

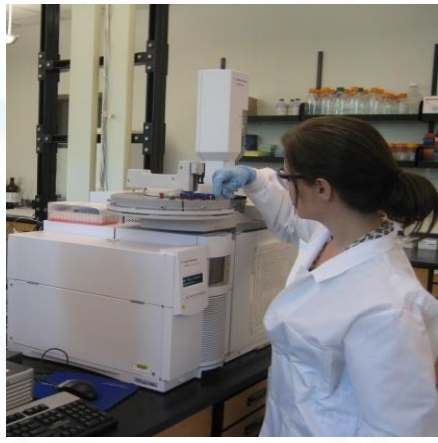

Tools for the analysis of Per-and Polyfluoroalkyl Substances (PFAS)

Jessica L. Reiner, Chemical Sciences Division

NIST
National Institute of Standards and Technology
U.S. Department of Commerce

MATERIAL MEASUREMENT LABORATORY

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National Institute of Standards and Technology

NIST is a non-regulatory Bureau within the Department of Commerce

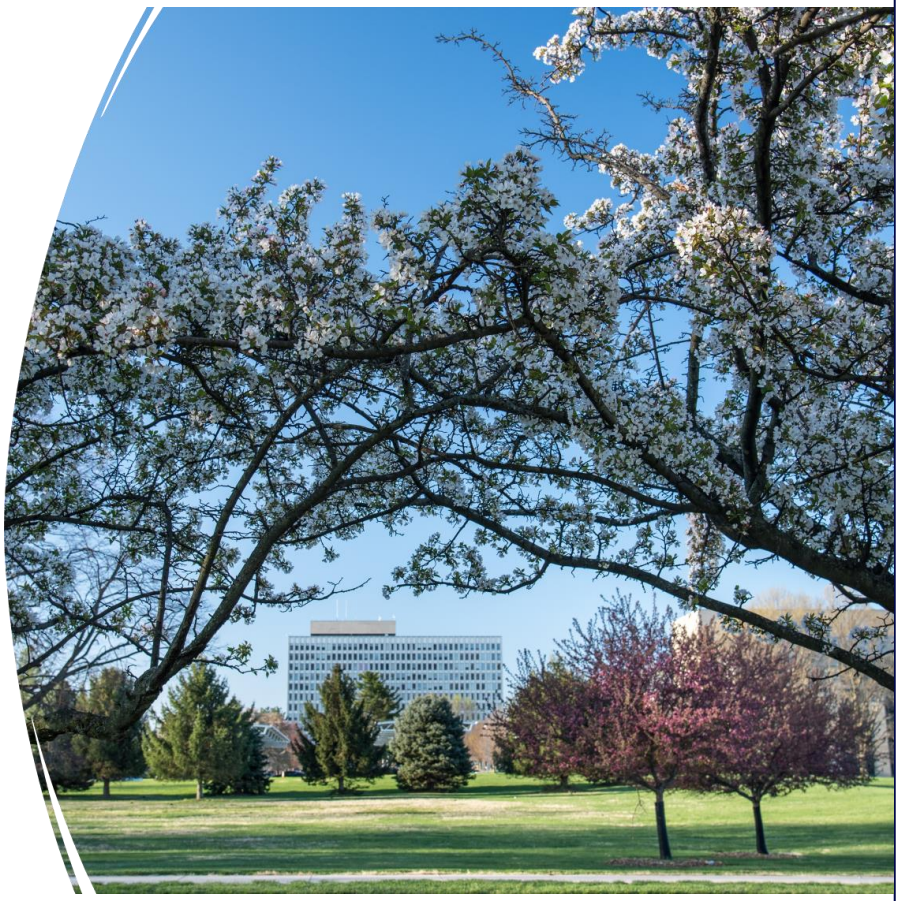
NIST mission … promote US innovation and industrial competitiveness by advancing measurement science, standards, and technology

The Chemical Sciences Division at NIST provides measurement services for a wide range of industries.

Provide traceability infrastructure for the nation for the measurement of chemical species in clinical, environmental, and food matrices

Develop new technologies based on separation and mass spectrometric techniques for measurement of chemical species

Assist industry to meet measurement goals



NIST Laboratory Programs

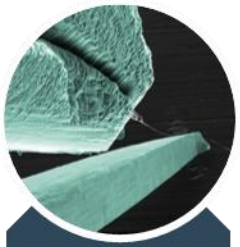

Material Measurement Laboratory

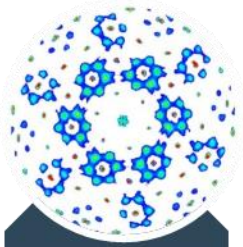

Physical Measurement Laboratory


Engineering Laboratory


Information Technology Laboratory


Communication Technology Laboratory


Center for Nanoscale Science and Technology


NIST Center for Neutron Research

Metrology Laboratories

Driving innovation through Measurement Science and Standards

Technology Laboratories

Accelerating the adoption and deployment of advanced technology solutions

National User Facilities

Providing world class, unique, cutting-edge research facilities

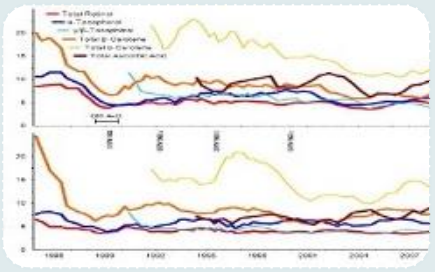
Measurement Services

Reference materials and data

- **1,200** Standard Reference Material products
- **100** Standard Reference Data products

User facilities

- National Synchrotron Light Source II at Brookhaven National Laboratory
- nSoft consortium at NIST Center for Neutron Research



Measurement quality assurance programs

- Cannabis
- Clinical measurements
- Dietary supplements
- Food nutrition and safety
- Marine environment

Reference Materials (RMs)

Standard Reference Materials (SRMs) are Certified Reference Materials (CRMs) issued by the National Institute of Standards and Technology (NIST)

Homogeneous, well-characterized materials used to validate measurements and improve the quality of analytical data

Support accurate and comparable measurements

SRMs are provided to support clinical, food, environmental, fuel, metal alloy, cement, and advanced materials analyses

SRMs for chemical measurements

- High Purity Neat Chemicals
  - Organic Calibration Solutions
  - Inorganic Calibration Solutions
  - Gas Mixture Standards
- Complex Matrix Standards
  - Advanced Materials
  - Biological Fluids/Tissues
  - Foods/Botanicals
  - Sediments/Soils/Particulates
  - House Dust

SRMs

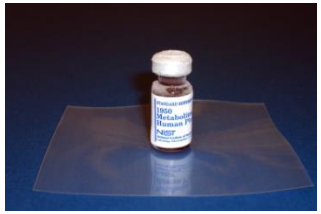
NIST has a variety of human SRMs including

- Serum, Plasma, Milk, Urine, Hair

NIST has a variety of natural matrix SRMs including

- Fish tissue, Mussel tissue, House dust

Measurements on these materials include chemical contaminants, elements, vitamins, metabolites, etc…



Use of Complex or Natural-Matrix SRMs

Method Development

You can analyze the SRM using a new analytical method as you develop it. If your result agrees with the assigned value, then your method will probably give good values for other similar samples

Method Validation

You can analyze the SRM and other samples typical of those that you will analyze (matrix, concentration) to demonstrate your method's scope of applicability and that your method has acceptable accuracy, repeatability, and selectivity. (AOAC recommends analysis of at least three materials, at least in duplicate, on at least two days.)

Quality Control (QC)

You can prepare and analyze the SRM the same way as you would an unknown sample. If your result for the SRM agrees with the assigned value, then your results for your own sample are probably right.

Traceability

You can prepare and analyze the SRM along with an in-house QC material over a set timeframe to establish values for your in-house QC, and then use that material for routine quality assurance.

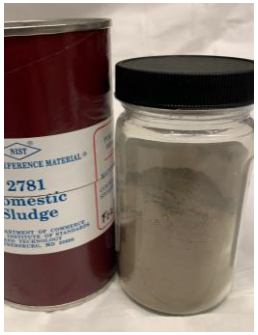
NIST's Role in PFAS Measurement

NIST (2004-present)

- NIST developed measurement methods for PFAS using LC-MS/MS
- Added PFAS values to existing SRM
- 15 materials with PFAS measurements
- Four **New** AFFF Reference Materials (7/2023)
- Working on contaminated soil, contaminated food, low level drinking water

Sediment	Tissue	Human Fluids	Calibration Standards	Other
2586 – Soil containing lead from paint	1946 – Lake Superior Fish Tissue	1957/1958 - Human Serum	RM 8446	2781 – Domestic Sludge
1936 – Great Lakes Sediment	1947 – Lake Michigan Fish Tissue	1950 - Human Plasma	RM 8447	2585 – House Dust

PFAS in Environmental Matrices



PFAS in Aqueous Film-Forming Foams (AFFF)

- Four individual formulations of AFFF (diluted and modified)
- Wide range of concentrations for up to 16 PFAS
- Designed for the identification and quantification of PFAS in AFFF

PFAS in Food

- Fish tissue (in production)
- Frozen meat (in progress)
  - Bull
  - Dairy cow
  - Porcine
- Plant materials (in progress)
  - Corn silage
  - Spinach
- Quality Assurance Programs
  - *Freeze-dried milk (cow)*
  - *Freeze-dried egg (chicken)*

Interlaboratory Studies for PFAS

NIST routinely coordinates interlaboratory studies where participating laboratories are given select materials and laboratories provide data for the concentration of PFAS (or other chemicals) in the materials.

- Quality Assurance Programs (QAPs) are interlaboratory studies aimed at providing results and feedback to laboratories, and sometimes subsequent interlaboratory studies, aimed at improving measurement capabilities of participating laboratories.

Interlaboratory Study for PFAS in AFFF

- Participating laboratories were sent four AFFF commercial mixtures and asked to provide quantitative data for specific PFAS.
- Project was supported in part by DOD SERDP Project ER18-1664.

National Institute of Standards and Technology Internal Report (NISTIR 8399)
https://doi.org/10.6028/NIST.IR.8399

Quality Assurance Program for PFAS in Food

- In 2023, as part of the Food Nutrition and Safety Measurements Quality Assurance Program (FNSQAP), three materials were sent to participating laboratories to measure select PFAS:
  - Frozen meat (beef)
  - Freeze-dried milk (cow)
  - Freeze-dried egg (chicken)
- Data is still being analyzed and a final report is expected soon.

NIST Data Tools for the Non-Targeted Analysis of PFAS

- NIST List of Possible Per- and Polyfluoroalkyl Substances
- PFAS in the NIST Mass Spectral Libraries
- Database Infrastructure for Mass Spectrometry (DIMSpec)

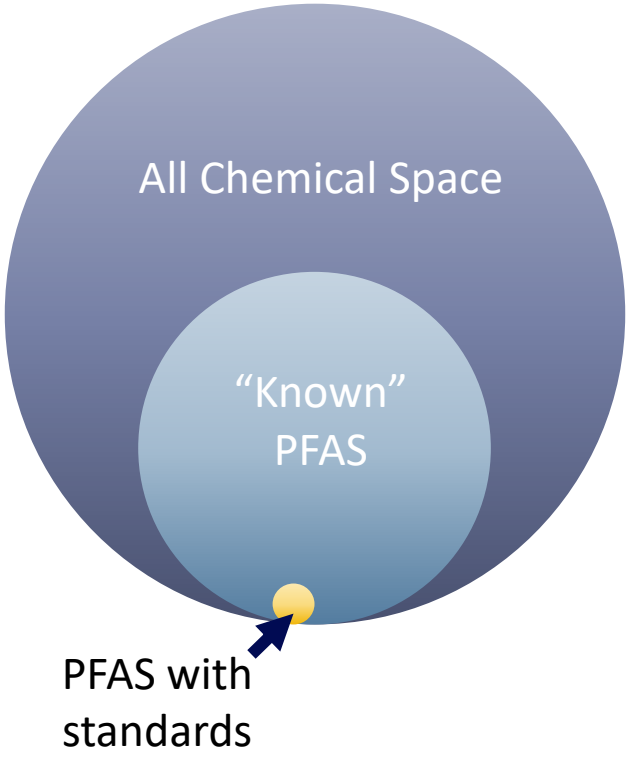
Per- and polyfluoroalkyl substances

Estimates for the total number of different PFAS in the environment and/or used in varying industries can be over 4,000.

There are a limited number of analytical standards available for these compounds.

- Estimated ~100 standards commercially available.
- This makes traditional targeted approaches (LC-MS/MS) more difficult

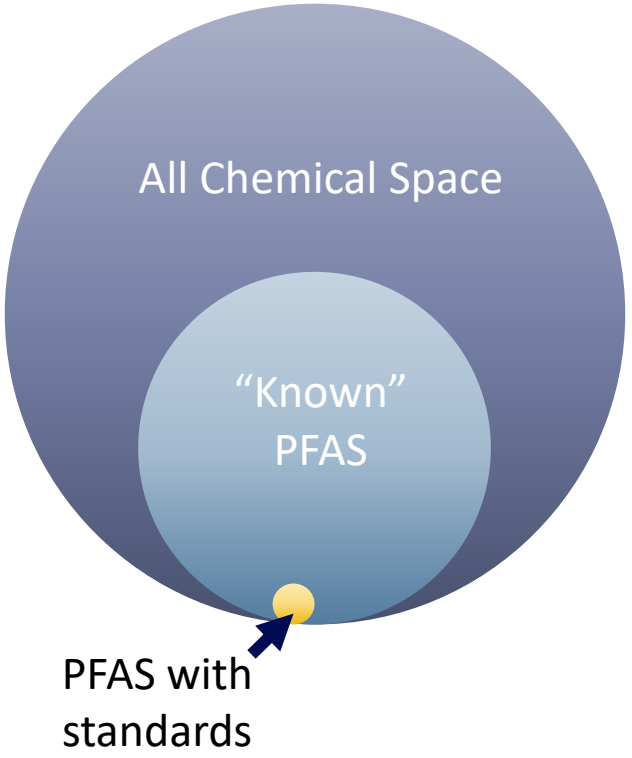
Non-Targeted Analysis and **Suspect Screening Analysis** are two approaches towards the detection of known and unknown PFAS without the availability of authentic analytical standards.



Non-Targeted Analysis

Non-targeted analysis (NTA) is a theoretical concept that can be broadly defined as the characterization of the chemical composition of any given sample without the use of *a priori* knowledge regarding the sample's chemical content.

Suspect screening analysis (SSA) is the identification of chemicals and/or chemical classes detected by an instrument, typically a mass spectrometer, by comparison to a predefined user list or library containing known chemicals of interest.



Benchmarking and Publications for Non-Targeted Analysis Working Group. https://nontargetedanalysis.org/

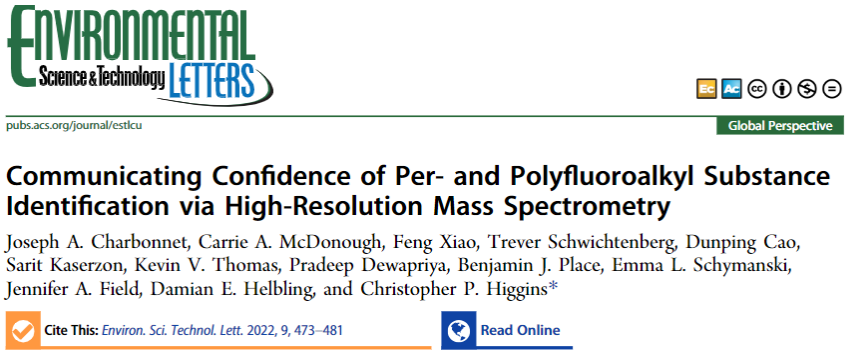
Standardized and Consistent Reporting of PFAS Identities

Naming protocols for PFAS have varied over the years.

- We recommend the use of compound identifiers and/or structural notation for reporting the discovery and identification of novel PFAS.

Use of standard protocols for stating the identification confidence of a novel PFAS.

- Charbonnet et al. provides a new scale for communicating the confidence for PFAS identification.



NIST Suspect List of Possible PFAS

Purpose: To create a central location for PFAS identified by peer-reviewed manuscripts, other documentations, or computational tools.

- Identities are attributed to discovery source.
- Structures (as InChI) are the key value (not name, acronym, elemental formula, etc.).
- Index values are constant
- Additional information (acronym, chemical class, etc.) available.

Built upon efforts by Colorado School of Mines, Oregon State University, and others.

Public contributions are allowed, does not require chemical registration or other official entry protocol.

NIST Suspect List of Possible Per- and Polyfluoroalkyl Substances

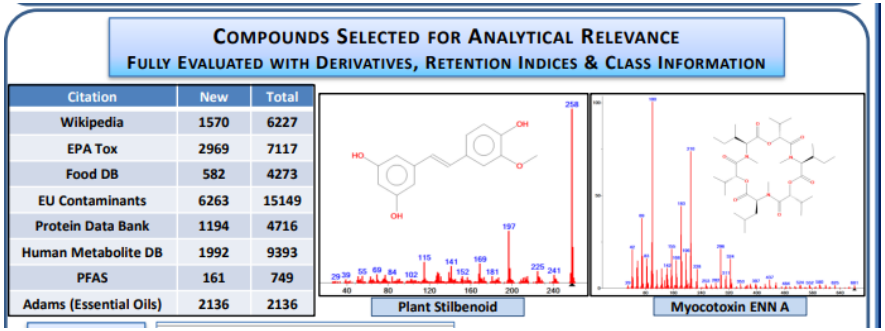
ID	CHEMICAL_NAME	INCHI	SMILES	INCHIKE	FORMUL	FIXEDMASS
1	1H-Perfluoro-3,3-bis(trifluorom	InChI=1S/C8HF13/c1-2-3(6(13,14)15,7(16,17)18)4(9,10)5(11,12)8(19,20)21/h1H	C#CC(C(C((	UEYXJPFQ	C8HF13	343.9870669
2	Bis(heneicosafluorodecyl)phosp	InChI=1S/C20H9F34O2P/c21-5(22,7(25,26)9(29,30)11(33,34)13(37,38)15(41,42)17	C(CP(=O)((	DEENCVDX	C20H9F34	957.9797256
3	Tris(2-(perfluorododecyl)ethyl)p	InChI=1S/C42H12F75O4P/c43-7(44,10(49,50)13(55,56)16(61,62)19(67,68)22(73,74	C(COP(=O)	JKDZBIHM	C42H12F7	2035.927562
4	2-Chloro-2-propenoic acid 3,3,4	InChI=1S/C9H6ClF9O2/c1-4(10)5(20)21-3-2-6(11,12)7(13,14)8(15,16)9(17,18)19/h	C=C(C(=O)	CVMPVWS	C9H6ClF9O	351.9912611
5	Bicyclo[2.2.1]hept-2-ene, 5,5,6-	InChI=1S/C10H6F10O/c11-6(12)4-1-2-5(3-4)7(6,13)21-10(19,20)8(14,15)9(16,17)1	C1=CC2CC	JZEKVGIW	C10H6F10	332.025897
6	3,3,4-Trifluoro-4-(heptafluoropr	InChI=1S/C12H8F10O/c13-8(14)6-4-1-2-5(3-4)7(6)9(8,15)23-12(21,22)10(16,17)11	C1=CC2CC	NGEYGRCI	C12H8F10	358.0415471
7	5-(Nonafluorobutyl)bicyclo[2.2.	InChI=1S/C11H9F9/c12-8(13,7-4-5-1-2-6(7)3-5)9(14,15)10(16,17)11(18,19)20/h1-2	C1=CC2CC	QAIOQFZL	C11H9F9	312.0560543
8	3-(Heptafluorobutyryl)camphor	InChI=1S/C14H15F7O2/c1-10(2)6-4-5-11(10,3)8(22)7(6)9(23)12(15,16)13(17,18)14	CC1(C)C2C	PEWOESYI	C14H15F7	348.0960273
9	Perfluorobutylsulfonamide	InChI=1S/C4H2F9NO2S/c5-1(6,3(9,10)11)2(7,8)4(12,13)17(14,15)16/h(H2,14,15,16	C(C(C(F)(F)	FUVKFLJW	C4H2F9NO	298.9662533
10	N-(3,4-Dichlorophenyl)-2,2,3,3,4	InChI=1S/C10H4Cl2F7NO/c11-5-2-1-4(3-6(5)12)20-7(21)8(13,14)9(15,16)10(17,18)	c1cc(c(cc1	INMDAGXI	C10H4Cl2F	356.9558166
11	N-(3,5-Dichlorophenyl)-2,2,3,3,4	InChI=1S/C10H4Cl2F7NO/c11-4-1-5(12)3-6(2-4)20-7(21)8(13,14)9(15,16)10(17,18)	c1c(cc(cc1	WGNKYUV	C10H4Cl2F	356.9558166
12	2-Propenoic acid, 2-methyl-, 2-[	InChI=1S/C28H28F17N3O8S/c1-6-48(9-10-54-19(50)46-16-8-7-14(4)17(11-16)47-2	CCN(CCOC	WUGSPVX	C28H28F1	889.1325656

https://data.nist.gov/od/id/mds2-2387

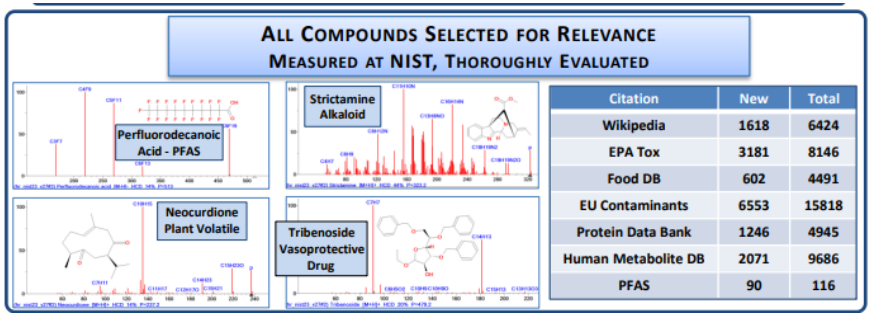
NIST Mass Spectral Libraries: 2023 Release

The NIST Mass Spectrometry Data Center have a total of 865 PFAS to their mass spectral libraries, with 251 PFAS added in the 2023 release.

- 161 empirical mass spectra added to the EI-MS library
- 90 empirical mass spectra added to the tandem MS library



Citation	New	Total
Wikipedia	1570	6227
EPA Tox	2969	7117
Food DB	582	4273
EU Contaminants	6263	15149
Protein Data Bank	1194	4716
Human Metabolite DB	1992	9393
PFAS	161	749
Adams (Essential Oils)	2136	2136

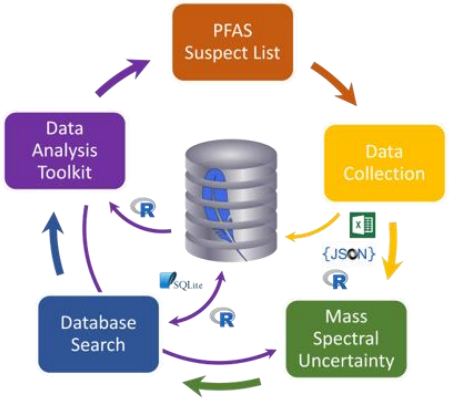


Citation	New	Total
Wikipedia	1618	6424
EPA Tox	3181	8146
Food DB	602	4491
EU Contaminants	6553	15818
Protein Data Bank	1246	4945
Human Metabolite DB	2071	9686
PFAS	90	116

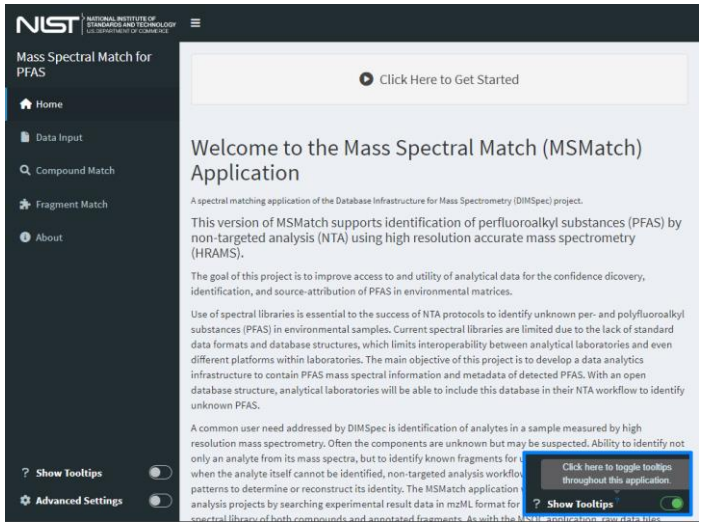
Database Infrastructure for Mass Spectrometry (DIMSpec)

Project funded by the DOD Strategic Environmental Research and Development Program (SERDP)

Objective: develop a data analytics infrastructure to contain PFAS mass spectral information and metadata of detected PFAS. With an open database structure, analytical laboratories will be able to include this database in their NTA workflow to identify unknown PFAS.

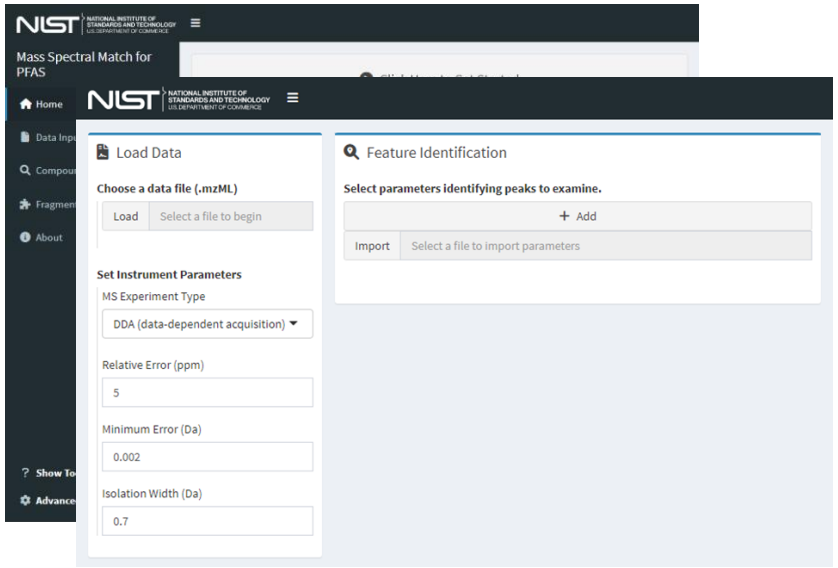


Database Infrastructure for Mass Spectrometry (DIMSpec)



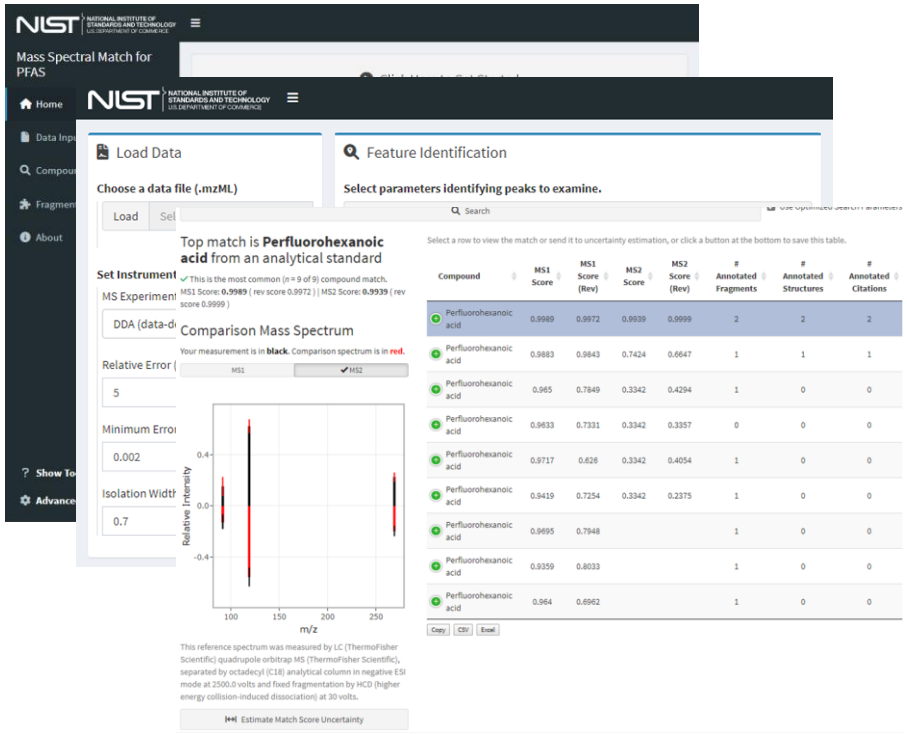
Mass Spectral Match (MSMatch) App

Database Infrastructure for Mass Spectrometry (DIMSpec)



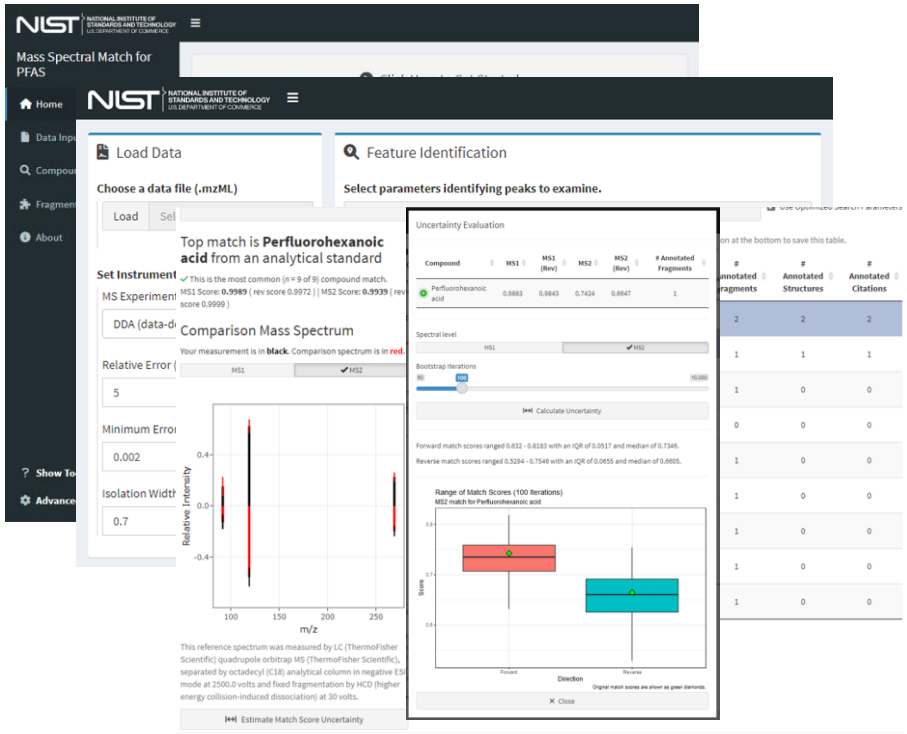
MSMatch – Data Load

Database Infrastructure for Mass Spectrometry (DIMSpec)



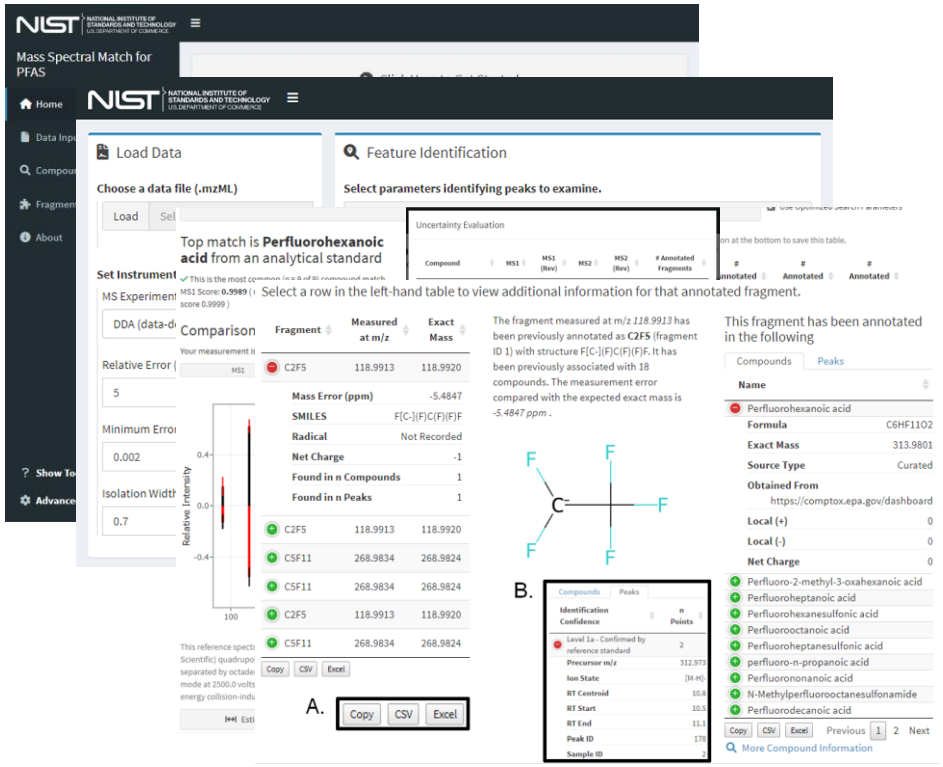
MSMatch – Compound Search

Database Infrastructure for Mass Spectrometry (DIMSpec)



MSMatch – Uncertainty Analysis

Database Infrastructure for Mass Spectrometry (DIMSpec)



MSMatch – Fragment Search

Questions?

For more information on any of the ongoing PFAS projects, feel free to reach out at:
pfas@nist.gov

To learn about NIST's PFAS Program go to:
https://www.nist.gov/programs-projects/and-polyfluoroalkyl-substances-pfas

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