The Role of HRMS in Searching for Xenobiotic Compounds in Environmental Media

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Office of Research and Development (ORD)
Center for Environmental Measurement and Modeling (CEMM)

August 3rd, 2020
NEMC The Environment in 2020: Past, Present and Future

Compound identification basis

Foundation: First step
Critical for home
Necessary
Everything else is built upon it

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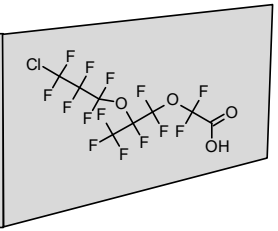
Compound Identification



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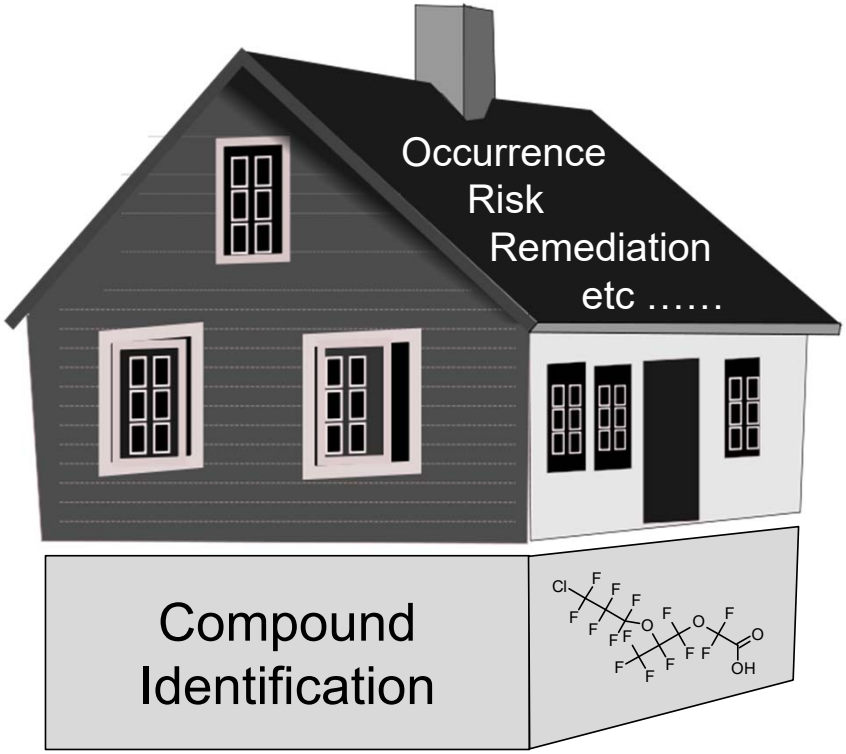


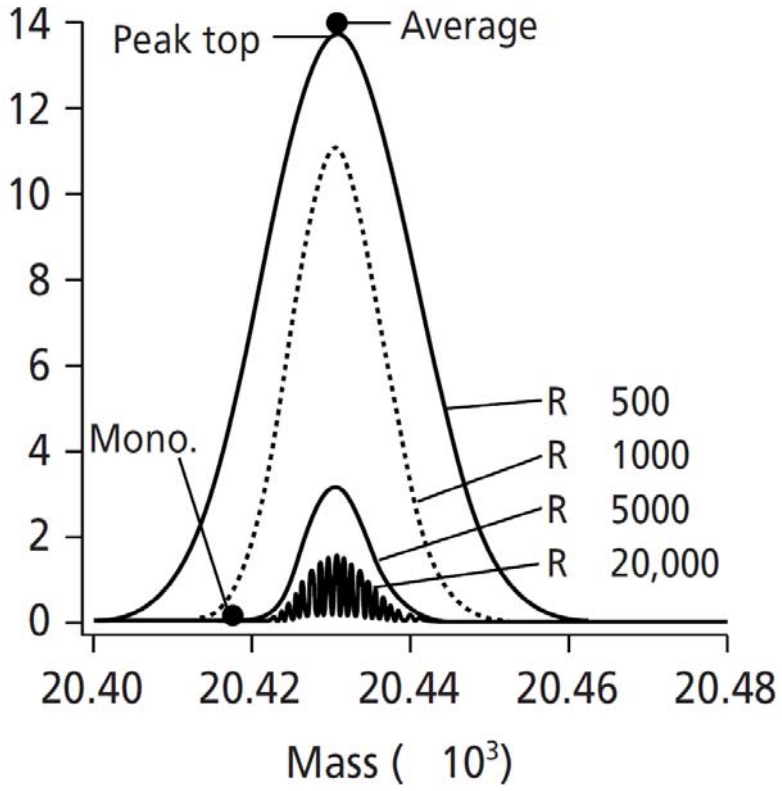
Mass Spectrometry Resolution?

LR MS or MS/MS

HRMS

Resolution is “the ability to “image” a detected ion in a mass spectrometer and differentiate it from any other”. *Balogh 2004 Debating Resolution and Mass Accuracy LCGC NORTH AMERICA VOLUME 22 NUMBER 2*

Mass Spectrometry Resolution?



Type	Resolving Power (FWHM)
FT-ICR-MS	1,000,000
FT-Orbitrap	100,000
High-Res-TOF	60,000
TOF	10,000
Quadrupole / IonTrap in UltraZoom mode	10,000
Quadrupole / Iontrap	1,000

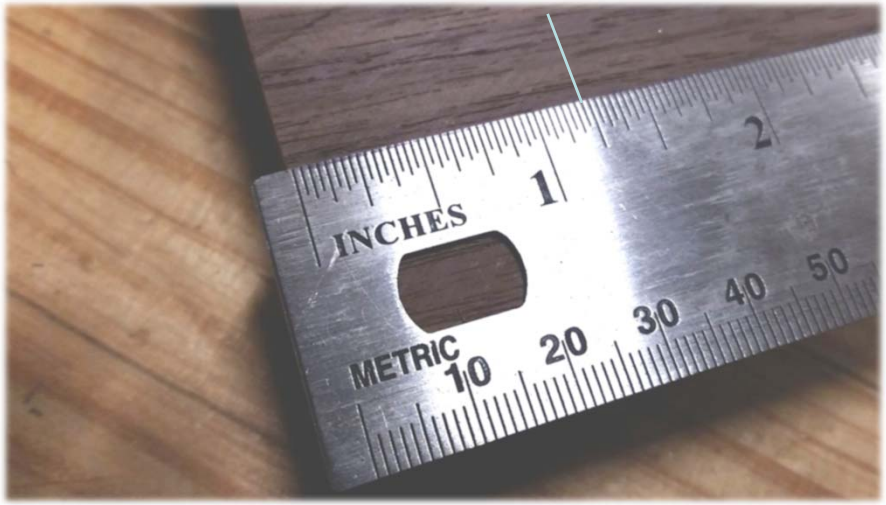
https://fiehnlab.ucdavis.edu/projects/seven-golden-rules/mass-resolution

Balogh 2004 Debating Resolution and Mass Accuracy
LCGC NORTH AMERICA VOLUME 22 NUMBER 2

Mass Accuracy

PFOA: MW 412.9 +/- 0.1 to 0.5 Da

MW 412.9964 +/- 0.0004 Da (1ppm)



photos by Mark Strynar

Mass accuracy is the ability to measure or calibrate the instrument response against a known entity. Usually expressed in parts per million (ppm), the measurement indicates the deviation of the instrument response from a known.

Balogh 2004 Debating Resolution and Mass Accuracy
LCGC NORTH AMERICA VOLUME 22 NUMBER 2

HRMS Measurable Parameters

Mass Accuracy

Resolution (FWHM method)

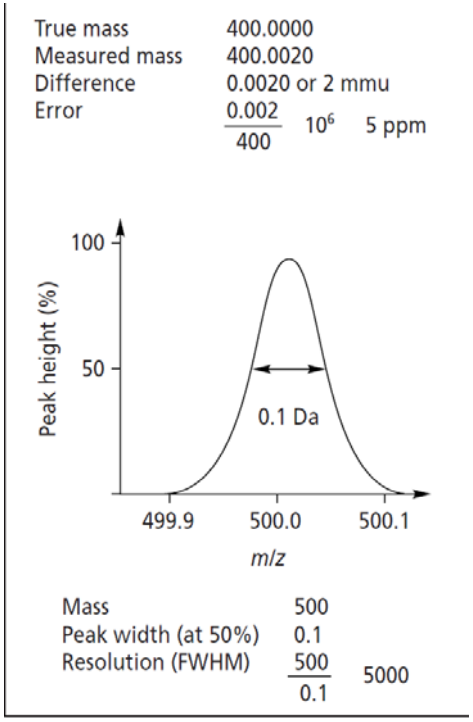


Figure 1: (Top) Mass accuracy determination and (bottom) the FWHM method for determining resolution for a mass spectrometer measured at a given ion.

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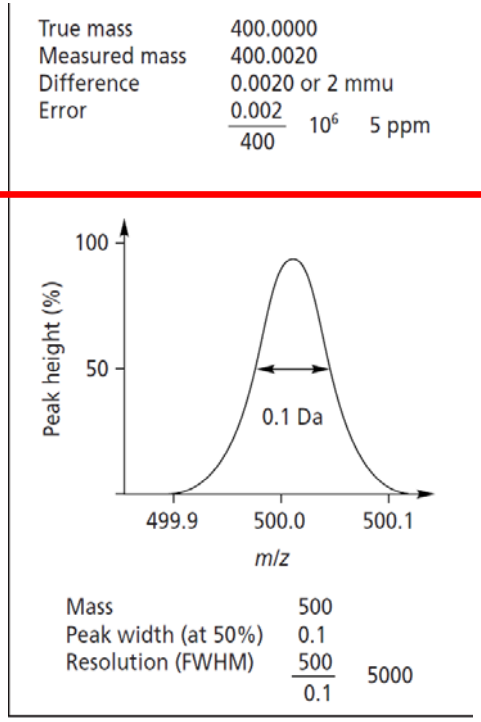

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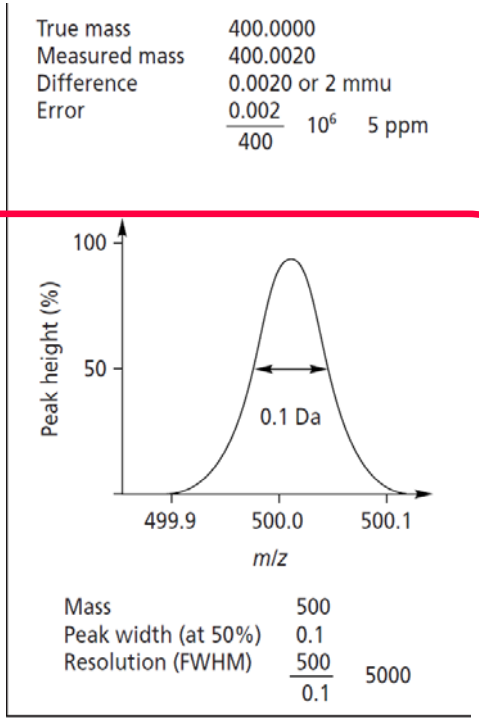

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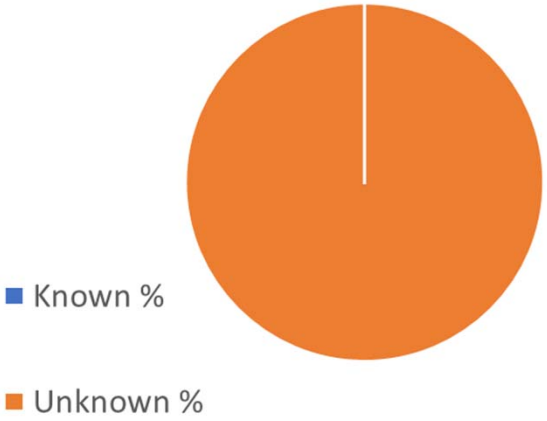
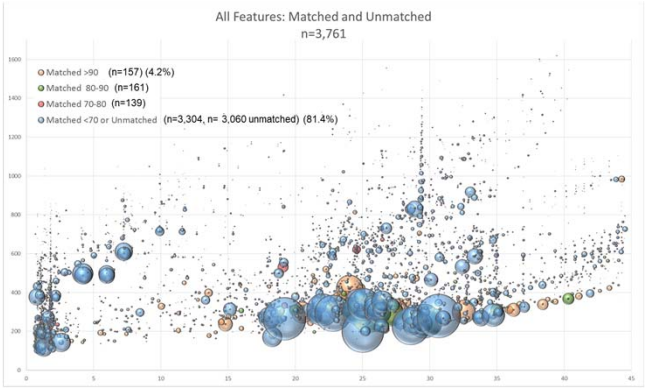
What is our sample analysis comfort level?





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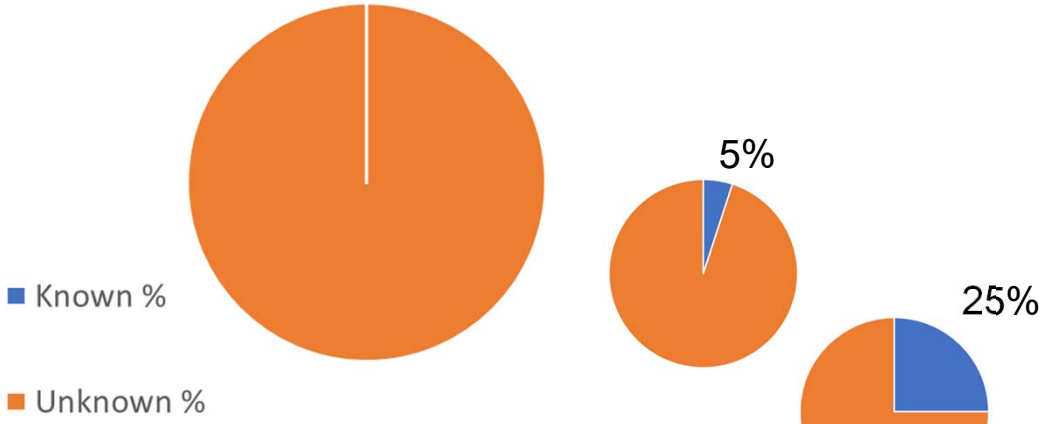
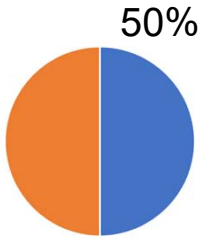
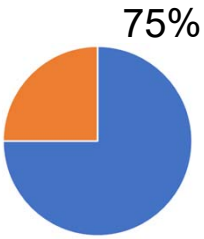
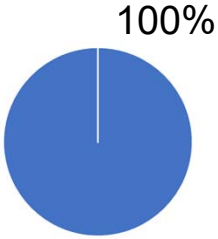
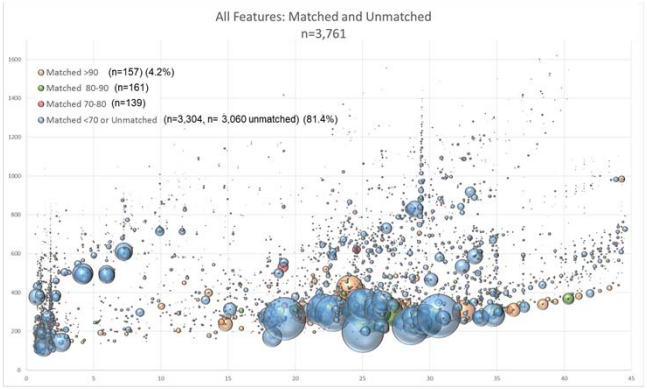






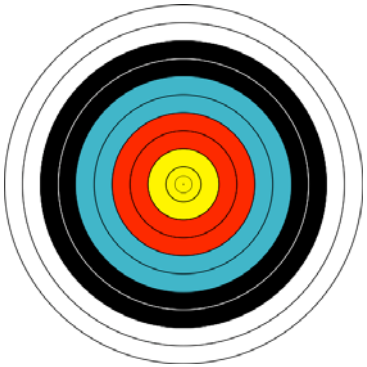




A few items defined

Targeted Analysis - analyzing for a suite of analytes with a validated method

e.g. How much Fipronil is in my water?



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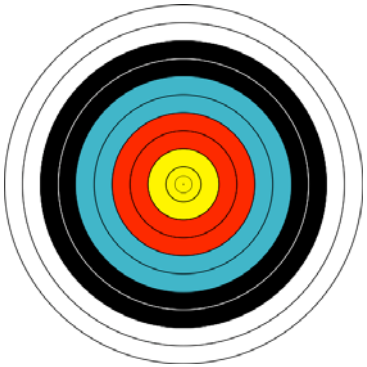

LRMS

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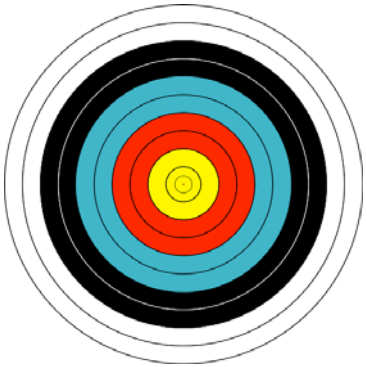

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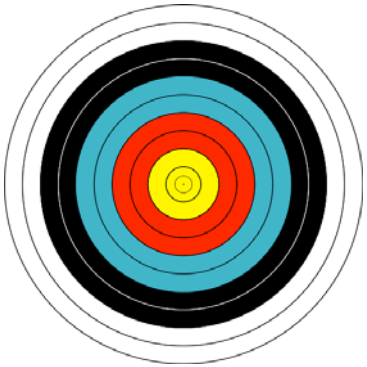

LRMS

HRMS

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e.g. What chemicals are in my water?

Suspect Screening – screening against a database of chemicals

Non-Targeted Analysis – novel compound identification

Some key questions we are all asking:

How good is good enough?

Can we give quantitative values of these chemicals?

How will this data be used?

What are the important analytes?

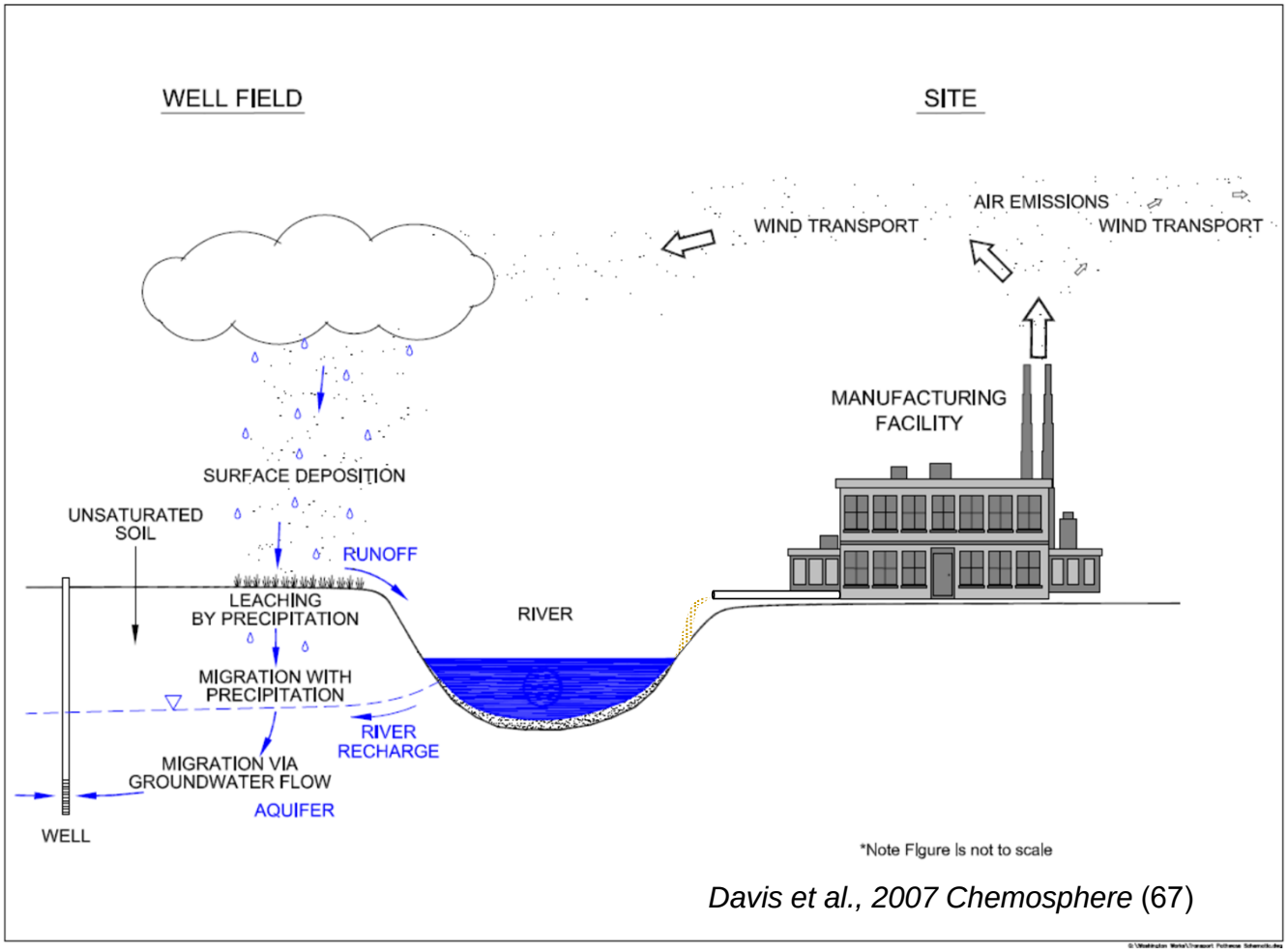
What is my confidence in identification?

What if I miss something?

HRMS is A tool in the environmental/analytical chemists tool belt:

- a powerful tool
- a very useful tool
- not the only tool

Conceptual Model of APFO Emission



Davis et al., 2007 Chemosphere (67)

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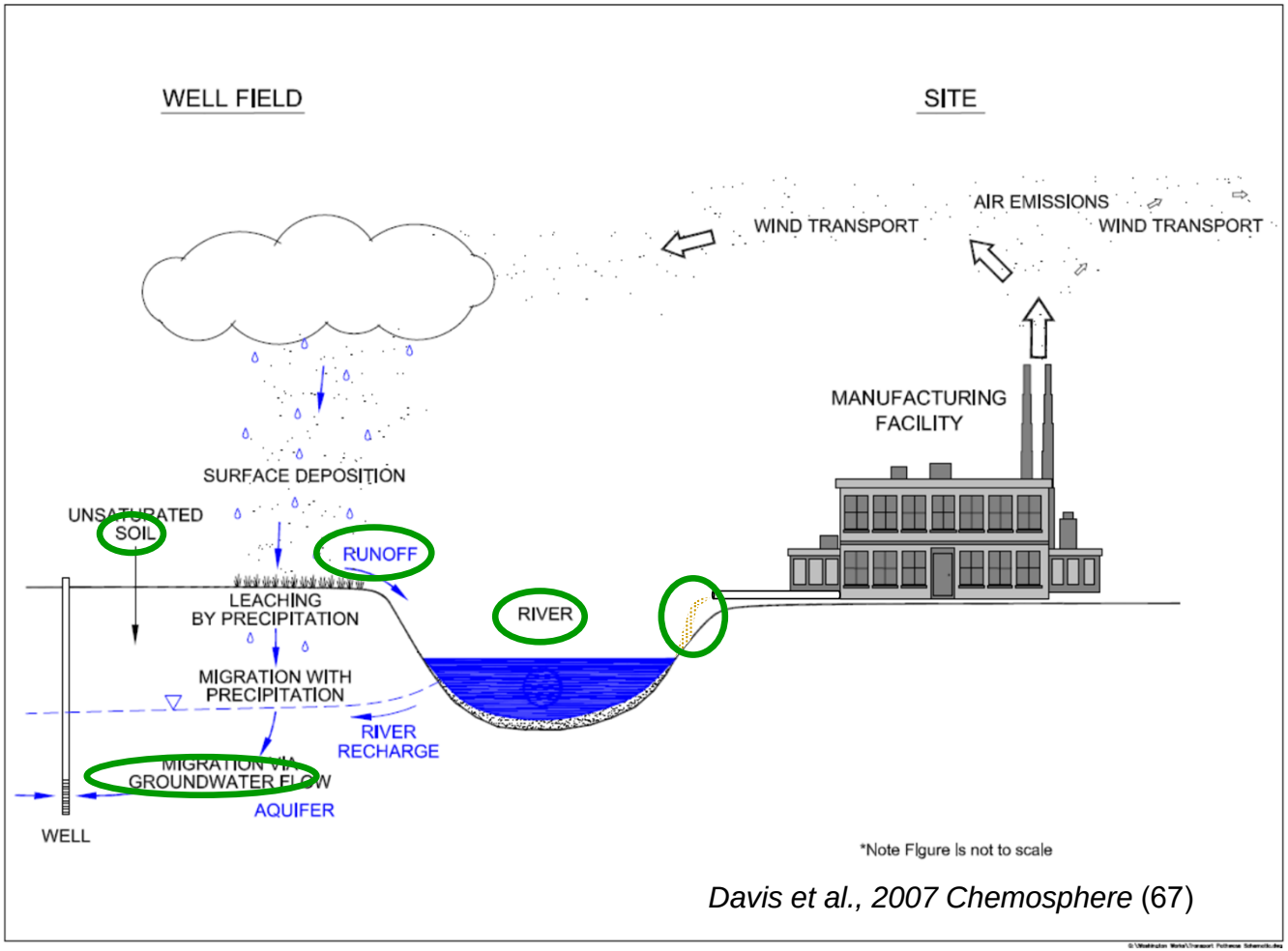

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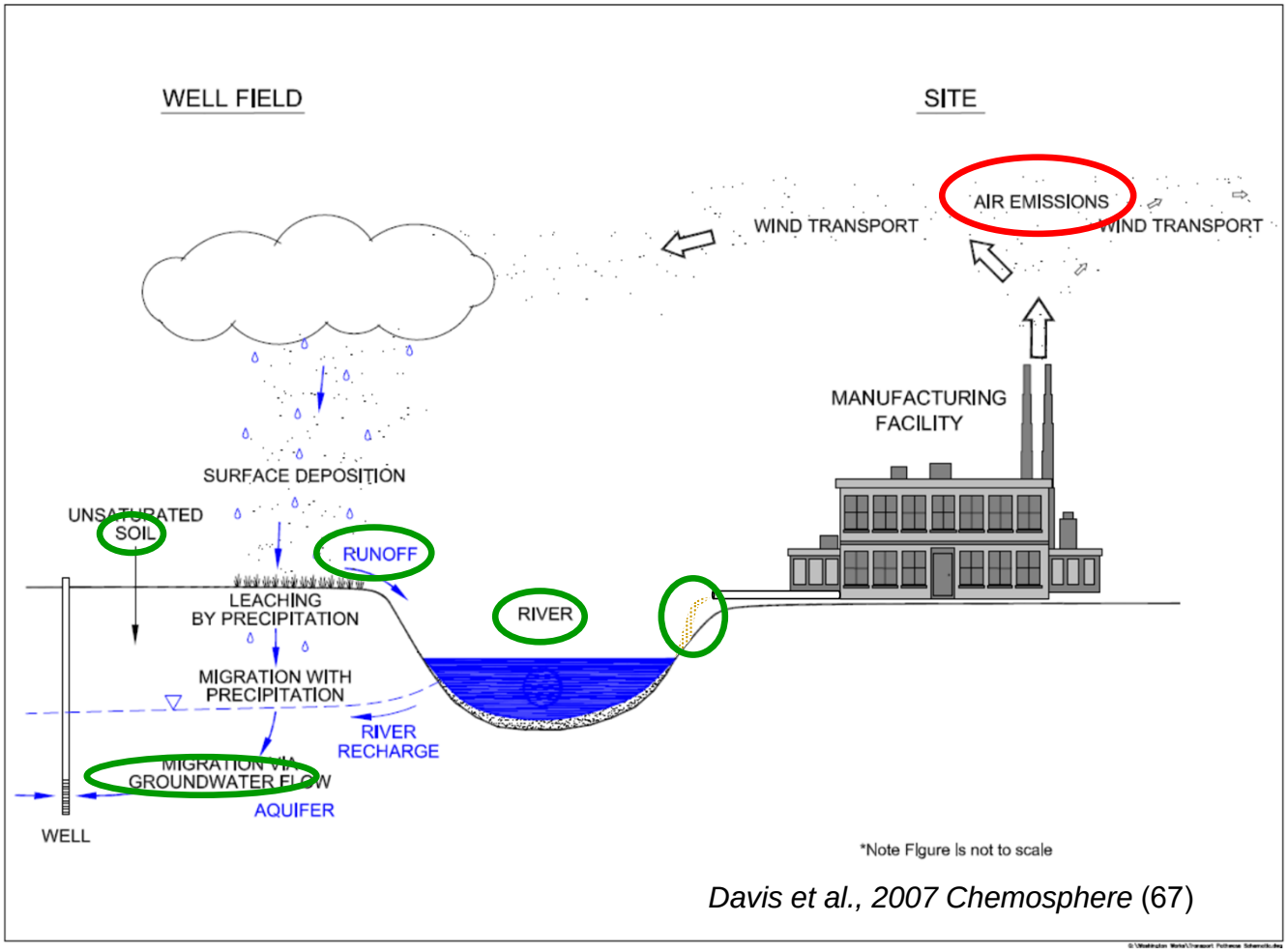

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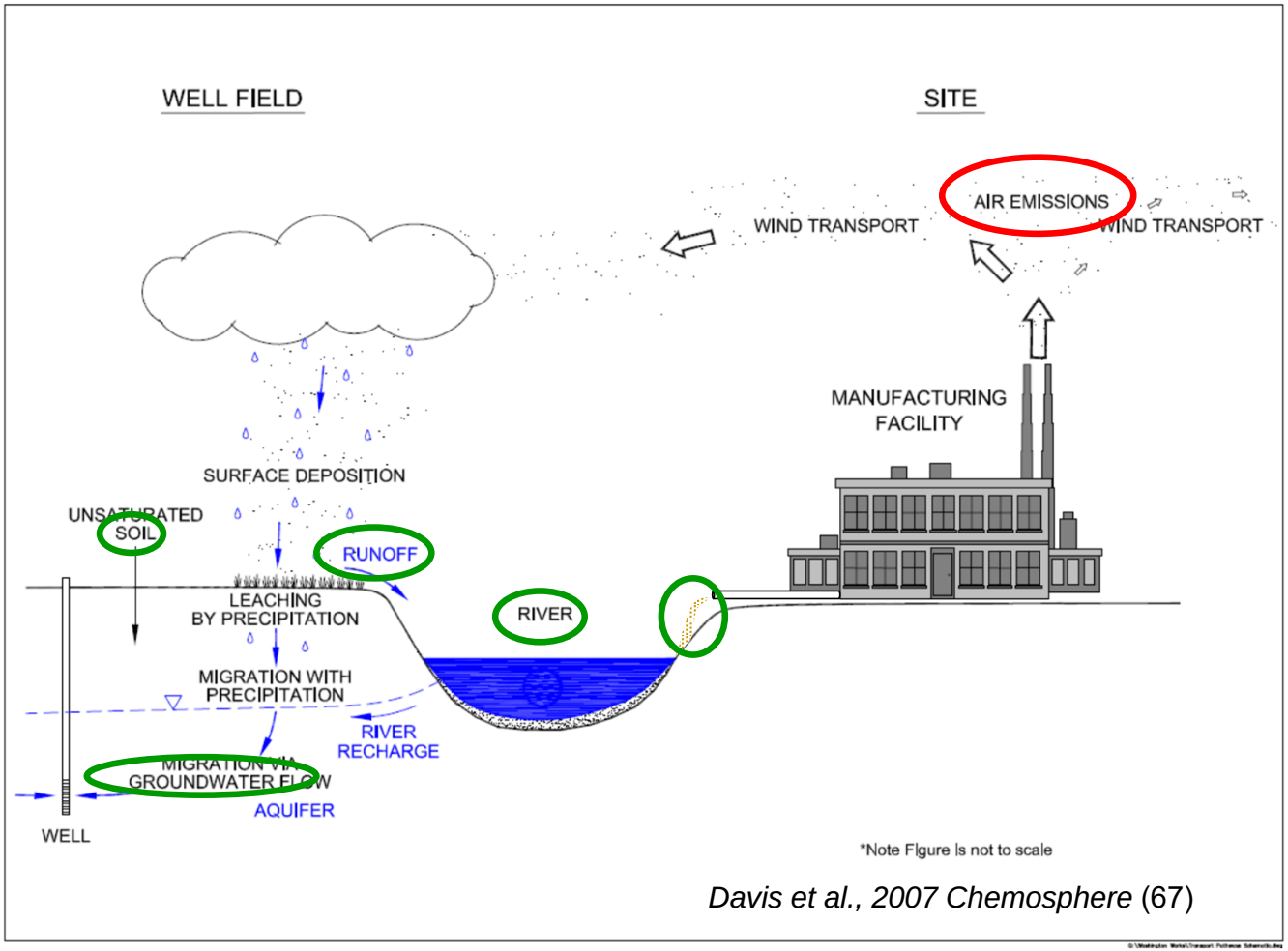

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HRMS Analysis to compare Samples:

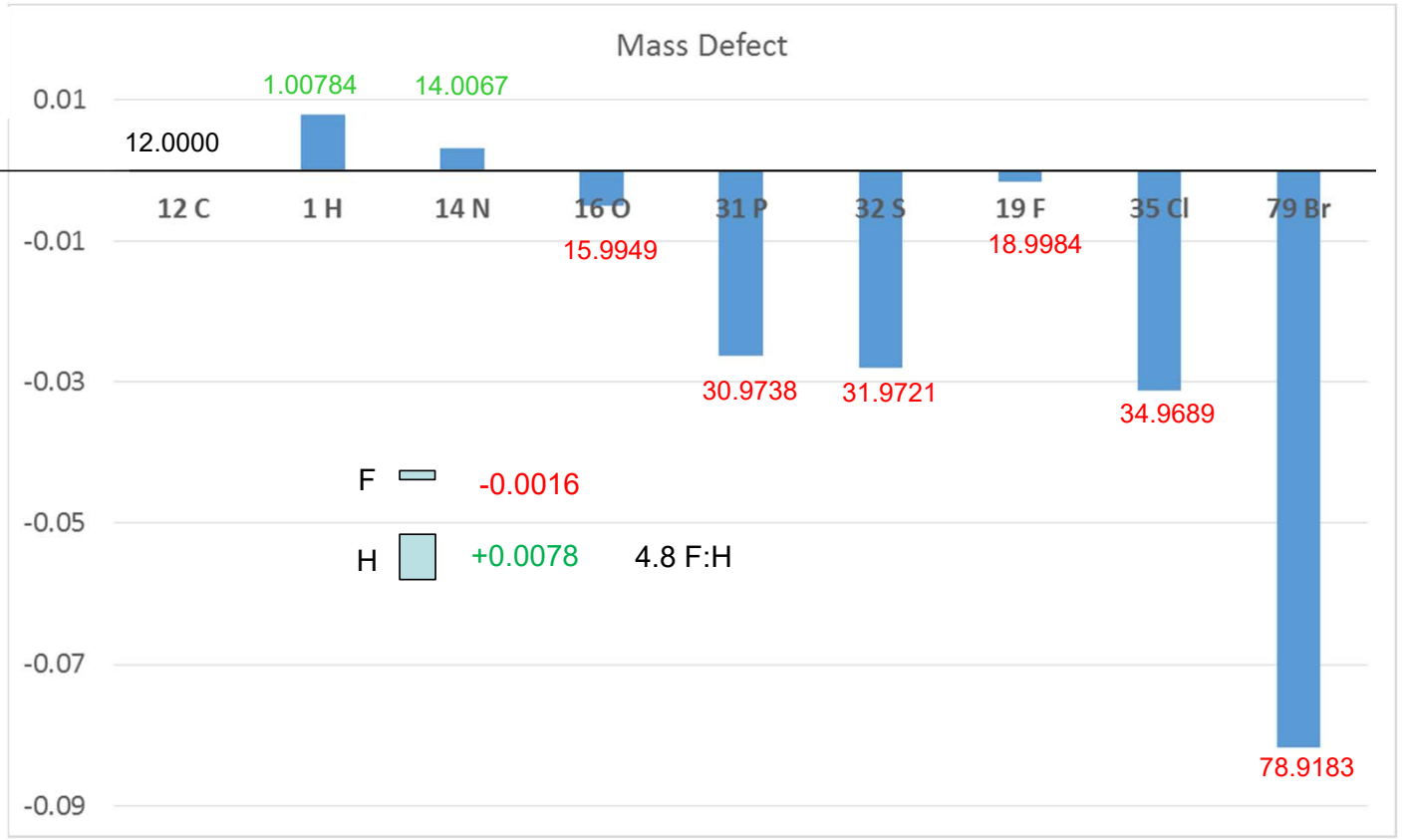
Upstream vs. downstream
Pretreatment vs post-treatment
Close vs distant
Upwind vs downwind
Surface vs deep
Etc….

Isotope Signatures: Negative Mass Defect

SOME KEY TOOLS

Positive Mass Defect

Negative Mass Defect



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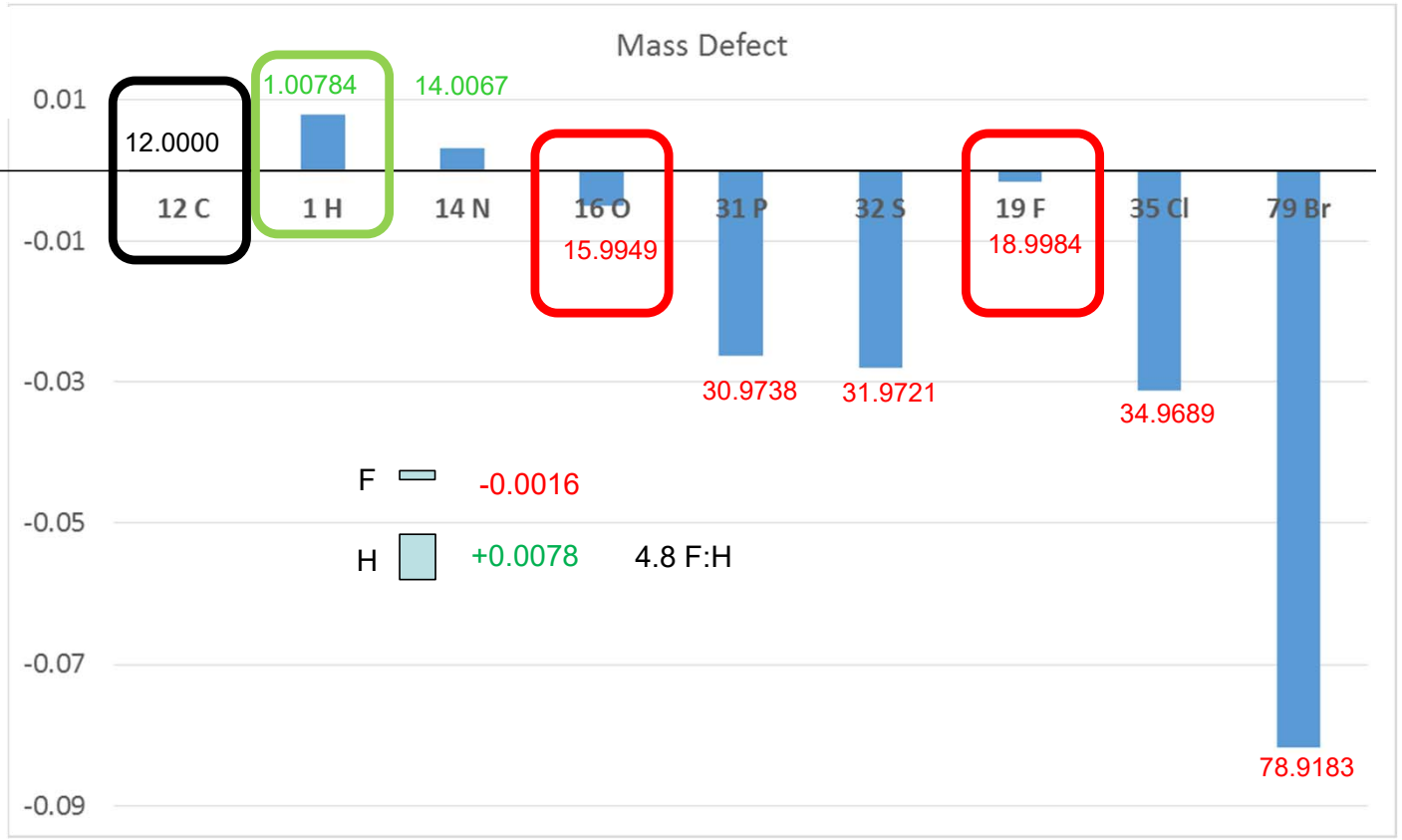

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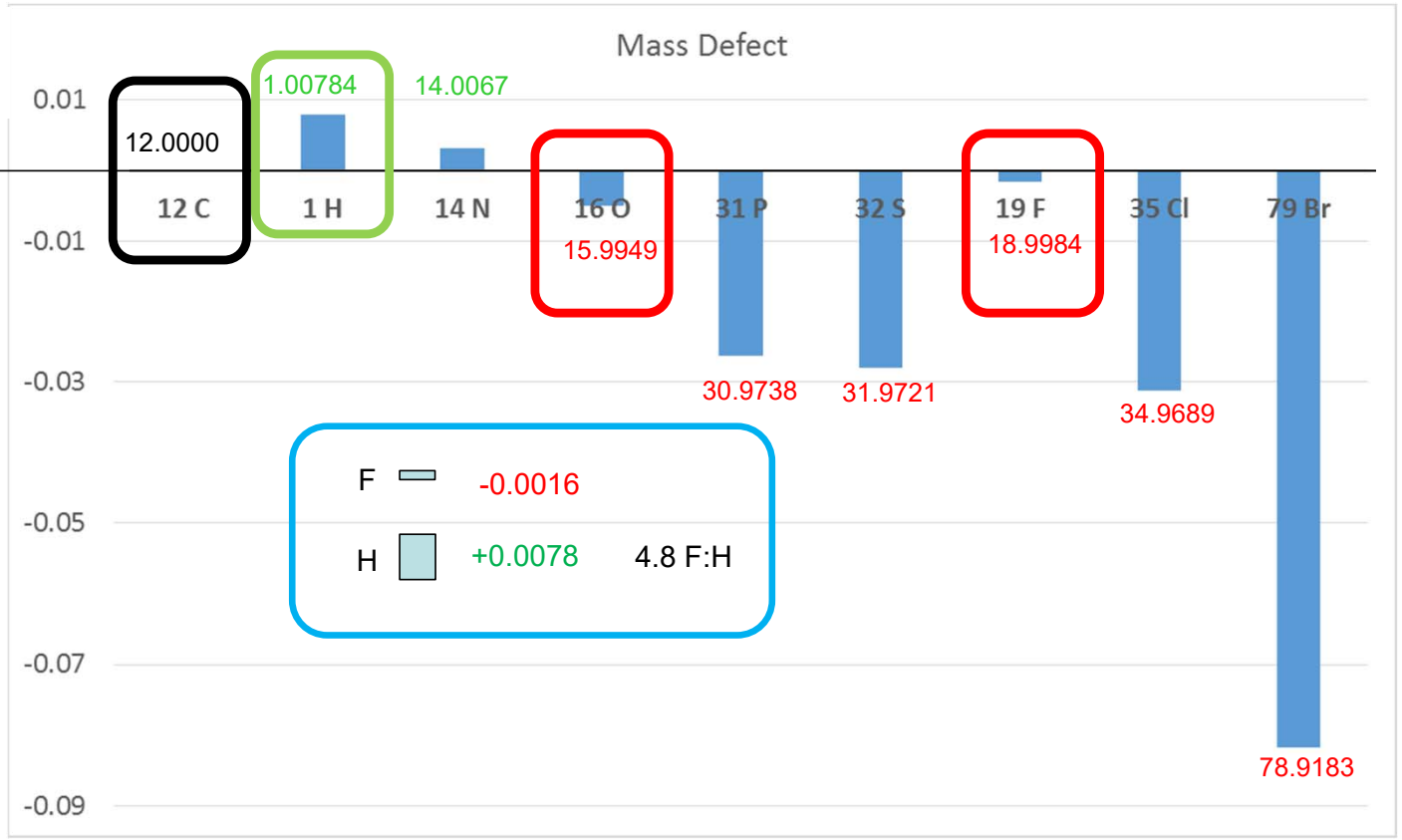

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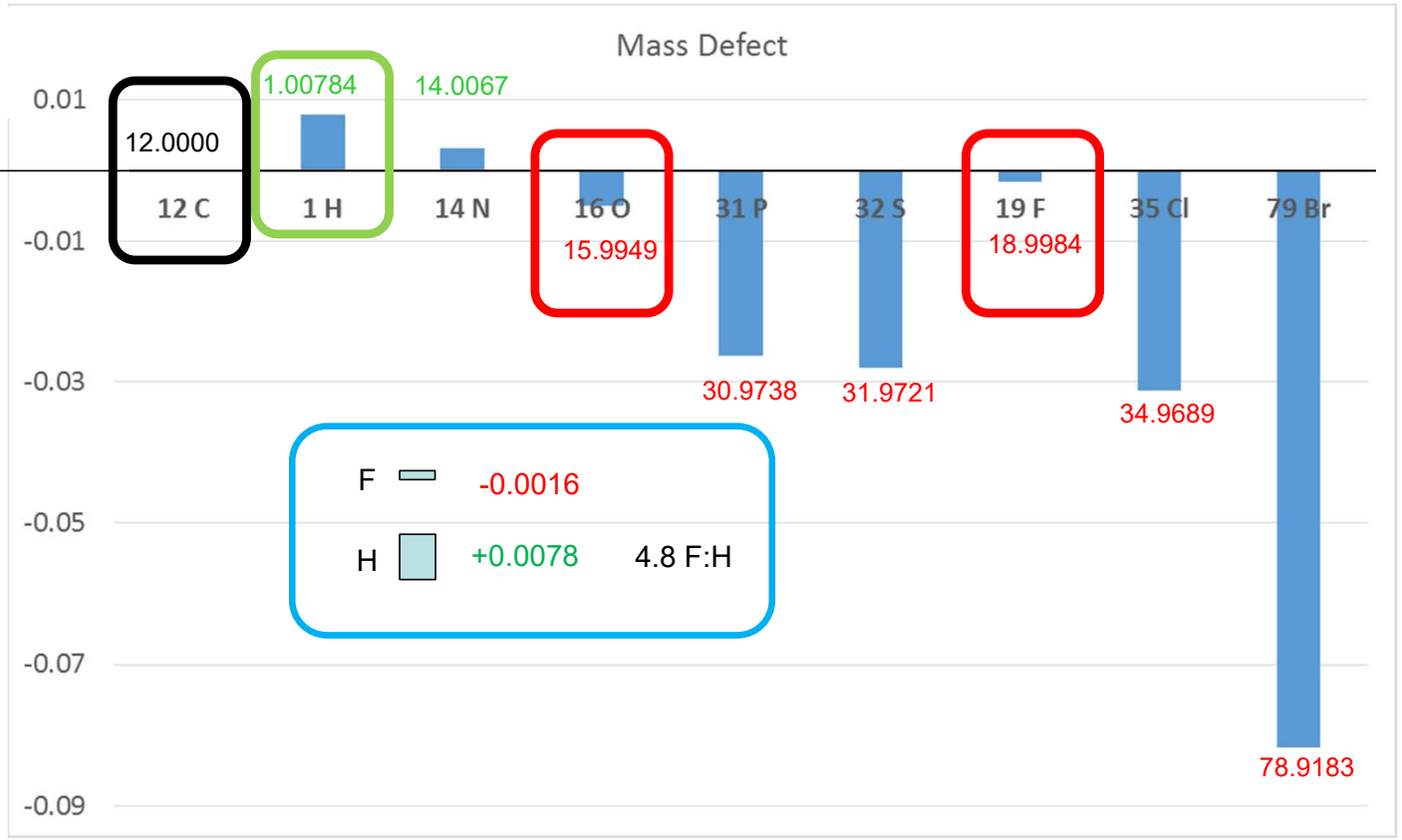
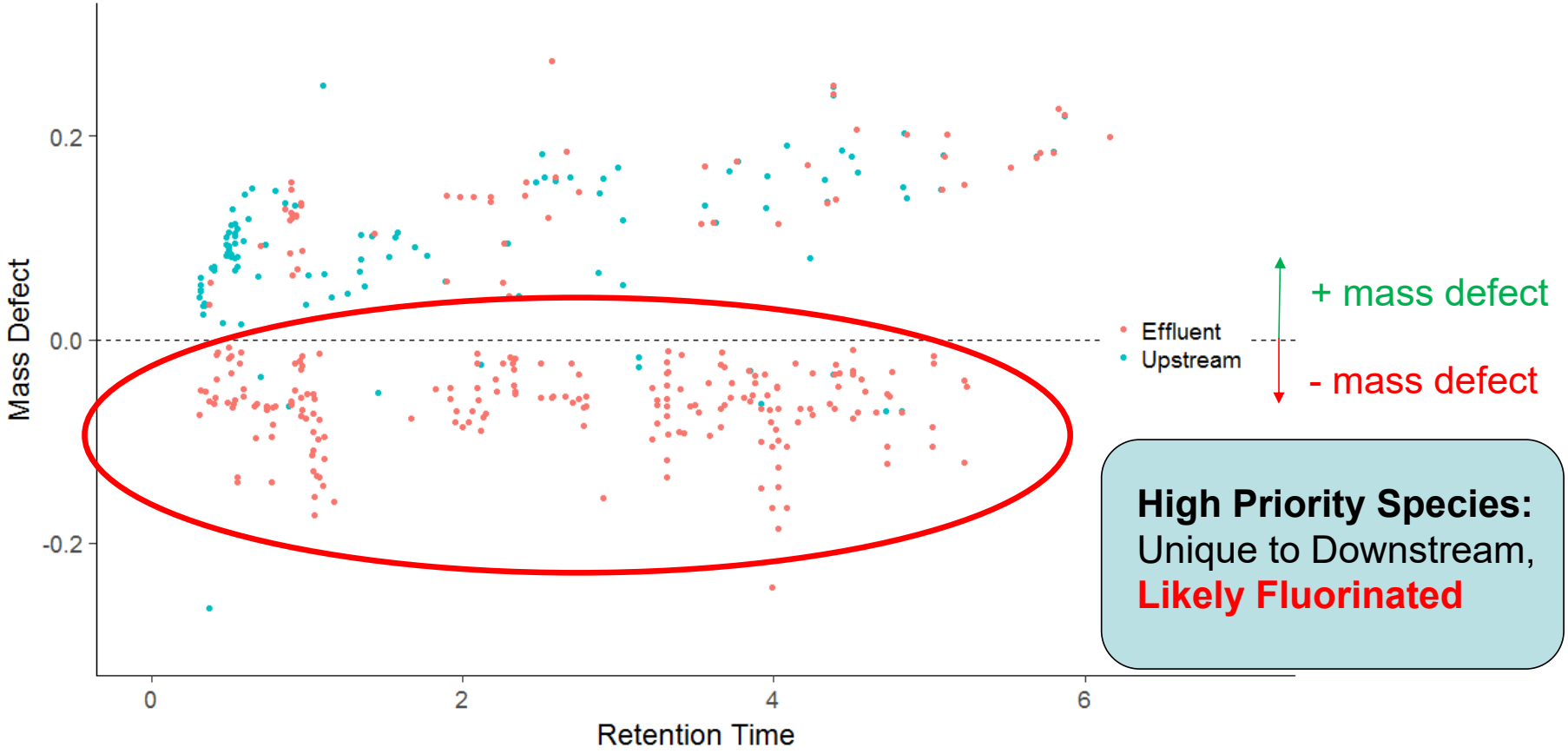


Octanoic Acid
($C_8H_{16}O_2$)
144.1150

PFOA
($C_8HF_{15}O_2$)
413.9773

Cape Fear River Sample Comparison

SOME KEY TOOLS

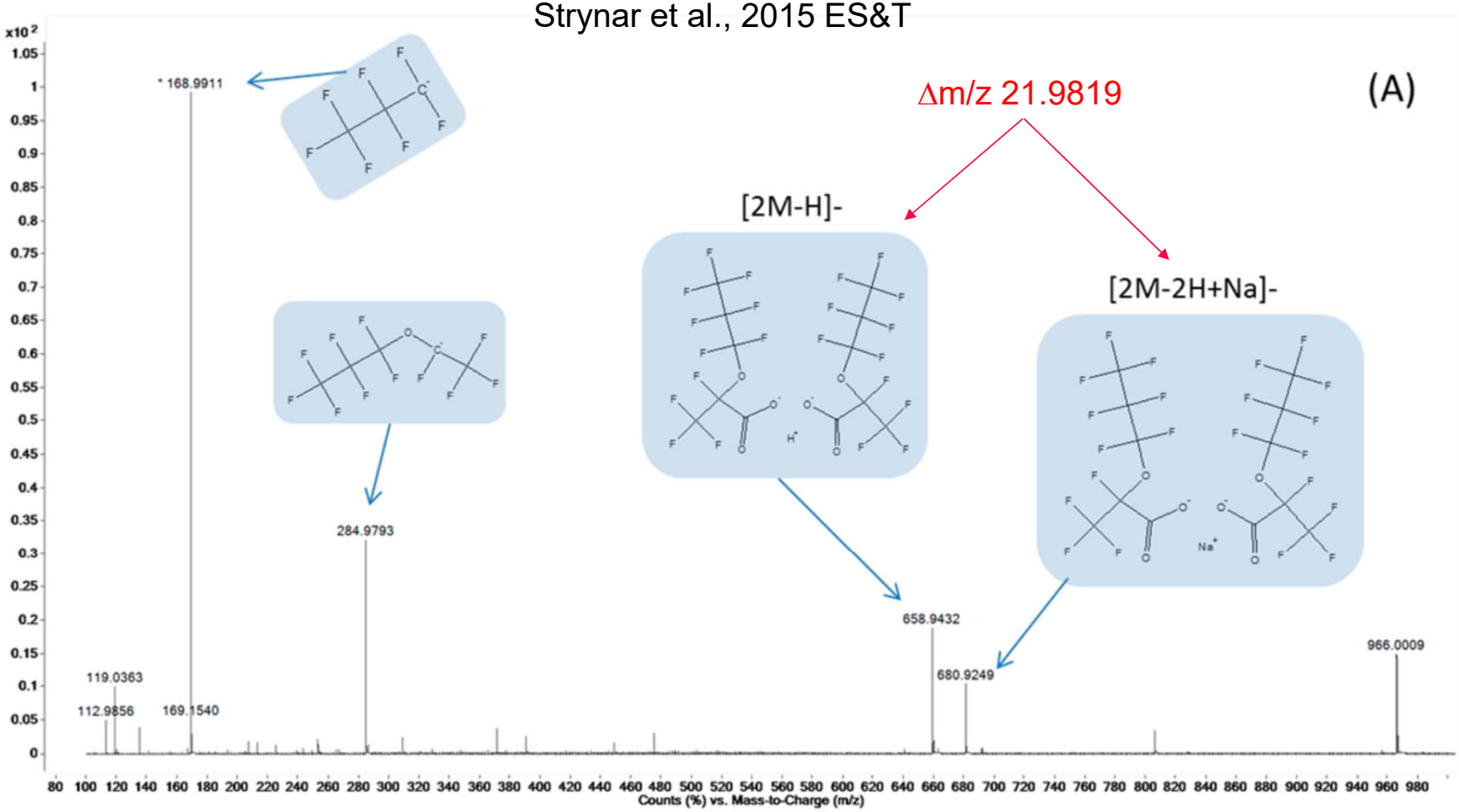


High Priority Species:
Unique to Downstream,
Likely Fluorinated

Gas Phase *n*-mers (HFPO-DA)

SOME KEY TOOLS

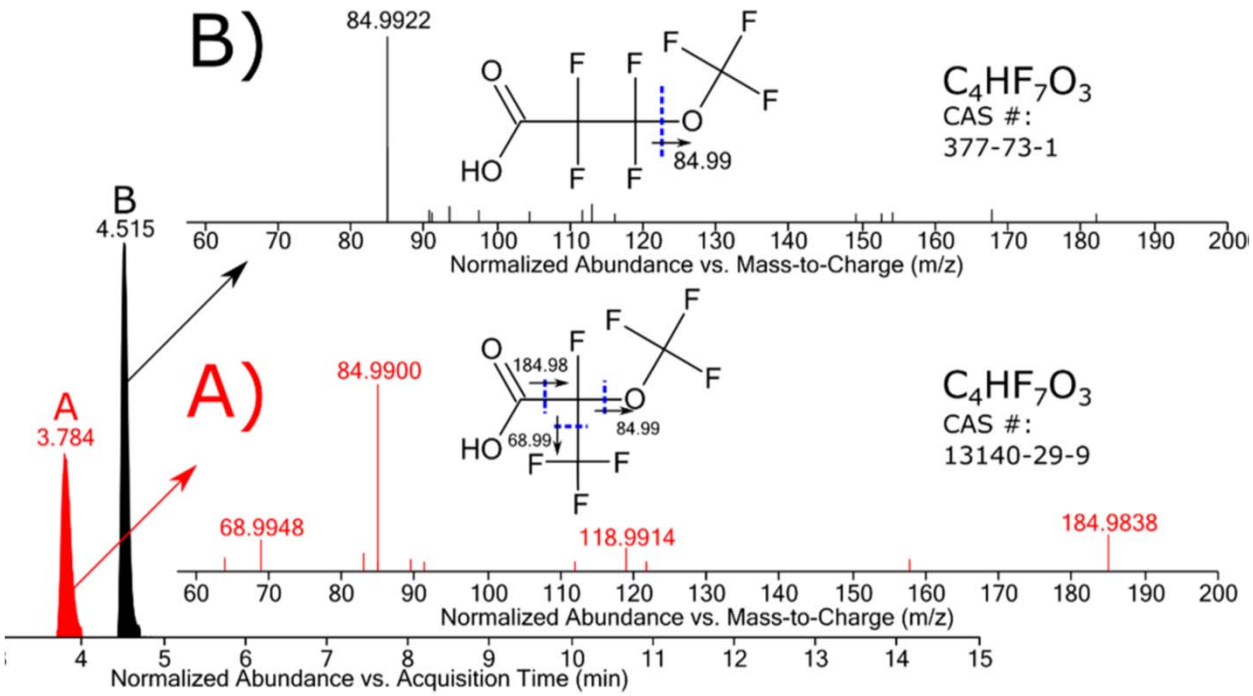
Strynar et al., 2015 ES&T



Have also seen:
K+
NH_4+
Trimers
tetramers

Diagnostic Fragment Ions contd.

SOME KEY TOOLS



McCord and Strynar ES&T 2019

Diagnostic Fragment Ions contd.

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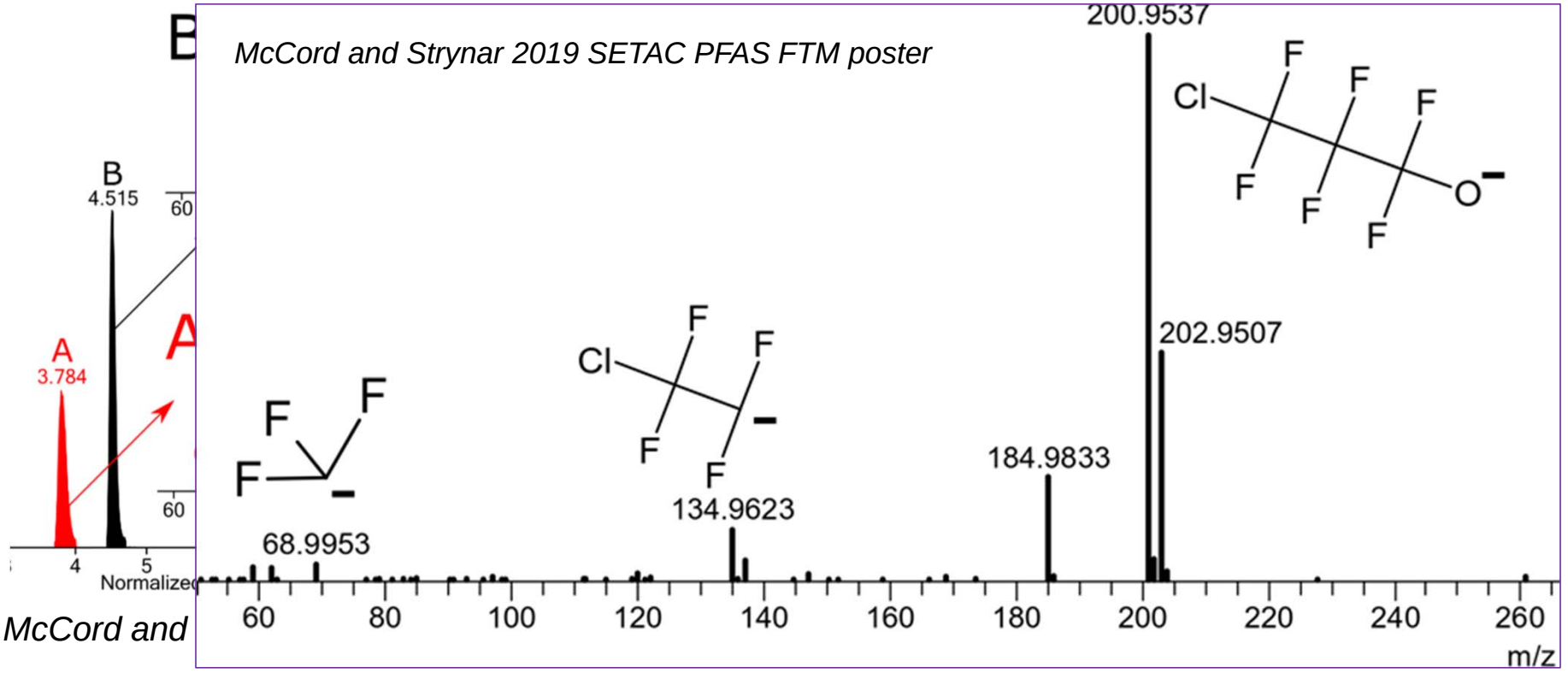
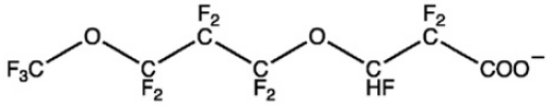


McCord and

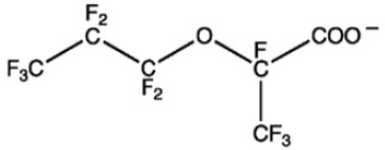
Post PFOA Stewardship Agreement

Fluoropolymer manufacture

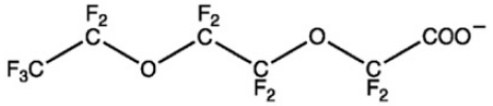
ADONA (CAS No. 958445-44-8)



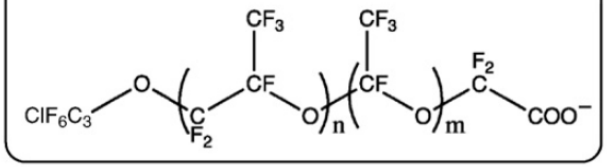
GenX (CAS No. 62037-80-3)



Asahi's product (CAS No. 908020-52-0)

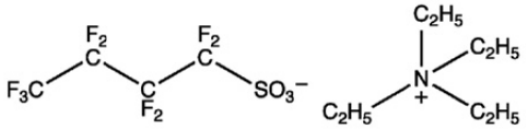


Solvay's product (CAS No. 329238-24-6)

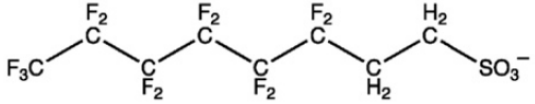


Metal plating

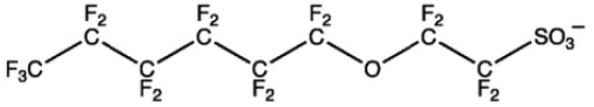
$N(Et)_4$-PFBS (CAS No. 25628-08-4)



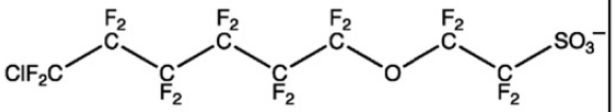
6:2 FTSA (CAS No. 27619-97-2)



F-53 (CAS No. 754925-54-7)



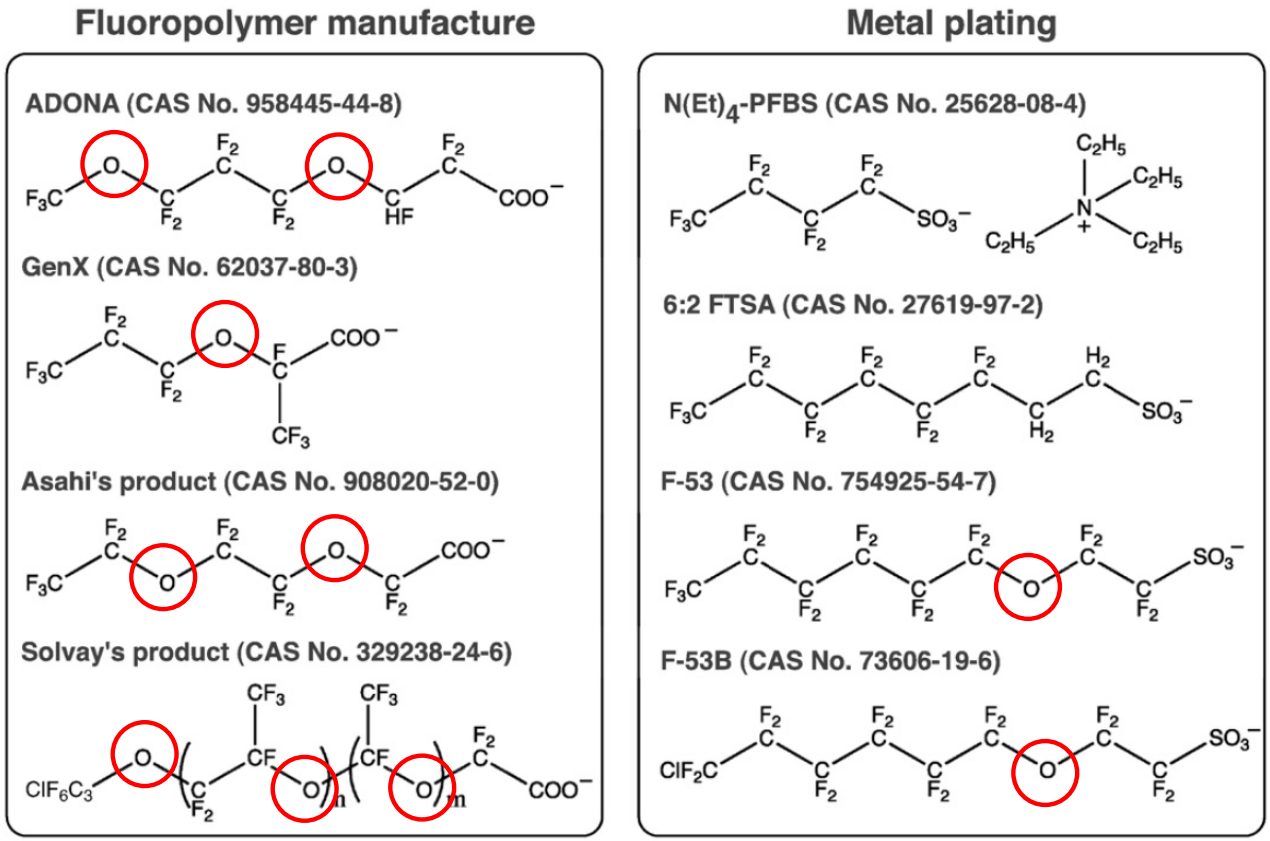
F-53B (CAS No. 73606-19-6)



Wang et al. *Environment International*, **2013,** *60,* pp 242–248

Post PFOA Stewardship Agreement

Ethers/Polyethers



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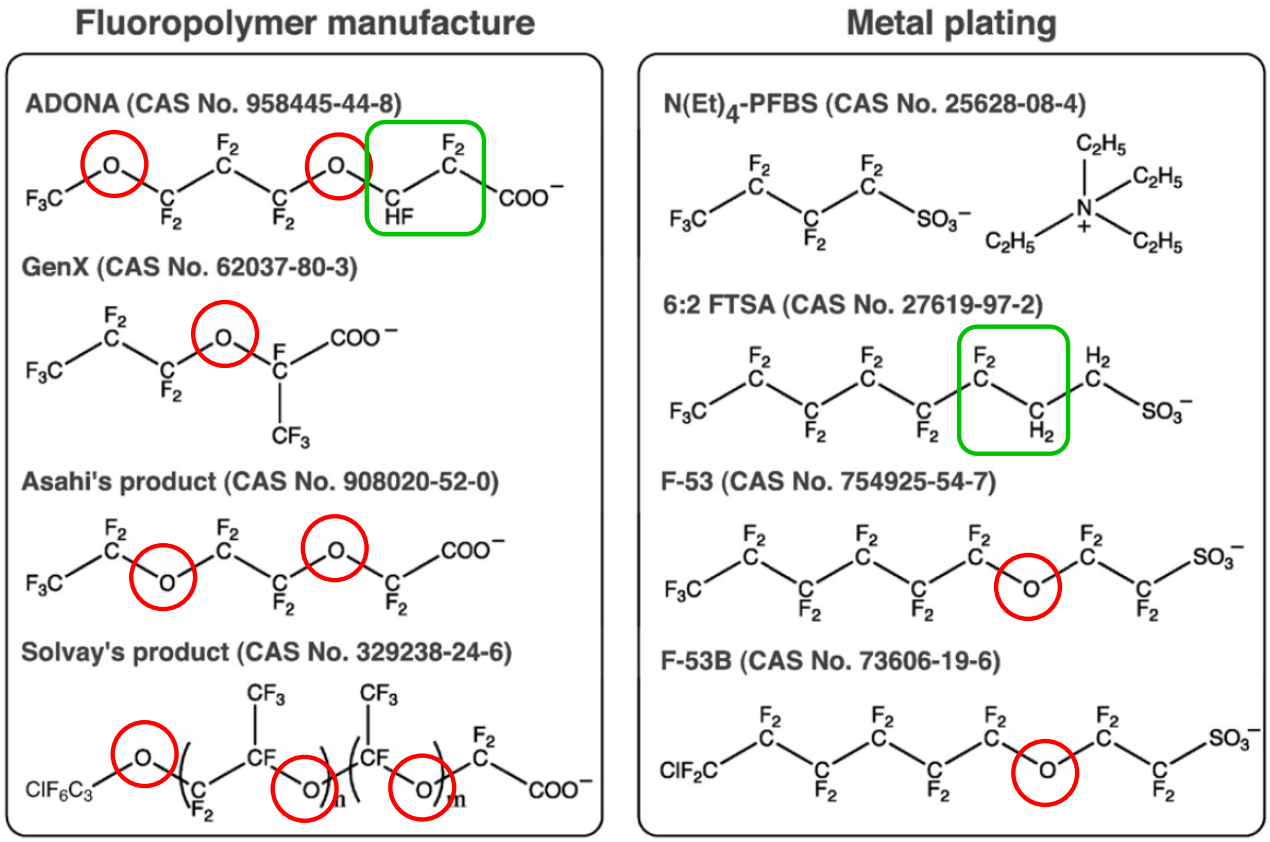
Ethers/Polyethers

Polyfluorinated



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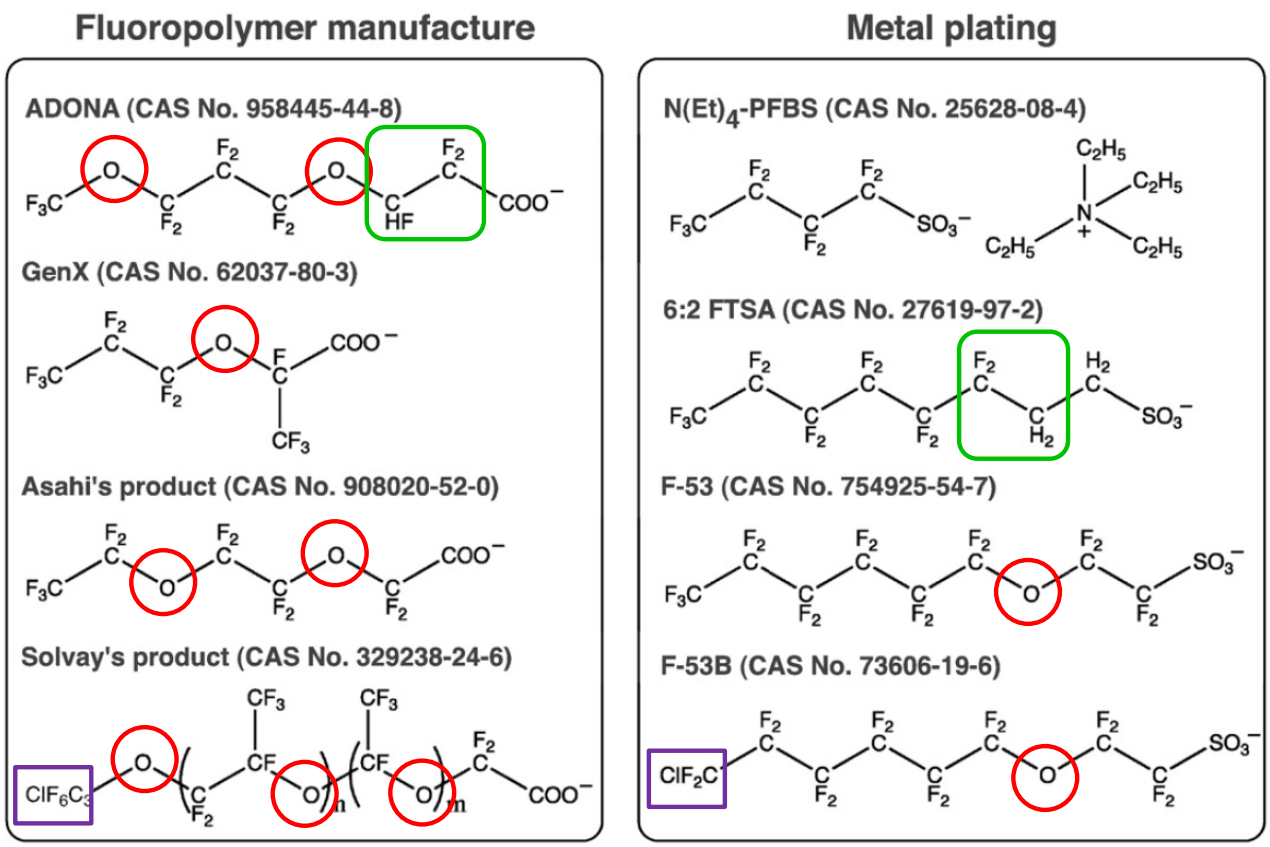
Post PFOA Stewardship Agreement

Ethers/Polyethers

Polyfluorinated

Chlorinated



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Environmental Science & Technology

November 2015

Article

pubs.acs.org/est

Identification of Novel Perfluoroalkyl Ether Carboxylic Acids (PFECAs) and Sulfonic Acids (PFESAs) in Natural Waters Using Accurate Mass Time-of-Flight Mass Spectrometry (TOFMS)

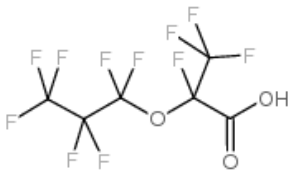
Mark Strynar,[*,†] Sonia Dagnino,[†,‡] Rebecca McMahen,[†,‡] Shuang Liang,[†,‡] Andrew Lindstrom,[†] Erik Andersen,[†] Larry McMillan,[§] Michael Thurman,[∥] Imma Ferrer,[∥] and Carol Ball[⊥]

Table 1. Accurate Mass of Polyfluorinated Compounds and In-Source Artifacts Found in Extracted Water Samples

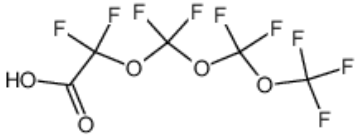
number	formula	CAS no.	name	[M][a]	$[M-H]^-$ m/z	$[2M-2H+Na]^-$ m/z	$[2M-H]^-$ m/z
Monoether PFECAs							
1	$C_3HF_5O_3$			179.9846	178.9773	380.9438	358.9619
2	$C_4HF_7O_3$			229.9813	228.9740	480.9372	458.9553
3	$C_5HF_9O_3$	863090-89-5		279.9782	278.9709	580.9310	558.9491
4	$C_6HF_{11}O_3$	13252-13-6	undecafluoro-2-methyl-3-oxahexanoic acid	329.9750	328.9677	680.9247	658.9427
5	$C_7HF_{13}O_3$			379.9718	378.9645	780.9182	758.9363
6	$C_8HF_{15}O_3$			429.9686	428.9613	880.9118	858.9299
Polyether PFECAs							
7	$C_7HF_{13}O_7$	39492-91-6	perfluoro-3,5,7,9,11-pentaoxadodecanoic acid	443.9515	442.9442	908.8776	886.8957
8	$C_6HF_{11}O_6$	39492-90-5	perfluoro-3,5,7,9-butaoxadecanoic acid	377.9598	376.9525	776.8942	754.9123
9	$C_5HF_9O_5$	39492-89-2	perfluoro-3,5,7-propaoxaoctanoic acid	311.9681	310.9608	644.9108	622.9289
10	$C_4HF_7O_4$	39492-88-1	perfluoro-3,5-dioxahexanoic acid	245.9764	244.9691	512.9274	490.9455
PFESAs							
11	$C_7HF_{13}O_5S$	66796-30-3[b]		443.9337	442.9264		
12	$C_7H_2F_{14}O_5S$			463.9399	462.9326		

3 Found in human serum Wilmington, NC (Kotlarz *EHP* accepted 2020)

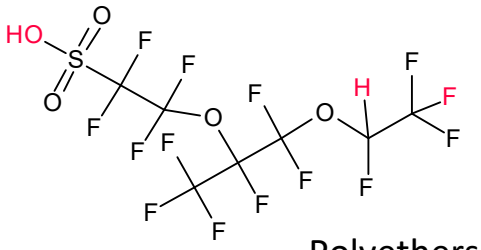
Example Structures



Monoether (6): GenX



Polyethers (4):



Polyethers sulfonates (2):

Environmental Science & Technology

November 2015

Article

pubs.acs.org/est

Identification of Novel Perfluoroalkyl Ether Carboxylic Acids (PFECAs) and Sulfonic Acids (PFESAs) in Natural Waters Using Accurate Mass Time-of-Flight Mass Spectrometry (TOFMS)

Mark Strynar,[*,†] Sonia Dagnino,[†,‡] Rebecca McMahen,[†,‡] Shuang Liang,[†,‡] Andrew Lindstrom,[†] Erik Andersen,[†] Larry McMillan,[§] Michael Thurman,[∥] Imma Ferrer,[∥] and Carol Ball[⊥]

Table 1. Accurate Mass of Polyfluorinated Compounds and In-Source Artifacts Found in Extracted Water Samples

number	formula	CAS no.	name	$[M]^a$	$[M-H]^-$ m/z	$[2M-2H+Na]^-$ m/z	$[2M-H]^-$ m/z
Monoether PFECAs							
1	$C_3HF_5O_3$			179.9846	178.9773	380.9438	358.9619
2	$C_4HF_7O_3$			229.9813	228.9740	480.9372	458.9553
3	$C_5HF_9O_3$	863090-89-5		279.9782	278.9709	580.9310	558.9491
4	$C_6HF_{11}O_3$	13252-13-6	undecafluoro-2-methyl-3-oxahexanoic acid	329.9750	328.9677	680.9247	658.9427
5	$C_7HF_{13}O_3$			379.9718	378.9645	780.9182	758.9363
6	$C_8HF_{15}O_3$			429.9686	428.9613	880.9118	858.9299
Polyether PFECAs							
7	$C_7HF_{13}O_7$	39492-91-6	perfluoro-3,5,7,9,11-pentaoxadodecanoic acid	443.9515	442.9442	908.8776	886.8957
8	$C_6HF_{11}O_6$	39492-90-5	perfluoro-3,5,7,9-butaoxadecanoic acid	377.9598	376.9525	776.8942	754.9123
9	$C_5HF_9O_5$	39492-89-2	perfluoro-3,5,7-propaoxaoctanoic acid	311.9681	310.9608	644.9108	622.9289
10	$C_4HF_7O_4$	39492-88-1	perfluoro-3,5-dioxahexanoic acid	245.9764	244.9691	512.9274	490.9455
PFESAs							
11	$C_7HF_{13}O_5S$	66796-30-3[b]		443.9337	442.9264		
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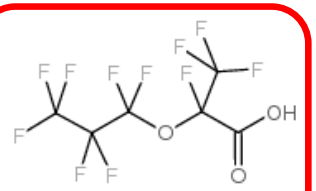

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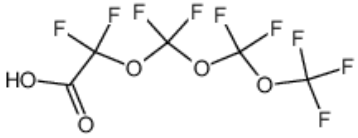

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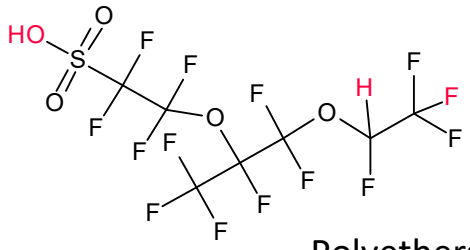

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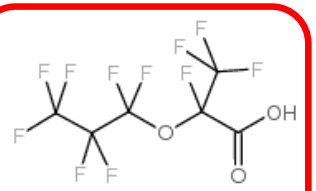

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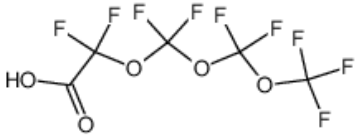

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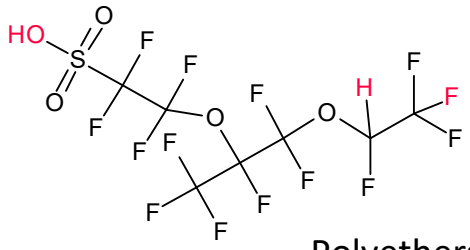


Polyethers sulfonates (2):

Data Mining

Trends

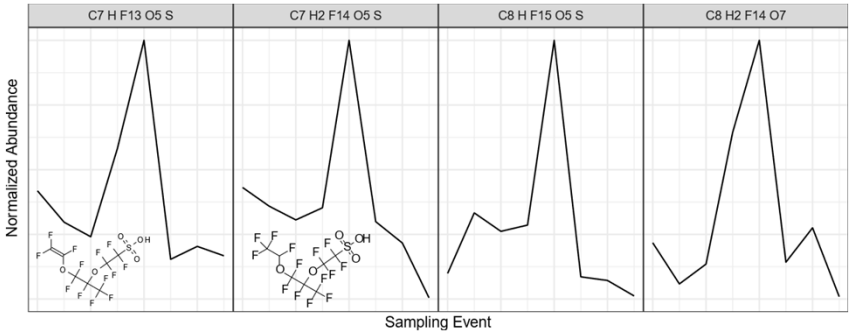
Clustering

Fingerprinting

Previously Undiscovered

McCord and Strynar ES&T
DOI: 10.1021/acs.est.8b06017
Environ. Sci. Technol. 2019, 53, 4717−4727

Data Mining



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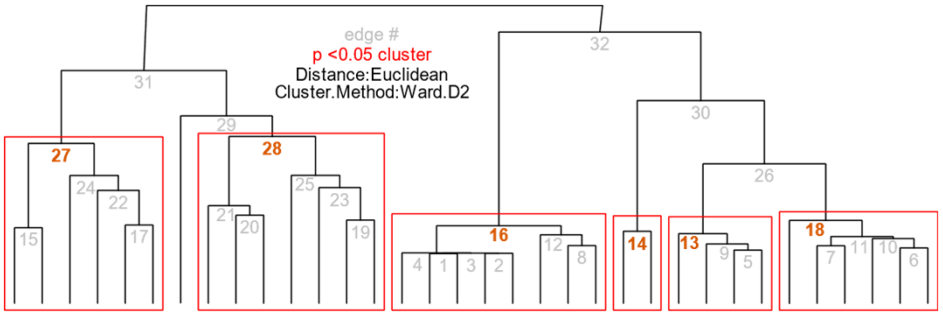

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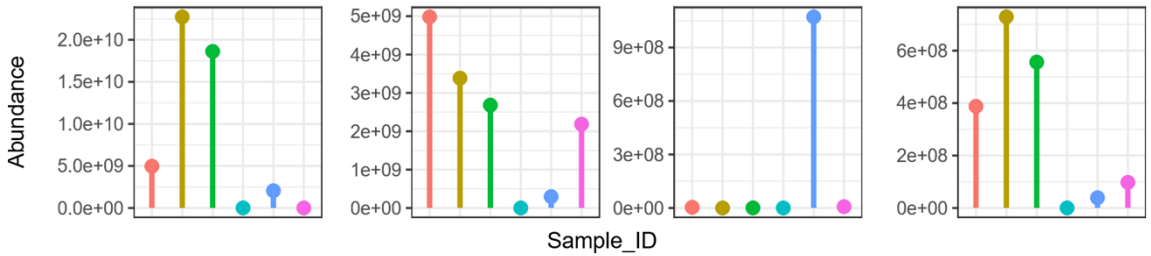

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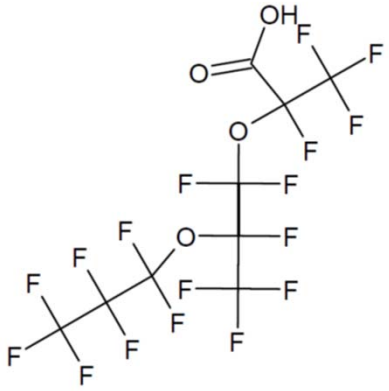
Retrospective Analysis

N=20 NC monitoring Wells (M-H)

HFPO-TA CAS 13252-14-7

DTXSID00892442



Molecular Formula: $C_9HF_{17}O_4$

Monoisotopic Mass: 495.960338 Da

[M-H]-: 494.953061 Da

Pan et al., 2017 ES&T

DOI: 10.1021/acs.est.7b02259

Xiaoqing River China near fluoropolymer production facility

Found in water, carp and nearby human serum

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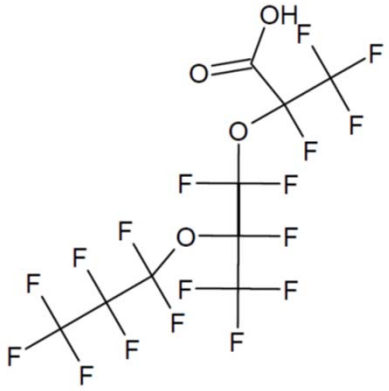

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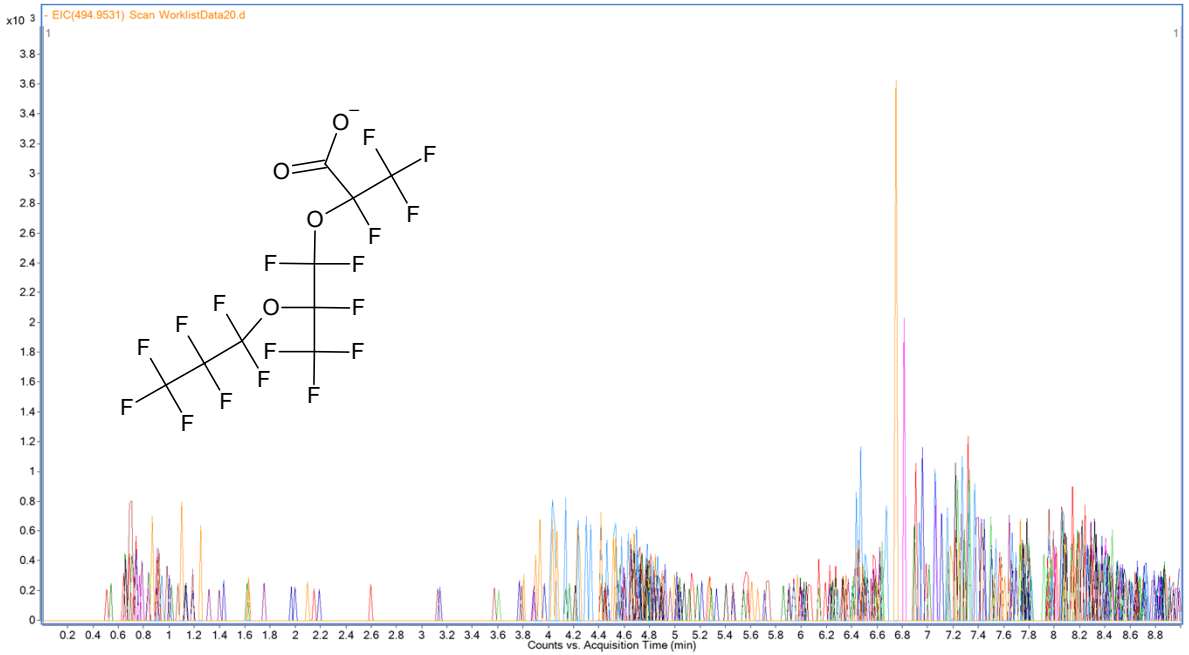

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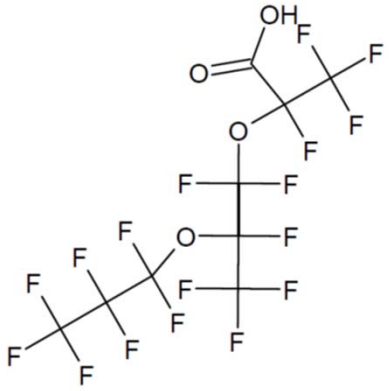

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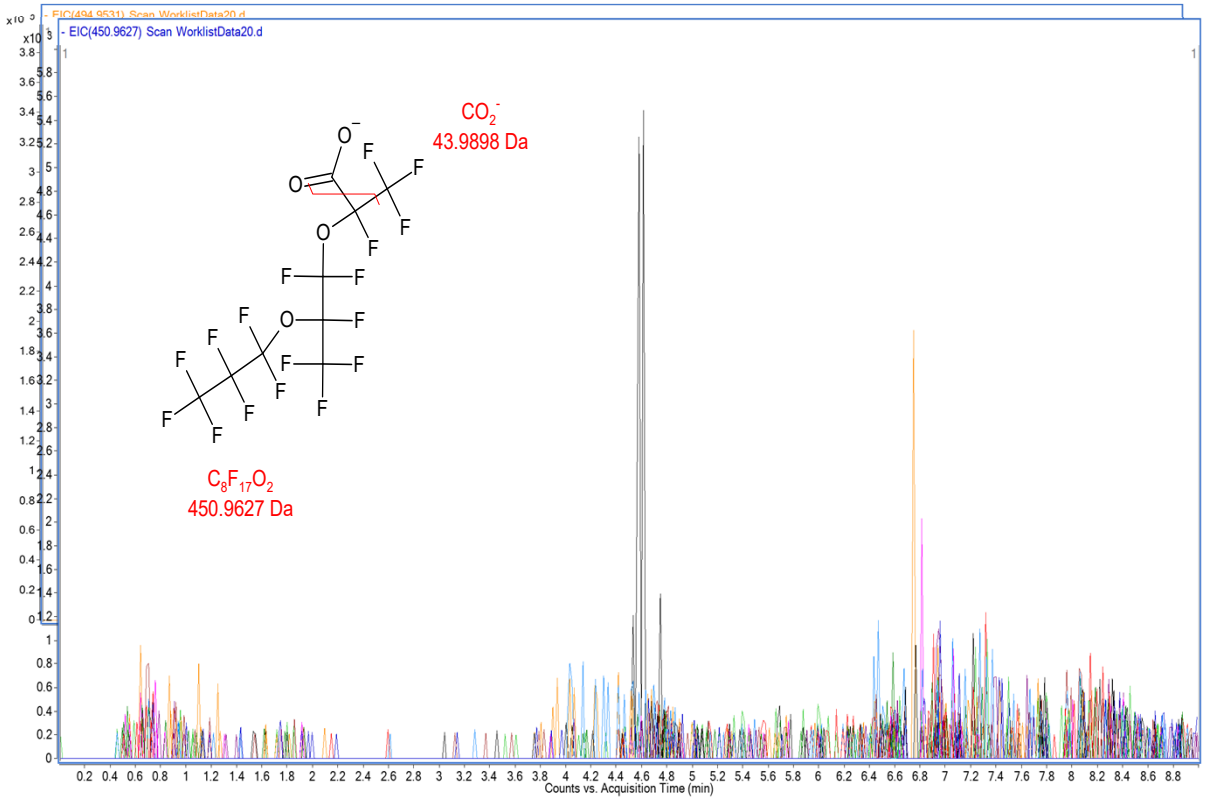

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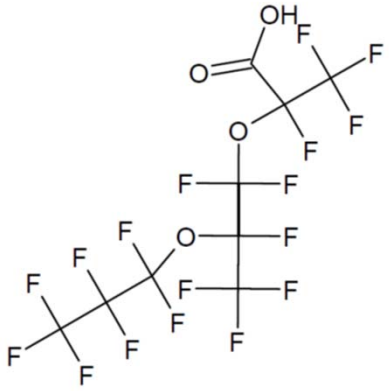

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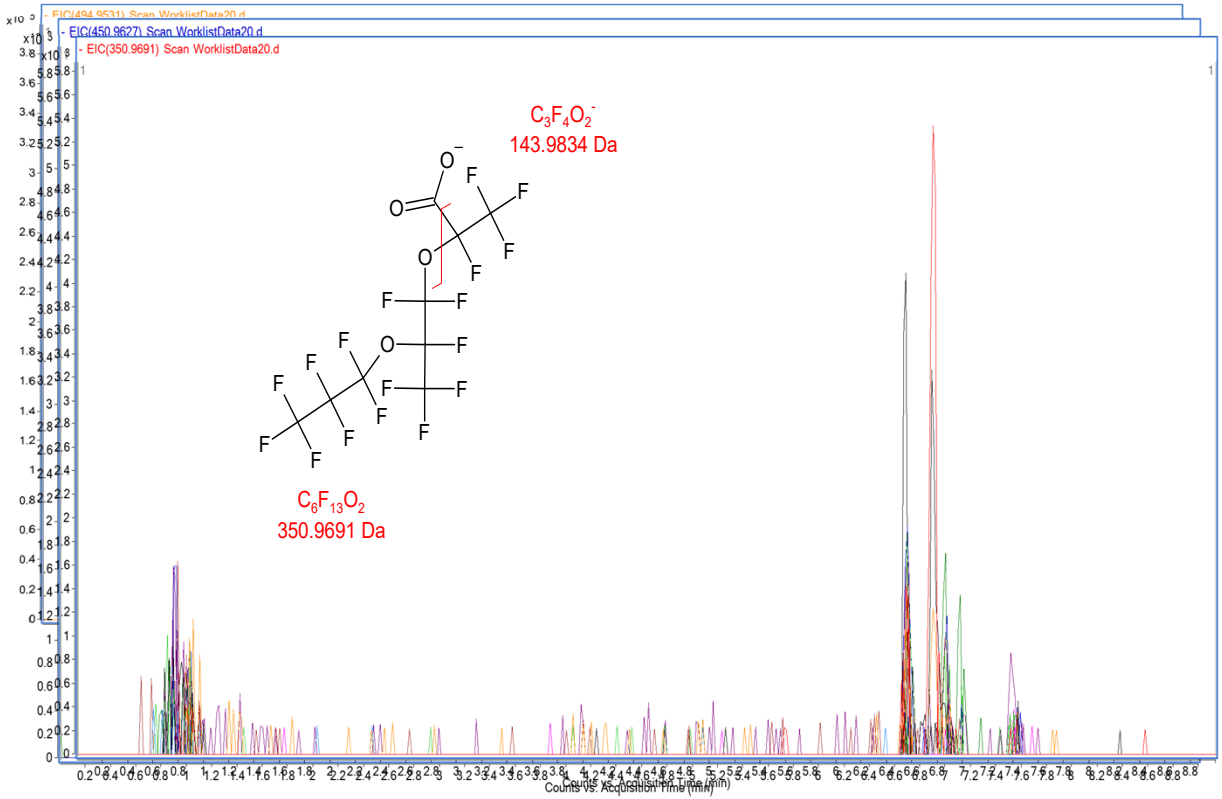

Pan et al., 2017 ES&T

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Xiaoqing River China near fluoropolymer production facility

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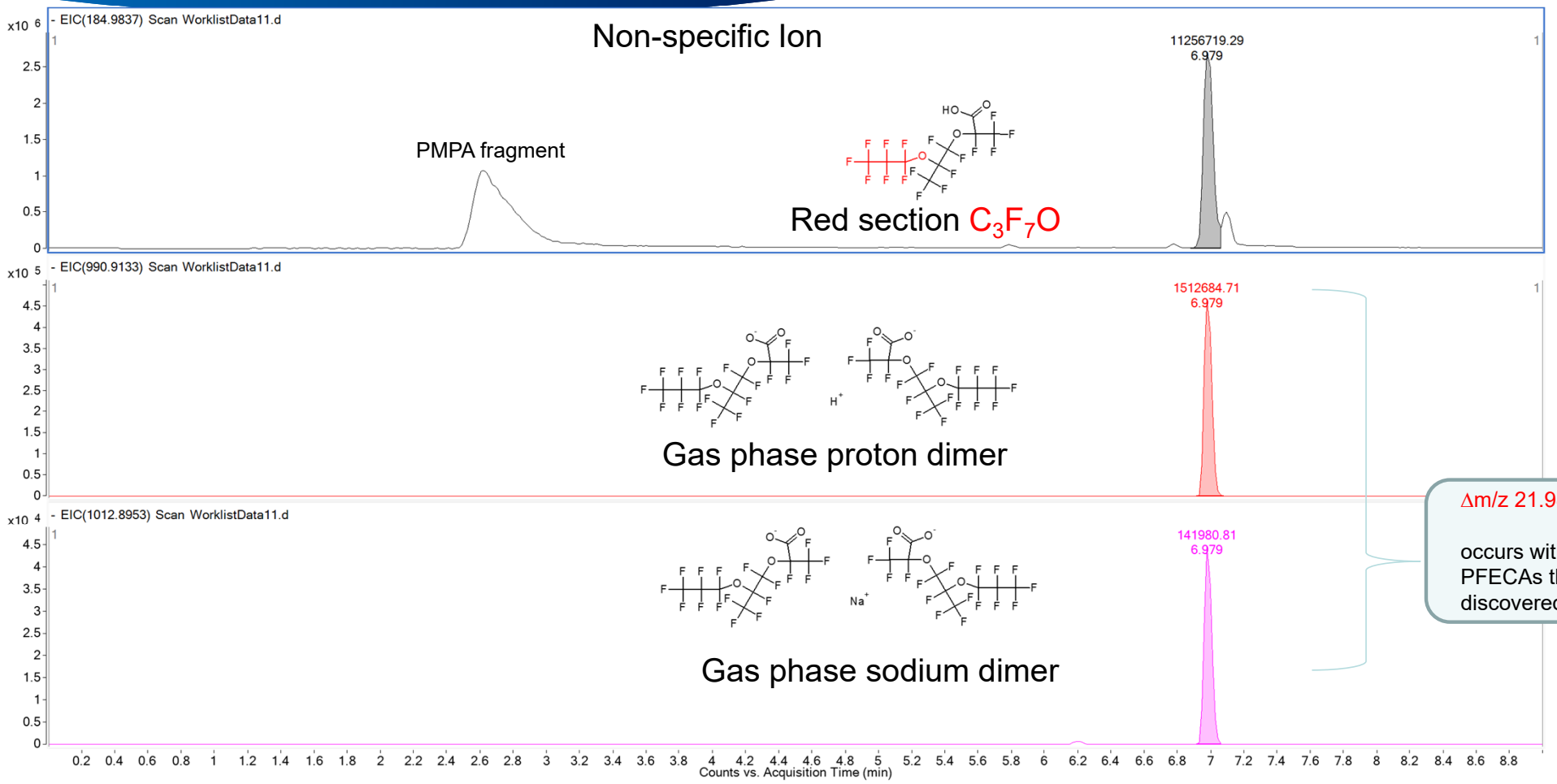
Retrospective Analysis

Three TOFMS ions consistent with HFPO-TA

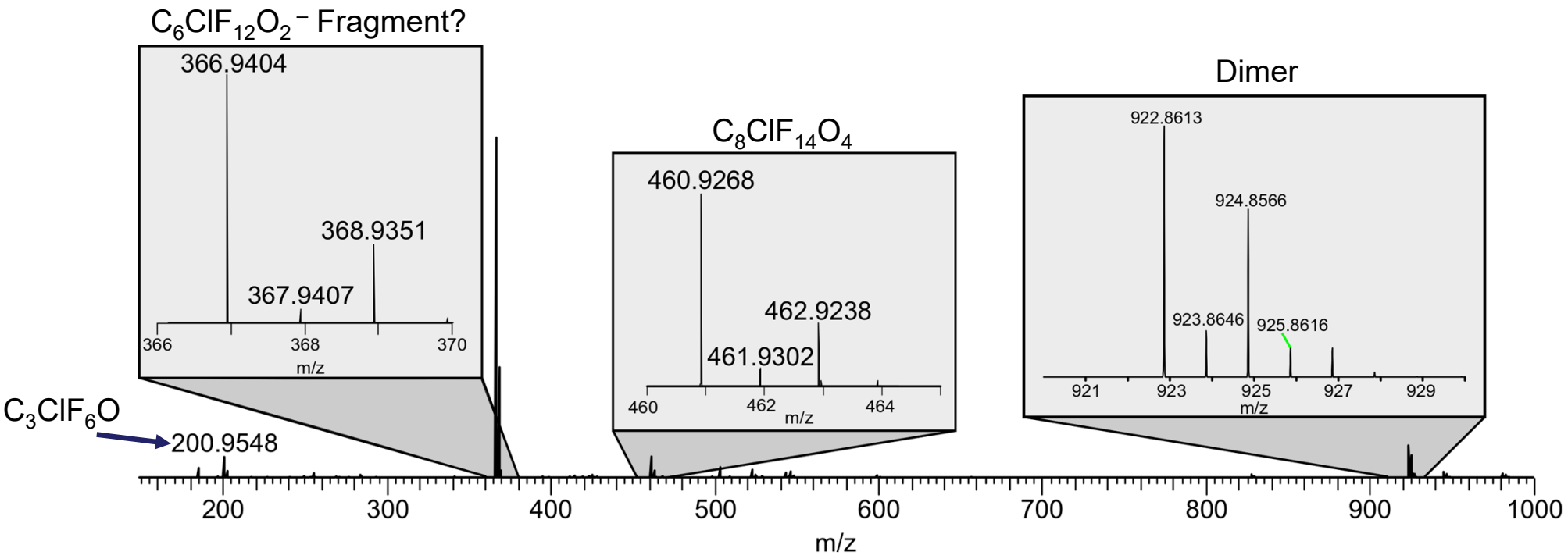


Δm/z 21.9819

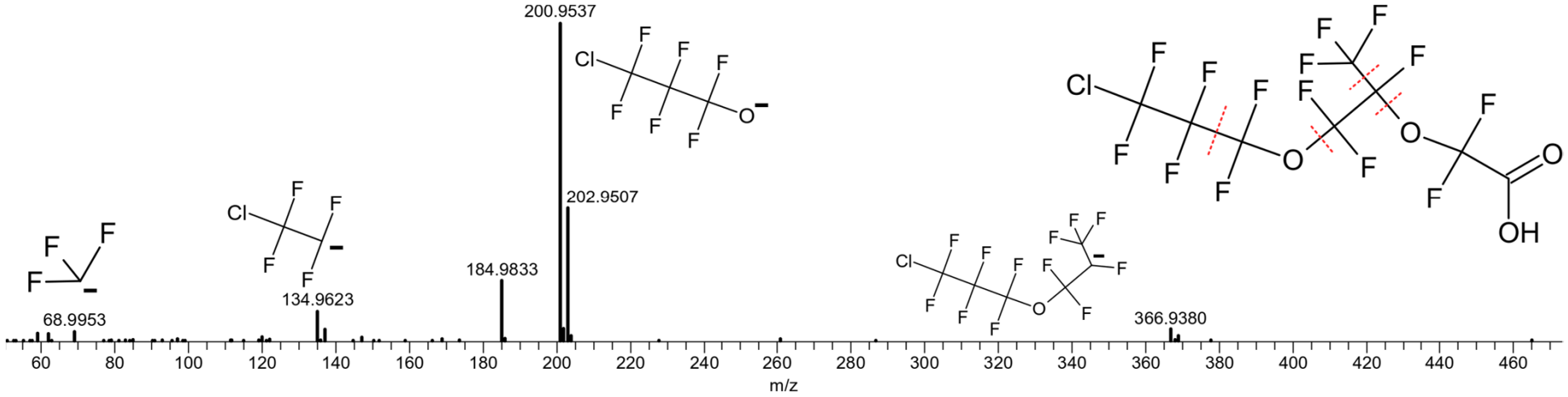
occurs with all PFECAs thus far discovered.

Novel Compound Identification

460.9268*2+1.00784 = 922.8614

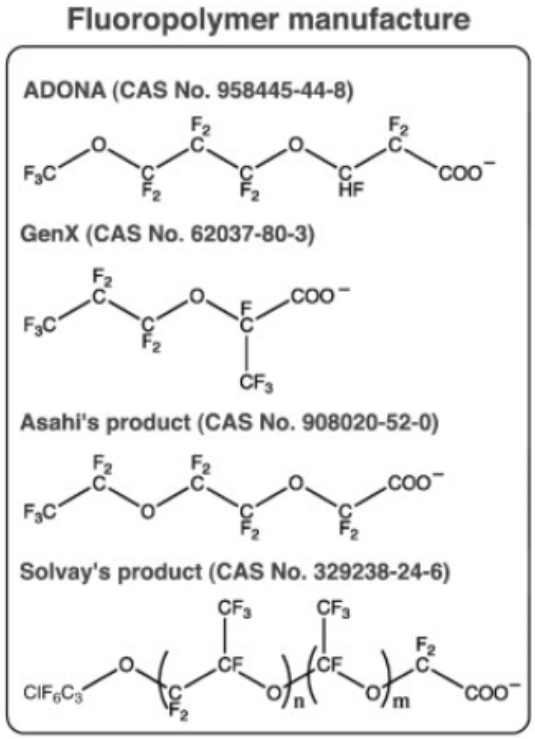


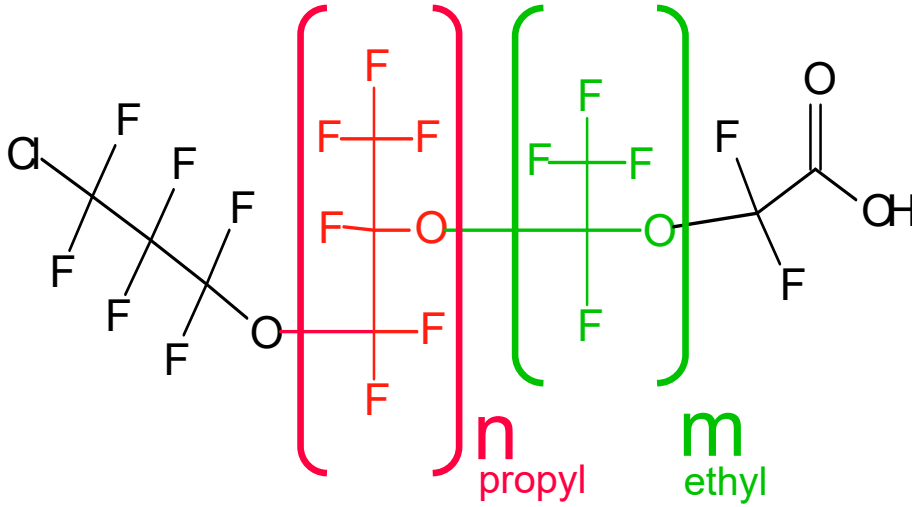
Structural Elucidation by MS/MS



- Unequivocal assignment of terminal Cl and ether positions based on MS/MS experiments
- Confirmation of Dimers and in-source fragments from prior slide, with additional experiments (not show)

Literature Support

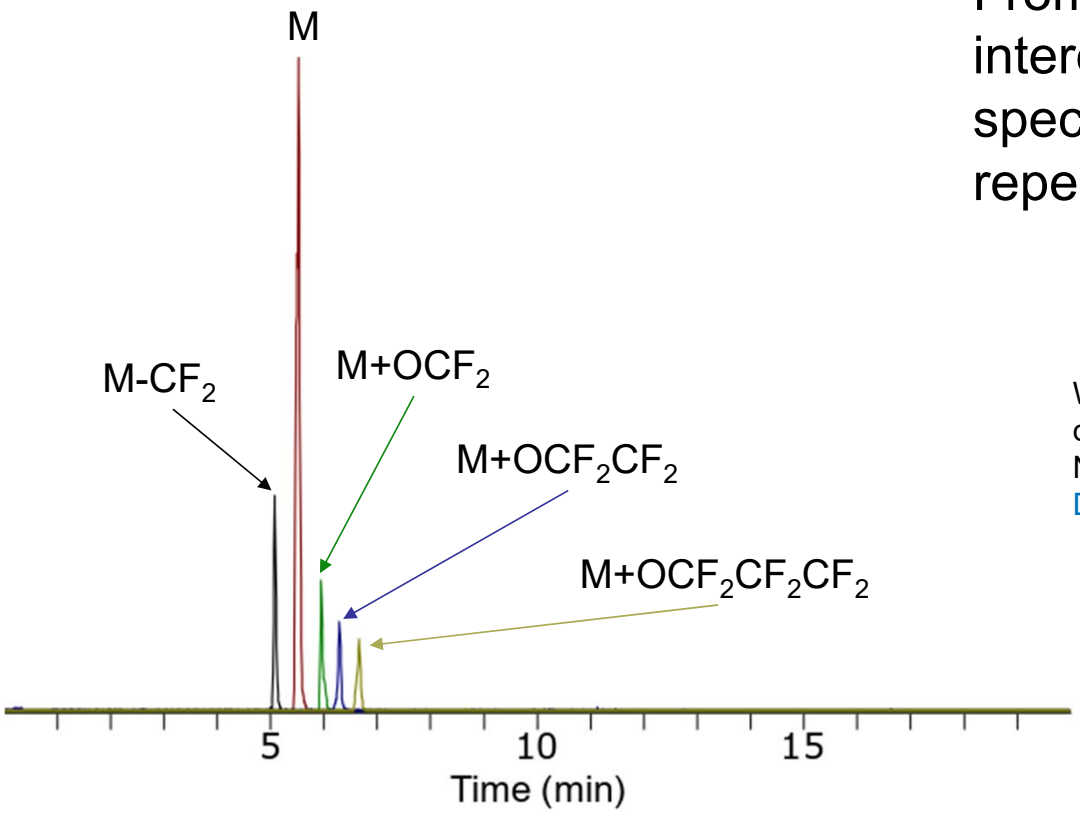




Chloro perfluoro polyether carboxylic acids ClPFPECAs(n,m)

Wang, Z., et al. (2013). Environ. Int. **60: 242.**
EFSA J, 8 (2) (2010), p. 1519, 10.2903/j.efsa.2010.1519

Homologous Fluoropolymer Series

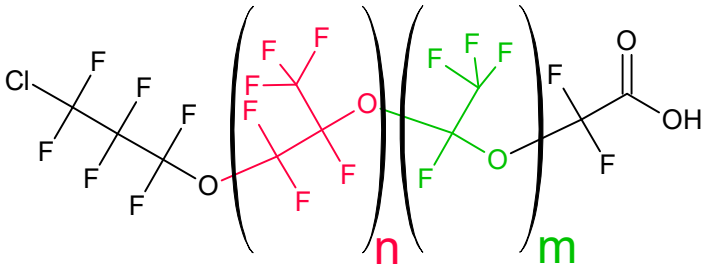


From single identified mass of interest we identified additional species related by CF_2 repeating units

Washington et al., 2020 Nontargeted mass-spectral detection of chloroperfluoropolyether carboxylates in New Jersey soils *Science*
DOI: 10.1126/science.aba7127

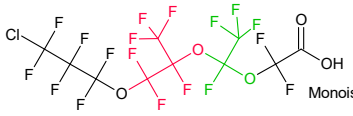
Structural Homologs

CAS 329238-24-6



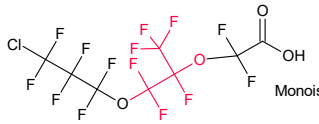
propyl, ethyl

ClPFECA 1,1



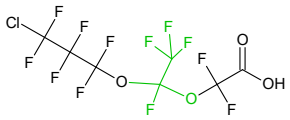
Monoisotopic Mass: 577.922508 Da

ClPFECA 1,0



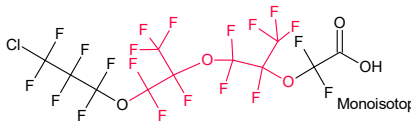
Monoisotopic Mass: 461.933981 Da

ClPFECA 0,1



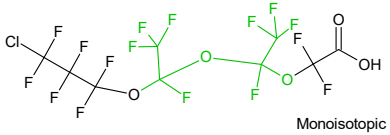
Monoisotopic Mass: 411.937175 Da

ClPFECA 2,0



Monoisotopic Mass: 627.919315 Da

ClPFECA 0,2



Monoisotopic Mass: 527.925702 Da

Some Take Home Points

- You only see what you are looking for
- HRMS has a role to discover the undiscovered
- HRMS should be used in concert with LRMS or other methods
- Retrospective analysis is possible

Questions?

Contact Information
strynar.mark@epa.gov

The views expressed in this presentation are those of the author(s) and do not necessarily represent the views or policies of the U.S. Environmental Protection Agency.