OLEM Perspective on Non-Targeted Analysis for Emergency Response

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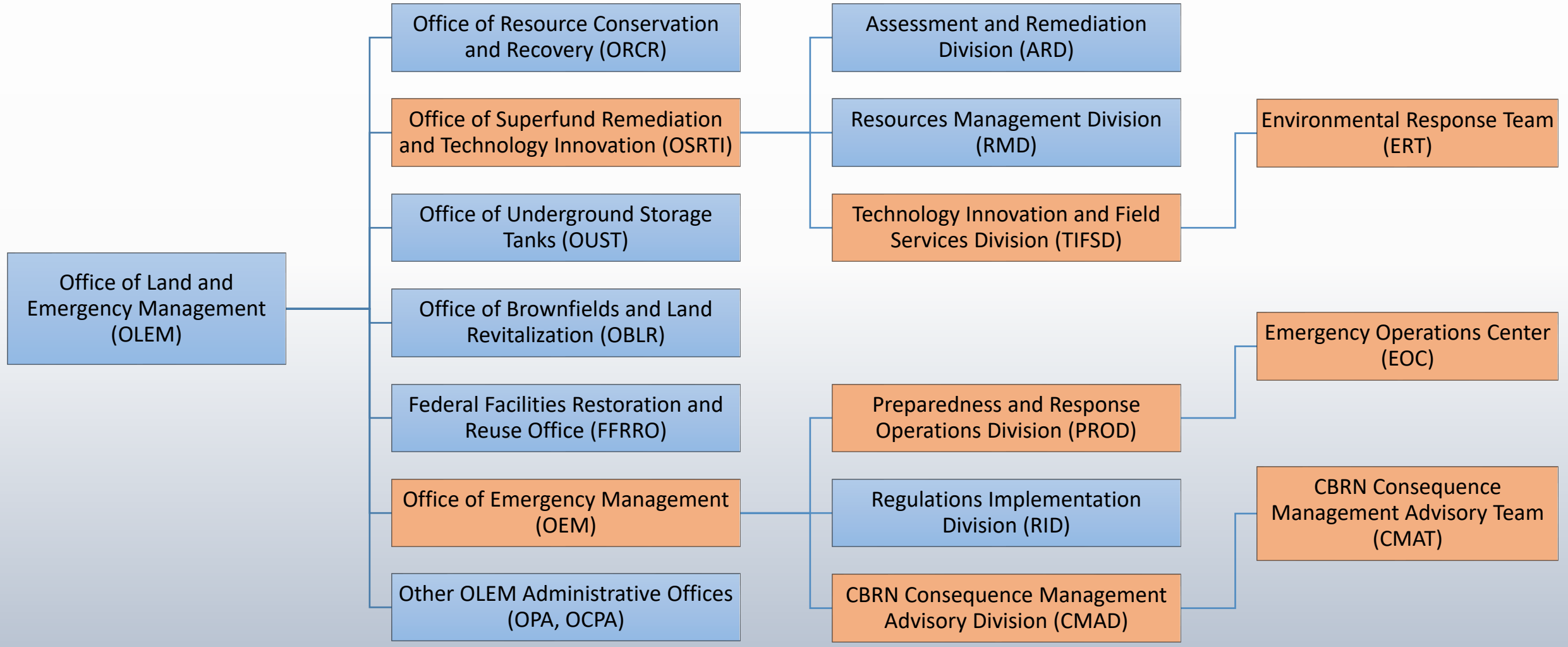
Office of Emergency Management

OLEM Organization



EPA's Emergency Response Authorities and Responsibilities

- EPA National Oil and Hazardous Substances National Contingency Plan (NCP)
  - Framework for responding to oil spills and hazardous substance releases
  - Covers emergency response authority under various EPA statutes
    - Oil Pollution Act (OPA)
    - Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA)
    - Clean Water Act (CWA)
- FEMA National Response Framework
  - Scalable, flexible, and adaptable guide for how the nation responds to disasters and emergencies
  - Uses National Incident Management System – key roles and responsibilities
  - Emergency Support Functions describe federal coordinating structures
  - ESF #10 – Oil and Hazardous Materials Response
    - EPA is ESF #10 Coordinator, primary agencies are EPA, DHS, USCG
    - Activated for Stafford Act response, at discretion of Secretary of Homeland Security, or in response to request for Federal support
    - EPA deployment contingent on Mission Assignment – specifies tasks and funding

Paths to EPA Involvement

Local Responders called to scene
- Often fire department
- Local public health or environmental agencies

Locals request state support
- State Department of Health, Environmental Quality, Environmental Protection, etc

State requests Federal or EPA support
- Regional office notified by state
- Regional OSC assigned

NRC staffed 24/7/365 by USGC
- Receives notifications of all releases
- Notifies relevant state and federal agencies

Regional Phone Duty OSC notified
- Authority to decide whether EPA response is appropriate

EPA Response OSC assigned
- Leads response
- Notifies Regional Response Team

OSC responsible for assessment, monitoring, response assistance, and evaluation during and after a response

Resources for OSCs – EPA Special Teams

CBRN Consequence Management Advisory Team (CMAT)

- CBRN experts
- Mobile labs for confirmatory analysis of chemical warfare agents and toxic industrial compounds (TICs) - PHILIS
- Aerial detection system for TICs and oil spills - ASPECT
- Laboratory network for surge capacity - ERLN

Environmental Response Team (ERT)

- Oil and hazmat response experts
- Air monitoring team
- Mobile trace atmospheric gas analyzers - TAGA
- Fate and transport modeling

Radiological Emergency Response Team (RERT)

- Radiation risk monitoring
- Cleanup of radioactive substances

National Criminal Enforcement Response Team (NCERT)

- Forensic evidence collection
- Law enforcement liaisons
- Protective escorts for responders

Potential Applications of NTA in OLEM Emergency Response Capabilities

- Non-targeted analysis (NTA) could be used to rapidly narrow down composition of unknown spills or intentional releases of unknown chemicals
  - Specific chemical composition is important for:
    - Determination of EPA authority – must be a listed hazardous waste, substance, etc under some EPA authority for responsible party financial liability
    - Selection of decontamination techniques and establishing clearance goals
- NTA may be able to be used to identify degradation products and/or complex mixtures of hazardous chemicals
  - Potentially useful for long-term monitoring in addition to emergency response
  - Potentially useful for determining the source of contamination using chemical profile matching
  - Potential applications for identification of chemical warfare agents (traditional and fourth generation) – limited laboratory capacity
  - Potential applications for identification of pharmaceutical based agents (fentanyl and analogs) – many potential agents

The Use of Non-Targeted Analysis for Rapid and Emergency Response

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Office of Research and Development

Office of Emergency Management

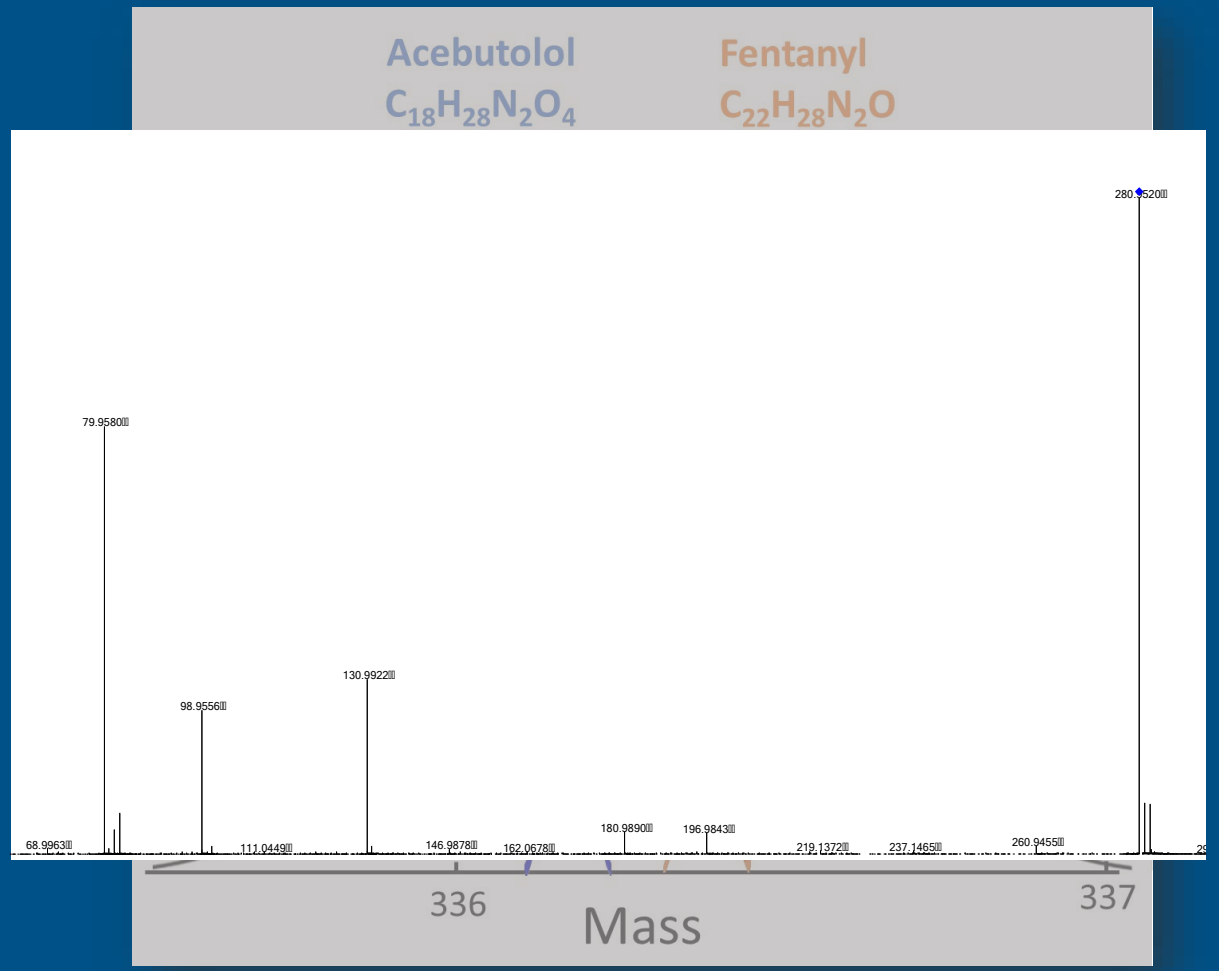
The views expressed in this presentation are those of the author(s) and do not necessarily represent the views or the policies of the U.S. Environmental Protection Agency (USEPA)

Why NTA in Rapid Response?

- In 2019, ~26,000 logged environmental discharges → 37% of unknown composition
  - "unknown oil", "unknown toxic chemicals", "unknown green liquid"
- NRT relies on a brick-and-mortar lab network called the Emergency Response Lab Network (ERLN)
- For on-scene analysis, Portable High-Throughput Integrated Laboratory Identification Systems (PHILIS) are staged at strategic locations
- ERLN and PHILIS utilize mostly targeted analytical chemistry methods, although some non-targeted work is done

Phillips et al., ET&C 2021.

NTA and High Resolution Mass Spectrometry (MS)



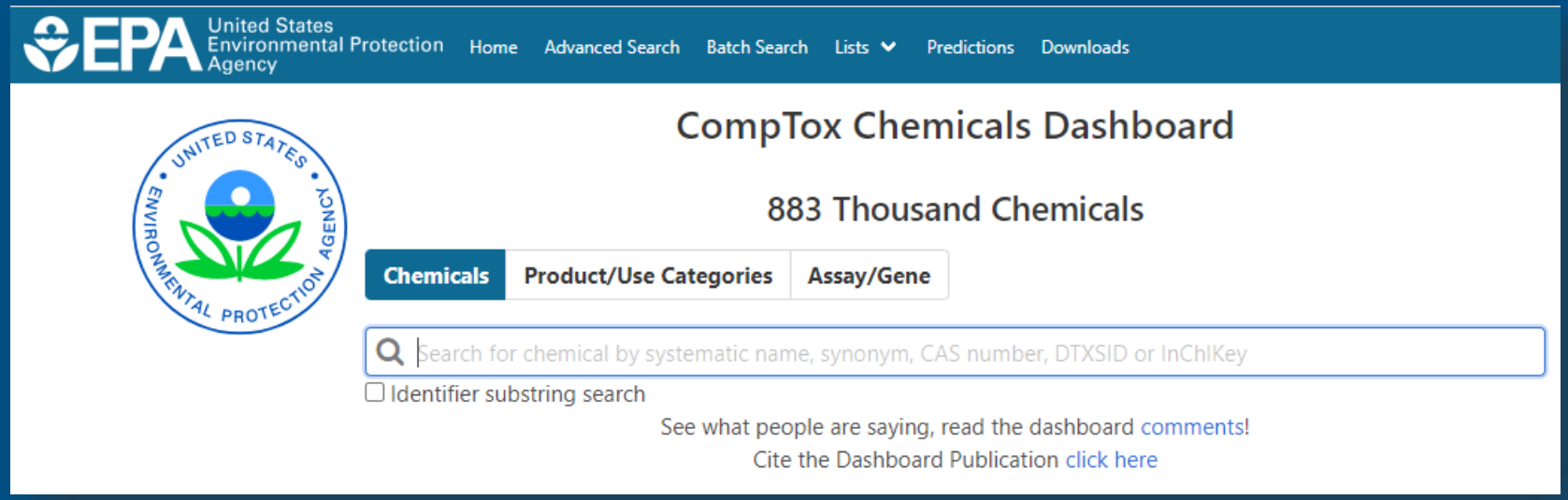
MS1:

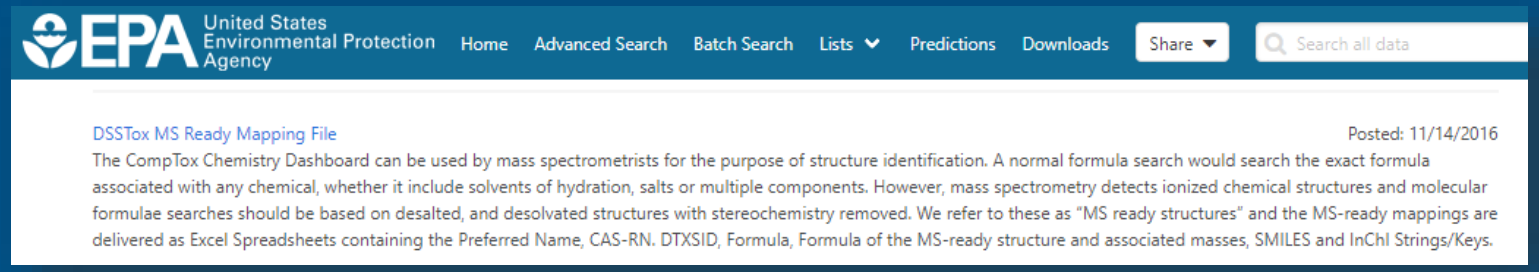
- Accurate mass of molecular ion
- Molecular formula prediction or matching

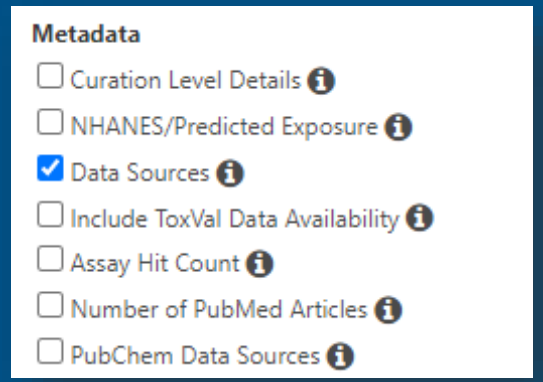
MS2:

- Fragmentation data used to match to spectral libraries (experimental or predicted)
- NTA utilizes both MS1 and MS2 data from HRMS, combined with informatics tools, for identification of unknown chemicals
- NTA is typically very slow and time-consuming

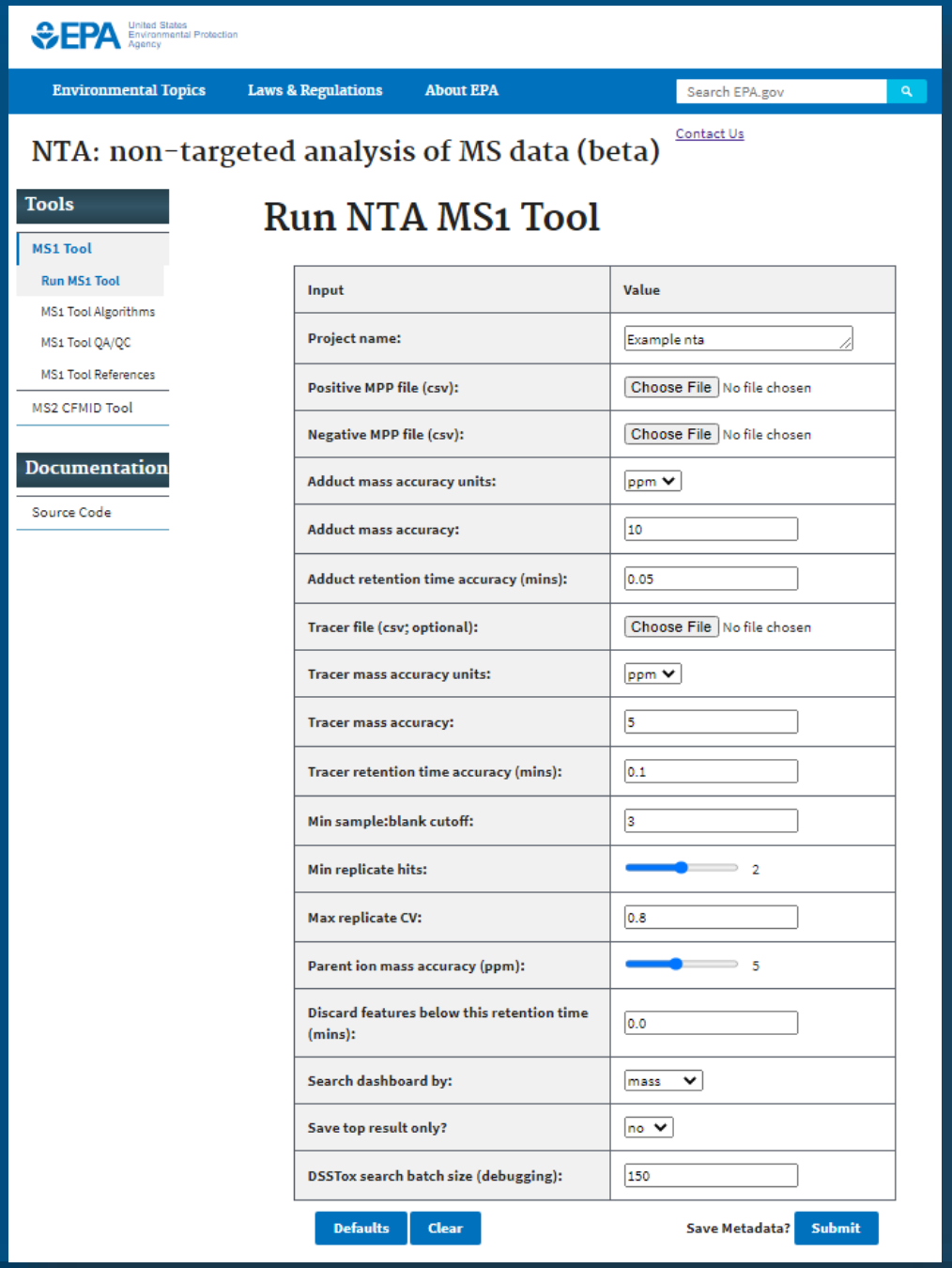
The Comptox Chemicals Dashboard

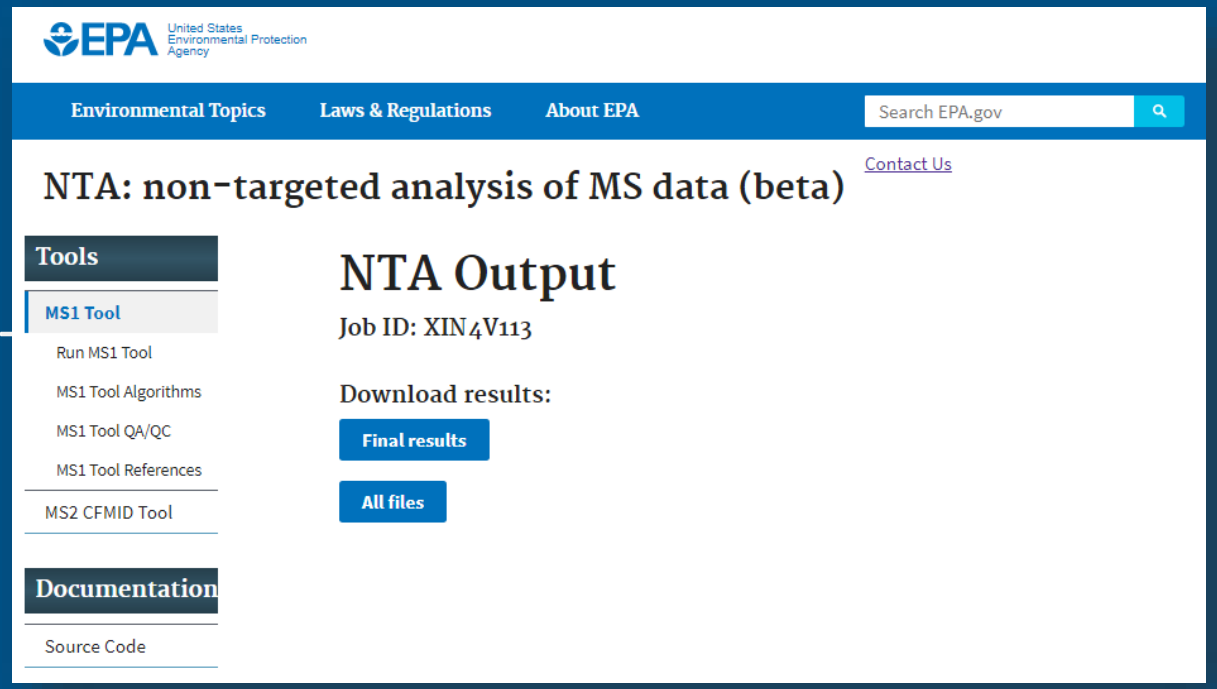






List Acronym	List Name	Last Updated	Number of Chemicals	List Description
FENTANYLS	LIST: Fentanyl Analogues	2021-04-22	67	A list of fentanyl analogues include both compounds developed by pharmaceutical companies and as designer drugs.





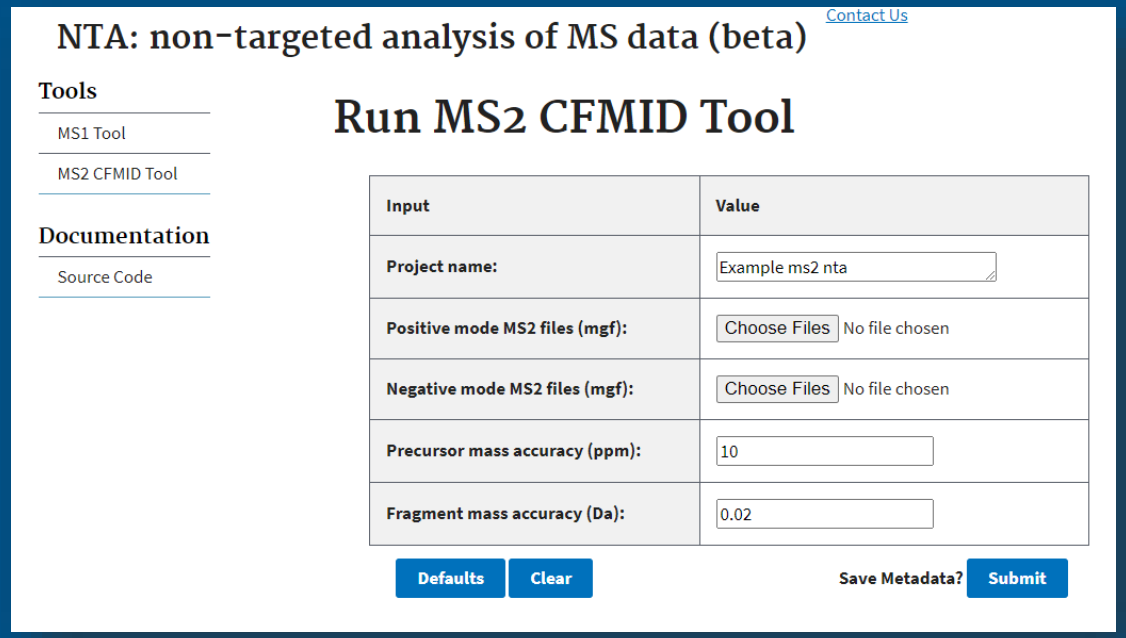
Param
clean-
searc

WebApp Output:

- QA/QC results of tracers
- Cleaned, unannotated file for stats analysis
- Cleaned, annotated file with chemicals
- Complete file with all details

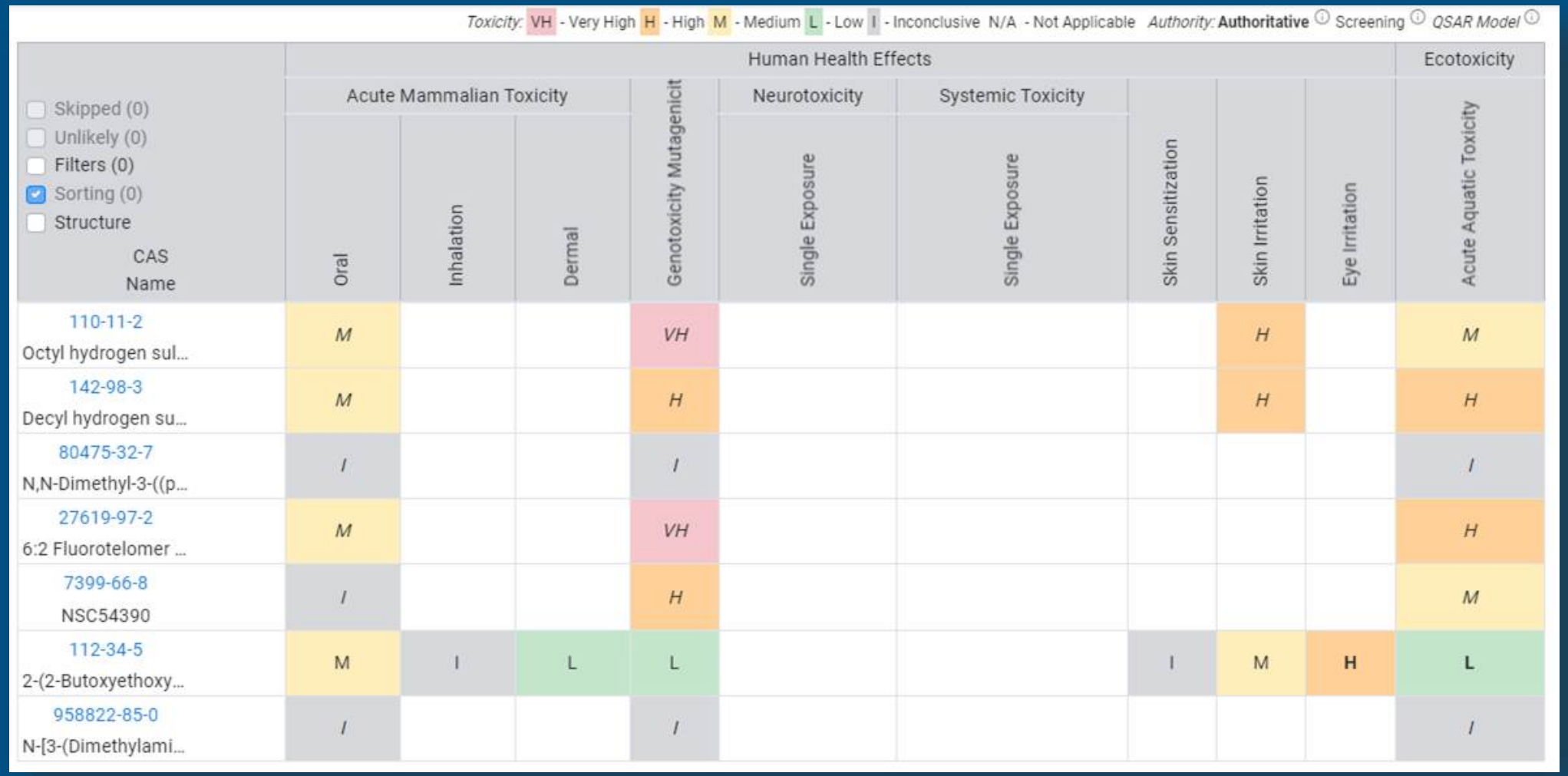
https://qed.edap-cluster.com/nta/

NTA WebApp:
MS2 Spectra Fragmentation Prediction



Competitive Fragmentation Modeling for Metabolite Identification (CFM-ID)

Hazard Comparison Dashboard



Toxicity: VH - Very High H - High M - Medium L - Low I - Inconclusive N/A - Not Applicable *Authority:* **Authoritative** Screening *QSAR Model*

- Skipped (0)
- Unlikely (0)
- Filters (0)
- Sorting (0)
- Structure

CAS Name	Human Health Effects									Ecotoxicity
	Acute Mammalian Toxicity			Genotoxicity Mutagenicit	Neurotoxicity	Systemic Toxicity	Skin Sensitization	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity
	Oral	Inhalation	Dermal		Single Exposure	Single Exposure				
110-11-2 Octyl hydrogen sul...	*M*			*VH*				*H*		*M*
142-98-3 Decyl hydrogen su...	*M*			*H*				*H*		*H*
80475-32-7 N,N-Dimethyl-3-((p...	*I*			*I*						*I*
27619-97-2 6:2 Fluorotelomer ...	*M*			*VH*						*H*
7399-66-8 NSC54390	*I*			*H*						*M*
112-34-5 2-(2-Butoxyethoxy...	M	I	L	L			I	M	**H**	**L**
958822-85-0 N-[3-(Dimethylami...	*I*			*I*						*I*

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

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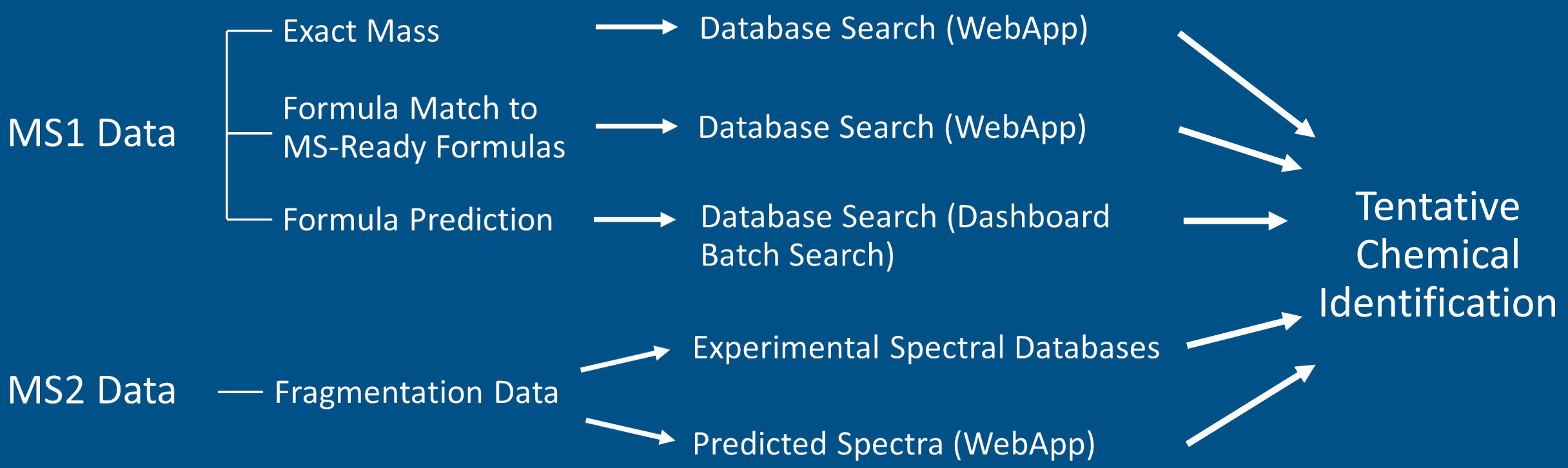
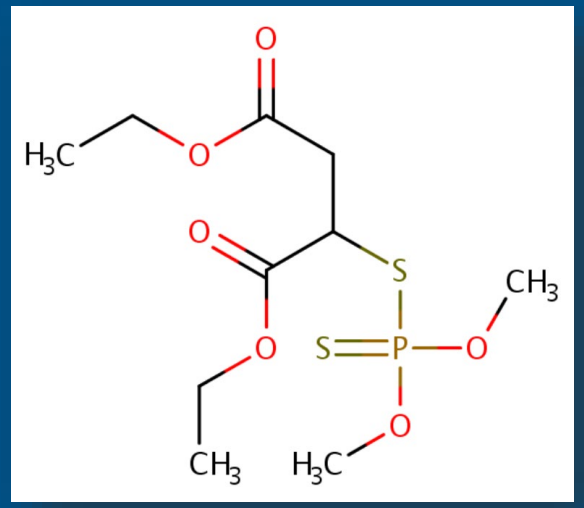
Putting it all together

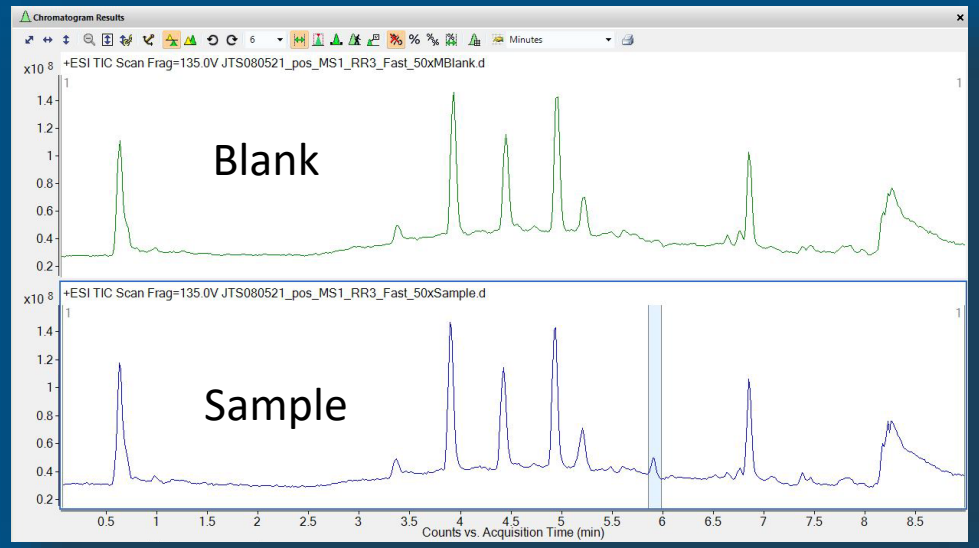


Mock Scenario 1: A Chemical Warfare Agent in Alcohol

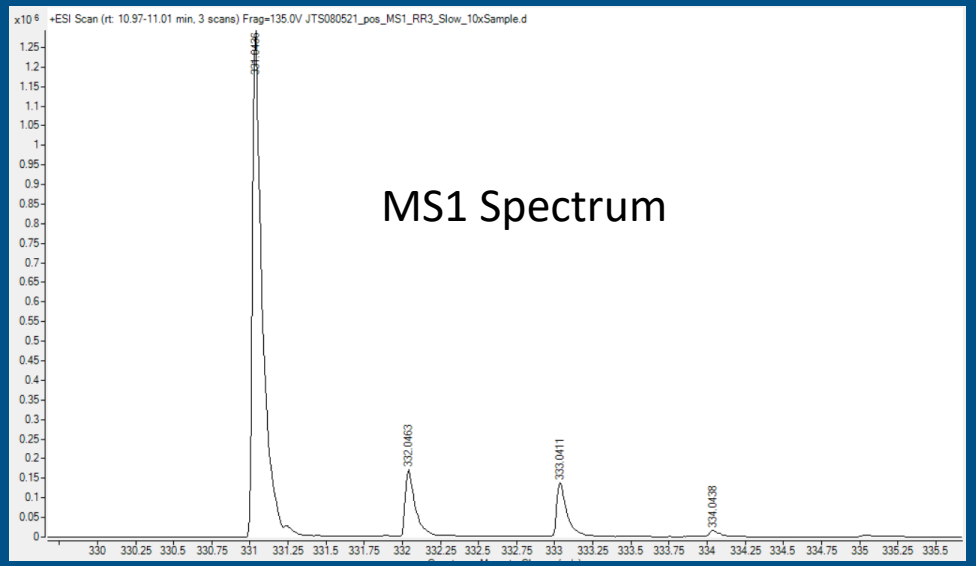
Malathion ($C_{10}H_{19}O_6PS_2$)

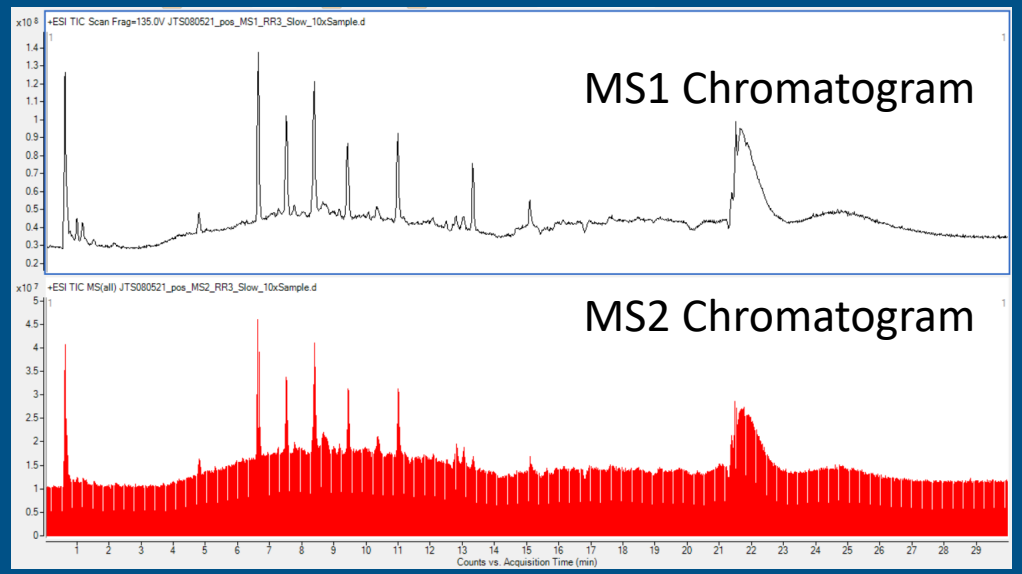


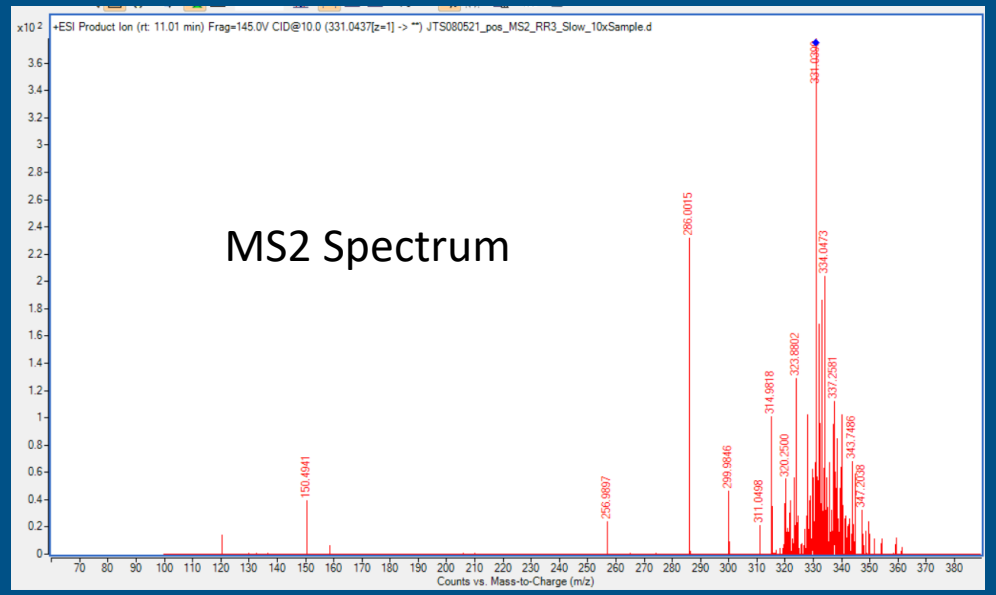
- Malathion is structurally similar to Novichok nerve agents, used in an attack in the UK in 2018
- It was spiked into pure ethanol
- The analyst was blind to the identity of the compound



Rapid Range Finding

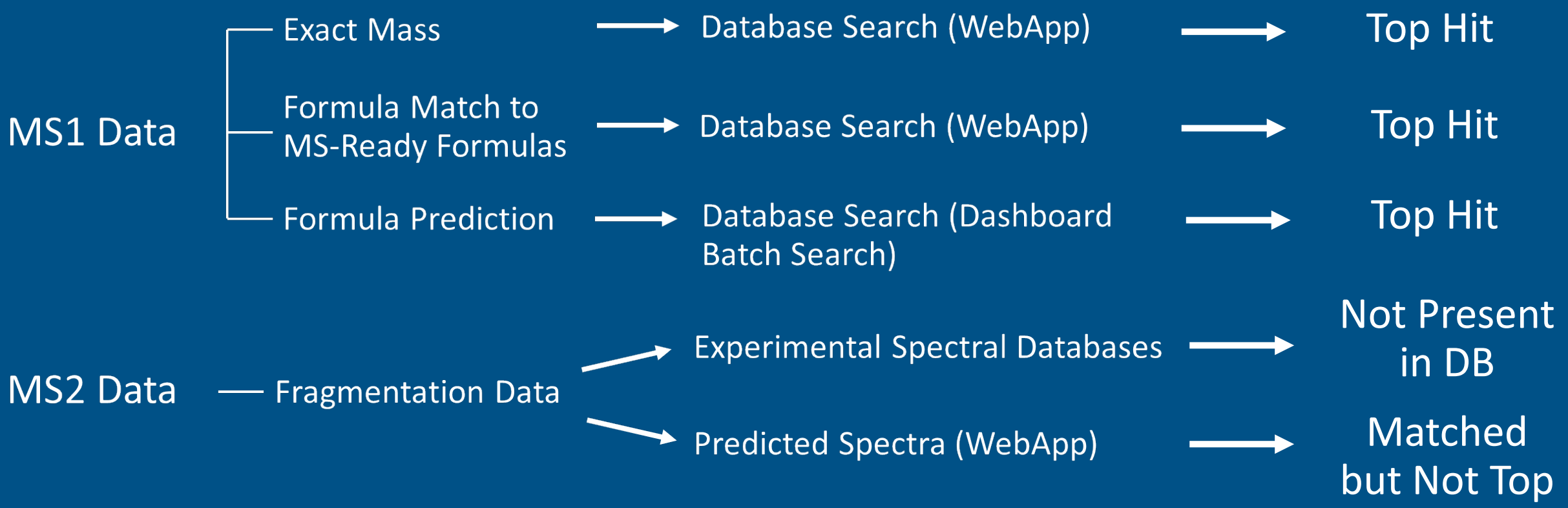






Long Method

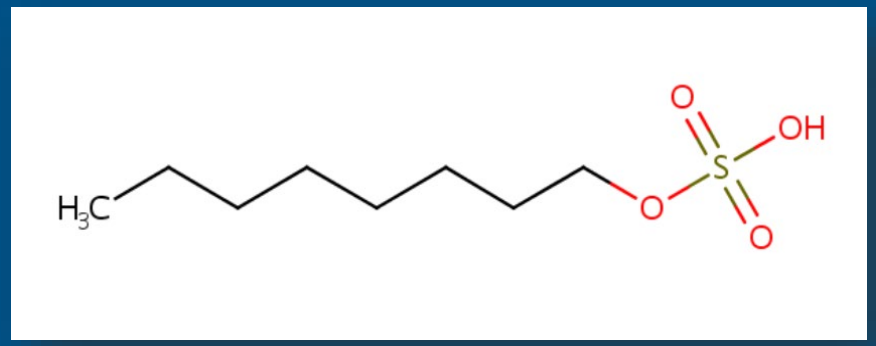
Mock Scenario 1: Choosing Best Hit



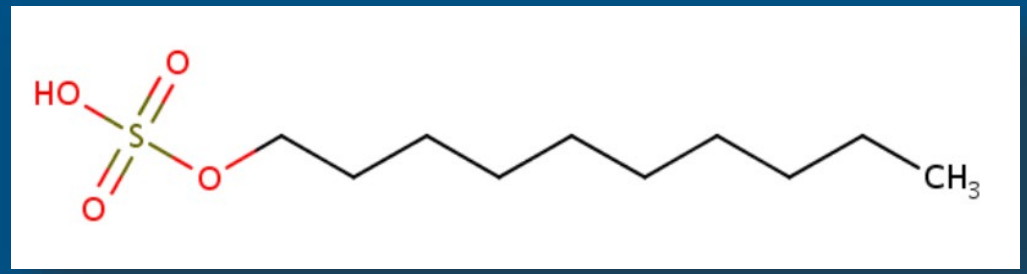
Analyst reported correct identification in 13 hours

Mock Scenario 2 – Aqueous Firefighting Foam (AFFF) Spilled into Surface Water

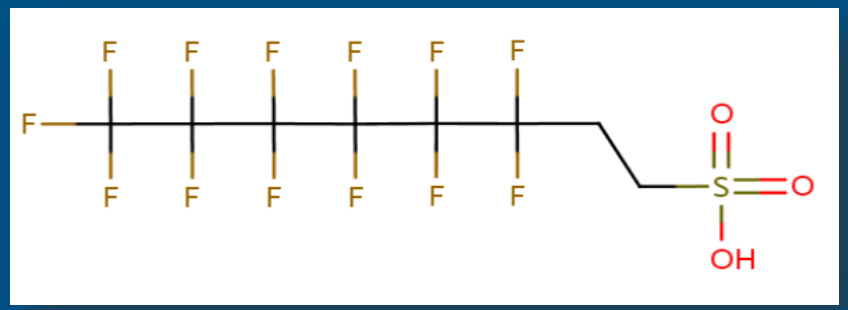
- Confident structure identification



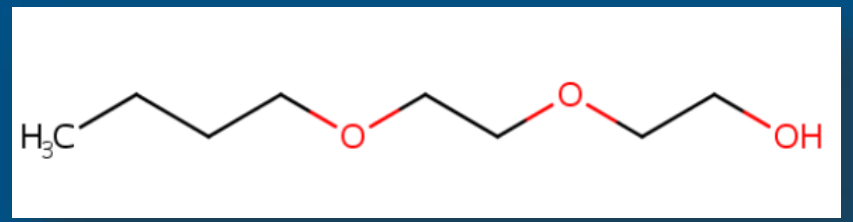
Octyl Hydrogen Sulfate



Decyl Hydrogen Sulfate

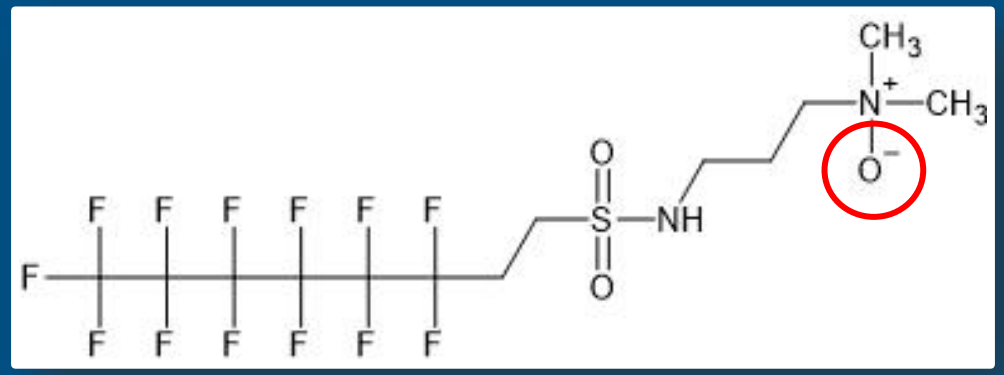


6:2 Fluorotelomer Sulfonic Acid

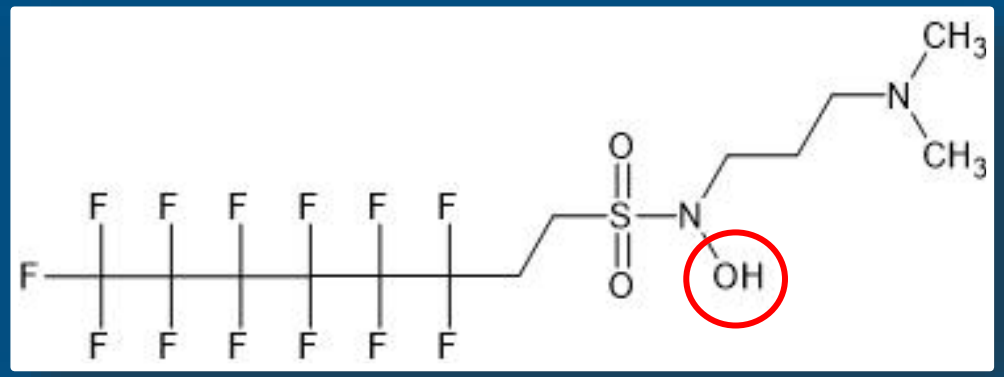


2-(2-Butoxyethoxy)ethanol

Mock Scenario 2 – Two Candidates



N,N-Dimethyl-3-((perfluorohexyl)ethylsulfonyl) aminopropanamine N-oxide



N-[3-(Dimethylamino)propyl]-3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-N-hydroxyoctane-1-sulfonamide

Summary of Conclusions

- NTA workflows have been adapted to cut down on response time
- Work best when the chemical of interest is at higher concentrations than the background
- NTA workflows can be applied to complex mixtures, but response times may increase

Future Work

- More scenarios in complex matrices
- Adapt methods to GC
- Get a chance to apply this to a real-world scenario

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