Per- and polyfluorinated compound (PFAS) analysis in cosmetic using high resolution accurate mass spectrometry

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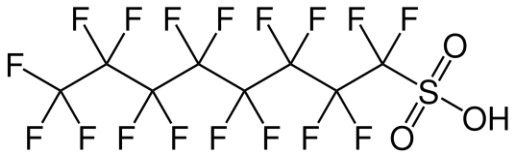
Presentation outline

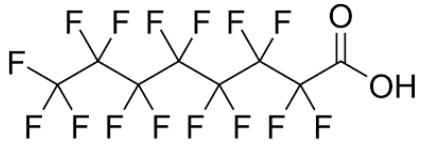
- **PFAS characterization** of consumer products are poorly understood; important piece of the PFAS lifecycle
- **Accurate mass spectrometry** methods improve characterization of PFAS in cosmetic products, increasing knowledge of PFAS “dark matter” and overall risk
- **SCIEX ZenoTOF 7600** increases the MS/MS fragmentation spectra sensitivity which is essential structural elucidation of novel PFAS
- **MS/MS spectra** can be used to confirm detection of known PFAS and discover novel PFAS … Molecule Profiler software

PFAS: poly- and perfluoroalkyl substances

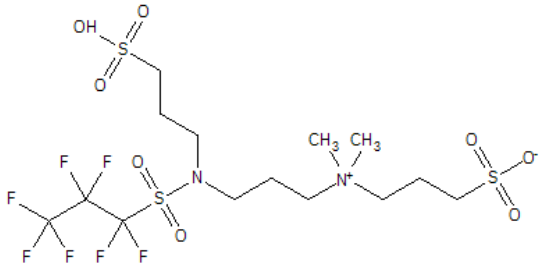
- ~5000 individual PFAS used in commerce, comprising >200 “use categories” (Glüge *et al.*, *Environ. Sci. Processes Impacts*, 2020)
- Consumer product characterization typically only monitors 20-30 PFAS
- Limited focus on consumer products
- **PFAS are numerous, diverse and complex!**



perfluorooctane sulfonic acid (PFOS)

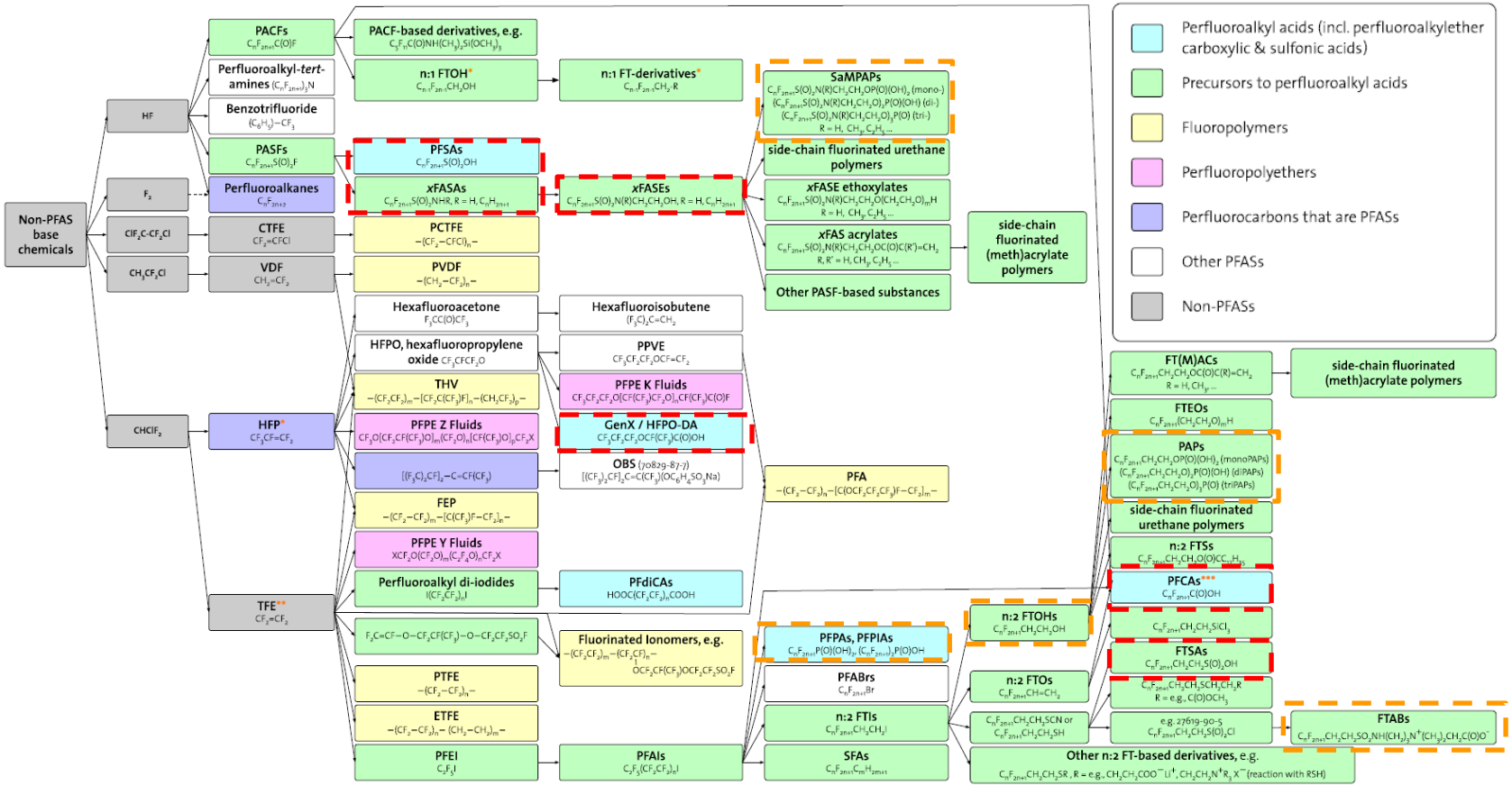


perfluorooctane carboxylic acid (PFOA)

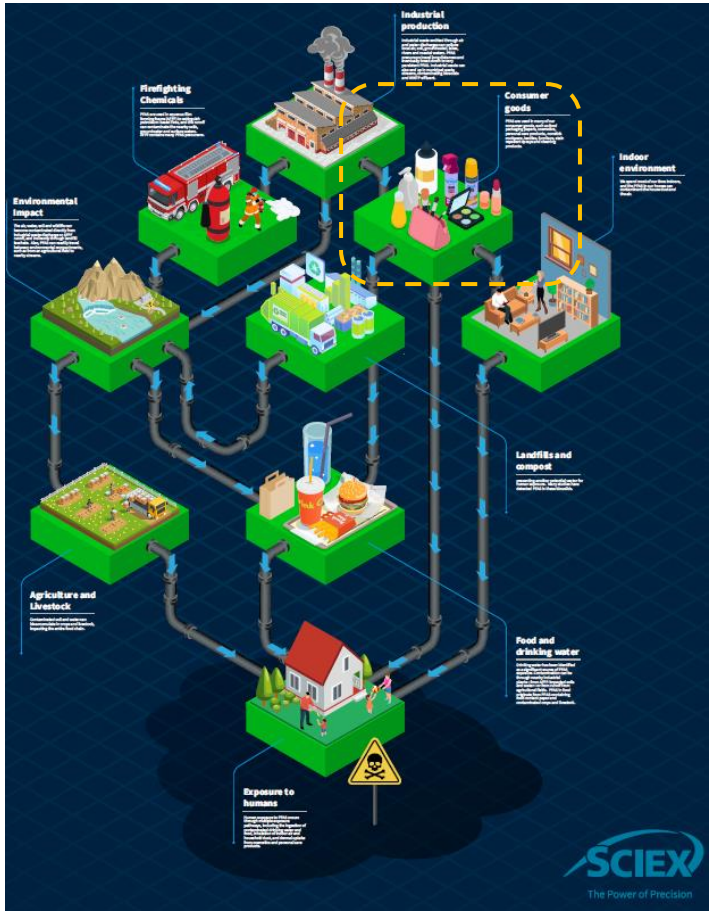


N-SPAmP-FPrSAPS

High complexity and diversity in the PFAS universe



Importance of the PFAS lifecycle



- The PFAS lifecycle is critical to understanding PFAS levels in humans
- Dermal exposure from personal care products (e.g., cosmetics) is not well understood
- Limited studies characterizing PFAS in cosmetics

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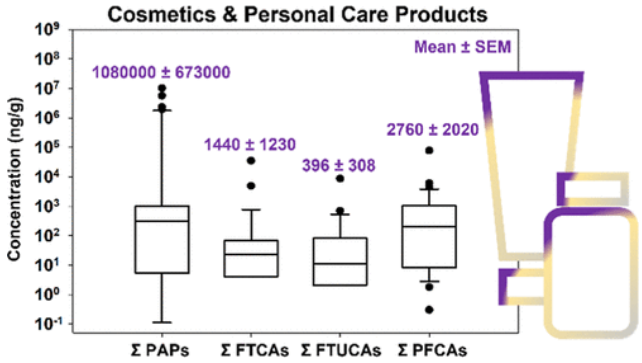
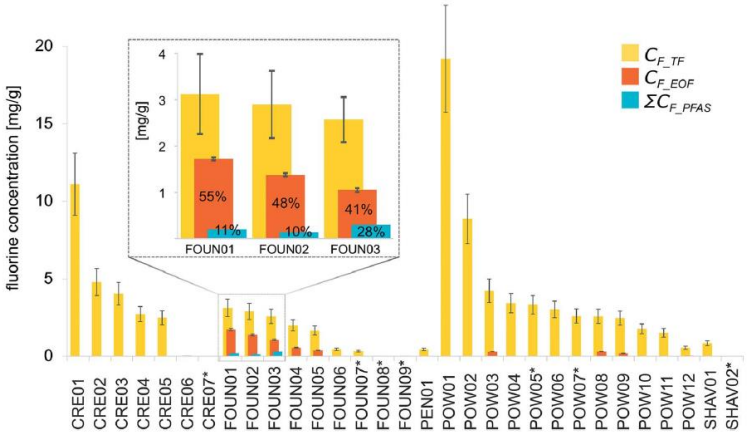
PFAS in personal care products



Harris *et al.* Environ. Sci. Technol. **2022**, *56*, 14594-14604



Schultes et al. Environ. Sci. Processes Impacts 2018 20, 1680

California bans cosmetics and apparel with PFAS

Sales prohibitions takes effect in 2025, with some exemptions

by Cheryl Hogue

September 30, 2022

PFAS is used in some cosmetics to make the product waterproof.

Credit: Shutterstock

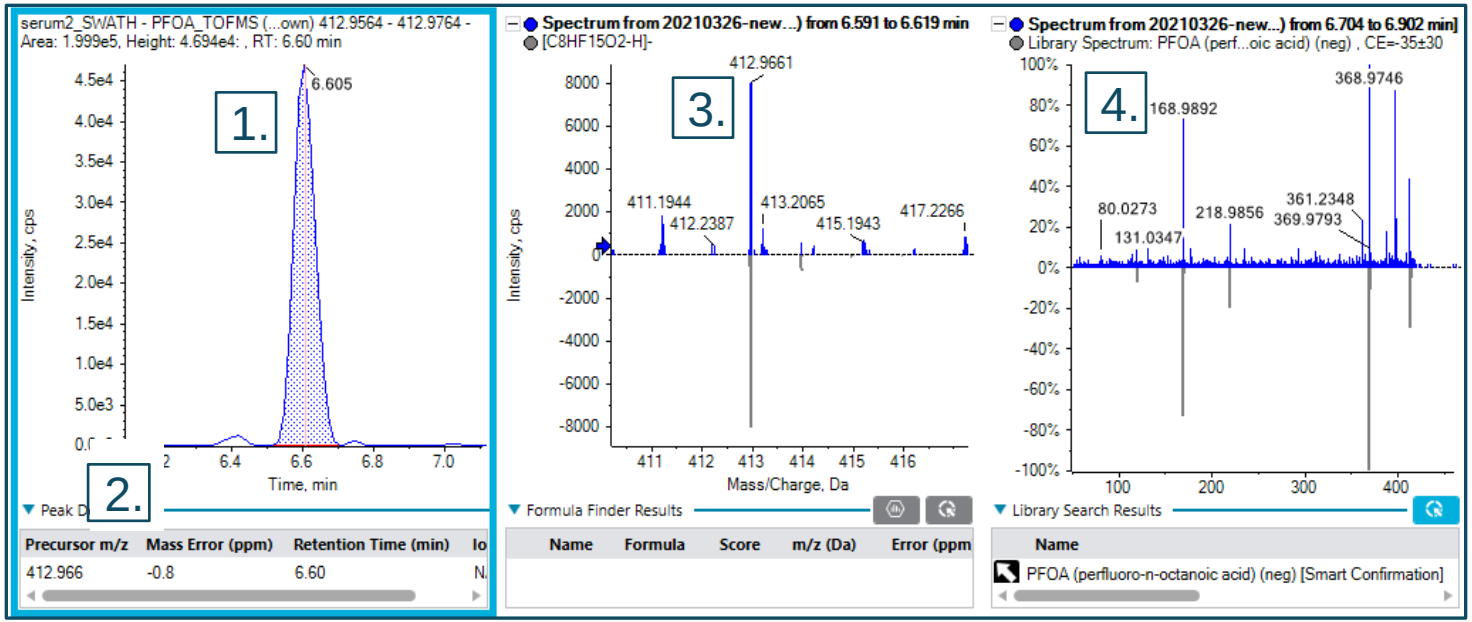
https://cen.acs.org/environment/persistent-pollutants/California-bans-cosmetics-apparel-PFAS/100/web/2022/09

Yellow bars = Total Fluorine (surrogate for total PFAS)

Blue bars = PFAS from targeted LC-MS measurement

Accurate MS: multiple lines of evidence for compound ID

1. Retention time (<2.5%) ✓➡ Not applicable for true unknown screening
2. High resolution accurate mass (<5 ppm) ✓
3. Isotope pattern (>80%) ✓
4. MS/MS fragmentation pattern match with MS/MS library ✓



ZenoTOF 7600 system

ZenoTOF 7600 system

QUALITATIVE FLEXIBILITY COMBINED WITH **QUANTITATIVE** POWER

- ZenoTOF 7600 system combines the flexibility of multiple fragmentation options
- High sensitivity MS/MS with the ZenoTOF 7600 system
- SCIEX OS software provides an intuitive workflow interface for easy acquisition and data processing

ZenoTOF 7600 system

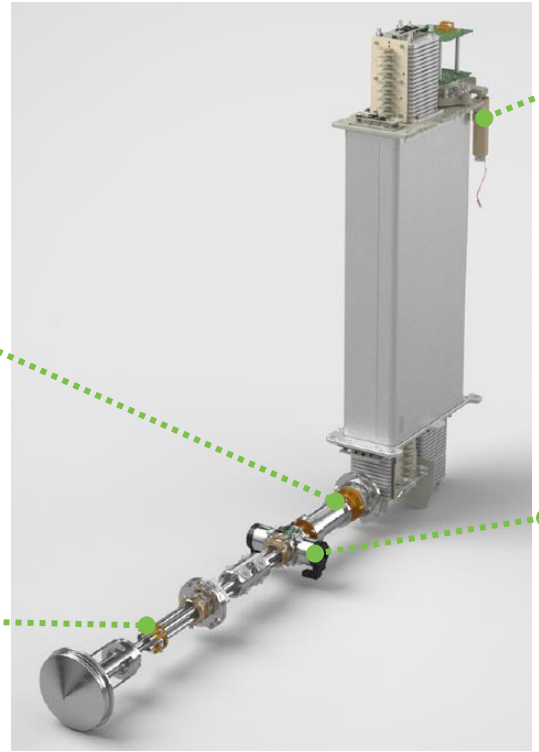
HARDWARE ADVANCEMENTS

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

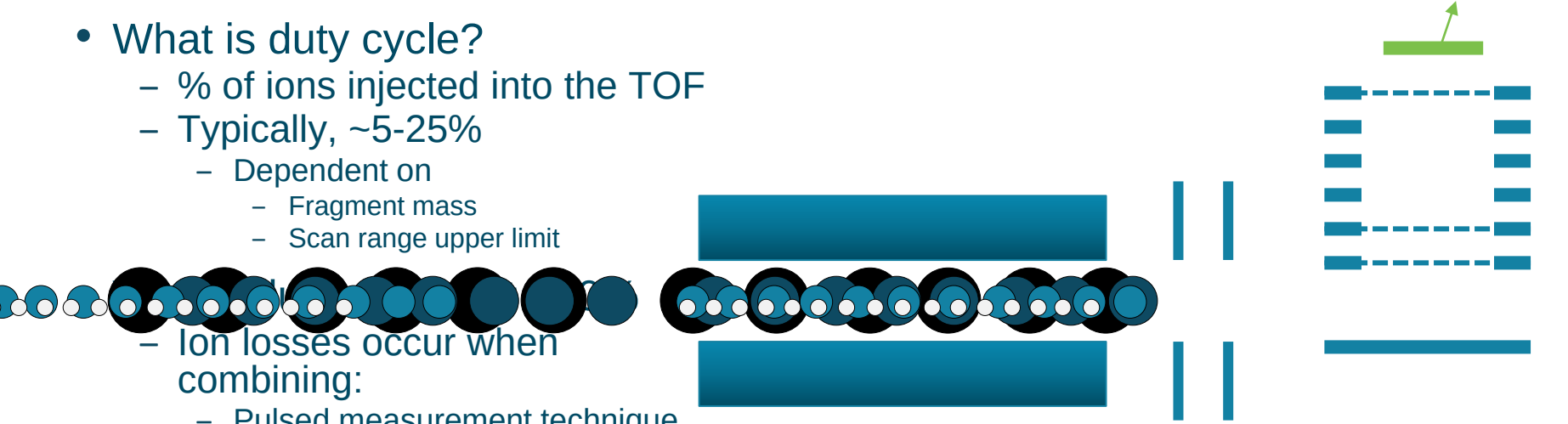
EAD cell
Complementary fragmentation with increased sensitivity using the EAD cell

MKT-28868-A

What is Duty Cycle?

… AND WHY IS DUTY CYCLE IMPORTANT?

- What is duty cycle?
  - % of ions injected into the TOF
  - Typically, ~5-25%
    - Dependent on
      - Fragment mass
      - Scan range upper limit
  - Ion losses occur when combining:
    - Pulsed measurement technique
      - TOF
    - Continuous ion beam
      - Quadrupole



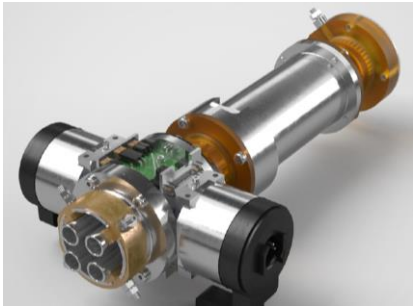
Quadrupole region
Continuous ion beam

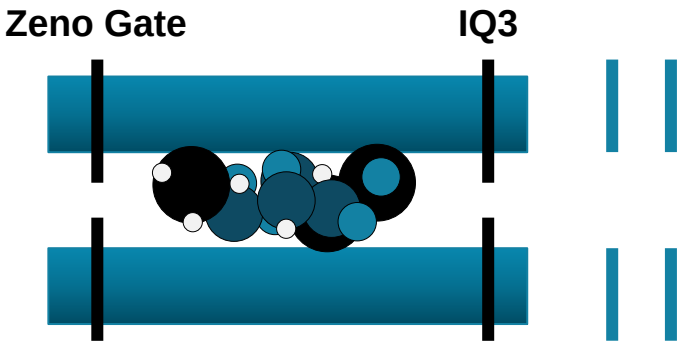
TOF accelerator
Ion pulsing

Zeno Trap for Improved Duty Cycle and MS/MS Sensitivity

FOR SENSITIVITY GAINS IN MS/MS

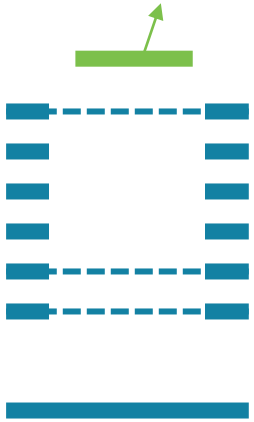
- The Zeno trap provides control of the ion beam from the collision cell into the accelerator
- Ions are gated then released based on potential energy
  - Generally, higher m/z ions are released first then followed by lower m/z ions
  - A wide range of ions now arrive in the accelerator to be pushed during the same pulse





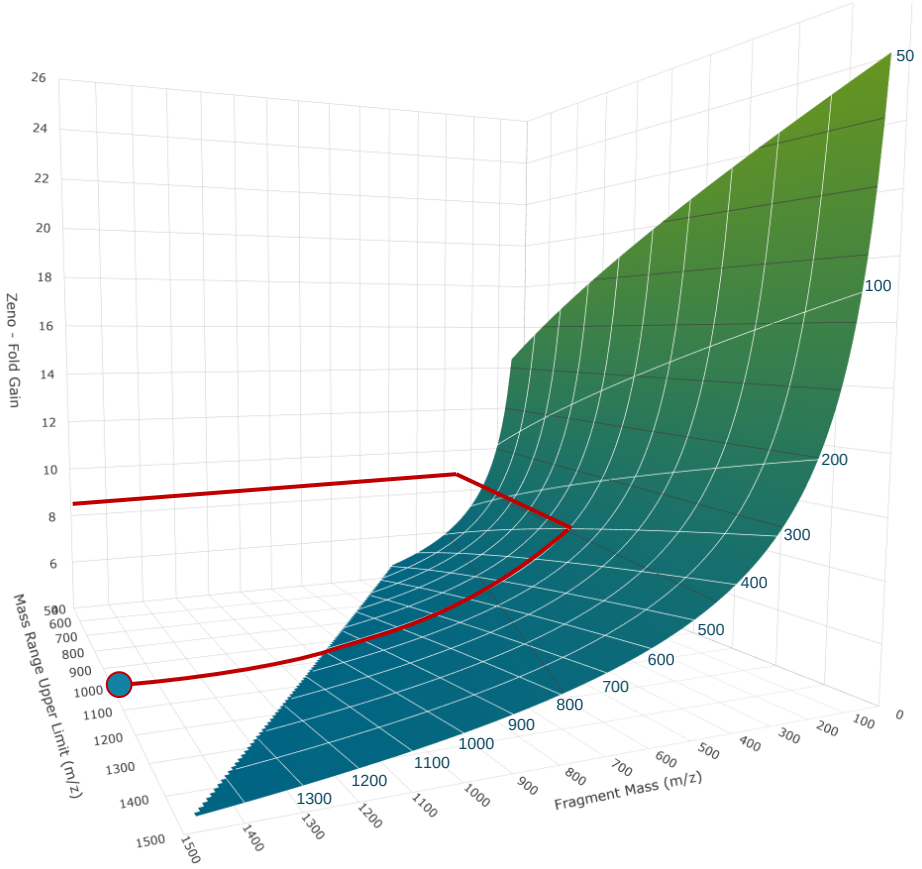
Quadrupole region
Continuous ion beam

≥90% of all ions injected into TOF region!



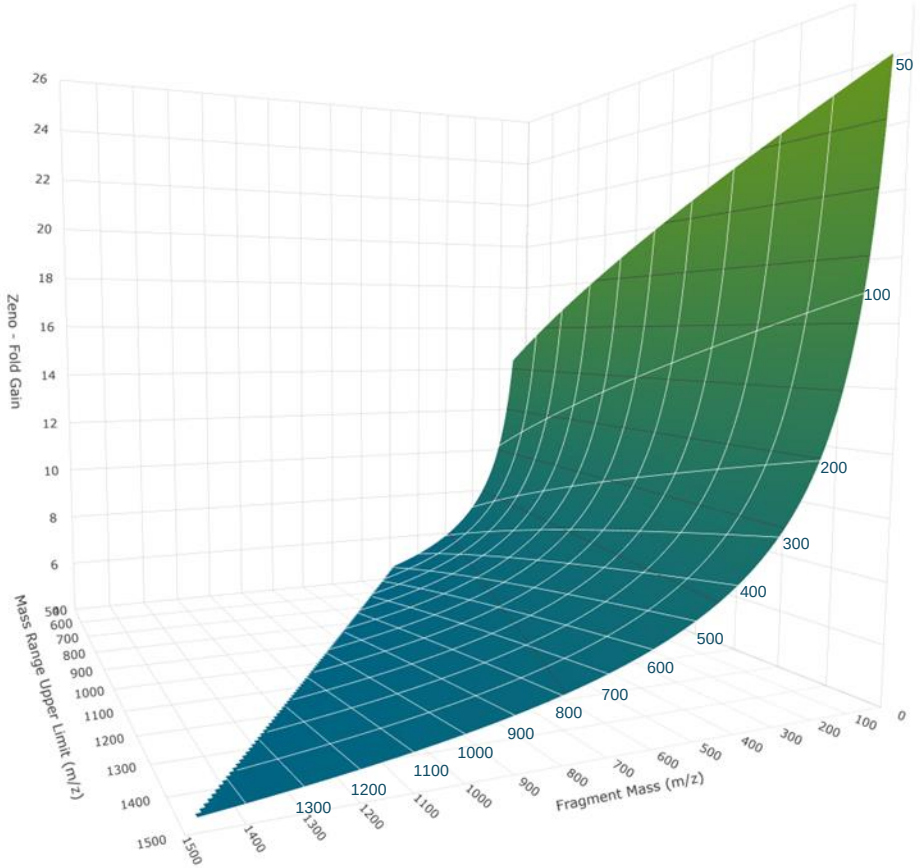
TOF accelerator
Ion Pulsing

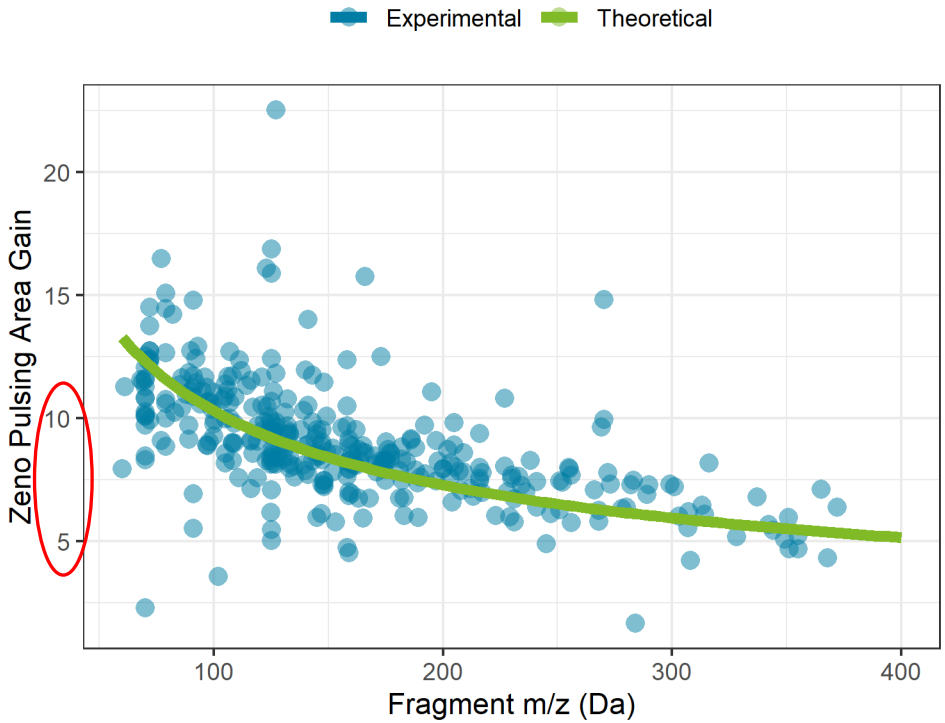
Zeno Trap for MS/MS Sensitivity



- When activated the Zeno trap ensures ≥90% recovery of duty cycle losses across the entire mass range
  - Observed gains depend on current duty cycle limitations
    - Higher m/z ions show gains ~ 4 to 8x depending on mass range and fragment mass
    - Lower m/z ions show gains up to >22 x depending on mass range and fragment mass
- Example
  - If scanning up to m/z = 1000
  - For a fragment at 300 Da
  - Expect ~8.5x gain in sensitivity

Experimental Gains





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

Methods

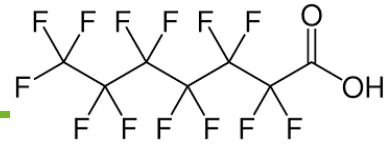
- Cosmetic extracts (foundation, concealer, creams)
- All samples identified as containing PFAS, labels were often vague
- Ultrasonication extraction, cleanup using SPE
- Acquisition using IDA on ZenoTOF 7600 system
- **Data processing:**
  - Targeted suspect screening covering multiple PFAS classes
  - MS/MS matching using SCIEX Fluorochemical 2.0 library
  - **Molecule Profiler** for novel PFAS identification

Suspect screening with MS/MS library matching

- Components list built from **legacy** PFAS (i.e., sulfonic and carboxylic acids, diPAPs)
- SCIEX Fluorochemical spectral library v2.0 contains MS/MS fragmentation spectra from ~250 PFAS compounds
- Confirmation criteria
  - retention time, if possible
  - precursor mass error (<5 ppm)
  - isotope pattern match
  - MS/MS library match

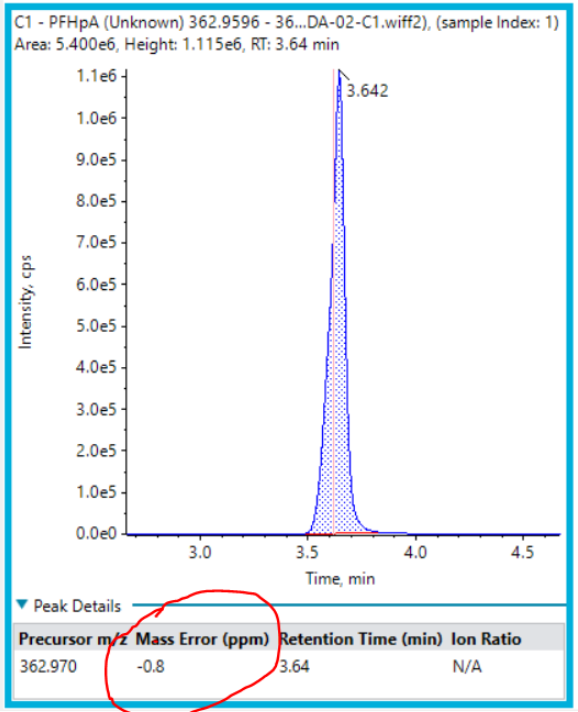
Also, unknown screening for novel PFAS!

C1 – PFHpA confirmation

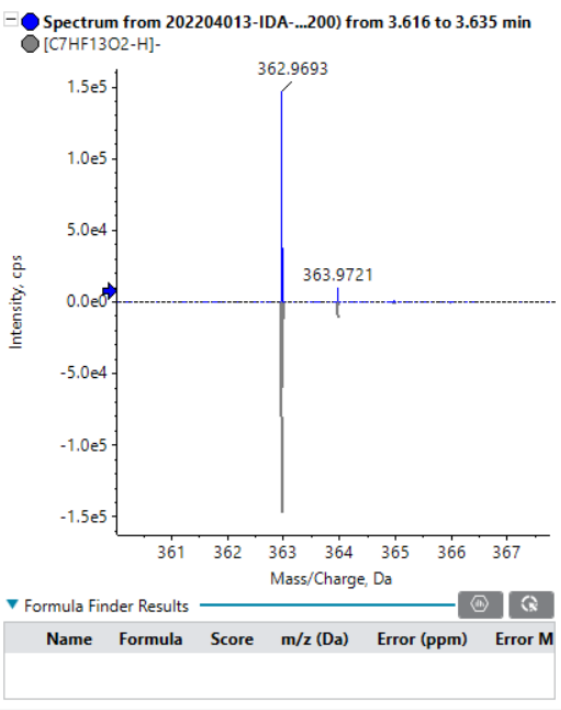


MS/MS library match for id confirmation

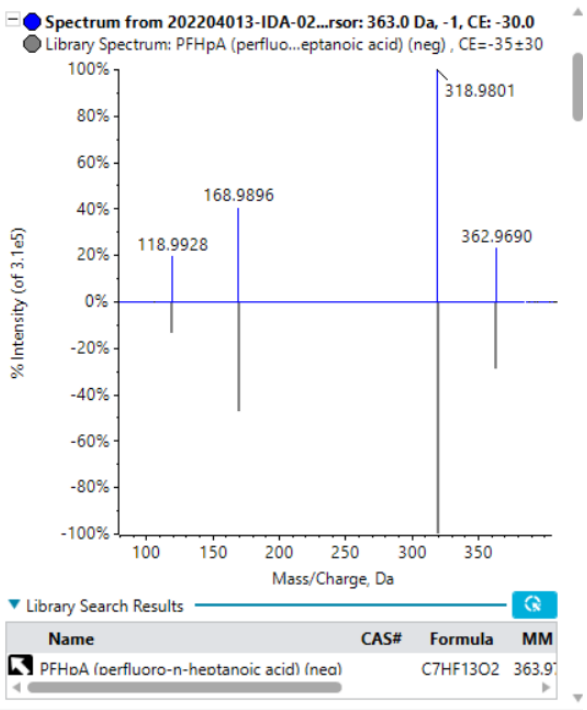
Precursor XIC



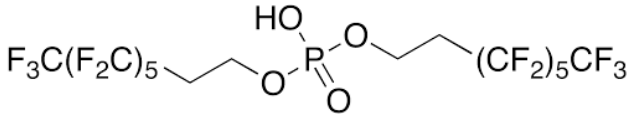
TOFMS (isotope pattern)



TOFMSMS (fragmentation pattern & library matching



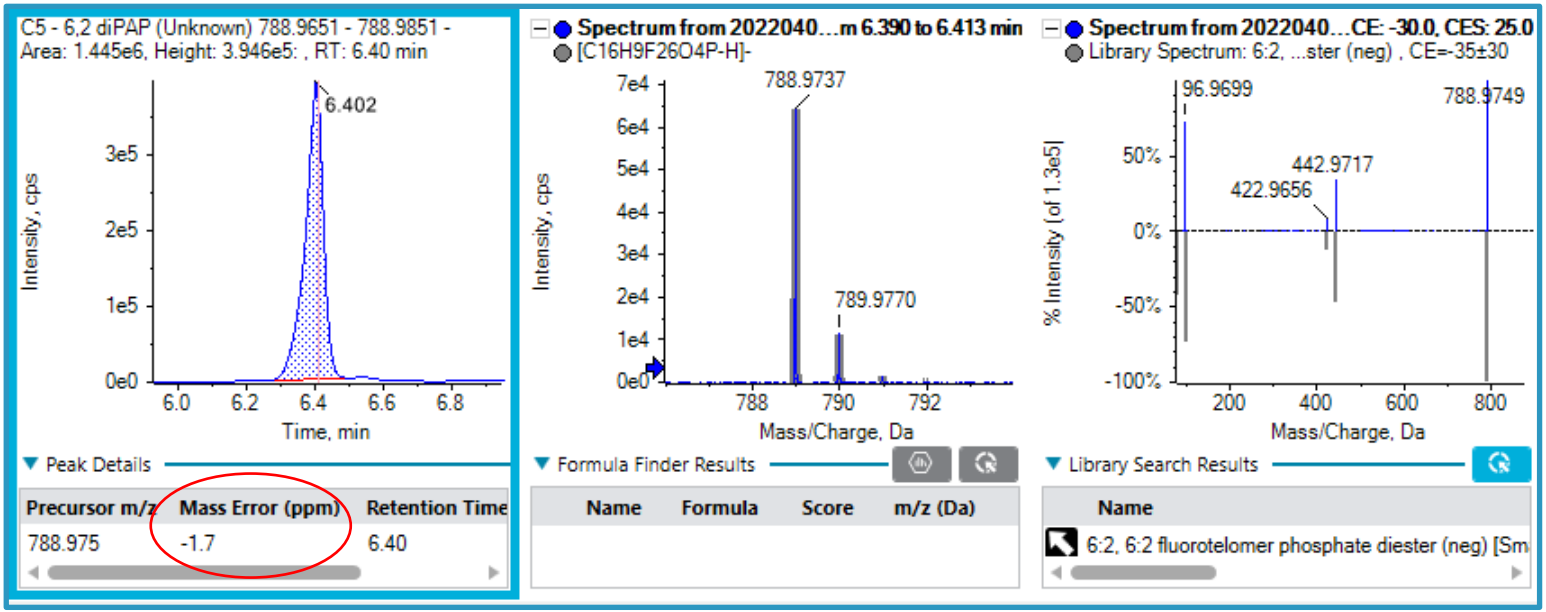
C5 – 6:2 diPAPs confirmation



Precursor XIC

TOFMS (isotope pattern)

TOFMSMS (fragmentation pattern & library matching)



MS/MS spectral library match for compound id

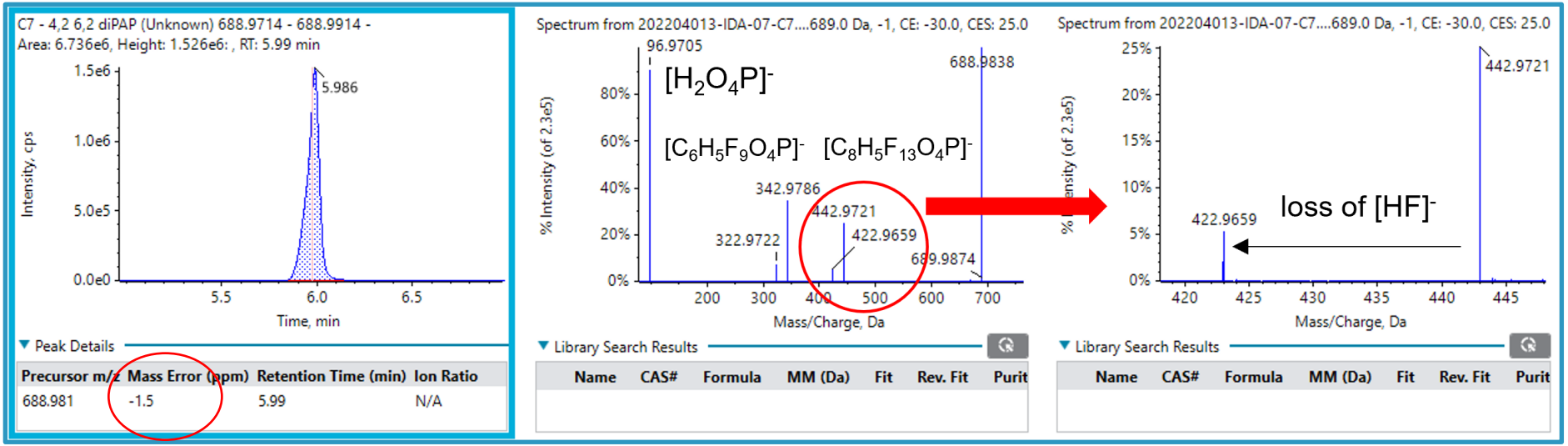
Detection of 6:2 diPAPs in a cosmetic sample. Compound confirmation achieved through precursor mass error (left panel), isotope pattern match (middle panel) and MS/MS spectrum match to SCIEX Fluorochemical High Resolution MS/MS library.

C7 – 4:2/6:2 diPAPs identification

MS/MS diagnostic fragment match for id confirmation

Precursor XIC

TOFMSMS (diagnostic fragment, *loss of HF*)



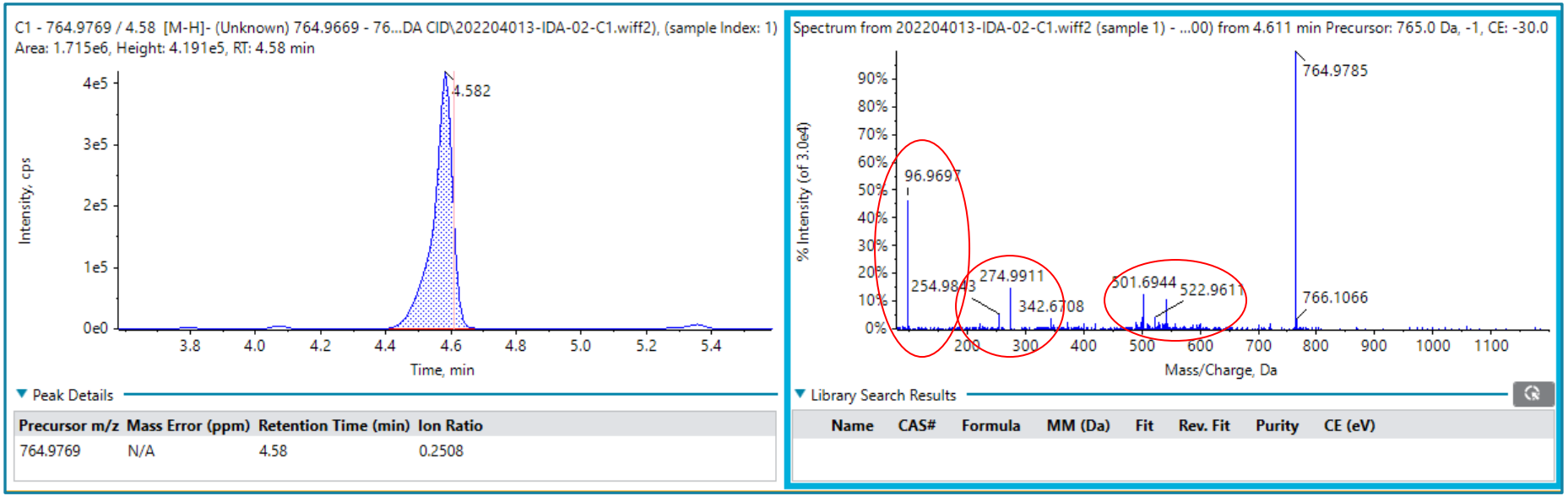
Detection of 4:2/6:2 diPAPs in a cosmetic sample. Compound confirmation shown by precursor mass error (left panel), and diagnostic fragments based on MS/MS of analogous diPAP compounds (right panels)

Cosmetics samples: detection summary

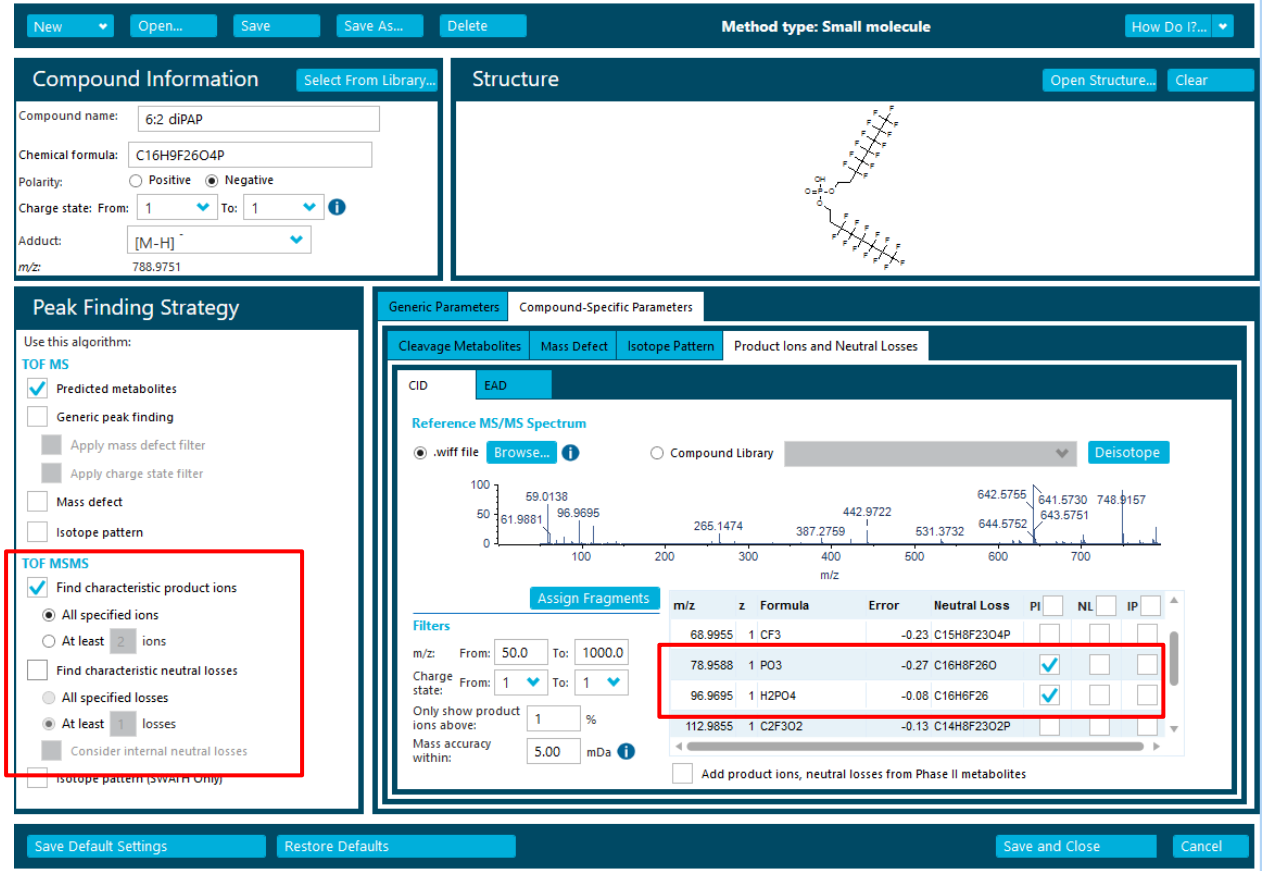
- **Suspect screening:**
  - **Not detected:** FTSs, PFSAs, PFPIAs, PFPA, PFECHS, Cl-PFOS, PFESA, sulfonamides ✘
  - **Detected:** PFCAs, FTCAs, FTUCAs, monoPAPs, diPAPs ✓
  - Samples varied by frequency of detection, concentration
- **Unknown screening:**
  - Evidence of novel diPAPs-like compounds
  - Negative mass balance (highly fluorinated), [PO4H2] fragment @m/z 96.9697

Unknown screening: detection of diPAPs-like compound

- negative mass defect
- [PO4H2] fragment @m/z 96.9697
- loss of $[HF]^-$ in fragments



Molecule Profiler results

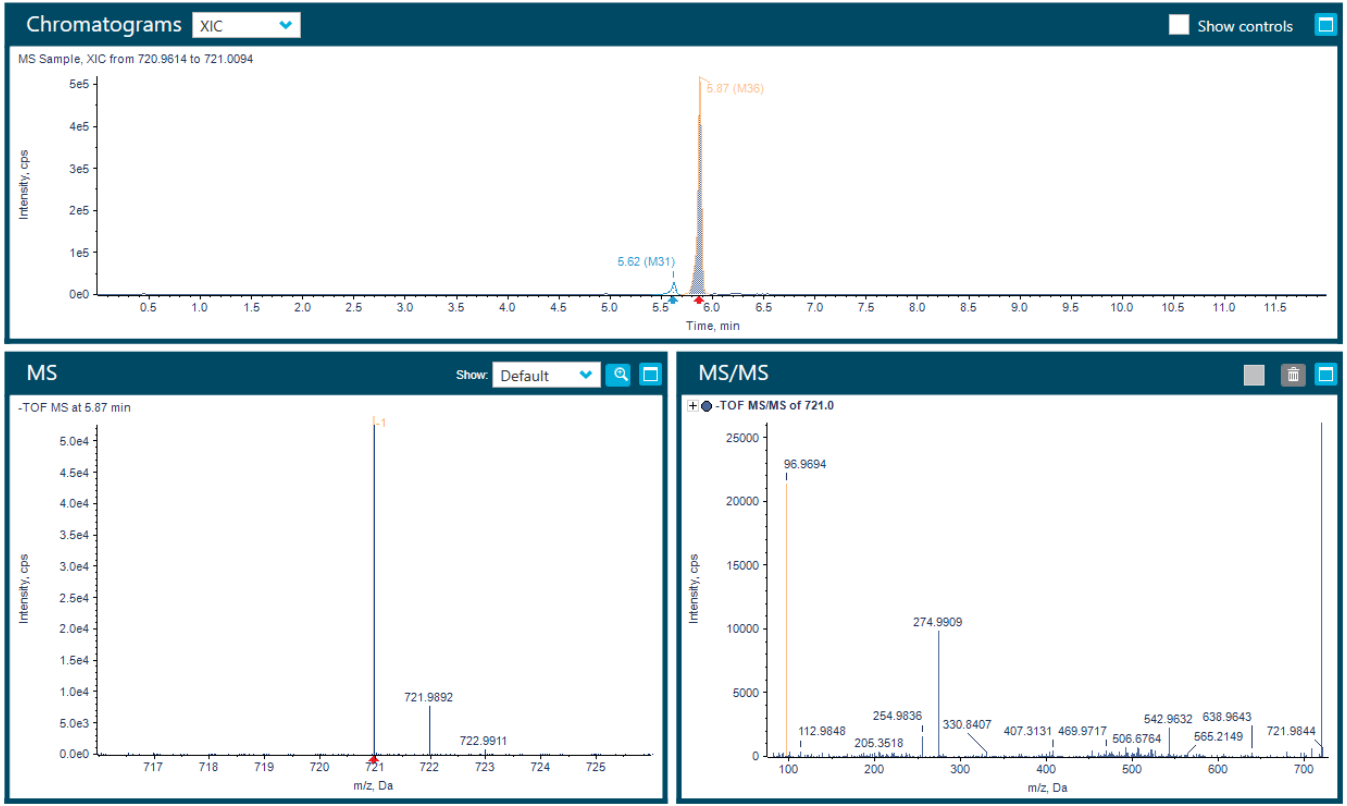


Goal: Identify precursors which contain user-specified fragments

- [H2PO4] = 96.9695

1. Upload representative .mol file (e.g. 6:2 diPAPs)
2. Select diagnostic fragments
3. Interrogate non-target data file

Molecule Profiler results



Example finding

- **m/z 720.9859, 5.87 min**

1. Negative mass balance
2. [H2PO4] fragment
3. Neutral loss of [HF]
4. Structure?

Summary

- SCIEX 7600 technology – **ZenoTrap** – improves MS/MS for enhanced PFAS characterization
- Suspect screening with MS/MS library searching for confirming detection of “known” PFAS
- Novel PFAS can be discovered – thorough and fast – using the SCIEX **Molecule Profiler** software
- Detection of several “expected” PFAS classes but also surprises

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Questions and answers

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