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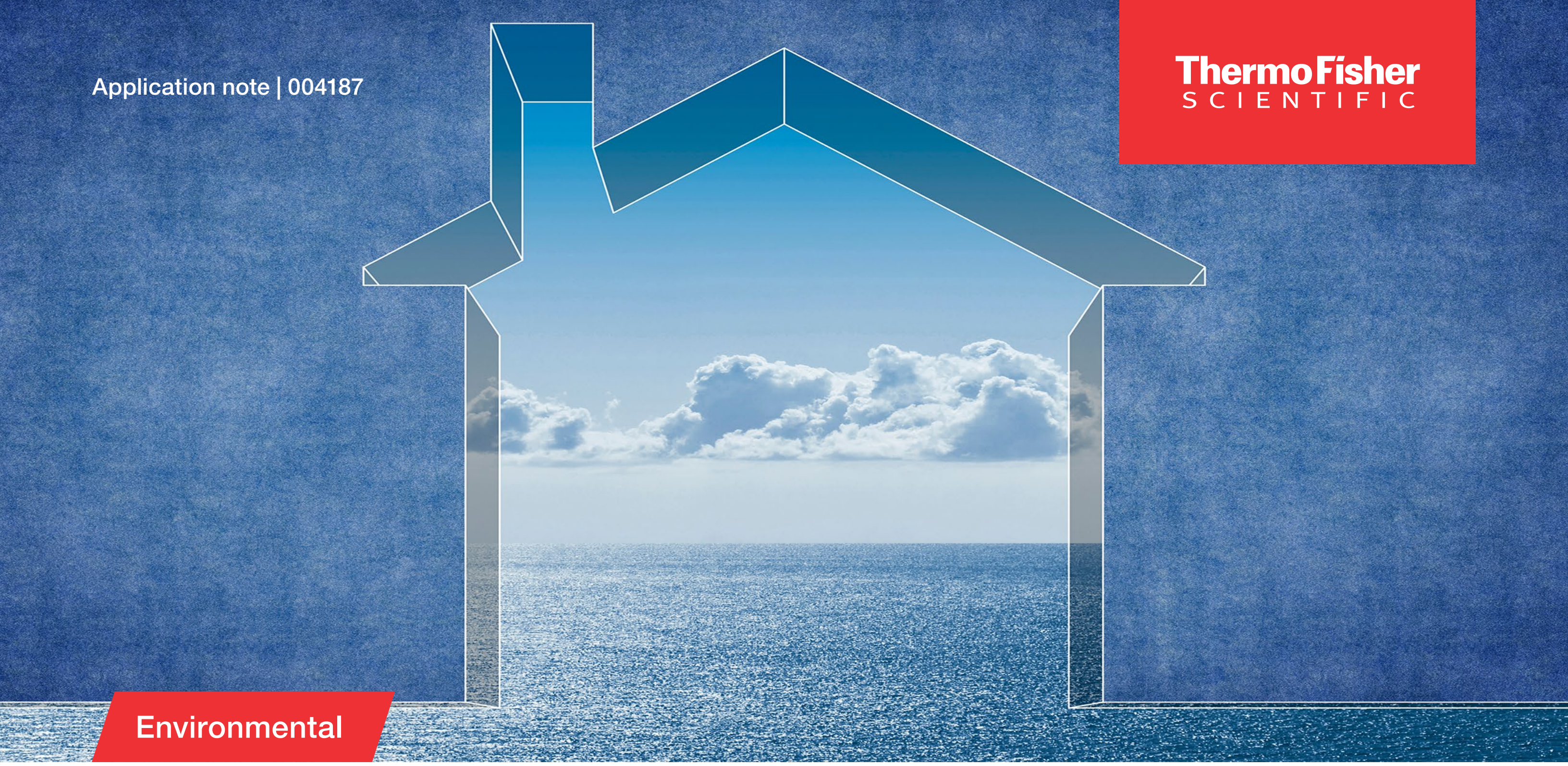

# Untargeted screening for volatile PFAS in indoor air using thermal desorption-GC Orbitrap mass spectrometry

## Authors

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## Keywords

Polyfluoroalkyl substances (PFAS), indoor air monitoring, thermal desorption, TD100-xr, gas chromatography-mass spectrometry, GC-MS, Orbitrap Exploris GC, HRAM, TRACE 1610 GC, EI, CI, ddMS[2], Compound Discoverer software, elemental composition, FreeStyle software

## Goal

The purpose of this application note is to demonstrate thermal desorption sampling coupled with the Thermo Scientific Orbitrap™ Exploris™ GC Mass Spectrometer and Thermo Scientific™ Compound Discoverer™ Software for effective and simple identification/screening of untargeted volatile PFAS in indoor air.

## Introduction

Per- and polyfluoroalkyl substances (PFAS) consist of one or more alkyl residues where all hydrogen atoms have been replaced by fluorine atoms. PFAS, often referred to as "forever chemicals," are used for their surfactant properties.[1] Volatile PFAS are also found in indoor air as they are widely used in consumer cleaning products and applied to fabrics and upholstery for surface protection. PFAS are known to cause a range of health problems. Neutral PFAS species (n-PFAS), such as fluorotelomer alcohols (FTOHs), fluorotelomer carboxylic acids (FTCAs), and perfluorooctanesulfonamides (FOSA), can degrade within the body and in the environment to form perfluorooctanoic acid (PFOA), which has been linked to cancer, reproductive and immune system toxicity, and other diseases at low concentrations.[2]

The thermal desorption (TD) technique provides an efficient way to conduct air monitoring. Stainless-steel tubes packed with sorbent sampling media can preconcentrate volatile species from several liters of air to be directly analyzed by GC-MS without any additional sample preparation prior to analysis.[3] Full scan data acquisition with HRAM allows all ions to be acquired at high mass selectivity and accuracy across the entire scan range. This provides a simple method setup to conduct untargeted compound screening with retrospective data mining capabilities.[4]

Non-targeted screening combined with HRAM GC-MS and TD represents a fast and broad analytical approach for providing a comprehensive picture of indoor air quality. Combined with Compound Discoverer software for data mining, this approach simplifies monitoring of thousands of organic contaminants in air, including volatile PFAS species. Analysis within this study investigated indoor air from three different locations (carpeted, non-carpeted, and cleaning supplies storage closet) in our facility located in San Jose, California. We demonstrated the simplicity and the potential of the untargeted screening workflow for volatile PFAS illustrated in Figure 1.

## Experimental design and workflow

### Sampling system

A Markes International™ TD100-xr™ Advanced thermal desorber with electronic flow control, equipped with a Markes International™ Internal Standard Addition / Dry Purge (ISDP) accessory for automated addition of gaseous internal standard, was used. The TD100-xr thermal desorption unit offers sequential, unattended analysis of up to 100 samples. Due to the use of Peltier cooling for refocusing in the trap, the TD100-xr eliminates both the cost and hassle of using a cryogenic fluid. Markes' systems also allow samples to be split and re-collected onto a clean sorbent tube at the tube desorption and/or trap desorption stages, providing "insurance" against failed runs and simplifying demonstration of complete analyte transfer and absence of analytical bias. Re-collection also allows for sample backup for storage purposes. The re-collection feature was used for replicate injections for samples to be run twice without the need for new spiked sorbent tubes during method optimization as well as for confirmation.

### Standard and sample preparation

Native PFAS standards—procured from Wellington Laboratories Inc., Cat. No. EPA-1633stk, and AccuStandard, Inc., Cat. No. FTOH-MIX-001 (Fluorotelomer Alcohols Mix 1), Cat. No. FTOH-004S (1:3 FTOH), Cat. No. M-1633-2/3A-CN-10X (EPA 1633 perfluorosulfonic acids and perfluorosulfonamides), and Cat. No. CLP-PS-3-10X (Toluene-d8)—were used for method optimization and for building the in-house Thermo-SJ-PFAS HRAM EI database and mass lists for the Thermo Scientific™ TraceGOLD™ TG-200MS GC Column used for this study.

PFAS Standard mix (1 ng/µL) was prepared in methanol and 5 µL was spiked on to the sorbent tubes using a Calibration Solution Loading Rig (CSLR™) purged with nitrogen.

Markes International™ PFAS Extended volume tubes (Thermo Fisher Cat. No. 76473-0942) were used for spiking standards and indoor air sampling. Markes International™ ACTI-VOC PLUS™, fast-flow pump kit was used for sampling indoor air into sorbent tubes for TD analysis. Pumped sampling is one of the most versatile methods for sampling VOCs and SVOCs. Using ACTI-VOC PLUS, precise volumes from 20 mL to

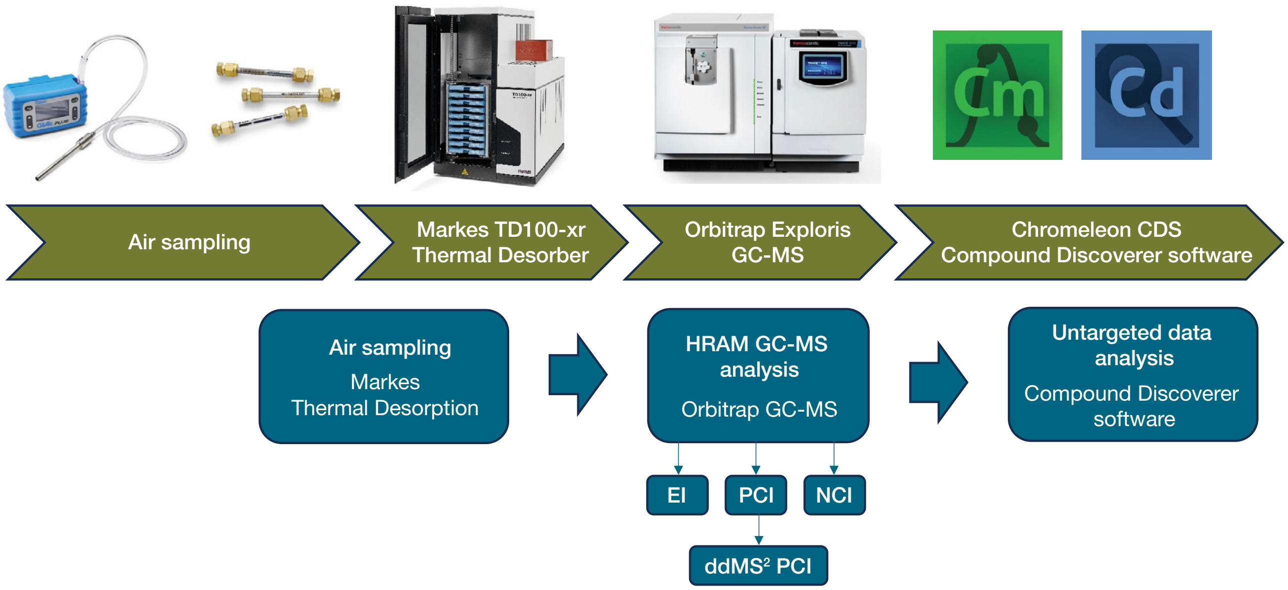


Figure 1. TD-GC-HRMS workflow for untargeted PFAS analysis in air.

several hundred liters can be drawn through the tubes, allowing analytes over a wide concentration range to be sampled and analyzed. Thirty-five liters of indoor air were sampled from the three different locations (carpeted, non-carpeted, and cleaning supplies storage closet).

## Method setup

Spiked standard tubes and indoor air samples were thermally desorbed, cryo-focused, and trapped at -28 °C onto the Markes International PFAS focusing trap (Thermo Fisher Cat. No. 76473-0940), which was desorbed at 250 °C for 8 min onto the GC analytical column. The focusing trap was heated to 300 °C for 3 min between injections to avoid carry-over.

**Table 1. TRACE 1610 GC - Orbitrap Exploris GC parameter settings.**

| TRACE 1610 GC parameters | |
|---|---|
| Injection mode | Splitless |
| GC aux heater (°C) | 250 |
| Carrier gas, flow (mL/min) | He, 1.2 |
| **Oven temperature program** | |
| Temperature (°C) | 40 |
| Hold time (min) | 2.0 |
| Rate (°C/min) | 15 |
| Temperature 2 (°C) | 250 |
| Hold time (min) | 3 |
| Rate 2 (°C/min) | 50 |
| Temperature 3 (°C) | 300 |
| Hold time 2 (min) | 3 |
| GC run time (min) | 23 |
| **Analytical column** | |
| TraceGOLD TG-200MS | 30 m × 0.25 mm × 1 µm (Cat. No. 26084-2960) |
| **Orbitrap Exploris GC mass spectrometer parameters** | |
| **EI mode** | |
| Transfer line temperature (°C) | 250 |
| Ion source type and temperature (°C) | Thermo Scientific™ ExtractaBrite™ electron ionization source, 250 |
| Aquisition mode | Full Scan |
| Mass range (*m/z*) | 50–700 |
| Resolution | 60,000 |
| Internal mass calibration | On |
| **CI mode** | |
| Transfer line temperature (°C) | 250 |
| Ion source type and temperature (°C) | ExtractaBrite, 150 |
| CI gas type and flow (mL/min) | Methane, 1.75 |
| Internal mass calibration | Off |
| **CI ddMS$^2$ mode** | |
| Scan range | 90–700 |
| Full Scan ➜ ddMS$^2$ | 4 scans |

Standards and samples were analyzed using the Thermo Scientific™ TRACE™ 1610 Series GC coupled to the Orbitrap Exploris GC mass spectrometer. Chromatographic separation was achieved on a TraceGOLD TG-200MS capillary column 30 m × 0.25 mm × 1.0 µm (Cat. No. 26084-2960). The trifluoropropylmethylpolysiloxane stationary phase of the TraceGOLD TG-200MS column provides an exceptionally inert phase for improved thermal stability, low column bleed, and reliable run-to-run and batch-to-batch reproducibility.[3] Its mid-polarity can resolve compounds that phenyl and cyano phases cannot due to fluorine in its stationary phase. GC-HRMS conditions are summarized in Table 1, while Table 2 shows the TD-100-xr parameters.

## Data acquisition

Data acquisition was carried out in full scan analysis. Additional MS method parameters for both EI and CI modes are summarized in Table 1. External mass calibration was performed prior to analysis, while characteristic ions representing column bleed were used as lock masses when scanning in EI to perform internal mass calibration. Sample acquisition and qualitative processing were performed using the Thermo Scientific™ Chromeleon™ version 7.3.2 Chromatography Data System (CDS) and Thermo Scientific™ FreeStyle™ Software, an application to view and qualitatively analyze raw MS data. Indoor untargeted air screening data full processing was done using Compound Discoverer software along with the Thermo Scientific™ Orbitrap™ GC-MS HRAM Contaminants Library, GC Orbitrap™ PFAS EI Database by the U.S. Environmental Protection Agency (EPA), and in-house curated PFAS HRAM EI database and mass list.

**Table 2. Markes International TD100-xr parameters (2-3 Stage Tube Desorb settings).**

| Parameter | Value |
|---|---|
| Tube type | PFAS Extended volume tubes (Cat. No. 76473-0942) |
| Split flow | 10 mL/min |
| Flow path temperature | 150 °C |
| Minimum carrier pressure | 5 psi |
| Automatic dry purge | 1 min at 50 mL/min |
| Tube desorption | 250 °C for 10 min at 50 mL/min |
| Trap purge | 1 min at 50 mL/min |
| Focusing trap | PFAS focusing trap (Cat. No. 76473-0940) |
| Focusing trap low temperature | -28 °C |
| Elevated trap purge temperature | 25 °C |
| Trap high temperature | 250 °C (8 min) |
| Trap heat rate | 28 °C/s |
| Split flow | 2 mL/min |

## Results and discussion

The Orbitrap Exploris GC-MS was used for accurate mass measurements in full-scan mode at 60,000 mass resolution (FWHM at *m/z* 200). Variable electron voltage (VeV) is an effective technique that can be implemented in the high-resolution, accurate-mass (HRAM) Orbitrap Exploris GC-MS Series. This highly efficient technology enables lower eV settings for electron ionization, essentially soft EI as previously described, and routinely delivers very robust tuning results. The softer EI technique promotes higher mass signals and increases sensitivity for compounds prone to extensive fragmentation.[5] Using the VeV technique, electron energy at 50 eV was optimal for PFAS analysis in EI mode.

Table 3 reports the list of PFAS compounds included in the standard mixture, and the corresponding EIC of MS quantitation peaks are shown in Figure 2. By thermally desorbing the PFAS compounds, we are able to trap and detect very volatile compounds that would be otherwise elute in the solvent front with liquid injections.

The Chromeleon CDS data file for the PFAS standard mix (5 ng) was imported as a raw data file in FreeStyle software. Mass spectra of each PFAS standard were curated by subtracting the background and checking the elemental composition and mass accuracy of the EI fragments (Appendix Figure A3). Spectra can be imported for library construction to non-target screening applications. These libraries can then be used by the Compound Discoverer software for identification of PFAS compounds.

### Indoor air analysis

Thirty-five liters of indoor air from three different locations—namely carpeted, non-carpeted, and a cleaning supplies storage closet in our facility—were collected at 300 mL/min using the ACTI-VOC low-flow pump into Markes PFAS Extended volume tubes. Pumped sampling tubes were desorbed and HRAM data was collected in both EI and CI ionization modes. Example of TIC chromatograms in EI and CI modes are shown in Figures A1 and A2 in the Appendix.

**Table 3. Component table of PFAS standard mix.**

| Name | Retention time (min) | CAS # | Chemical formula | MS quant. peak | MS conf. peak 1 | MS conf. peak 2 | MS conf. peak 3 |
|---|---|---|---|---|---|---|---|
| 1:3 FTOH | 2.92 | 461–18–7 | $C_4H_7F_3O$ | 77.0197 | 68.9947 | 91.0354 | 107.0303 |
| 5:1 FTOH | 3.07 | 423-46-1 | $C_6H_3F_{11}O$ | 91.0542 | 130.9915 | 68.9947 | 162.997 |
| d8-Toluene | 3.08 | 2037-26-5 | $C_6D_5CD_3$ | 98.098 | 100.1122 | – | – |
| 4:2 FTOH | 3.50 | 2043-47-2 | $C_6H_5F_9O$ | 95.0102 | 130.9915 | 127.0166 | 68.9947 |
| 5H4:1 FTOH | 3.95 | 355-80-6 | $C_5H_4F_8O$ | 130.9915 | 95.0103 | 113.0009 | 68.9947 |
| 7:1 FTOH | 4.58 | 307-30-2 | $C_8H_3F_{15}O$ | 130.9914 | 68.9946 | 99.993 | 180.9883 |
| PFBS( Perfluorobutanesulfonic acid) | 4.93 | 375-73-5 | $C_4HF_9O_3S$ | 162.9977 | 68.9947 | 113.0009 | 130.9915 |
| 6:2 FTOH | 5.08 | 647-42-7 | $C_8H_5F_{13}O$ | 95.0102 | 127.0165 | 68.9946 | 296.0054 |
| 8:1 FTOH | 5.35 | 423-56-3 | $C_9H_3F_{17}O$ | 130.9914 | 68.9947 | 180.9883 | 99.993 |
| PFPS ( Perfluoropentanesulfonic acid) | 5.71 | 2706-91-4 | $C_5HF_{11}O_3S$ | 180.9883 | 68.9947 | 162.9977 | 130.9915 |
| 6:3FTOH | 6.33 | 80806-68-4 | $C_9H_7F_{13}O$ | 130.9914 | 68.9947 | 180.9883 | 115.0542 |
| 8:2 FTOH | 6.54 | 678-39-7 | $C_{10}H_5F_{17}O$ | 130.9914 | 68.9947 | 180.9883 | 95.0103 |
| 9ME-8:2FTOH | 7.30 | 31200-98-3 | $C_{11}H_5F_{19}O$ | 130.9914 | 68.9947 | 180.9883 | 95.0102 |
| 10:2 FTOH | 7.80 | 865-86-1 | $C_{12}H_5F_{21}O$ | 130.9914 | 68.9947 | 180.9883 | 95.0102 |
| 12:2FTOH | 8.96 | 39239-77-5 | $C_{14}H_5F_{25}O$ | 130.9914 | 68.9947 | 180.9883 | 95.0103 |
| N-MeFBSE | 9.95 | 34454-97-2 | $C_7H_8F_9NO_3S$ | 325.989 | 68.9947 | 130.9915 | 262.0273 |
| N-me-PFOSA | 10.03 | 31506-32-8 | $C_9H_4F_{17}NO_2S$ | 93.9956 | 68.9947 | 280.9818 | 130.9915 |
| 1:8:1FTdiOH | 10.12 | 754-96-1 | $C_{10}H_6F_{16}O_2$ | 130.9914 | 68.9947 | 180.9883 | 95.0102 |
| PFOSA | 10.15 | 754-91-6 | $C_8H_2F_{17}NO_2S$ | 79.9801 | 68.9947 | 230.9853 | 130.9915 |
| Sulfuramid | 10.34 | 4151-50-2 | $C_{10}H_6F_{17}NO_2S$ | 447.9987 | 68.9947 | 108.0114 | 130.9915 |
| Et-FOSA-AcOH | 11.94 | 2991-50-6 | $C_{12}H_8F_{17}NO_4S$ | 134.962 | 68.9947 | 146.962 | 130.9915 |

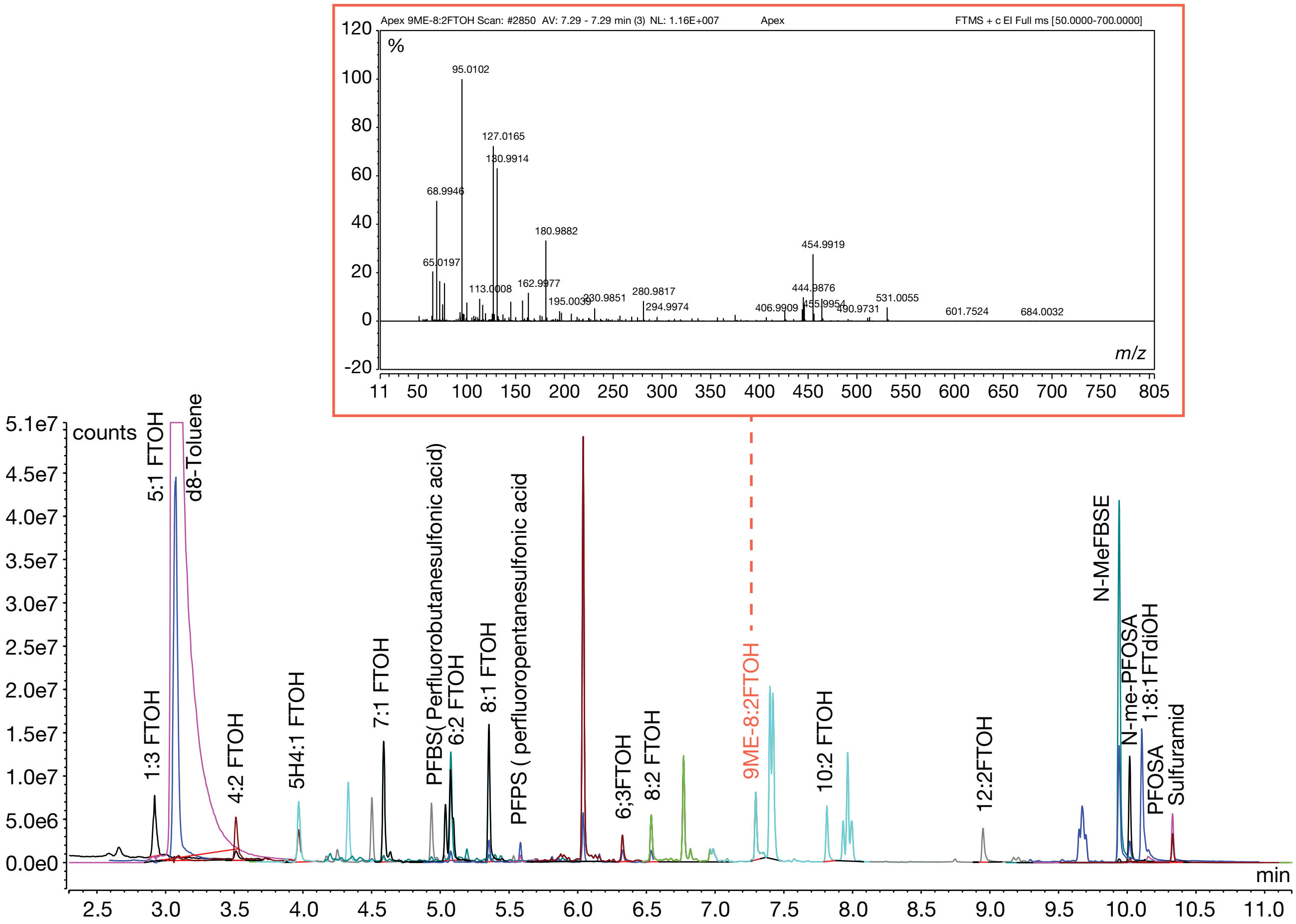


**Figure 2. Extracted ion chromatogram (EIC) of PFAS standards mix (5 ng) on a TraceGOLD TG-200MS column in Full-scan EI mode.** The inset shows the HRAM spectrum for 9ME-8:2FTOH.

## Untargeted screening of indoor air for PFAS using Compound Discoverer software

Compound Discoverer software is a powerful platform providing a comprehensive solution for the untargeted analysis including PFAS in complex matrices. The GC-EI or CI workflows contain a pre-assembled combination of customizable interconnected nodes with parameters optimizable for the analysis of PFAS (Figure 3). These workflows leverage formula prediction based on HRAM and spectral best fit. Descriptive statistics and differential analysis nodes enable the visualization of statistical differences seen in different PFAS species amongst the three different locations of sampled indoor air in our study. The result exporter node is used to export results from Compound Discoverer software in text as well as csv file formats. These files can be imported into Chromeleon CDS for setting up targeted analysis.

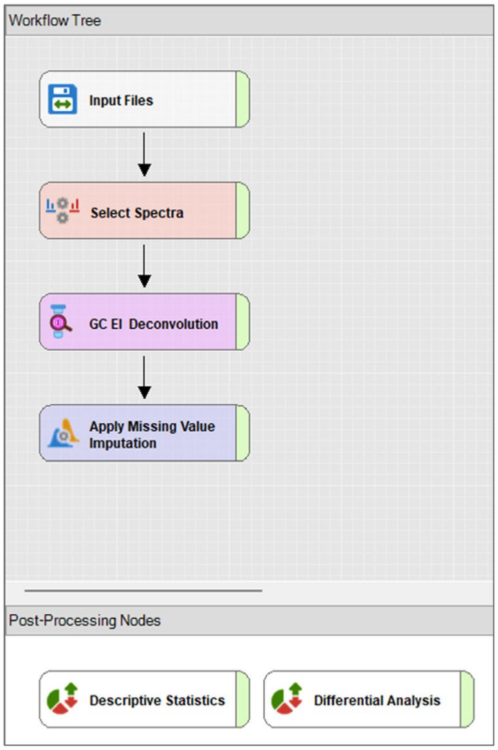
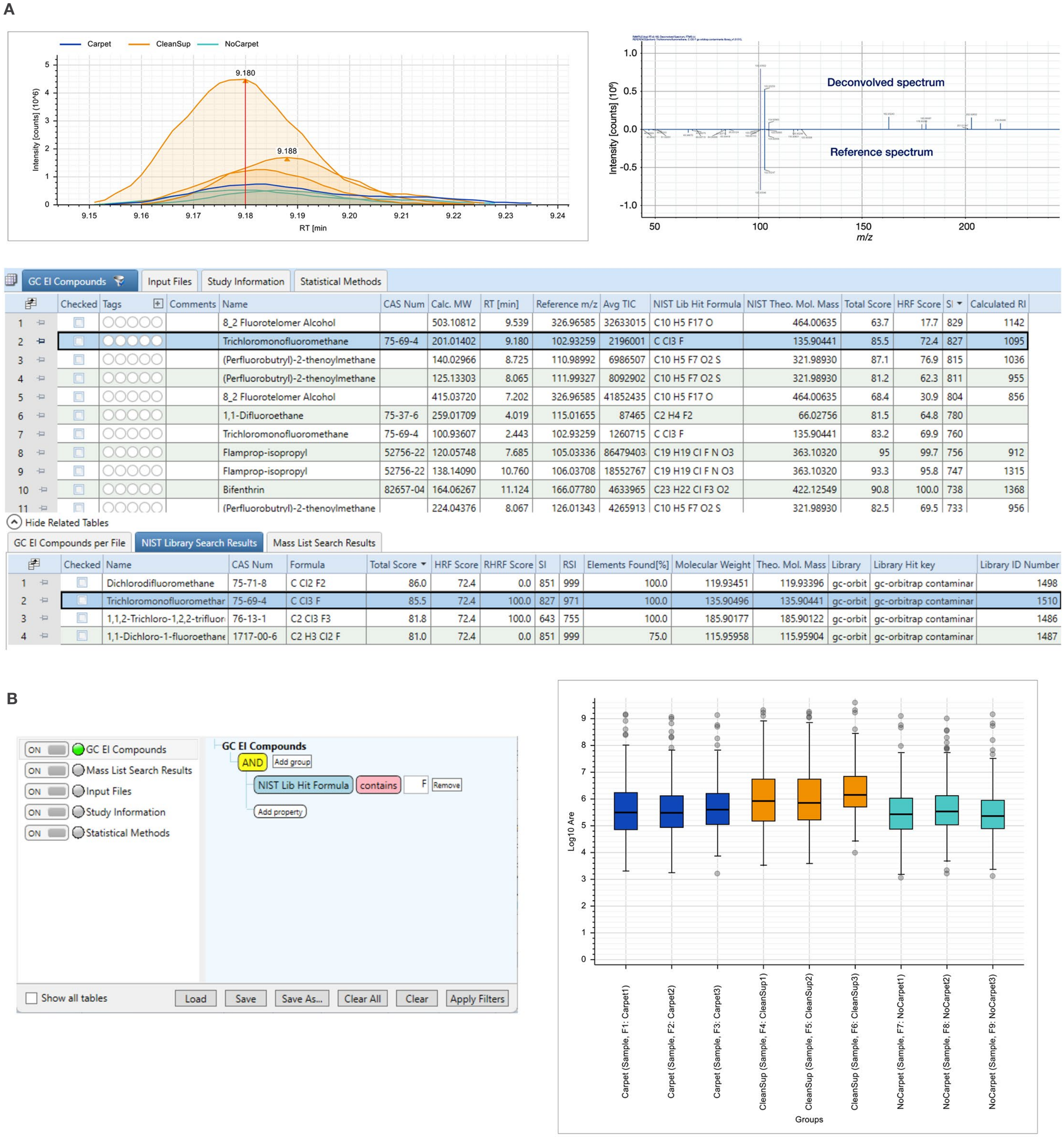


**Figure 3. GC-EI workflow in Compound Discoverer software.**

GC-EI results can be filtered for PFAS-specific compounds by applying a filter to the library hit formula that specifically contains fluorine. Formula prediction is constrained by a maximum of 50 fluorine atoms to provide optimal coverage for the observable chemical space where PFAS reside.[6] More than 2,000 compounds were identified in the present indoor air study, which was shortlisted to 100 compounds by adding a fluorine filter to the NIST library hit formula. Other filters like total score, high resolution filtering (HRF) score, and search index (SI) score can be applied to further simplify the compound list. Figure 4 (A,B) shows GC-EI results filtered for fluorine.



|  | Checked | Tags | Comments | Name | CAS Num | Calc. MW | RT [min] | Reference m/z | Avg TIC | NIST Lib Hit Formula | NIST Theo. Mol. Mass | Total Score | HRF Score | SI | Calculated RI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | ☐ | ○○○○○ |  | 8_2 Fluorotelomer Alcohol |  | 503.10812 | 9.539 | 326.96585 | 32633015 | C10 H5 F17 O | 464.00635 | 63.7 | 17.7 | 829 | 1142 |
| 2 | ☐ | ○○○○○ |  | Trichloromonofluoromethane | 75-69-4 | 201.01402 | 9.180 | 102.93259 | 2196001 | C Cl3 F | 135.90441 | 85.5 | 72.4 | 827 | 1095 |
| 3 | ☐ | ○○○○○ |  | (Perfluorobutryl)-2-thenoylmethane |  | 140.02966 | 8.725 | 110.98992 | 6986507 | C10 H5 F7 O2 S | 321.98930 | 87.1 | 76.9 | 815 | 1036 |
| 4 | ☐ | ○○○○○ |  | (Perfluorobutryl)-2-thenoylmethane |  | 125.13303 | 8.065 | 111.99327 | 8092902 | C10 H5 F7 O2 S | 321.98930 | 81.2 | 62.3 | 811 | 955 |
| 5 | ☐ | ○○○○○ |  | 8_2 Fluorotelomer Alcohol |  | 415.03720 | 7.202 | 326.96585 | 41852435 | C10 H5 F17 O | 464.00635 | 68.4 | 30.9 | 804 | 856 |
| 6 | ☐ | ○○○○○ |  | 1,1-Difluoroethane | 75-37-6 | 259.01709 | 4.019 | 115.01655 | 87465 | C2 H4 F2 | 66.02756 | 81.5 | 64.8 | 780 |  |
| 7 | ☐ | ○○○○○ |  | Trichloromonofluoromethane | 75-69-4 | 100.93607 | 2.443 | 102.93259 | 1260715 | C Cl3 F | 135.90441 | 83.2 | 69.9 | 760 |  |
| 8 | ☐ | ○○○○○ |  | Flamprop-isopropyl | 52756-22 | 120.05748 | 7.685 | 105.03336 | 86479403 | C19 H19 Cl F N O3 | 363.10320 | 95 | 99.7 | 756 | 912 |
| 9 | ☐ | ○○○○○ |  | Flamprop-isopropyl | 52756-22 | 138.14090 | 10.760 | 106.03708 | 18552767 | C19 H19 Cl F N O3 | 363.10320 | 93.3 | 95.8 | 747 | 1315 |
| 10 | ☐ | ○○○○○ |  | Bifenthrin | 82657-04 | 164.06267 | 11.124 | 166.07780 | 4633965 | C23 H22 Cl F3 O2 | 422.12549 | 90.8 | 100.0 | 738 | 1368 |
| 11 | ☐ | ○○○○○ |  | (Perfluorobutryl)-2-thenoylmethane |  | 224.04376 | 8.067 | 126.01343 | 4265913 | C10 H5 F7 O2 S | 321.98930 | 82.5 | 69.5 | 733 | 956 |

|  | Checked | Name | CAS Num | Formula | Total Score | HRF Score | RHRF Score | SI | RSI | Elements Found[%] | Molecular Weight | Theo. Mol. Mass | Library | Library Hit key | Library ID Number |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | ☐ | Dichlorodifluoromethane | 75-71-8 | C Cl2 F2 | 86.0 | 72.4 | 0.0 | 851 | 999 | 100.0 | 119.93451 | 119.93396 | gc-orbit | gc-orbitrap contaminar | 1498 |
| 2 | ☐ | Trichloromonofluoromethar | 75-69-4 | C Cl3 F | 85.5 | 72.4 | 100.0 | 827 | 971 | 100.0 | 135.90496 | 135.90441 | gc-orbit | gc-orbitrap contaminar | 1510 |
| 3 | ☐ | 1,1,2-Trichloro-1,2,2-trifluor | 76-13-1 | C2 Cl3 F3 | 81.8 | 72.4 | 100.0 | 643 | 755 | 100.0 | 185.90177 | 185.90122 | gc-orbit | gc-orbitrap contaminar | 1486 |
| 4 | ☐ | 1,1-Dichloro-1-fluoroethane | 1717-00-6 | C2 H3 Cl2 F | 81.0 | 72.4 | 0.0 | 851 | 999 | 75.0 | 115.95958 | 115.95904 | gc-orbit | gc-orbitrap contaminar | 1487 |

ON ● GC EI Compounds
ON ○ Mass List Search Results
ON ○ Input Files
ON ○ Study Information
ON ○ Statistical Methods

GC EI Compounds
AND Add group
NIST Lib Hit Formula contains F Remove
Add property

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Figure 4. (A) GC-EI results in Compound Discoverer software filtered for fluorine; (B) GC-EI results in Compound Discoverer software showing filter and differential analysis between sample groups.

The PCI workflow in Compound Discoverer software, schematized in Figure 5, is used to confirm the compounds identified in the EI workflow. All nodes can be customized depending on which library or identification route the user chooses to employ.[7] The GC-CI workflow can also be used to process PCI dd-MS$^2$ data acquisition. The built-in CI workflow enabled searching our PCI dd-MS$^2$ data against online databases like the Thermo Scientific™ mzCloud™ mass spectral fragmentation library and ChemSpider. The structure proposal capability enabled applying a Fragment Ion Search, or FISh, score by performing *in silico* fragmentation of the proposed compound, critical to pinpoint the right hit from similar *m/z*.

As shown in Figure 6, 6:2 FTOH was identified at RT 5.08 min based on the library hit formula. Despite the library match, several ions missing from the experimental spectra result in low SI score. This can be attributed to the low concentration of the detected analyte as well as co-elution of background matrix compounds present at higher concentrations.

To address this challenge, Compound Discoverer software uses the HRF score, which represents the percentage of the spectrum that is explained by the chemical formula proposed by the library hit. In this example, a HRF score of 98.2 is achieved.

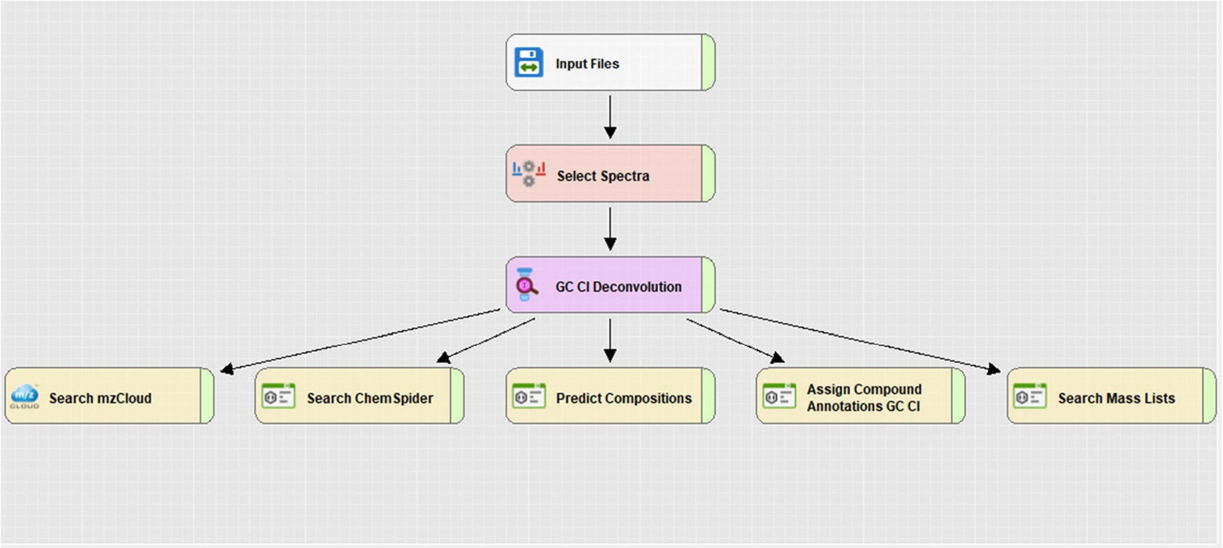
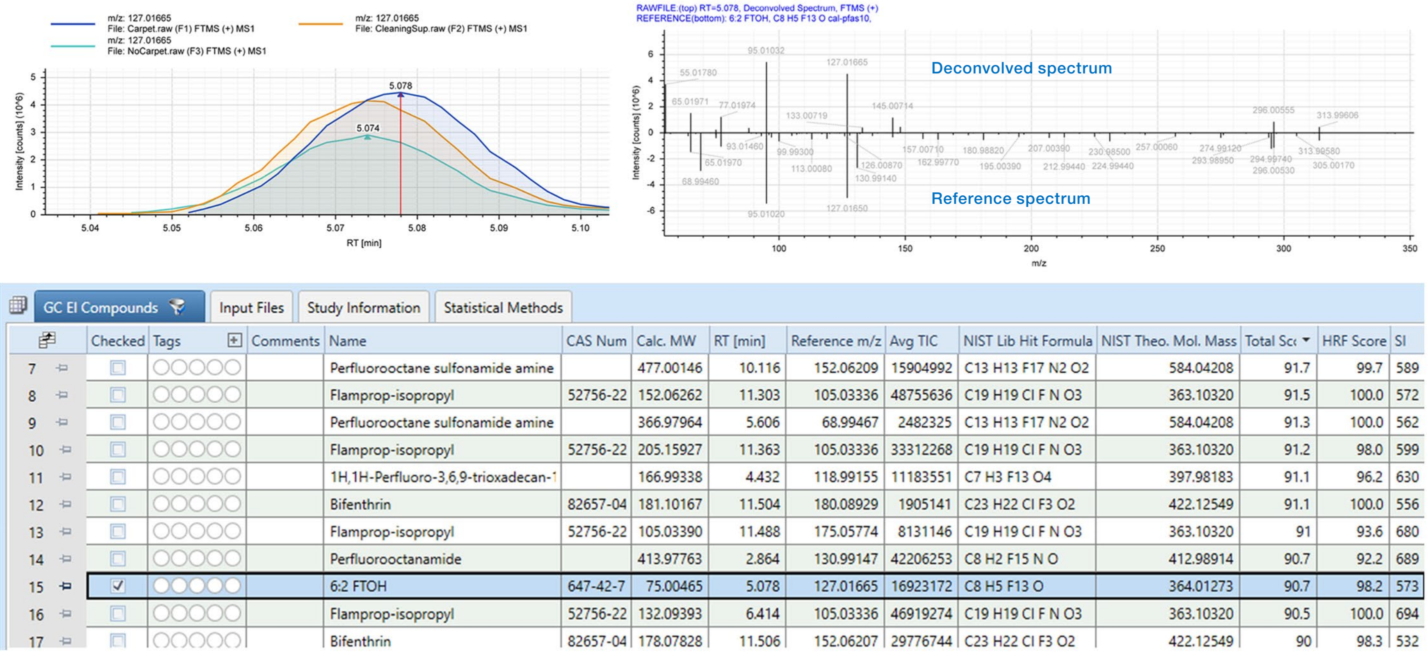


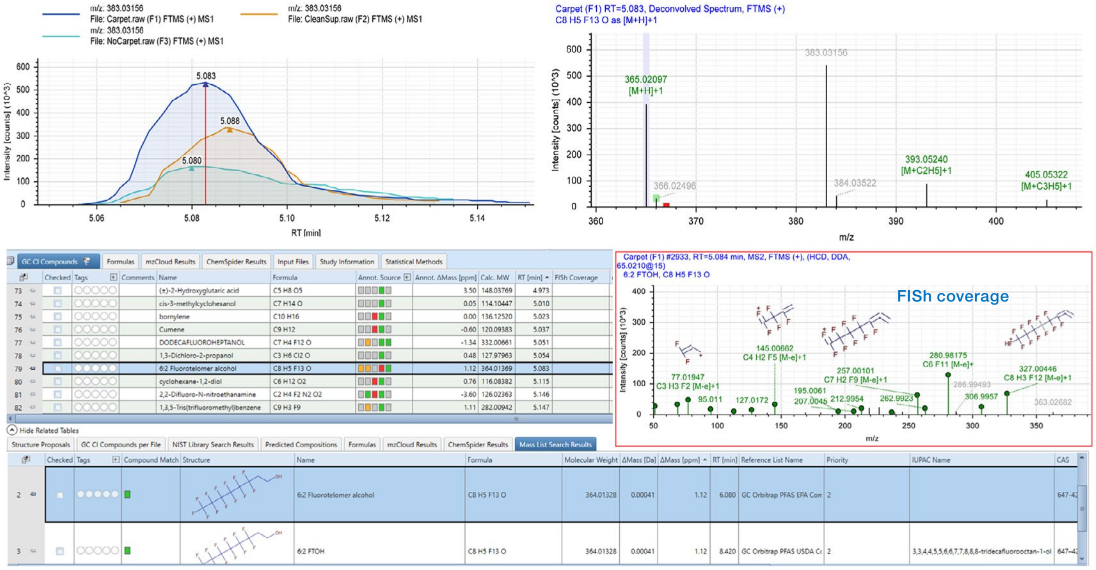
Figure 5. PCI workflow in Compound Discoverer software.



| | | Checked | Tags | Comments | Name | CAS Num | Calc. MW | RT [min] | Reference m/z | Avg TIC | NIST Lib Hit Formula | NIST Theo. Mol. Mass | Total Sc | HRF Score | SI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7 | | ☐ | ○○○○○ | | Perfluorooctane sulfonamide amine | | 477.00146 | 10.116 | 152.06209 | 15904992 | C13 H13 F17 N2 O2 | 584.04208 | 91.7 | 99.7 | 589 |
| 8 | | ☐ | ○○○○○ | | Flamprop-isopropyl | 52756-22 | 152.06262 | 11.303 | 105.03336 | 48755636 | C19 H19 Cl F N O3 | 363.10320 | 91.5 | 100.0 | 572 |
| 9 | | ☐ | ○○○○○ | | Perfluorooctane sulfonamide amine | | 366.97964 | 5.606 | 68.99467 | 2482325 | C13 H13 F17 N2 O2 | 584.04208 | 91.3 | 100.0 | 562 |
| 10 | | ☐ | ○○○○○ | | Flamprop-isopropyl | 52756-22 | 205.15927 | 11.363 | 105.03336 | 33312268 | C19 H19 Cl F N O3 | 363.10320 | 91.2 | 98.0 | 599 |
| 11 | | ☐ | ○○○○○ | | 1H,1H-Perfluoro-3,6,9-trioxadecan-1 | | 166.99338 | 4.432 | 118.99155 | 11183551 | C7 H3 F13 O4 | 397.98183 | 91.1 | 96.2 | 630 |
| 12 | | ☐ | ○○○○○ | | Bifenthrin | 82657-04 | 181.10167 | 11.504 | 180.08929 | 1905141 | C23 H22 Cl F3 O2 | 422.12549 | 91.1 | 100.0 | 556 |
| 13 | | ☐ | ○○○○○ | | Flamprop-isopropyl | 52756-22 | 105.03390 | 11.488 | 175.05774 | 8131146 | C19 H19 Cl F N O3 | 363.10320 | 91 | 93.6 | 680 |
| 14 | | ☐ | ○○○○○ | | Perfluorooctanamide | | 413.97763 | 2.864 | 130.99147 | 42206253 | C8 H2 F15 N O | 412.98914 | 90.7 | 92.2 | 689 |
| 15 | | ☑ | ○○○○○ | | 6:2 FTOH | 647-42-7 | 75.00465 | 5.078 | 127.01665 | 16923172 | C8 H5 F13 O | 364.01273 | 90.7 | 98.2 | 573 |
| 16 | | ☐ | ○○○○○ | | Flamprop-isopropyl | 52756-22 | 132.09393 | 6.414 | 105.03336 | 46919274 | C19 H19 Cl F N O3 | 363.10320 | 90.5 | 100.0 | 694 |
| 17 | | ☐ | ○○○○○ | | Bifenthrin | 82657-04 | 178.07828 | 11.506 | 152.06207 | 29776744 | C23 H22 Cl F3 O2 | 422.12549 | 90 | 98.3 | 532 |

Figure 6. Example of PFAS data mining using library match for indoor air samples.

Excessive fragmentation in EI analysis can hinder detection of the molecular ion. Confirmation of the molecular ion can be performed through PCI analysis along with additional structural information using ddMS$^2$ data. Using our previous example of 6:2 FTOH, the exact mass of its molecular ion (*m/z* 364.0369) was confirmed with a mass error of 1.12 ppm using both M+H and respective methane reagent adduct ions (Figure 7). In addition, the structure proposal generated from the MS$^2$ data was used in *in silico* fragmentation. Comparison of the experimental and expected fragmentation of the molecular ion produced a FISh coverage score of 80% to the expected fragmentation pattern.



GC CI Compounds | Formulas | mzCloud Results | ChemSpider Results | Input Files | Study Information | Statistical Methods

| | Checked | Tags | Comments | Name | Formula | Annot. Source | Annot. ΔMass [ppm] | Calc. MW | RT [min] | FISh Coverage |
|---|---|---|---|---|---|---|---|---|---|---|
| 73 | ☐ | ○○○○○ | | (±)-2-Hydroxyglutaric acid | C5 H8 O5 | ⬜⬜⬜🟩⬜ | 3.50 | 148.03769 | 4.973 | |
| 74 | ☐ | ○○○○○ | | cis-3-methylcyclohexanol | C7 H14 O | ⬜⬜⬜🟩⬜ | 0.05 | 114.10447 | 5.010 | |
| 75 | ☐ | ○○○○○ | | bornylene | C10 H16 | ⬜⬜🟥🟩⬜ | 0.00 | 136.12520 | 5.023 | |
| 76 | ☐ | ○○○○○ | | Cumene | C9 H12 | ⬜⬜🟥🟩⬜ | -0.60 | 120.09383 | 5.037 | |
| 77 | ☐ | ○○○○○ | | DODECAFLUOROHEPTANOL | C7 H4 F12 O | ⬜🟧⬜🟩🟩 | -1.34 | 332.00661 | 5.051 | |
| 78 | ☐ | ○○○○○ | | 1,3-Dichloro-2-propanol | C3 H6 Cl2 O | ⬜⬜⬜🟩⬜ | 0.48 | 127.97963 | 5.054 | |
| 79 | ☐ | ○○○○○ | | 6:2 Fluorotelomer alcohol | C8 H5 F13 O | 🟧🟧⬜🟥🟩 | 1.12 | 364.01369 | 5.083 | |
| 80 | ☐ | ○○○○○ | | cyclohexane-1,2-diol | C6 H12 O2 | ⬜⬜🟥🟩⬜ | 0.76 | 116.08382 | 5.115 | |
| 81 | ☐ | ○○○○○ | | 2,2-Difluoro-N-nitroethanamine | C2 H4 F2 N2 O2 | ⬜🟩🟥🟩⬜ | -3.60 | 126.02363 | 5.146 | |
| 82 | ☐ | ○○○○○ | | 1,3,5-Tris(trifluoromethyl)benzene | C9 H3 F9 | ⬜🟧⬜🟩⬜ | 1.11 | 282.00942 | 5.147 | |

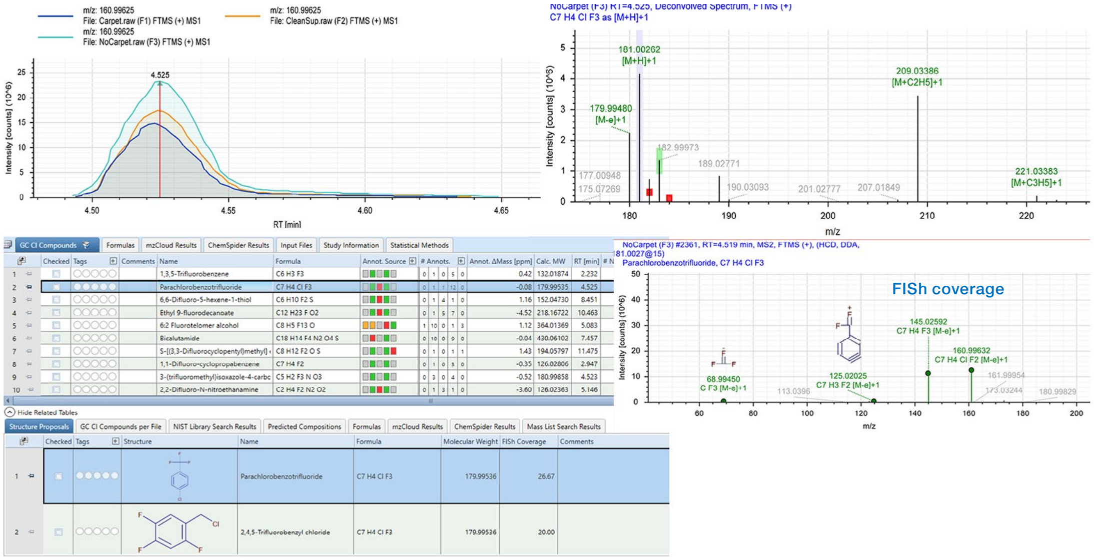
Hide Related Tables

Structure Proposals | GC CI Compounds per File | NIST Library Search Results | Predicted Compositions | Formulas | mzCloud Results | ChemSpider Results | Mass List Search Results

| | Checked | Tags | Compound Match | Structure | Name | Formula | Molecular Weight | ΔMass [Da] | ΔMass [ppm] | RT [min] | Reference List Name | Priority | IUPAC Name | CAS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | ☐ | ●●●●● | 🟩 | | 6:2 Fluorotelomer alcohol | C8 H5 F13 O | 364.01328 | 0.00041 | 1.12 | 6.080 | GC Orbitrap PFAS EPA Con | 2 | | 647-42 |
| 3 | ☐ | ○○○○○ | 🟩 | | 6:2 FTOH | C8 H5 F13 O | 364.01328 | 0.00041 | 1.12 | 8.420 | GC Orbitrap PFAS USDA C | 2 | 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctan-1-ol | 647-42 |

Figure 7. Identification of 6:2 FTOH using PCI ddMS$^2$ data, accurate *m/z* 364.0369, and FISh coverage.

Compounds that were not present in our PFAS library were also identified through the Compound Discoverer workflow. An example of this is parachlorbenzotrifluoride, eluting at 4.525 min, tentatively identified through the ChemSpider database search. The compound with accurate *m/z* 179.9953 was PCI amenable and displayed respective M+H ion and methane adducts. A FISh score of 26 was obtained through fragment matching, highlighting the need for further investigation (Figure 8). Using the information obtained in PCI on the molecular ion and proposed chemical formula, revisiting data collected in EI can provide further insight.



GC CI Compounds | Formulas | mzCloud Results | ChemSpider Results | Input Files | Study Information | Statistical Methods

| | Checked | Tags | Comments | Name | Formula | Annot. Source | # Annots. | Annot. ΔMass [ppm] | Calc. MW | RT [min] |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | ☐ | ○○○○○ | | 1,3,5-Trifluorobenzene | C6 H3 F3 | ⬜🟩⬜🟩⬜ | 0 1 0 5 0 | 0.42 | 132.01874 | 2.232 |
| 2 | ☐ | ●●●●● | | Parachlorobenzotrifluoride | C7 H4 Cl F3 | ⬜🟩🟥🟩⬜ | 0 1 1 12 0 | -0.08 | 179.99535 | 4.525 |
| 3 | ☐ | ○○○○○ | | 6,6-Difluoro-5-hexene-1-thiol | C6 H10 F2 S | ⬜🟩🟥🟩⬜ | 0 1 4 1 0 | 1.16 | 152.04730 | 8.451 |
| 4 | ☐ | ○○○○○ | | Ethyl 9-fluorodecanoate | C12 H23 F O2 | ⬜🟩🟥🟩⬜ | 0 1 5 7 0 | -4.52 | 218.16722 | 10.463 |
| 5 | ☐ | ○○○○○ | | 6:2 Fluorotelomer alcohol | C8 H5 F13 O | 🟧🟧⬜🟥🟩 | 1 10 0 1 3 | 1.12 | 364.01369 | 5.083 |
| 6 | ☐ | ○○○○○ | | Bicalutamide | C18 H14 F4 N2 O4 S | ⬜🟥⬜🟩⬜ | 0 10 0 9 0 | -0.04 | 430.06102 | 7.457 |
| 7 | ☐ | ○○○○○ | | S-[(3,3-Difluorocyclopentyl)methyl] | C8 H12 F2 O S | ⬜🟩⬜🟩🟥 | 0 1 0 1 1 | 1.43 | 194.05797 | 11.475 |
| 8 | ☐ | ○○○○○ | | 1,1-Difluoro-cyclopropabenzene | C7 H4 F2 | ⬜🟩⬜🟩⬜ | 0 1 0 3 0 | -0.35 | 126.02806 | 2.947 |
| 9 | ☐ | ○○○○○ | | 3-(trifluoromethyl)isoxazole-4-carbc | C5 H2 F3 N O3 | ⬜🟩⬜🟩⬜ | 0 3 0 4 0 | -0.52 | 180.99858 | 4.523 |
| 10 | ☐ | ○○○○○ | | 2,2-Difluoro-N-nitroethanamine | C2 H4 F2 N2 O2 | ⬜🟩🟥🟩⬜ | 0 1 3 1 0 | -3.60 | 126.02363 | 5.146 |

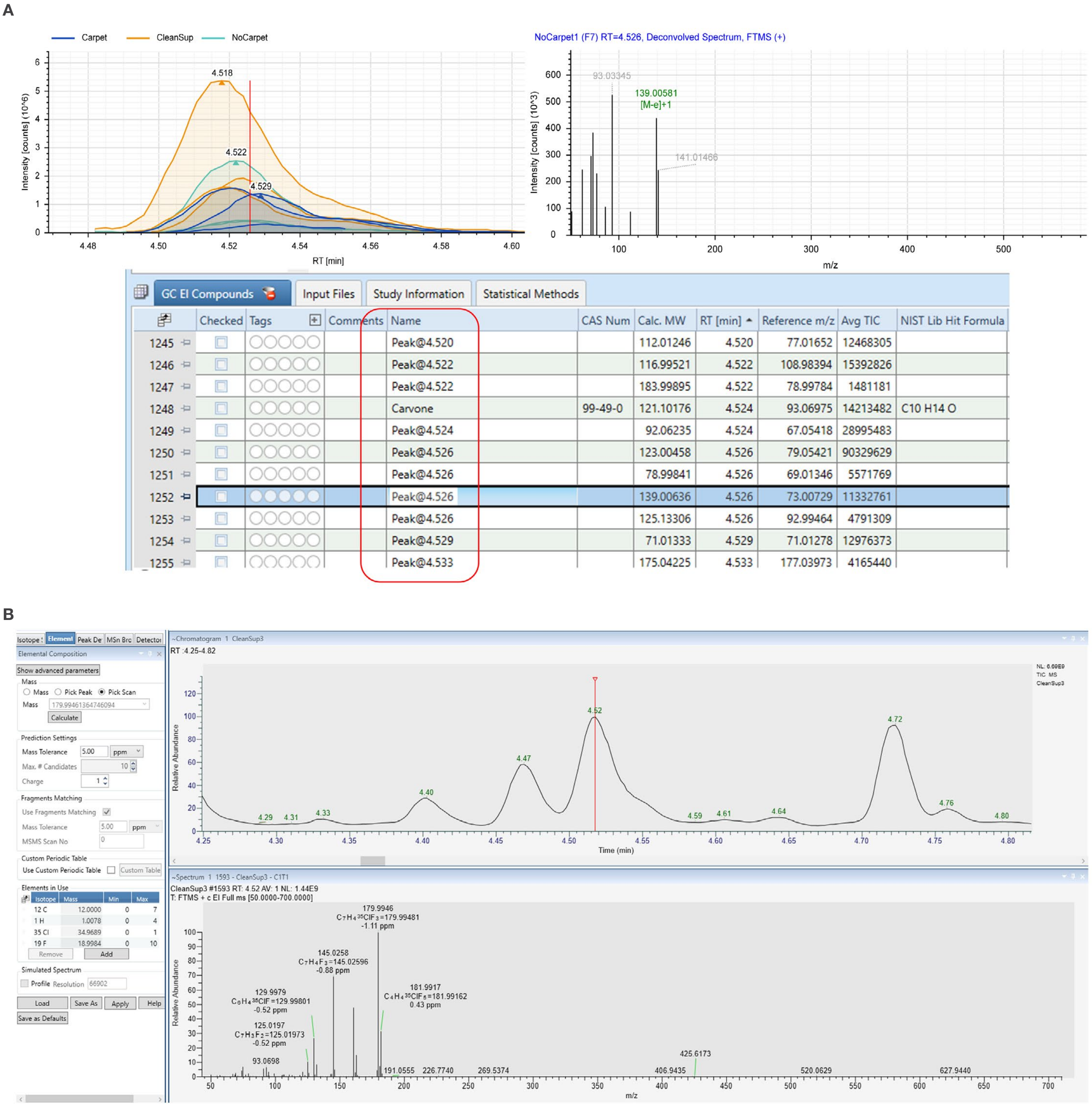
Hide Related Tables

Structure Proposals | GC CI Compounds per File | NIST Library Search Results | Predicted Compositions | Formulas | mzCloud Results | ChemSpider Results | Mass List Search Results

| | Checked | Tags | Structure | Name | Formula | Molecular Weight | FISh Coverage | Comments |
|---|---|---|---|---|---|---|---|---|
| 1 | ☐ | ●●●●● | | Parachlorobenzotrifluoride | C7 H4 Cl F3 | 179.99536 | 26.67 | |
| 2 | ☐ | ○○○○○ | | 2,4,5-Trifluorobenzyl chloride | C7 H4 Cl F3 | 179.99536 | 20.00 | |

Figure 8. Example of PFAS data mining for unknowns in indoor air samples using ChemSpider match and FISh coverage.

In our EI analysis, several co-eluted peaks were identified at the same retention time (Figure 9A). The peak at 4.52 min was further investigated using the FreeStyle software. The match formula proposed from ChemSpider in our PCI analysis was used to confirm elemental composition and mass accuracy of the EI fragments. Elemental composition analysis confirmed that the compound is indeed a PFAS, and EI fragments observed are part of the compound identified in PCI.



| | Checked | Tags | Comments | Name | CAS Num | Calc. MW | RT [min] ▲ | Reference m/z | Avg TIC | NIST Lib Hit Formula |
|---|---|---|---|---|---|---|---|---|---|---|
| 1245 | ☐ | ○○○○○ | | Peak@4.520 | | 112.01246 | 4.520 | 77.01652 | 12468305 | |
| 1246 | ☐ | ○○○○○ | | Peak@4.522 | | 116.99521 | 4.522 | 108.98394 | 15392826 | |
| 1247 | ☐ | ○○○○○ | | Peak@4.522 | | 183.99895 | 4.522 | 78.99784 | 1481181 | |
| 1248 | ☐ | ○○○○○ | | Carvone | 99-49-0 | 121.10176 | 4.524 | 93.06975 | 14213482 | C10 H14 O |
| 1249 | ☐ | ○○○○○ | | Peak@4.524 | | 92.06235 | 4.524 | 67.05418 | 28995483 | |
| 1250 | ☐ | ○○○○○ | | Peak@4.526 | | 123.00458 | 4.526 | 79.05421 | 90329629 | |
| 1251 | ☐ | ○○○○○ | | Peak@4.526 | | 78.99841 | 4.526 | 69.01346 | 5571769 | |
| 1252 | ☐ | ○○○○○ | | Peak@4.526 | | 139.00636 | 4.526 | 73.00729 | 11332761 | |
| 1253 | ☐ | ○○○○○ | | Peak@4.526 | | 125.13306 | 4.526 | 92.99464 | 4791309 | |
| 1254 | ☐ | ○○○○○ | | Peak@4.529 | | 71.01333 | 4.529 | 71.01278 | 12976373 | |
| 1255 | ☐ | ○○○○○ | | Peak@4.533 | | 175.04225 | 4.533 | 177.03973 | 4165440 | |

Elemental Composition

Mass: ○ Mass ○ Pick Peak ● Pick Scan

Mass: 179.99461364746094

Prediction Settings

Mass Tolerance: 5.00 ppm

Max. # Candidates: 10

Charge: 1

Fragments Matching

Use Fragments Matching: ☑

Mass Tolerance: 5.00 ppm

MSMS Scan No: 0

Custom Periodic Table

Use Custom Periodic Table: ☐

Elements in Use

| Isotope | Mass | Min | Max |
|---|---|---|---|
| 12 C | 12.0000 | 0 | 7 |
| 1 H | 1.0078 | 0 | 4 |
| 35 Cl | 34.9689 | 0 | 1 |
| 19 F | 18.9984 | 0 | 10 |

Simulated Spectrum

☐ Profile Resolution 66902

CleanSup3 #1593 RT: 4.52 AV: 1 NL: 1.44E9

T: FTMS + c EI Full ms [50.0000-700.0000]

179.9946 $C_7H_4{}^{35}ClF_3$=179.99481 -1.11 ppm

145.0258 $C_7H_4F_3$=145.02596 -0.88 ppm

129.9979 $C_6H_4{}^{35}ClF$=129.99801 -0.52 ppm

125.0197 $C_7H_3F_2$=125.01973 -0.52 ppm

181.9917 $C_4H_4{}^{35}ClF_5$=181.99162 0.43 ppm

Figure 9. (A) EI data with co-eluted peaks at 4.526 min that were present in all indoor air samples; (B) elemental composition of the peak at 4.52 min from an indoor air sample analyzed in Freestyle software confirms the PFAS compound.

## Conclusions

This study successfully demonstrated the effectiveness of thermal desorption (TD) coupled with high-resolution accurate-mass (HRAM) gas chromatography - Orbitrap mass spectrometry (GC-MS) as a powerful approach for untargeted screening of volatile PFAS in indoor air. Thermal desorption, while reducing the need for complex extraction and sample preparations, boosted sensitivity by concentrating volatile PFAS present in air. HRAM delineated target compounds from background noise or matrix interference for precise measurements.

Untargeted PFAS screening was performed by using a top-tier ensemble of Thermo Scientific™ software entailing Chromeleon CDS for instrument control and acquisition combined with FreeStyle software and Compound Discoverer software for data analysis for a simplified screening approach. Qualitative data analysis was facilitated by FreeStyle software through data visualization and HRAM data curation. Compound Discoverer software streamlined compound identification and comparative analyses, and provided extensive filtering and data graphics display capabilities. Also, the built-in EI/CI workflows for GC-MS together with variable electron voltage (VeV) for softer ionization provided complementary fragmentation information enhancing confidence of PFAS identification. Integrated libraries, databases, and robust statistical analysis tools available in Compound Discoverer software enabled rapid and precise insights to the untargeted screening approach, greatly simplifying interpretation.

Data demonstrate the presence of many volatile PFAS in indoor air. Air samples analyzed from the three areas under study—carpeted, non-carpeted, and cleaning supplies storage closet—represent common areas with exposure to consumer cleaning products. Occurrence of volatile PFAS in indoor air confirms the off-gassing and persistence of these “forever chemicals” resulting from use of consumer cleaning products. As expected, indoor air from the carpeted and cleaning closet had the largest amount of these chemicals with concentrations ≤0.01-0.03 ppt. PFAS detected were predominantly fluoropolymers containing fluorotelomer or fluoroalkyl sulfonate moieties.

Overall, the proposed approach delivers high analytical confidence, simplified workflow integration, and the ability to uncover emerging or unexpected PFAS species, providing environmental and industrial laboratories with a valuable tool for air quality monitoring.

## Acknowledgment

The authors sincerely acknowledge Markes International Inc. for loaning the Markes International TD100-xr Advanced Thermal Desorber for this study.

### References

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# Appendix

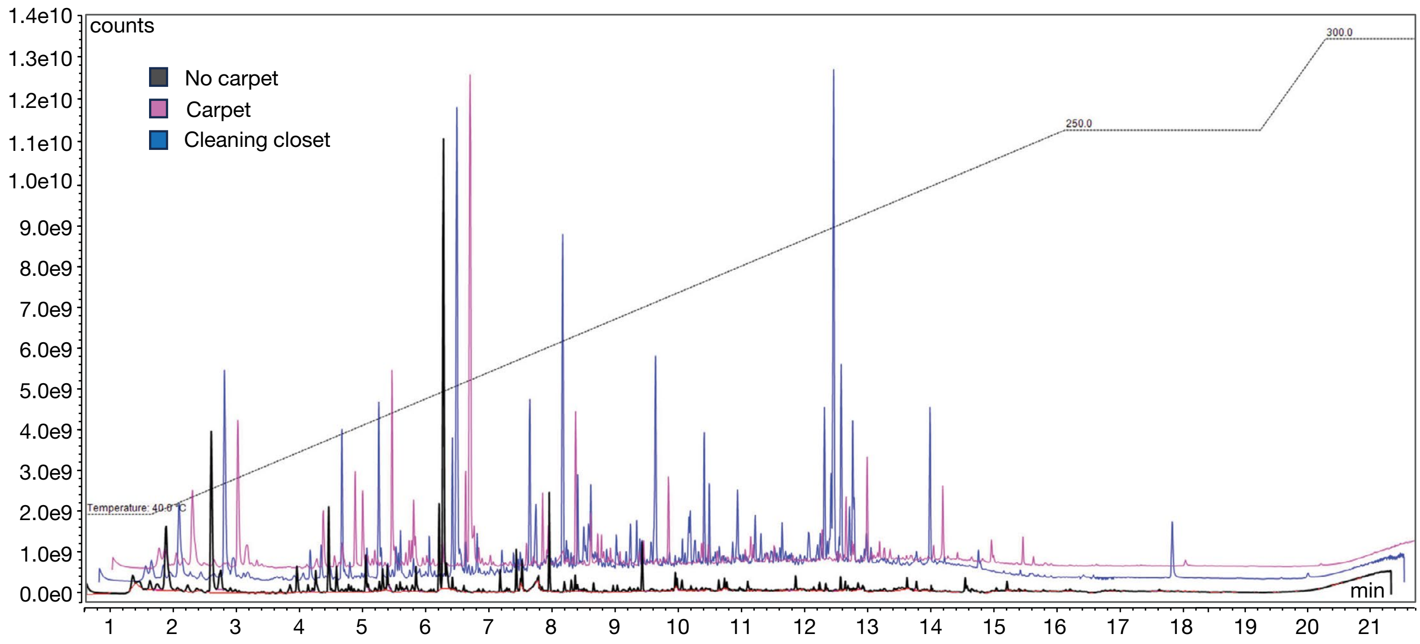


Figure A1. Total ion chromatogram of three different indoor air samples in EI Full Scan mode.

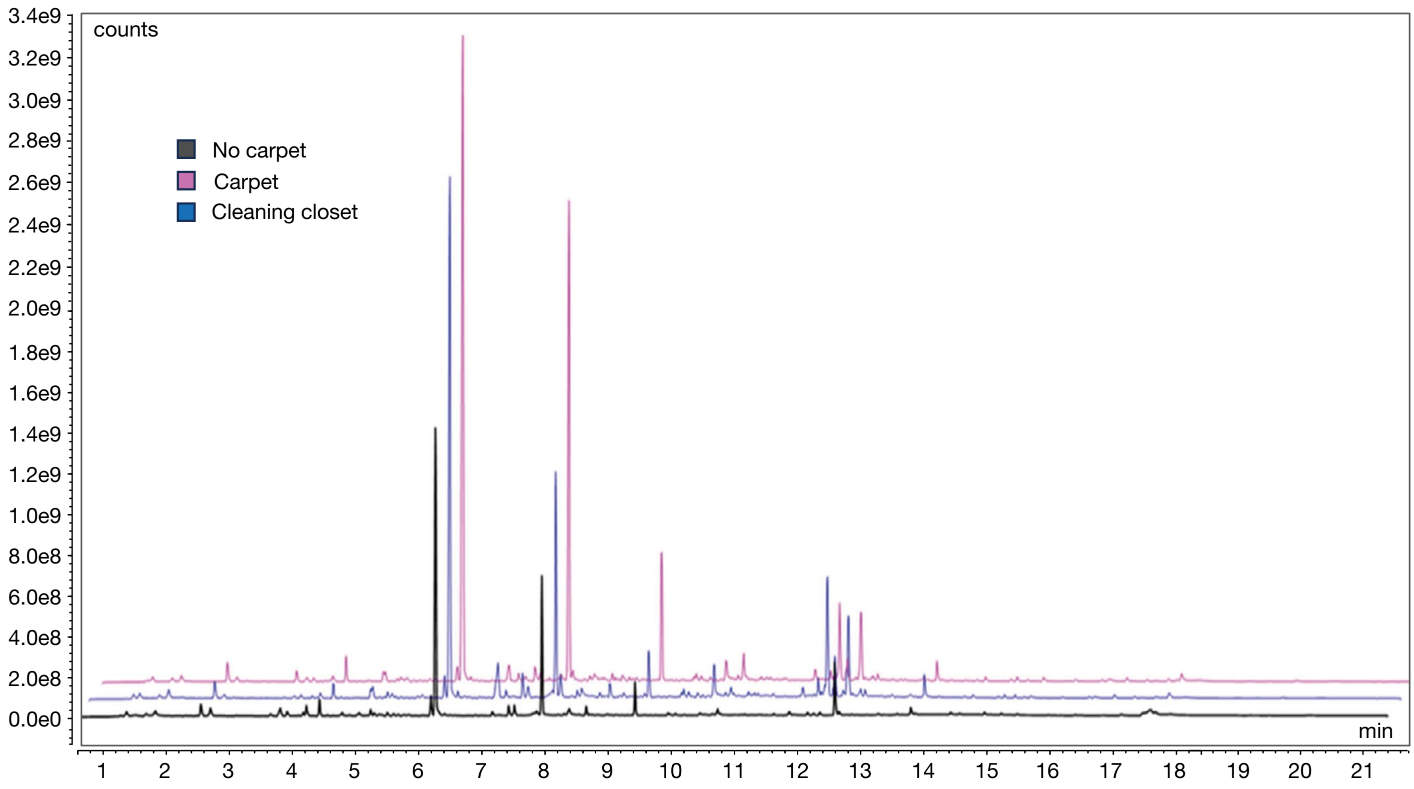
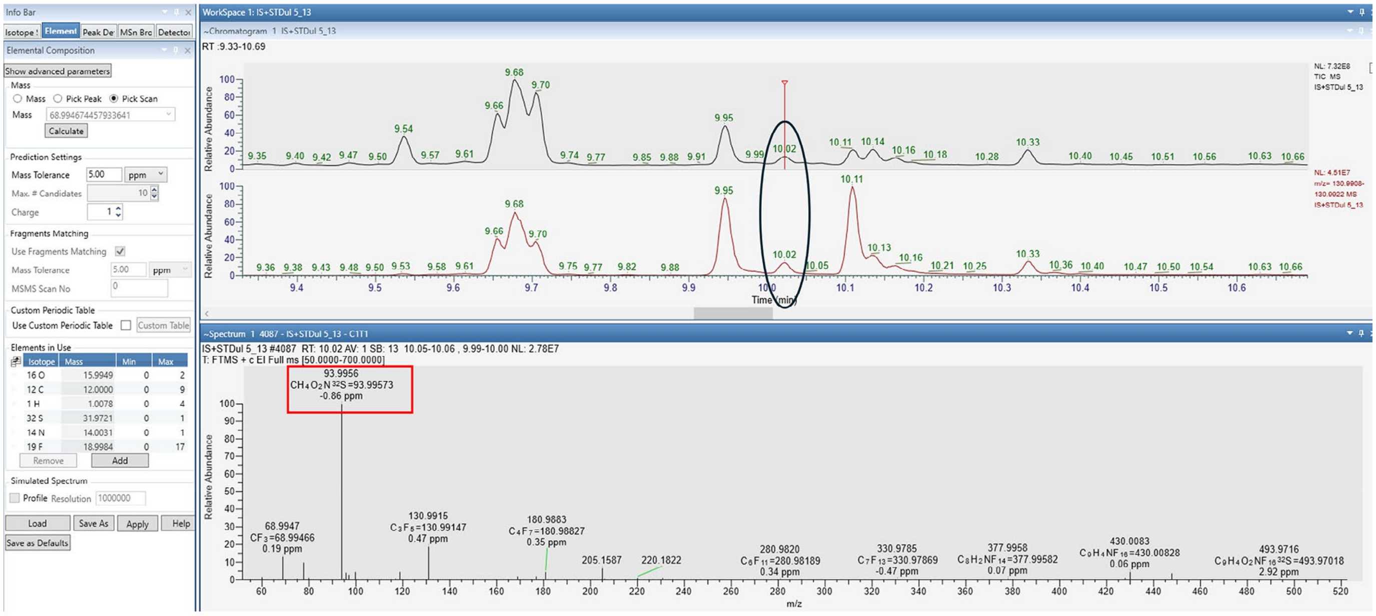


**Figure A2. Total ion chromatogram of three different indoor air samples in positive CI mode (Full Scan filter from a PCI ddMS$^2$ method).** Note fewer peaks as compared to EI acquisition in Figure A1.

**A**



Mass

○ Mass ○ Pick Peak ● Pick Scan

Mass: 68.994674457933641

Prediction Settings

Mass Tolerance: 5.00 ppm

Max. # Candidates: 10

Charge: 1

Fragments Matching

Use Fragments Matching ☑

Mass Tolerance: 5.00 ppm

MSMS Scan No: 0

Custom Periodic Table

Use Custom Periodic Table ☐ Custom Table

Elements in Use

| Isotope | Mass | Min | Max |
|---|---|---|---|
| 16 O | 15.9949 | 0 | 2 |
| 12 C | 12.0000 | 0 | 9 |
| 1 H | 1.0078 | 0 | 4 |
| 32 S | 31.9721 | 0 | 1 |
| 14 N | 14.0031 | 0 | 1 |
| 19 F | 18.9984 | 0 | 17 |

Simulated Spectrum

☐ Profile Resolution 1000000

IS+STDul 5_13 #4087 RT: 10.02 AV: 1 SB: 13 10.05-10.06 , 9.99-10.00 NL: 2.78E7

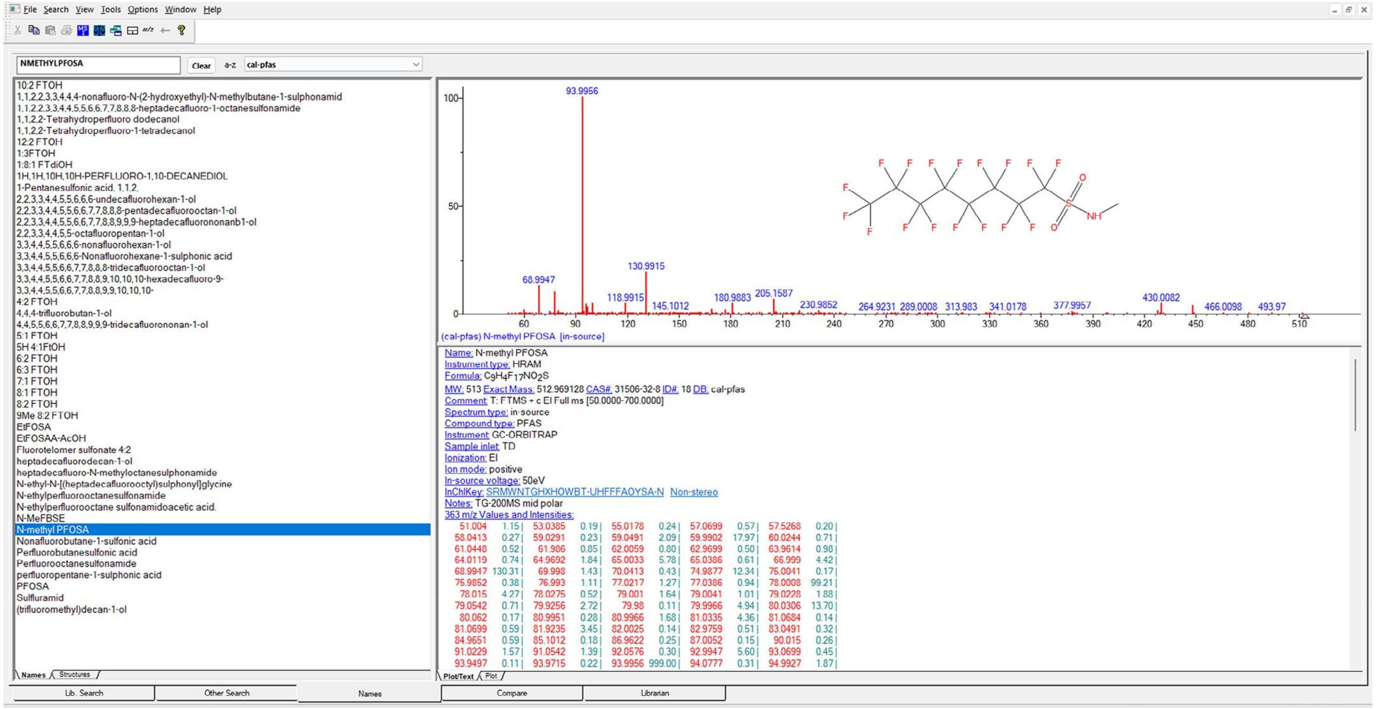
T: FTMS + c EI Full ms [50.0000-700.0000]

93.9956

$CH_4O_2N^{32}S$ =93.99573

-0.86 ppm

**B**



NMETHYLPFOSA

10:2 FTOH
1,1,2,2,3,3,4,4,4-nonafluoro-N-(2-hydroxyethyl)-N-methylbutane-1-sulphonamid
1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-1-octanesulfonamide
1,1,2,2-Tetrahydroperfluoro dodecanol
1,1,2,2-Tetrahydroperfluoro-1-tetradecanol
12:2 FTOH
1:3FTOH
1:8:1 FTdiOH
1H,1H,10H,10H-PERFLUORO-1,10-DECANEDIOL
1-Pentanesulfonic acid, 1,1,2,
2,2,3,3,4,4,5,5,6,6,6-undecafluorohexan-1-ol
2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluorooctan-1-ol
2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononanb1-ol
2,2,3,3,4,4,5,5-octafluoropentan-1-ol
3,3,4,4,5,5,6,6,6-nonafluorohexan-1-ol
3,3,4,4,5,5,6,6,6-Nonafluorohexane-1-sulphonic acid
3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctan-1-ol
3,3,4,4,5,5,6,6,7,7,8,8,9,10,10,10-hexadecafluoro-9-
3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-
4:2 FTOH
4,4,4-trifluorobutan-1-ol
4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononan-1-ol
5:1 FTOH
5H 4:1FtOH
6:2 FTOH
6:3 FTOH
7:1 FTOH
8:1 FTOH
8:2 FTOH
9Me 8:2 FTOH
EtFOSA
EtFOSAA-AcOH
Fluorotelomer sulfonate 4:2
heptadecafluorodecan-1-ol
heptadecafluoro-N-methyloctanesulphonamide
N-ethyl-N-[(heptadecafluorooctyl)sulphonyl]glycine
N-ethylperfluorooctanesulfonamide
N-ethylperfluorooctane sulfonamidoacetic acid.
N-MeFBSE
N-methyl PFOSA
Nonafluorobutane-1-sulfonic acid
Perfluorobutanesulfonic acid
Perfluorooctanesulfonamide
perfluoropentane-1-sulphonic acid
PFOSA
Sulfluramid
(trifluoromethyl)decan-1-ol

Name: N-methyl PFOSA
Instrument type: HRAM
Formula: $C_9H_4F_{17}NO_2S$
MW: 513 Exact Mass: 512.969128 CAS#: 31506-32-8 ID#: 18 DB: cal-pfas
Comment: T: FTMS + c EI Full ms [50.0000-700.0000]
Spectrum type: in-source
Compound type: PFAS
Instrument: GC-ORBITRAP
Sample inlet: TD
Ionization: EI
Ion mode: positive
In-source voltage: 50eV
InChIKey: SRMWNTGHXHOWBT-UHFFFAOYSA-N Non-stereo
Notes: TG-200MS mid polar
363 m/z Values and Intensities:

```
  51.004   1.15|  53.0385   0.19|  55.0178   0.24|  57.0699   0.57|  57.5268   0.20|
 58.0413   0.27|  59.0291   0.23|  59.0491   2.09|  59.9902  17.97|  60.0244   0.71|
 61.0448   0.52|   61.986   0.85|  62.0059   0.80|  62.9699   0.50|  63.9614   0.98|
 64.0119   0.74|  64.9692   1.84|  65.0033   5.78|  65.0386   0.61|   66.999   4.42|
 68.9947 130.31|   69.998   1.43|  70.0413   0.43|  74.9877  12.34|  75.0041   0.17|
 75.9852   0.38|   76.993   1.11|  77.0217   1.27|  77.0386   0.94|  78.0008  99.21|
  78.015   4.27|  78.0275   0.52|   79.001   1.64|  79.0041   1.01|  79.0228   1.88|
 79.0542   0.71|  79.9256   2.72|    79.98   0.11|  79.9966   4.94|  80.0306  13.70|
  80.062   0.17|  80.9951   0.28|  80.9966   1.68|  81.0335   4.36|  81.0684   0.14|
 81.0699   0.59|  81.9235   3.45|  82.0025   0.14|  82.9759   0.51|  83.0491   0.32|
 84.9651   0.59|  85.1012   0.18|  86.9622   0.25|  87.0052   0.15|   90.015   0.26|
 91.0229   1.57|  91.0542   1.39|  92.0576   0.30|  92.9947   5.60|  93.0699   0.45|
 93.9497   0.11|  93.9715   0.22|  93.9956 999.00|  94.0777   0.31|  94.9927   1.87|
```

Figure A3. (A) Curation of N-methyl PFOSA at RT 10.02 in Freestyle software with the elemental composition showing *m/z* 93.9956 EI fragment at less than 1 ppm mass accuracy; (B) Curated HRAM spectra for N-methyl PFOSA after import into in-house curated PFAS HRAM EI database.

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