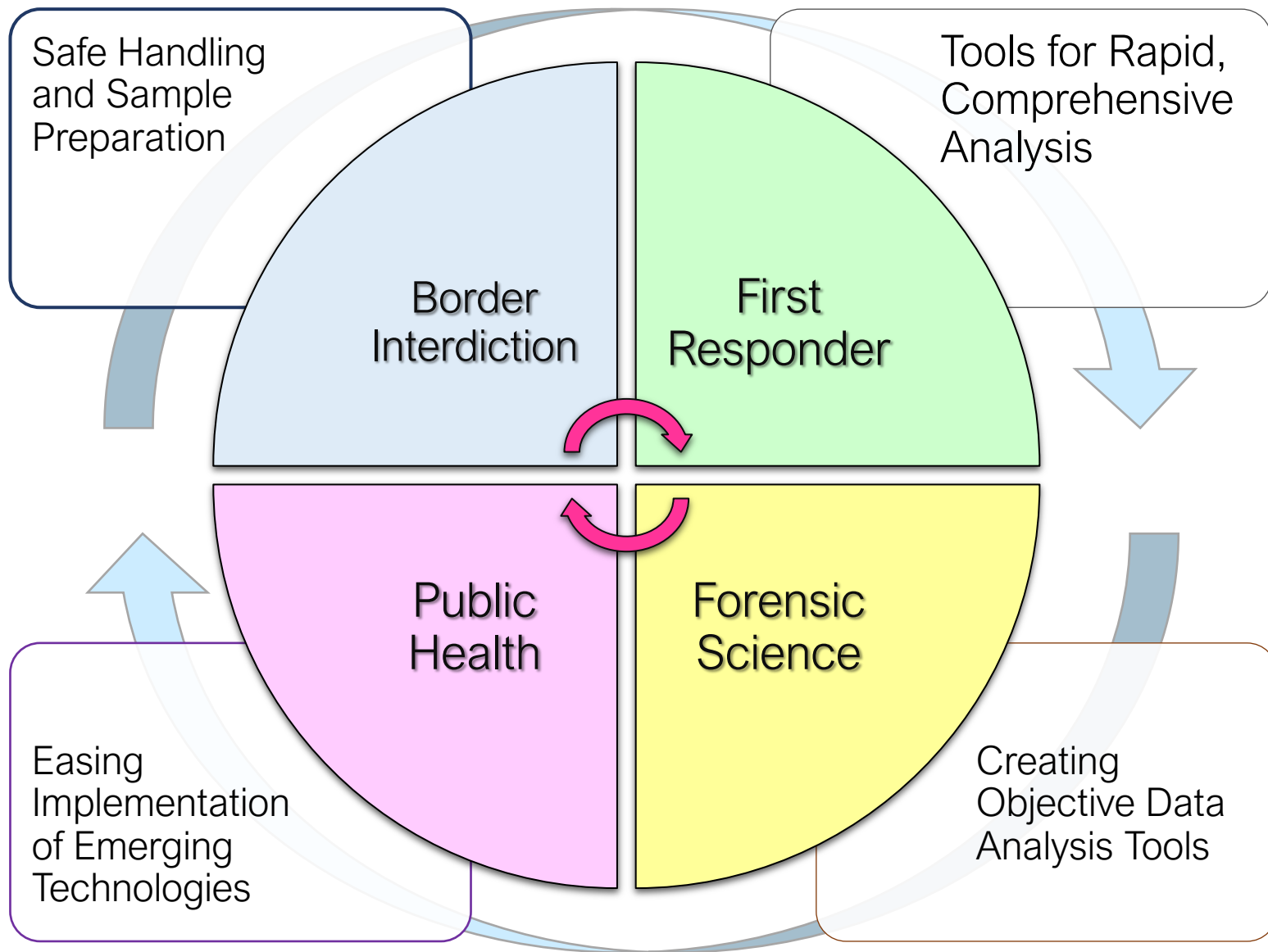


Rapid Drug Analysis & Research (RaDAR): Enabling Near Real-Time Drug Surveillance

Edward Sisco, Research Chemist
CSTE Briefing – May 11th, 2023



Research Philosophy:

Support other local, state, and federal partners address **critical measurement challenges** surrounding drug detection by developing **implementable solutions** through **collaborative research**.

Lowering Barriers to Implementation

- Working with forensic laboratories on ways to help lower implementation barriers for new technology
- Efforts include:
 - Collaborative development of methods for analysis
 - Objective identification of method limitations
 - Publishing validated methods in peer-reviewed literature
 - Creating documentary implementation packages
 - SOPs, validation plan, validation workup, maintenance, and training documents
 - Creating spectral libraries and algorithms for data analysis
 - Webinars and workshops
 - Hands on, on-site training
- See need for similar pipeline in the public health / drug checking space

NIST PUBLIC DATA REPOSITORY 1.10.0 About

Data Publication
Templates for the Implementation of DART-MS for Seized Drug Analysis
Part of the Forensics Science Data Collection
Edward Sisco, Amber Burns ▶
Contact: [Edward Sisco](#).. ▶
Identifier: [doi:10.18434/mds2-2424](#)
Version: 1.2 ... ▶ Revised: 2021-09-27

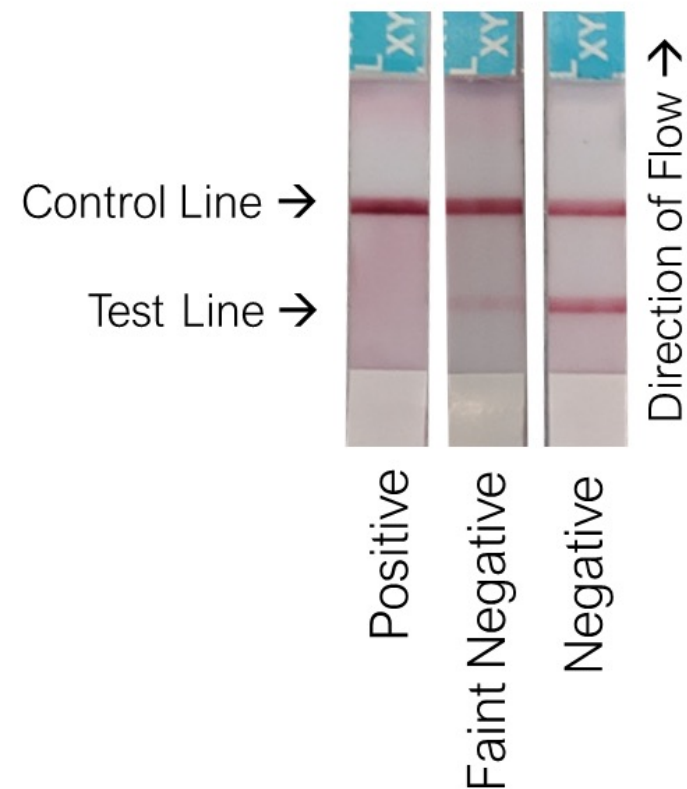
Abstract

This dataset includes templates to assist with laboratory implementation of direct analysis in real time mass spectrometry (DART-MS) for seized drug analysis. These templates should be modified as necessary to meet the needs of the particular laboratory. Certain commercial equipment, instruments, or materials are identified in this paper in order to specify the experimental procedure adequately. Such identification is not intended to imply recommendation or endorsement by NIST, nor is it intended to imply that the materials or equipment identified are necessarily the best available for the purpose. These opinions, recommendations, findings, and conclusions do not necessarily reflect the views or policies of NIST or the United States Government.

Research Topics: Forensics: Drugs and toxicology
Forensics Research Topics: *Drugs and toxicology*

Xylazine Test Strips

- Working with Johns Hopkins on evaluation of xylazine test strips
- Sensitive down to $\sim 2 \mu\text{g/mL}$
- Lidocaine will produce positive results
 - 77 Compounds tested against
 - Does not react to other α_2 -agonists
- Accuracy of real-world samples 98%



REMEDY

- Joint effort with DEA-STRL to speed up identification of emerging substances
- Provide reference data and reference materials to the community
 - Available at no cost to labs
- Seized material supplied to NIST and DEA-STRL for characterization

Reference Material Cover Sheet

DEA Special Testing and Research Laboratory

22624 Dulles Summit Court, Dulles, Virginia USA 20166-9509

Phone: (703)668-3300 FAX: (703) 668-3321

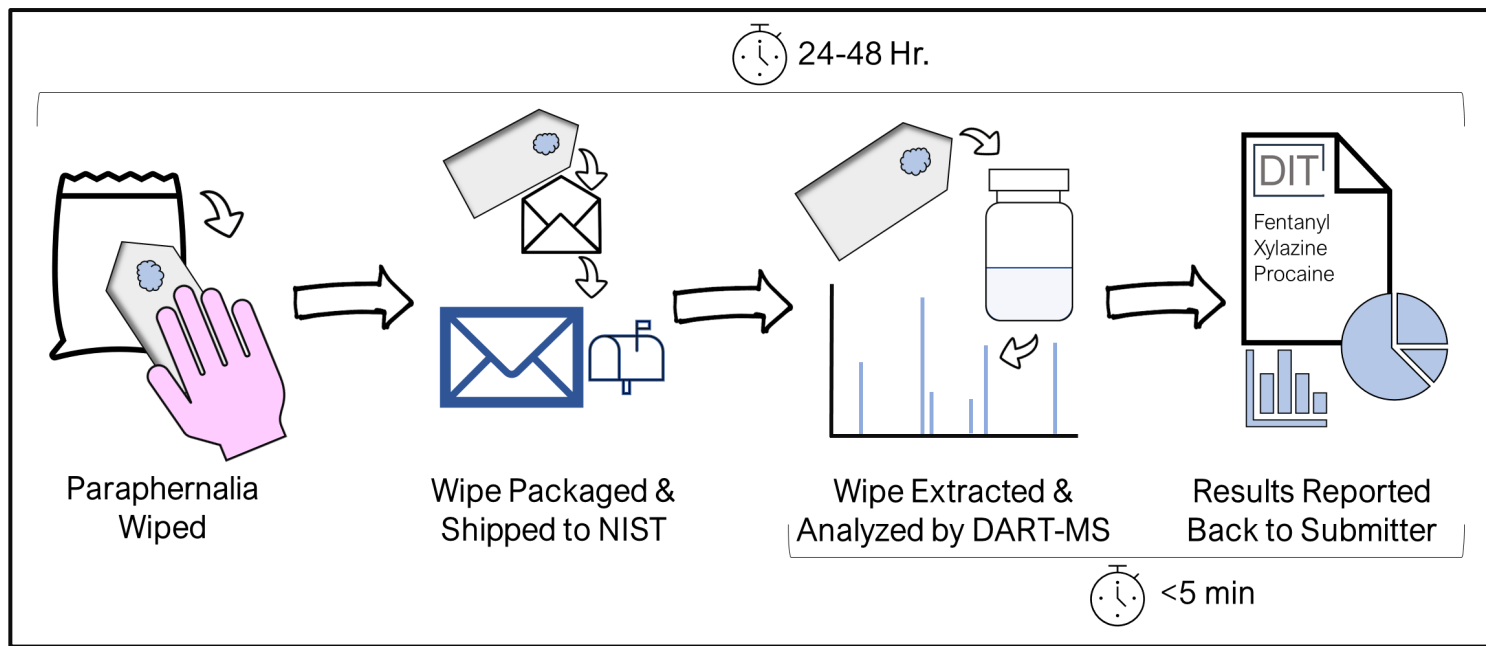
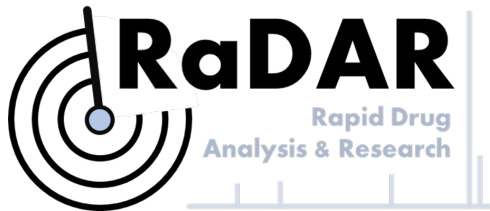
Designated for Qualitative Use Only

Compound Name:	N-methyl-N-isopropyltryptamine Fumarate	
IUPAC Name:	N-(2-(1H-indol-3-yl)ethyl)-N-methylpropan-2-aminium Fumarate	
Synonyms:	N-(2-(1H-indol-3-yl)ethyl)-N-methylpropan-2-aminium (2E)-but-2-enedioate, MiPT Fumarate, N-[2-(1H-indol-3-yl)ethyl]-N-methylpropan-2-amine (2E)-but-2-enedioic acid	
Source:	NIST	Molecular Formula: C ₁₄ H ₂₀ N ₂ · C ₄ H ₄ O ₄
Unique Identifier:	PSS0146	Molecular Weight: 332.39
Date of Authentication:	October 19, 2021	
Appearance:	Tan Powder	
Purity (mass fraction):	92.96%	
Expanded Uncertainty:	1.09% (95% confidence)	
Data Obtained / Notes:	National Institute of Standards and Technology (NIST): NMR(1D, 2D), GC-MS, GC-FID, Raman, LC-MS, DART-MS Special Testing and Research Laboratory (STRL): NMR(1D, 2D), GC-MS, GC-FID, FTIR, UHPLC. The purity is determined by NMR analysis.	
Melting Point (°C):	NA	
Identification Determined by:	Structural Elucidation	
Recommended Storage:	Store in Freezer	
Expiration of Certification:	3 Years from Date of Authentication/Verification. This material must be checked for continued use.	
Literature Spectra Reference:	The data is generated by the National Institute of Standards and Technology, and the Special Testing and Research Laboratory. See the following attachments.	
Traceability:		
Purity Method:	Quantitative HNMR	
ISTD Used for Purity:	Maleic Acid (Sigma Aldrich Lot BCBV7235) Purity: 99.98±0.13%	
ISTD Purity Traceable to:	NIST SRM 84I (KHP)	

The purity result and associated uncertainty are traceable to the above referenced National Institute of Standards and Technology certified reference material (NIST SRM) and method.

The Special Testing and Research Laboratory certifies that this standard meets the specifications stated on this certificate through the expiration date when stored unopened as recommended.

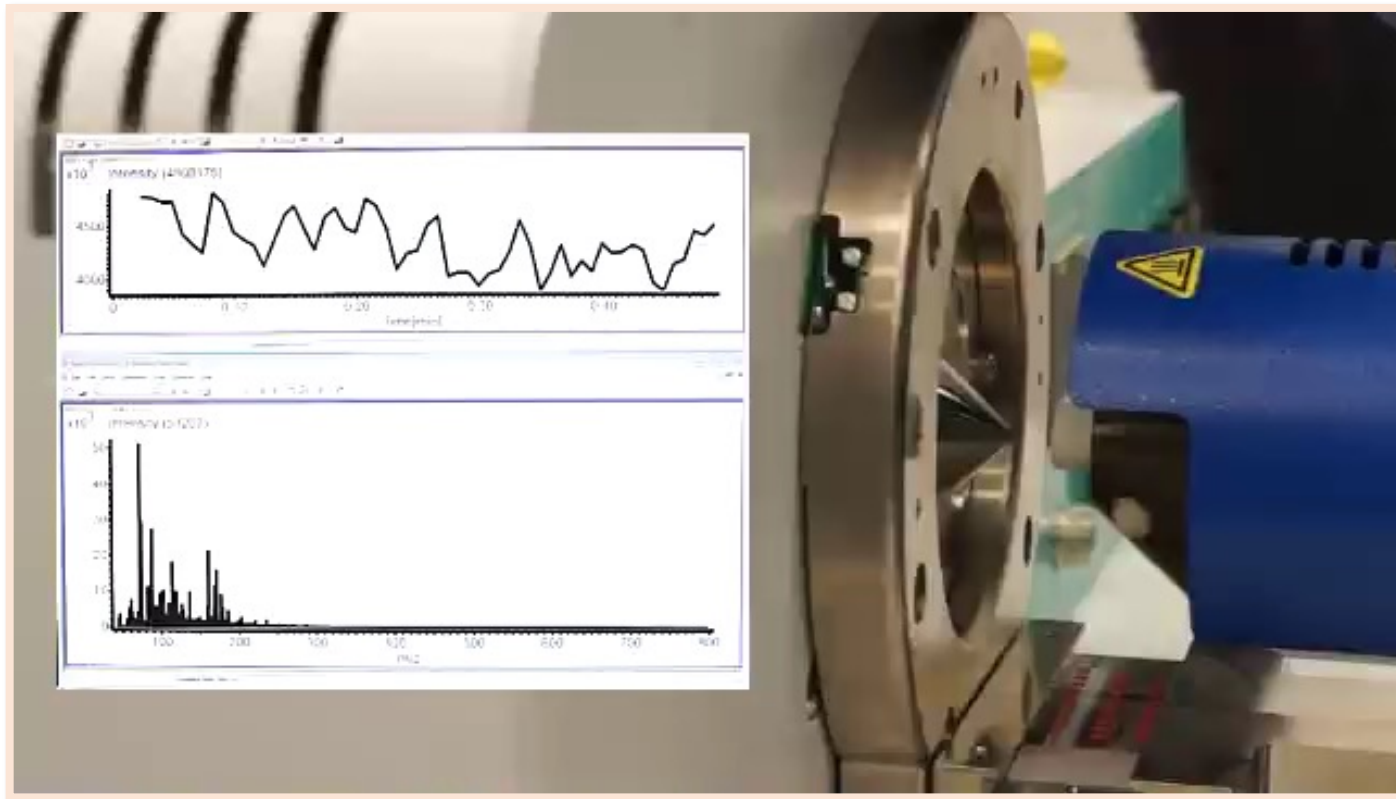
Structure



Since October 2021, NIST, Maryland State Police, Maryland Dept. of Health, and others have implemented DART-MS for the rapid screening of drug residue from paraphernalia obtained at harm reduction sites across the state and from law enforcement task forces across the state. The goal of the partnership is to allow public safety and public health officials to obtain more timely and complete picture of the drug landscape across the state.



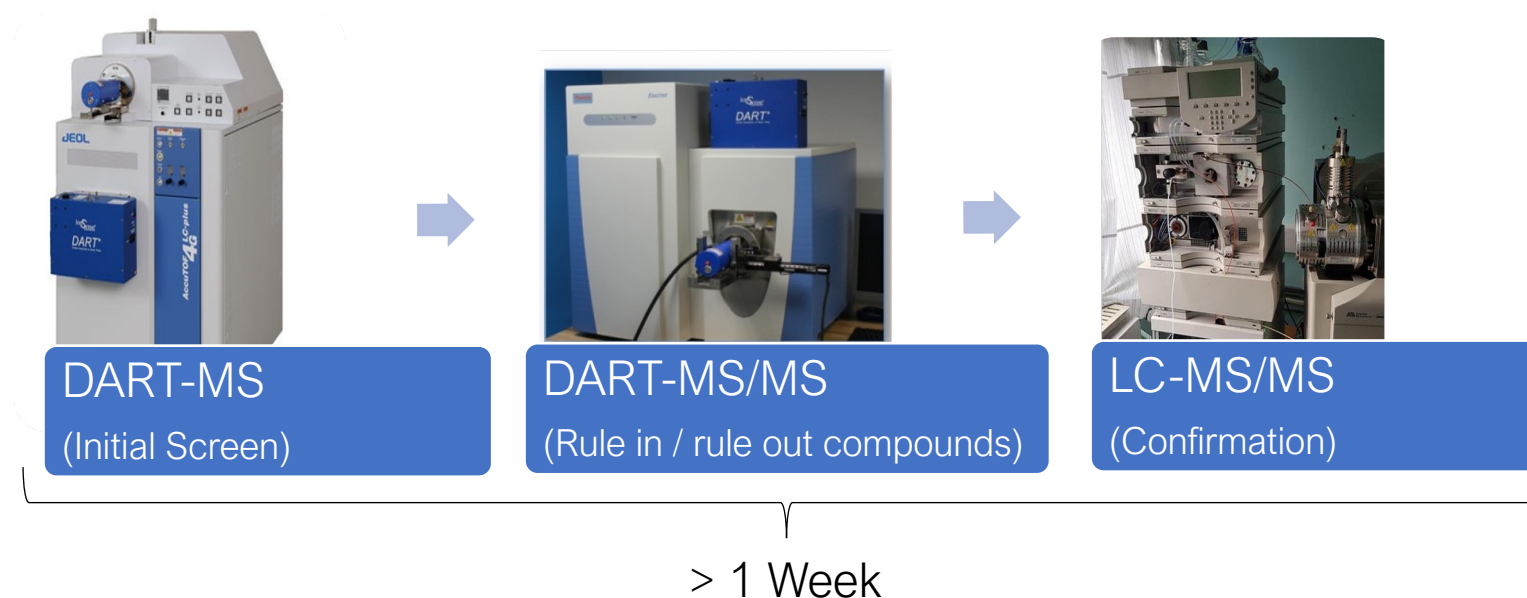
DART-MS



- Cannot differentiate some isomers
- How we use DART-MS is not quantitative
- Different compounds will produce different levels of responses based on their chemical properties
- Cannot detect some cutting agents
 - Flour, sugar, baby powder, salt, citric acid
- In complex samples we may not be able to detect all compounds
- Typically, cannot detect compounds below ~0.5 % wt in a sample

Additional Testing

- Roughly 7.5 % of samples produced a result warranting further study
 - New compound, isomers, low result scores
- Led to the development of a confirmation platform for samples with potential additional compounds



Sharing the Data

- Collaborators and NIST sign a Materials Transfer Agreement
 - *NIST is conducting the Research Project as part of NIST's research mission and not as part of any law enforcement function of any entity. NIST will make every effort to avoid participating in any legal proceeding, including avoiding the provision of oral or written testimony, in accordance with 15 C.F.R. Part 15, Subpart B.*
- Collected samples are placed in barcoded envelopes and mailed to NIST
 - Envelopes contain optional lines to fill out
 - Item sampled is the only line of interest to us
- Results provided back via spreadsheet
- Collaborating agency handles any further dissemination

RaDAR Sample

Do not lick the envelope



0001

Sample #: _____

Date Collected: _____

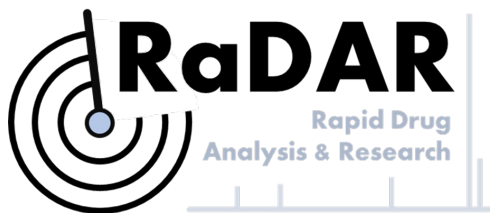
Location / Site: _____

Item Sampled: _____

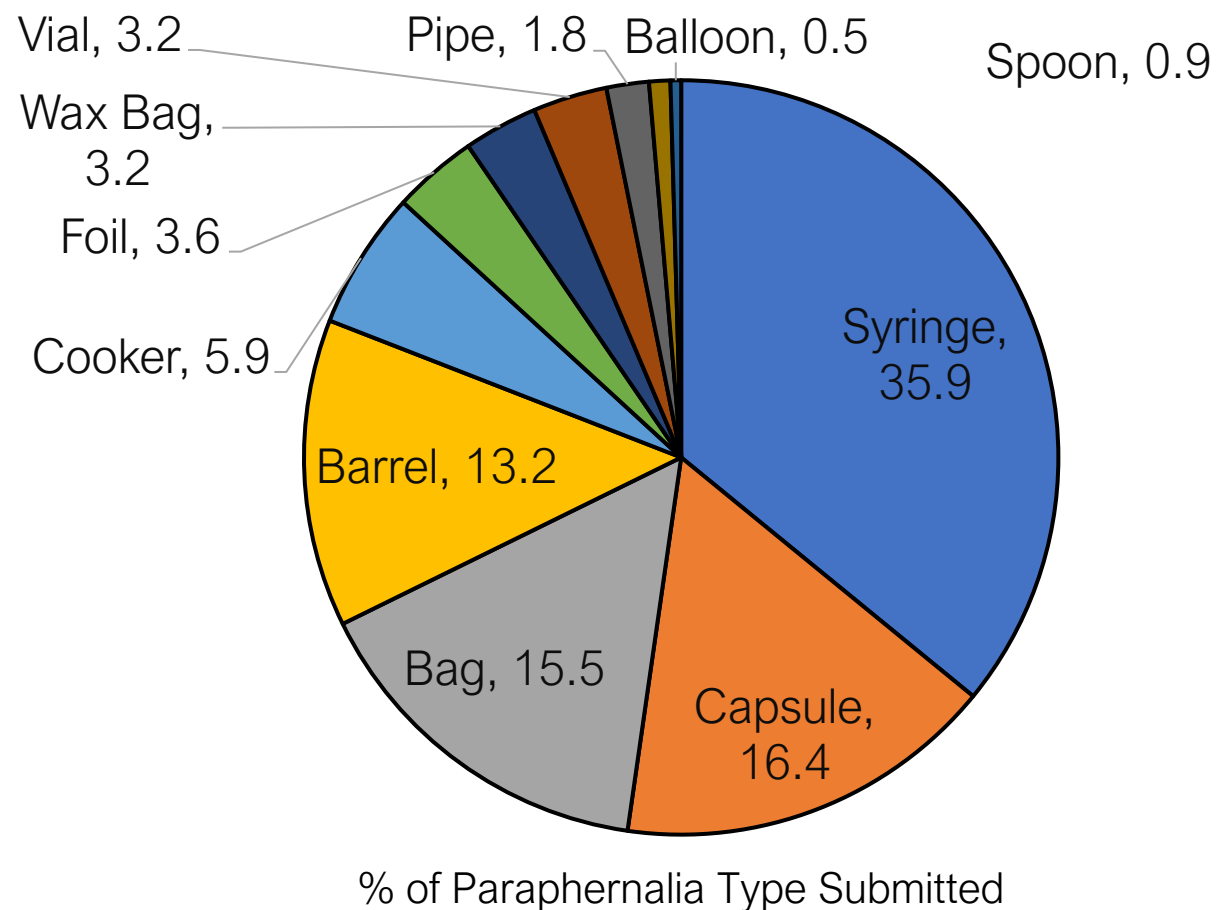


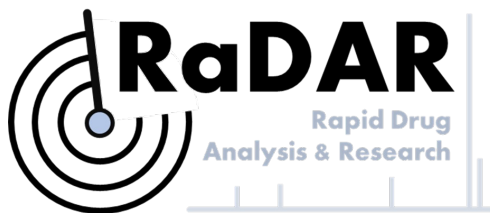
	A	B	C	D	E	F	G	H	I
1	Reviewed	NIST_ID	Site_ID	Wipe_Swab	Item	Agency	Location/State	Collection_Date	Run_Date
2	✓	0001	9991	Swab	Baggie	MDH	Site 1	9/22/2022	9/28/2022
3	✓	0002	9992	Swab	Syringe	MDH	Site 1	9/23/2022	9/28/2022
4	✓	0003	9993	Swab	Capsules	MDH	Site 2	9/30/2022	10/6/2022
5	✓	0004	9994	Swab	Baggie	MDH	Site 2	9/30/2022	10/6/2022
6	✓	0005	9995	Wipe	Syringe	MDH	Site 3	10/1/2022	10/8/2022
7	✓	0006	9996	Wipe	Scale	MDH	Site 3	10/1/2022	10/9/2022
8	✓	0007	9997	Wipe	Pipe	MDH	Site 4	10/2/2022	10/10/2022
9	✓	0008	9998	Wipe	Straw	MDH	Site 4	10/2/2022	10/11/2022
10									
11									

J	K	L	M	N	O
Compound_1	Compound_2	Compound_3	Compound_4	Compound_5	Other relevant information
Fentanyl	Cocaine	Xylazine	Quinine		
No Compounds Detected					
Quinine	Fentanyl	4-ANPP	Phenethyl 4-ANPP		Possible Quetiapine
Xylazine	Fentanyl				
Methamphetamine					
No Compounds Detected					
Cocaine	Acetaminophen				
Fentanyl	Xylazine	4-ANPP			

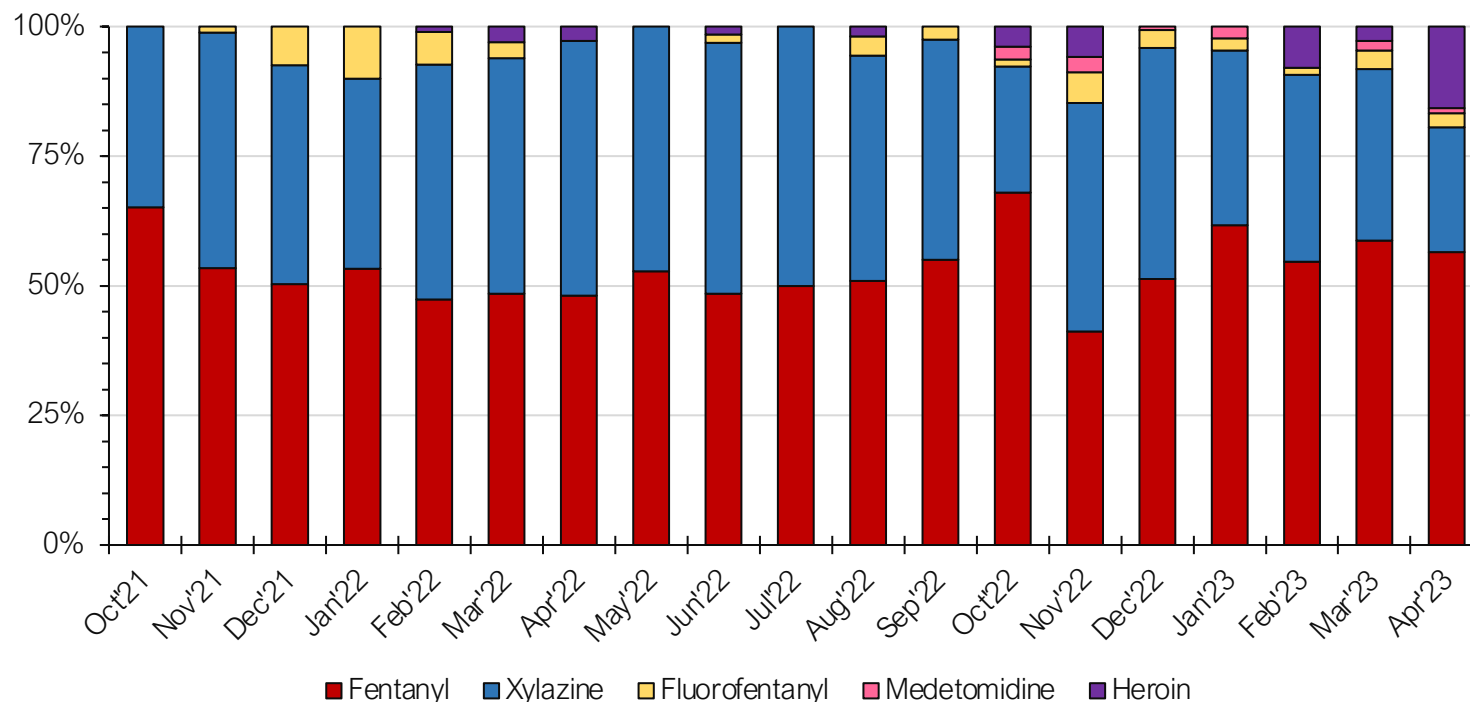


- Started in October 2021 with 2 LE task forces and 8 SSPs in Maryland
- Developed methodology for sampling, analysis, and data interpretation
- Moved out of pilot in October 2022
 - All 22 SSPs in Maryland, and 5+ LE task forces
 - Began testing of syringes
- Since October 2022, we have:
 - Incorporated 4 additional cities/states
- We are currently seeking additional collaborators

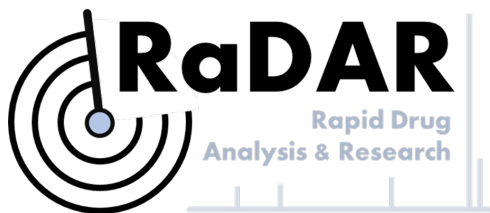




- As of May 1st, 2023
 - 2500+ samples analyzed from 35 unique sites / task forces across 5 states
 - 74 unique compounds identified
 - First to identify 7 new compounds in the state of Maryland
 - First to identify 2 new compounds in the country
- Near real-time surveillance has
 - Enabled forensic laboratories to better prepare for, detect, and track emerging compounds
 - Forced conversations between criminal justice, law enforcement, and public health

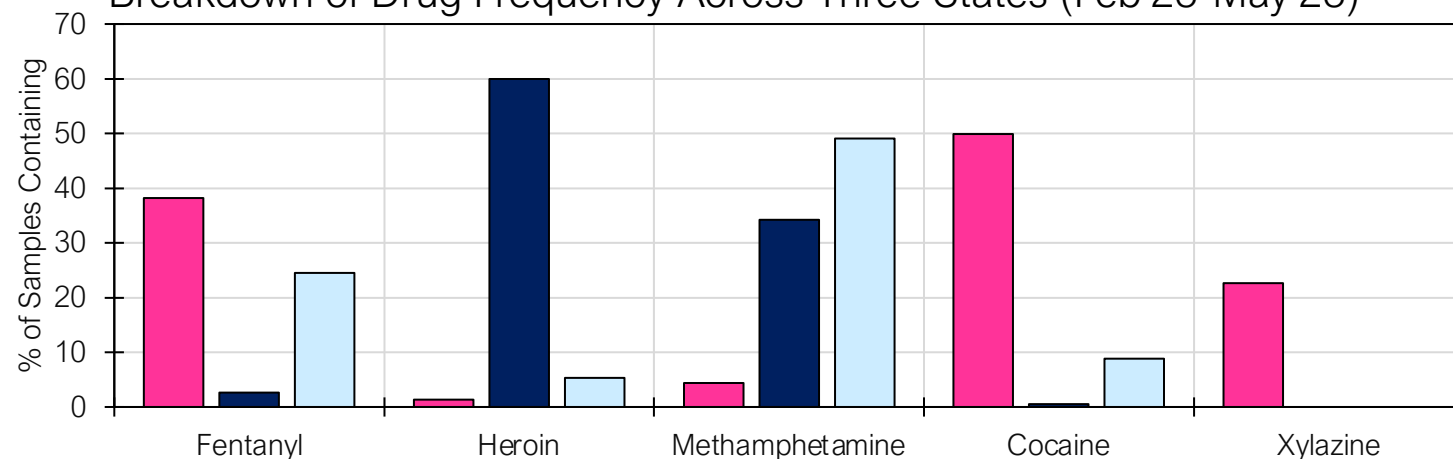


Top 10 Compounds (Previous 3 Months, All Sites):
 Cocaine, Fentanyl, Quinine, Xylazine, Methamphetamine,
 Caffeine, 4-ANPP, Phenacetin, Heroin, Phenylephrine

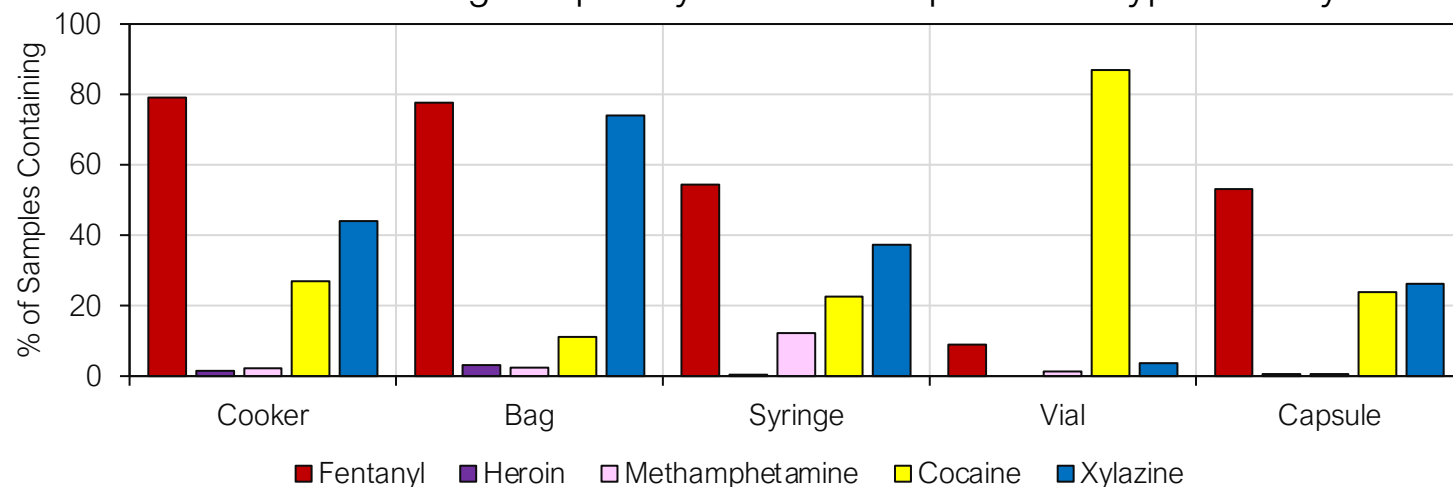


- As of May 1st, 2023
 - 2500+ samples analyzed from 35 unique sites / task forces across 5 states
 - 74 unique compounds identified
 - First to identify 7 new compounds in the state of Maryland
 - First to identify 2 new compounds in the country
- Near real-time surveillance has
 - Enabled forensic laboratories to better prepare for, detect, and track emerging compounds
 - Forced conversations between criminal justice, law enforcement, and public health

Breakdown of Drug Frequency Across Three States (Feb'23-May'23)



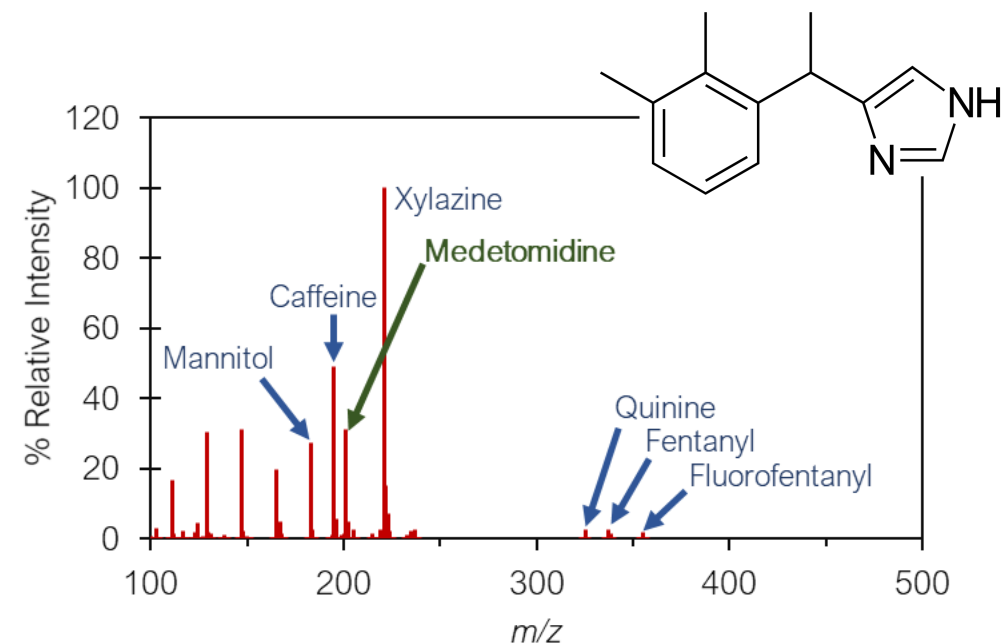
Breakdown of Drug Frequency Across Paraphernalia Type in Maryland



Identifying New Compounds

“New” compounds that have been identified in samples from Maryland include:

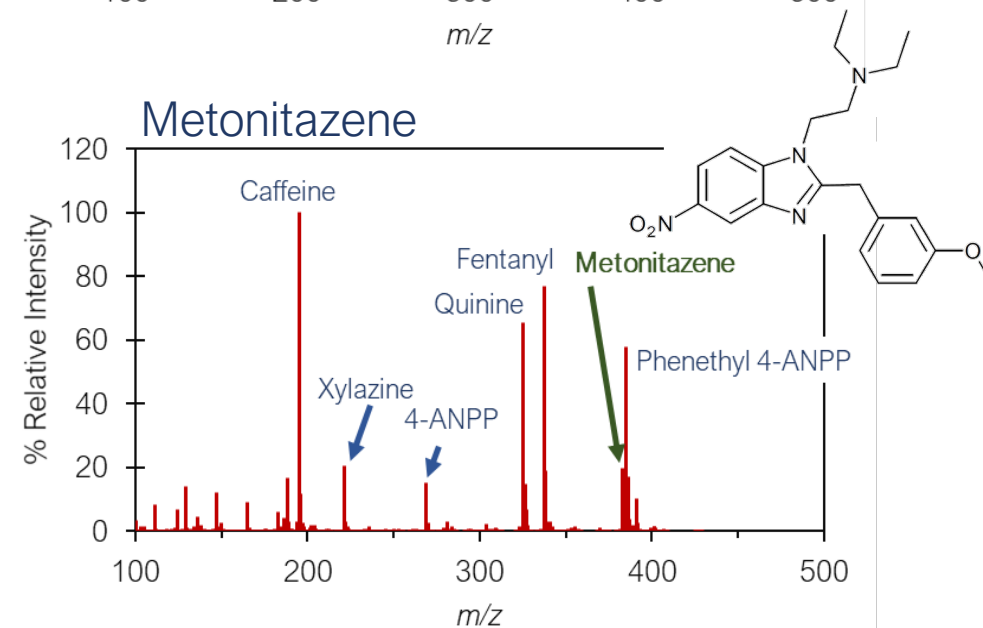
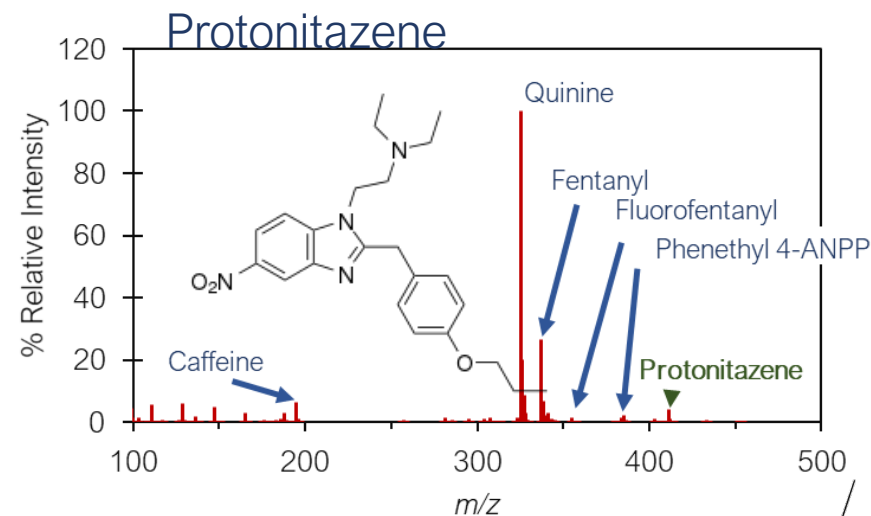
- Medetomidine
 - Veterinary sedative / analgesic that is used in a similar fashion to xylazine
 - Always detected with fentanyl and xylazine
 - First seen in July 2022, detected in ~1 sample / month
- Metonitazene & Protonitazene
- Bromazolam & Meclonazepam



Identifying New Compounds

“New” compounds that have been identified in samples from Maryland include:

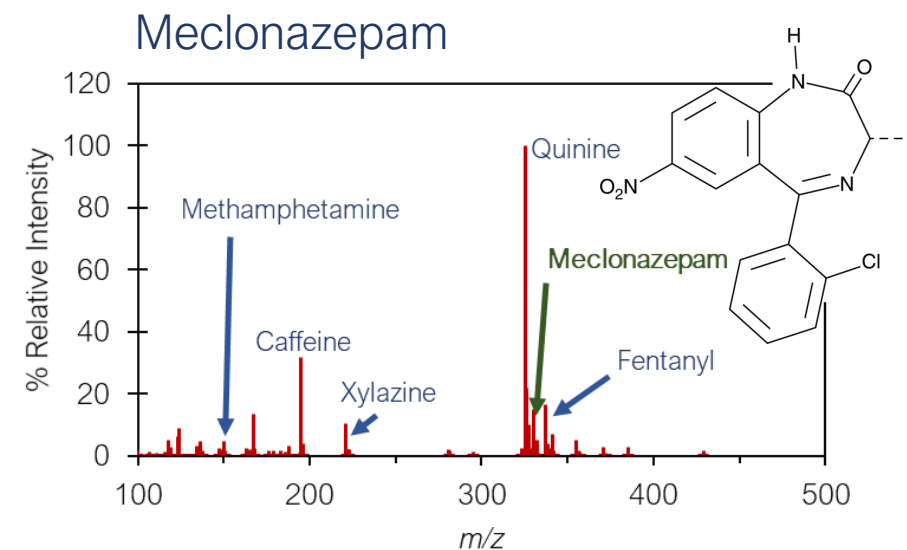
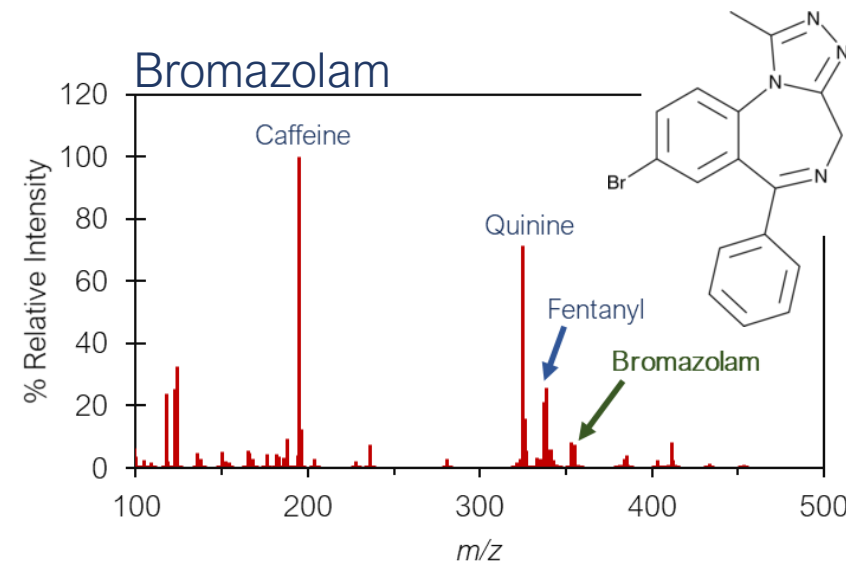
- Medetomidine
- Metonitazene & Protonitazene
 - (P) First seen in November 2021, detected in 1 sample
 - (P) Detected with fentanyl and quinine
 - (M) First seen in October 2022, detected in 1 sample
 - (M) Detected with fentanyl, quinine, and xylazine
- Bromazolam & Meclonazepam



Identifying New Compounds

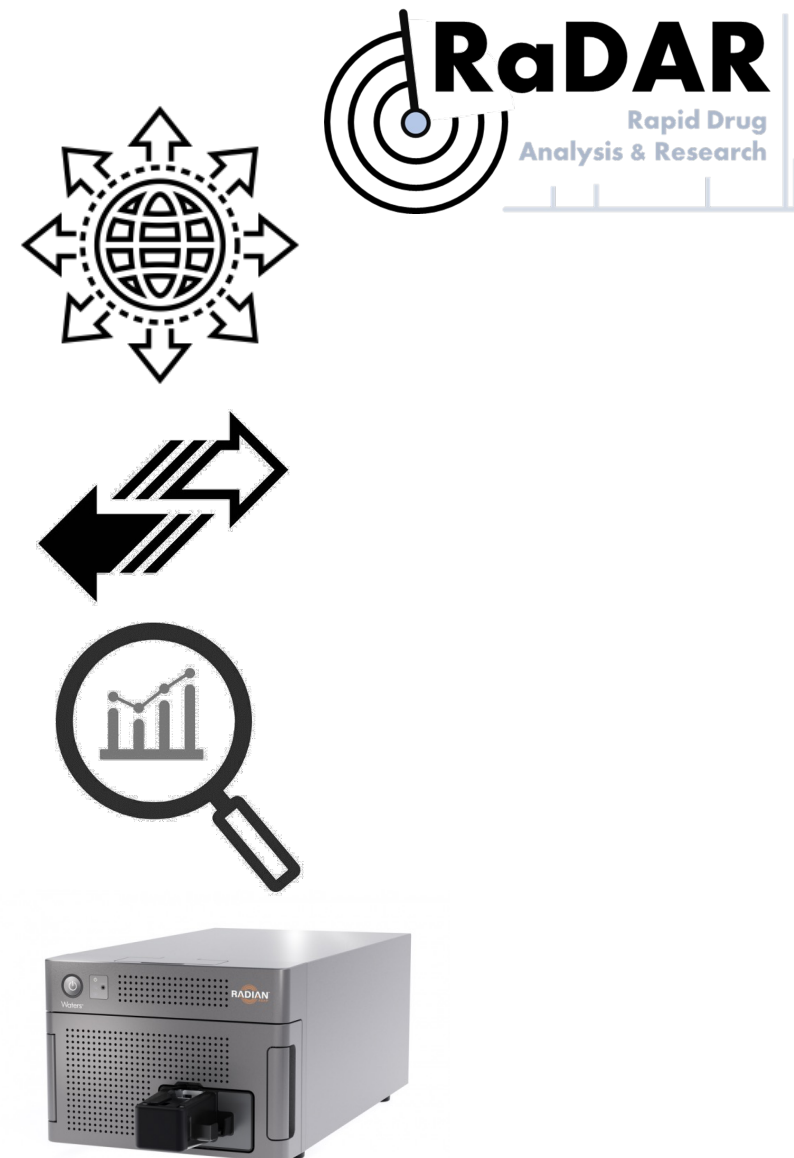
“New” compounds that have been identified in samples from Maryland include:

- Medetomidine
- Metonitazene & Protonitazene
- Bromazolam & Meclonazepam
 - (B) First seen in January 2022 and still being observed
 - (M) First seen in October 2021, not observed since February 2022
- Always detected with fentanyl and (usually) xylazine



Short Term Project Goals

- Expand geographic coverage to test platform in areas where drug landscape differs
 - Bringing on West Coast locations, Mid-West, and Northeast
- Work to transition routine testing approach to others
- Development of quant / semi-quant methods
 - Can we provide rapid quantitative information?
 - Enable rapid identification of “bad batches” and greater intelligence
 - *Investigating use of test strip solutions to accomplish this*
- Bring to small footprint / lower cost mass spec
- Identify other potential technologies that generate comprehensive drug profiles



1. Identify Technology

Work with labs to identify challenges and potential technology solutions

2. Method Development

Bring technology in-house and work to collaboratively develop methods. Develop databases and algorithms, if necessary.

3. Method Validation

Complete, and publish foundational validation. Make all validation materials available to the community.

4. Implementation & Training

Assist labs with implementation via training, workshops, webinars, etc.

5. Interlab. Studies & Test Method Development

Work with adopting labs to run necessary interlab. studies then develop a consensus test method.

**Widespread Adoption
+
Reachback Support**

**Mid-Term Goal:
Emerging Technology Implementation and Validation Pipeline**

Questions, Comments, or Interested in Collaborating?

Edward.Sisco@nist.gov
RaDAR@nist.gov

MMWR

DOI: 10.15585/mmwr.mm7217a2



Analysis

DOI: 10.1016/j.forc.2023.100489



Medetomidine

DOI:10.1111/1556-4029.15242

