EPA United States Environmental Protection Agency

The Use of Non-Targeted Analysis for Rapid and Emergency Response: Demonstration Through Mock Scenarios

John T. Sloop, Alex Chao, Jennifer Gundersen, Allison L. Phillips, Jon R. Sobus, Elin M. Ulrich, Antony J. Williams, Seth R. Newton

The views expressed in this presentation are those of the author(s) and do not necessarily represent the views or the policies of the U.S. Environmental Protection Agency (USEPA)

Office of Research and Development
Center for Computation Toxicology and Exposure, Chemical Characterization and Exposure Division

Monday, May 23, 2022

Rapid Response Background

- Office of Land and Emergency Management (OLEM)
- EPA's emergency response authorities and responsibilities
  - National Oil and Hazardous Substances National Contingency Plan (NCP)
  - FEMA National Response Framework
- Paths to EPA involvement
  - State requesting Federal or EPA support
  - National Response Center (NRC) assigns On-Scene Coordinator (OSC) to release if EPA response is deemed appropriate

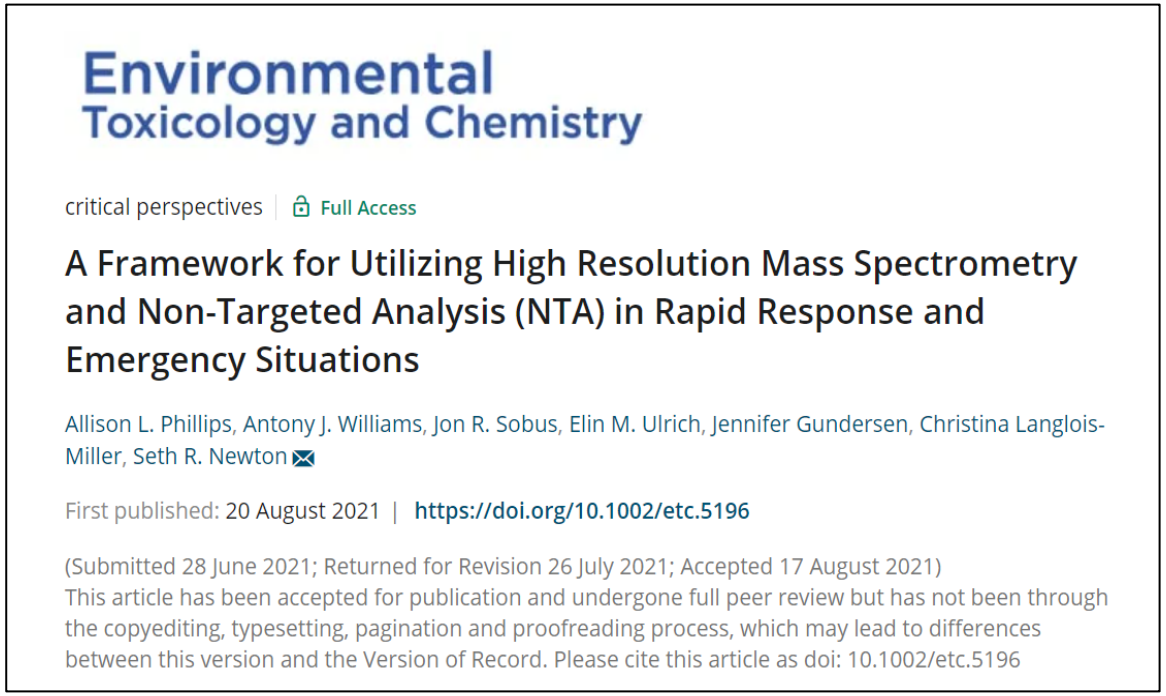
Why NTA in Rapid Response?

- In 2021, over 25,000 calls logged by the National Response Center (NRC) reporting environmental discharges → 30% of an unknown composition
  - "Unknown oil", "unknown toxic chemicals", "unknown green liquid"
- Of those of an unknown composition, over 70% reported to penetrate a body of water near the release
- NRC relies on a brick-and-mortar lab network called Emergency Response Lab Network (ERLN)
- For on-scene analyses, Portable High-Throughput Integrated Laboratory Identification Systems (PHILIS)
  - Staged at strategic locations across the contiguous US (24-hour response time)

Phillips et al., ET&C 2021.

Framework paper

- Laid the framework of how NTA could be applied in the field of rapid response
- High-resolution mass spectrometry (HRMS) vs. traditional, low-resolution instrumentation
- NTA has been proven as a tool for identifying unknowns
  - Even in rapid response scenarios



Environmental
Toxicology and Chemistry

critical perspectives | Full Access

A Framework for Utilizing High Resolution Mass Spectrometry and Non-Targeted Analysis (NTA) in Rapid Response and Emergency Situations

Allison L. Phillips, Antony J. Williams, Jon R. Sobus, Elin M. Ulrich, Jennifer Gundersen, Christina Langlois-Miller, Seth R. Newton

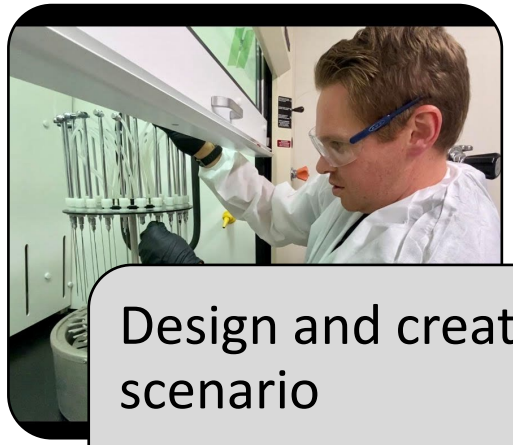
First published: 20 August 2021 | https://doi.org/10.1002/etc.5196

(Submitted 28 June 2021; Returned for Revision 26 July 2021; Accepted 17 August 2021)
This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/etc.5196

Phillips et al., ET&C 2021. Strynar et al., ES&T 2015, 49, 11622-11630. Newton et al., Environ. Poll. 2018, 234, 297-306. Hollender et al., 2017. Bader et al., 2016.

Summary of “mock scenarios”

- Created samples intended to mimic situations in which a rapid response would be necessary

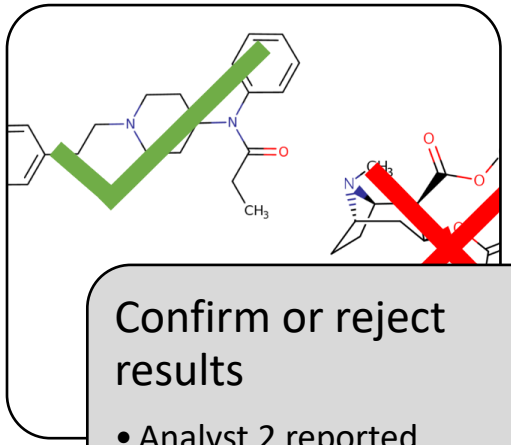


Design and create scenario

- Analyst 1 planned scenario
- Prepared individual samples

Conduct the scenario

- Analyst 2 performed any additional sample prep
- Collected, processed, and analyzed data
- Assigned identity to unknown compound(s)



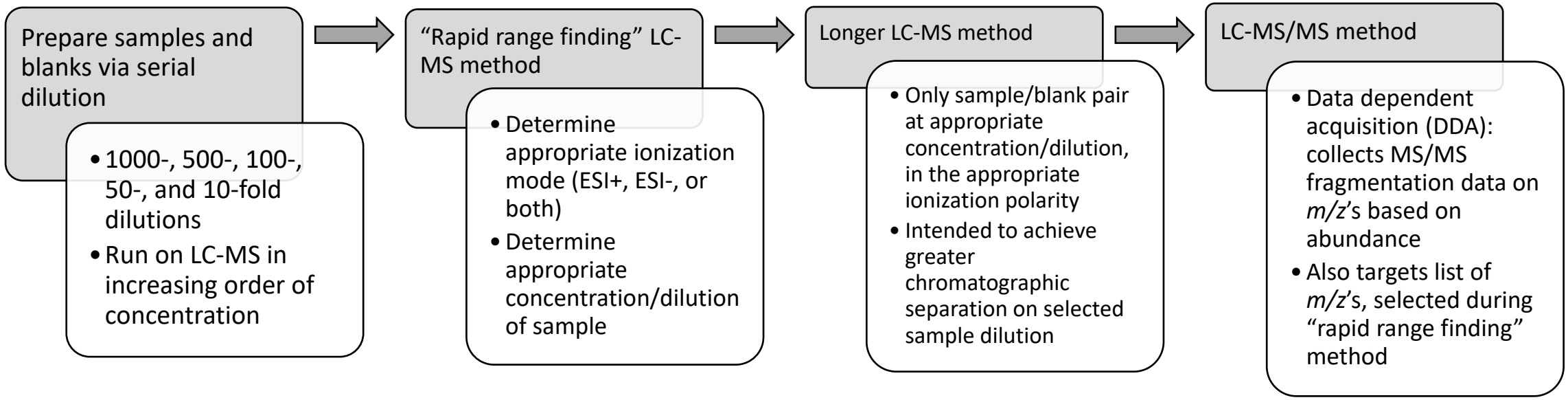
Confirm or reject results

- Analyst 2 reported assigned identities to Analyst 1
- Analyst 1 confirmed or rejected results of analysis

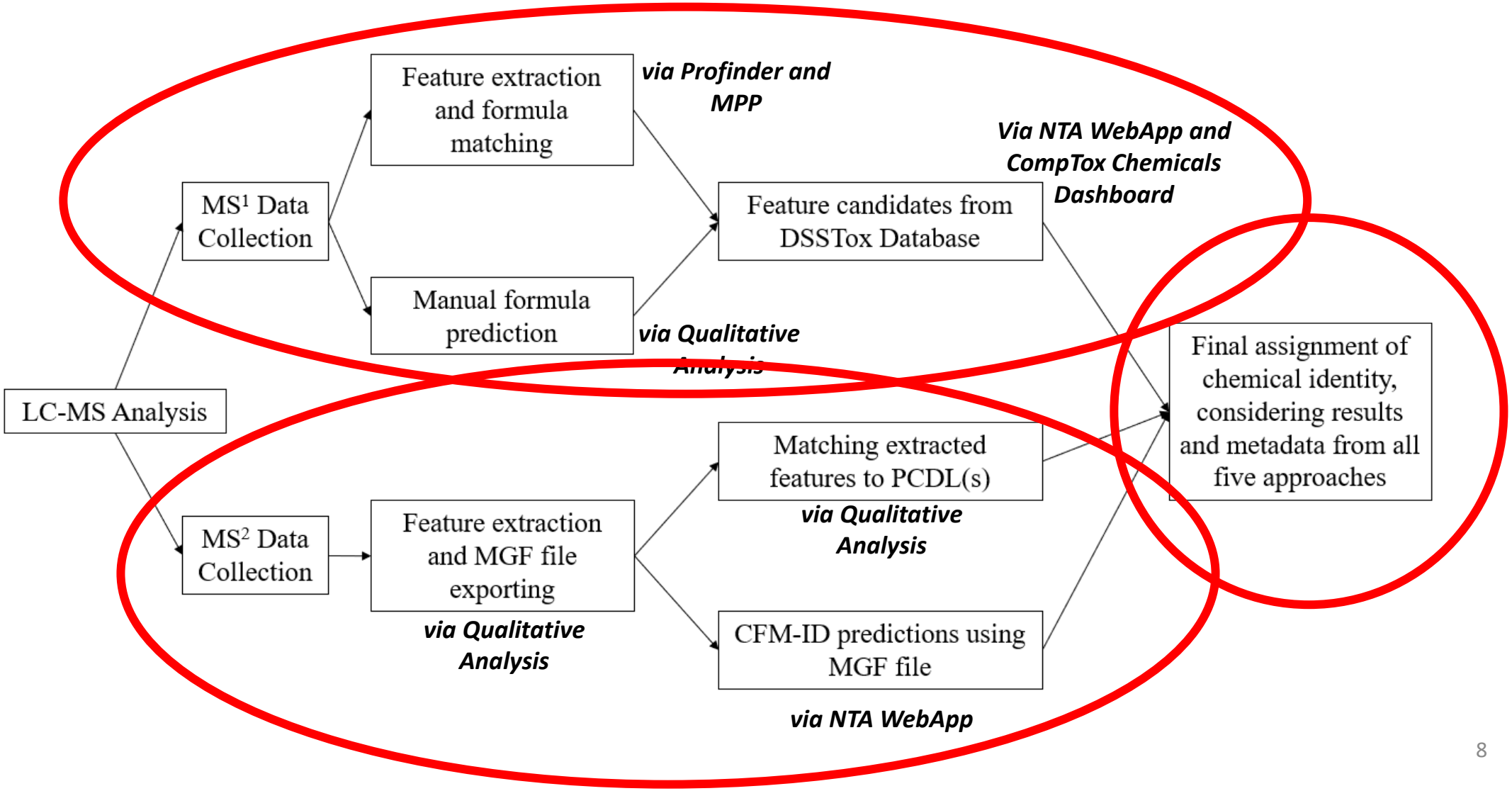
Defining Metrics for Success

1. Speed of analysis
2. Confidence in the eventual chemical identifications
3. Degree of hazard assessment that can be performed
4. Transferability of the designed NTA method/workflow

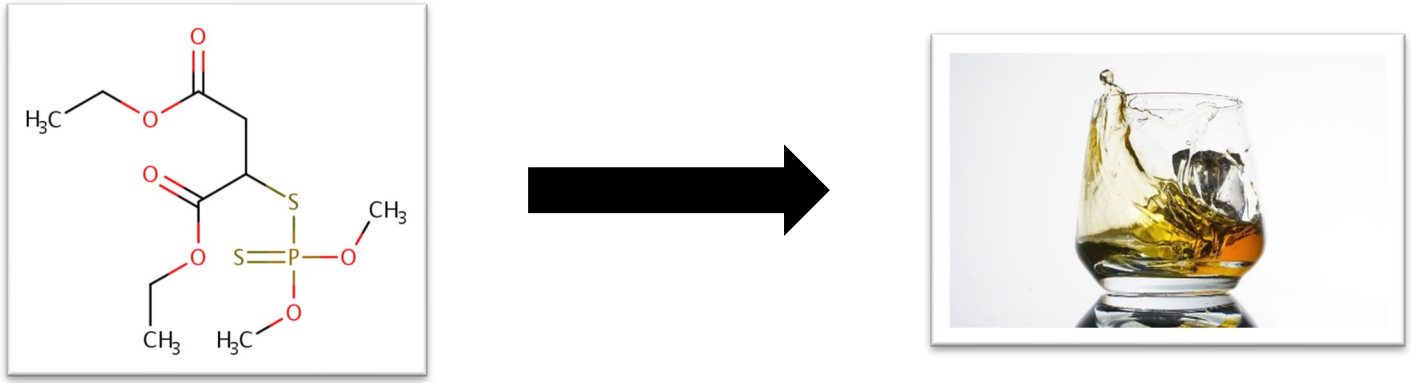
Data collection workflow



Data processing approach



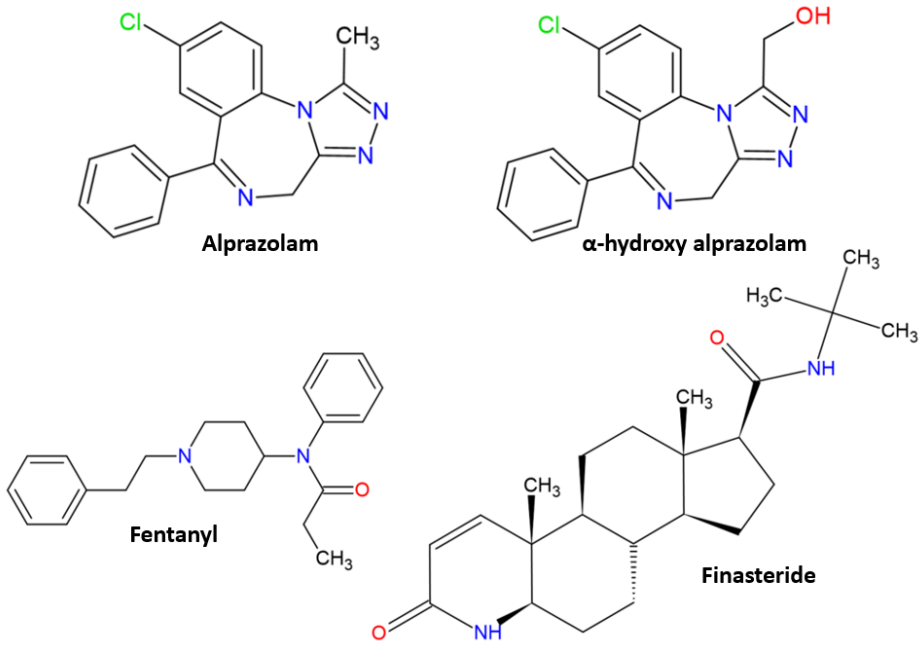
Mock scenario 1: Nerve agent spiked into alcoholic beverage



- Malathion ($C_{10}H_{19}O_6PS_2$) is structurally similar to Novichok nerve agents (used in an attack in the UK in 2018)
  - Spiked into pure ethanol
- Top hit for all MS^1 data processing approaches
- No spectra present in PCDL, and matched via CFM-ID, but not “top”
- Reported correct identification in 13 hours

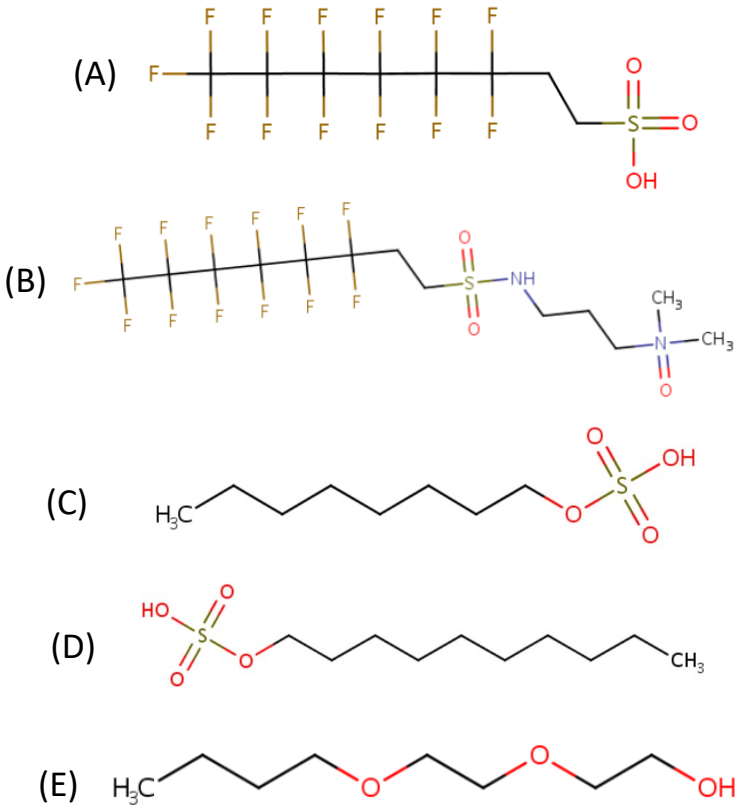
Mock scenario 2: Raid on Clandestine Fentanyl Laboratory (i.e., a “drug house”)

- Scenario: drug house raided under suspicion of fentanyl processing with another illicit drug
- Typical sampling of “drug houses” includes traditional (surface wipes of non-porous materials) and non-traditional sampling (porous materials)
- Results:
  - α-hydroxy alprazolam top hit for all MS^1 approaches, and matched with CFM-ID MS^2 spectra
  - Finasteride top hit for all MS^1 approaches, and matched MS^2 spectra via PCDL



Mock scenario 3: AFFF spill into surface water

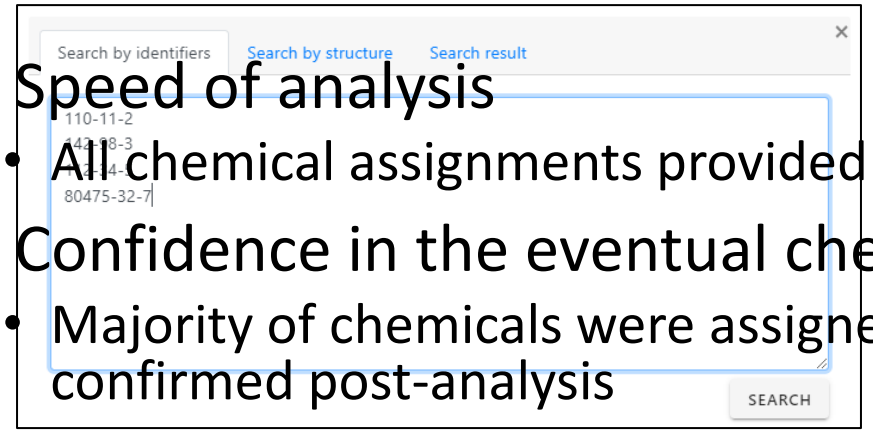
- Aqueous Film Forming Foam (AFFF) mixture (Solberg Type 6) spiked into surface water
- Selected a total of 14 features for further investigation
- Multiple features assigned a structure
  - Two features (one ESI+, one ESI-) related to the same chemical
  - Five unique chemicals
  - Confirmed via literature review

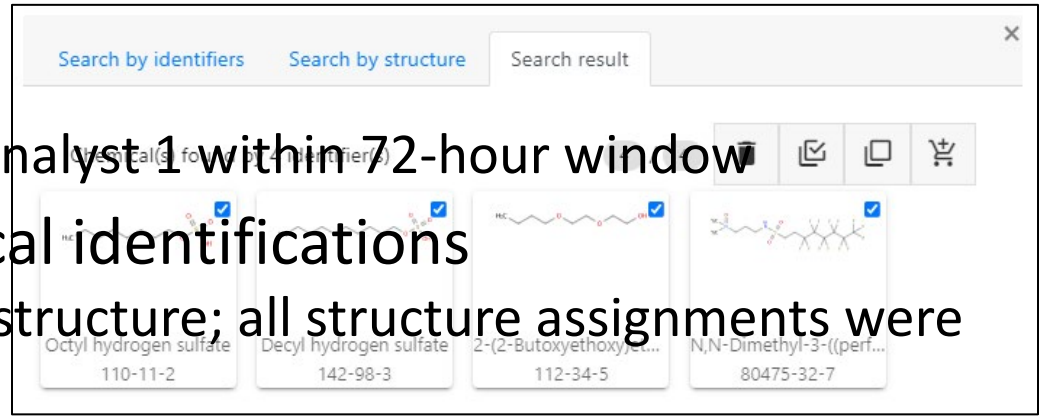


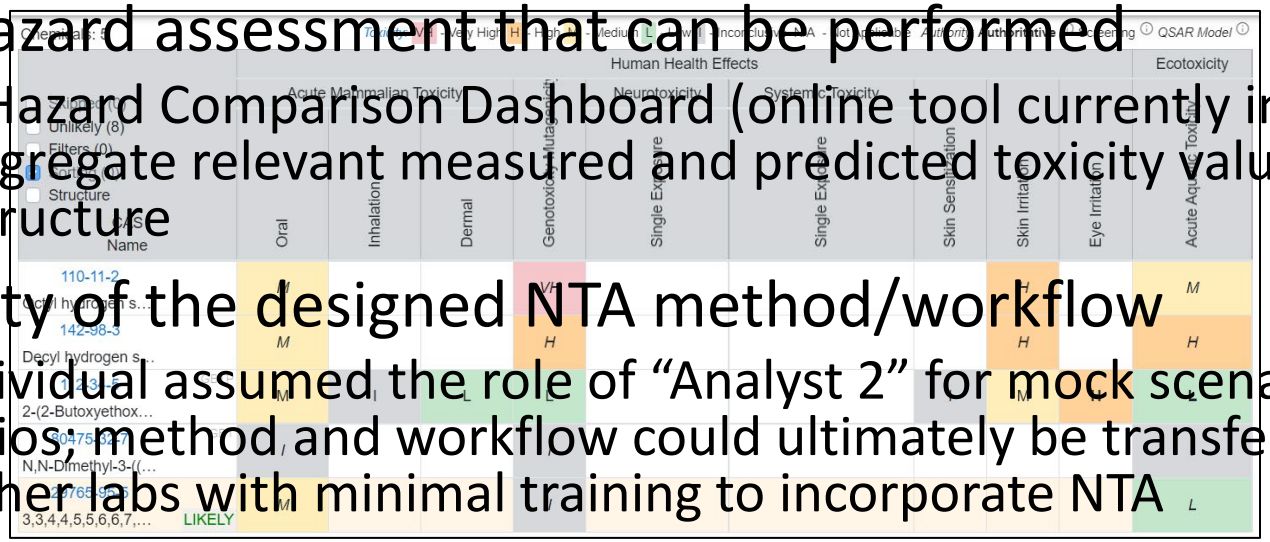
(A) 6:2 fluorotelomer sulfonic acid; (B) N,N-Dimethyl-3-((perfluorohexyl)ethylsulfonyl)aminopropanamine N-oxide; (C) Octyl hydrogen sulfate; (D) Decyl hydrogen sulfate; (E) 2-(2-Butoxyethoxy)ethanol

Addressing the Metrics for Success

1. Speed of analysis
   - All chemical assignments provided to Analyst 1 within 72-hour window
2. Confidence in the eventual chemical identifications
   - Majority of chemicals were assigned a structure; all structure assignments were confirmed post-analysis
3. Degree of hazard assessment that can be performed
   - Utilized the Hazard Comparison Dashboard (online tool currently in development at USEPA) to aggregate relevant measured and predicted toxicity values for chemicals assigned a structure
4. Transferability of the designed NTA method/workflow
   - Different individual assumed the role of "Analyst 2" for mock scenario 2 than the other scenarios; method and workflow could ultimately be transferred to regional, state, and other labs with minimal training to incorporate NTA







Current limitations of our approach

- All mock scenarios included “known” chemicals (all present in DSSTox)
  - Even if single structure cannot be determined, can still collect useful information, and later perform *de novo* NTA
- Qualitative, not quantitative
  - Methods are being developed to estimate concentrations of compounds without standards via quantitative NTA (qNTA); improving hazard assessment
- Only explored LC-MS, not GC-MS
  - GC-MS NTA workflows are currently being further developed, hoping to perform GC-MS mock scenarios soon

Conclusions

- Situations where traditional, targeted methods cannot elucidate the identity of an unknown → NTA is a useful, additional analytical tool
- The three mock scenarios presented showcase the applicability of NTA approaches
- The success of each mock scenario against the identified metrics for success was discussed
  - Level of success increases as complexity of specific scenario decreases
- Future work:
  - Incorporating quantitative NTA approaches for concentration estimates, improving hazard assessment
  - Attempting this approach on a real sample/situation
  - Exploring GC-MS NTA methods for rapid response scenarios

EPA United States Environmental Protection Agency

Acknowledgements

- EPA ORD and Oak Ridge Institute for Science and Education (ORISE)
- The NTA WebApp team
- The HCD team
- Jarod Grossman of Agilent

Contact Information:
Sloop.John@epa.gov