



Developing an Interpretation Workflow for Toxicology Cases Involving NPS

Society of Forensic Toxicologists (SOFT) Annual Meeting – Tuesday October 31, 2023

Workshop 11: Forensic Interpretation of Novel Psychoactive Substances in Challenging Cases

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INTRODUCTION

- **Center for Forensic Science Research & Education**

- Associate Director
 - Toxicology & Chemistry
- Program Manager
 - NPS Discovery

- **Thomas Jefferson University**

- Assistant Program Director
 - MS in Forensic Toxicology
- Faculty / Lecturer



DISCLOSURES

- I have no conflicts of interest to disclose.
- I am a scientist and employee of FRFF / CFSRE, a 501(c)(3) non-profit research and educational facility.
- CFSRE's NPS Discovery program is funded in part by the National Institute of Justice (NIJ), Office of Justice Programs (OJP), U.S. Department of Justice (DOJ).
 - Award Number: 15PNIJ-22-GG-04434-MUMU
 - The opinions, findings, conclusions and/or recommendations expressed in this publication are those of the author(s) and do not necessarily represent the official position or policies of the U.S. Department of Justice.



NIJ | *National Institute
of Justice*

STRENGTHEN SCIENCE. ADVANCE JUSTICE.



TOXICOLOGY TESTING AND INTERPRETIVE STRATEGY



THE CFSRE & OUR LAB

- The Center for Forensic Science Research and Education (CFSRE)
 - 501(c)(3) non-profit research and educational facility
 - Surveillance & Casework



Waters Xevo® G2-S LC-QTOF-MS



Sciex X500R LC-TOF-MS



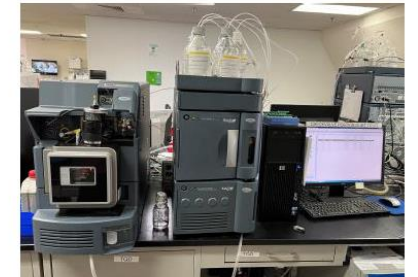
Sciex TripleTOF® 5600+ LC-TOF-MS



Agilent 6495 LC-QQQ-MS



Agilent 6430 LC-QQQ-MS



Waters TQS LC-QQQ-MS



Waters TQD LC-QQQ-MS



Agilent 5975 GC-MS



Agilent 5975 GC-MS

COMPARISON OF ANALYTICAL METHODS

SCREENING ASSAYS

- Immunoassay / ELISA
 - Leveraging the benefits of cross reactivity
- GC-MS
 - Defined scope vs. vast library databases

SCREENING ASSAYS

- LC-QTOF-MS
 - Non-targeted acquisition method
 - Targeted data processing method
 - **Library database containing >1,100 analytes**

CONFIRMATORY ASSAYS

- LC-QQQ-MS
 - Targeted acquisition methods
 - Class or subclass specific
 - Quantitative vs. qualitative



CONFIRMATORY ASSAYS

- LC-QTOF-MS
 - Qualitative confirmation
 - [Same assay as screening]
 - Library database containing >1,100 analytes



INTERPRETATION OF CASES INVOLVING NPS

MDI INFORMATION SHARED

- Case history / circumstances
- Police reports
- Death investigator report
 - Scene photos
- Autopsy report
- Medical records / prescriptions
- Crime lab results
- Other toxicology results***
- Other relevant information
 - Drug use history



TOXICOLOGY TESTING & INTERPRETATION

- Specimens available and tested
- Testing performed and scope of testing
 - Limitations of testing (e.g., sample preparation)
- Results (qualitative vs. quantitative)
 - Reference concentration ranges
 - Drug-drug interactions

NPS EVALUATION & INTERPRETATION

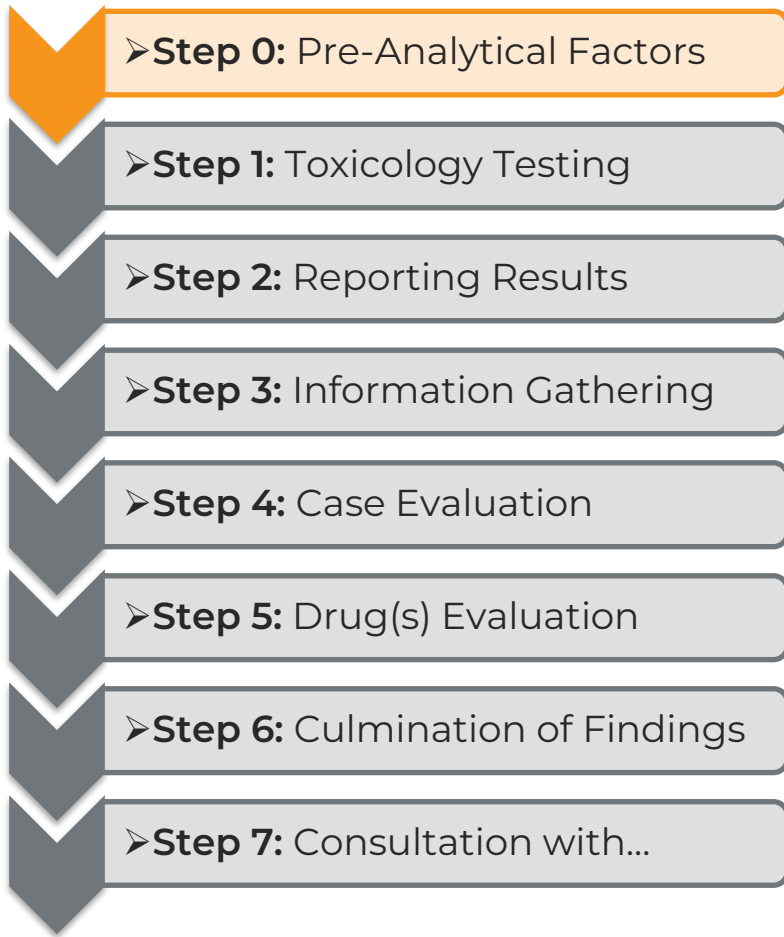
- What is known about the drug? Any published literature?
 - Chemistry, pharmacology, toxicity, adverse effects, etc.
- Have there been other forensic / clinical cases?
- Is the drug related to other known drugs? (e.g., analogue)
- Ultimately, is the drug the only identifiable culprit??



INTERPRETATION WORKFLOW



INTERPRETATION WORKFLOW

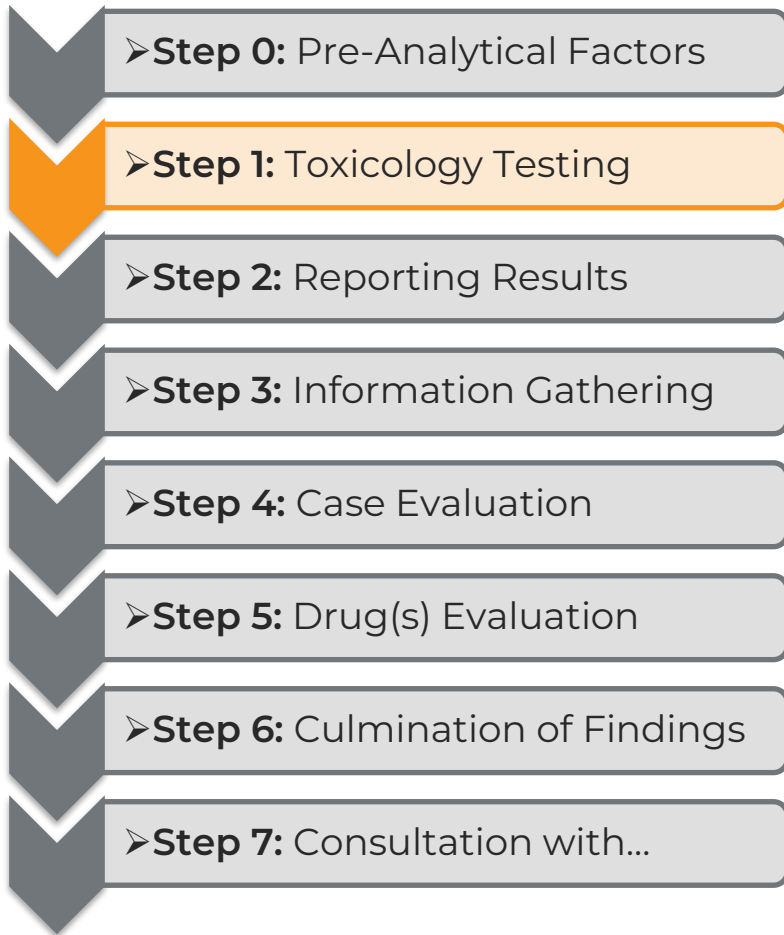


- Refer to Dani Mata's presentation ~20 mins ago...

- **Factors**

- Case type
- Sample type
- Tube type
- Storage conditions
- Sample state (e.g., clotted, low volume, etc.)
- Everything else prior to lab
- ...

INTERPRETATION WORKFLOW



- **Toxicology Testing**

- Arguably the most important piece to the puzzle
- Good interpretation should consider testing conducted
 - Could lead to blind spots and unanswered questions

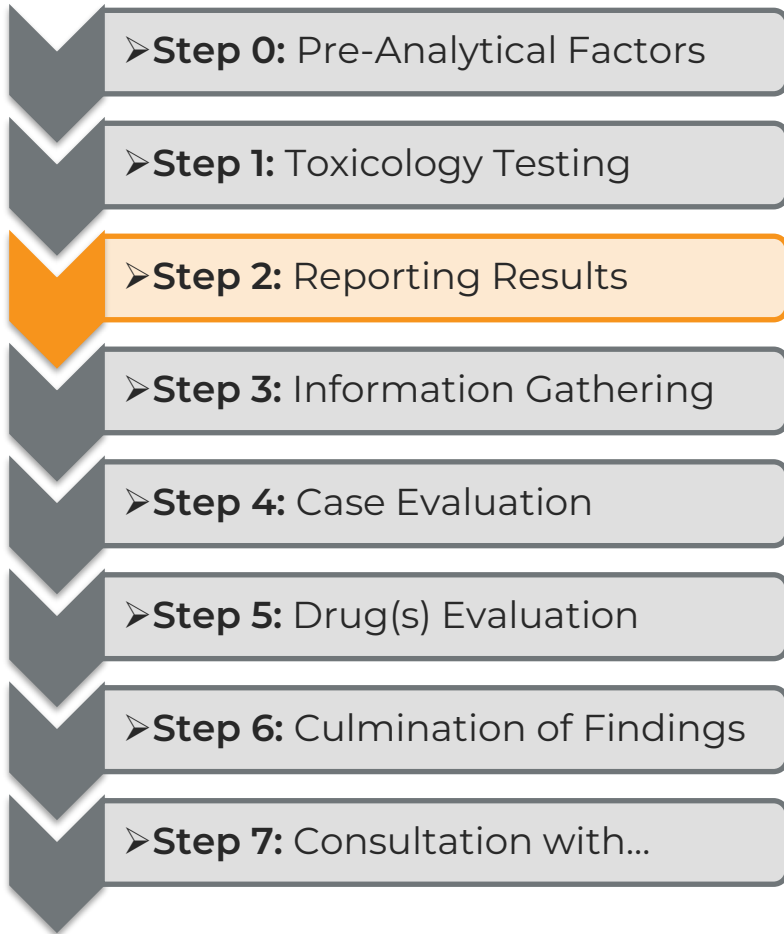
- **Decisions:**

- What testing can be / is performed?
- Targeted vs. non-targeted testing (i.e., comprehensive or not)
- Qualitative vs. quantitative testing

- **Interpretation can only be as good as testing performed**

- You can't interpret what you don't know
- But... results are only as good as sample submission / state

INTERPRETATION WORKFLOW



▪ Reporting Results

- What results are reported vs not reported? And why?
- What's requested for testing?
 - Drug may not be on report but may be in the data (e.g., unconfirmed)
 - Related to scope of testing

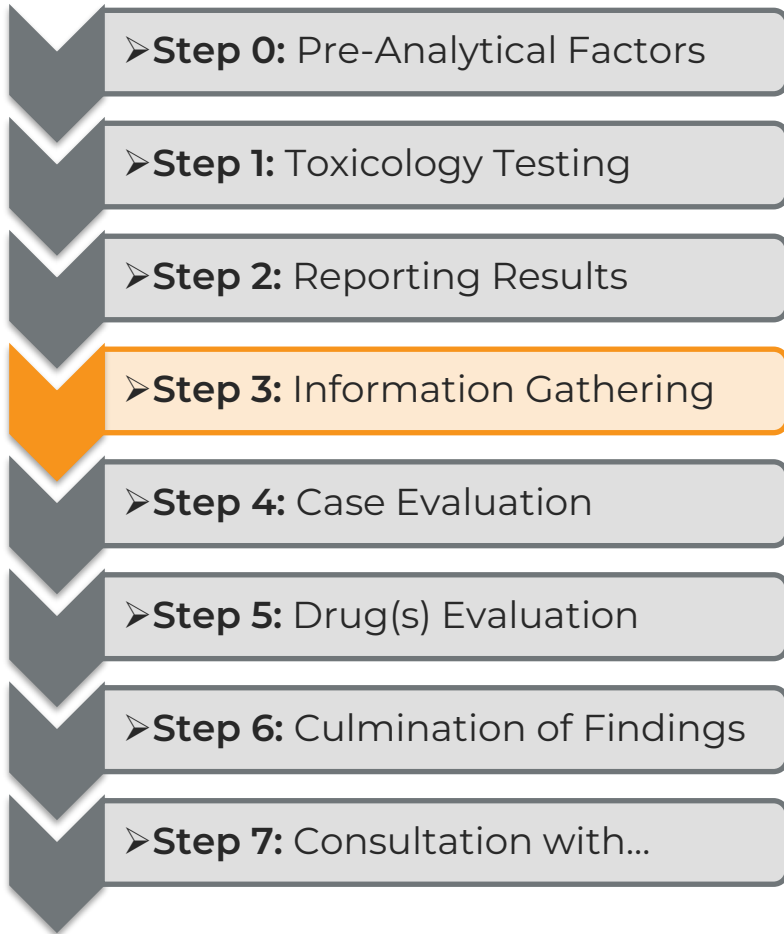
Results and Conclusions:

Exhibit #	Analyte	Concentration
1	Levamisole	Positive
1	Lidocaine	Positive
1	Monoethylglycinexylidide	Posit
1	Fentanyl	Posit
1	Norfentanyl	Posit
1	4-ANPP	Posit
1	Cocaine	Posit
1	Benzoylcegonine	Posit
1	Norcocaine	Positive
1	Cocaethylene	Positive
1	Trazodone	Positive
1	mCPP	Positive

Results and Conclusions:

Exhibit #	Analyte	Concentration
1	<i>N,N</i> -Dimethylpentylone	360 ng/mL
1	Pentylone	74 ng/mL

INTERPRETATION WORKFLOW



- **Information Gathering**

- All relevant case information may impact interpretation

- **Important Documents:**

- Case history / circumstances
- Police reports
- Death investigator report
- Scene photos
- Autopsy report
- Medical records / prescriptions
- Crime lab results / Tox results***
- Other relevant information
- Drug use history

**BOARD OF MEDICOLEGAL INVESTIGATIONS
OFFICE OF THE CHIEF MEDICAL EXAMINER**

Central Office: 501 N.E. 27th St., Oklahoma City, OK 73105
Eastern Division: 1115 West 17th Street, Tulsa, Oklahoma 74107

REPORT OF INVESTIGATION BY MEDICAL EXAMINER

DECEDENT First-Middle-Last Names (Please avoid use of initials): JOHN MARION GRANT
Age: 60
Birth Date: 4/12/1961
Race: BLACK
Sex: M

HOME ADDRESS - No. - Street, City, State: 1301 NORTH WEST STREET, MCALESTER, OK

EXAMINER NOTIFIED BY NAME - TITLE (AGENCY, INSTITUTION, OR ADDRESS): JAMES HUNTER - AGENT IN CHARGE - OFFICE OF INSPECTOR GENERAL
DATE: 10/28/2021
TIME: 15:30

INJURED OR BECAME ILL AT ADDRESS:	CITY:	COUNTY:	TYPE OF PREMISES:	DATE:	TIME:
1301 NORTH WEST STREET	MCALESTER	PITTSBURG	PENAL INSTITUTION	10/28/2021	16:00

LOCATION OF DEATH:	CITY:	COUNTY:	TYPE OF PREMISES:	DATE:	TIME:
1301 NORTH WEST STREET	MCALESTER	PITTSBURG	PENAL INSTITUTION	10/28/2021	16:21

BODY VIEWED BY MEDICAL EXAMINER:	CITY:	COUNTY:	TYPE OF PREMISES:	DATE:	TIME:
1115 WEST 17TH STREET	TULSA	TULSA	AUTOPSY SUITE	10/29/2021	9:20

TRANSPORTATION INJURY: DRIVER PASSENGER PEDESTRIAN
 TYPE OF VEHICLE: AUTOMOBILE LIGHT TRUCK HEAVY TRUCK BICYCLE MOTORCYCLE OTHER

DESCRIPTION OF BODY

EXTERNAL PHYSICAL EXAMINATION	ROTOR	LIVOR	EXTERNAL OBSERVATION	NOSE	MOUTH	EARS
Jaw: <input checked="" type="checkbox"/> Complete	Color: <input checked="" type="checkbox"/> PURPLE	Beard: <input type="checkbox"/> STUBBLE	Hair: <input type="checkbox"/> SHORT	BLOOD: <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Neck: <input checked="" type="checkbox"/> Adam's	Label: <input type="checkbox"/>	Eyes: Color: <input type="checkbox"/> BROWN	Muscle: <input type="checkbox"/> SLIMBLE	OTHER: <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Arms: <input checked="" type="checkbox"/> Paresis	Posterior: <input checked="" type="checkbox"/>	Opacities: <input type="checkbox"/>				
Legs: <input checked="" type="checkbox"/> Paresis	Anterior: <input type="checkbox"/>	Pupils: R: 3 MM, L: 4 MM				
Decomposed: <input type="checkbox"/>	Regard: <input type="checkbox"/>	Body Length: 22.28, Body Weight: _____				

Significant observations and injury documentation: (Please use space below)
 JUDICIAL EXECUTION BY LETHAL INJECTION

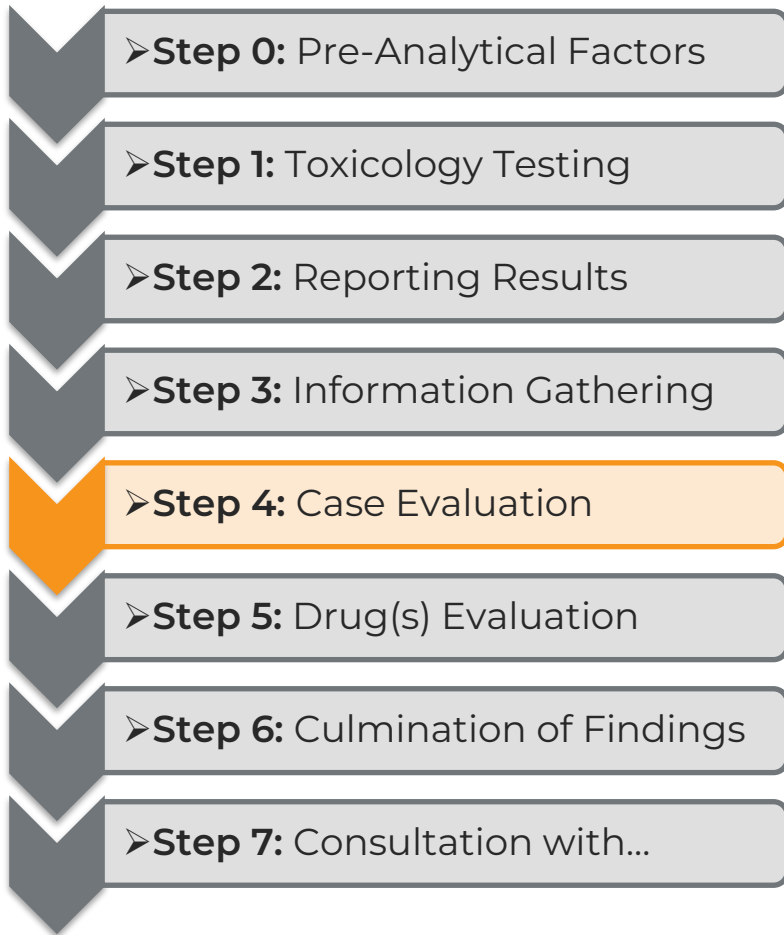
Probable Cause of Death: JUDICIAL EXECUTION BY LETHAL INJECTION
 Manner of Death: Natural Accident Suicide Homicide Unknown Pending Not assigned
 Case disposition: Autopsy YES Authorized by: JEREMY SHELTON, M.D. Penitentiary: JEREMY SHELTON, M.D. Not a medical examiner case

Other significant conditions contributing to death (but not resulting in the underlying cause given): Not assigned

MEDICAL EXAMINER: JEREMY SHELTON, M.D., 1115 W 17th Street, Tulsa, OK 74107
 I hereby state that, after receiving notice of the death described herein, I conducted an investigation as to the cause and manner of death, as required by law, and that the facts contained herein regarding such death are true and correct to the best of my knowledge.
 Signature of Medical Examiner: [Signature] JEREMY SHELTON, M.D.
 Date Case Initiated: 10/28/2021
 Date Case Printed: 1/24/2022

Case Number: 2107045 Page 1 of 1

INTERPRETATION WORKFLOW



- **Case Evaluation**

- Organizing, comparing, synthesizing, researching, etc.

- **Important Factors:**

- Manner of death

- Autopsy findings – pulmonary edema, etc.

- Impairment, signs/symptoms, toxidrome, etc.

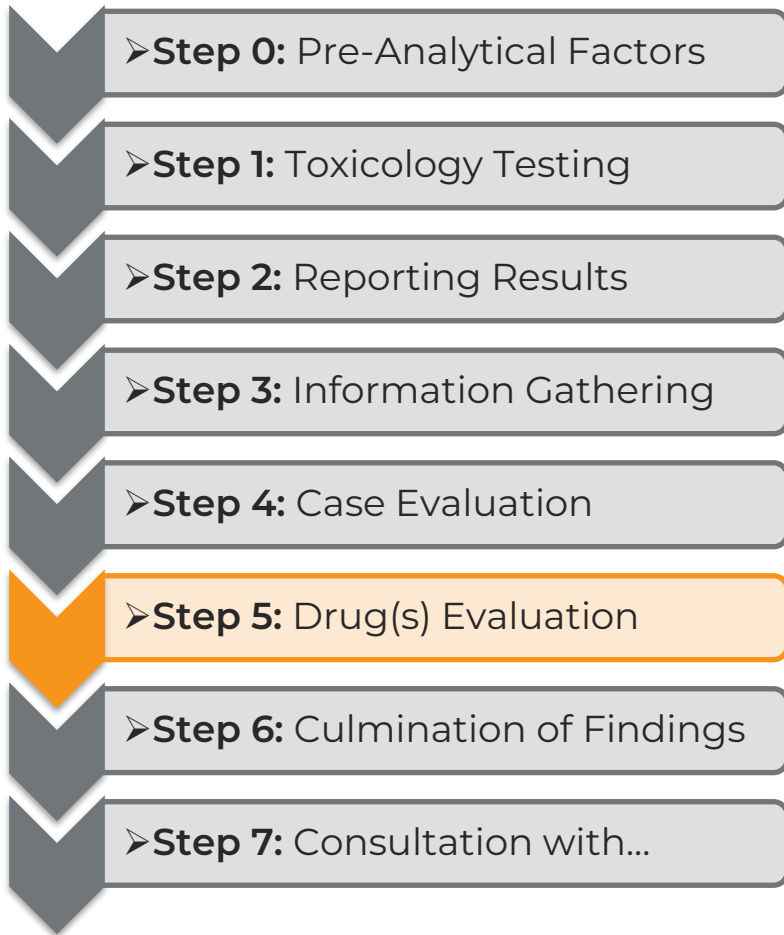
- Drug chemistry – does it match the toxicology results?

- Is the drug illegal in that state? Federally?

- **Establishing what you know vs. don't know**

- Ask questions to gain access to additional information

INTERPRETATION WORKFLOW



- **Drug Evaluation**

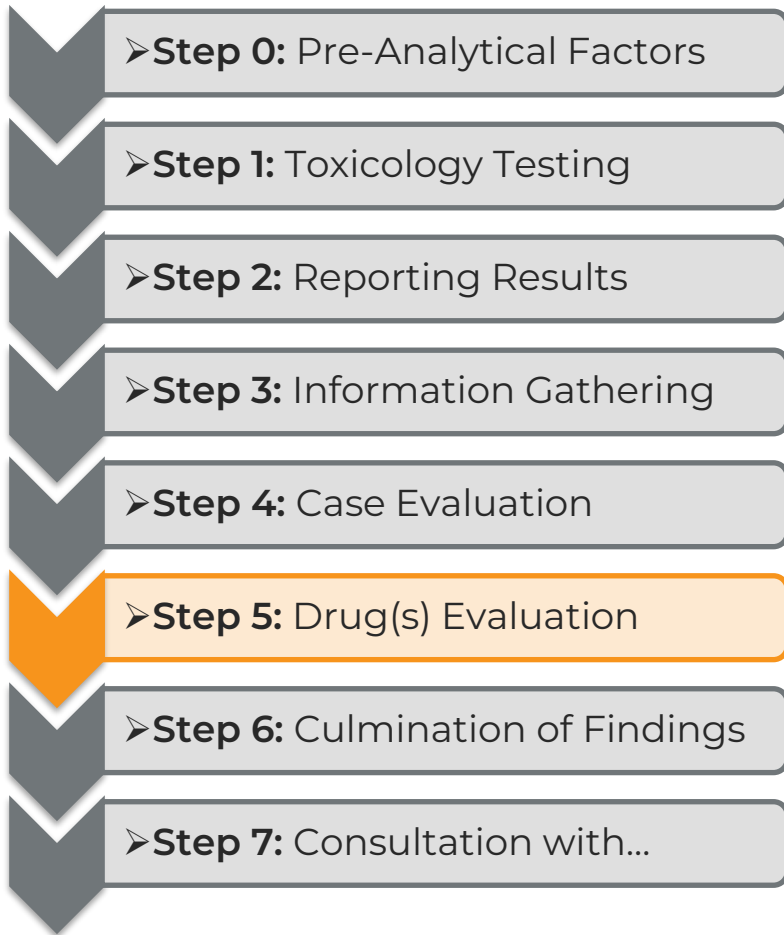
- So... what do the toxicology findings really mean?
- There is a lot to consider, depending on complexity of case
- Not all information may be available

- **Toxicology / Analytical Chemistry**

- What drug or drugs are present?
 - Linked to testing performed and scope of testing
- What's the quality of the testing and results?
- Are the results qualitative or quantitative?

- Are there adverse effects reported in the literature?

INTERPRETATION WORKFLOW



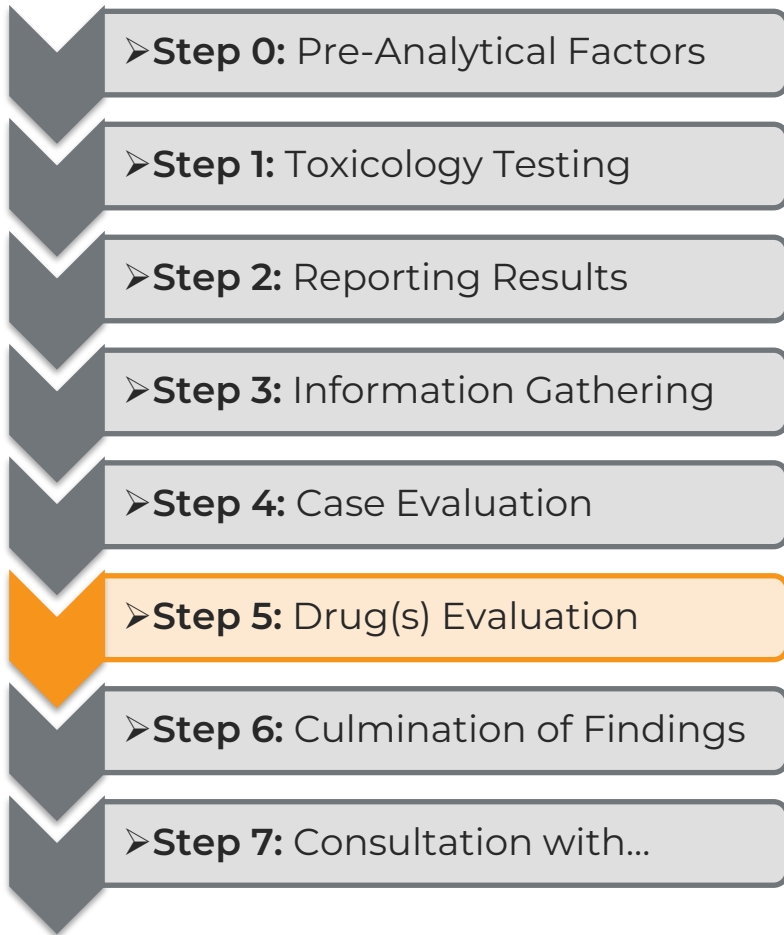
- **Drug Evaluation**

- **Pharmacology (Pharmacodynamics)**

- Is the pharmacology of the drug(s) known?
 - Comparison to other drugs / analogues, if necessary
- What drug classes are present?
- Activity vs. potency – the drug vs. its analogues
- Comparing potency vs. concentrations observed in cases
 - Sometimes forensic cases provide first data on pharmacology of drug
- Drug interactions – co-positivity / additive effects

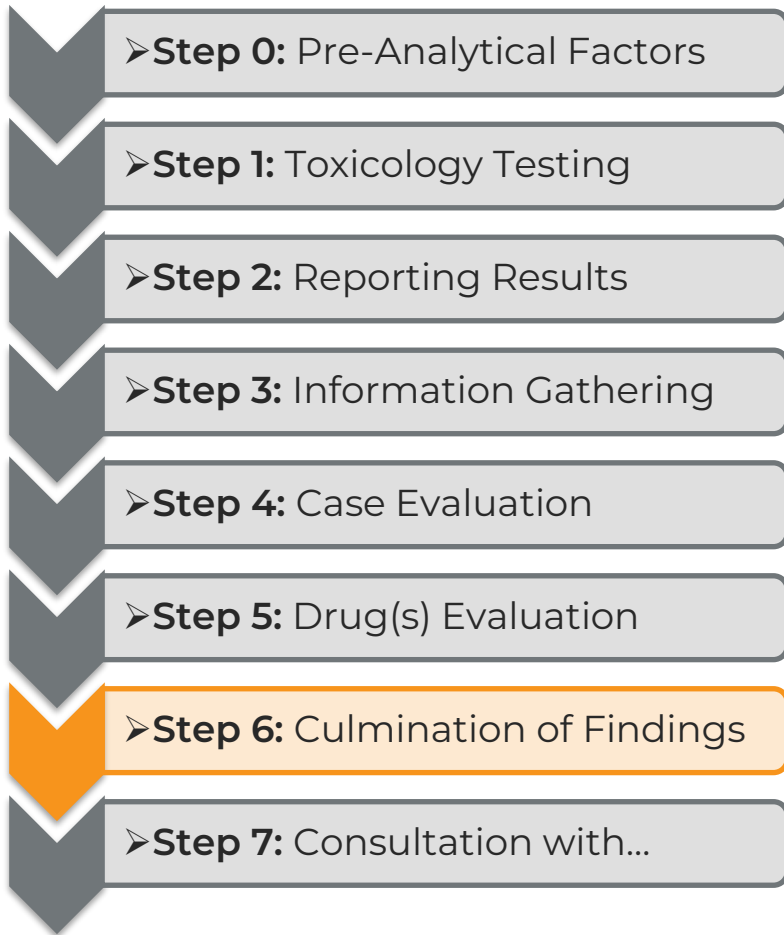
- *Examples:*
 - *W18*
 - *Synthetic cannabinoids in 2023*
 - *Fentanyl precursors / analogues*

INTERPRETATION WORKFLOW

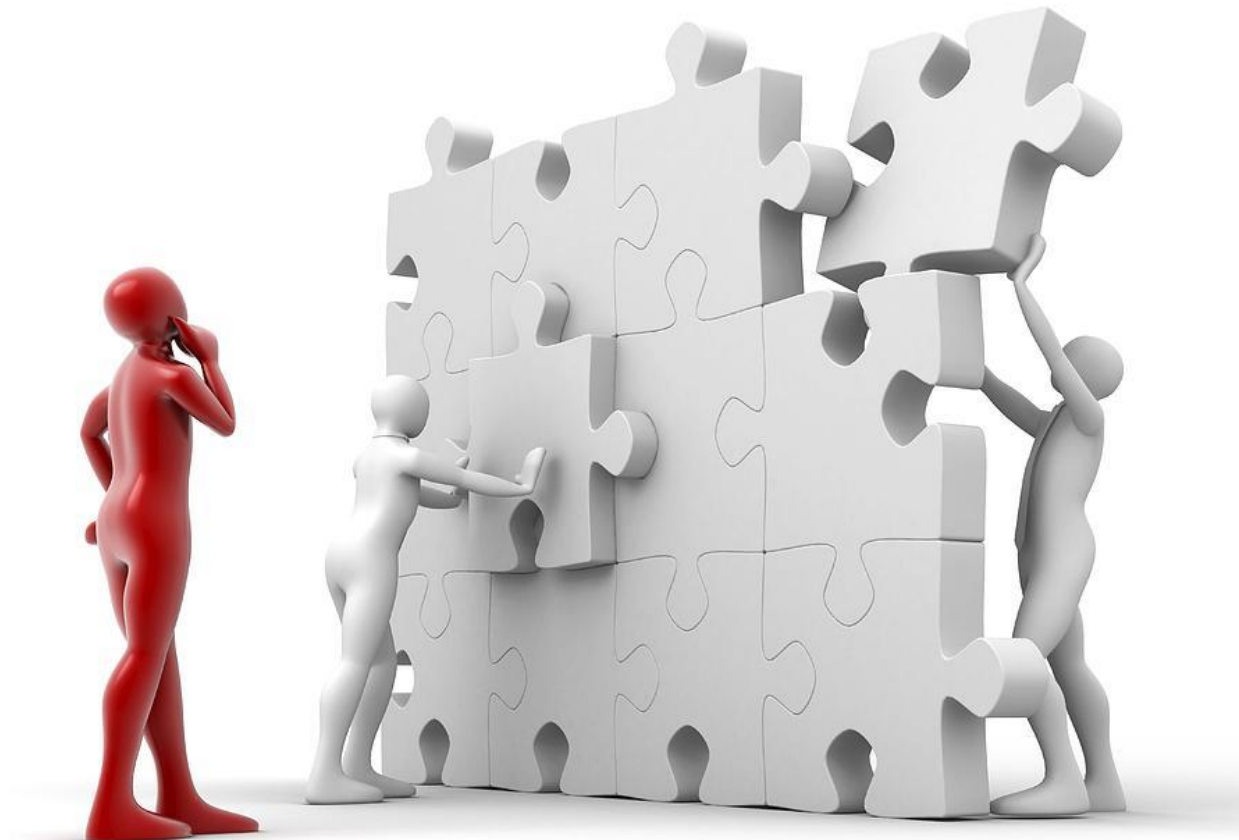


- **Drug Evaluation**
- **Pharmacology (Pharmacokinetics)**
 - Is the metabolism known? What are the primary metabolites?
 - Are you testing for the right target in correct matrix?
 - Example: synthetic cannabinoid metabolites in urine
 - Are there common / shared metabolites?
 - Do metabolites retain activity?
- **All linked back to:**
 - Case evaluation
 - Samples and information available
 - Circumstances / situation of the case

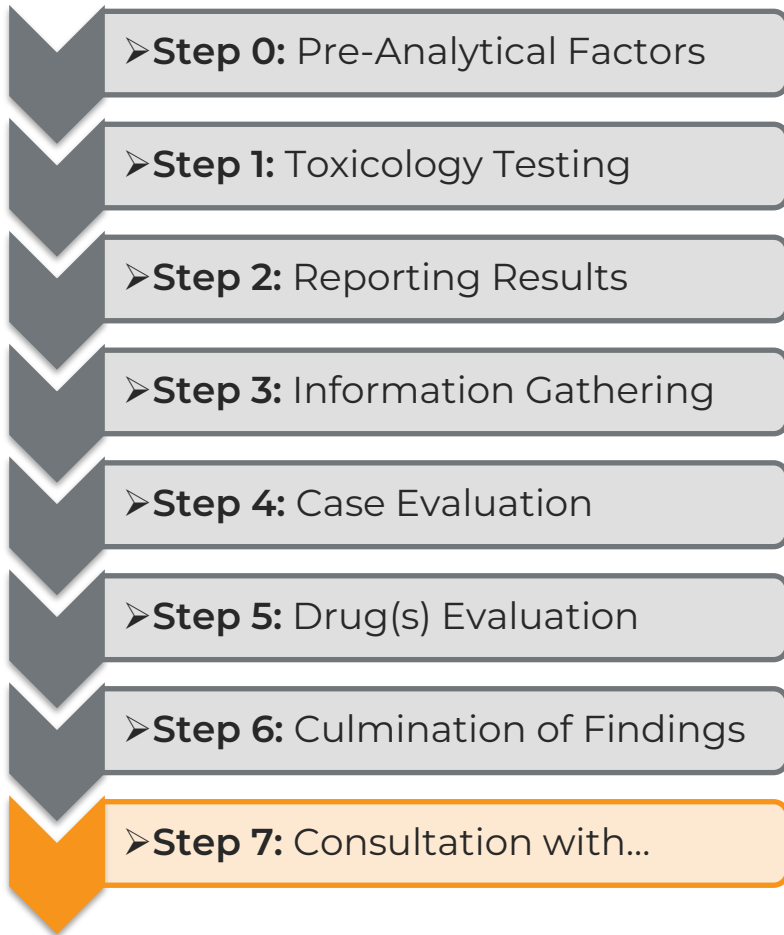
INTERPRETATION WORKFLOW



▪ Culmination of Findings



INTERPRETATION WORKFLOW



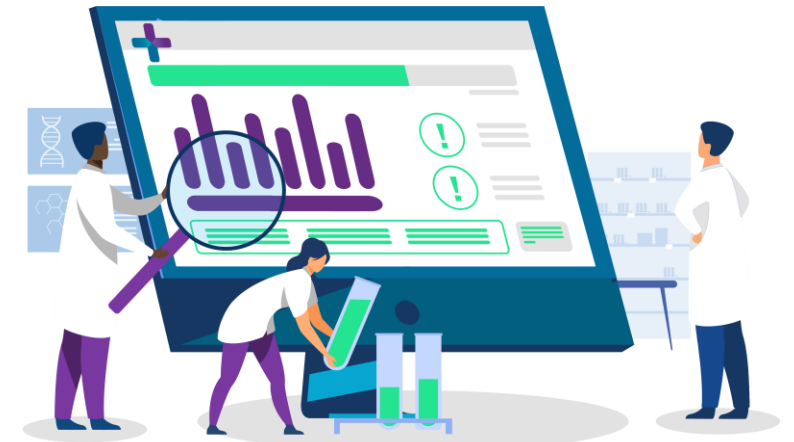
- **Consultation with...**

- Medical examiner
- Law enforcement
- Clinicians / physicians
- Attorneys
- Peers / other toxicologists

- **Education / Outreach**

- Public health agencies
- Media/public

- **Manner:** Conversations, expert opinions, testimony

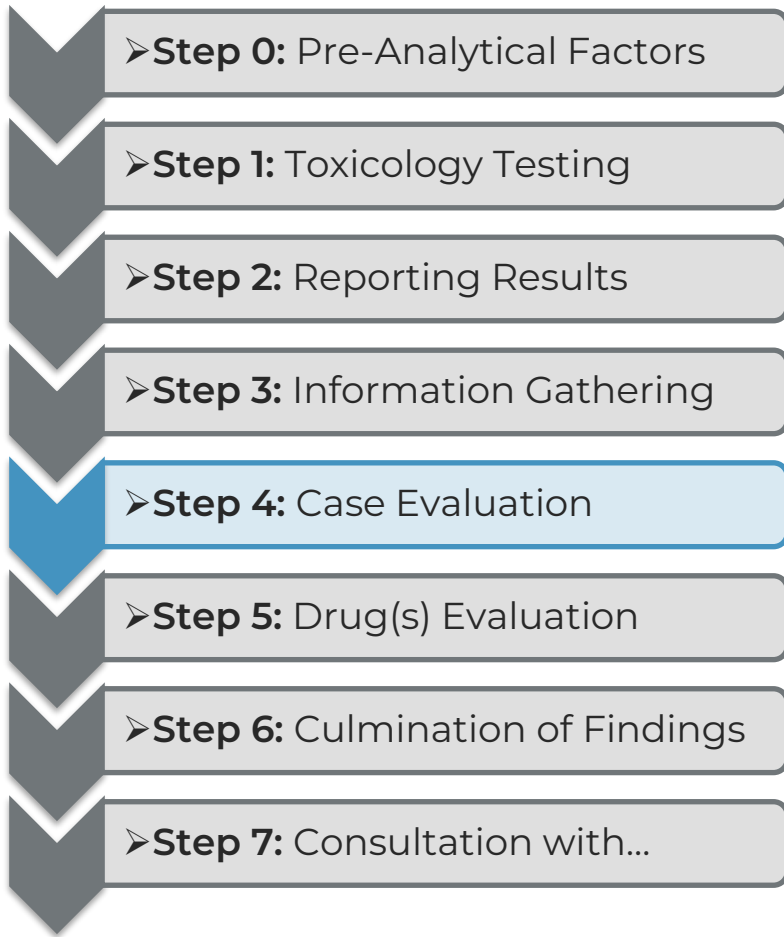




CASE EXAMPLE

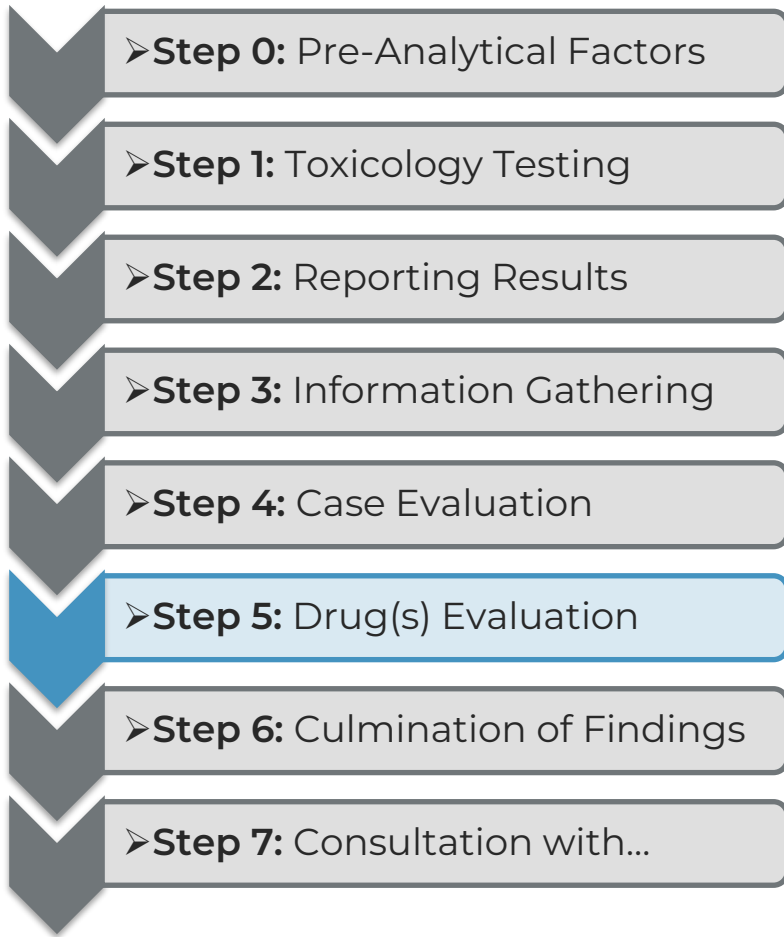


CASE EXAMPLE



- 2019 medicolegal death investigation
- Police respond to discover decedent
- Recover drug paraphernalia near the body
- Body transported to MEO, full autopsy perform
 - Needle puncture marks
 - Pulmonary edema
- Blood, urine and vitreous sent for toxicology testing
- Comprehensive testing undertaken
- Results reported back to the MEO

CASE EXAMPLE



▪ Toxicology:

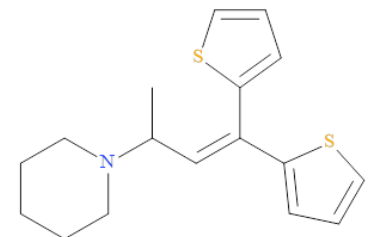
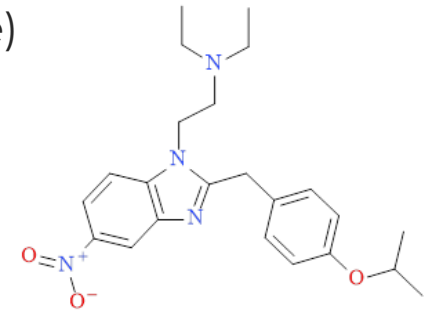
- Isotonitazene (0.9 ng/mL), Piperidylthiambutene (0.5 ng/mL)
- Ethanol (147 mg/dL), caffeine, alprazolam (100 ng/mL), lamotrigine (1.1 µg/mL), and amphetamine (43 ng/mL)

▪ Chemistry:

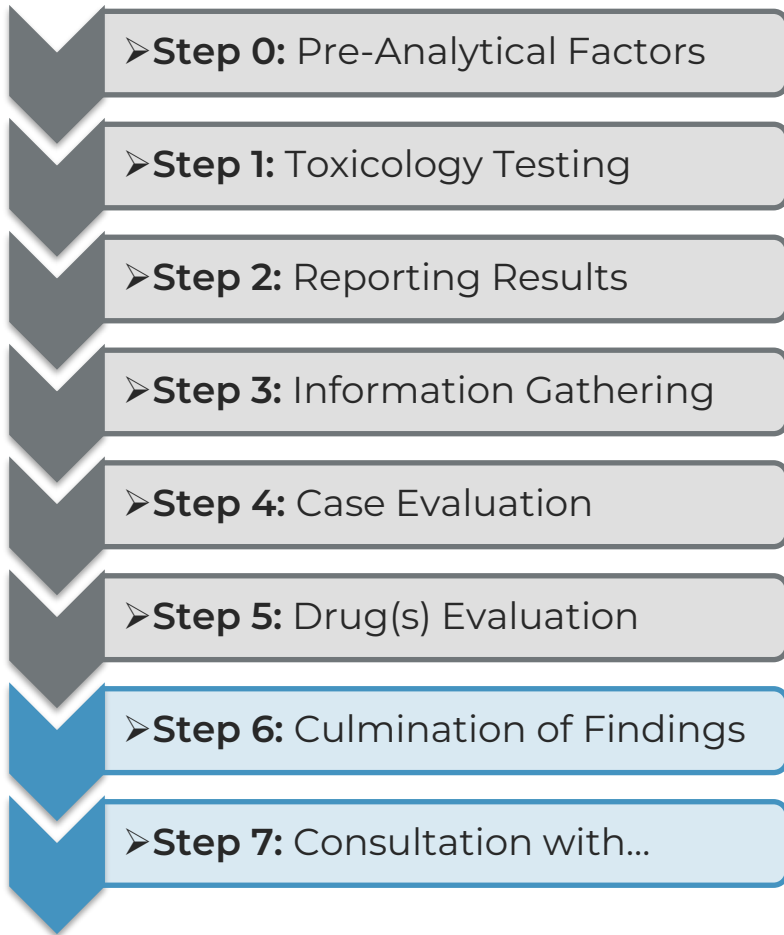
- Spoon (Isotonitazene, Piperidylthiambutene)
- Syringe (Isotonitazene)

▪ Drug Evolution

- Pharmacology?
- Toxicology?
- Polydrug use – drug-drug interactions?



CASE EXAMPLE



- **Medical Examiner Consultation & Interpretation:**
 - No anatomical cause of death
 - Other drugs largely unremarkable on their own
- **Manner of Death:**
 - Accident
- **Cause of Death:**
 - Acute isotonitazene and piperidylthiambutene intoxication
- **Other Significant Conditions:**
 - Ethanol, alprazolam, and lamotrigine ingestion



DISCUSSION & CONCLUSIONS

ACKNOWLEDGEMENTS

- **CFSRE Team**

- Barry Logan
- Sara Walton
- Josh DeBord
- Mandi Mohr
- Melissa Fogarty
- Alyssa Reyes
- Brianna Stang
- Alexis Quinter
- Max Denn
- Many others!

- **NMS Labs**

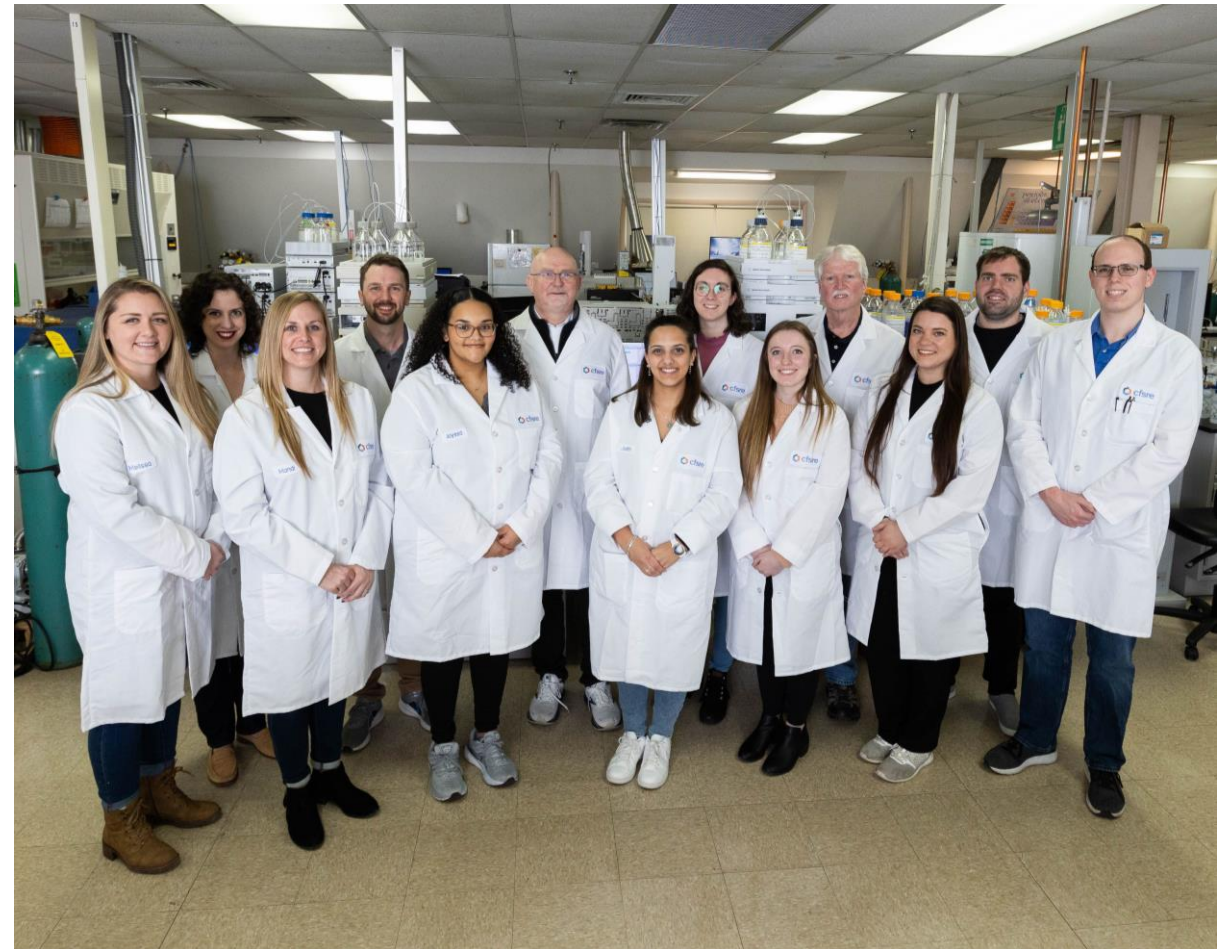
- Donna Papsun

- **Funding Agencies**

- NIJ

- **Collaborators & Partners**

- Forensic
- Clinical
- Medical Examiners
- Coroners
- Crime Labs
- Etc.





cfsre



NPS DISCOVERY

THANK YOU! **QUESTIONS?**



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