Moving beyond monitoring legacy per and polyfluoroalkyl substances (PFAS)

Screening strategies for the growing list.

James Pyke, Jerry Zweigenbaum, Tarun Anumol
Agilent Technologies, Inc.

Agilent
Trusted Answers

PFAS related products

Common household products and industrial uses

Non-stick surfaces

Grease-proof food packaging

Surfactants and lubricants

Fire-fighting foams

Stain guards

Water repellents

PFAS related products

Common laboratory materials

Solvent caps, filters and tubing

Caps on samples vials

Pump seals, frits, degasser materials

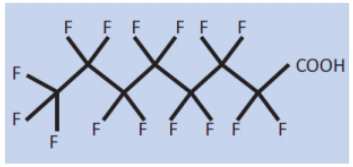
Air conditioning filters

Gloves/Coats

Sample preparation consumables

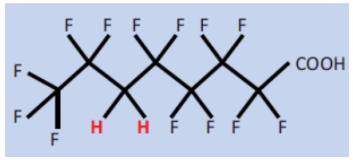
PFAS

Perfluoroalkyl substance



ALL H atoms linked to C in alkyl chain are substituted with F

Polyfluoroalkyl substance



SOME *(but not all)* H atoms linked to C alkyl chain are substituted with F

- Thermal & Chemical stability: grease-proof food packaging, stain repellents
- Zwitterionic properties: surfactants
- Surface-tension lowering: fire-fighting foams

PFAS

Concern Grows Over Tainted Drinking Water

Vermont, New Hampshire and New York expand efforts to find out how much of a potentially toxic chemical is in drinking water

England since August 2014, when a resident of Hoosick Falls, N.Y., near the Vermont border, tested his drinking water and found high levels of the acid. The man was concerned because his father, a former employee of the town's plastics plant that used PFOA, died of cancer.

of PFOA contamination. The state in March sampled PFOA levels up to 620 parts per trillion in private Litchfield wells, well above the 100-parts-per-trillion level at which New Hampshire officials start to consider the amount unsafe. Tests in Merrimack measured as high as 1,600 parts per trillion.

environment

Williamtown water contamination highlights dangers of PFOS and PFOA

Qantas faces $180,000 fine over toxic foam spill at Brisbane Airport

21 April 2017 - 04:56pm - First published 21 April 2017 - 11:02am
By Ruth McCosker

Qantas has been hit with an investigation notice while residents continue to be warned not to eat seafood following a toxic spill into Brisbane's waterways.

On Monday, April 10, 22,000 litres of a firefighting foam containing perfluorinated compounds was spilled from a Qantas hangar at Brisbane Airport.

c&en

Volume 94 Issue 20 | pp. 20-22
Issue Date: May 16, 2016 | Web Date: May 11, 2016

Perfluorinated chemicals taint drinking water

Are there toxins in your fast food packaging?

CBS NEWS

QLD News

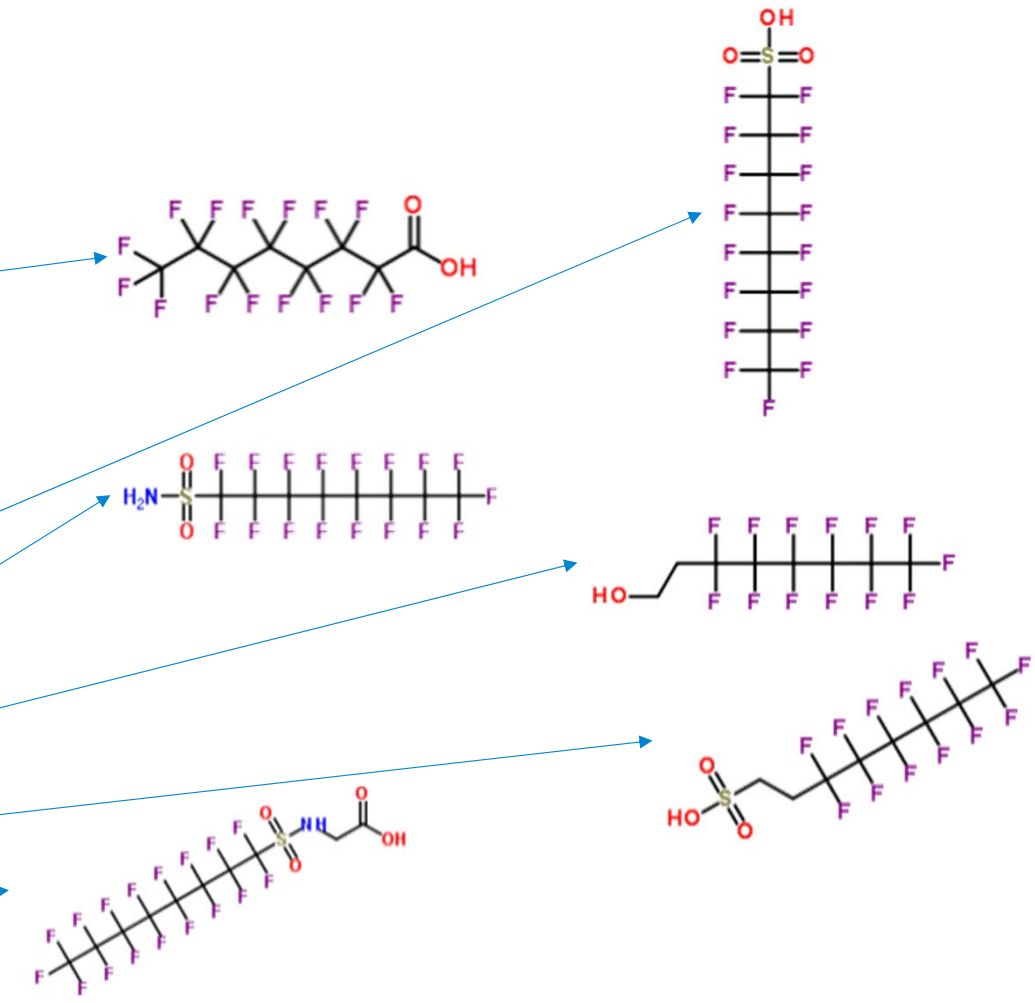
Brisbane River seafood warning still in effect

Chris Honnery, The Courier-Mail
April 20, 2017 8:49pm

Regulated PFAS monitoring

Common target compounds

Compound	Formula	Abbreviation
Perfluoroalkylcarboxylic acids (PFCAs)		
Perfluro-n-butanoic acid	$C_4HF_7O_2$	PFBA
Perfluoro-n-pentanoic acid	$C_5HF_9O_2$	PFPeA
Perfluoro-n-hexanoic acid	$C_6HF_{11}O_2$	PFHxA
Perfluoro-n-heptanoic acid	$C_7HF_{13}O_2$	PFHpA
Perfluoro-n-octanoic acid	$C_8HF_{15}O_2$	PFOA
Perfluoro-n-nonanoic acid	$C_9HF_{17}O_2$	PFNA
Perfluoro-n-decanoic acid	$C_{10}HF_{19}O_2$	PFDA
Perfluoro-n-undecanoic acid	$C_{11}HF_{21}O_2$	PFUdA
Perfluoro-n-dodecanoic acid	$C_{12}HF_{23}O_2$	PFDoA
Perfluoro-n-tridecanoic acid	$C_{13}HF_{25}O_2$	PFTrDA
Perfluoro-n-tetradecanoic acid	$C_{14}HF_{27}O_2$	PFTeDA
Perfluoro-n-pentadecanoic acid	$C_{15}HF_{29}O_2$	PFPeDA
Perfluorinated sulfonates (PFSAs)		
Perfluoro-1-butanesulfonate	$C_4F_9SO_3^-$	PFBS
Perfluoro-1-hexanesulfonate	$C_6F_{13}SO_3^-$	PFHxS
Perfluoro-1-octanesulfonate	$C_8F_{17}SO_3^-$	PFOS
Perfluoro-1-decanesulfonate	$C_{10}F_{21}SO_3^-$	PFDS
Perfluorinated sulfonamides (FOSA)		
Perfluoro-1-octansulfonamide	$C_8H_2F_{17}NO_2S$	FOSA
N-Methylperfluoro-1-octanesulfonamide	$C_9H_4F_{17}NO_2S$	N-MeFOSA
N-Ethylperfluoro-1-octanesulfonamide	$C_{10}H_6F_{17}NO_2S$	N-EtFOSA
Perfluorinated sulfonamidoethanols (FOSE)		
2-(N-methylperfluoro-1-octanesulfonamido)-ethanol	$C_{11}H_8F_{17}NO_3S$	N-MeFOSE
2-(N-ethylperfluoro-1-octanesulfonamido)-ethanol	$C_{12}H_{10}F_{17}NO_3S$	N-EtFOSE
Fluorinated Telomer Sulfonates (FTS)		
1H,1H,2H,2H-Perfluorohexanesulfonic acid	$C_6H_5F_9SO_3$	4:2 FTS
1H,1H,2H,2H-perfluorooctane sulfonate	$C_8H_5F_{13}SO_3$	6:2 FTS
1H,1H,2H,2H-Perfluorodecanesulfonic acid	$C_{10}H_5F_{17}SO_3$	8:2 FTS
Perflourinated sulfonamidoacetic acids (FOSAA)		
Perfluorooctane sulfonamidoacetic acid	$C_{10}H_4F_{17}NO_4S$	FOSAA
N-methylperfluorooctane sulfonamidoacetic acid	$C_{11}H_6F_{17}NO_4S$	N-MeFOSAA
N-ethylperfluorooctane sulfonamidoacetic acid	$C_{12}H_8F_{17}NO_4S$	N-EtFOSAA

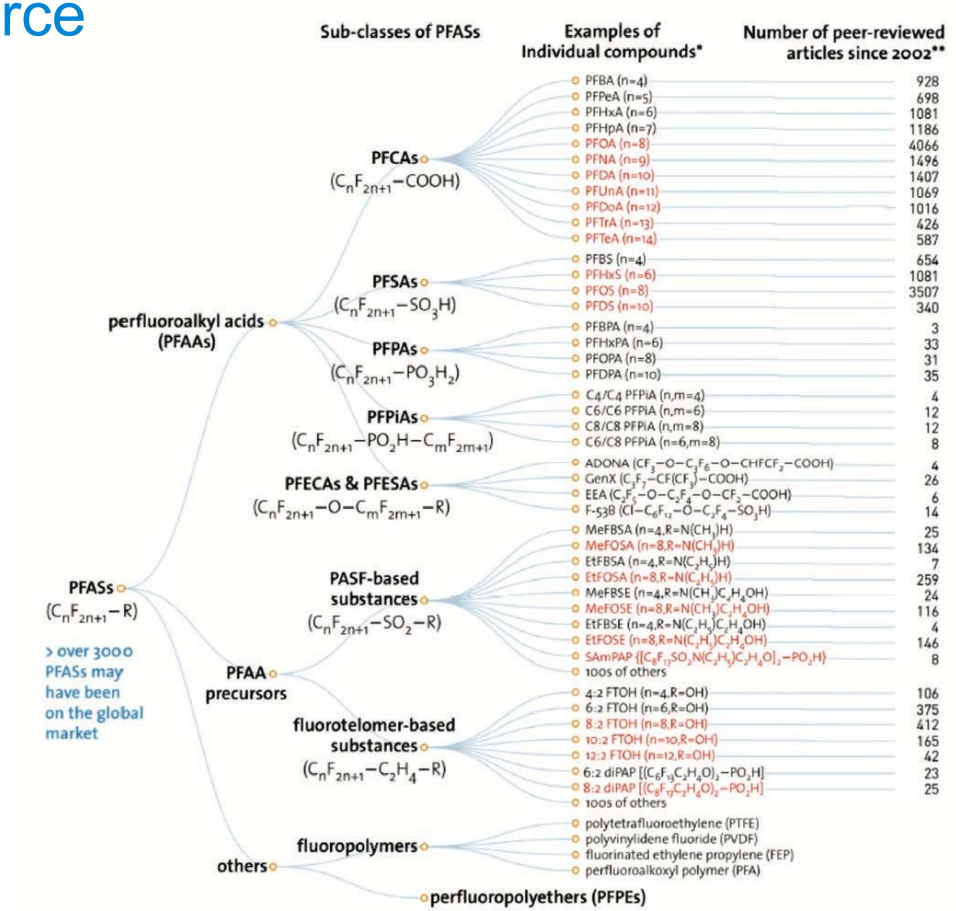


>4000 PFAS compounds in commerce

Common Acronyms

PFCA	Perfluoroalkylcarboxylic acid
PFOA	Perfluorooctanecarboxylic acid
PFAS	Perfluoroalkylsulfonate
PFOS	Perfluorooctanesulfonate
PFASi	Perfluoroalkylsulfinate
FOSA	Perfluorooctanesulfonamide
FOSAA	Perfluorooctanesulfonamidoacetic acid
FOSE	Perfluorooctanesulfonamidoethanol
FTOH	Fluorinated telomer alcohol (-OH functional group)
FTA	Fluorinated telomer acid
FTUA	Fluorinated telomer unsaturated acid
FTS	Fluorinated telomer sulfonate
PFAPA	Perfluoroalkylphosphonic acid
PFPi	Perfluoroalkylphosphinate
PAP	Mono-substituted polyfluoroalkylphosphate ester
diPAP	Di-substituted polyfluoroalkylphosphate ester
PFAI	Perfluoroalkyl iodide
SFA	Semifluorinated alkane
FTI	Fluorinated telomer iodide
FTO	Fluorinated telomer olefin
FTAC	Fluorinated telomer acrylate

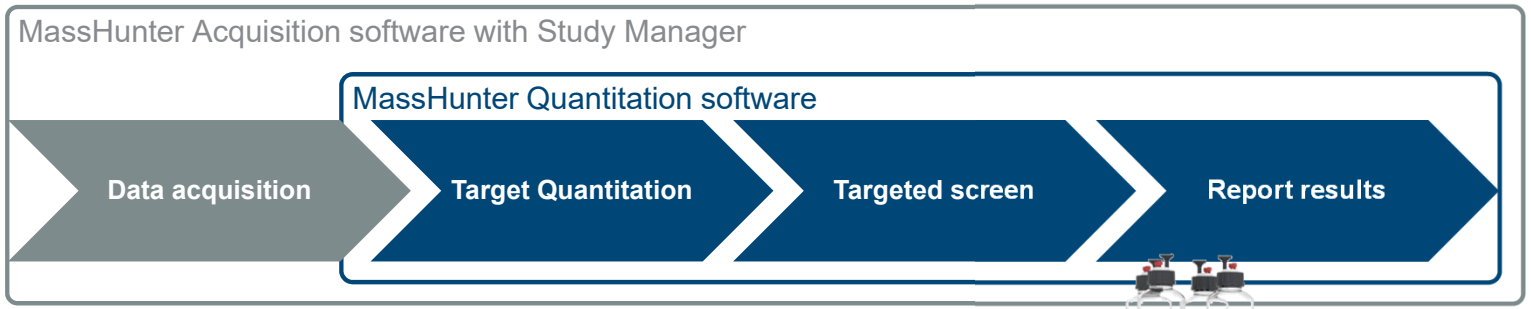
https://www.well-labs.com/docs/pfc_reference_handling_guide.pdf

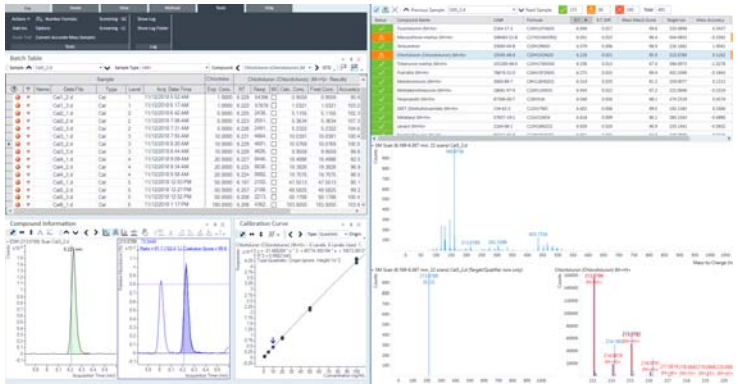


Wang, Z et al. (2017). Environ. Sci. Technol. 51, 2508-2518.

Aim

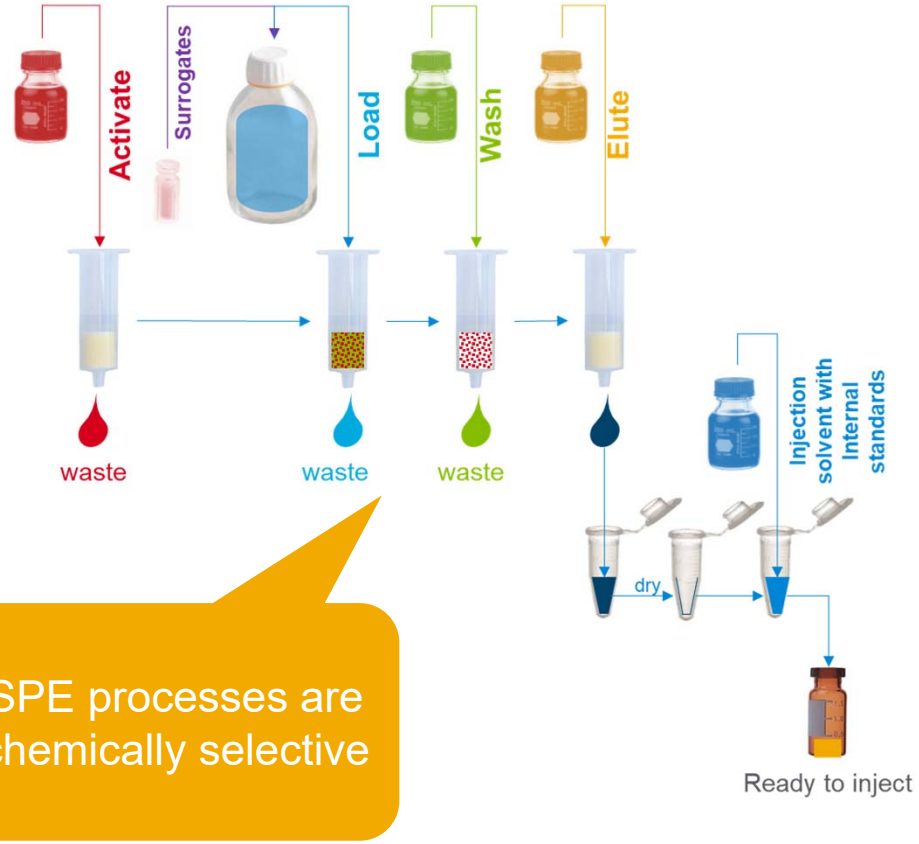
Simplified and simultaneous Target quantitation and Suspect screening





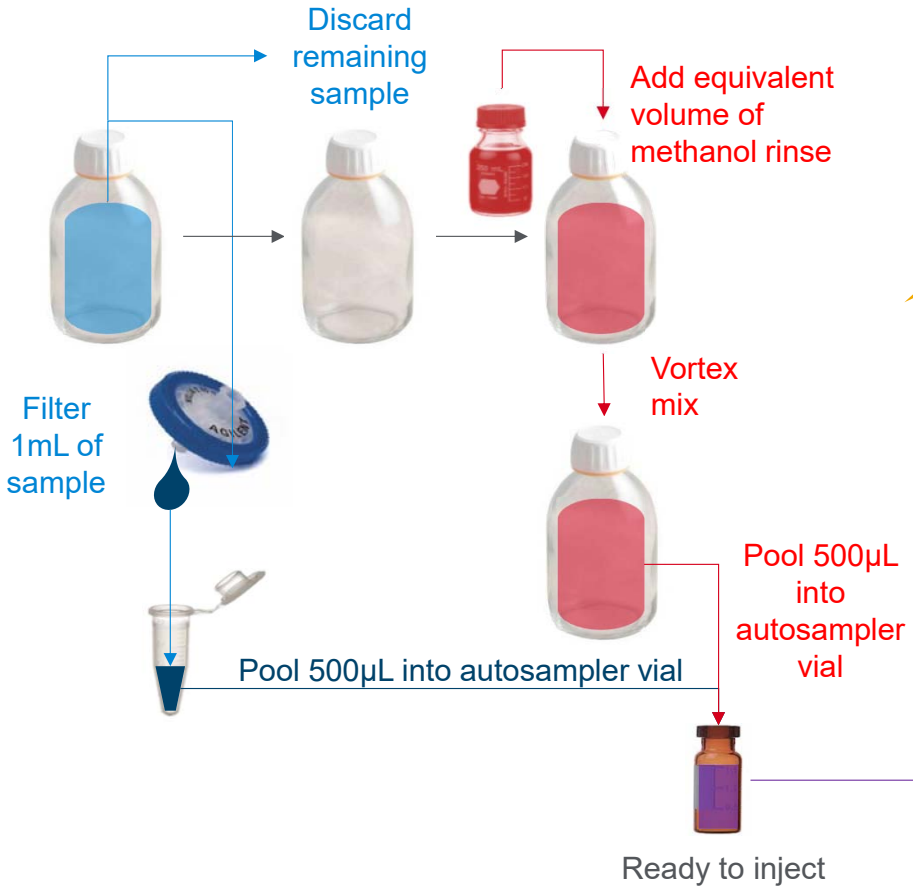
Sampling for screening

Traditional SPE is selective



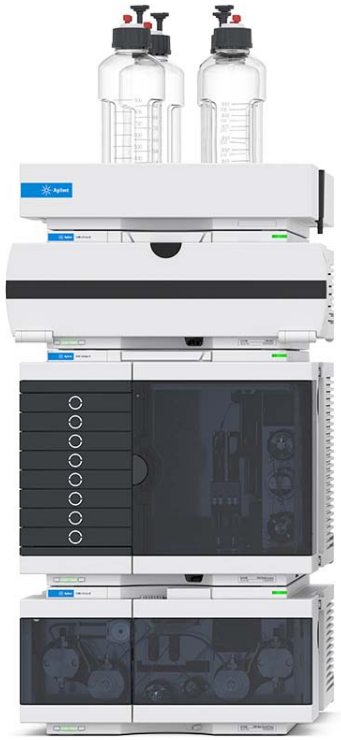
Sampling for screening

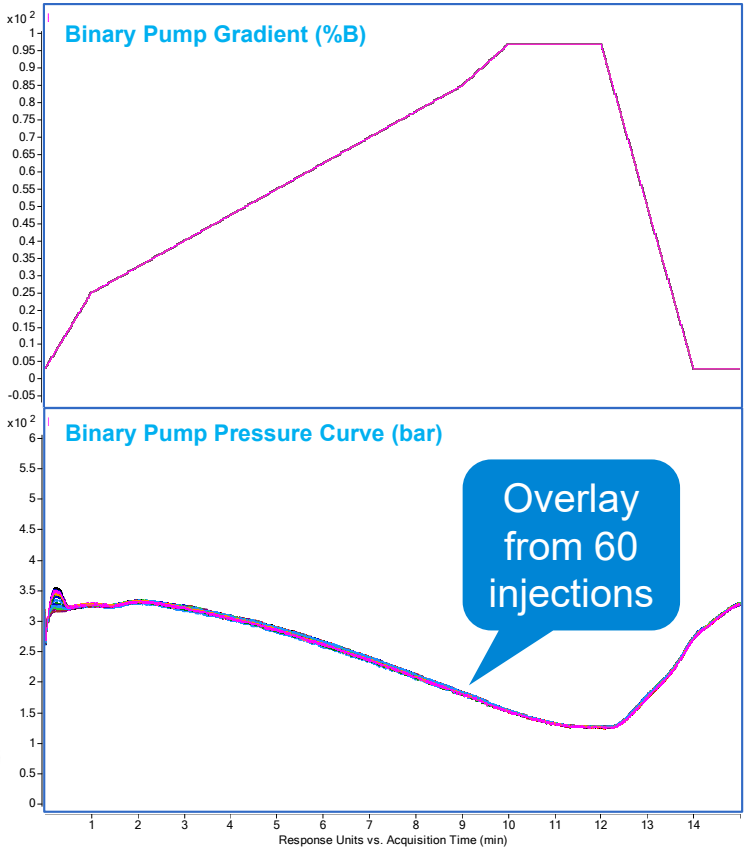
Move to direct injection to broaden the screen



Need to insure the sample vessel is rinsed with organic solvent

Agilent 1290 Infinity II UHPLC conditions

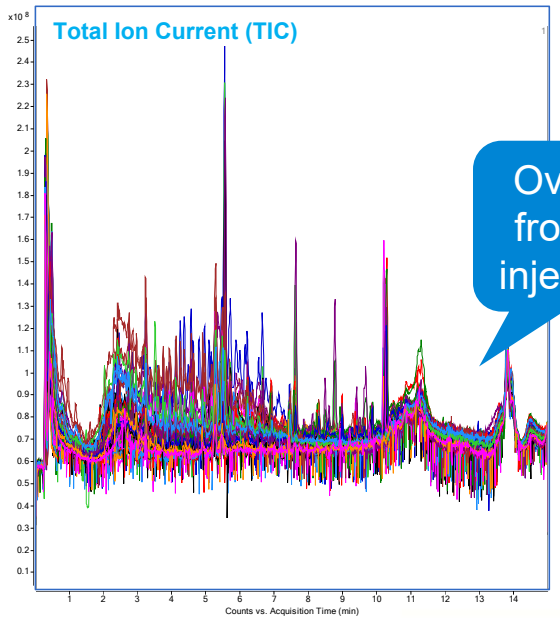




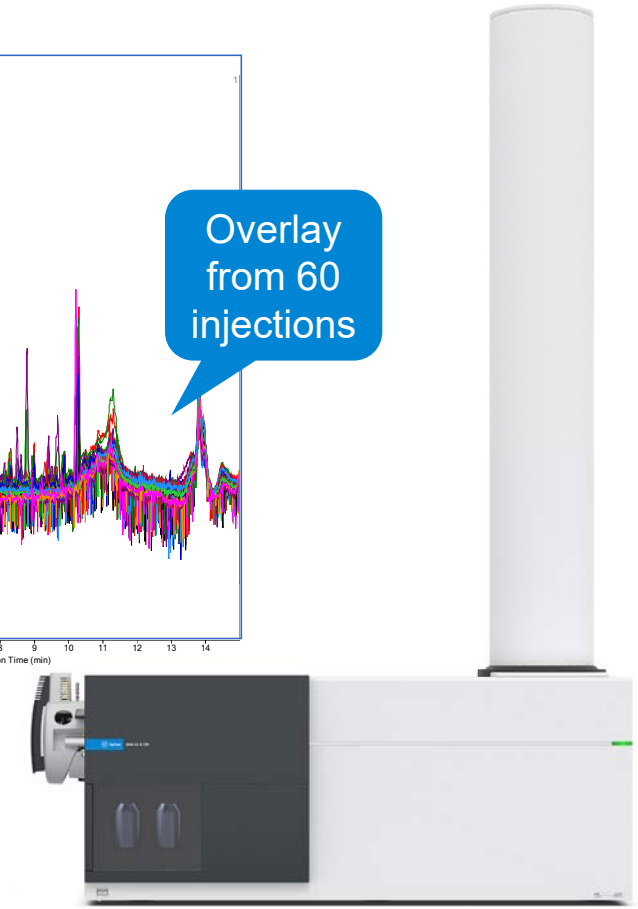
High Speed Pump (G7120A)	Solvent A: 5mM ammonium acetate in water Solvent B: Neat acetonitril
	Flow Rate: 0.4 mL/min Max Pressure Limit: 1300 bar
	Gradient: Time (min) %B 0.00 3.00 1.00 25.00 9.00 85.00 10.00 97.00 12.00 97.00 14.00 3.00 15.00 3.00 Stop time: 15.00 min
Multisampler (G7167B)	Injection Volume: 30 µL Multiwash: Seat back flush and needle wash with 5s each of 100% isopropanol, then 100% acetonitrile, then 100% water
Multicolumn Thermostat (G7116B)	Column Temperature: 30°C Column: Agilent InfinityLab Poroshell HPH-C18 2.1 × 100 mm, 1.9 µm (p/n 695675-702)

Agilent 6546 LC/Q-TOF LC/MS system (G6546A) conditions

Agilent Jet-Stream Ion Source	Drying Gas Temp: 320 °C Drying Gas Flow: 8 L/min Nebulizer: 35 psi Sheath Gas Temp: 350 °C Sheath Gas Flow: 11 L/min Capillary Voltage: 3500 V Nozzle Voltage: 0 V Fragmentor Voltage: 115 V
Tune mode	Ion Polarity: Negative Mass Range: Low (1700m/z) Slicer mode: High resolution
Acquisition mode	50-1100 m/z Rate: 6 spectra/sec Collision Energy: 0, 10, 20 V
	Reference Mass Correction: Enabled using bottle A 119.03632 $(M-H)^-$ adduct of purine 980.016375 $(M+Ac)^-$ adduct of HP-0921

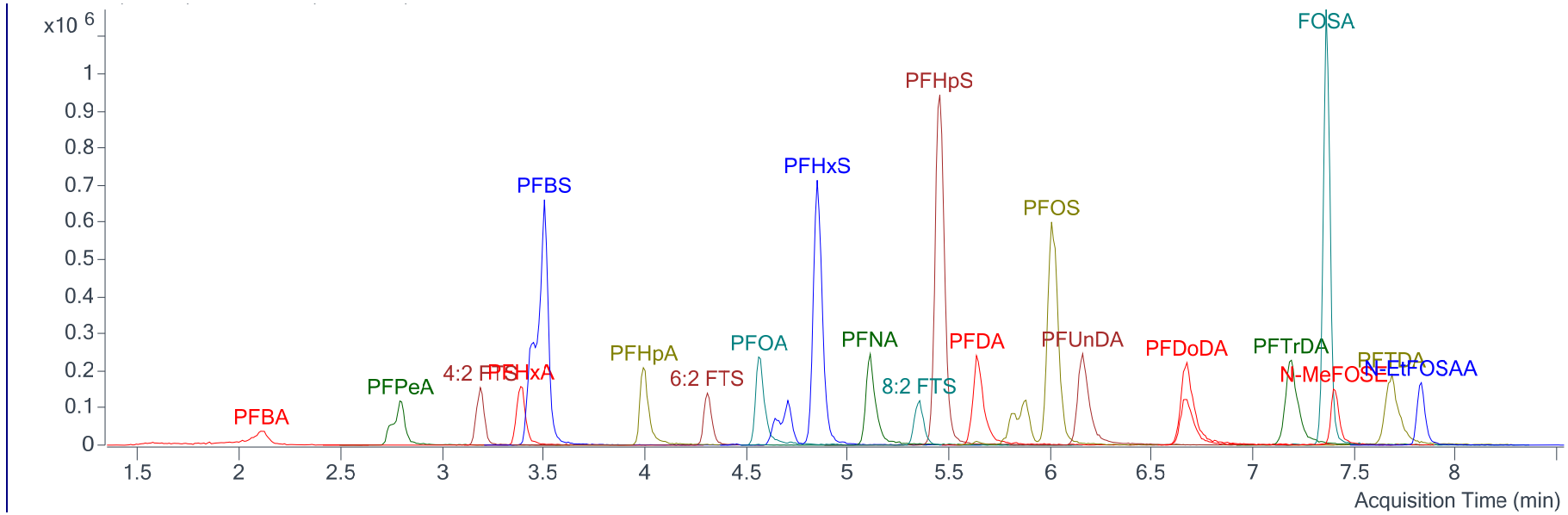


Overlay from 60 injections



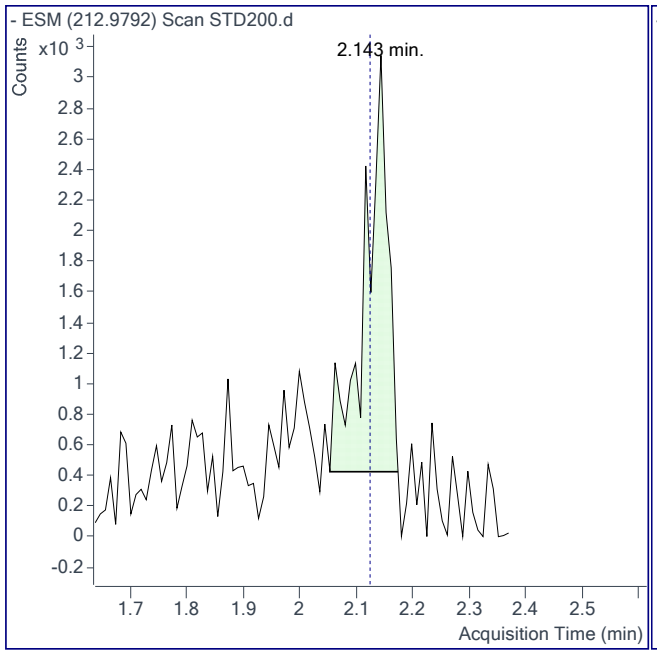
Quantitative analysis results

Separation of the target compounds

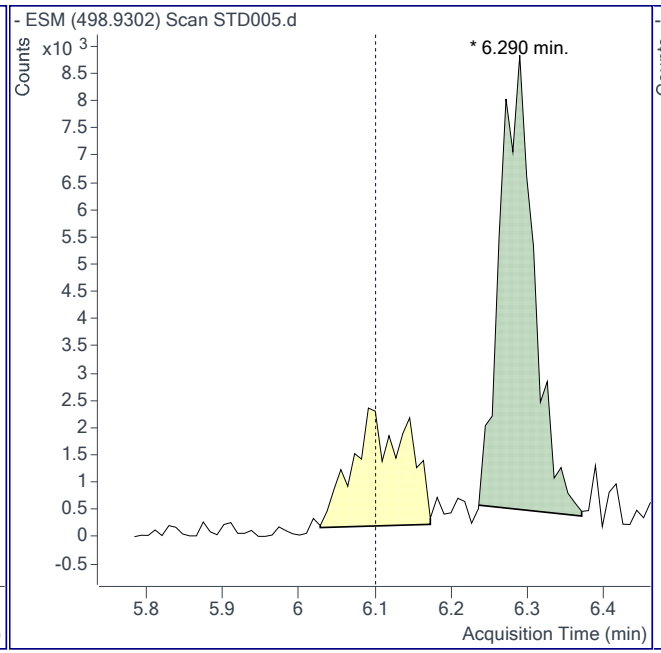


Quantitative analysis results

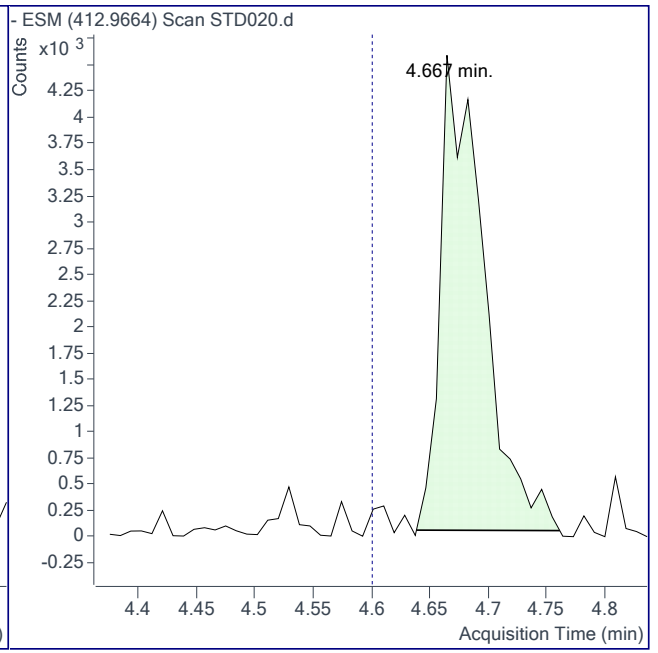
Lower Limit of Detection



PFBA @ 200 ng/L



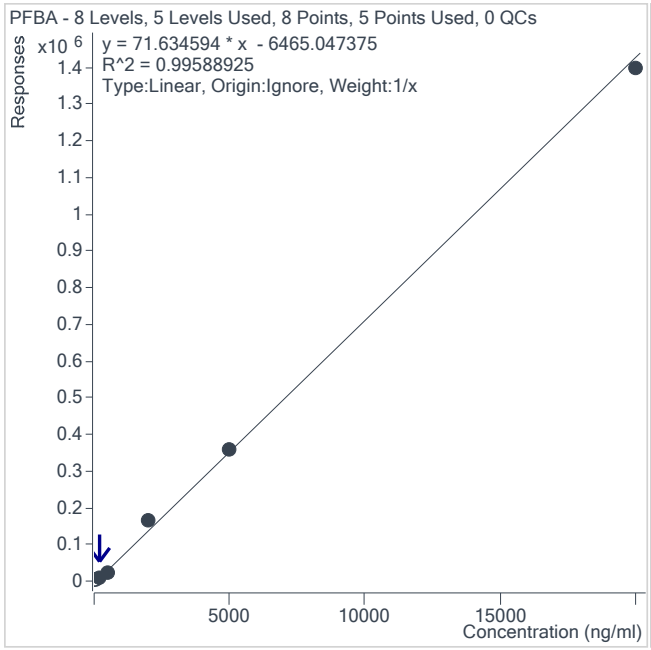
PFOS @ 5 ng/L

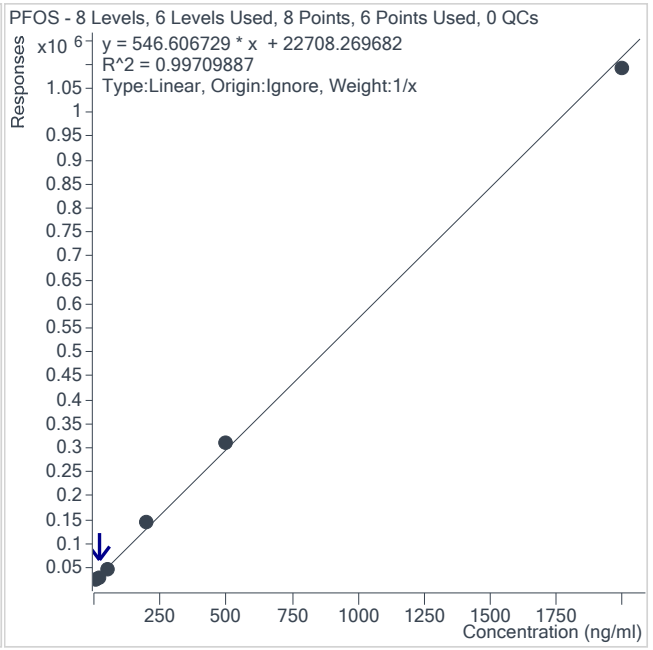


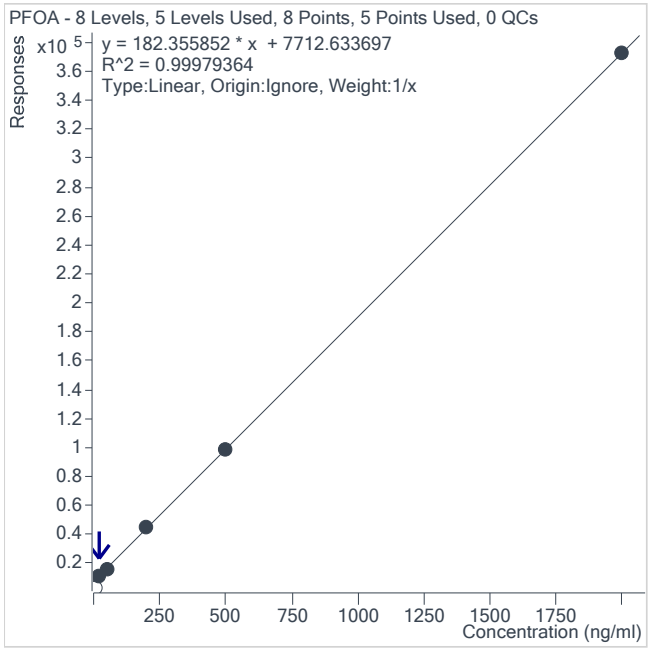
PFOA @ 20 ng/L

Quantitative analysis results

Dynamic range







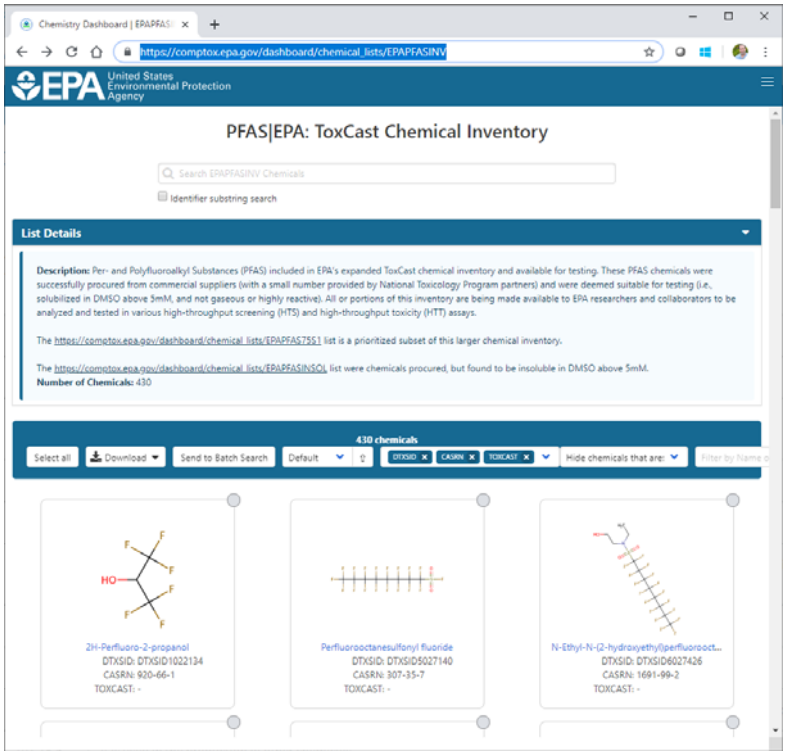
PFBA 200 – 20000 ng/L

PFOS 5 – 2000 ng/L

PFOA 20 – 2000 ng/L

Monitoring suspect PFAS

PFAS/EPA: ToxCast Chemical Inventory



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

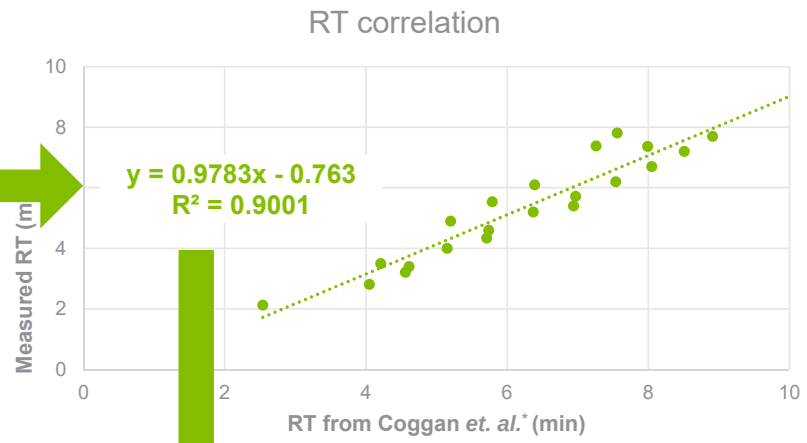
How to rapidly screen for PFAS with more confidence, without standards?

- Focus search criteria:
  - on mass accuracy
  - on expected retention time
- Use all data possible to make a putative identification

Monitoring suspect PFAS

Adding focus through Retention Time (RT) ***Projection***

Compound Name	RT (min)
Perfluorobutanoic acid	2.13
Perfluoropentanoic acid	2.81
4:2 Fluorotelomer sulfonic acid	3.21
Perfluorohexanoic acid	3.40
Perfluorobutanesulfonic acid	3.50
Perfluoroheptanoic acid	4.00
6:2 Fluorotelomer sulfonic acid	4.34
Perfluorooctanoic acid	4.60
Perfluorohexanesulfonic acid	4.90
Perfluorononanoic acid	5.20
Perfluoroheptanesulfonic acid	5.54
8:2 Fluorotelomer sulfonic acid	5.40
Perfluorodecanoic acid	5.72
Perfluorooctanesulfonic acid	6.10
Perfluoroundecanoic acid	6.20
Perfluorododecanoic acid	6.70
Perfluorotridecanoic acid	7.20
Perfluorotetradecanoic acid	7.70
Perfluorooctanesulfonamide	7.37
2-(N-Methylperfluorooctanesulfonamido)acetic acid	7.38
2-(N-Ethylperfluorooctanesulfonamido)acetic acid	7.81
4,8-Dioxa-3H-perfluorononanoic acid	4.56
(2E)-3,4,4,5,5,6,6,7,7,8,8,8-Dodecafluoro-2-octenoic acid	4.44
2-Perfluorooctyl ethanoic acid	5.66
2-Perfluorodecyl ethanoic acid	6.83
2H-Perfluoro-2-octenoic acid	4.40
2H-Perfluoro-2-decenoic acid	5.64
2H-Perfluoro-2-dodecenoic acid	6.79
Ethyl heptafluorobutyrate	3.20
2H,2H,3H,3H-Perfluorooctanoic acid	4.41
3-Perfluoroheptylpropanoic acid	5.68
Perfluoropentanesulfonic acid	3.83
Perfluorononanesulfonic acid	6.07
Perfluorodecanesulfonic acid	6.60
Perfluorododecanesulfonic acid	7.52
Perfluoro(2-((6-chlorohexyl)oxy)ethanesulfonic acid)	5.84
2-[(8-Chloro-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-hexadecafluorooctyl)oxy]-1,1,2,2-tetrafluoroethanesulfonic acid	6.92
10:2 Fluorotelomer sulfonic acid	7.11
N-Methylperfluorooctanesulfonamide	8.15
8:2 Fluorotelomer sulfonamide	8.52
N-[(1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-Heptadecafluorooctyl)sulfonyl]glycine	6.14
N-Methyl-N-(2-hydroxyethyl)perfluorooctanesulfonamide	8.17
N-Ethyl-N-(2-hydroxyethyl)perfluorooctanesulfonamide	8.51
Phosphonic acid, (tridecafluorohexyl)-	3.22
PFOPA	4.35
Perfluorodecylphosphonic acid	5.57
6:2 Fluorotelomer phosphate diester	7.92
6:2/8:2 Fluorotelomer phosphate diester	8.48
8:2 Fluorotelomer phosphate diester	8.90
Bis(tridecafluorohexyl)phosphinic acid	7.39
(Heptadecafluorooctyl)(tridecafluorohexyl)phosphinic acid	8.07
Bis(heptadecafluorooctyl)phosphinic acid	8.60
Ammonium bis(N-ethyl-2-perfluorooctylsulfonaminoethyl)phosphate	9.35



21 measured RT's

32 projected RT's

Analytical and Bioanalytical Chemistry (2019) 411:3507–3520
https://doi.org/10.1007/s00216-019-01829-8

RESEARCH PAPER

Check for updates

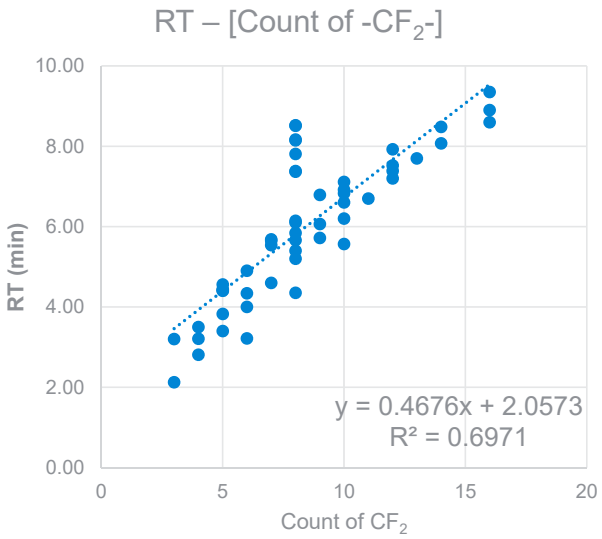
A single analytical method for the determination of 53 legacy and emerging per- and polyfluoroalkyl substances (PFAS) in aqueous matrices

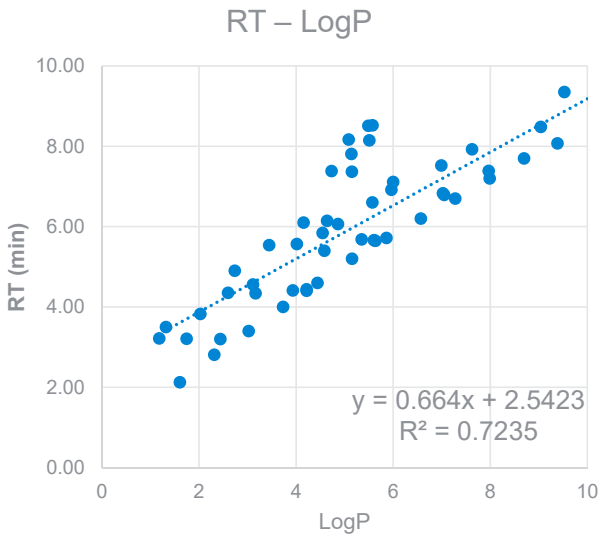
Timothy L. Coggan[1] · Tarun Anumol[2] · James Pyke[2] · Jeff Shimeta[1] · Bradley O. Clarke[1]

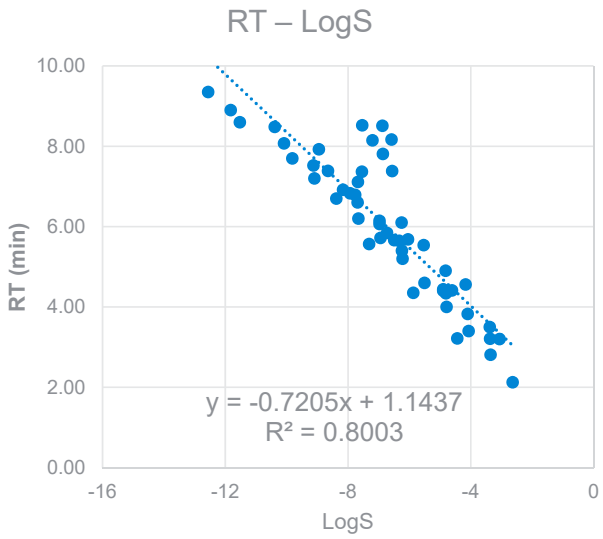
Received: 30 November 2018 / Revised: 27 February 2019 / Accepted: 3 April 2019 / Published online: 9 May 2019

Monitoring suspect PFAS

Adding focus through Retention Time (RT) ***Prediction***

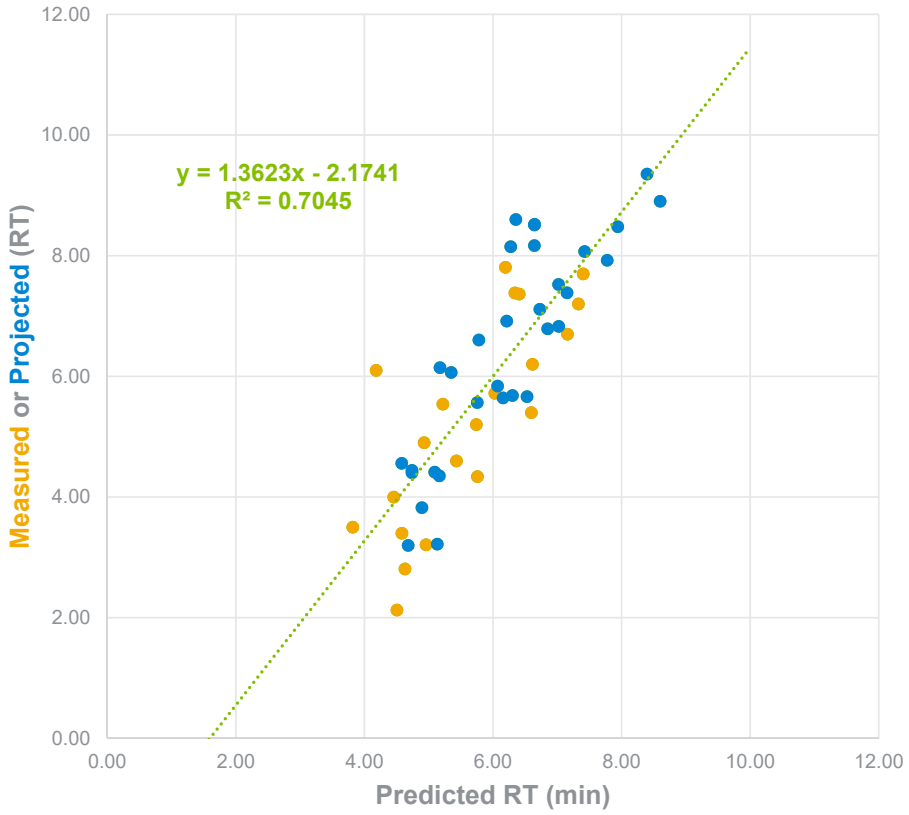






Monitoring suspect PFAS

Adding focus through Retention Time (RT) ***Prediction***



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

Journal of Cheminformatics

RESEARCH ARTICLE Open Access

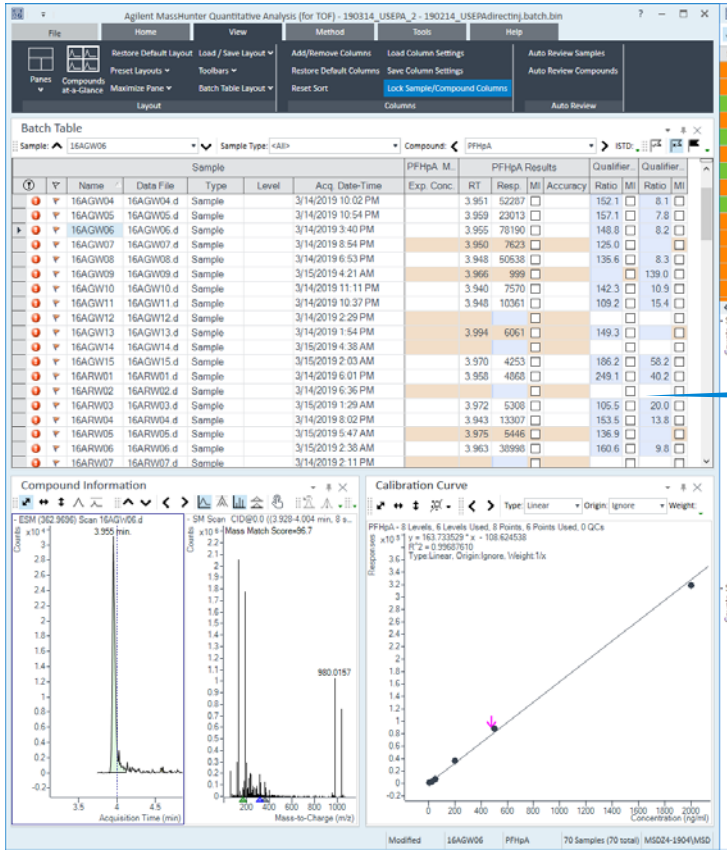
OPERA models for predicting physicochemical properties and environmental fate endpoints

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

29 physiochemical properties in addition to the count of -CF_2- used to create prediction model

Monitoring suspect PFAS

Simultaneous Quantitation and Screening



Filter compounds that are Verified, Needs Review, Not Detected

Filter Targets and Suspects

Set outliers flags according to SANTE guidelines

MassHunter Quantitative 'Batch-at-a-glance' view

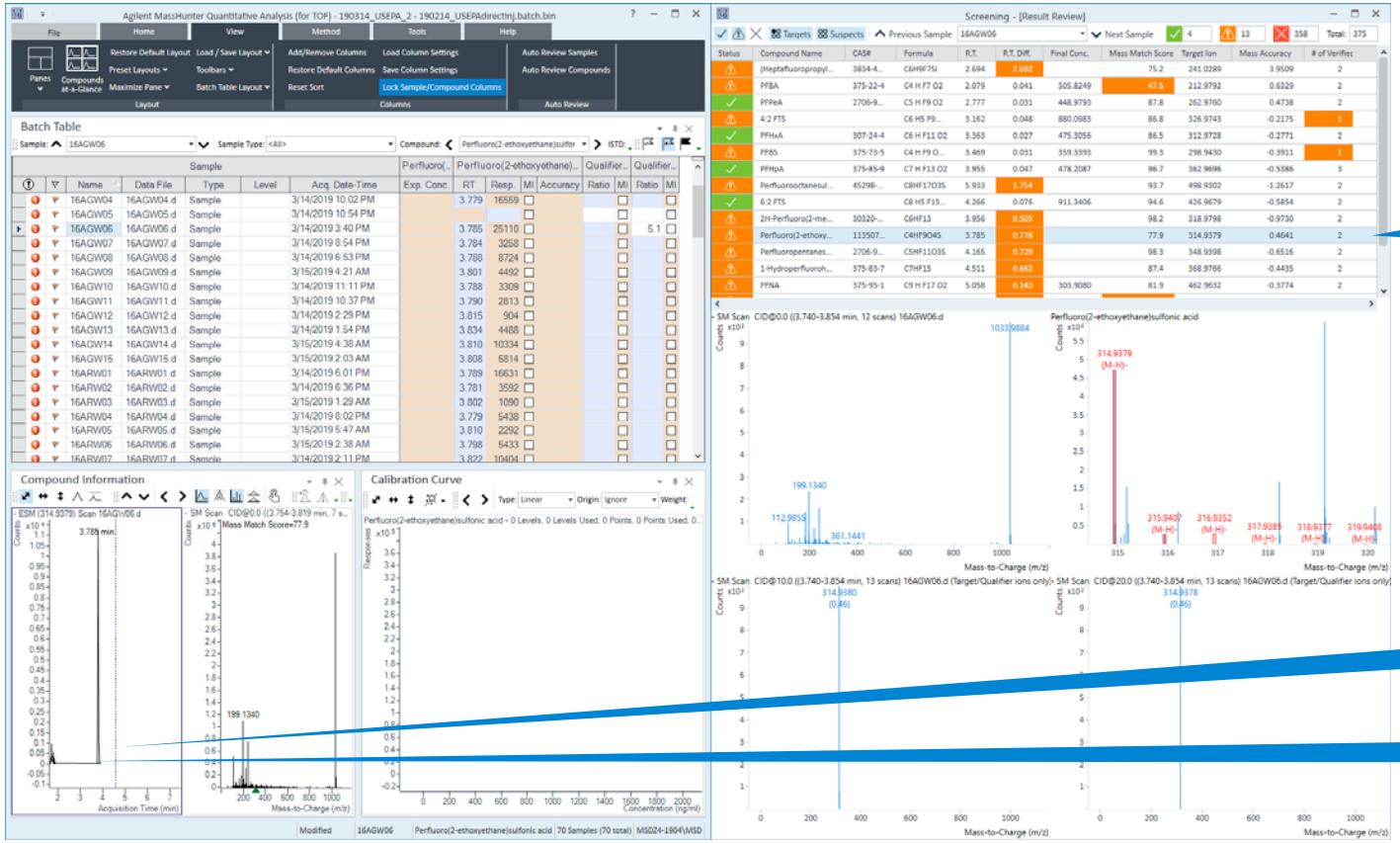
New Screener Tool

Review Isotope pattern match

Review Fragments

Monitoring suspect PFAS

Simultaneous Quantitation and Screening



PFAS Suspect

Predicted RT

Measured RT

Monitoring suspect PFAS

Screening summary PDF report

Screening Summary Report

Agilent | Trusted Answers

Sample name: 16AGW06 **Good** 4 **Warning** 17 **Error** 354

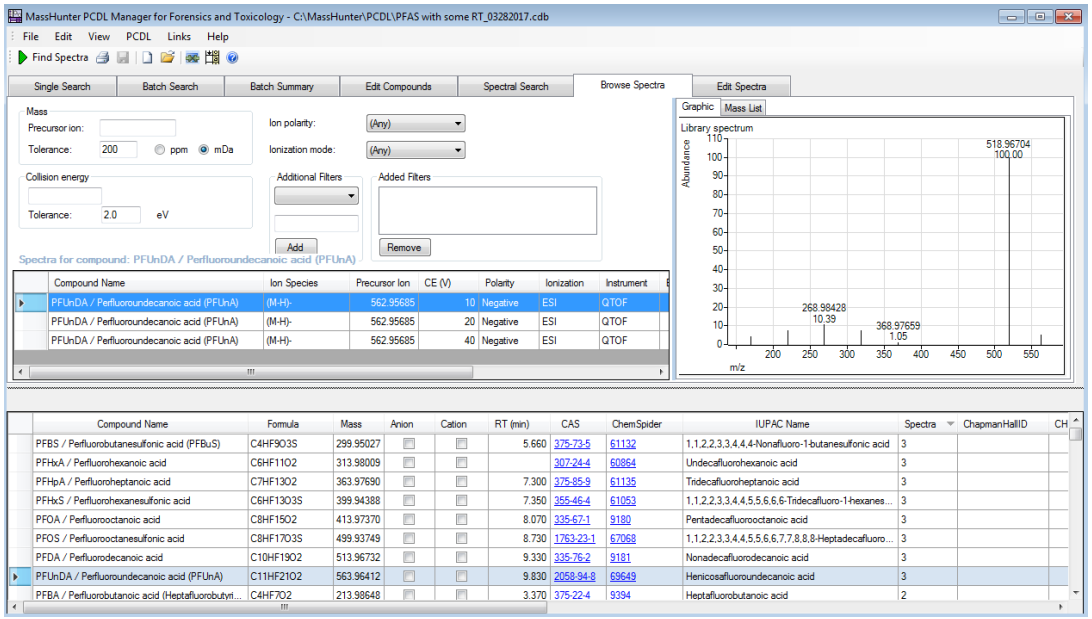
Status	Screening Summary Report	Formula	R.T.	R.T. Diff.	Match Score	Target Ion	Mass Accuracy	# of Qualified Ions	Final Conc.
!	(Heptafluoropropyl)trimethylsilane	C6H9F7Si	2.694	2.692		241.0289	3.95 PPM	2	
+	PFBA	C4 H F7 O2	2.079	0.041		212.9792	0.63 PPM	2	472.7851
+	PFPeA	C5 H F9 O2	2.777	0.031		262.9760	0.47 PPM	2	448.9793
!	4:2 FTS	C6 H5 F9 O3 S	3.162	0.048		326.9743	-0.22 PPM	1	880.0983
+	PFHxA	C6 H F11 O2	3.363	0.036		312.9728	-0.28 PPM	2	475.3056
!	PFBS	C4 H F9 O3 S	3.469	0.031		298.9430	-0.39 PPM	1	359.3393
!	3H-Perfluorobutanoic acid	C4H2F6O2	3.530	0.499		194.9886	-1.07 PPM	1	
!	Perfluorooctanesulfonate	C8HF17O3S	5.933	1.754		498.9302	-1.26 PPM	2	
+	6:2 FTS	C8 H5 F13 O3 S	4.266	0.076		426.9679	-0.59 PPM	2	911.3406
!	2H-Perfluoro(2-methylpentane)	C6HF13	3.956	0.505		318.9798	-0.97 PPM	2	
!	Perfluoro(2-ethoxyethane)sulfonic acid	C4HF9O4S	3.785	0.778		314.9379	0.46 PPM	2	
!	Perfluoropentanesulfonic acid	C5HF11O3S	4.165	0.729		348.9398	-0.65 PPM	2	
!	1-Hydroperfluoroheptane	C7HF15	4.511	0.662		368.9766	-0.44 PPM	2	
!	PFNA	C9 H F17 O2	5.058	0.143		462.9632	-0.38 PPM	2	303.9080
!	2,3,3,3-Tetrafluoro-2-(perfluoropentoxy)propan-1-ol	C8H3F15O2	4.526	0.718		414.9821	0.81 PPM	2	
!	1H-Perfluorohexane	C6HF13	3.956	1.326		318.9798	-0.97 PPM	2	
!	((Perfluorooctyl)ethyl)phosphonic acid	C10H6F17O3P	5.300	0.485		526.9710	4.37 PPM	1	
!	4-[3-(Perfluorobutyl)-1-propyloxy]benzyl alcohol	C14H13F9O2	6.167	0.221		383.0699	2.89 PPM	1	
!	(Perfluorooctyl)propanoyl chloride	C11H4ClF17O	5.927	0.137		508.9606	-2.22 PPM	1	
!	PFOS	C8 H F17 O3 S	5.933	0.167		498.9302	-1.23 PPM	2	63.0760
!	FOSA			0.015			PPM	1	0.4484

Flagging RT outlier

Flagging number of verified ions

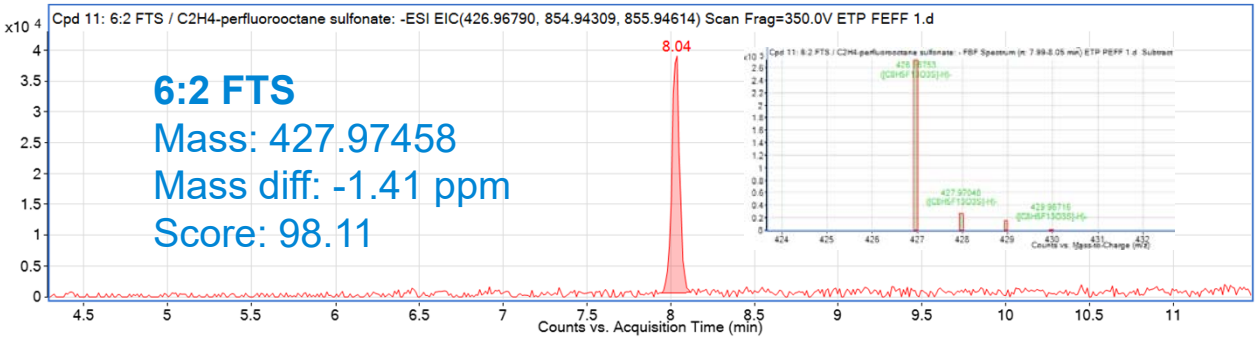
Targeted Suspect Screening

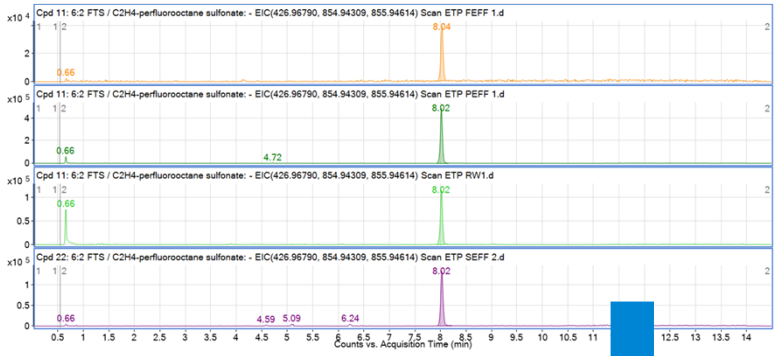
Custom PFAS database with >150 compounds
MS/MS spectra and retention time data available for a subset of compounds



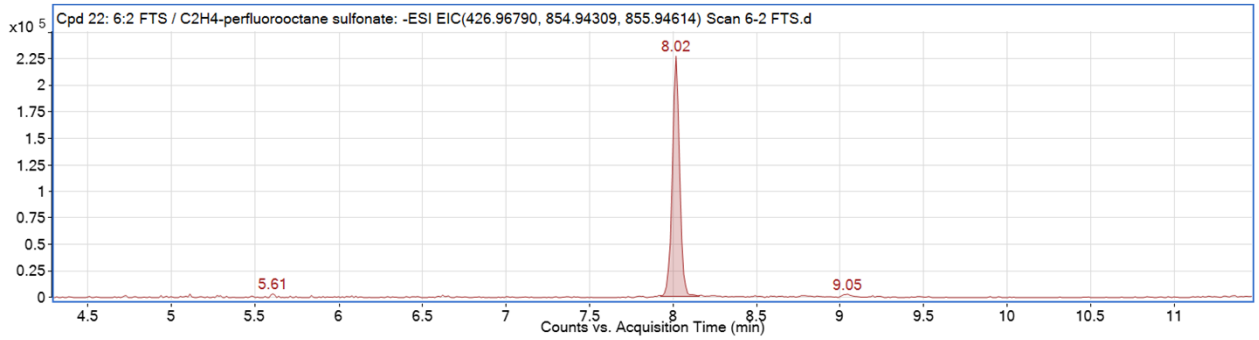
Targeted Suspect Screening Results

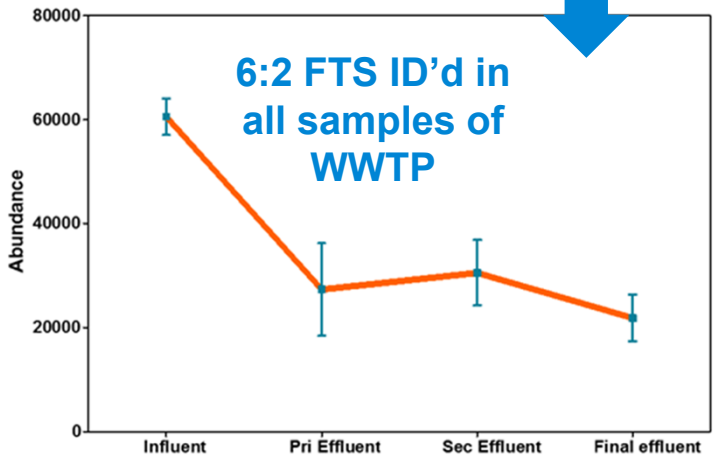
WWTP1 Final Effluent





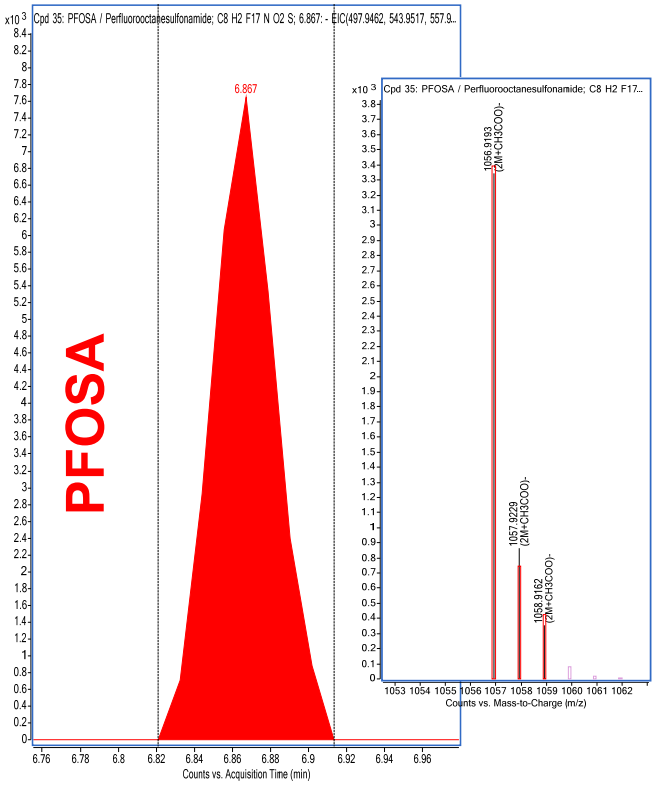
Standard

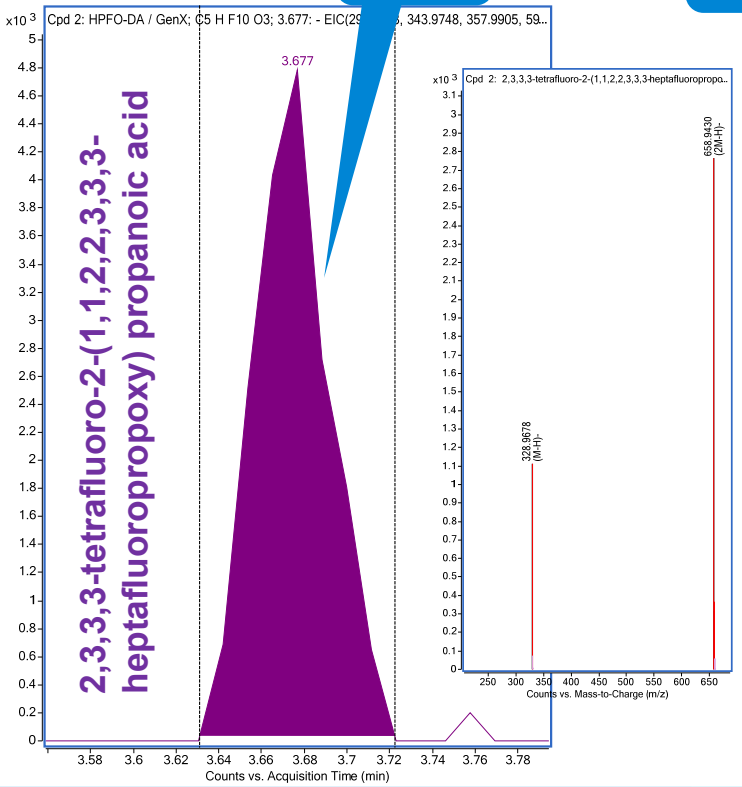


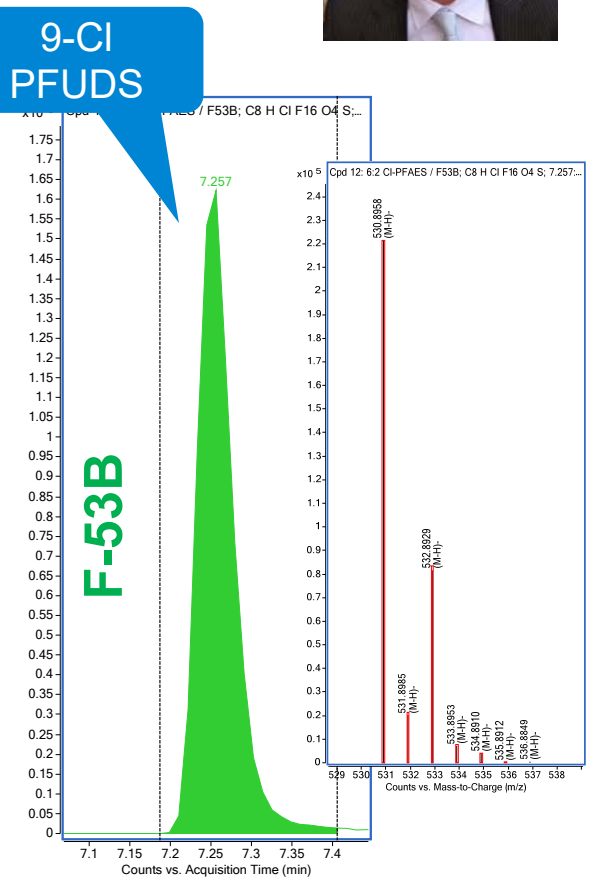


Targeted Suspect Screening Results

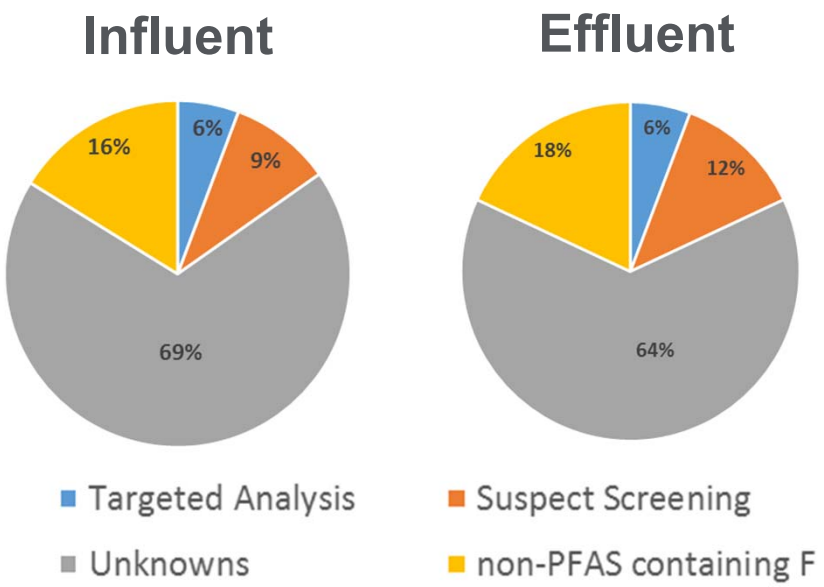
Additional PFAS identified with LC-Q/TOF







Targeted Suspect Screening Results



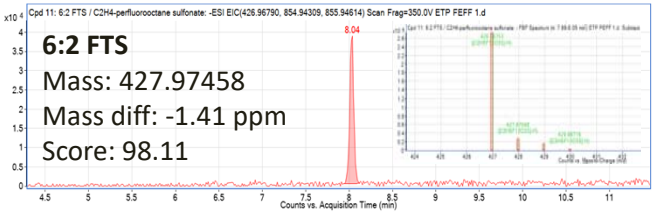
- **Targeted:** Only captured ~6% of compounds
- **Suspects:** 10-16% of fluorinated compounds
- **Unknowns:** 66-81% of fluorinated compounds
- Large portion of fluorinated anionic compounds in sample unknowns

60-70% of fluorine containing molecules in these samples is ‘unknown’

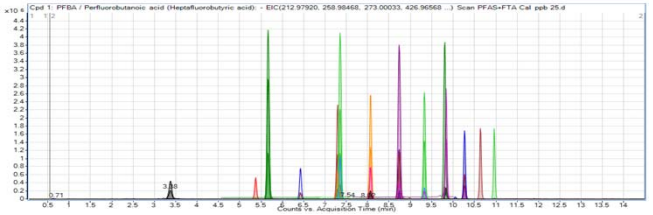
Complete Workflow

Known knowns
Expanded targeted list (~50 compounds)

Known unknowns
Expanded PFAS database



Continually refining targeted method



Unknown unknowns
Adding identified compounds to database list

Measuring PFAS by LC-IM-Q/TOF

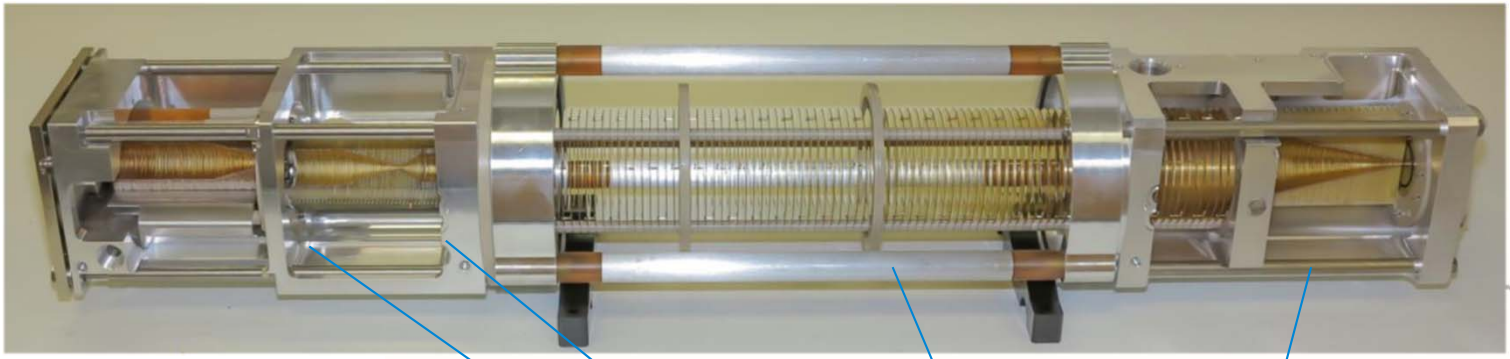
The ultimate tool for PFAS identification

“Rapid Assessment of Isomeric Diversity in PFAS by Ion Mobility Spectrometry-Mass Spectrometry (IMS-MS)”

James Dodds & Erin Baker , NC State

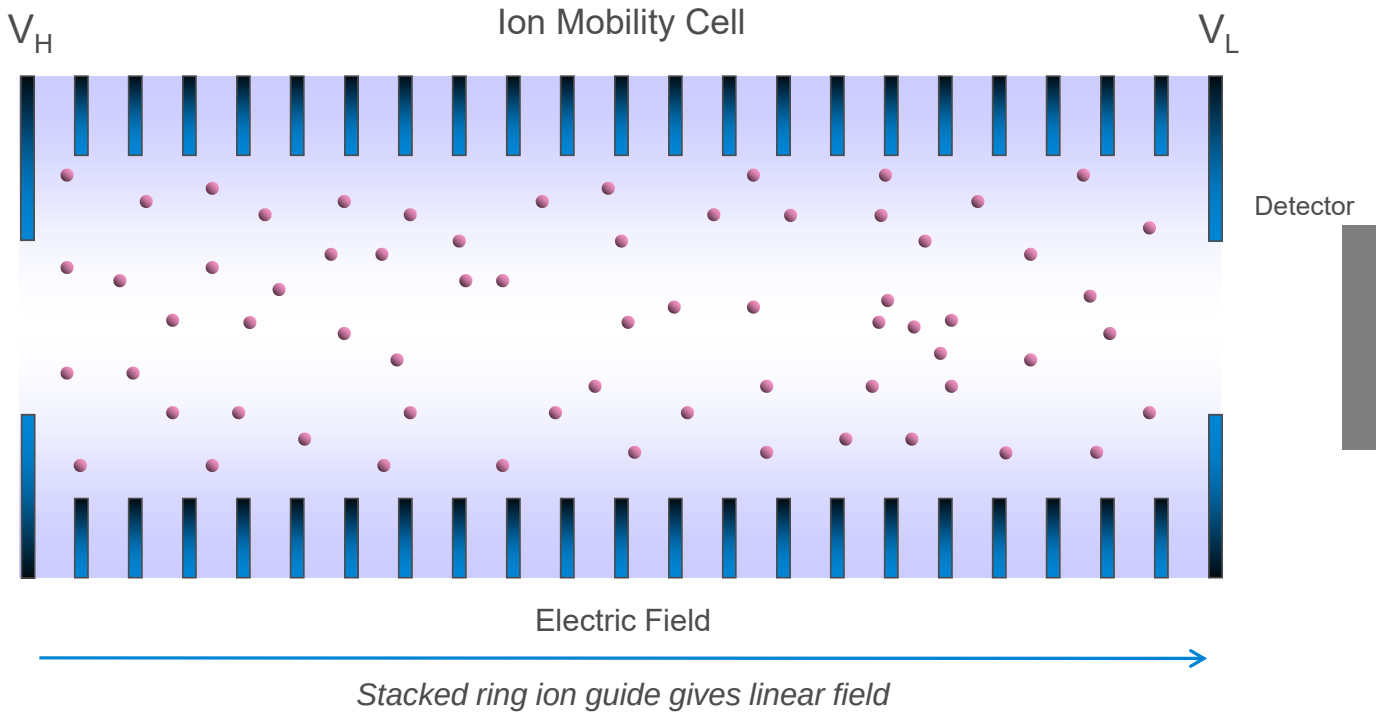
Agilent 6560 IM-Q/TOF

Ion path design



Agilent 6560 IM-Q/TOF

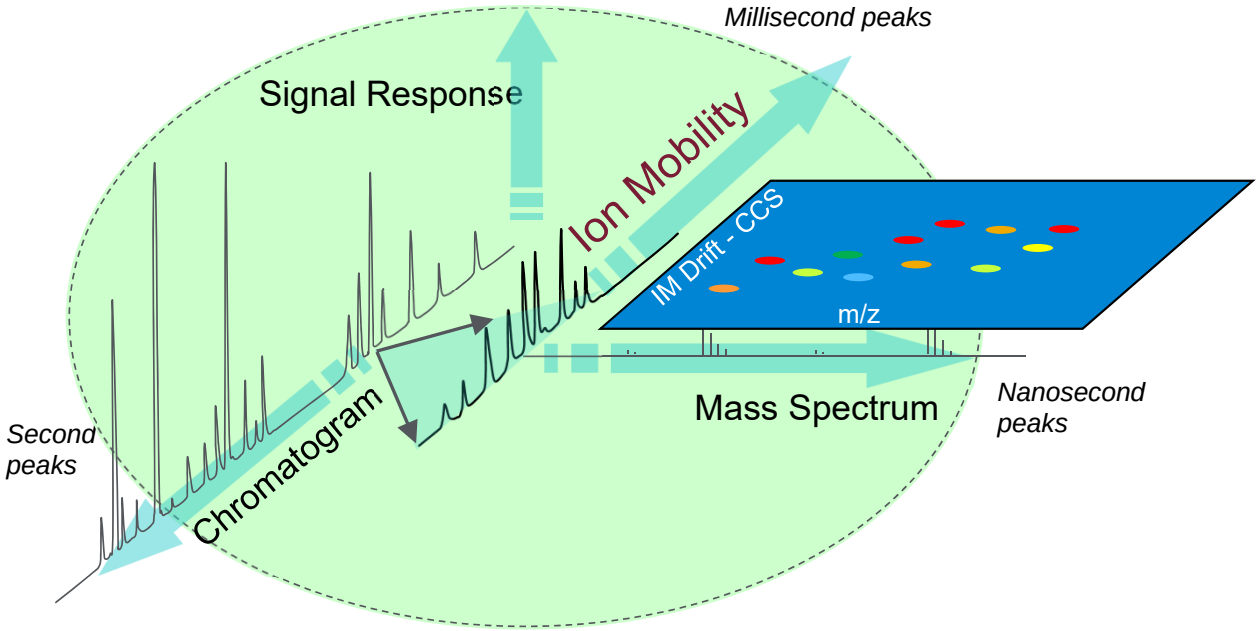
Basic operational principle of Ion Mobility for conventional DC uniform field IMS



$$v = K\,E \;\propto \frac{e\,E}{P\,\sqrt{T}\,\Omega}$$

Measuring PFAS by LC-IM-Q/TOF

An additional dimension of separation

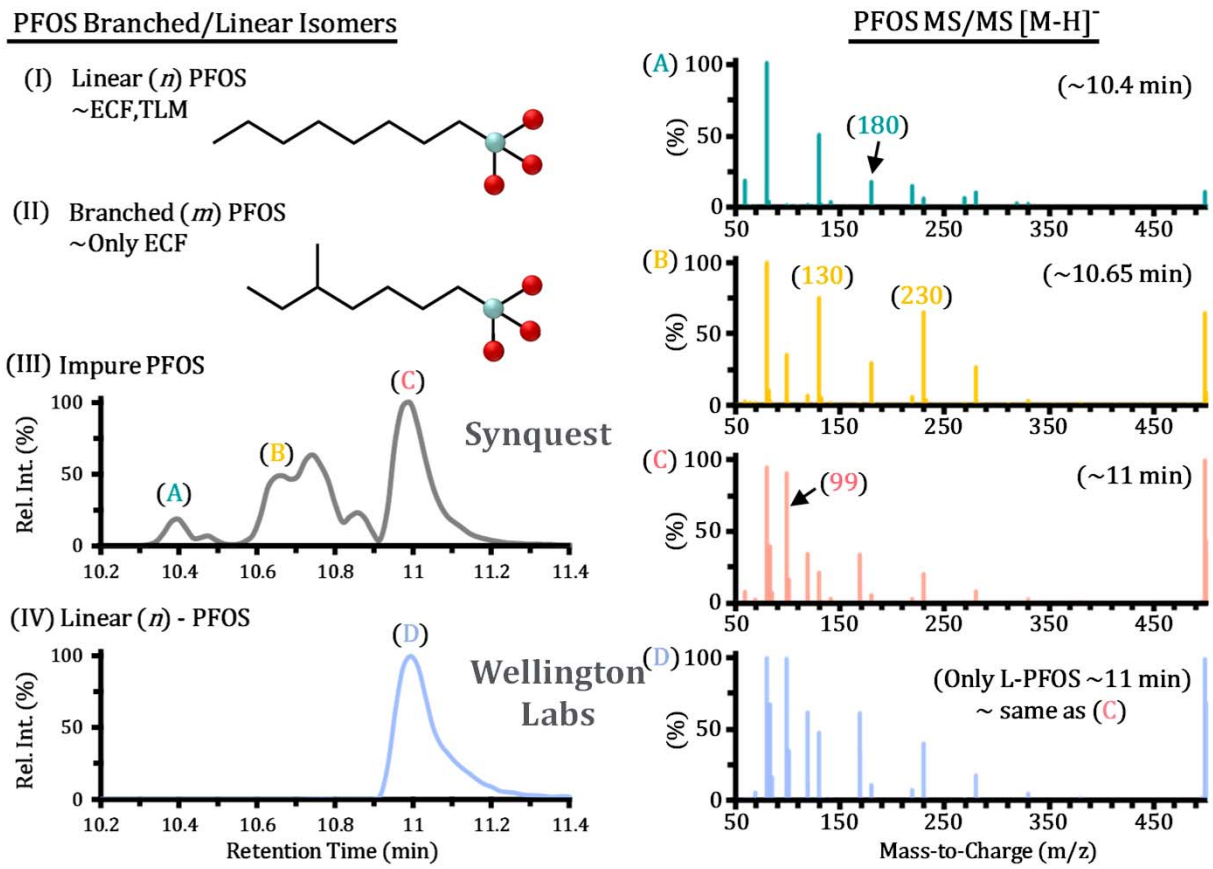


Combining the Power of Accurate Mass and Structural Characterization

With Current UHPLC (and GC) Separations

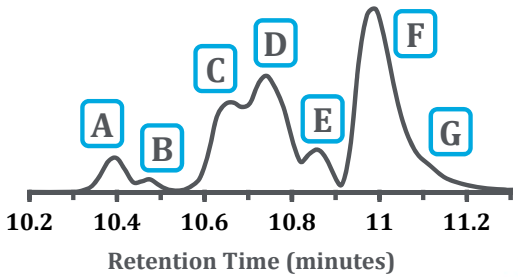
Measuring PFAS by LC-IM-Q/TOF

Mass Spectrometry data



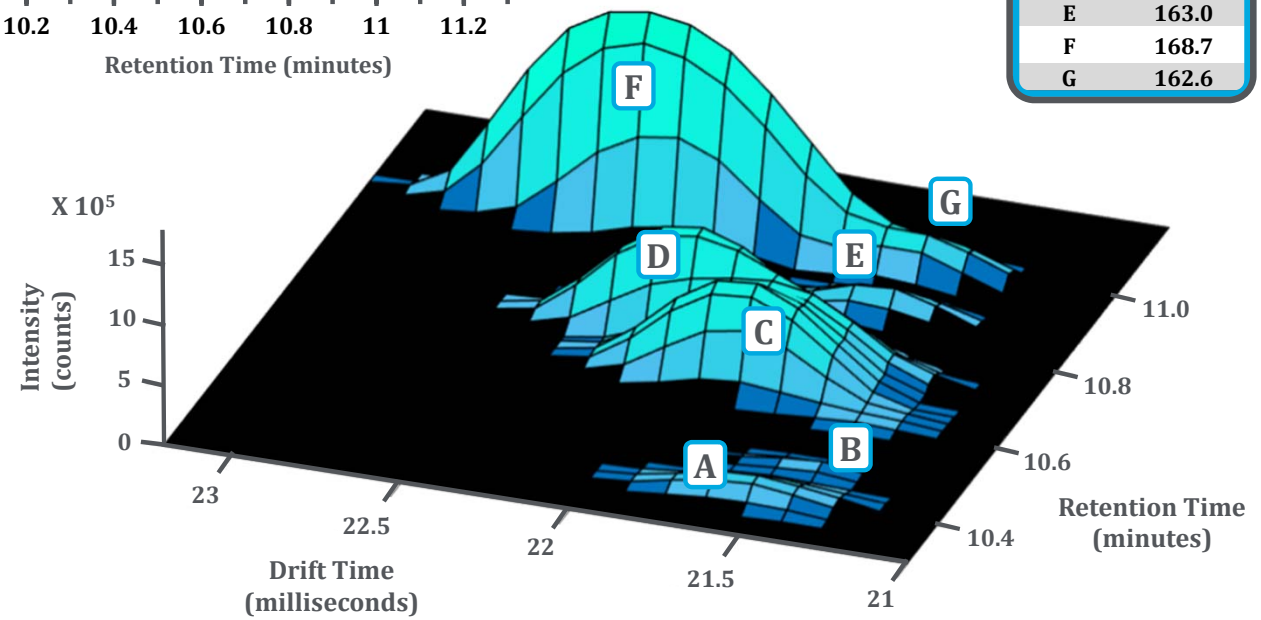
Measuring PFAS by LC-IM-Q/TOF

PFOS Conformations resolved by IM



LC-IMS-MS for PFOS
Extracted m/z (498.93)

Peak	CCS (Å²)
A	162.7
B	162.0
C	164.6
D	165.8
E	163.0
F	168.7
G	162.6



Summary

- TQ→QTOF→IM/QTOF resolving PFAS reveals complexity of the problem
- Simultaneous target quantitation and suspect screening workflow
- Need for direct injection methods for broad screening
- Adding confidence to putative identifications using RT projection and prediction

Acknowledgements

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