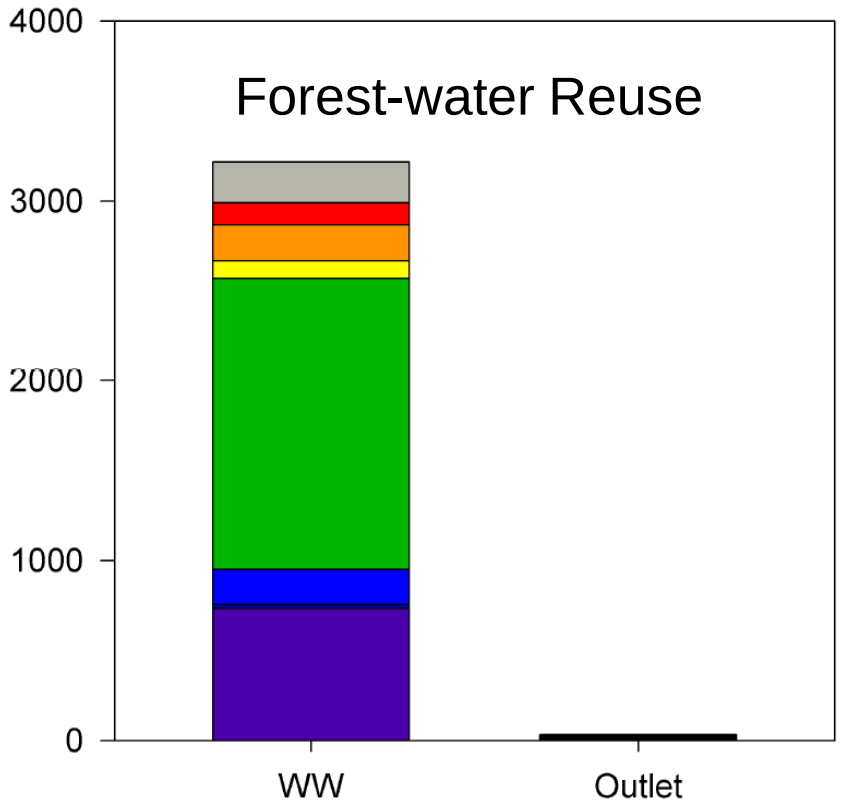
How does environmental input of emerging contaminants differ between conventional systems and forest-water reuse systems?

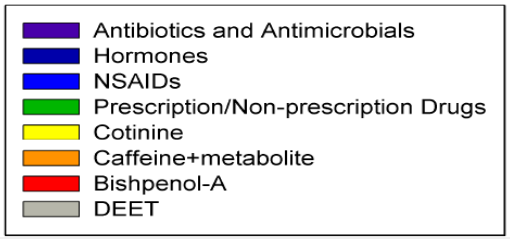
WW release

"Pharmaceutical and Personal Care Product (PPCP) Occurrence, Distribution, and Export at a Forest-Water Reuse System." 2016. Dissertation, NC State Univ.

Total summed PPCP concentrations greater downstream of conventional system

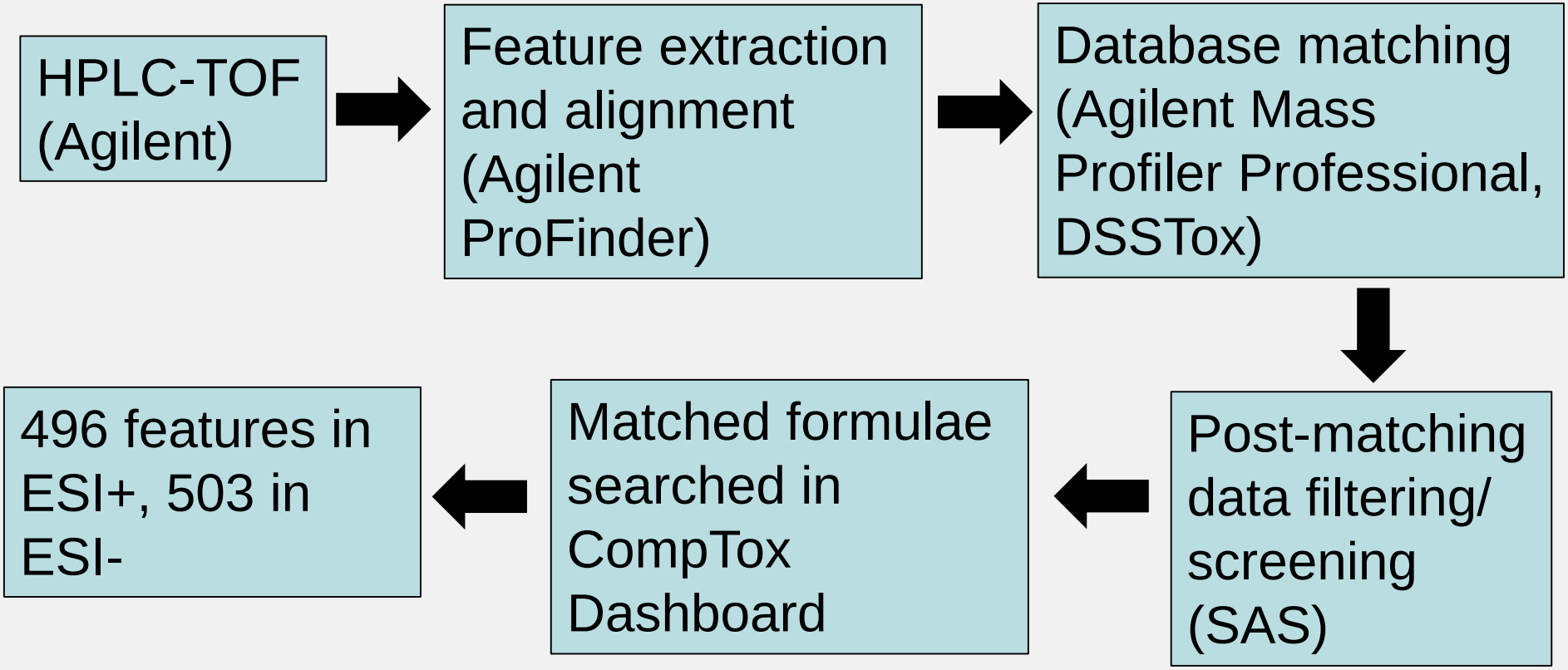






"Pharmaceutical and Personal Care Product (PPCP) Occurrence, Distribution, and Export at a Forest-Water Reuse System." 2016. Dissertation, NC State Univ.

Non-targeted analysis workflow



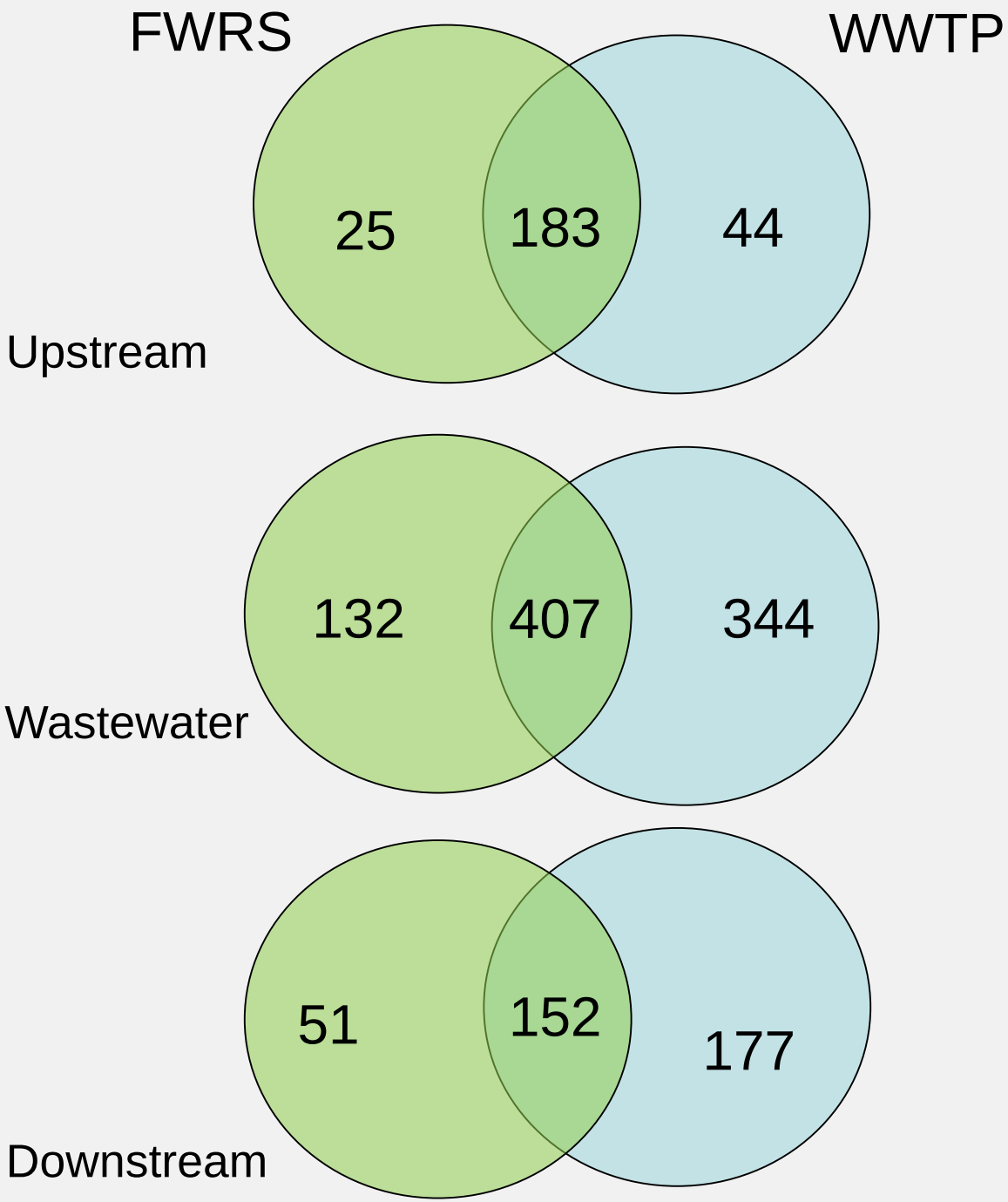
Average DB-Matched Chemicals per site/location

	FWRS	WWTP
Upstream	128	132
Wastewater	367	460
Downstream	123	202

FWRS= Forest-water Reuse System
WWTP=Wastewater Treatment Plant

"Pharmaceutical and Personal Care Product (PPCP) Occurrence, Distribution, and Export at a Forest-Water Reuse System." 2016. Dissertation, NC State Univ.

Number of unique/similar matched chemicals between sites



"Pharmaceutical and Personal Care Product (PPCP) Occurrence, Distribution, and Export at a Forest-Water Reuse System." 2016. Dissertation, NC State Univ.

EPA United States Environmental Protection Agency

Tentative Candidates:

Top 50 most frequently occurring in ESI-

	INPUT	DTXSID	CASRN	PREFERRED NAME	MOL FOR	MONOISC	EXPOCAS	EXPOCAS
2	C6H12O2	DTXSID30	123-86-4	Butyl acetate	C6H12O2	116.08372	Y	6.43e-05
3	C7HF7S	DTXSID20	651-84-3	2,3,5,6-Tetrafluoro-4-(trifluoromethyl)benzene-1-thiol	C7HF7S	249.96871	-	-
4	C8H16Br2O	DTXSID70	7239-41-0	Butane, 1,1'-oxybis(4-bromo-	C8H16Br2	285.95679	-	-
5	C14H8BrClN2	DTXSID00	83800-98-	2-(4-bromophenyl)-4-chloroquinazoline	C14H8BrC	317.95593	-	-
6	C10H10O10S3	DTXSID10	121227-24	2-Hydroxy-1,2-dihydronaphthalene-1,2,3-trisulfonic acic	C10H10O1	385.94361	-	-
7	C18H15Cl3O6	DTXSID20	69799-33-	BUELLOLIDE	C18H15Cl3	431.99342	-	-
8	C2H5O6P	DTXSID60	13147-57-	Phosphoglycolate	C2H5O6P	155.98237	-	-
9	C5H5ClN2S	DTXSID60	49844-90-	4-Chloro-2-methylthiopyrimidine	C5H5ClN2	159.98619	-	-
10	C8H6F2N2O	DTXSID00	105391-65	5-(Difluoromethoxy)-1H-indazole	C8H6F2N2	184.04481	-	-
11	C8H10O3S	DTXSID40	80-48-8	Methyl toluene-4-sulfonate	C8H10O3S	186.03506	-	-
12	C9H12O3S	DTXSID60	15763-76-	Sodium 4-isopropylbenzenesulfonate	C9H11NaC	222.03265	Y	1.6e-07
13	C9H15FO4	DTXSID40	1216897-1	ML-10	C9H15FO4	206.09543	-	-
14	C12H18O3S	DTXSID60	28261-72-	Diisopropylbenzenesulphonic acid	C12H18O3	242.09766	-	-
15	C13H22O4	DTXSID50	2155-60-4	Butanedioic acid, methylene-, dibutyl ester	C13H22O4	242.15180	-	-
16	C10H14O5S	DTXSID30	688763-13	2-(3,4-dimethoxyphenyl)sulfonylethanol	C10H14O5	246.05619	-	-
17	C9H5Cl3N4	DTXSID90	101-05-3	Anilazine	C9H5Cl3N	273.95797	Y	9.34e-08
18	C17H26O4	DTXSID30	23513-14-	(6)-Gingerol	C17H26O4	294.18310	-	-
19	C21H22NS	DTXSID60	6322-87-8	1-Benzyl-4-(benzylsulfanyl)-2,6-dimethylpyridin-1-ium i	C21H22IN	447.05177	-	-
20	C14H9ClF3NO3	DTXSID70	74274-36-	Benzoic acid, 2-amino-5-(2-chloro-4-(trifluoromethyl)ph	C14H9ClF3	331.02230	-	-
21	C16H17N3O4S	DTXSID90	15686-71-	Cephalexin	C16H17N3	347.09397	Y	4.82e-08
22	C16H30O7S	DTXSID70	2373-38-8	Butanedioic acid, sulfo-, 1,4-bis(1,3-dimethylbutyl) este	C16H29Na	388.15316	-	-
23	C13H11IN2O3	DTXSID90	91718-17-	Barbituric acid, 5-allyl-5-(p-iodophenyl)-	C13H11IN	369.98144	-	-
24	C17H14F3N3O2S	DTXSID00	169590-42	Celecoxib	C17H14F3	381.07588	Y	2.55e-07
25	C12H19Cl3O8	DTXSID10	56038-13-	Sucralose	C12H19Cl3	396.01455	Y	2.92e-07
26	C16H14INO2S	DTXSID00	920505-56	2-Iodo-N-[2-(3-methyl-1-benzothiophen-2-yl)ethyl]fura	C16H14IN	410.97899	-	-
27	C8HF15O2	DTXSID80	335-67-1	PFOA	C8HF15O2	413.97370	Y	5.56e-06
28	C9H15Cl6O4P	DTXSID90	13674-87-	TDCPP	C9H15Cl6	427.88391	Y	1.81e-07
29	C25H28N6O	DTXSID00	138402-11	Irbesartan	C25H28N6	428.23245	Y	2.88e-07
30	C12H4Cl2F6N4OS	DTXSID40	120068-37	Fipronil	C12H4Cl2F	435.93870	Y	2.65e-08
31	C17H16Br2N2O4	DTXSID00	5573-43-3	STK052309	C17H16Br2	469.94768	-	-
32	C17H13Br2ClO4	DTXSID80	6976-54-1	[2-bromo-1-(6-bromo-1,3-benzodioxol-5-yl)propyl] 4-ch	C17H13Br2	473.88691	-	-
33	C33H30N4O2	DTXSID80	144701-48	Telmisartan	C33H30N4	514.23687	Y	3.26e-07
34	C38H52N6O7	DTXSID90	198904-31	Atazanavir	C38H52N6	704.38974	Y	4.44e-07
35	CH4O4S	DTXSID30	870-72-4	Sodium hydroxymethanesulfonate	CH3NaO4S	133.96497	Y	1.86e-08
36	C5H8F3NS	DTXSID10	61170-54-	2,2-Dimethyl-1-[(trifluoromethyl)sulfanyl]aziridine	C5H8F3NS	171.03295	-	-
37	C10H20O2	DTXSID90	334-48-5	Decanoic acid	C10H20O2	172.14632	Y	4.18e-05
38	C12H24O3	DTXSID00	3006-82-4	Hexaneperoxoic acid, 2-ethyl-, 1,1-dimethylethyl ester	C12H24O3	216.17254	-	-
39	C6H10N3O4S	DTXSID50	88347-81-	[(2-Azido-3-methoxy-3-oxopropyl)sulfanyl]acetic acid	C6H9N3O4	219.03137	-	-
40	C11H10O3S	DTXSID50	65505-16-	2,5-Dimethyl-3-thiofuroylfuran	C11H10O3	222.03506	-	-

Sheet1 | negative mode matches | positive mode matches

EPA United States Environmental Protection Agency

Tentative Candidates:

Top 50 most frequently occurring in ESI+

	A	B	C	D	E	F	G	H
1	INPUT	DTXSID	CASRN	PREFERRED NAME	MOL FOR	MONOISO	EXPOCAS	EXPOCAST
2	C5H5N4	DTXSID80	39910-65-	2-azidopyridine	C5H4N4	120.04359	-	-
3	C9H18Cl3(	DTXSID50	13674-84-	Tris(2-chloroisopropyl)phosphate	C9H18Cl3(	326.00082	Y	1.75e-07
4	C22H30N2	DTXSID70	466-49-9	Aspidospermine	C22H30N2	354.23072	-	-
5	C18H24O2	DTXSID00	50-28-2	17beta-Estradiol	C18H24O2	272.17763	Y	3.2e-08
6	C22H30N2	DTXSID70	466-49-9	Aspidospermine	C22H30N2	354.23072	-	-
7	C15H33NC	DTXSID10	70592-80-	C10-16-Alkyldimethylamines oxides	C15H33NC	243.25621	-	-
8	C10H9FO4	DTXSID10	5292-47-7	Dimethyl 2-fluoroterephthalate	C10H9FO4	212.04848	-	-
9	C12H14O4	DTXSID70	84-66-2	Diethyl phthalate	C12H14O4	222.08920	Y	6.94e-05
10	C12H22N2	DTXSID30	952-45-4	Cycloleucylleucine	C12H22N2	226.16812	-	-
11	C15H33NC	DTXSID10	70592-80-	C10-16-Alkyldimethylamines oxides	C15H33NC	243.25621	-	-
12	C16H32N6	DTXSID80	82911-03-	1H-1,3-Diazepin-2-amine, N,N'-(1,2-ethanediylbis	C16H34I2N	596.08326	-	-
13	C22H30N2	DTXSID70	466-49-9	Aspidospermine	C22H30N2	354.23072	-	-
14	C5H4N4	DTXSID50	120-73-0	Purine	C5H4N4	120.04359	-	-
15	C12H10O2	DTXSID60	127-63-9	Diphenylsulfone	C12H10O2	218.04015	Y	2.34e-07
16	C13H25NS	DTXSID50	87630-35-	N-Triisopropylsilylpyrrole	C13H25NS	223.17562	-	-
17	C12H13NC	DTXSID00	5234-68-4	Carboxin	C12H13NC	235.06669	Y	1.52e-08
18	C16H19NC	DTXSID30	86811-09-	Litoxetine	C16H19NC	241.14666	-	-
19	C16H9N3	DTXSID90	97869-49-	Propanedinitrile, 9-acridinyl-	C16H9N3	243.07964	-	-
20	C16H21NC	DTXSID00	2503-80-2	MY 12-62c	C16H21NC	243.16231	-	-
21	C18H24O2	DTXSID00	50-28-2	17beta-Estradiol	C18H24O2	272.17763	Y	3.2e-08
22	C17H25NC	DTXSID60	113-48-4	MGK-264	C17H25NC	275.18852	Y	2.65e-07
23	C18H37NC	DTXSID10	7545-23-5	N,N-Bis(2-hydroxyethyl)tetradecamide	C18H37NC	315.27734	-	-
24	C20H39N5	DTXSID30	2533-20-2	6-Heptadecyl-1,3,5-triazine-2,4-diamine	C20H39N5	349.32054	-	-
25	C17H34N6	DTXSID10	88172-27-	2,2-Diethyl-N~1~,N~3~-bis(4-methylpiperazin-1-y	C17H34N6	354.27432	-	-
26	C21H39NC	DTXSID70	82919-37-	Decanedioic acid, methyl 1,2,2,6,6-pentamethyl-4	C21H39NC	369.28790	-	-
27	C18H39O7	DTXSID50	78-51-3	Tris(2-butoxyethyl) phosphate	C18H39O7	398.24334	Y	9.29e-05
28	C21H41F3(	DTXSID60	100556-70	3-(Hexadecyloxy)-2-(2,2,2-trifluoroethoxy)propar	C21H41F3(	398.30077	-	-
29	C20H40N6	DTXSID40	562834-07	L-Lysinamide, L-leucyl-L-isoleucylglycyl-	C20H40N6	428.31110	-	-
30	C25H49N5	DTXSID60	192563-92	N-[1-(Octadecyloxy)-4-(2H-tetrazol-5-yl)butan-2-	C25H49N5	451.38862	-	-
31	C23H46N6	DTXSID10	189131-49	CHEMBL418591	C23H46N6	486.35296	-	-
32	C6H11F3O	DTXSID90	130156-55	1,1,1-trifluoro-2-[(2-methoxyethoxy)methoxy]etl	C6H11F3O	188.06602	-	-
33	C14H29NC	DTXSID30	136-26-5	N,N-Bis(2-hydroxyethyl)decanamide	C14H29NC	259.21474	-	-
34	C15H30N6	DTXSID10	94031-01-	Tris(((2-aminoethyl)amino)methyl)phenol	C15H30N6	310.24810	-	-
35	C17H18F2	DTXSID70	296276-80	N,N'-Bis[2-(4-fluorophenyl)ethyl]thiourea	C17H18F2	320.11587	-	-
36	C17H33N5	DTXSID10	798541-22	L-Valyl-L-lysyl-L-alanyl-L-alanine	C17H33N5	387.24816	-	-
37	C25H50N6	DTXSID90	74037-60-	Methanol, (4,6-bis(bis(butoxymethyl)amino)-s-tr	C25H50N6	530.37918	-	-
38	C13H25NC	DTXSID50	39711-79-	N-Ethyl-4-menthane-3-carboxamide	C13H25NC	211.19361	Y	1.29e-07
39	C14H27NC	DTXSID60	2397-75-3	2-(Dibutylamino)ethyl methacrylate	C14H27NC	241.20417	-	-
40	C8H16N6C	DTXSID90	27640-22-	Bis(N-carbamyl-N-nitroso)hexamethylenediamin	C8H16N6C	260.12330	-	-

Sheet1 | negative mode matches | positive mode matches

Conclusions

- NTA requires integration of many resources
  - Challenges- data processing, ID confidence
- The US EPA's CompTox Chemistry Dashboard provides data and functionality for environmental chemists using HRMS and NTA
- Using the Dashboard, analysis of wastewaters and water-reuse systems is ongoing

Acknowledgements

NC State Univ
Elizabeth Nichols
Melanie Hedgespeth
Damian Shea

UNC-CH
Wanda Bodnar
Leonard Collins

EPA NCCT
Tony Williams
Chris Grulke
John Wambaugh
Kamel Mansouri*
Jeff Edwards
Ann Richard
Jennifer Smith

EPA NERL
Katherine Phillips
Kristin Isaacs
Kathie Dionisio
Jon Sobus
Mark Strynar
Elin Ulrich
Seth Newton
Jarod Grossman
Sarah Laughlin-Toth*
Aurelie Marcotte*

*ORISE Research Participant

EPA United States Environmental Protection Agency

Questions?

- mceachran.andrew@epa.gov
- http://orcid.org/0000-0003-1423-330X