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NPS
DISCOVERY

Case Studies in Clinical Toxicology

Alex J Krotulski, PhD – CFSRE / NPS Discovery

ISSED Webinar: Analytical Toxicology for Novel Psychoactive Substances – September 16, 2021

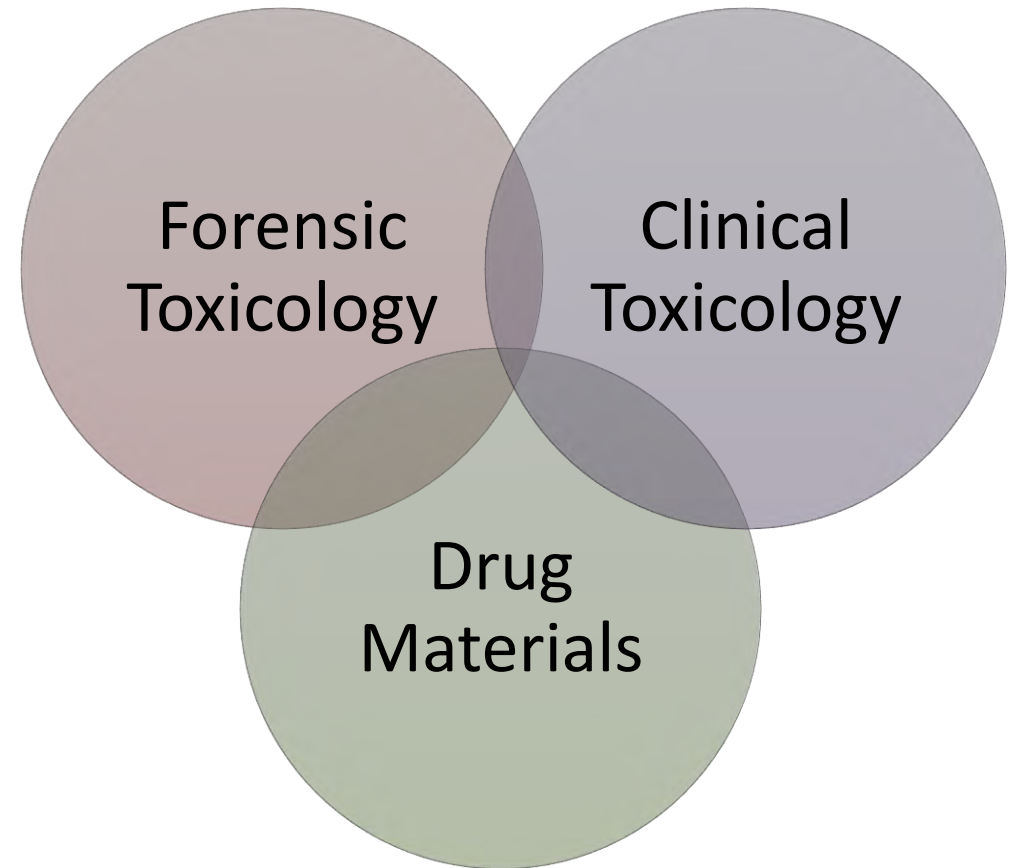
Brief Introduction

- **Alex J Krotulski, PhD**
 - Associate Director – CFSRE
 - Program Manager – NPS Discovery
 - Forensic Toxicologist / Chemist
- 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.



Clinical Toxicology Testing for NPS

- Clinical intoxications and emergency department admissions
- **Vital** component to determining NPS impacts
- Yet it is rare for clinical samples to be tested for NPS
 - Especially current / newer generations
- Hospital urine drug screens have utility
- Clinical NPS testing usually requires specialized interest (and approvals)



Sites Collaborating with NPS Discovery

- Collaborators:
 - Emergency departments
 - Poison centers
- Samples received:
 - Blood, serum, plasma, oral fluid
 - Biological specimens
 - Residuals discards
 - Drug materials
- Clinical signs, symptoms, outcomes, use history, etc.



Case Series



Case #1 – Mistaken Identity (2017)

- 17-year-old male
- Became apneic and unresponsive while en route to school
- On arrival, administered naloxone by bystander
 - 4 mg IN
- Patient transported to local ED



Case #1 – Mistaken Identity (2017)

- 17-year-old male
- Became apneic and unresponsive while en route to school
- On arrival, administered naloxone by bystander
 - 4 mg IN
- Patient transported to local ED
- Clinical observations:
 - Heart rate: 125 b/min (↑)
 - Respiratory rate: 18 br/min (↑)
 - Oxygen saturation: 100%
 - Pupils 4 mm in diameter
 - Neurologic exam: nonfocal
- Blood and urine samples collected for toxicology testing
 - **GC-MS: Caffeine only**

Case #1 – Mistaken Identity (2017)

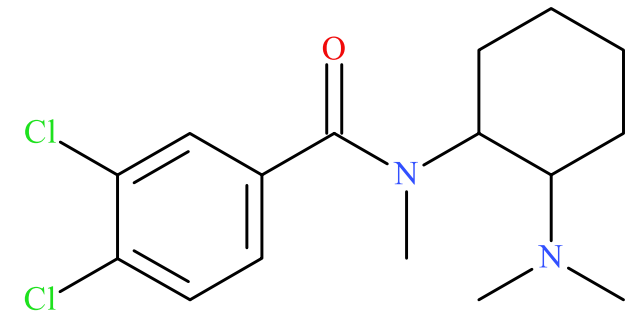
- Individual reported snorting “crushed Xanax”
 - Received from a friend
 - Crushed pill fragments
 - Negative for alprazolam
- Denied use of opioids



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- Expanded toxicology testing for NPS:
 - Caffeine
 - **U-47700 (282.4 ng/mL)**
 - **U-47700 Metabolites**
 - Naloxone



Case #2 – “Everything Under the Sun” (2020)

- 63-year-old male
 - Behaving erratically in public
 - Tachycardic, hypertensive, and hyperthermic
 - Required multiple doses of antipsychotics and benzodiazepines
- In ED, found to have acute kidney injury and rhabdomyolysis
- Admitted to taking “everything under the sun” on a multi-day binge

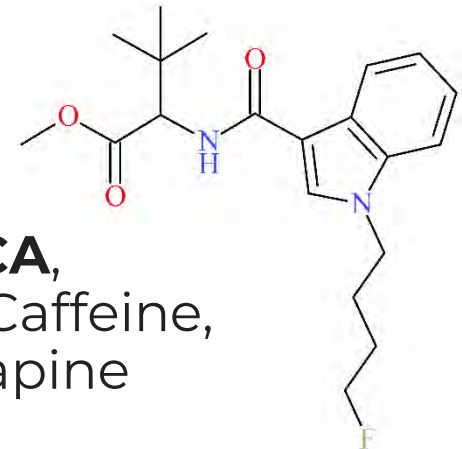


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- Hospital urine drug screen:
 - + Amphetamines
 - + Opiates
- Samples sent for further testing
 - Blood, urine, serum, and plasma

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- Hospital urine drug screen:
 - + Amphetamines
 - + Opiates
- Samples sent for further testing
 - Blood, urine, serum, and plasma
- Toxicology Results:
 - Blood: **4F-MDMB-BICA**, Methamphetamine, Caffeine, Sertraline, and Quetiapine



Case #3 – A Day At The Airport (2021)

- 32-year-old female
 - No known past medical history
 - Passed out at airport with subsequent drowsiness
 - Uneventful transport to ED
- Clinical signs and symptoms:
 - Somnolence
 - Confusion
 - Hallucinations
 - HR 41 (↓)
 - BP 139/90 (↑)
 - RR 18 (↑)
 - O2 100% on room air
 - Temperature 37.4



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 - BP 139/90 (↑)
 - RR 18 (↑)
 - O2 100% on room air
 - Temperature 37.4
- Recovered small plastic bag with “pressed blue pills”
 - Stated to be fentanyl / “M-30s”
- Pertinent physical exam findings:
 - GCS of 13 on initial presentation
 - Profound and persistent sedation
 - Ataxia
 - Right gaze preference
- Discharged six days after admission
 - Hospital course was complicated by aspiration pneumonia

Case #3 – A Day At The Airport (2021)

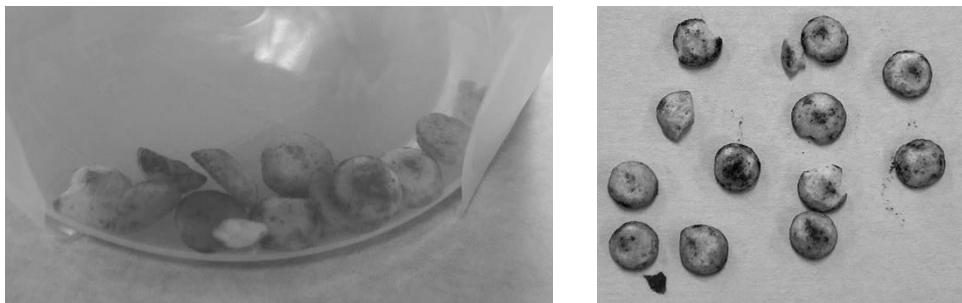
- “Pressed Blue Pills”
 - Do not look like pills
 - GC-MS: Negative
 - LC-QTOF-MS: Negative



- Patient may have used “M-30s”
that were not recovered

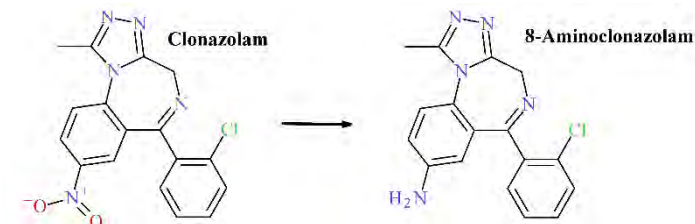
Case #3 – A Day At The Airport (2021)

- “Pressed Blue Pills”
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- Patient may have used “M-30s” that were not recovered

- Hospital urine drug screen:
 - + Fentanyl
 - + Opiates
 - + Benzodiazepines
- Expanded toxicology results:
 - Blood 4.5 hours after presentation
 - Fentanyl: 2.7 ng/mL
 - Norfentanyl: 2.5 ng/mL
 - **8-Aminoclonazepam: 2.3 ng/mL**



Clinical Case Takeaways

- What do you test for when someone says they took “everything” or conversely “nothing”?
- Do clinical signs and symptoms match toxicology results? If no, what’s next?
- User may not be aware of the drugs they are using
 - Or the drug combinations / amount
- Follow-up surveys can provide useful information / collect any and all information available
- Seek expanded toxicology testing, especially for NPS
 - Labs must remain aware of what to test for
 - E.g., Synthetic cannabinoid metabolites in urine (may not be routine)
- Drug materials can be helpful or could be a red herring



Recent Clinical Trends



Synthetic Cannabinoids Presenting Like Opioids?

- Respiratory failure in confirmed synthetic cannabinoid overdose
– *Clinical Toxicology*
- <https://doi.org/10.1080/15563650.2021.1975734>

CLINICAL TOXICOLOGY
<https://doi.org/10.1080/15563650.2021.1975734>

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SHORT COMMUNICATION

Check for updates

Respiratory failure in confirmed synthetic cannabinoid overdose

Alex F. Manini^a, Alex J. Krotulski^b, Jonathan Schimmel^a, Lisa Allen^c, Yasmin L. Hurd^d, Lynne D. Richardson^e, Kavey Vidal^f and Barry K. Logan^{b,f}

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ABSTRACT
Context: Synthetic cannabinoids (SCs) are a structurally heterogenous synthetic class of drugs of abuse. The objective was to describe the incidence of acute respiratory failure in Emergency Department (ED) patients with confirmed SC exposure, and to investigate the association between SC overdose with respiratory failure compared to non-SC overdose.
Methods: This was an observational cohort of ED patients ≥ 18 years with suspected cannabinoid overdose between 2015 and 2020 at two tertiary-care hospitals. Patient serum was analyzed *via* liquid chromatography/quadrupole time-of-flight mass spectrometry using a library with >800 drugs including novel psychoactive substances. The primary outcome was acute respiratory failure.
Discussion: Of 83 patients with suspected cannabinoid overdose, there were 29 confirmed SC overdoses: 5F-MDMB-PICA ($n=18$) and its metabolite 5OH-MDMB-PICA ($n=16$), ADB-FUBINACA ($n=4$), AB-CHIMINACA ($n=4$), AB-FUBINACA ($n=1$), AB-PINACA ($n=1$), MDMB-4en-PINACA ($n=1$), and 4F-MDMB-BINACA ($n=1$). Overall, incidence of acute respiratory failure was 31.3% (95%CI 21.6–42.4). Compared to non-SC overdose, confirmed SC overdose was significantly associated with respiratory failure (25.0% SC vs. 4.2% non-SC, $p=0.05$).
Conclusion: This study demonstrates that SCs are associated with respiratory failure. Since respiratory depression is a potentially lethal adverse effect of SC overdose, future research is warranted.

ARTICLE HISTORY
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KEYWORDS
Synthetic cannabinoids; synthetic cannabinoid receptor agonists; SCRAAs; respiratory failure; naloxone



Benzodiazepines Present in Opioid Overdose Cases

- Notes from the Field: Illicit Benzodiazepines Detected in Patients Evaluated in Emergency Departments for Suspected Opioid Overdose — Four States, October 6, 2020–March 9, 2021
 - *Morbidity and Mortality Weekly Report (MMWR)*
- https://www.cdc.gov/mmwr/volumes/70/wr/mm7034a4.htm?s_cid=mm7034a4_w

The screenshot shows the CDC website header with the logo and tagline "Centers for Disease Control and Prevention CDC 24/7: Saving Lives, Protecting People™". A search bar and "Advanced Search" link are visible. Below the header is a blue banner for "Morbidity and Mortality Weekly Report (MMWR)". The article title is prominently displayed in a large, bold font. Below the title, the issue information "Weekly / August 27, 2021 / 70(34);1177–1179" is shown. The author list includes Kim Aldy, Desiree Mustaquim, Sharan Campleman, Alison Meyn, Stephanie Abston, Alex Krotulski, Barry Logan, Matthew R. Gladden, Adrienne Hughes, Alexandra Amaducci, Joshua Shulman, Evan Schwarz, Paul Wax, Jeffrey Brent, Alex Manini, and the Toxicology Investigators Consortium Fentolog Study Group. A "View author affiliations" link is provided at the end of the author list.

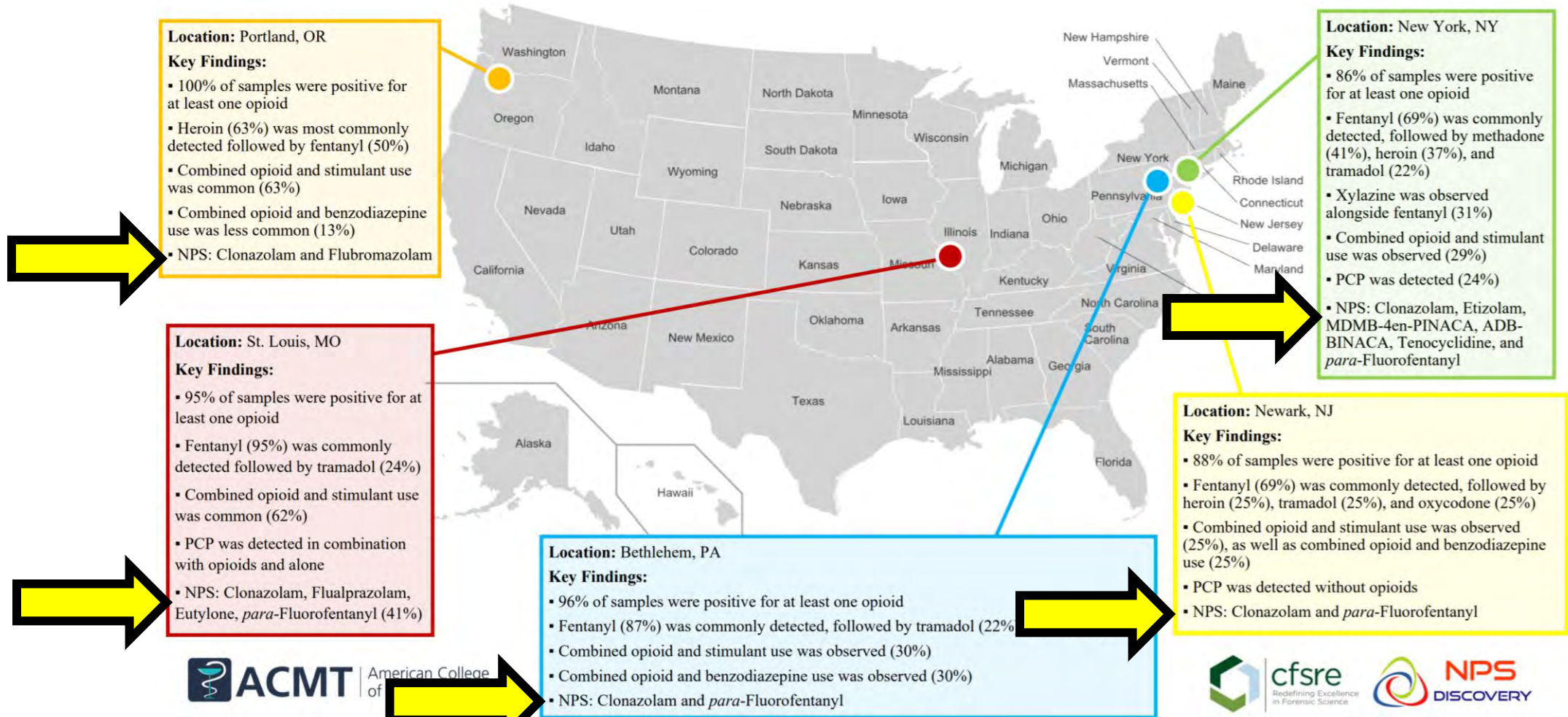


Concurrent and/or Concomitant NPS Use

- Speedballs
- Coc/Meth + NPS Opioids
- Goofballs
- Eutylone + Fentanyl
- Tranq Dope
- Xylazine + Fentanyl
- Benzo Dope
- Isotonitazene + Flualprazolam
- SCRA Dope
- 5F-ADB + Fentanyl
- Opioid Dope?
- Brophine + Fentanyl



“New” NPS Continue to Appear – Extent Unknown

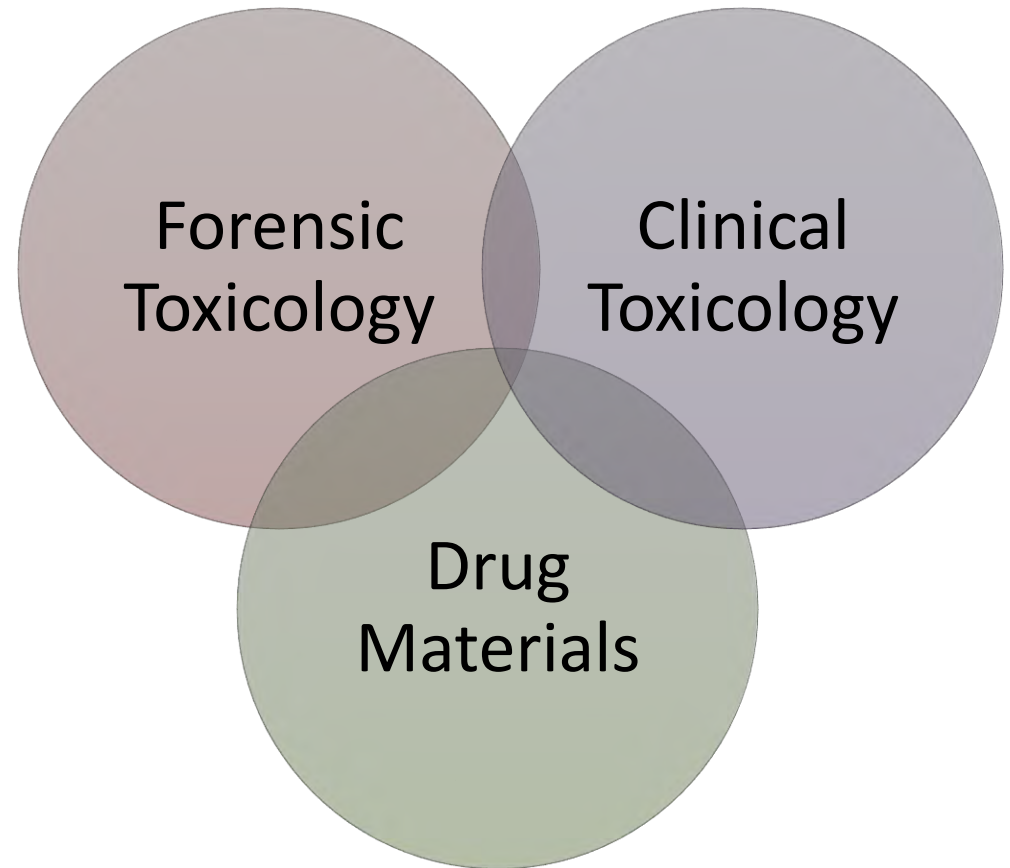


Discussion / Conclusions



Discussion / Conclusions

- NPS continue to appears in clinical scenarios
- Expanded toxicology testing is necessary and useful
- Investigate *strange* clinical signs and symptoms
 - Are the toxicology “correct”?
- **Share information !!!**



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- ACMT
 - ToxIC Fentanyl Study Group
- *And many others !*



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