Novel PFAS analysis using high resolution accurate mass spectrometry

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Global Technical Marketing, SCIEX

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MKT-28000-A

SCIEX
The Power of Precision

Presentation outline

- Brief PFAS introduction
- Importance of accurate mass spectrometry in PFAS analysis
- 4 projects:
  - Resolving endogenous interferences in human plasma/blood
  - Interferences in food matrices
  - Alternative fragmentation technique (EAD) for structural elucidation of PFAS in fire-fighting foams
  - Kendrick mass defects for the detection of novel PFAS from “GenX” contaminated river water and sediment in North Carolina, USA

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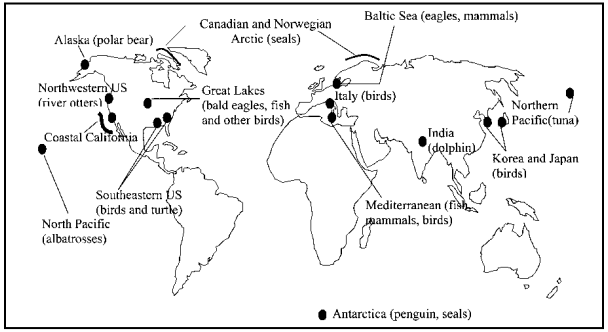
PFAS: poly- and perfluoroalkyl substances

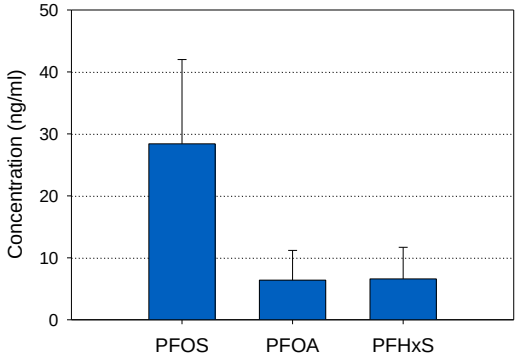
IN 2001, TWO *MONITORING* STUDIES DREW ATTENTION TO THE GLOBAL CONTAMINATION OF PFAS …

Wildlife (PFOS only)

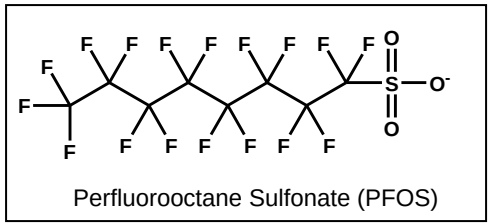


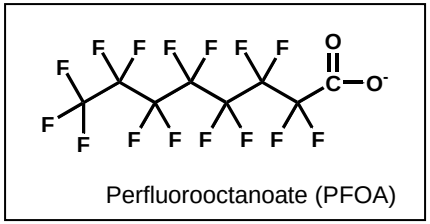
Giesy & Kannan, ES&T, 2001, 35, 1339-1342

Human Serum – United States



Hansen et al., ES&T, 2001, 35, 766-770

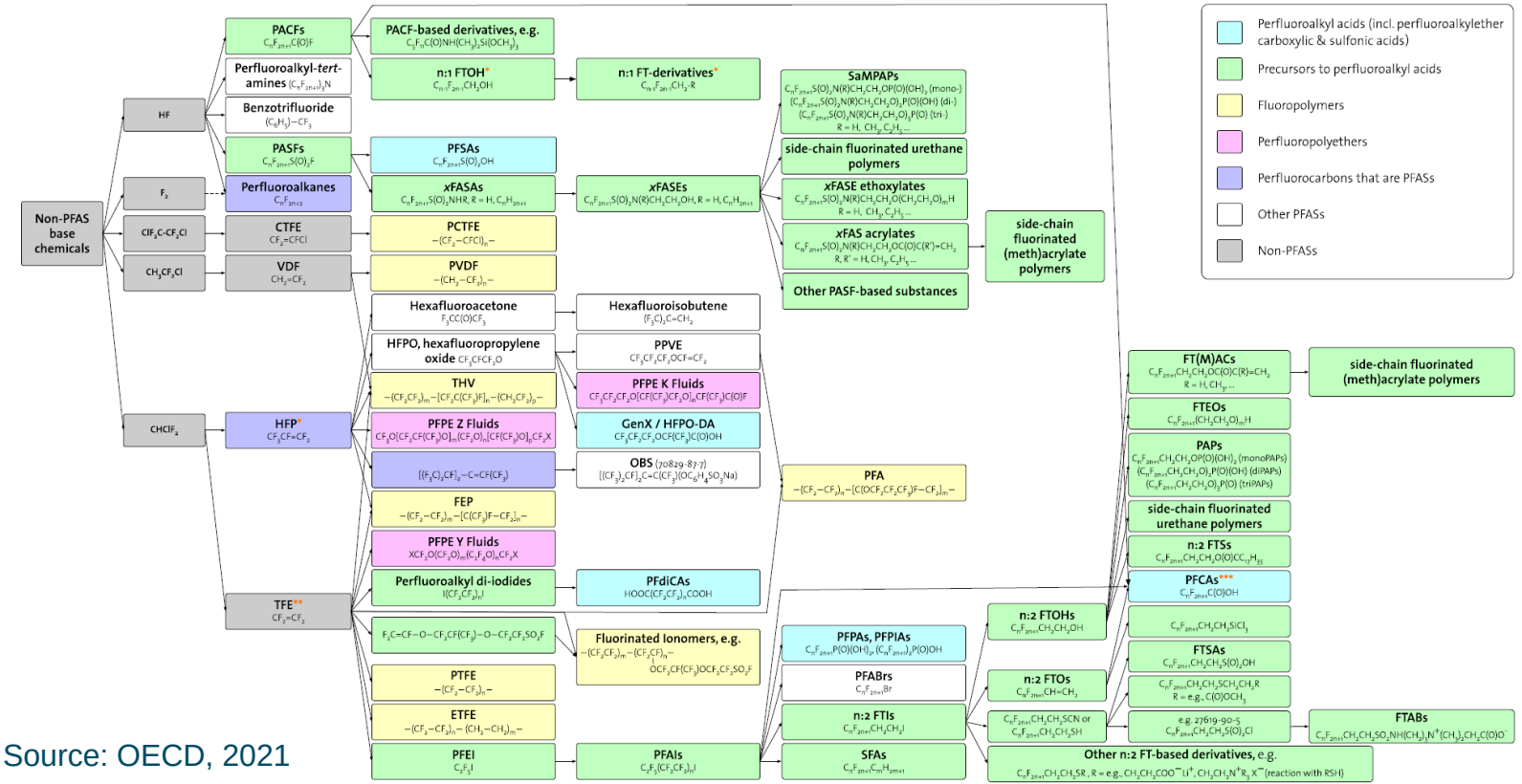




- Used primarily for their water and oil repellency properties (e.g. “stain resistance”) but also as surfactants (e.g. fire-fighting foam or AFFF)
- ~5000 individual PFAS used in commerce, comprising >200 “use categories” (Glüge *et al.*, *Environ. Sci. Processes Impacts*, 2020)
- **PFAS are numerous, diverse and complex!**

PFAS uses

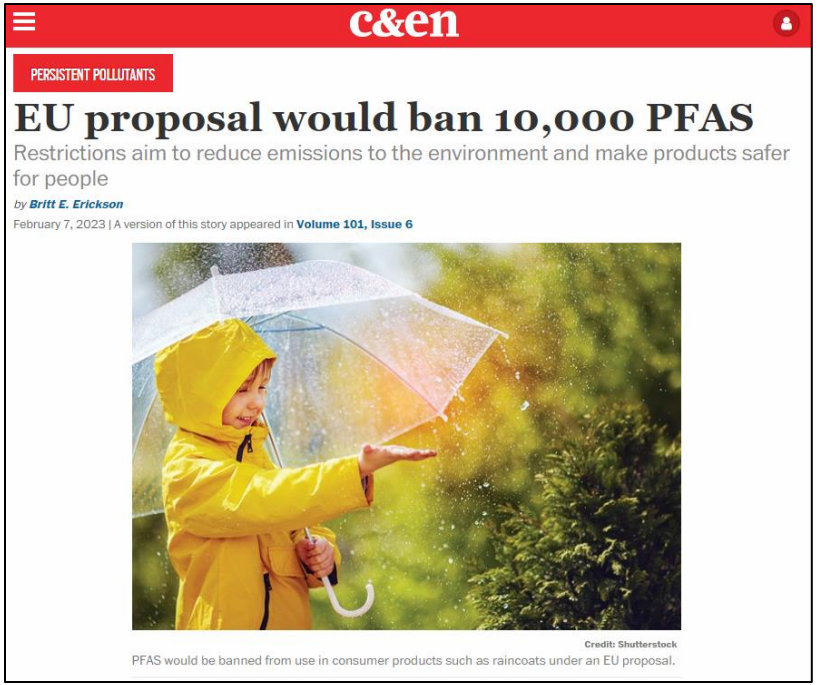
PFAS are complex!



Source: OECD, 2021

PFAS regulations: proposed EU ban

- **February 2023:** European Chemicals Agency (ECHA) proposed ban of production, use and sale of 10,000 PFAS in the European Union



c&en

PERSISTENT POLLUTANTS

EU proposal would ban 10,000 PFAS

Restrictions aim to reduce emissions to the environment and make products safer for people

by **Britt E. Erickson**

February 7, 2023 | A version of this story appeared in **Volume 101, Issue 6**

Credit: Shutterstock

PFAS would be banned from use in consumer products such as raincoats under an EU proposal.

Feb. 14, 2023, 5:00 AM; Updated: Feb. 14, 2023, 1:17 PM

'Staggering' Impact Foreseen on US Firms From EU PFAS Ban (2)

Pat Rizzuto
Reporter

Listen

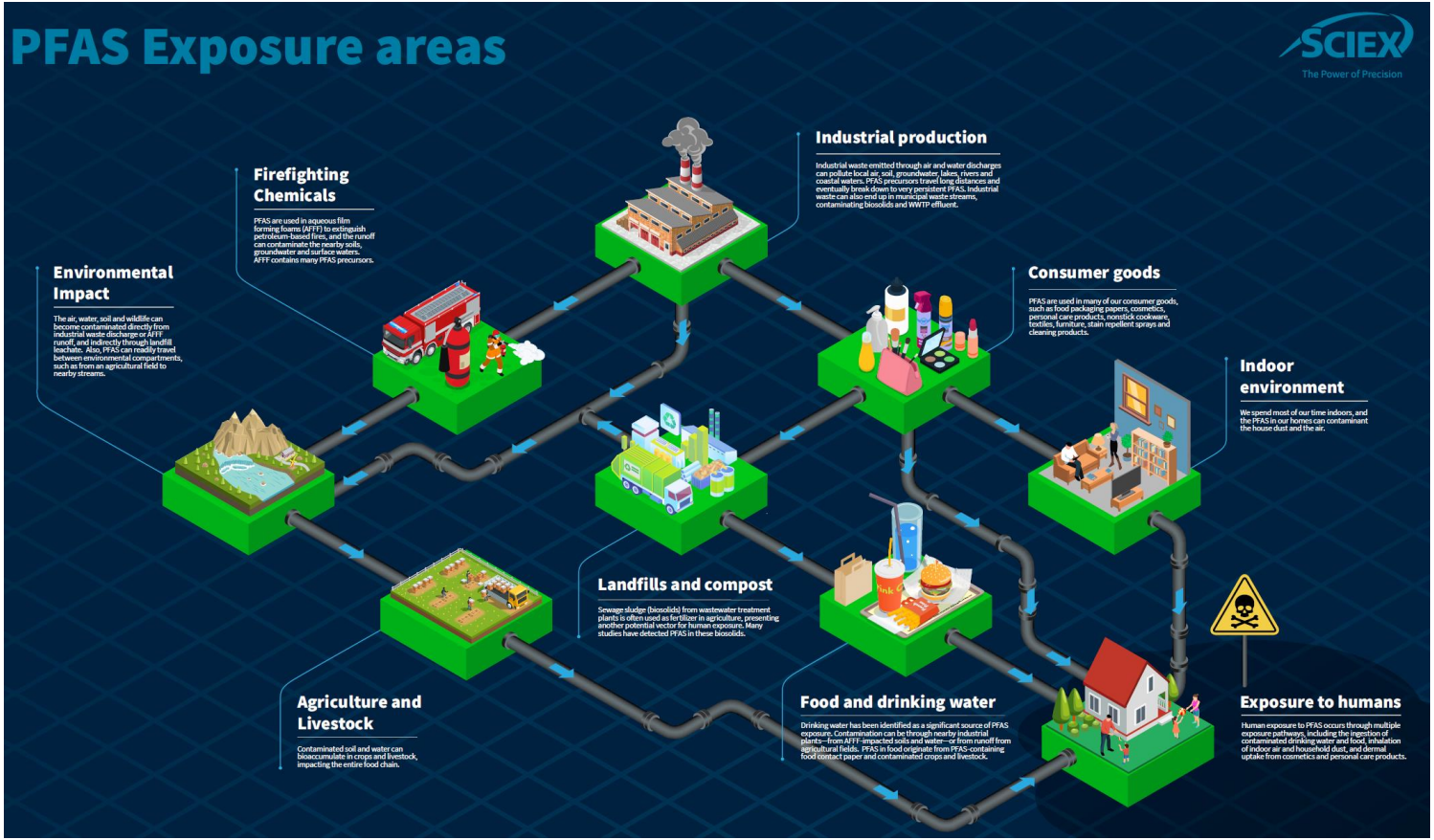
- Proposed PFAS ban could affect any exporter to the EU
- European Chemicals Agency to discuss proposal on April 5
- Practice Center: International Trade (Bloomberg Law subscription)

Related Stories

Ban On PFAS Use And Production Proposed In European Union (1)
Feb. 7, 2023, 11:00 AM

Source: Bloomberg Law. February 14, 2023

Sources of human exposure: PFAS lifecycle



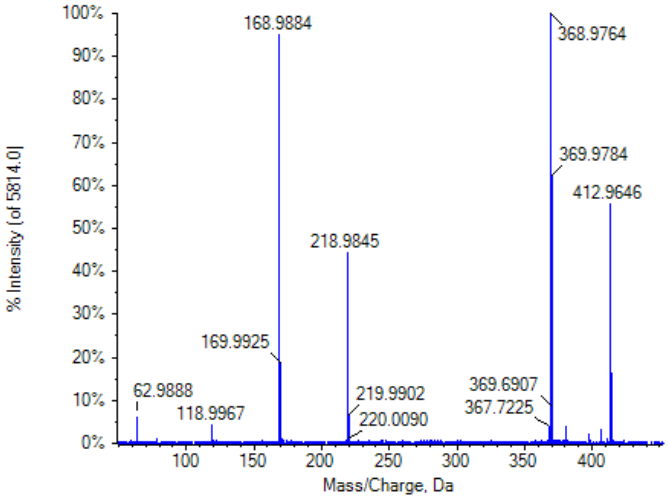
Unique features of a QTOF versus TripleQuad

- Q1 (mass filter) and Q2 (collision cell) are same as TripleQuad
- Q3 is replaced by very fast scanning time-of-flight tube (TOF)
  - Allows for *high quality, accurate mass* full scan MS data
  - Precursor scans (TOF MS) and fragment scans (TOF MSMS)
- Applications?
  - High resolution MRM quantitation (MRMHR); accurate mass fragments results in greater compound specificity
  - Nontarget acquisition with suspect screening; MS/MS product scan for compound confirmation
  - Unknown compound ID

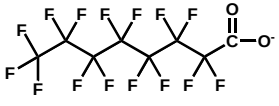
X500R QTOF

Why accurate mass spectrometry for PFAS?

- Compounds will break apart into characteristic fragments which generally represent pieces of the original (precursor) molecule
- **Fragmentation pattern can reveal the chemical structure**
- TOF instruments obtain high resolution fragment masses resulting in greater specificity



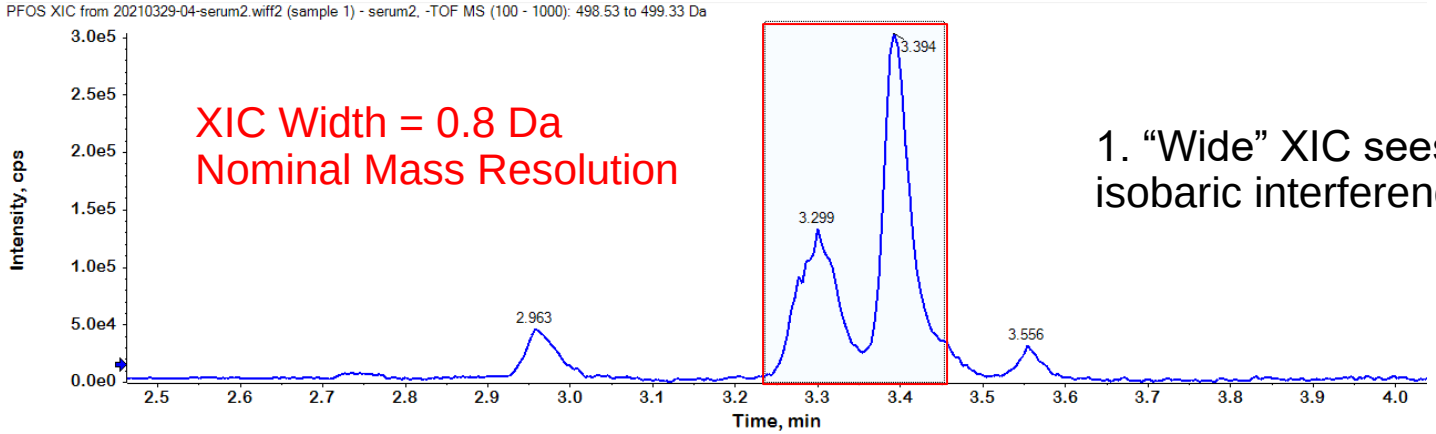
Perfluorooctanoate (PFOA)



PFOS Interferences In Serum

Serum Sample – “Nominal Mass” XIC for PFOS

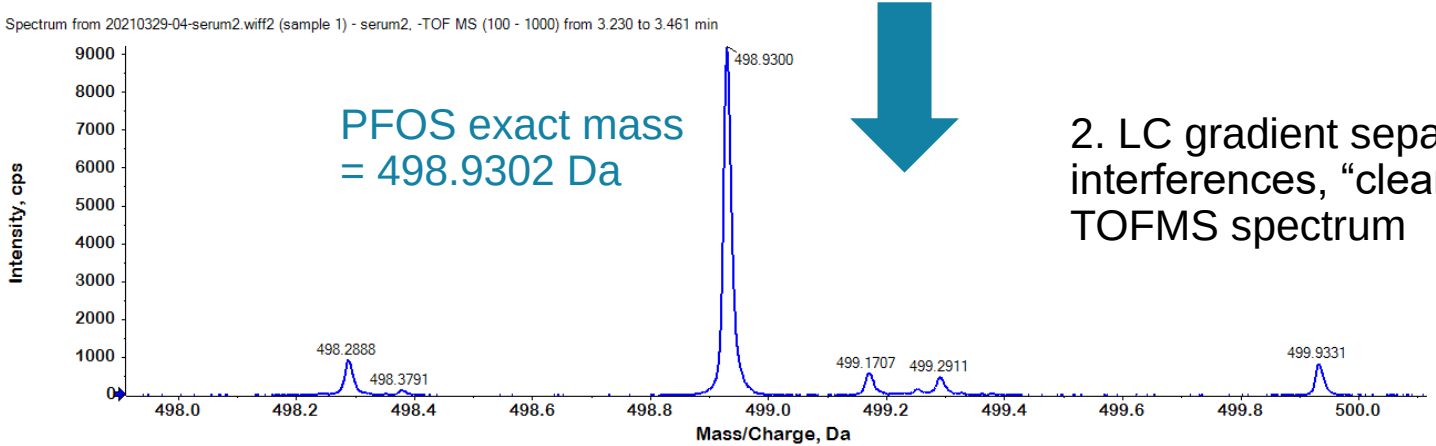
XIC



XIC Width = 0.8 Da
Nominal Mass Resolution

1. “Wide” XIC sees several isobaric interferences

TOFMS

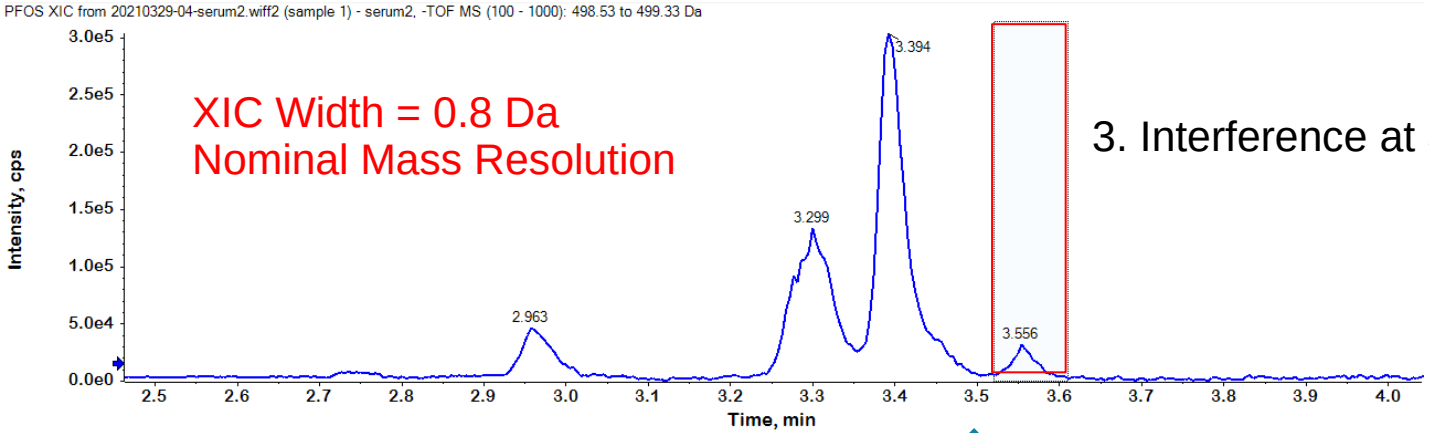


PFOS exact mass
= 498.9302 Da

2. LC gradient separates interferences, “clean” TOFMS spectrum

Serum Sample – “Nominal Mass” XIC for PFOS

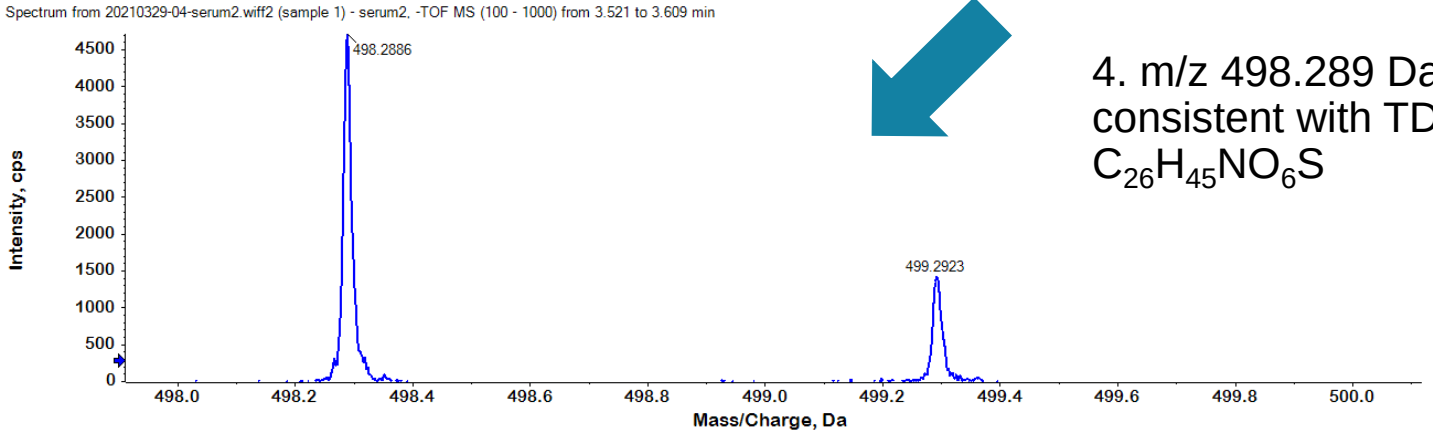
XIC



XIC Width = 0.8 Da
Nominal Mass Resolution

3. Interference at 3.6 min

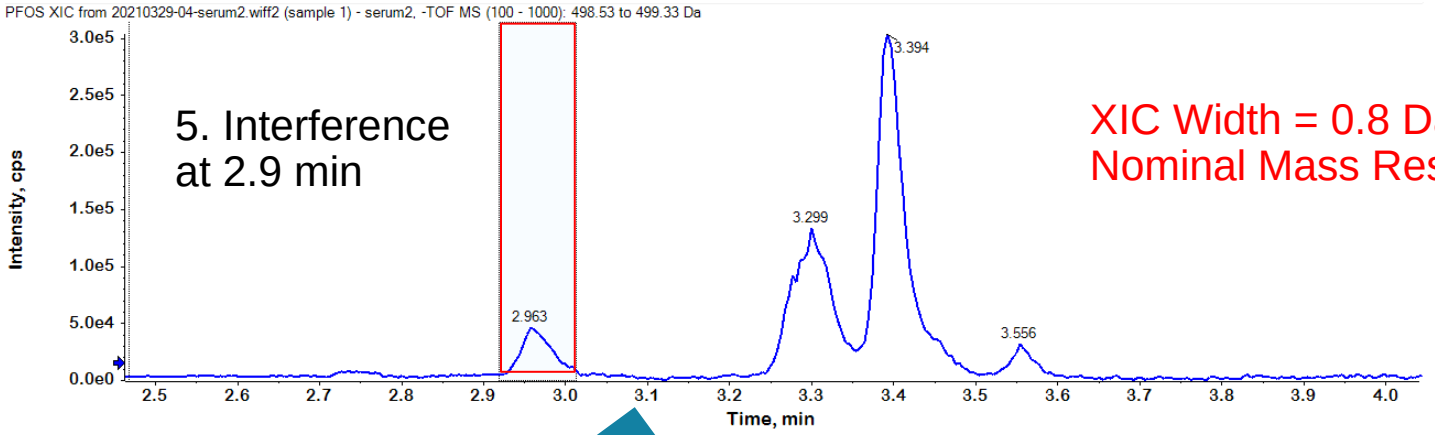
TOFMS



4. m/z 498.289 Da, consistent with TDCA, $C_{26}H_{45}NO_6S$

Serum Sample – “Nominal Mass” XIC for PFOS

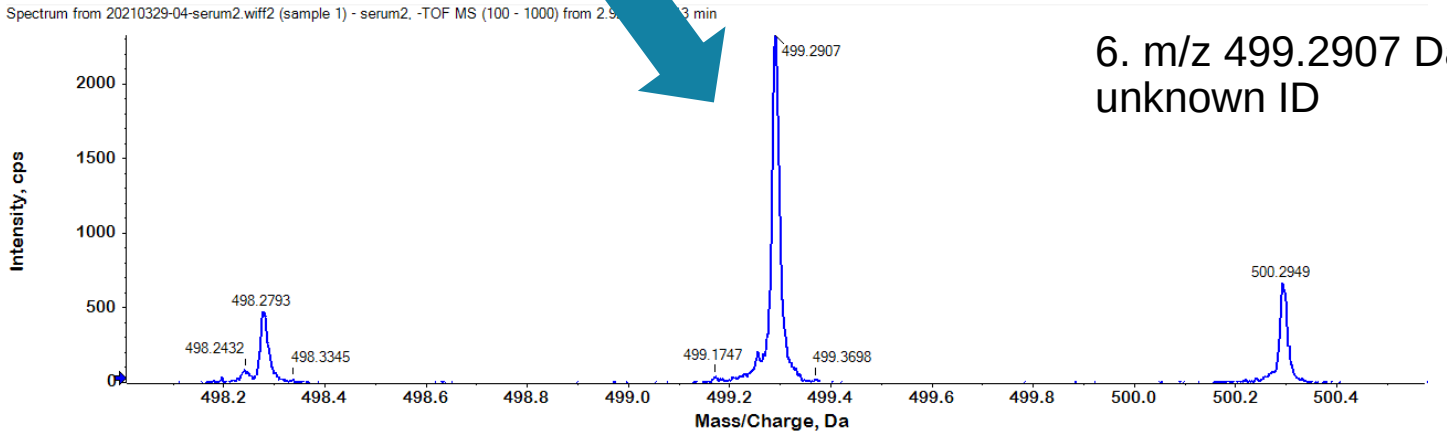
XIC



5. Interference at 2.9 min

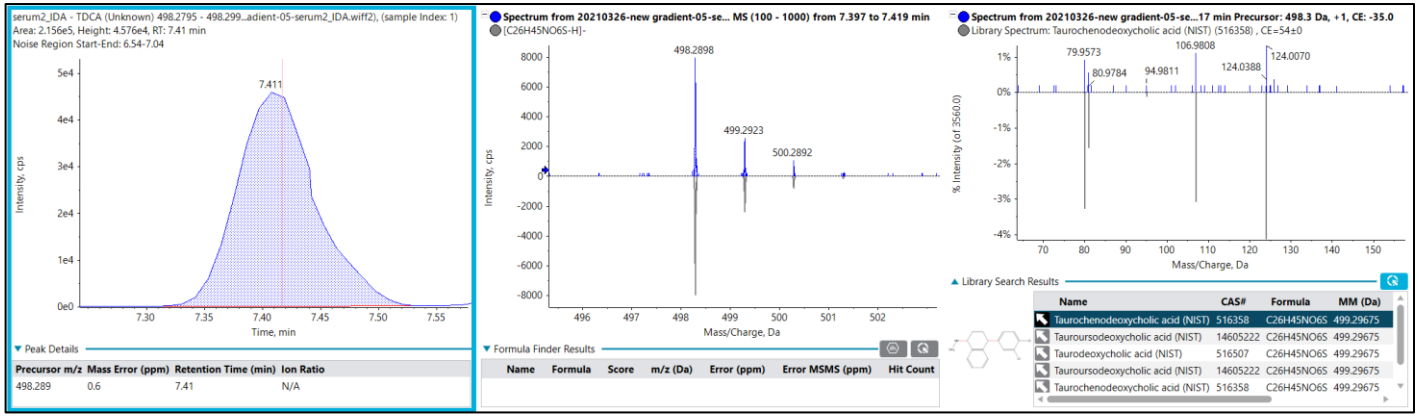
XIC Width = 0.8 Da
Nominal Mass Resolution

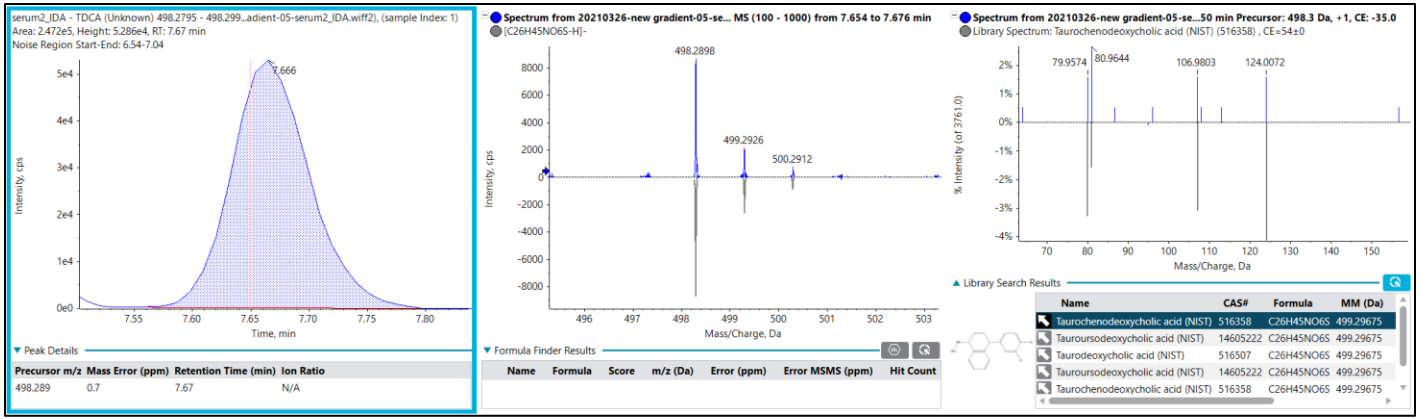
TOFMS



6. m/z 499.2907 Da, unknown ID

PFOS Interference Identification via MS/MS Library Matching



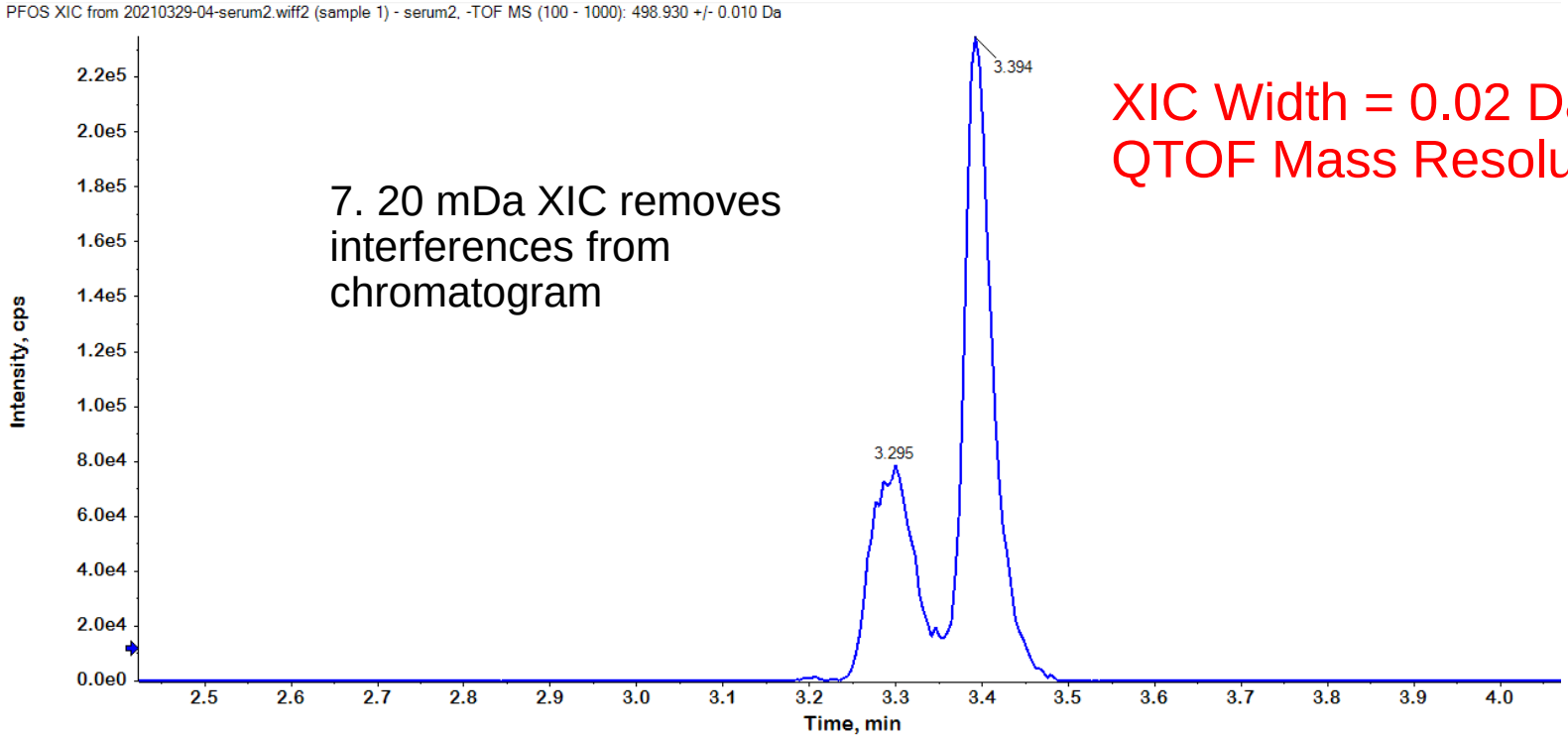


1. Extended LC gradient shows 2 compounds

2. Interferences have characteristic $[SO3]^-$ fragment

3. MS/MS library match to taurine-based cholic acids

Serum Sample – HRMS XIC for PFOS



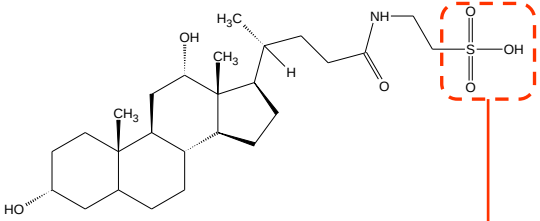
7. 20 mDa XIC removes interferences from chromatogram

XIC Width = 0.02 Da
QTOF Mass Resolution

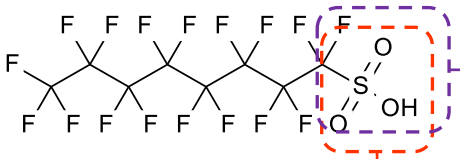
Reducing interferences in food matrices

PFOS interference in egg extract

Taurodeoxycholic acid (TDCA)
Exact mass = 498.2895

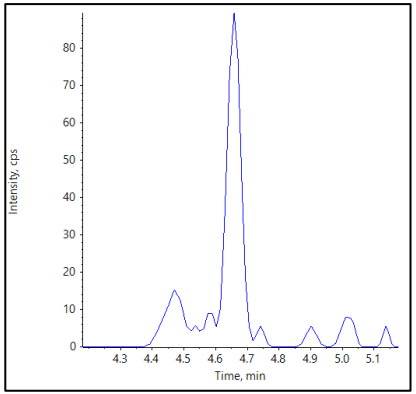


PFOS
Exact mass = 498.9302



499 > 98.9556
[FSO_3^-] fragment

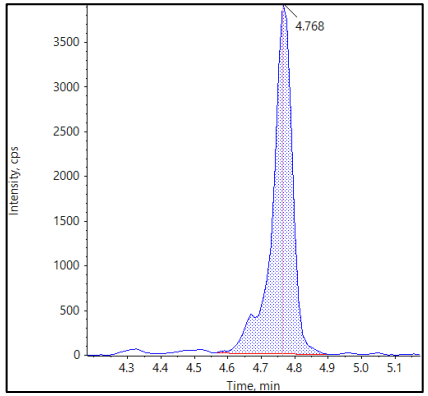
Very low signal in PFOS-specific transition

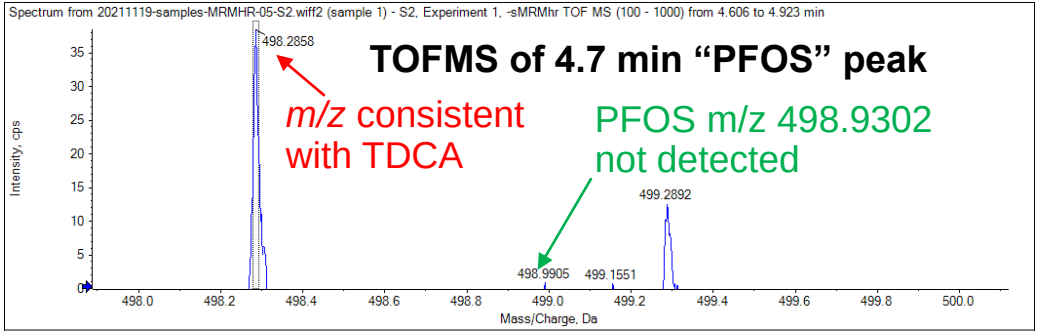


Egg extract

499 > 79.9574
[SO_3^-] fragment

TDCA or PFOS?





PFPeA interference

NOTE: PFAS with only one specific MS/MS transition (e.g. PFBA, PFPeA) should be verified using a second chromatographic separation method (i.e. the use of a secondary LC elution on a different analytical column and eluent) or another MS method (e.g. the use of high resolution MS).

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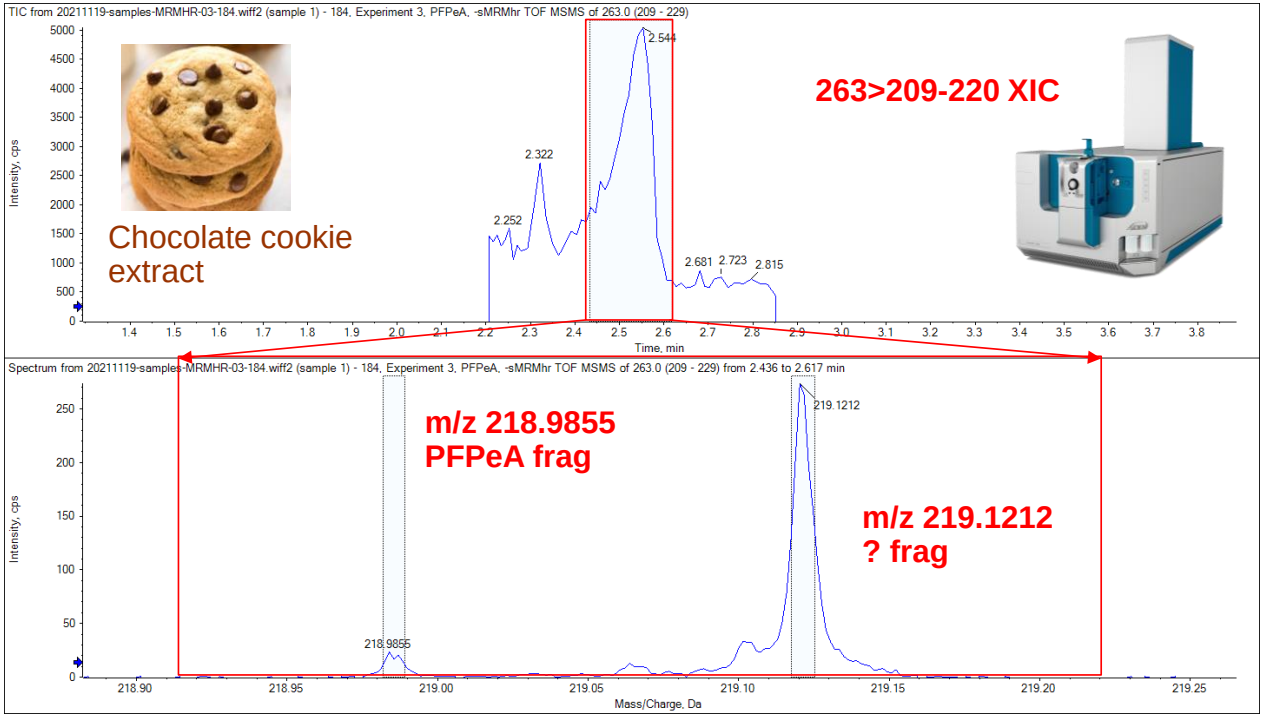
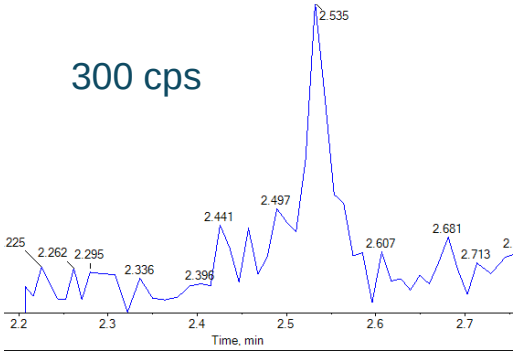
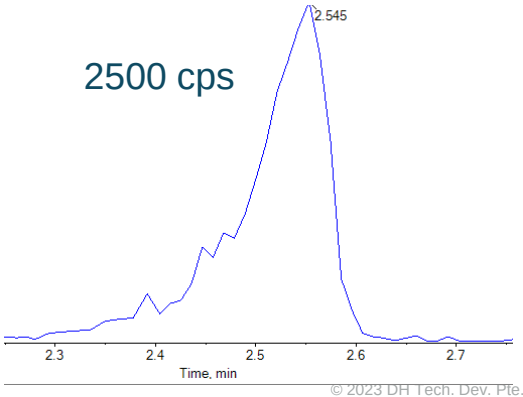
Peak co-eluting with PFPeA, but sample was confirmed to not contain PFPeA by a secondary method – what is this?



XIC of 218.9855 (PFPeA)



XIC of 219.1212 (?)



EAD fragmentation for improved PFAS structure elucidation in AFFF

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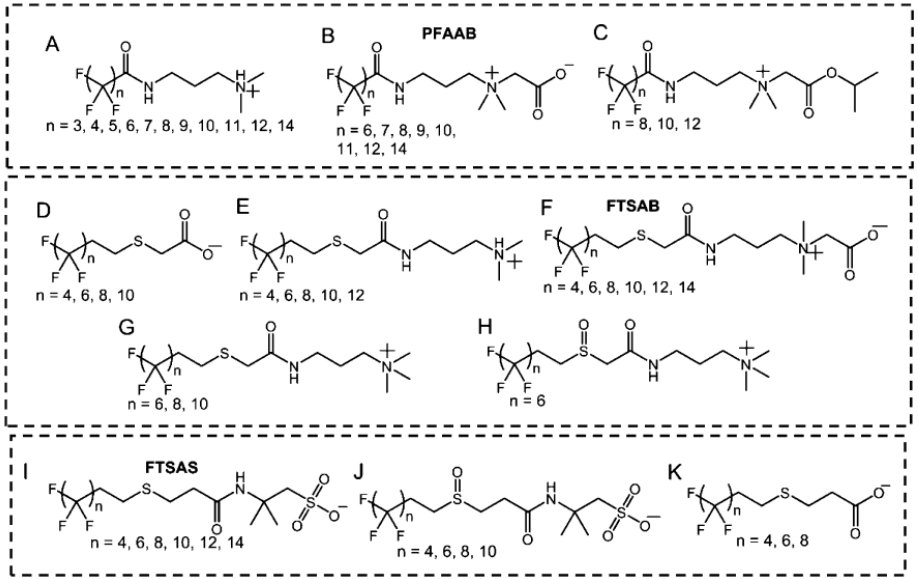
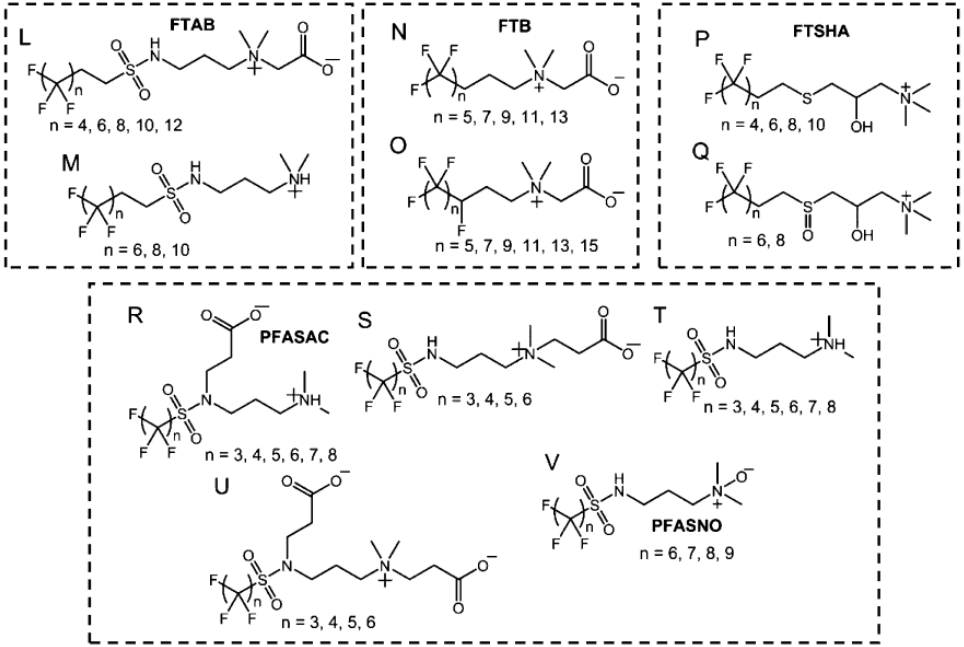
Introduction: characterizing PFAS in AFFF



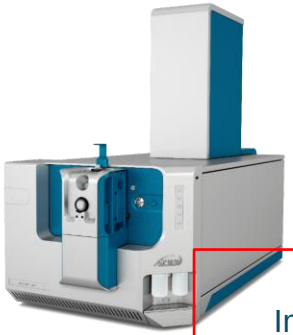
Unique AFFF-derived PFAS contain perfluorinated tail and complex alkyl headgroups



Source: D'Agostino & Mabury. *Environ. Sci. Technol.* **2014**, 48(10): 121-129

ZenoTOF 7600 system

HARDWARE ADVANCEMENTS

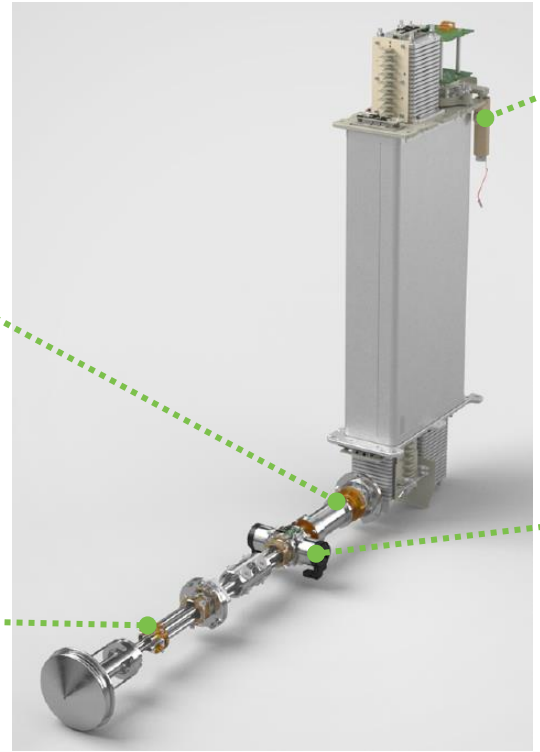


New

Zeno trap
Improved MS/MS duty cycle gain ≥90%

New

New Q0 design for improved ion transmission and maintenance



New

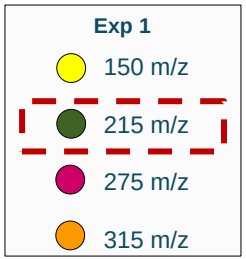
Wide dynamic range

- 5GHz, 10bit ADC with 40GHz TDC timing with 25 psec detection rate. High speed pulse counting to maintain resolution and mass accuracy >130Hz and over 5 orders LDR

New

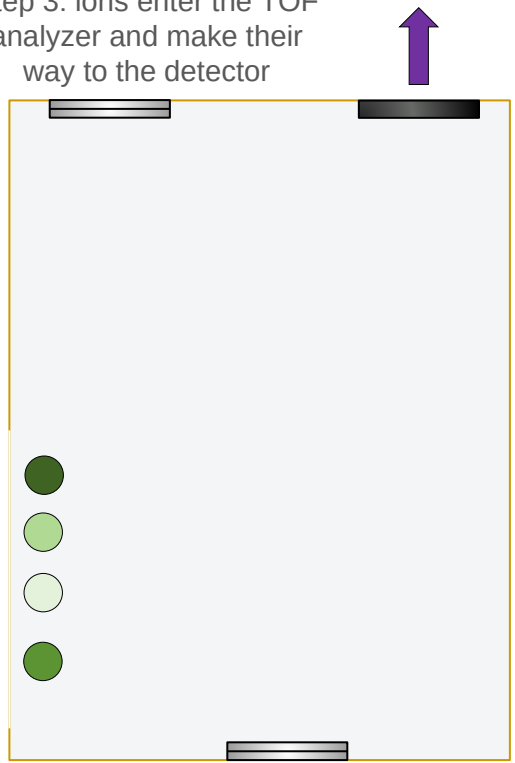
Complementary fragmentation with increased sensitivity using the EAD cell

Electron activated dissociation (EAD)



Step 2: fragmentation in EAD cell with optimized KE

Step 3: ions enter the TOF analyzer and make their way to the detector

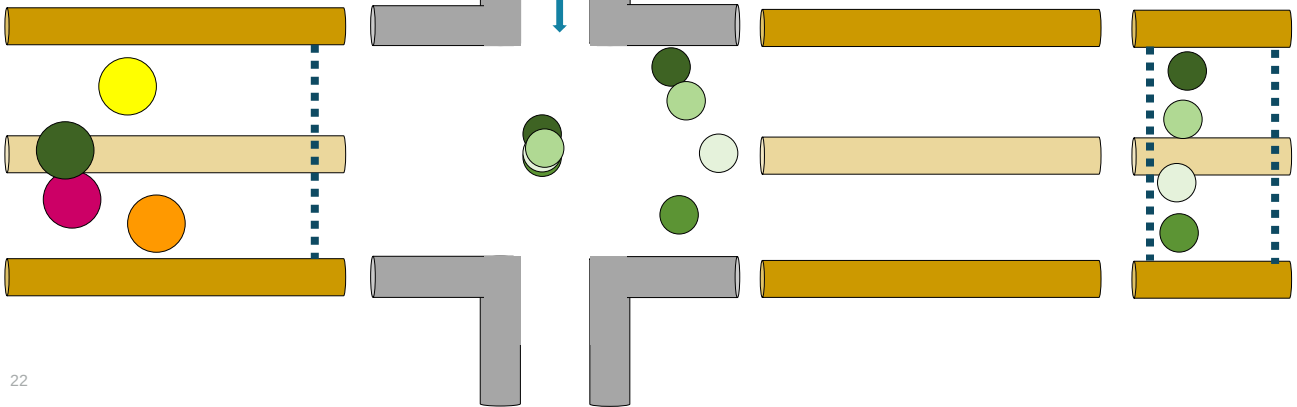


Electrons

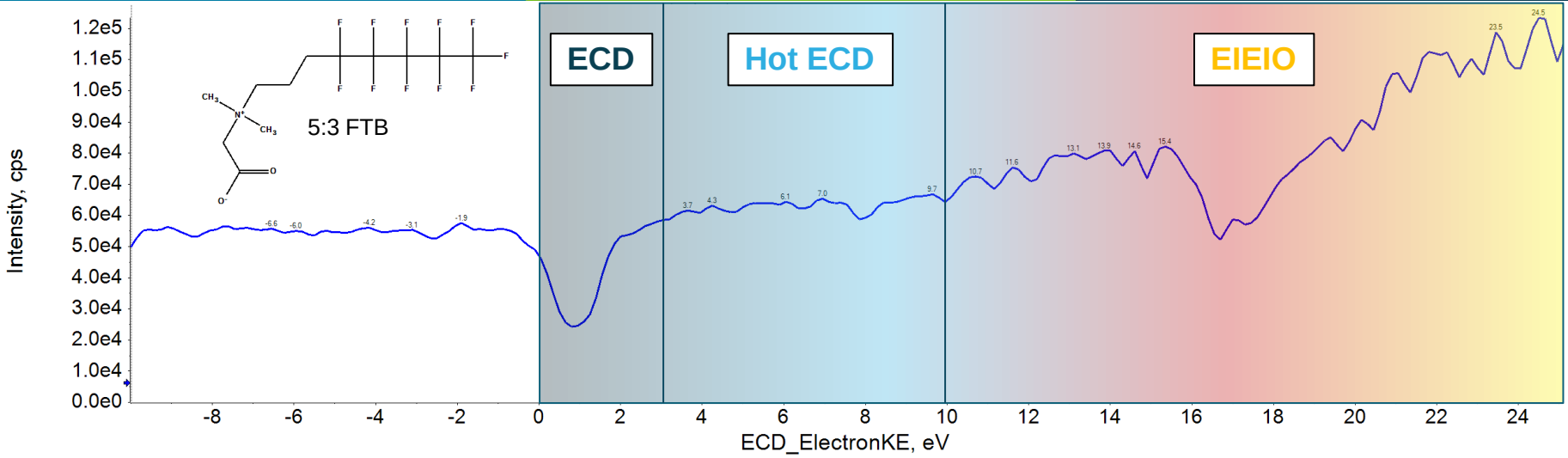
Step 1: selection of analyte ion in Q1 (215 m/z)

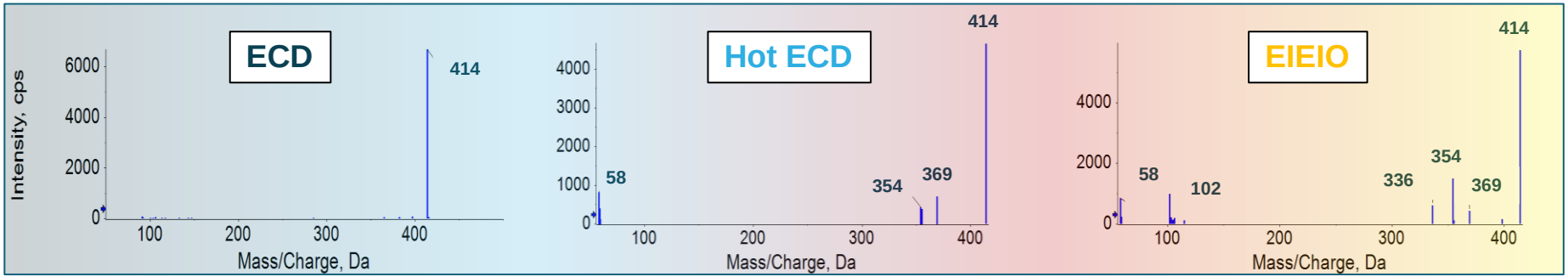
Step 2: ions travel through Q2

Step 3: Zeno trap stores all fragment ions



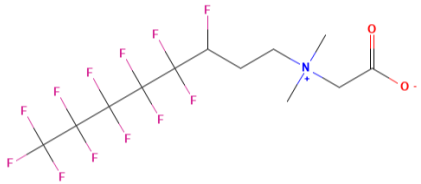
Ramping the kinetic energy



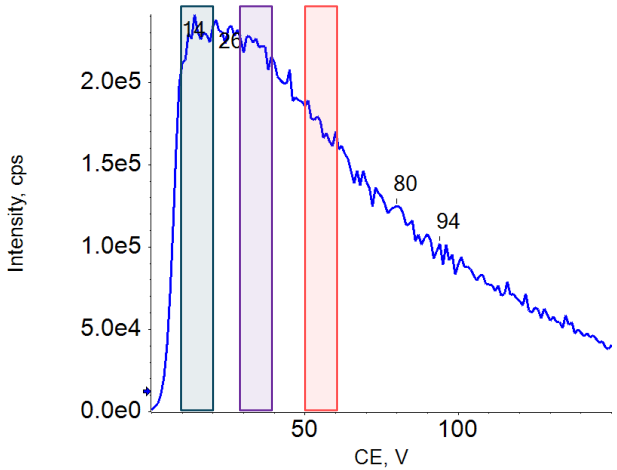


Where does EAD become useful?

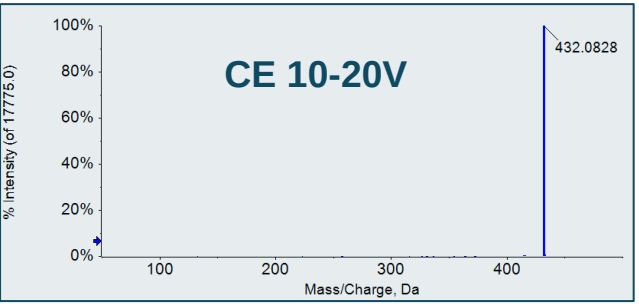
Using CID

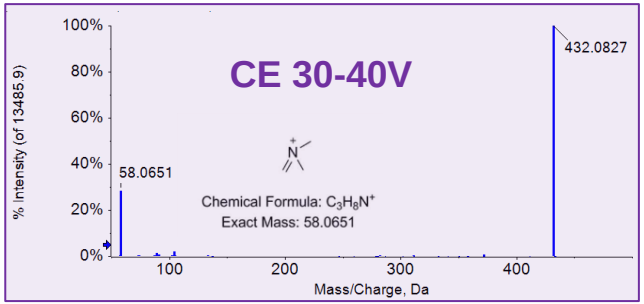


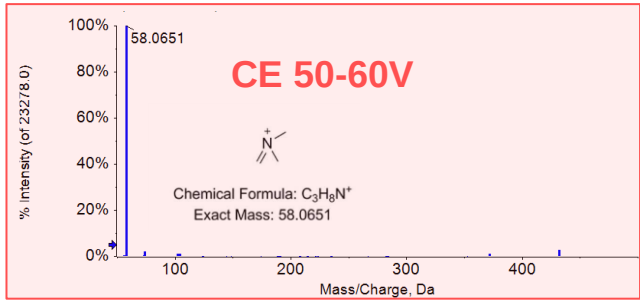
5:1:2 FTB



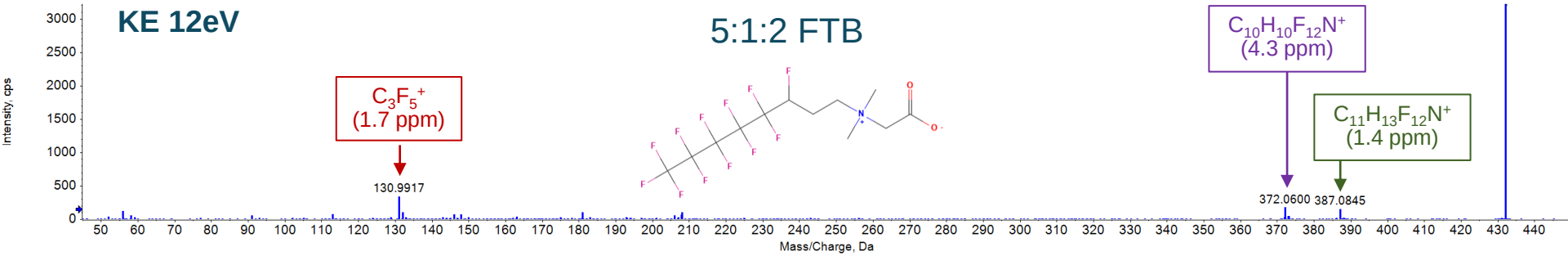
Fragments	Formula
432.0827 (Parent)	$C_{12}H_{14}F_{12}NO_2^+$
58.0651	$C_3H_8N^+$

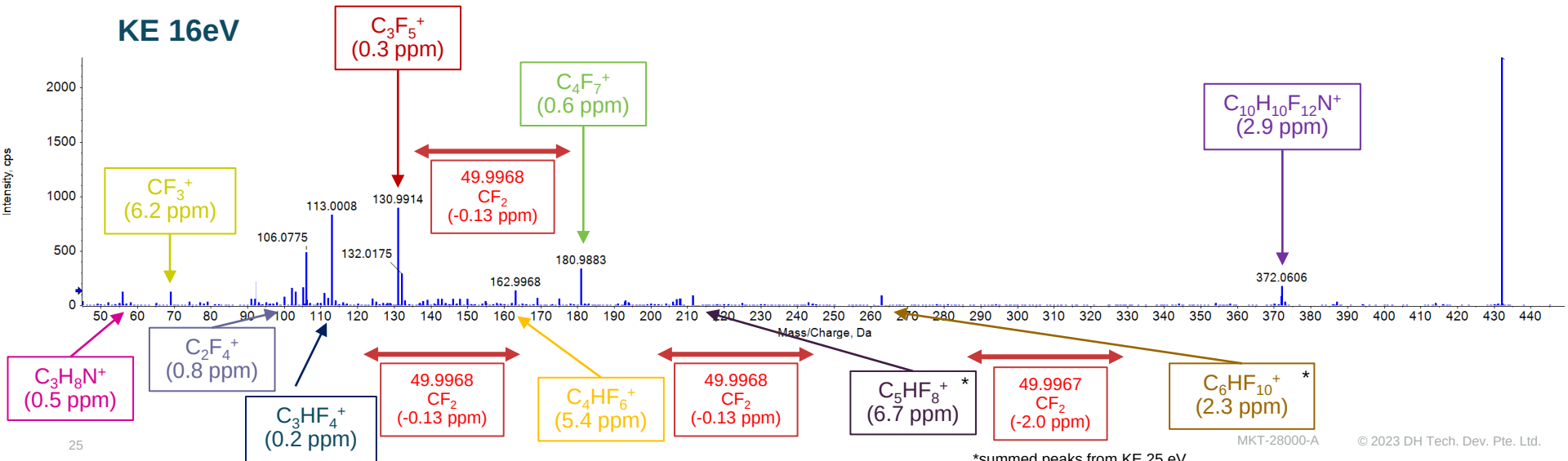






Where does EAD become useful?

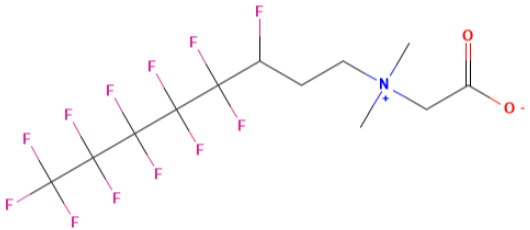




*summed peaks from KE 25 eV

Where does EAD become useful?

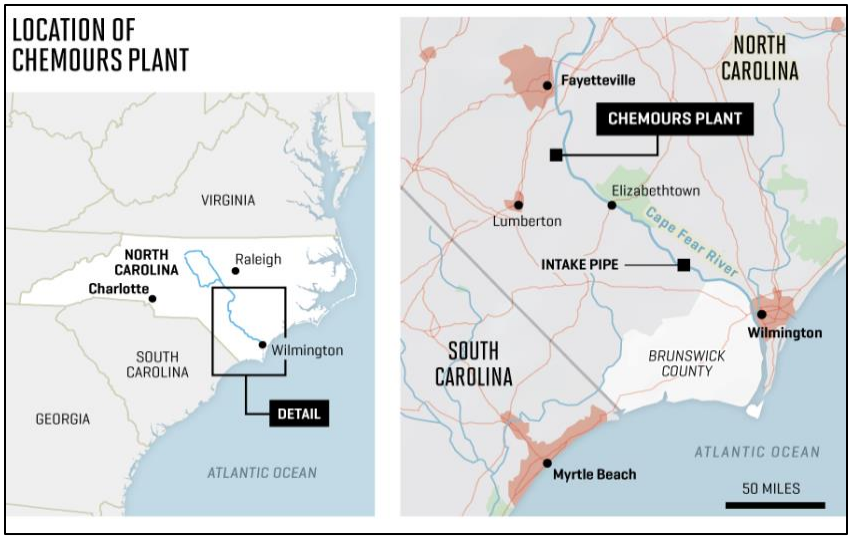
5:1:2 FTB

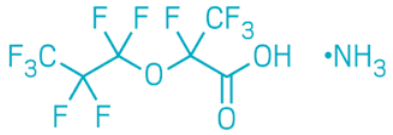


Calculated fragments formulas	CID	EAD
$C_{12}H_{14}F_{12}NO_2^+$ (Parent)	✓	✓
$C_{11}H_{13}F_{12}N^+$		✓
$C_{10}H_{10}F_{12}N^+$		✓
$C_6HF_{10}^+$		✓
$C_5HF_8^+$		✓
$C_4F_7^+$		✓
$C_4HF_6^+$		✓
$C_3F_5^+$		✓
$C_3HF_4^+$		✓
$C_3H_8F_{12}NO^+$		✓
$C_2F_4^+$		✓
CF_3^+		✓
$C_3H_8N^+$		✓
$C_3H_8N^+$	✓	✓

Suspect screening for novel PFAS in river water and sediment from North Carolina

Chemours plant: GenX contamination

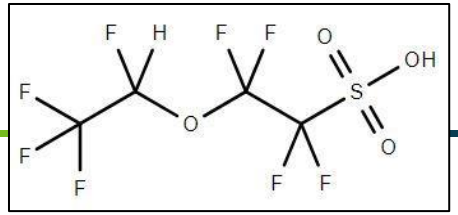


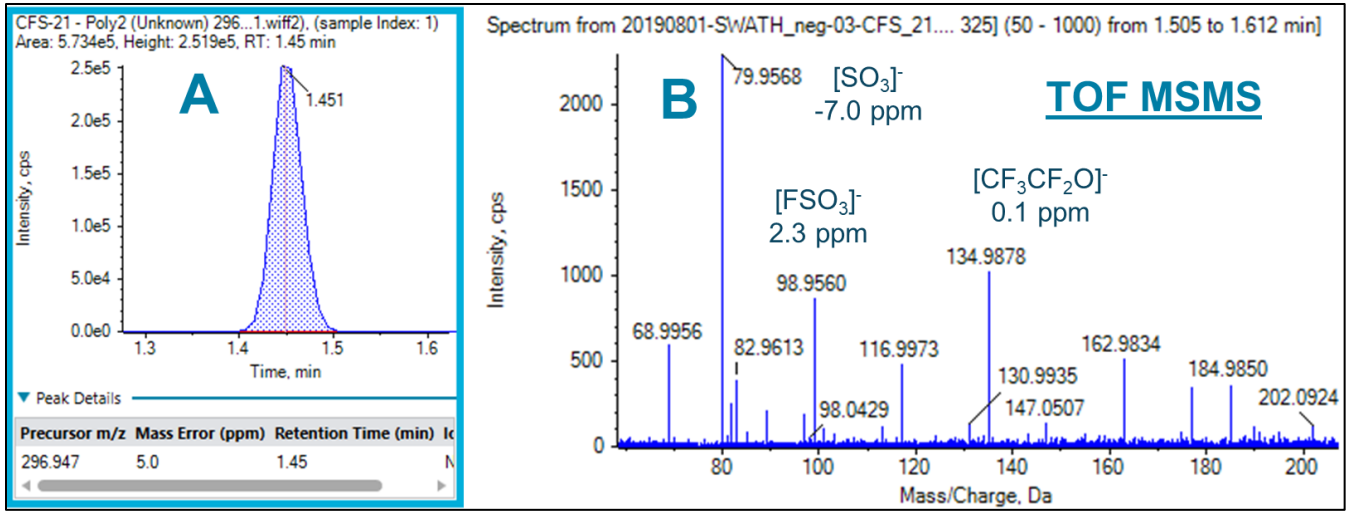


GenX

Many other “novel” ether-based PFAS!

Suspect screening: NVHOS



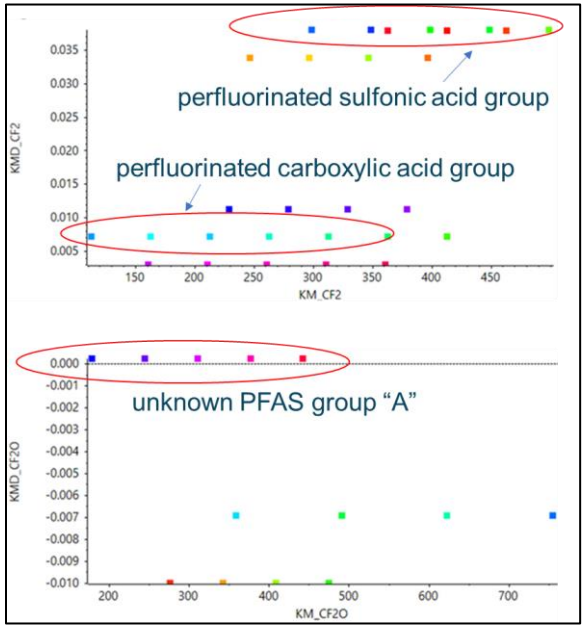


No MS/MS library entry

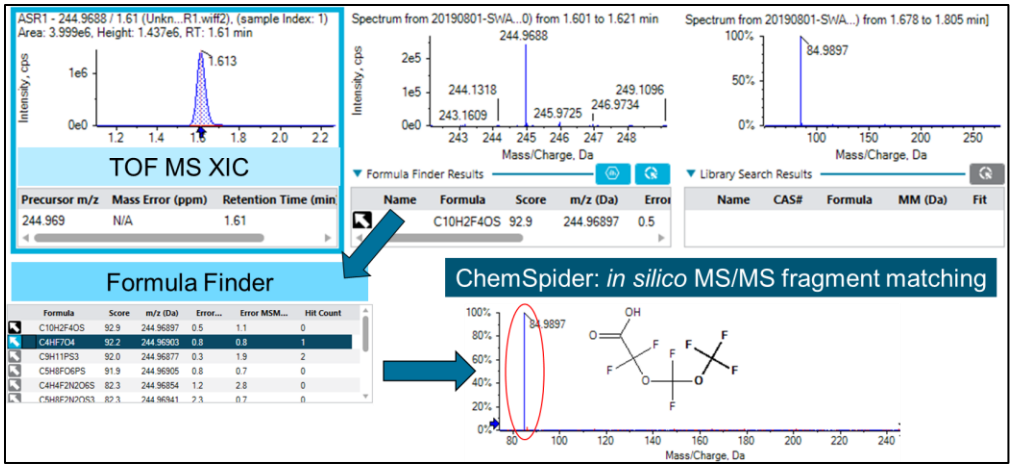
MS/MS spectrum matched to theoretical fragments from literature

Identification of NVHOS ($C_4F_8H_2O_4S$) in Cape Fear River sediment using suspect screening. Left panel (A) shows TOF MS XIC with good mass error (5 ppm). Right panel (B) shows TOF MS MS spectrum with matches to theoretical fragments. Identification confidence level 2b.

Kendrick mass defect filtering to detect novel PFAS



KMD plots from river water and sediment samples. Nine groups of homologs were identified in the KMD plot with repeating units of -CF2- (top) and -CF2O- (bottom).



Non-target analysis workflow using Formula Finder and ChemSpider in Analytics module of SCIEX OS software for the identification of PFO_2HxA in Cape Fear River aquifer water.

Summary

- Latest QTOF technology can address new PFAS research questions
- Despite 20+ years of PFAS research, many questions remain
- NTA analysis of consumer products improves our understanding of PFAS exposure and risk
- EAD fragmentation with SCIEX ZenoTOF 7600 system enhances the structural elucidation of PFAS “dark matter”
- Advanced data processing techniques (Kendrick mass defect plots) can further improve novel PFAS detection

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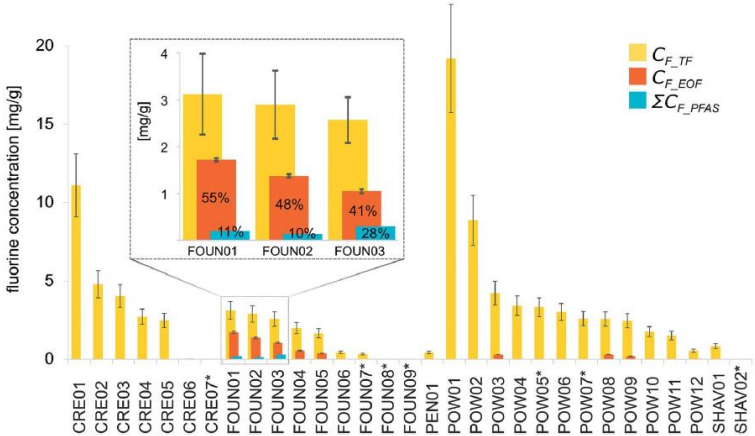
Accurate mass spectrometry for the characterization of PFAS in **cosmetic samples**

Why is this important?

- Routes of human exposure still not properly understood
- >5000 PFAS compounds used in commerce, *targeted monitoring lists include 20-30 compounds*
- Methods needed to improve understanding of PFAS risk



Yellow bars = Total Fluorine (surrogate for total PFAS)

Blue bars = PFAS from targeted LC-MS measurement

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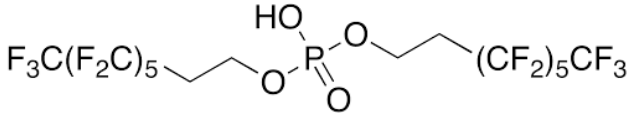
Methods

- 13 cosmetic extracts (foundation, concealer, creams)
- All samples identified as containing PFAS, labels were often vague
- Ultrasonication extraction, cleanup using SPE
- Acquisition using IDA on ZenoTOF 7600 system, PFAS-modified LC
- **Data processing**
  - Targeted suspect screening covering multiple PFAS classes
  - MS/MS library matching using SCIEX Fluorochemical library

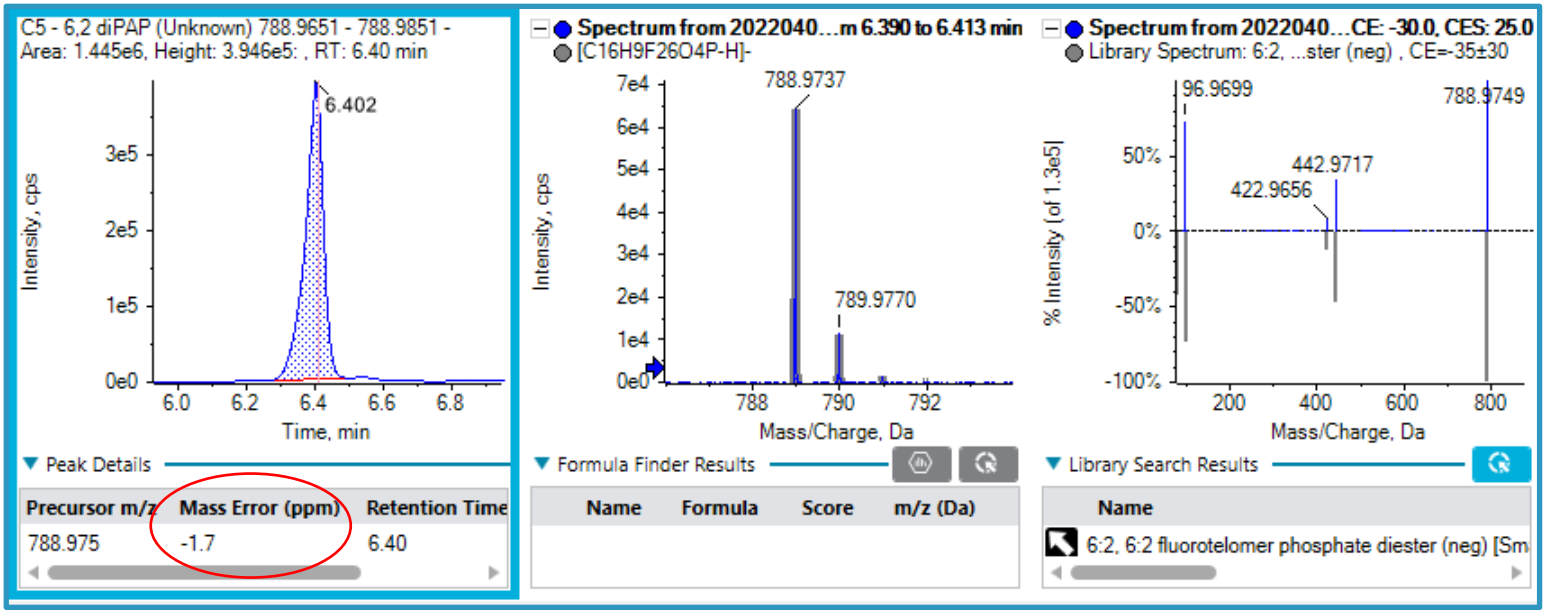
C5 – 6:2 diPAPs confirmation



Precursor XIC

TOFMS (isotope pattern)

TOFMSMS (fragmentation pattern & library matching)



MS/MS spectral library match for compound id

Detection of 6:2 diPAPs in a cosmetic sample. Compound confirmation achieved through excellent precursor mass error (left panel), good isotope pattern match (middle panel) and MS/MS spectrum match to SCIEX Fluorochemical High Resolution MS/MS library.

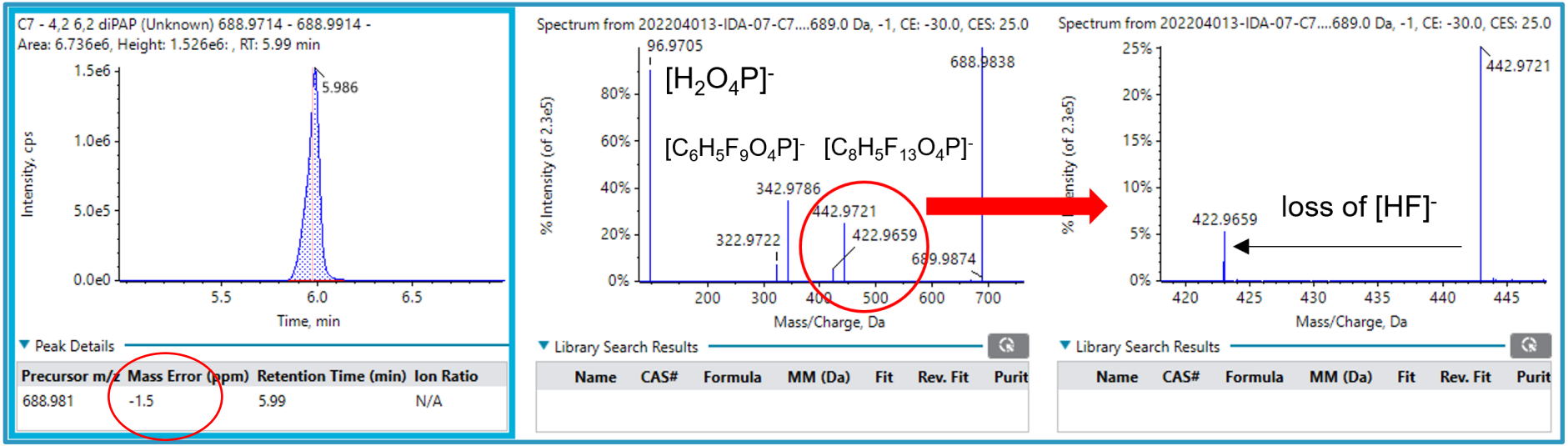
C7 – 4:2/6:2 diPAPs identification

MS/MS diagnostic fragment match for id confirmation

SCIEX The Power of Precision

Precursor XIC

TOFMSMS (diagnostic fragment, *loss of HF*)



Detection of 4:2/6:2 diPAPs in a cosmetic sample. Compound confirmation shown by excellent precursor mass error (left panel), and diagnostic fragments based on MS/MS of analogous diPAP compounds (right panels)