EPA Tools and Resources Webinar:
PFAS and Emerging Contaminant Technology Transfer to States and Tribes

Tim Buckley and Jon Sobus
US EPA Office of Research and Development

State Partners:
*Sinisa Urban, **Maryland Department of Health***
*Andri Dahlmeier, **Minnesota Pollution Control Agency***
*Wendy Linck, **California Water Boards***

October 18, 2023

ROAR Project Team

(Regional-ORD Applied Research)

State Partners

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California Water Boards

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- Erica Kalve

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- Andri Dahlmeier
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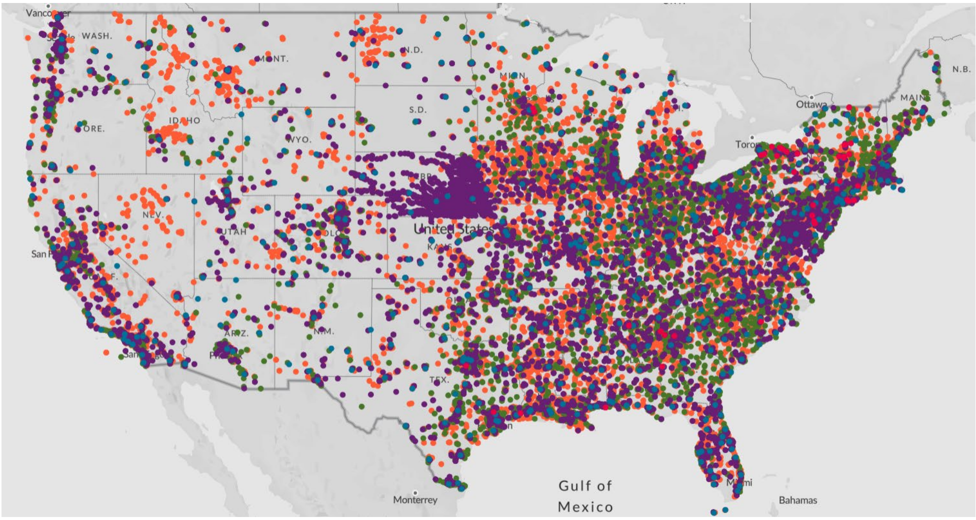
- Rosie Rushing

Public Health Rationale

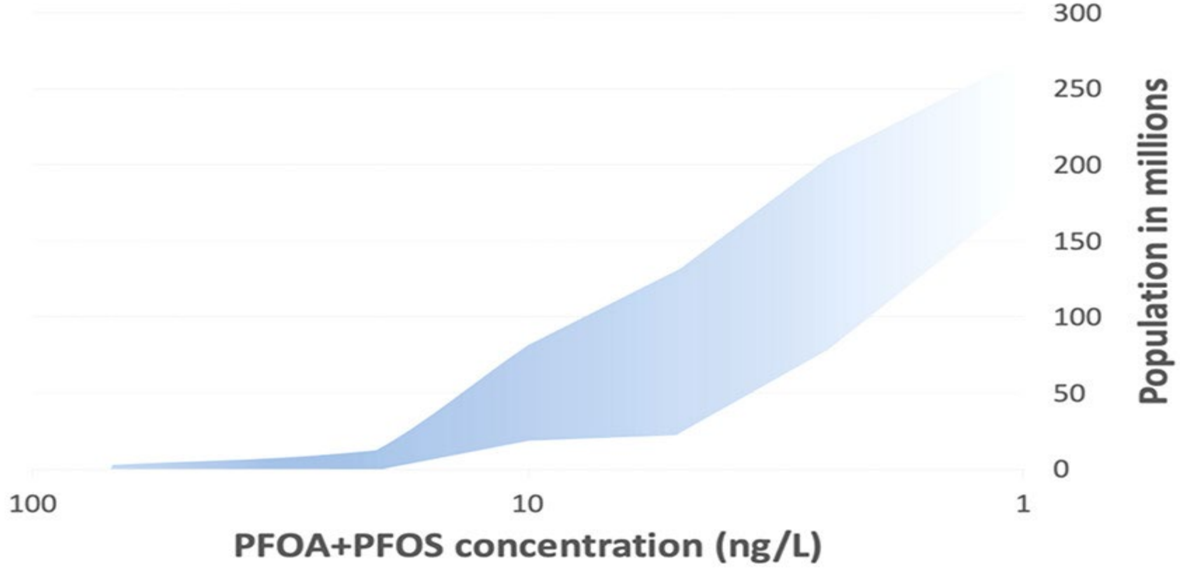
- States across the country impacted by PFAS contamination of water resources
  - PFAS manufacture and use is widespread
  - >200 M US residents have PFOS/PFOA in drinking water > 1 ng/L (Andrews and Naidenko, 2020)
  - Current characterization of environmental occurrence limited to a handful PFAS; additional PFAS contamination suspected
- Number of PFAS in commerce vastly exceeds traditional monitoring capability
  - 1400 PFAS identified across 200 use categories (Glűge et al. 2020)
  - Thousands PFAS exist (n=12,034 CompTox Chemical Dashboard (https://comptox.epa.gov/dashboard/chemical-lists/PFASMASTER)
  - Targeted methods accommodate approximately 40 PFAS
- To protect public health and water resources, more dynamic and comprehensive characterization of PFAS and other emerging contaminants is needed (Vandenberg et al. 2023)

Sites known or suspected of making, using or releasing PFAS (n=41,828)



Different colors points represent PFAS known users; suspected users; airports previously required to use AFFF; landfills and waste disposal facilities'; and sewage and waste treatment plants.

Estimated population-wide exposure to PFOA and PFOS from drinking water in the United States



Source: https://www.ewg.org/interactive-maps/2021_suspected_industrial_discharges_of_pfas/map/

United States Environmental Protection Agency

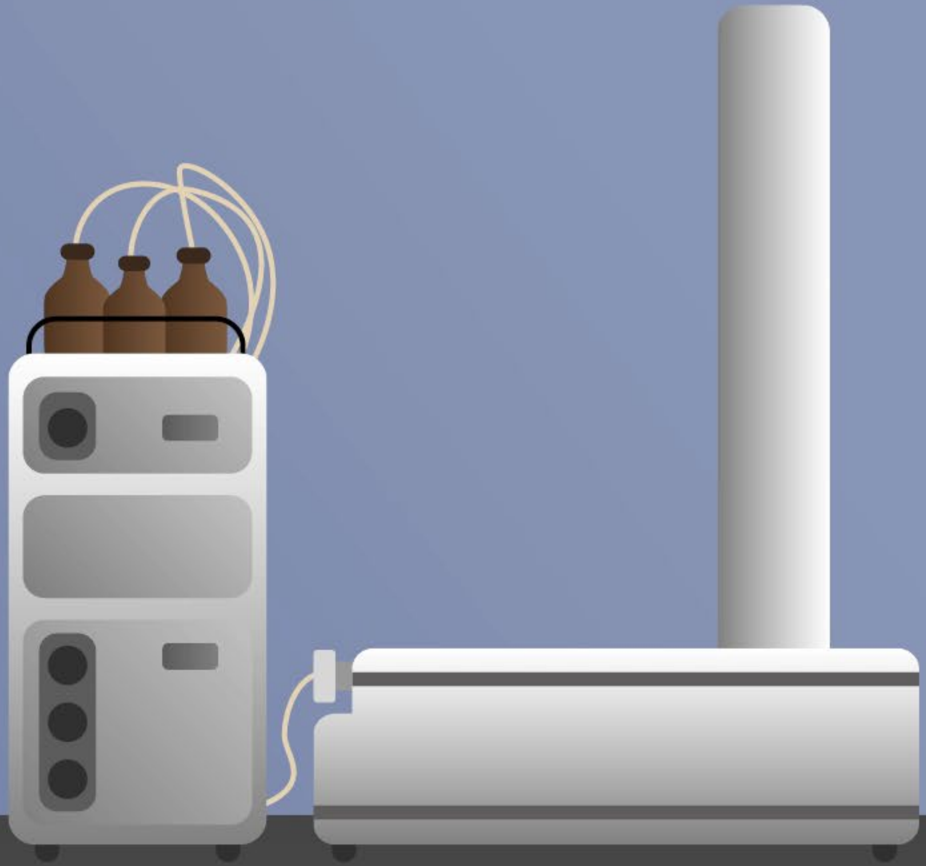
Non-Targeted Analysis (NTA) is a Transformative Solution

Measurement Method with Enormous Capability

- Chemical discovery – characterization of the chemical composition of any given sample without *a priori* knowledge of the sample's chemical content
- Large chemical space
- Achieved through technological advances in HRMS, computing, and data workflows

Challenges

- High-Resolution Mass Spectrometry (HRMS) cost
- Need for high-end computing (speed & memory)
- Combined expertise in analytical chemistry and data science
- Complex & special considerations relating to study design, QA/QC, data acquisition, analysis, reporting, communications



High-resolution mass spectrometer

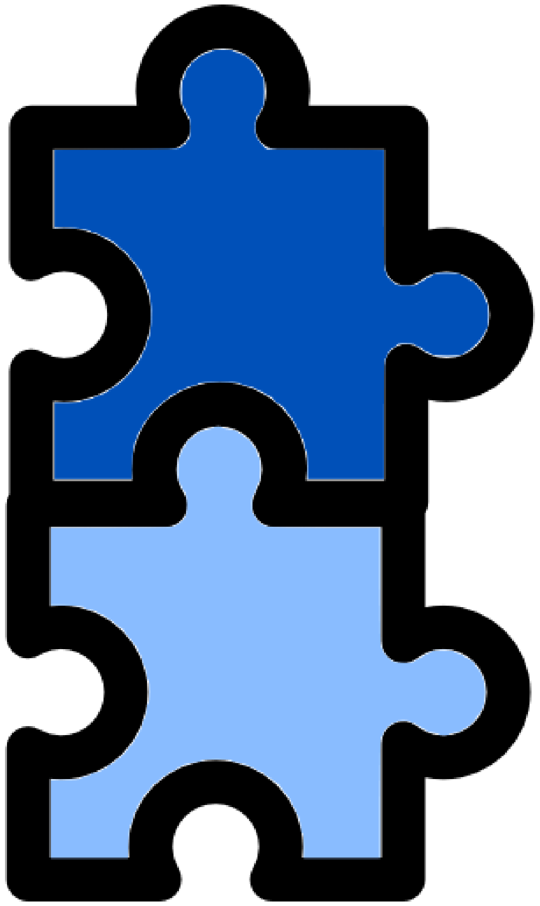
NTA: Right Place/Right Time

Advances in measurement technology

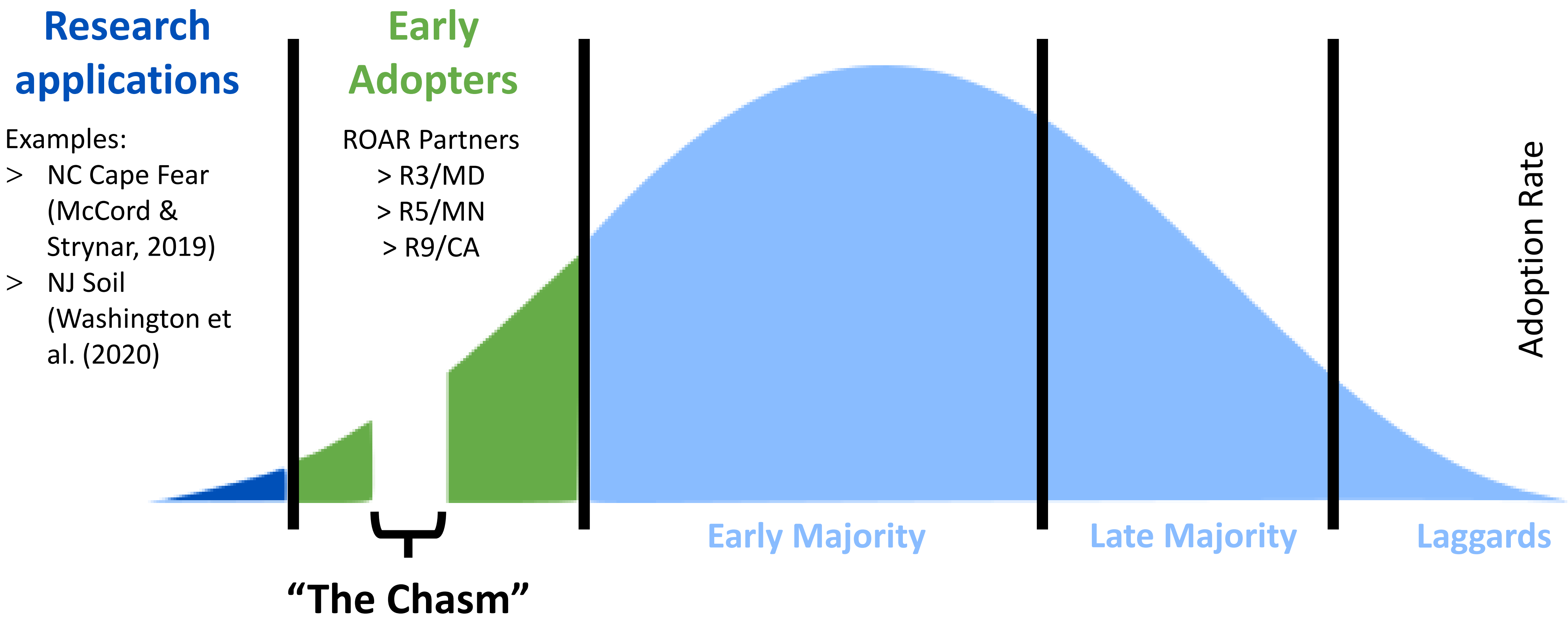
> Detection of emerging PFAS using HRMS platforms to perform NTA, including PFAS not measured in targeted analysis techniques

Heightened awareness of public health threats

> State concerns over public health threats from PFAS contamination in water resources



Technology Adoption Curve



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Pathway to the ROAR Project

1 ORD labs provide novel and critical support to states in identifying PFAS contamination supporting regulatory action

2 State/stakeholder demand for ORD laboratory PFAS NTA support exceeds availability

3 ORD Regional Science Liaisons hold workshop drawing large state, region and federal interest (Oct 2021) ~1000 attendees

4 ORD developing methods and workflows to enable broad application of NTA

5 **EPA Regions 3 ,5 & 9 team with ORD to develop ROAR proposal**

Objective: To build capacity and empower states/tribes/regions to access high-resolution mass spectrometry NTA knowledge and tools to independently apply NTA in their management of PFAS and other contaminants of emerging concern (CECs)

Maryland DEPARTMENT OF HEALTH

MINNESOTA POLLUTION CONTROL AGENCY

CALIFORNIA Water Boards

Applications of NTA for PFAS in Maryland:

Sinisa Urban, PhD, Maryland Department of Health

MD, MN & CA Common Interests

- PFAS contamination of water resources
- Heightened public / media interest
- Targeted analysis indicates widespread contamination
- PFAS contamination beyond targeted (n=40) suspected
- More complete PFAS assessment needed to protect public health and help identify sources
- Have NTA capability; need help with implementation

NEWS

Minnesota, 3M reach settlement ending $5 billion lawsuit

By **BOB SHAW** | Pioneer Press

PUBLISHED: February 20, 2018 at 3:41 p.m. | UPDATED: February 20, 2018 at 10:58 p.m.

Maryland investigating ‘forever chemicals’ near industrial plant in Cecil County

Timothy B. Wheeler

Jul 19, 2023

https://www.bayjournal.com/news/pollution/maryland-investigating-forever-chemicals-nearindustrialplant-in-cecil-county/article_f0c3195c-1ce7-11ee-937d-6b7e9ab39a5d.html

CLIMATE & ENVIRONMENT

‘This is taking too long’: California community awaits cleanup of PFAS-contaminated wells

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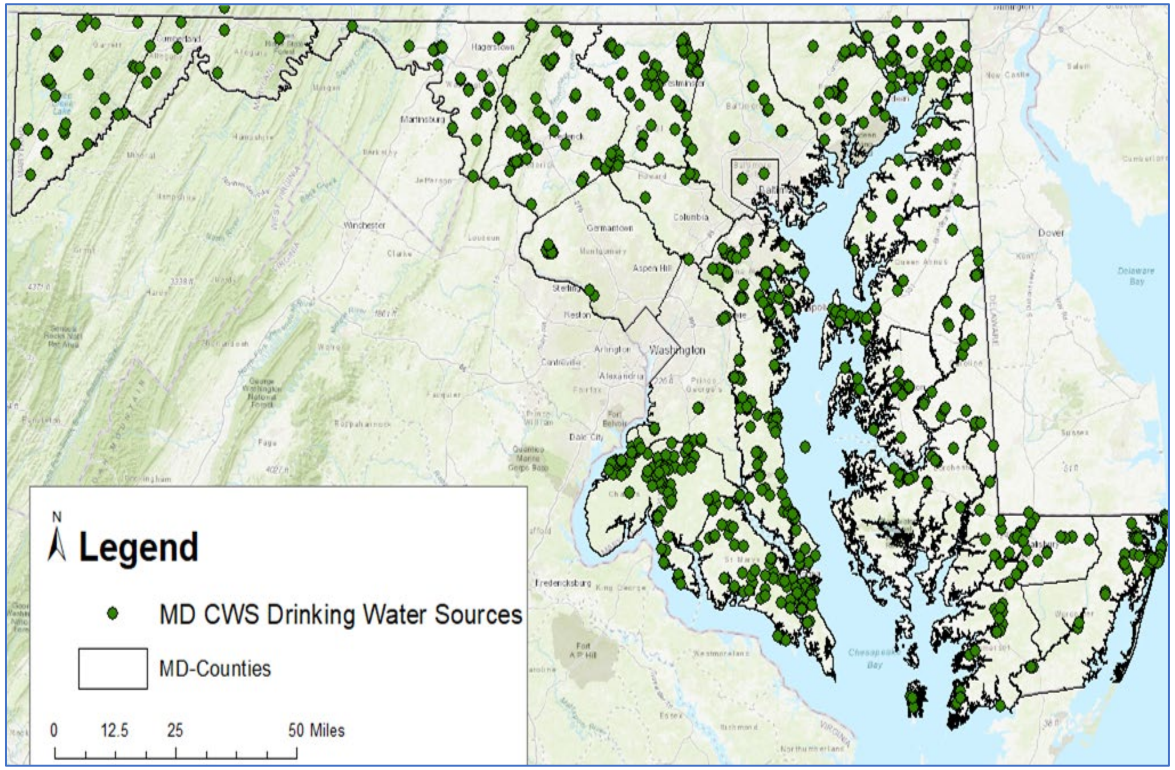
Partnership with R3/Maryland

Background: Large-scale drinking water surveillance program to understand presence of PFAS in finished drinking water, recently expanded to wastewaters, biosolids, fish & crabs

Motivation: To identify the presence of any additional PFAS and to understand their potential source(s) & fate(s)

Paradigm study: Approximately 50 drinking water samples collected in relation to an industrial release

Implementation barriers: Need for workflows and spectral libraries to generate high-confidence identifications of PFAS



https://mde.maryland.gov/PublicHealth/Pages/PFAS-Landing-Page.aspx

Maryland Department of the Environment

Maryland DEPARTMENT OF HEALTH

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Applications of NTA for PFAS in California:

Wendy Linck, California Water Boards

Partnership with R9/California

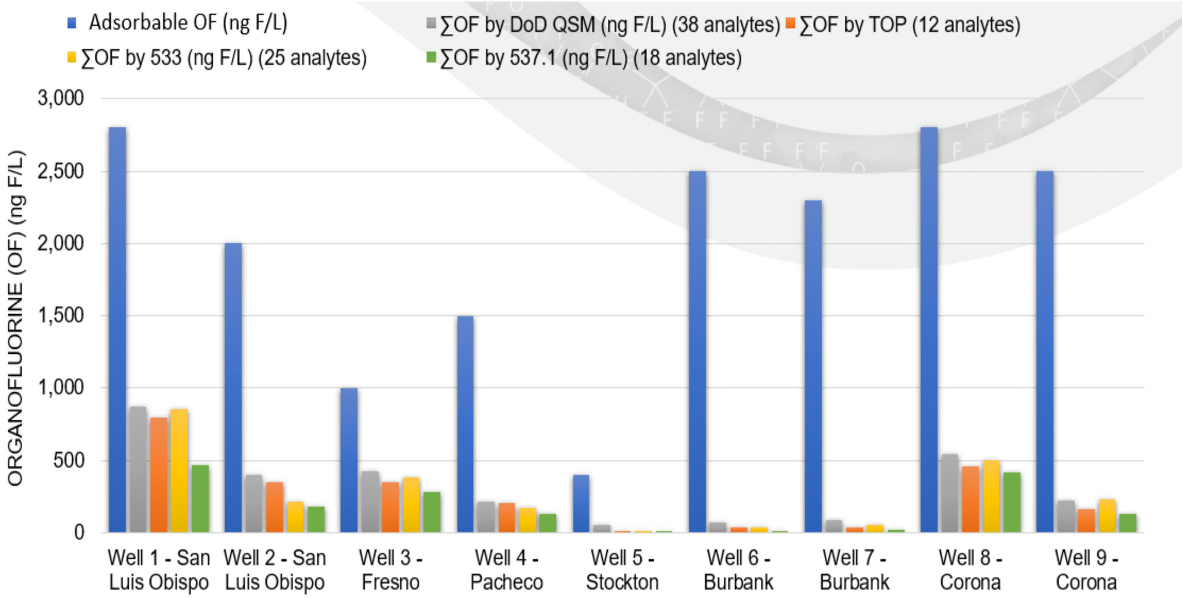
Background: Pilot study to compare and understand utility of various analytical techniques for PFAS, including NTA

Motivation: To use combinations of analytical techniques to elucidate patterns and trends in the content of PFAS in drinking water to support investigations on sources and treatment technologies

Study: Approximately 4,000 drinking water supply wells to be sampled including ~1,000 to be analyzed with NTA

Implementation barriers: Need for study design that considers a multi-technique, multi-year data collection and analysis protocol

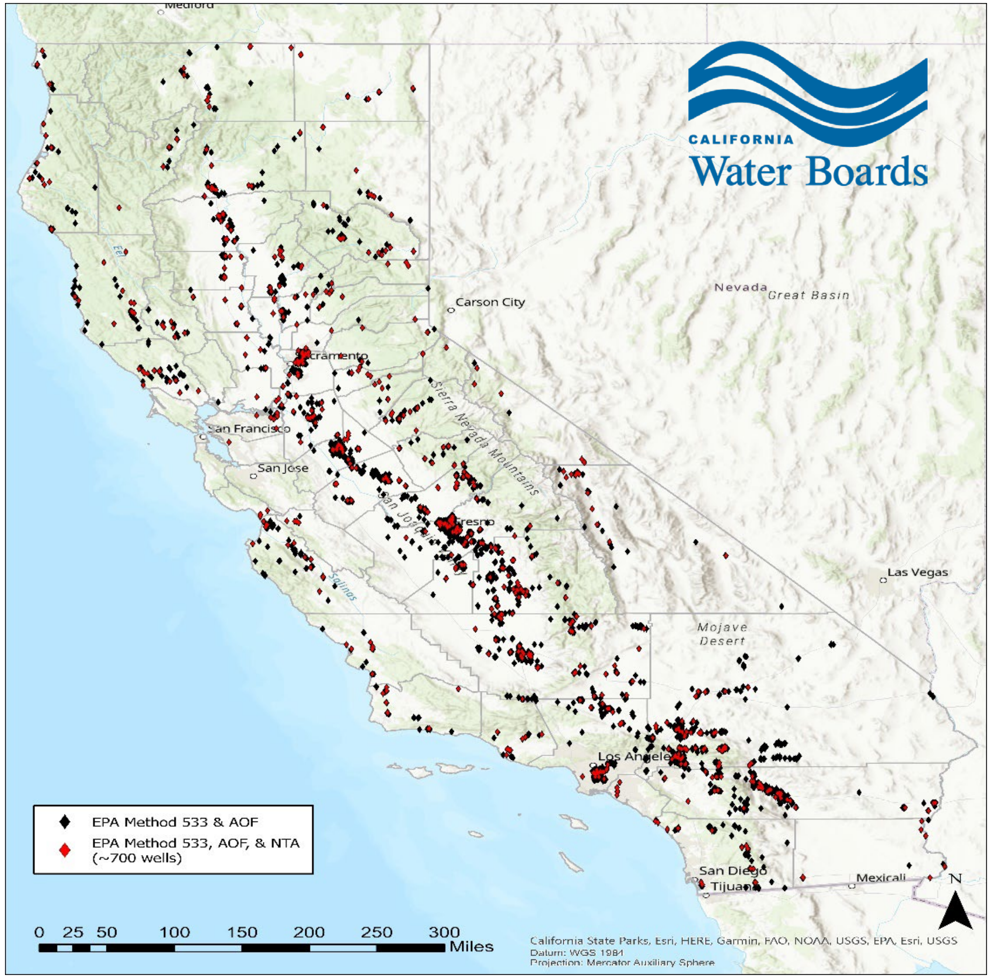
CALIFORNIA Water Boards



Partnership with R9/California and Beyond

Needs: ORD provides expertise in NTA and study plan design that have been critical as their support helps to ensure data that are collected for this large-scale project will be of known and useful quality. The results from this project will impact how PFAS are monitored in CA and support an approach to regulate “total PFAS” in drinking water

Outcomes: Enhanced capability of Water Boards for NTA and a continued relationship with EPA/ORD on the advancement of monitoring for and treatment of PFAS and other contaminants of emerging concern (CECs)



United States Environmental Protection Agency

Applications of NTA for PFAS in Minnesota:

Andri Dahlmeier, Minnesota Pollution Control Agency

Partnership with R5/Minnesota

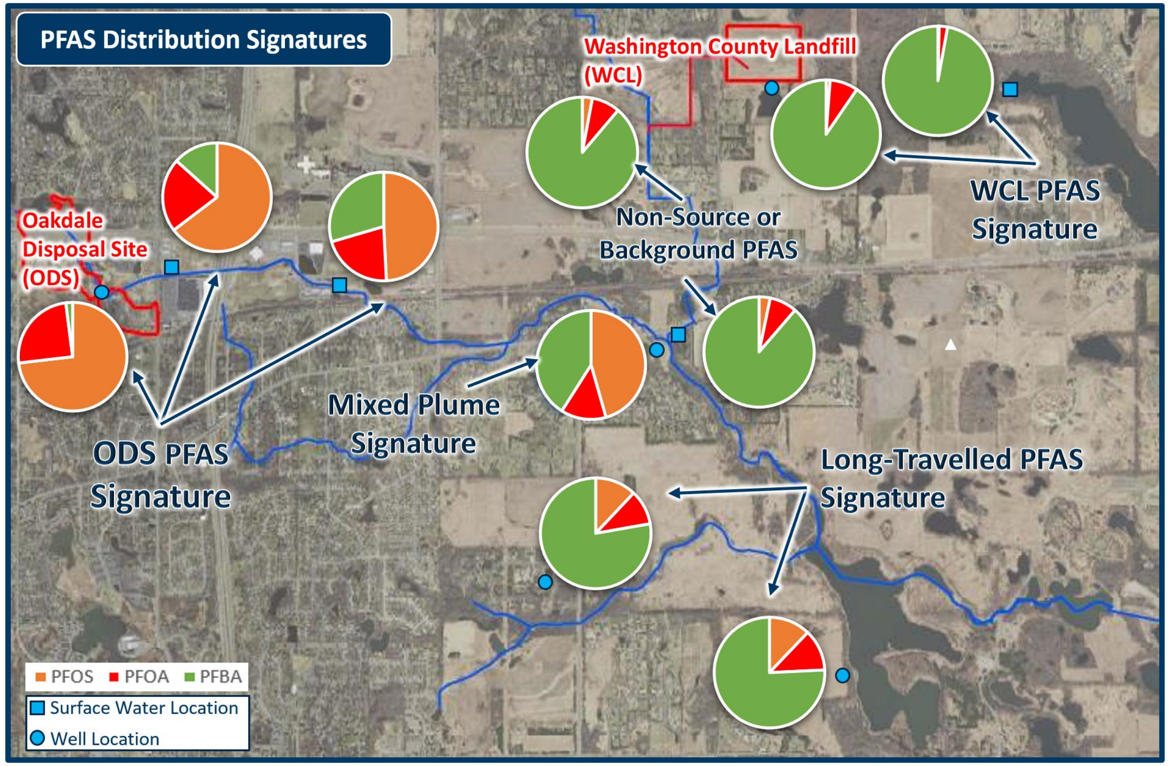
Background: Ongoing surveillance of surface and groundwater contamination in relation to two known point sources

Motivation: To identify the presence of any additional PFAS and to understand their fate and transport behaviors

Study: Approximately 20 samples of surface and groundwater samples collected from upstream, at, and downstream of each point source for NTA

Implementation barriers: Need for tools and statistical modeling resources to support identification of probable PFAS

MINNESOTA POLLUTION CONTROL AGENCY

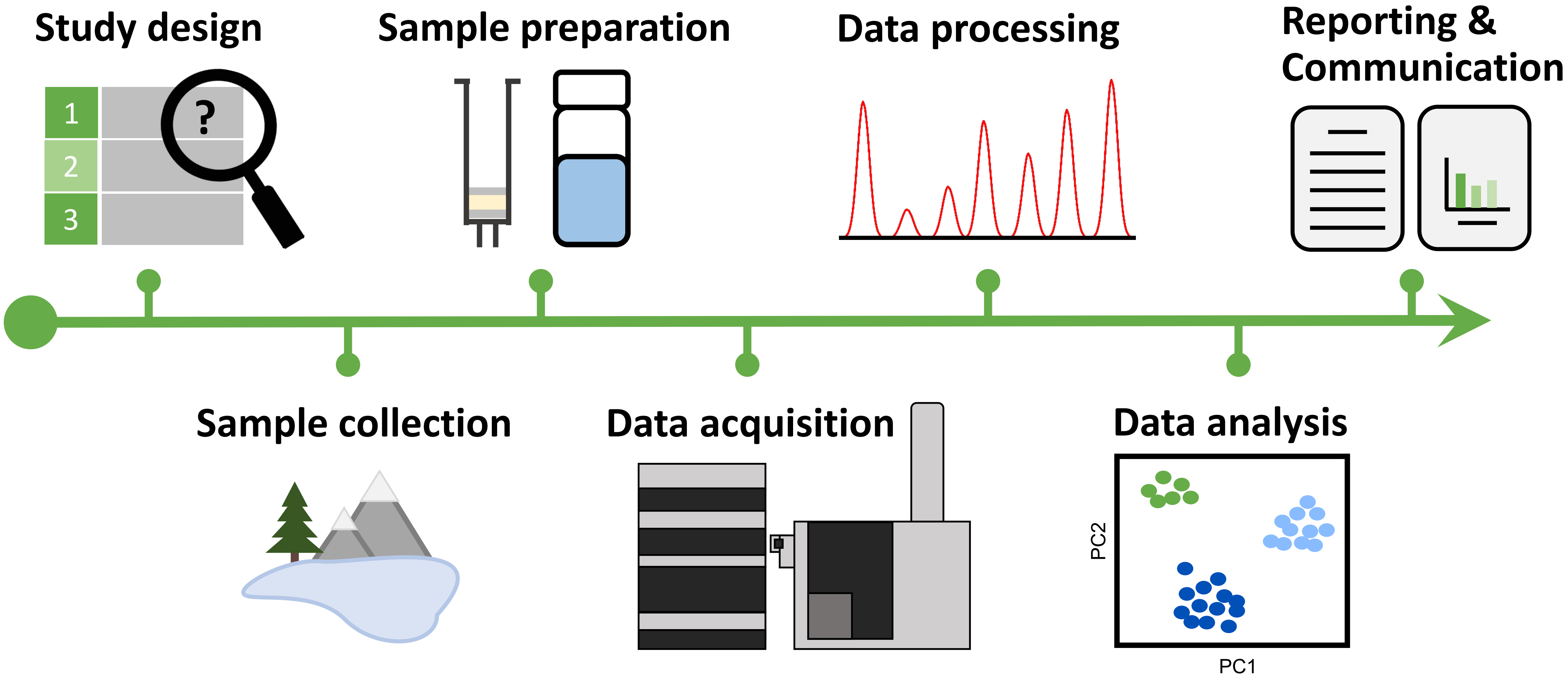


ORD Tools and Resources:

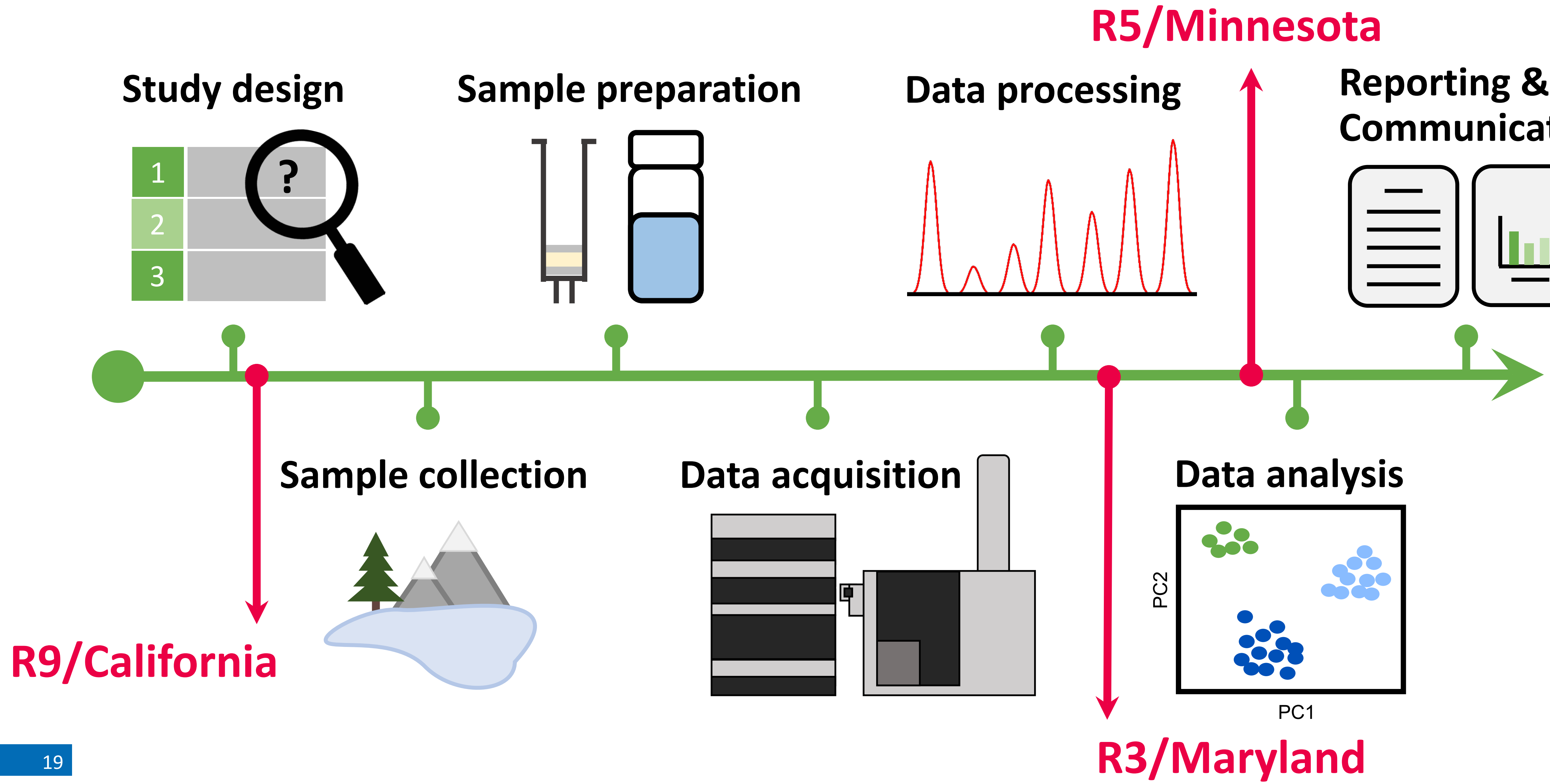
Jon Sobus, ORD/Center for Computational Toxicology and Exposure

United States
Environmental Protection
Agency

General NTA Workflow

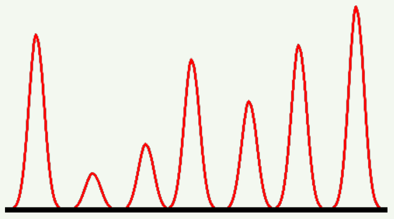


General NTA Workflow



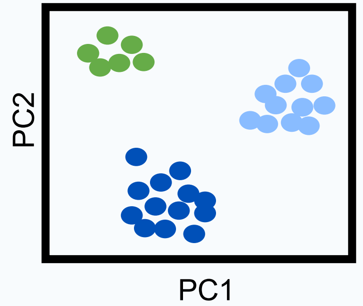
General Data Processing & Analysis Steps

Data processing

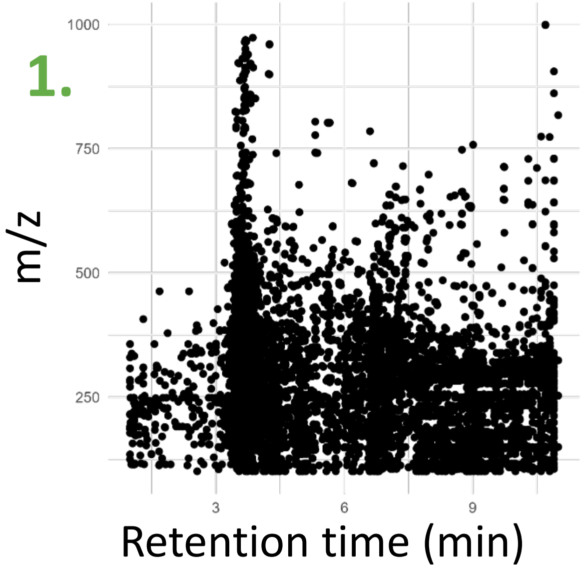


1. Extract chemical features
2. Assign chemical formulas
3. Assign chemical structures
4. Estimate chemical concentrations
5. Examine research hypotheses

Data Analysis

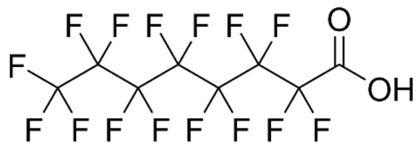


1.



2. $C_8HF_{15}O_2$

3.



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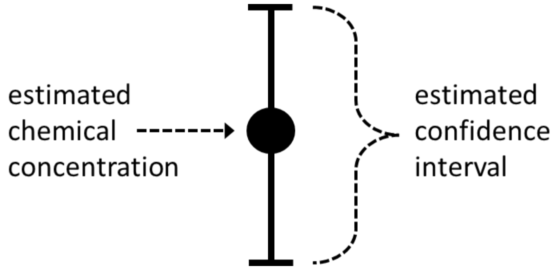
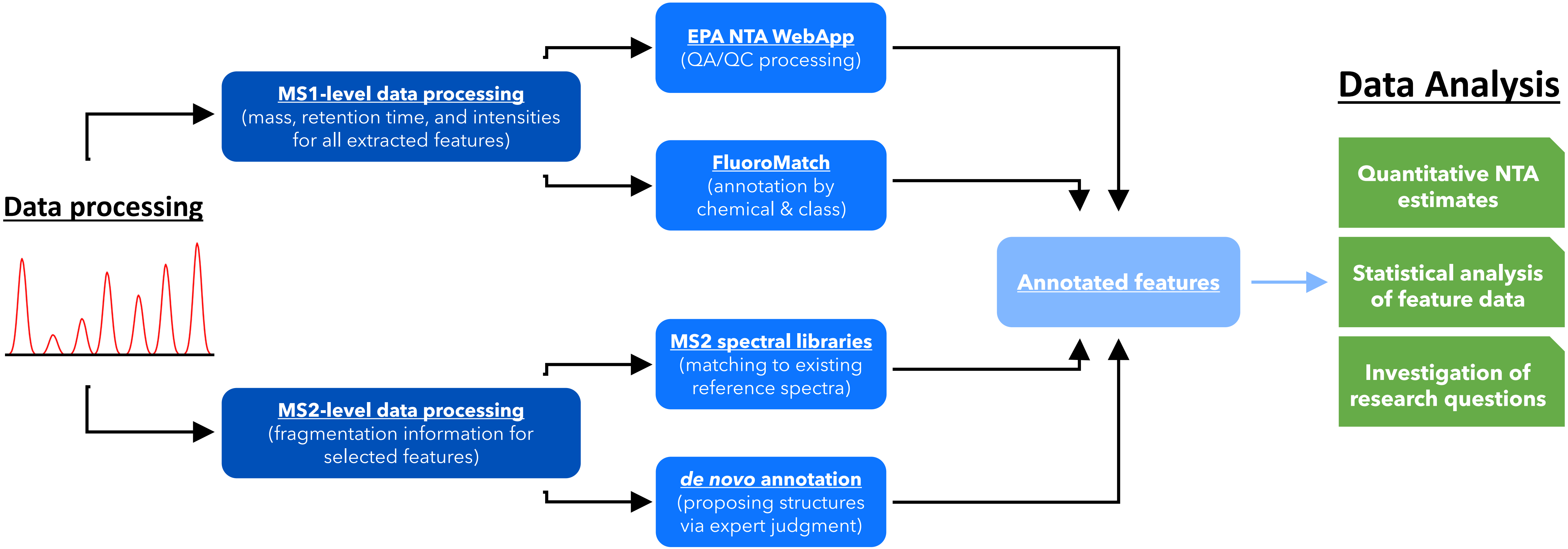


5.

- Trend analysis
- Source identification
- Exposure & risk estimation

ROAR Data Processing & Analysis Steps



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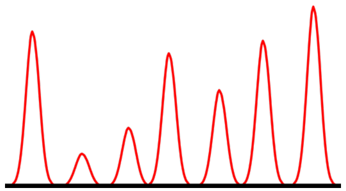
ROAR Data Processing & Analysis Steps

Data processing



MS1-level data processing
(mass, retention time, and intensities for all extracted features)

EPA NTA WebApp
(QA/QC processing)

FluoroMatch
(annotation by chemical & class)

MS2-level data processing
(fragmentation information for selected features)

MS2 spectral libraries
(matching to existing reference spectra)

***de novo* annotation**
(proposing structures via expert judgment)

Annotated features

Data Analysis

Quantitative NTA estimates

Statistical analysis of feature data

Investigation of research questions

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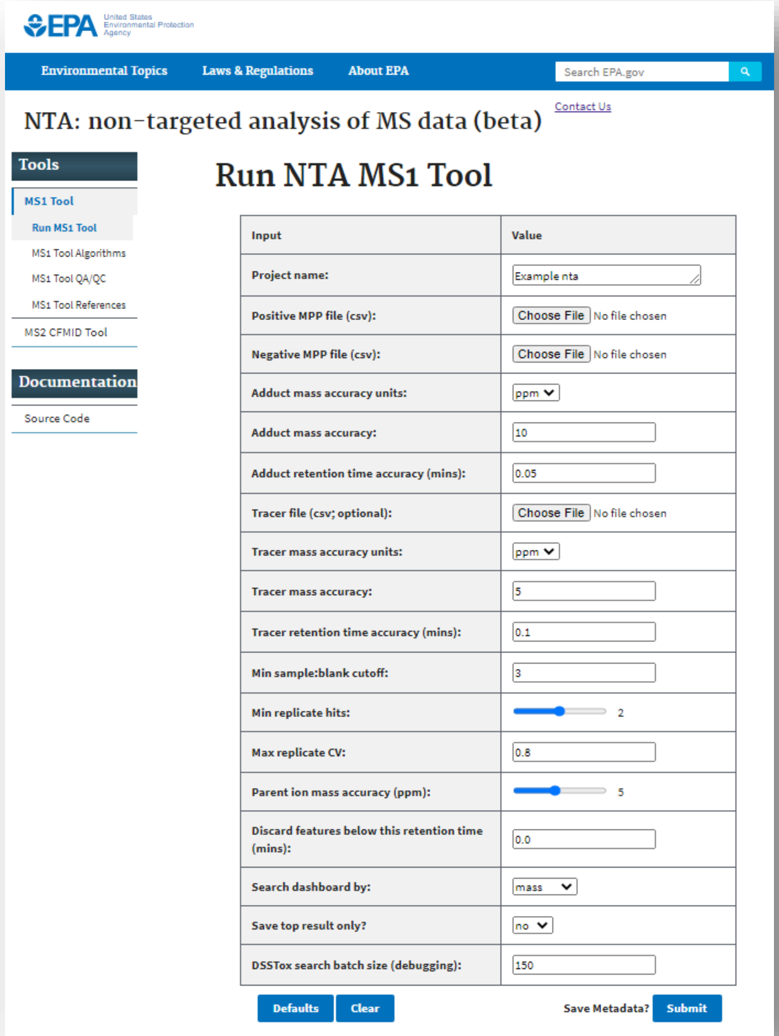
MS1 Data Processing Tools

MS1-level data processing
(mass, retention time, and intensities for all extracted features)
→
EPA NTA WebApp
(QA/QC processing)
→
Annotated features

The translation of MS1-level data into annotated identifications requires data cleaning, flagging & QC checks that include:

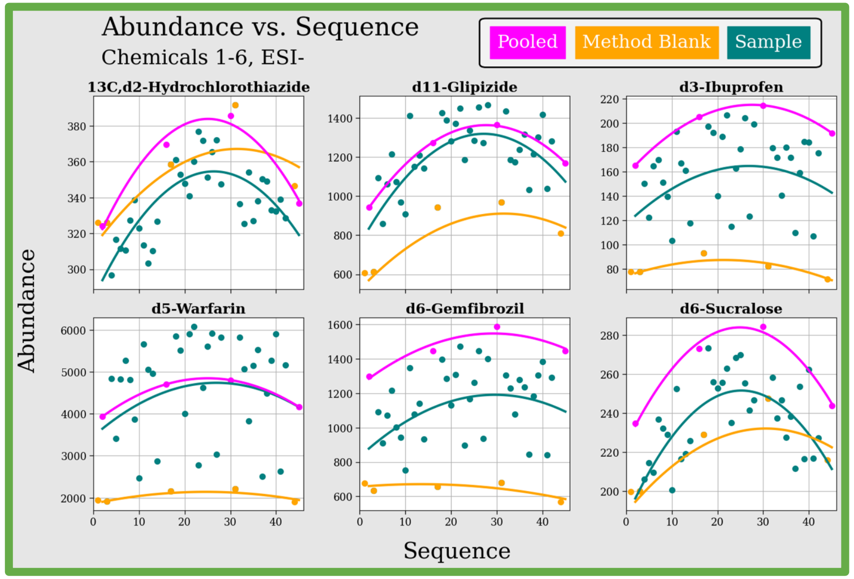
- Examination that expected features (“tracers”) are present
- Examination that instruments are meeting required specifications
- Annotation of related chemical signals (“adducts”)
- Removal of data artifacts and flagging of questionable signals
- Examination of matrix and batch effects

EPA NTA WebApp for MS1 Data Processing



Example outputs:

Chemical Name	DTXSID	Ionization Mode	Mass Error (ppm)	RT Difference (min)	Precision (max %CV)	Detection Frequency (%)
acetaminophen-d3	DTXSID50480414	ESI+	3.20	0.06	12	100
albuterol-d9	DTXSID10675541	ESI+	2.52	0.00	20	100
amitriptyline-d6	DTXSID501349824	ESI+	2.14	0.09	18	100
amlodipine-d4	DTXSID50661983	ESI+	8.59	0.09	35	97.8
atenolol-d7	DTXSID101027977	ESI+	2.59	0.02	15	100
Caffeine-13C3	DTXSID20437172	ESI+	2.45	0.02	17	100
carbamazepine-d8	DTXSID401349821	ESI+	0.79	0.12	22	100
diltiazem-d3	DTXSID801016193	ESI+	1.61	0.05	15	100
fluoxetine-d5	DTXSID50661983	ESI+	0.41	0.10	18	100
glipizide-d11	DTXSID601349827	ESI+	4.51	0.13	20	100
metoprolol-d7	DTXSID30648858	ESI+	2.92	0.07	16	100
norethindrone-d6	DTXSID401349857	ESI+	0.48	0.11	14	100
paroxetine-d4	DTXSID101349822	ESI+	1.58	0.05	32	100
sertraline-d3	DTXSID201349825	ESI+	0.35	0.08	23	100
sulfamethoxazole-d4	DTXSID101016780	ESI+	3.68	0.09	15	100
triamterene-d5	DTXSID701349820	ESI+	1.25	0.05	29	100
trimethoprim-d9	DTXSID10662219	ESI+	2.19	0.04	15	100
verapamil-d6	DTXSID801349823	ESI+	0.39	0.08	28	100
warfarin-d5	DTXSID801016155	ESI+	1.62	0.17	19	100
gemfibrozil-d6	DTXSID601028063	ESI-	0.29	0.16	12	100
glipizide-d11	DTXSID601349827	ESI-	1.19	0.04	22	100
hydrochlorothiazide-13C,d2	DTXSID00662001	ESI-	0.92	0.06	8	100
ibuprofen-d3	DTXSID00481299	ESI-	1.01	0.15	12	100
sucralose-d6	DTXSID301339960	ESI-	1.62	0.01	12	100
warfarin-d5	DTXSID801016155	ESI-	0.13	0.03	11	100



"Tracer" Performance Table:

> Mass accuracy
> Retention time drift
> Measurement precision
> Reproducibility

Run Sequence Plots:

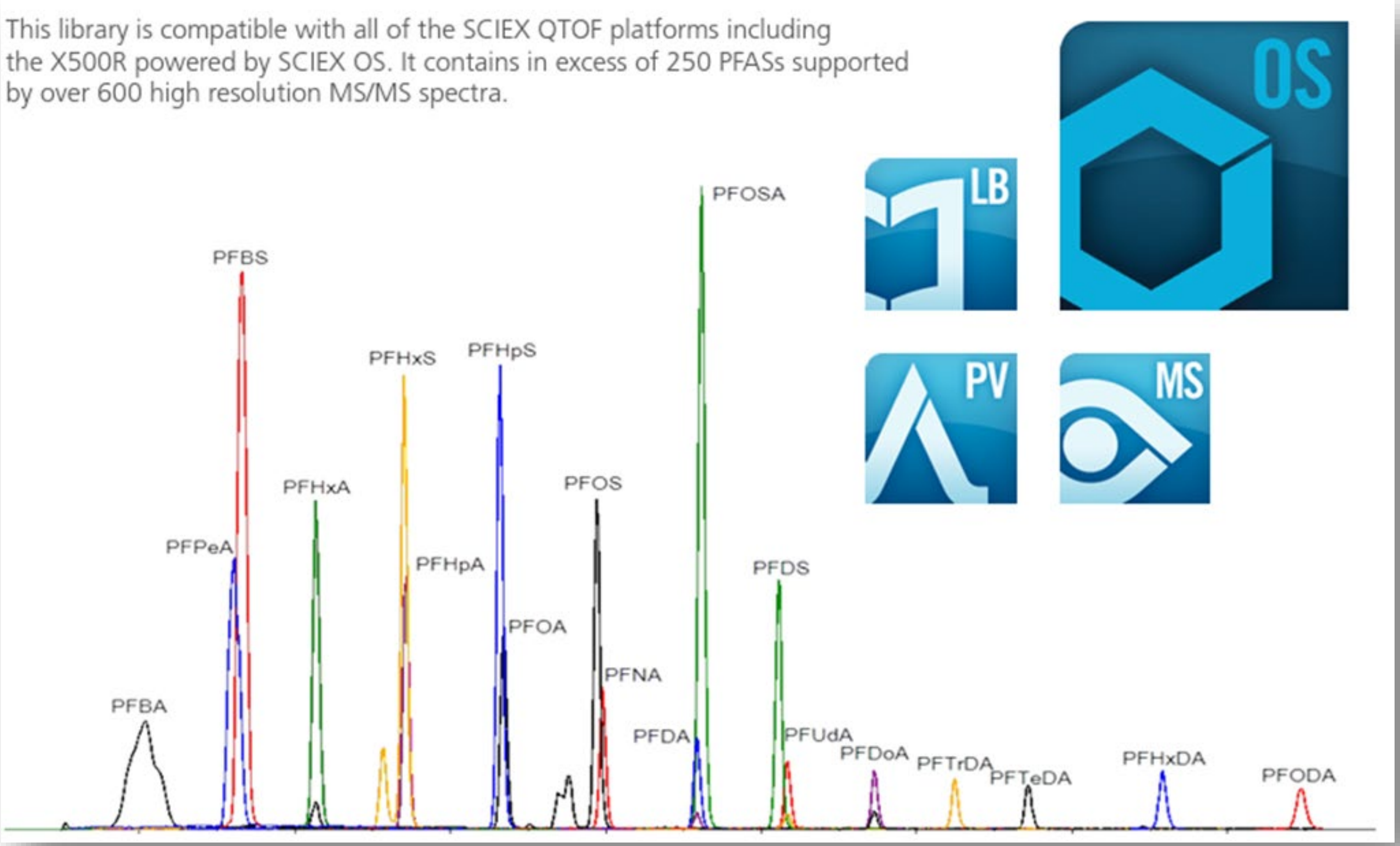
> Matrix suppression
> Matrix enhancement
> Measurement stability
> Batch effects

Annotation via MS2 Spectral Libraries

MS2-level data processing (fragmentation information for selected features) → **MS2 spectral libraries** (matching to existing reference spectra) → **Annotated features**

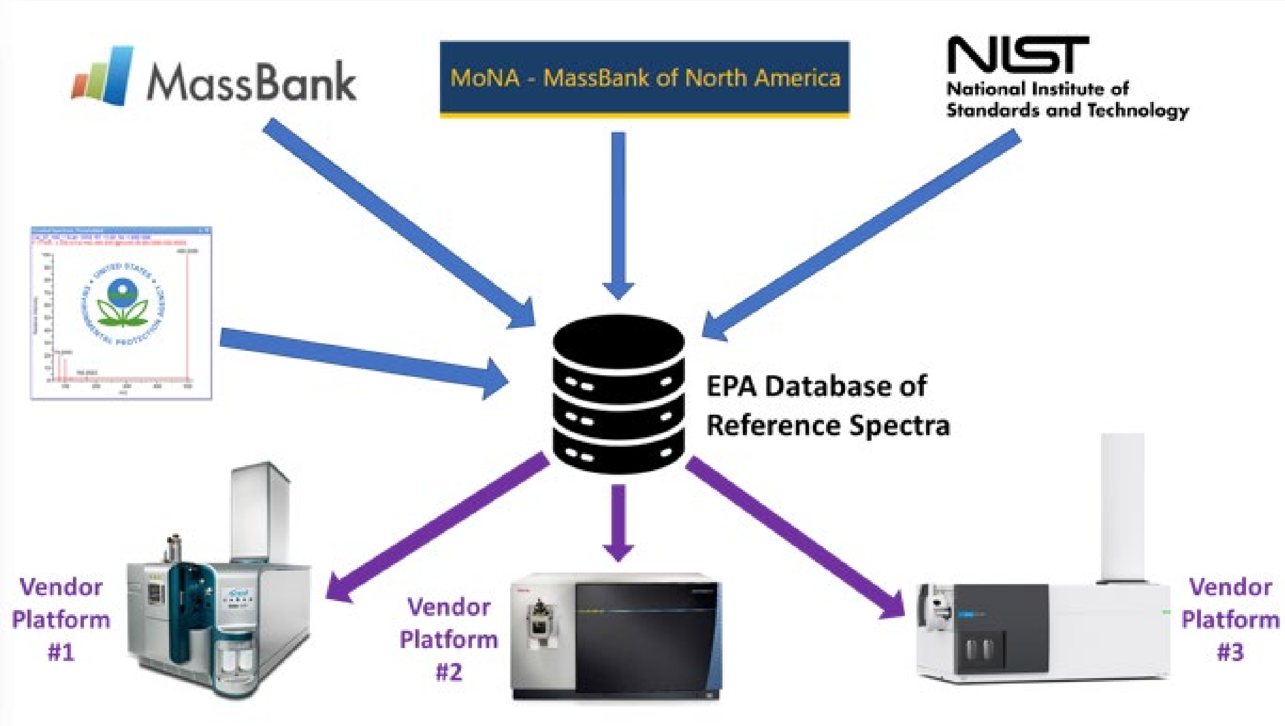
The translation of MS2 level data into annotated identifications involves utilization of spectral libraries

- Vendors curate purchasable spectral libraries for use on their platforms (e.g., *Sciex Fluorochemical library)*
- Libraries can also draw upon in-house data, public data, and *in-silico* predictions



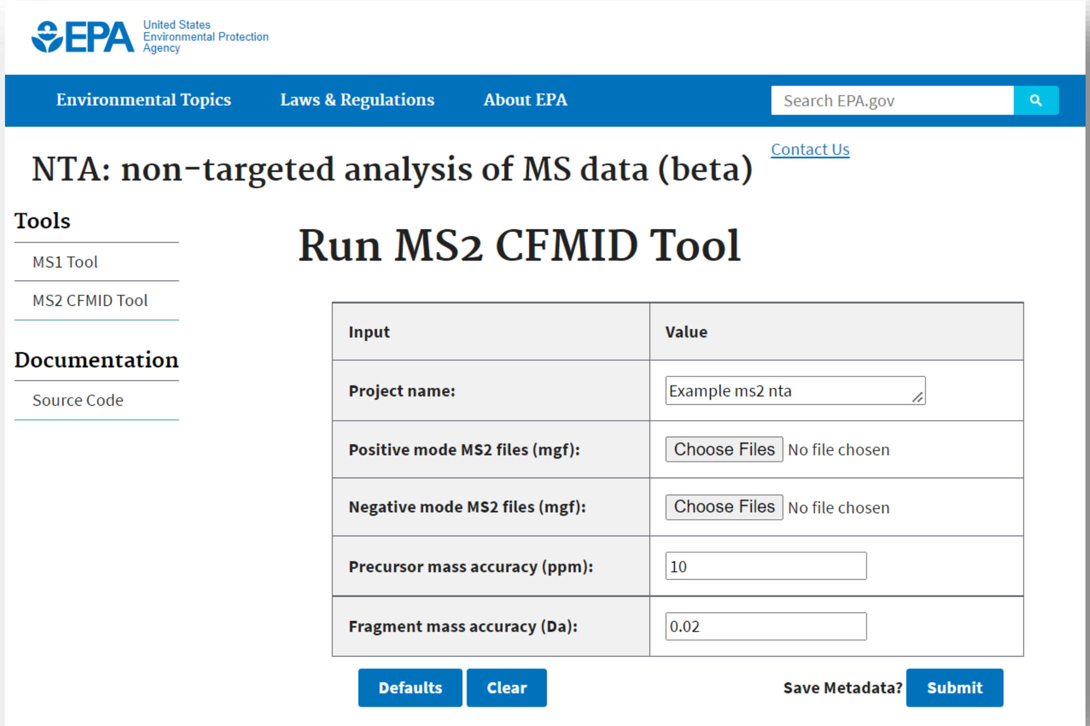
Annotation via MS2 Spectral Libraries

Library spectra from public domain



Matching against real spectra for hundreds of known PFAS

Predicted spectra from *in silico* tool



Matching against predicted spectra for more than 1M substances

Communication of ROAR Project Results

Roles & Responsibilities:

> States "own" their data and assume sole responsibility for reporting
> EPA's role is advisory
> EPA & state partners publish jointly with state permission

Unique considerations related to NTA study communications:

> New chemicals may be discovered amidst a large chemical space
> Discoveries prompt a pipeline of additional research (exposure, hazard, risk)
> There may be uncertainties related to chemical IDs and quantitative estimates
> Complex, intensive analyses require extended data processing time
> A need exists for standardized and transparent reporting

Summary: Closing the "chasm"

State challenges/needs:

- **Harmonized, well-defined approaches for NTA**
  - Study design
  - Data processing
  - Data analysis
- **Generic and more comprehensive libraries for compound ID**
- **Interpretation and communication strategies and tools**

Strategies to overcome barriers:

- **Tools and workflows to standardize NTA procedures:**
  - BP4NTA products (nontargetedanalysis.org)
  - EPA NTA WebApp
  - Strategies for analyzing big(ger) data
- **Harmonization of existing spectra, collection of new spectra, and prediction of *in silico* spectra**
- **Development of a desk statement, educational videos, and reporting tools**

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Conclusions

There is a great scientific & public health rationale for expanding use of NTA

> Address the gap between the number of chemicals that threaten human & environmental health and the number of chemicals that we currently measure

State environmental and public health agencies are motivated with early adoption in MD, MN and CA

> EPA has partnered with each state to identify and overcome barriers to NTA implementation

All three states are positioned to evaluate, report, and act on PFAS (including novel analytes) detected in water resources

> Possible via environmental characterization beyond targeted analysis

Contacts

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