



# Breaking Barriers that Limit Non-Targeted Analysis Through Stakeholder Engagement and Outreach

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*BP4NTA Past-Chairs, Chair, and Vice-Chair*

<sup>1</sup>Shimadzu Scientific Instruments

<sup>2</sup>Food and Drug Administration

<sup>3</sup>Environmental Protection Agency

<sup>4</sup>Connecticut Agricultural Experiment Station

# Acknowledgements

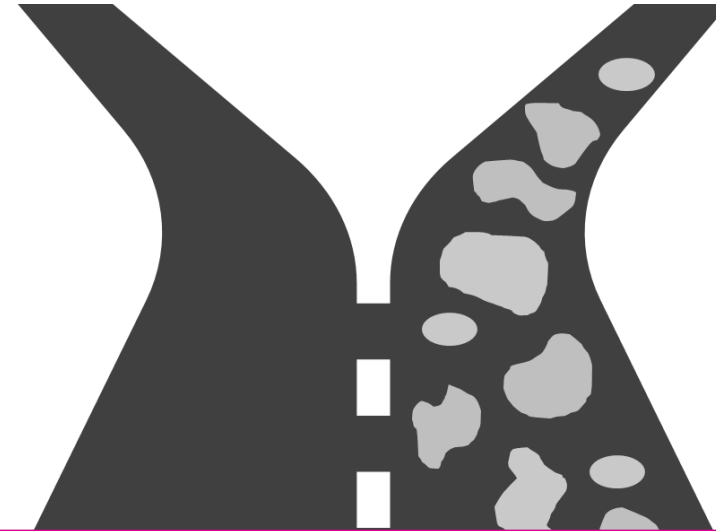
## Committee members:

Sara Nason (Co-chair)  
Yong-lai Feng (Co-chair)  
Jon Sobus  
Ruth Marfil-Vega  
James McCord  
Stéphane Bayen  
Christine Fisher  
Alli Phillips  
Greg Johnson  
John Sloop  
Keaton Nahan  
Esra Mutlu  
Angela Batt



Thank you to all who have come to our discussion meetings!

# Today's Road Trip



- Non-Targeted Analysis
- Best Practices 4 Non-Targeted Analysis
- Outcomes from Stakeholders Engagement and Outreach

# Non-Targeted Analysis (NTA): What it is

## **NON-TARGETED ANALYSIS**

The characterization of the chemical composition of any given sample without the use of a priori knowledge regarding the sample's chemical content.

The resulting detections may be used to classify samples (using the entire chemical profile), and/or subsequent analyses may focus on the identification of individual chemicals.


Also referred to as “non-target screening” and “untargeted screening”.

## **SUSPECT SCREENING**

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.

# Non-Targeted Analysis (NTA): Advantages

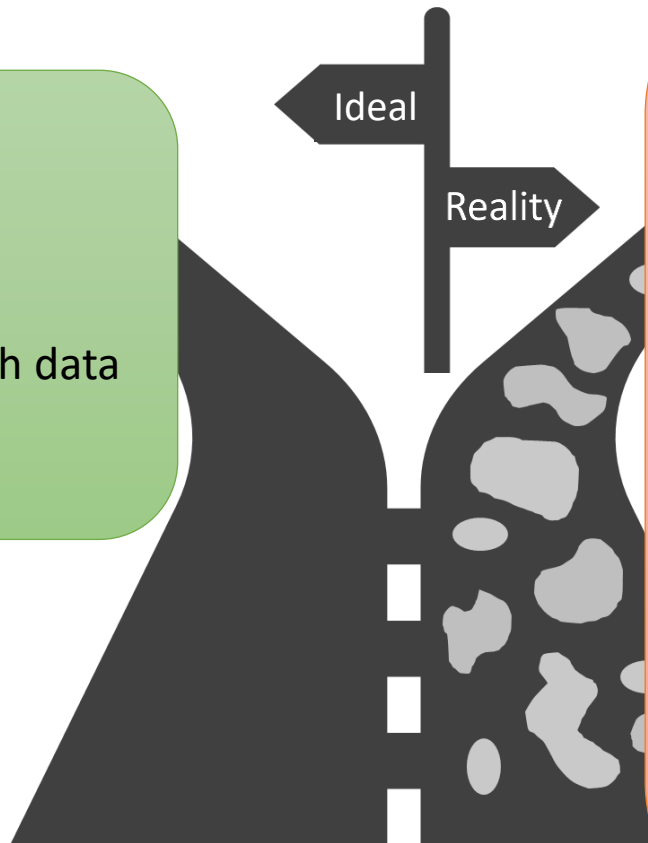
- Classify samples (e.g., adulterated vs. authentic)
- Identify unknown/unexpected compounds
- HRMS generates information-rich data
- Enable versatile workflows
- Allow retrospective analysis



NTA is a tool  
for more than  
identifying  
unknowns

# What does the Application of NTA look like for the Analysis of Unknowns?

- Classify samples (e.g., adulterated vs. authentic)
- Identify unknown/unexpected compounds
- HRMS generates information-rich data
- Enable versatile workflows
- Allow retrospective analysis



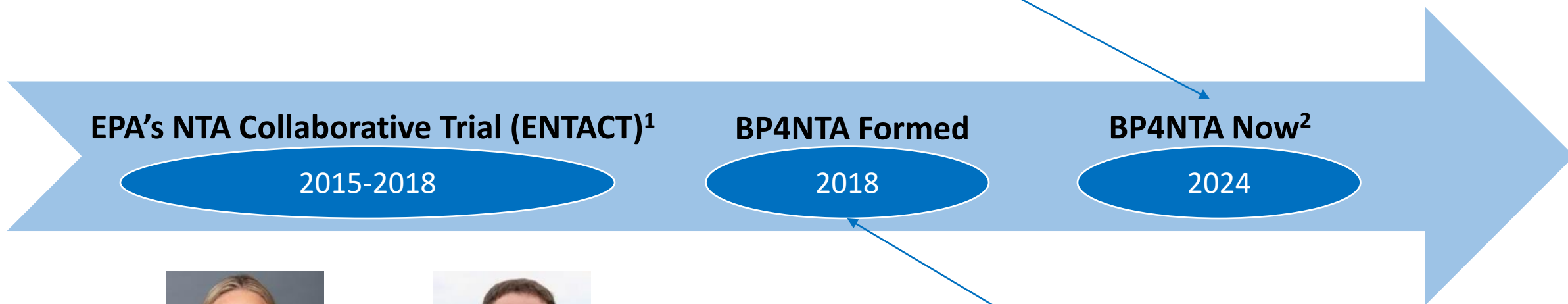
## Challenges

- Limited reporting quality-poor reproducibility
- Ability to compare data/results between labs
- Ensuring quality data (lack of accreditation)
- Performance assessment
- Lack of reference materials/methods/standards
- Lack of understanding & community-wide adopted definitions
- Uncertainty
- Complex workflows
- Time-intensive analysis
- Incomplete databases
- Valuable outputs for diverse stakeholders (quantitative NTA-qNTA...)
- Sustainable storage of large amounts of data



<https://nontargetedanalysis.org/>

A consensus-based working group formed to address challenges in mass spectrometry-based non-targeted analysis (NTA) studies by developing best practices and harmonizing standards in support of the scientific community and decision makers.



**EPA's NTA Collaborative Trial (ENTACT)<sup>1</sup>**

2015-2018

**BP4NTA Formed**

2018

**BP4NTA Now<sup>2</sup>**

2024



Elin Ulrich  
(EPA)



Benjamin Place  
(NIST)

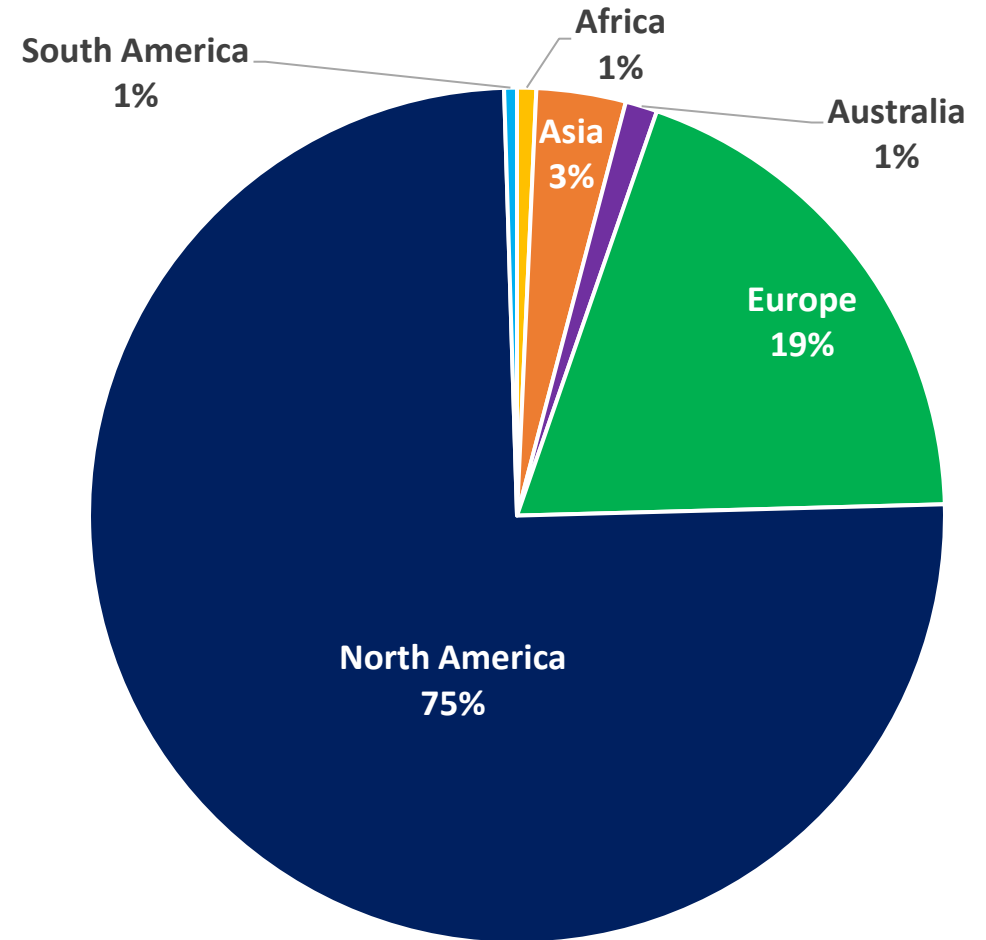
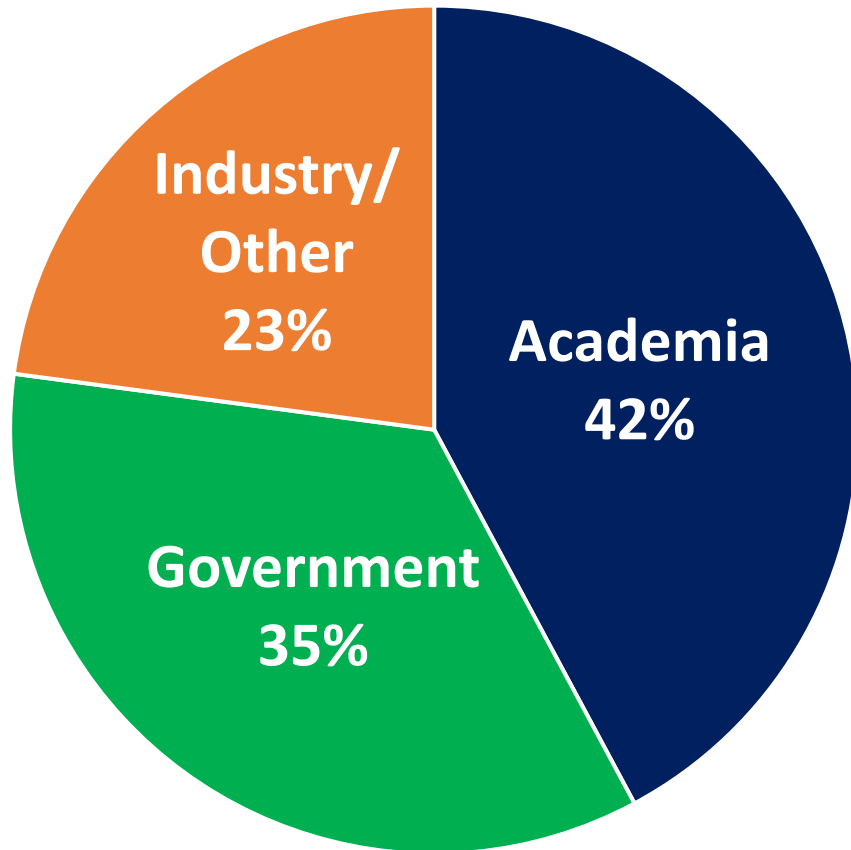
“a diverse working group consisting of industry, academic, and government representatives dedicated to clarifying the definitions and methods for Non-Targeted Analysis by publications and presentations”

<sup>1</sup>Ulrich et al. *Anal Bioanal Chem.* 2019. <https://doi.org/10.1007/s00216-018-1435-6>

<sup>2</sup>Place et al. *Anal. Chem.* 2021. <https://pubs.acs.org/doi/10.1021/acs.analchem.1c02660>



**~300 Members – September 2023**  
**~415 Members – April 2024**





# Leadership and Structure



**Chair:** James McCord

**Vice Chair:** Sara Nason

**Past Chair(s):** Ruth Marfil-Vega  
Christine Fisher

**Secretary:** Robert Young


















**Treasurer:** Stephan Baumann

**Technical Liaison:** Jon Sobus

**Operational Liaison:** Gabby Black



# BP4NTA is Addressing Challenges in NTA!

Challenge	Educational Materials	Study Reporting Tool	Study Planning Tool	Performance Manuscript	Databases /Libraries	Link to Tox/Fate
Lack of demand for NTA data						...
Not knowing when NTA is appropriate						
Lack of physical resources					...	
Lack of knowledge (laboratory)						
Lack of data processing tools					...	...
Inability to ensure data quality					...	
Lack of comparability between labs					...	
Lack of knowledge (end-users)						...



= Completed product available



= We are working on it

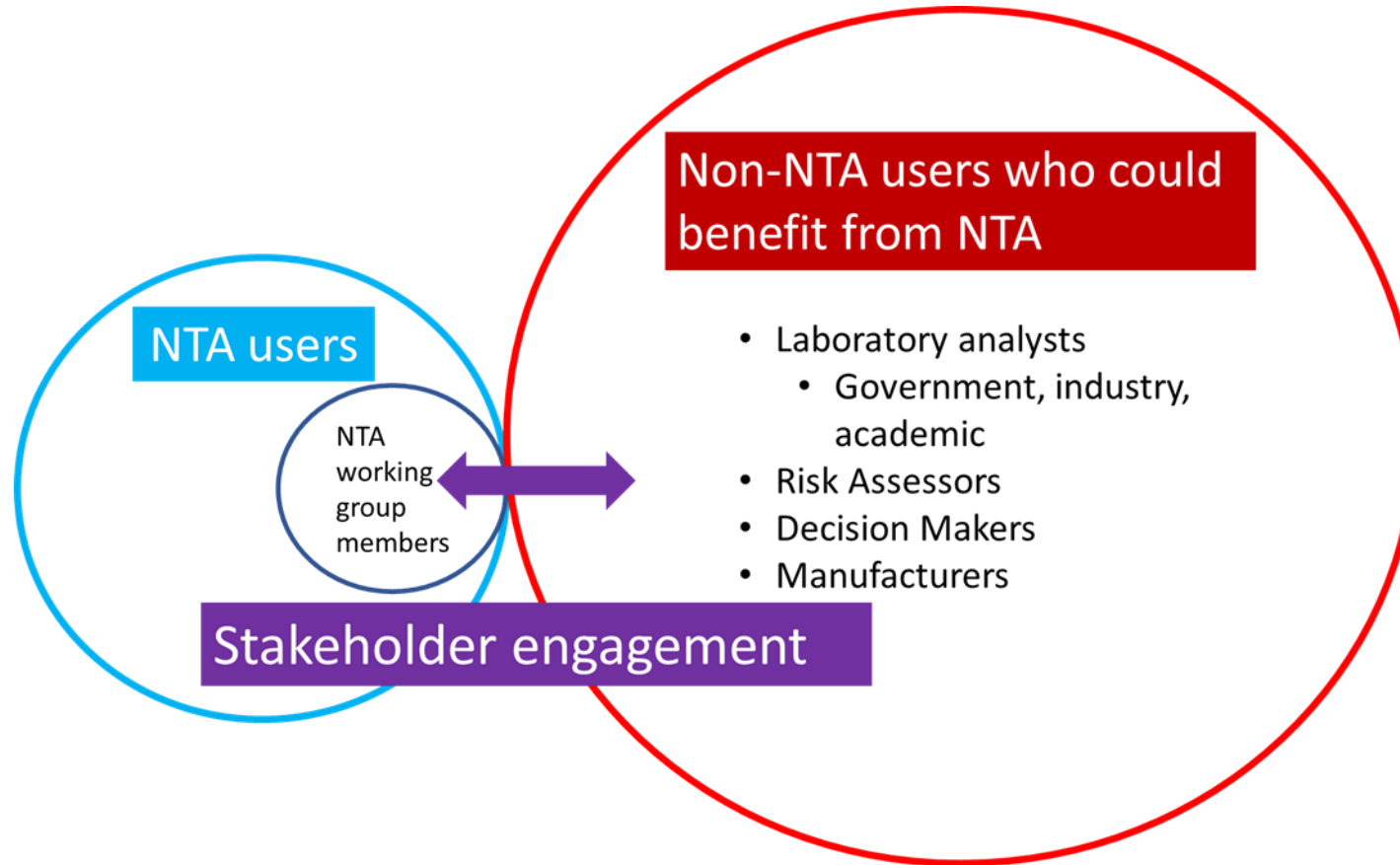
... = We are just getting started

# What BP4NTA has accomplished so far

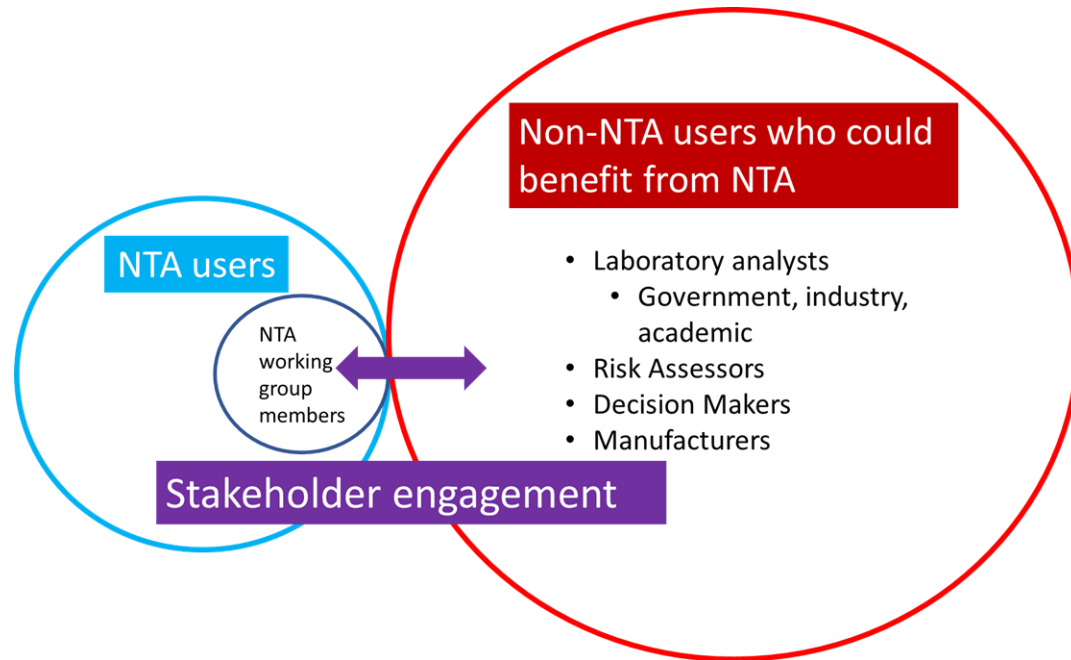
- Dissemination of scientific knowledge through the publication of six (6) peer-reviewed manuscripts and presentations at various conferences:
  - Introducing BP4NTA: [Place & Ulrich et al. \*Anal. Chem.\* 2021](#)
  - Describing & evaluating the Study Reporting Tool (SRT): [Peter & Phillips et al. \*Anal. Chem.\* 2021](#)
  - Promoting SRT use in exposure science: [Phillips & Peter et al. \*J Exp Sci Envi Epid\* 2023](#)
  - Proposing a tool to assess NTA chemical space: [Black & Lowe et al. \*ABC\* 2022](#)
  - Describing current approaches for NTA performance assessment: [Fisher & Peter et al. \*ABC\* 2022](#)
  - On/off-line prioritization of features (Collaboration: Krueve & Szabo): [Szabo et al. \*ABC\* 2024](#)
- Distribution of scientific and applied knowledge, and other relevant information in [WEBSITE](#) and through social media:
  - Reference content, SRT, NTA literature, Job postings, New member requests, Educational materials (videos/flyers/etc.)
- Seminar series keeps BP4NTA members abreast of NTA research across disciplines and sparks collaborations – during monthly meeting (available to members only)



# Stakeholder Outreach: Identifying and Prioritizing NTA Challenges



# Stakeholder Outreach: Identifying and Prioritizing NTA Challenges



## Stakeholder Committee Goal:

Meet with various stakeholder groups to determine the drivers and barriers affecting NTA adoption

# Stakeholder Outreach: Stakeholders' Participation



# Focus Group Meeting Format

- Attendee introductions
- Introduction to BP4NTA
- Define NTA
- Discussion questions
- Follow-up poll



# Discussion Questions

- Do you currently use NTA methods in your work? How?
- What are the biggest opportunities for using NTA methods in your field?
- What are the biggest barriers inhibiting NTA method use in your lab?
- How are NTA results reported and used in your field?
- What resources would be useful for incorporating more NTA methods in your work?
- Are you interested in participating in the creation/testing of these resources?



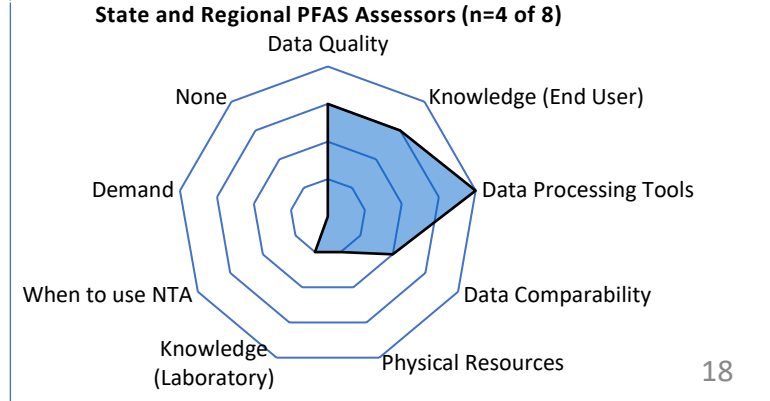
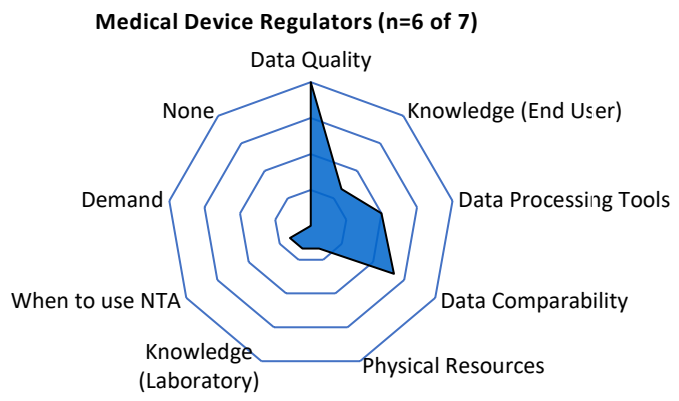
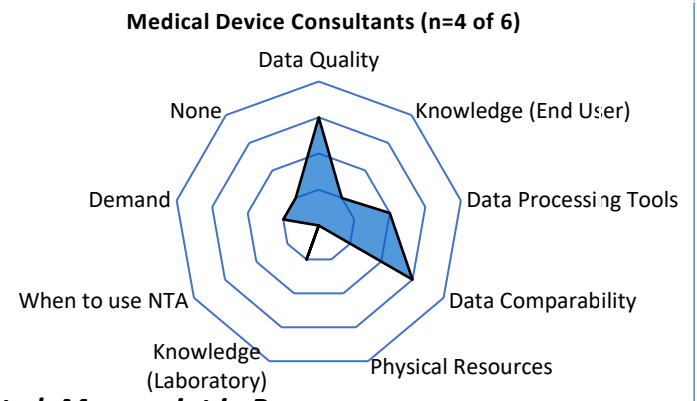
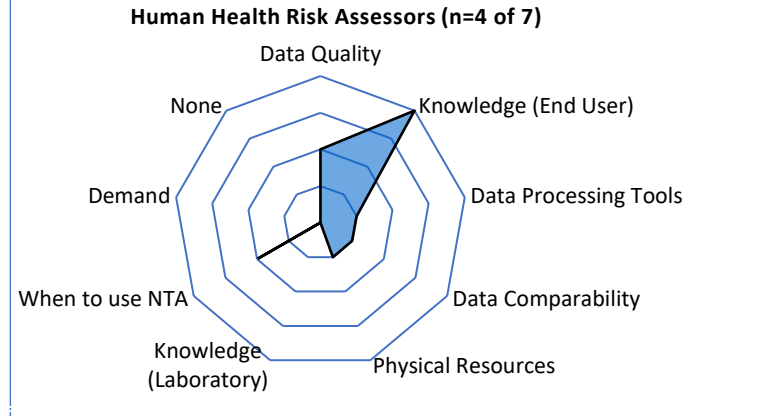
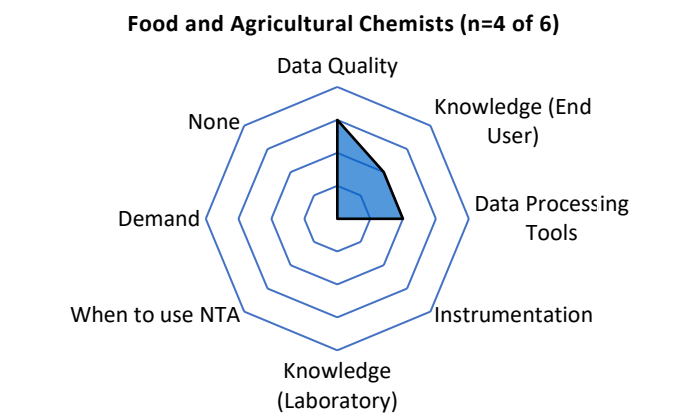
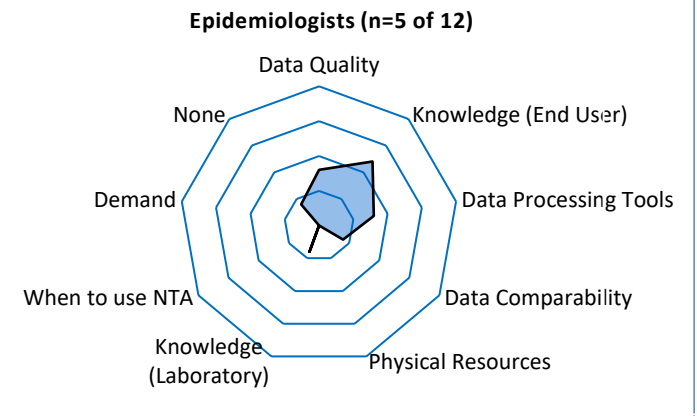
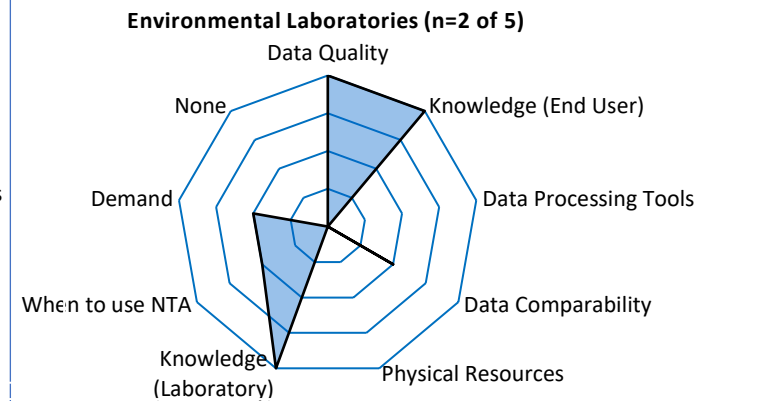
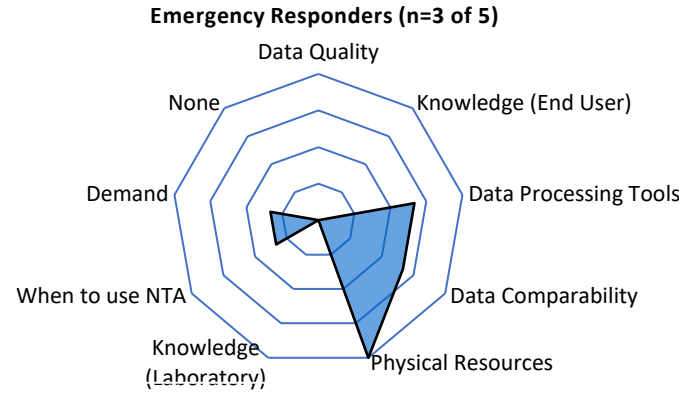
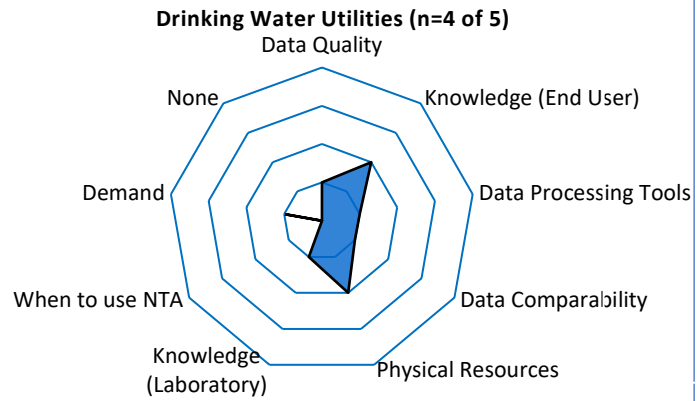
# Follow-up Poll

- **Barriers** to adoption
- **Potential efforts** useful for the stakeholders
- Current BP4NTA efforts relevant to stakeholders
- Relevant conferences and meetings

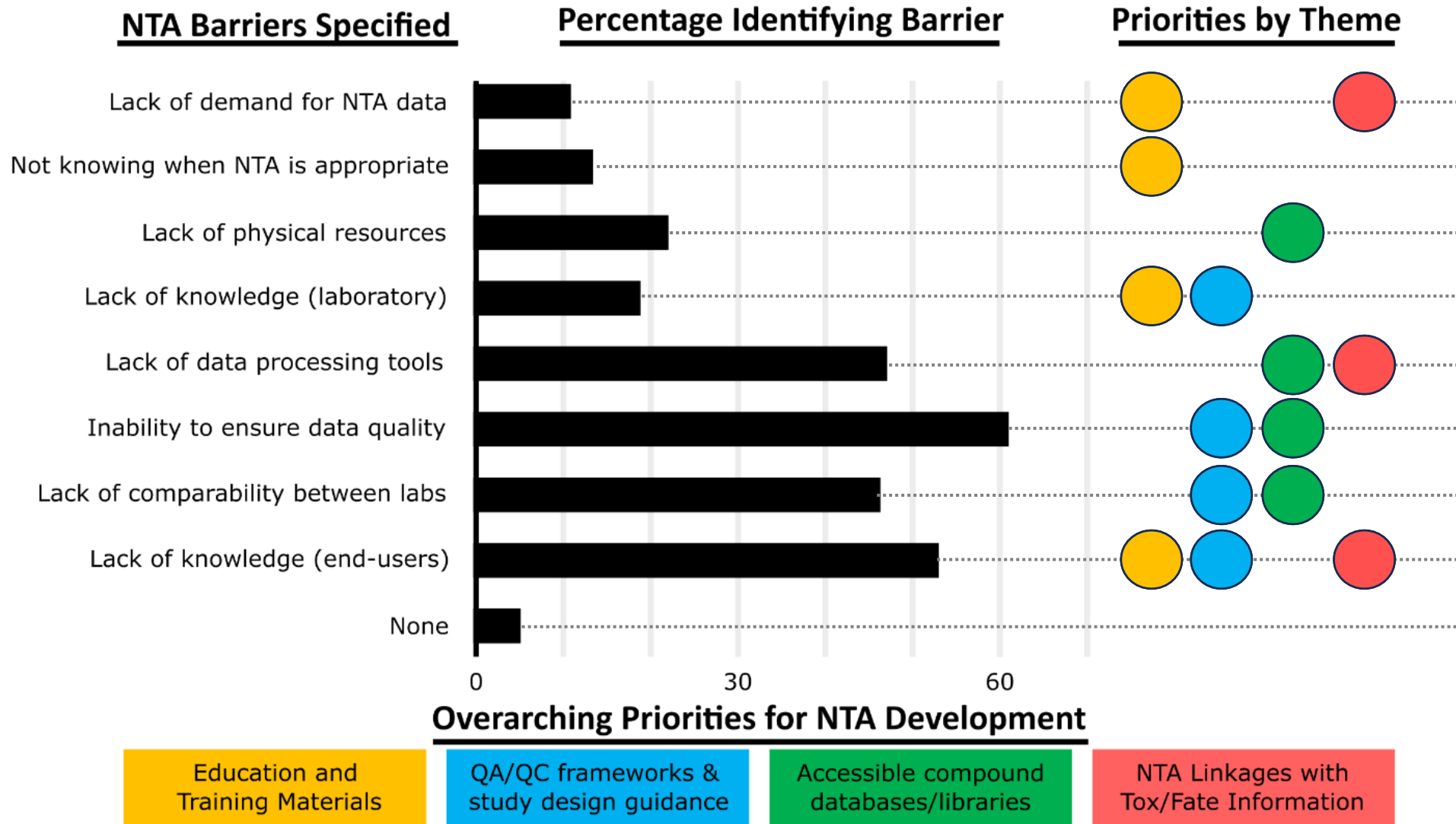
1. Lack of fundamental scientific understanding (laboratory analysts)
2. Lack of fundamental scientific understanding (end users of data)
3. Lack of access to necessary resources (e.g., instrumentation, lab space, personnel)
4. Lack of access to tools for data processing and analysis
5. Inability to ensure data quality (e.g. lack of accreditation opportunities, reference methods, established performance benchmarks)
6. Lack of ability to compare NTA data between labs
7. Lack of demand for NTA data
8. Lack of structure for determining when NTA analysis of a sample is appropriate
9. None of these

1. A standardized NTA method published by a government agency or other organization
2. Performance testing opportunities for NTA
3. NTA specific reference materials (e.g., open source databases and libraries)
4. NTA specific analytical standards
5. NTA training opportunities at workshops, conferences, or webinars
6. Materials for helping regulators and non-scientists understand NTA data (e.g., videos and fact sheets)

# Non-Targeted Analysis (NTA): Challenges



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# Proposed Actions Items to Address Challenges

Increasing Resources Needed



Category	Small Resource Requirements	Moderate Resource Requirements	Large Resource Requirements
<b>Education and Training Materials</b>	<ul style="list-style-type: none"> <li>• Fact sheets</li> <li>• Case studies</li> <li>• Tutorial videos</li> </ul>	<ul style="list-style-type: none"> <li>• Workshop training materials</li> <li>• Official author guidelines</li> </ul>	<ul style="list-style-type: none"> <li>• Intensive training courses with completion certificates</li> <li>• Multi-laboratory studies</li> </ul>
<b>QA/QC frameworks and study design guidance</b>	<ul style="list-style-type: none"> <li>• Study reporting guidelines</li> <li>• Single laboratory validation studies</li> </ul>	<ul style="list-style-type: none"> <li>• Guidance for study planning, workflow development, and QA/QC assessment</li> <li>• Harmonized study reporting requirements</li> </ul>	<ul style="list-style-type: none"> <li>• Universal reference mixtures and materials</li> <li>• Performance testing/accreditation</li> <li>• Multi-laboratory validation studies</li> </ul>
<b>Accessible Compound Databases and Libraries</b>	<ul style="list-style-type: none"> <li>• Community input for open-source databases/libraries</li> <li>• Submission templates for open-source libraries</li> </ul>	<ul style="list-style-type: none"> <li>• Curation, collation, and annotation of available data by research area</li> <li>• Integration of advanced information for library annotation (e.g., RT prediction, chemical space coverage)</li> </ul>	<ul style="list-style-type: none"> <li>• Institutionally sponsored efforts to close data gaps in accessible mass spectral information</li> </ul>
<b>NTA Linkages with Toxicity and Fate Information</b>	<ul style="list-style-type: none"> <li>• Incorporation of existing toxicity data within existing NTA databases</li> <li>• Development of quantitative models and approaches (e.g., qNTA) to link NTA results with toxicity values</li> </ul>	<ul style="list-style-type: none"> <li>• Expansion and validation of quantitative models and approaches (e.g., increased scope, number of applications and laboratory implementations)</li> </ul>	<ul style="list-style-type: none"> <li>• Institutionally sponsored efforts to develop quantitative tools that link NTA and toxicity data for risk estimation</li> </ul>

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- Defined an initial roadmap to address the challenges for NTA implementation
  - Categorized and prioritized the challenges
  - Identified action items to address them
- Prepared a peer-reviewed manuscript to disseminate outcomes (Nason & McCord et al.)
- Incorporated outcomes into BP4NTA's activities
- Started presenting outcomes at conferences relevant to stakeholders to expand engagement



## **We want you!**

**Accomplishing these goals requires concerted effort  
across similar groups, organizations, agencies, etc.!**

**See an effort you are interested in?  
Join us!**

**Part of a group working on something similar?  
Let's collaborate!**



**Access the website**  
of the Benchmarking and Publications  
for Non-Targeted Analysis (BP4NTA)  
workgroup

**Become a member**  
of BP4NTA



# Thank you!

Ruth Marfil-Vega (Past-Chair)  
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Sara Nason (Vice-Chair): [sara.nason@ct.gov](mailto:sara.nason@ct.gov)

