cfsre | NPS DISCOVERY

Monitoring the North American Drug Supply and Responding in Real-Time

Reducing Harm From Drugs in Aotearoa – Wellington, New Zealand – Monday December 1, 2025

Alex J. Krotulski, PhD – Center for Forensic Science Research and Education, Pennsylvania, USA

FUNDING DISCLOSURE

- **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-24-GK-00981-COAP
  - The opinions, findings, conclusions and/or recommendations expressed in this presentation are those of the author(s) and do not necessarily represent the official position or policies of the U.S. Department of Justice.

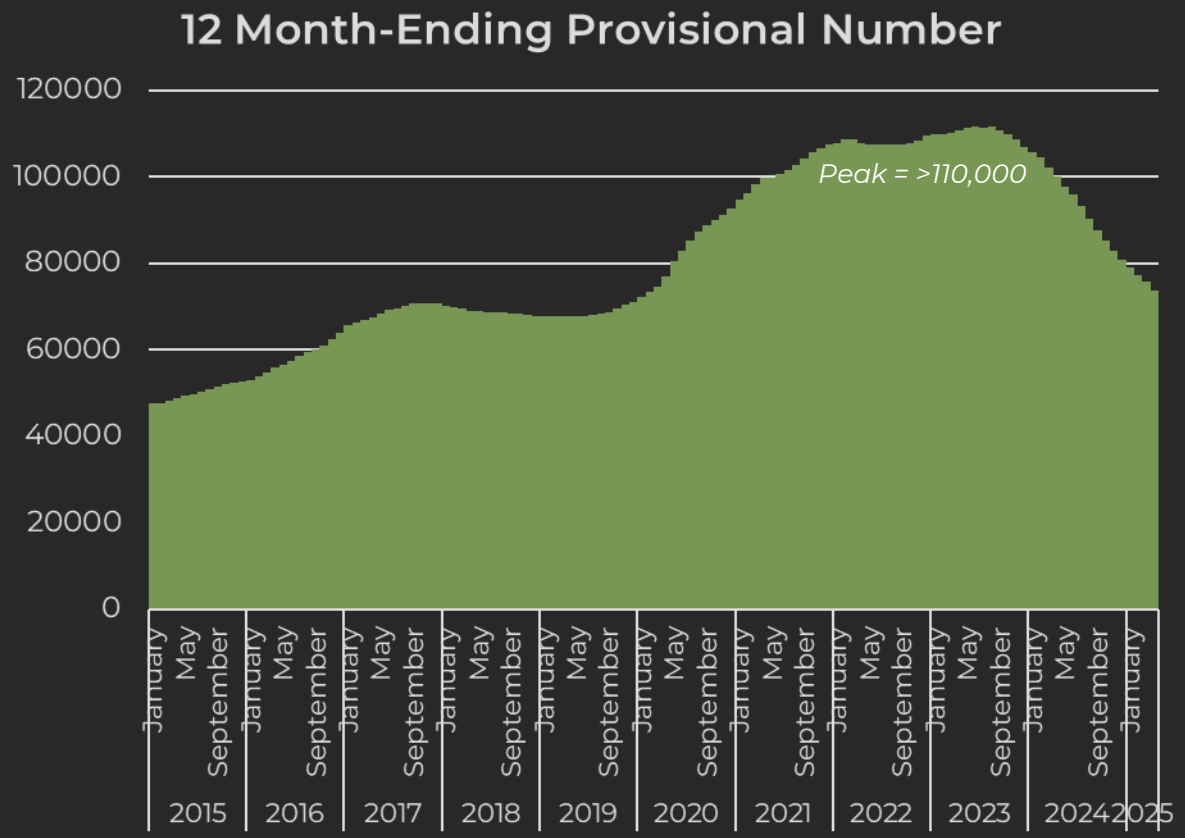
- CFSRE's NPS Discovery program also receives funding, either directly or indirectly, from a variety of agencies and entities, including Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH).

PROBLEM STATEMENT

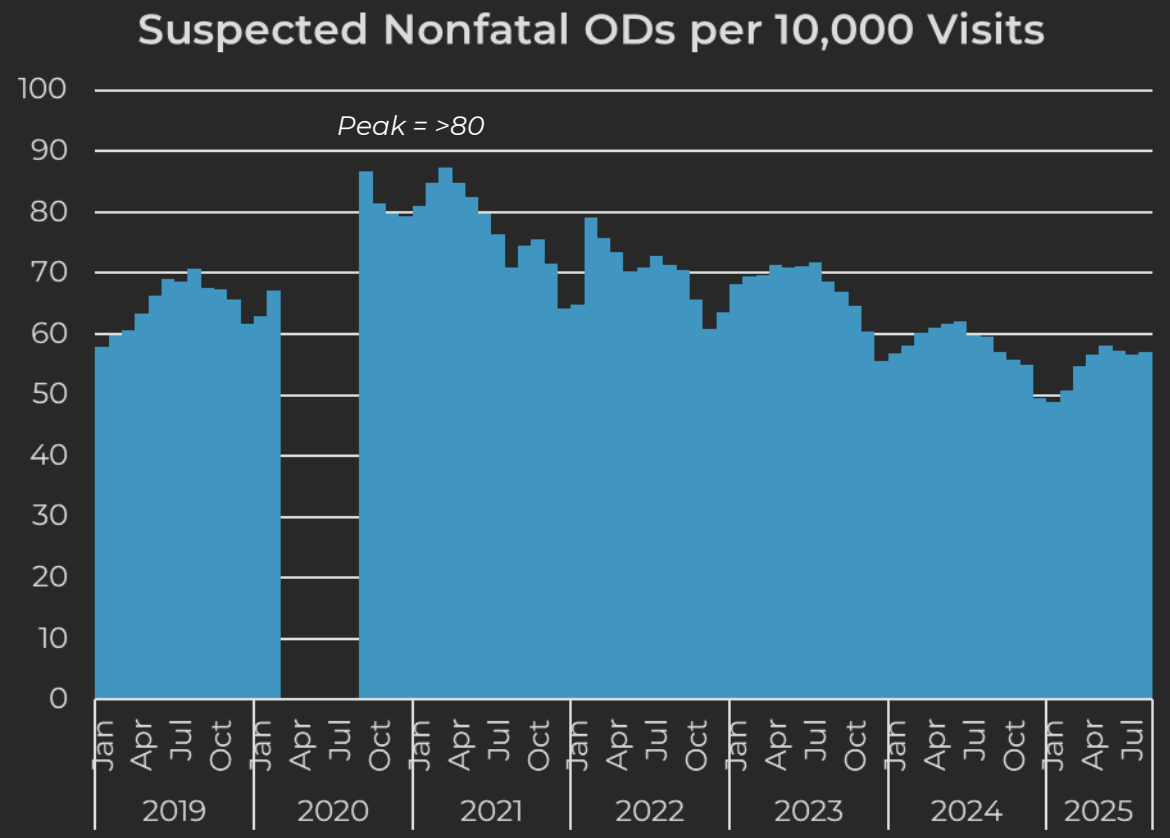
cfsre | NPS DISCOVERY

U.S. DRUG-RELATED DEATHS & HOSPITALIZATIONS

FATAL DRUG OVERDOSES



NON-FATAL DRUG OVERDOSES



cfsre | NPS DISCOVERY

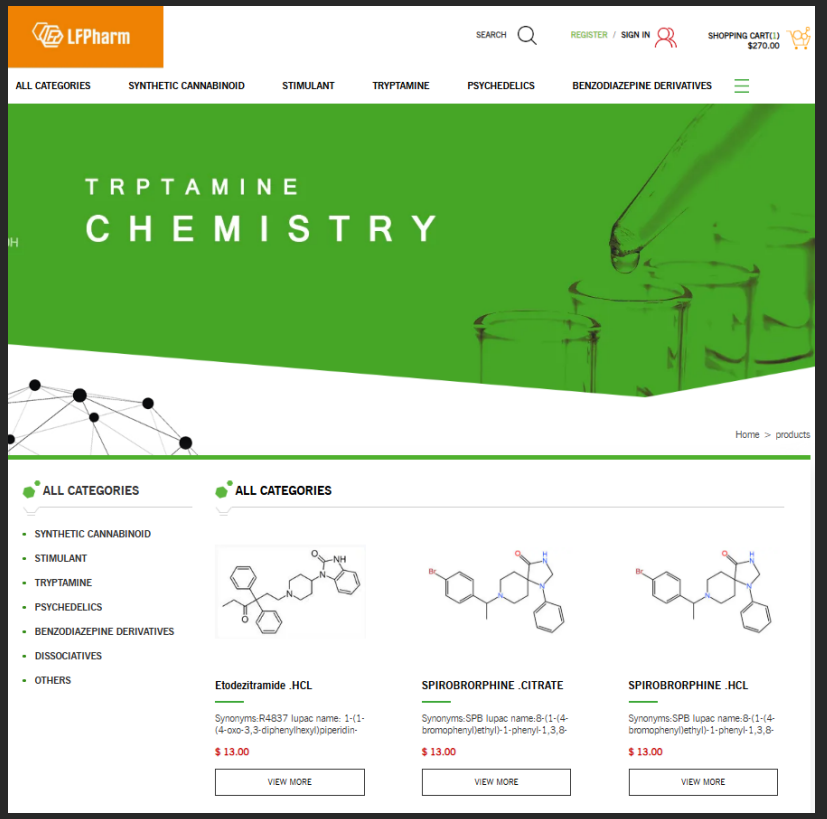
Source: U.S. Centers for Disease Control & Prevention

DISTINCT U.S. DRUG MARKETS

STREET DRUG SUPPLY

SMOKE SHOPS

ONLINE MARKETPLACES



cfsre | NPS DISCOVERY

DISTINCT U.S. DRUG MARKET PRODUCTS

STREET DRUG SUPPLY

SMOKE SHOPS

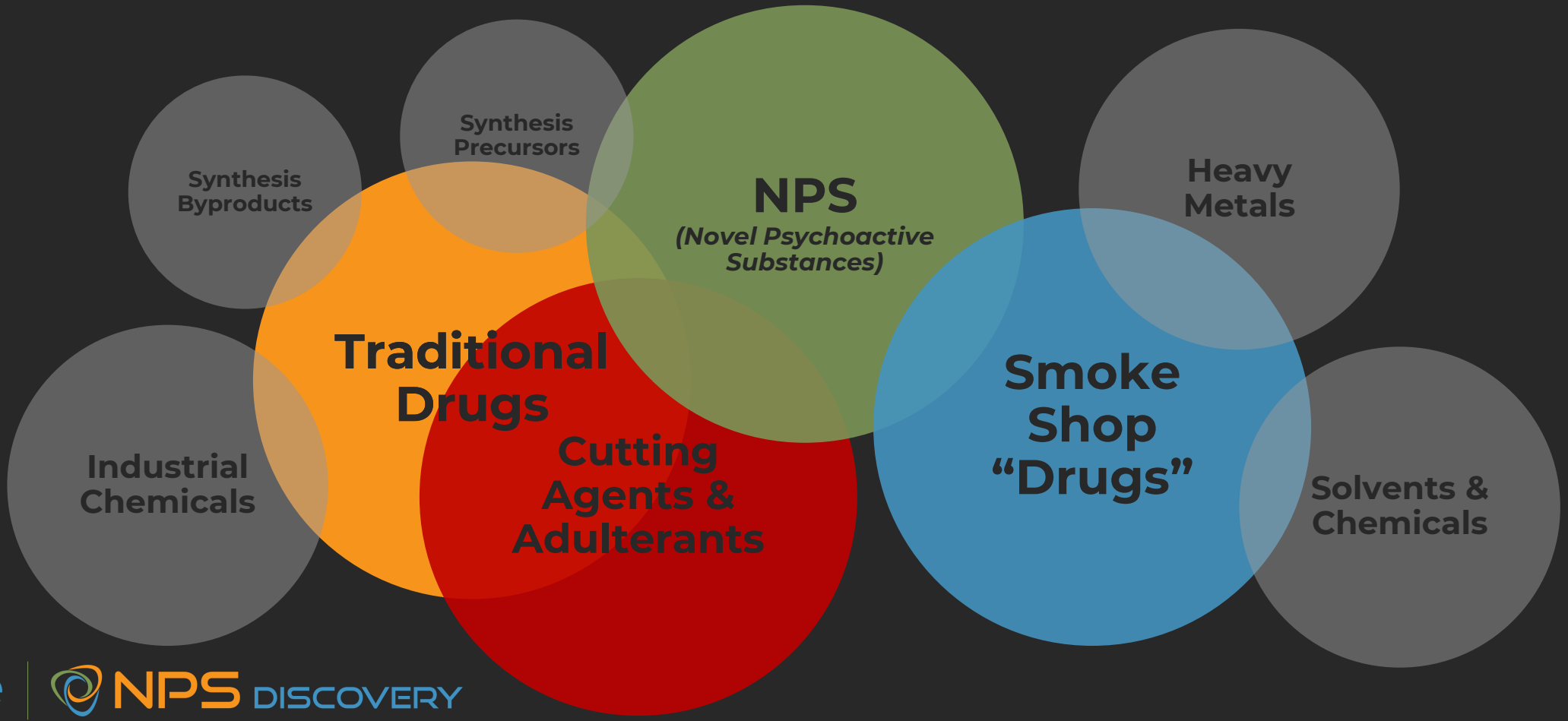
ONLINE MARKETPLACES

ILLICIT — QUASI-LEGAL — LEGAL ("LEGAL")

cfsre | NPS DISCOVERY

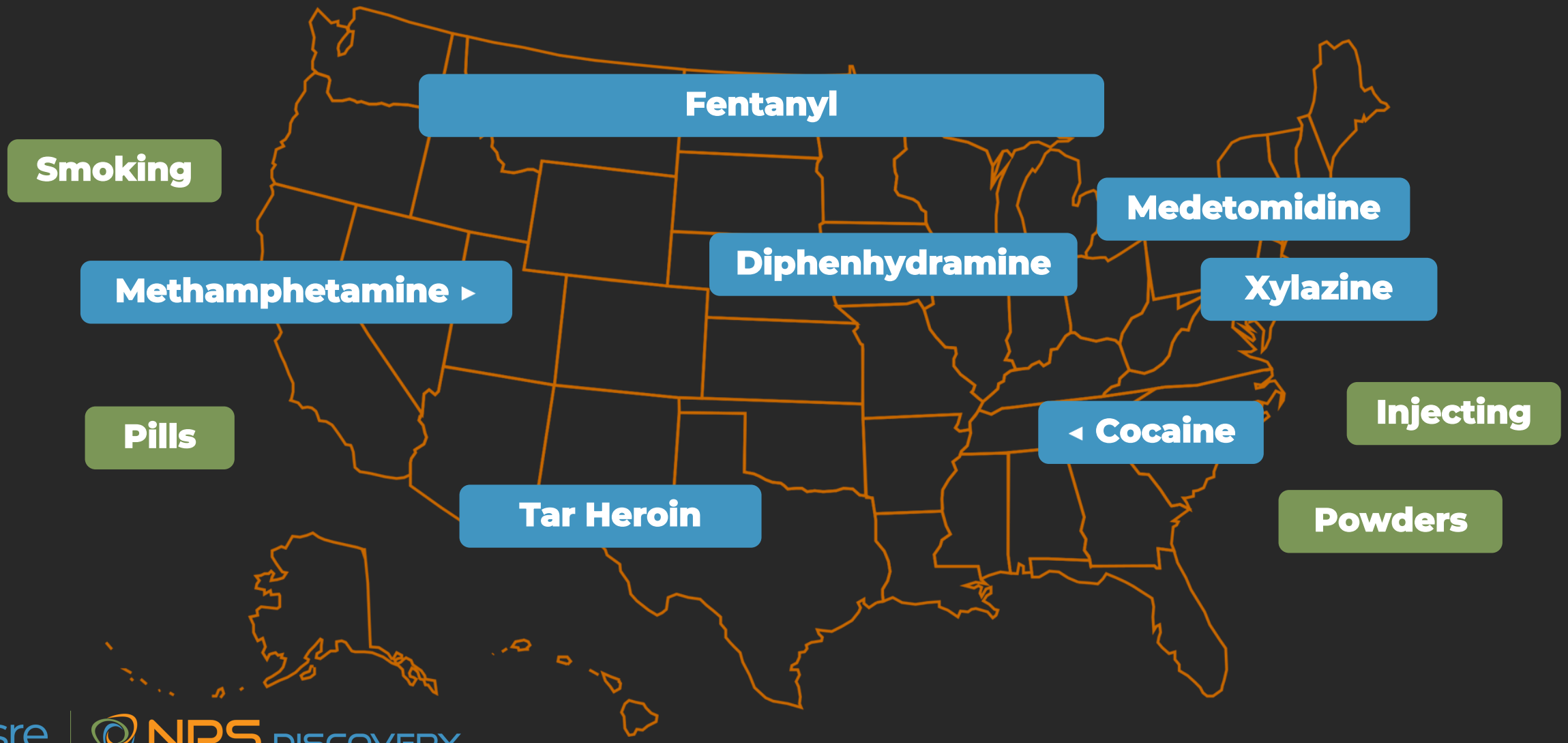
OVERLAPPING DRUG SUPPLIES & SOURCES

STREET DRUG SUPPLY | **SMOKE SHOPS** | **ONLINE MARKETPLACES**



cfsre | NPS DISCOVERY

GEOGRAPHICAL DIVERSITY IN THE U.S.



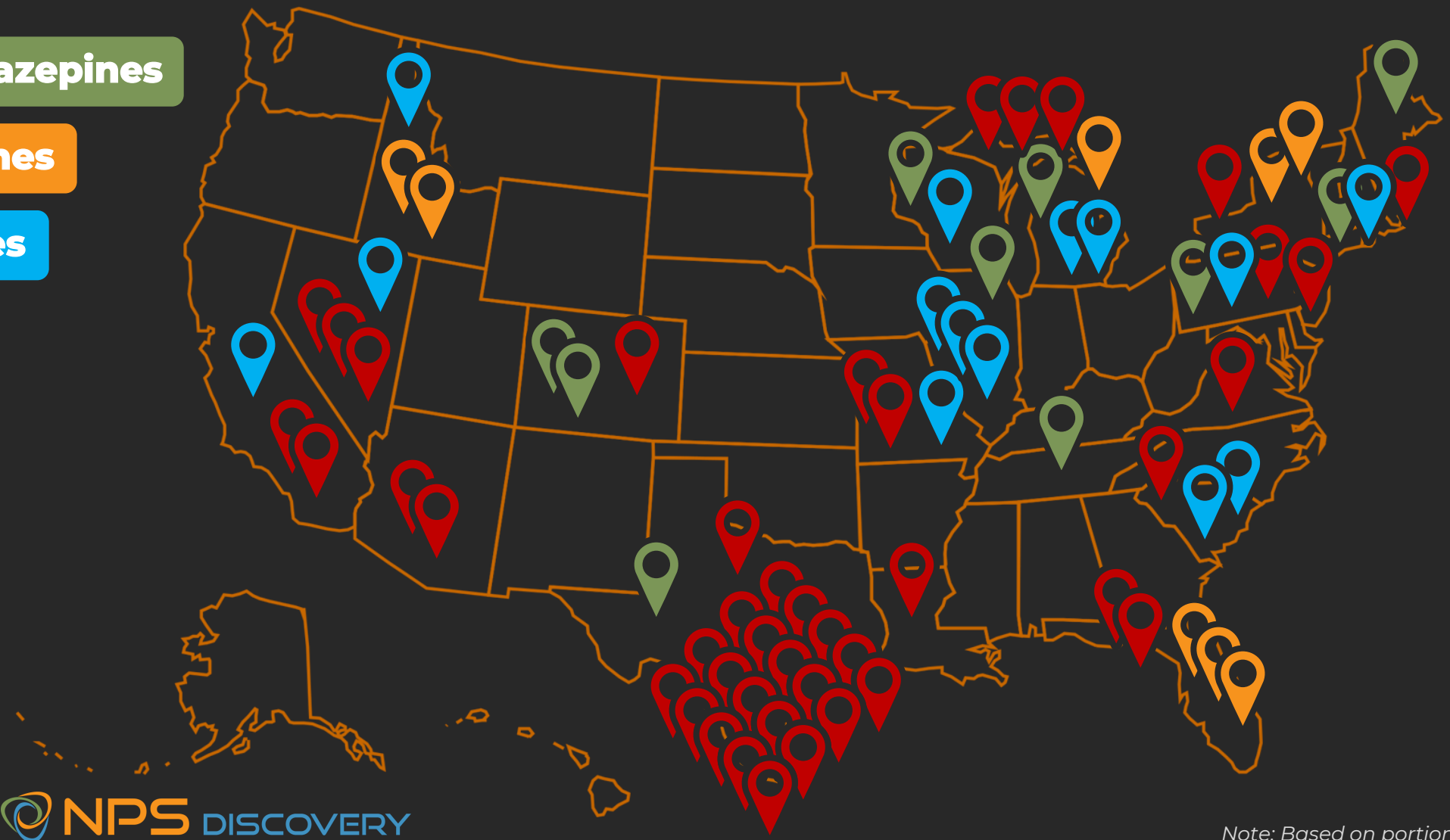
GEOGRAPHICAL DIVERSITY IN THE U.S.

Benzodiazepines

Cathinones

Nitazenes

SCRAs



cfsre | NPS DISCOVERY

Note: Based on portion of 2025 cases.

SOLUTION & APPROACH

cfsre | NPS DISCOVERY

CFSRE'S NPS DISCOVERY PROGRAM

- Launched in 2018, **NPS Discovery** is an **open-access drug early warning system** operating in the United States and housed at the Center for Forensic Science Research & Education (CFSRE)
  - Primary focus on **analytically confirmed** detections of NPS and other substances (when possible)

- Maintain extensive **collaborations and partnerships** with vast variety of public health and safety organizations (federal, state, and local) within North America and around the world

DRUG MATERIAL	RECREATIONAL	CLINICAL	FORENSIC
Customs & Border	Drug Use Survey	Non-Fatal Overdose	Impaired Driving
Street Drug Supply	Recreational Drug Use	Hospital Settings	Drug Facilitated Crime
Interdiction & Forensic	Drug Forums	Treatment Centers	Fatal Overdose

cfsre | NPS DISCOVERY

OPEN-ACCESS DRUG EARLY WARNING SYSTEM

Surveillance & Monitoring

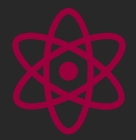
- Fatal Overdoses
- Non-Fatal Overdoses
- Recreational Drug Use
- Impaired Driving
- Local Drug Seizures
- Customs Interdiction

Outbreak Testing

- Emergent Harms & Overdose
- Rapid Turnaround
- Drug Materials
- Biological Specimens
- Public Health Interpretation

Drug Checking

- Public Health
- Harm Reduction
- Point-of-Use
- Market Analysis
- All Types of Drug Materials
- Use Information
- Survey Responses

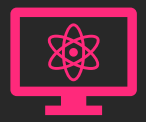


Test Purchases

- Smoke Shops, Gas Stations, & Corner Stores
- Recreational Supplies
- Gray Market Websites
- The Dark Web

Dissemination

- New Drug Monographs
- Trend Reports
- Public Alerts
- Year In Review
- Drug Checking Reports
- Clinical Reports
- Scope Recs.
- NPS Naming Guides

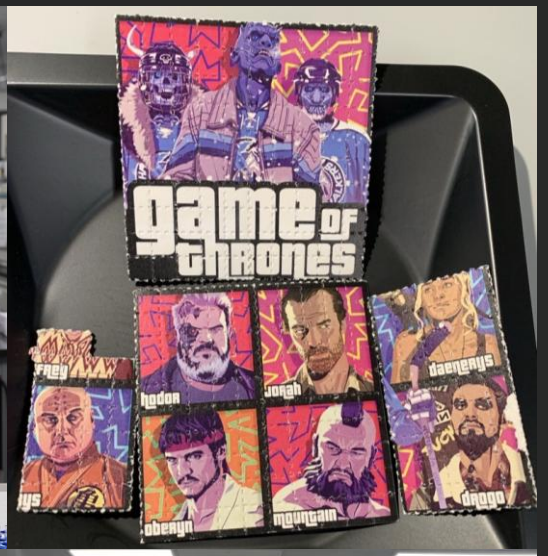


Resources

- Open-Access Web Repository
- *Forensically Relevant Drugs Database*
- Drug Checking Database
- Analytical Spectral Library
- Expert Review & Interpretation

cfsre | NPS DISCOVERY

OPEN-ACCESS DRUG EARLY WARNING SYSTEM



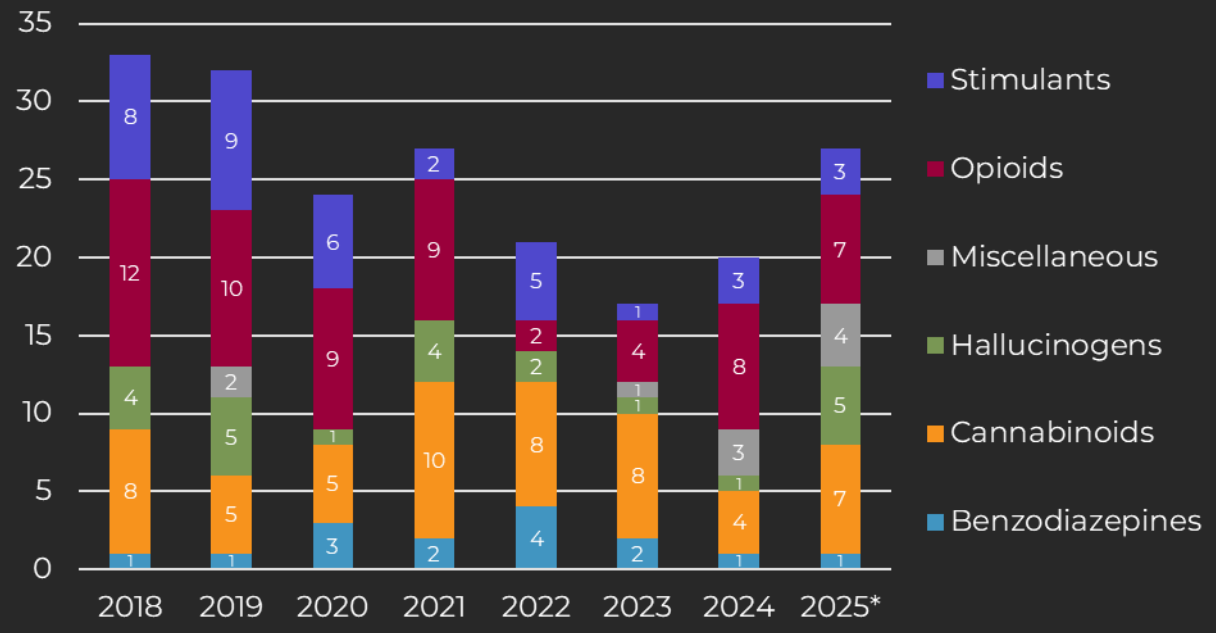
cfsre | NPS DISCOVERY

RESULTS & IMPACT

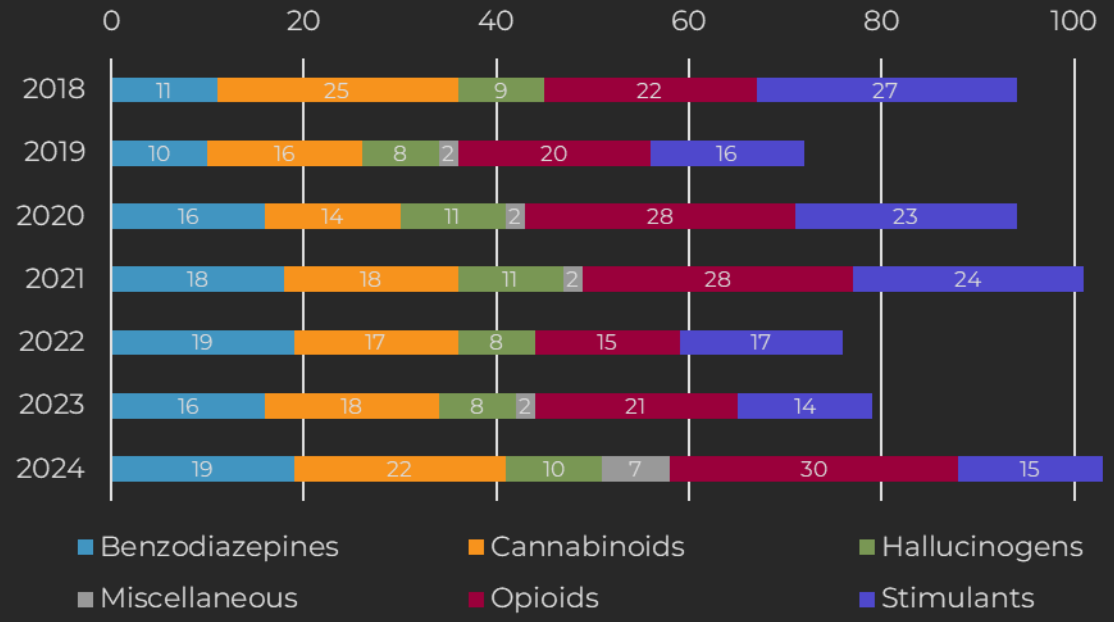
cfsre | NPS DISCOVERY

NPS DISCOVERIES

- Our program has reported **201+ newly discovered** NPS in the U.S. (**27+** in 2025)
  - **NPS opioids** remain the largest subclass, followed by **cannabinoids** and **stimulants**

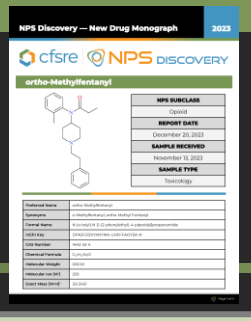


- In total, our program has **identified 296+** NPS in the U.S. (**103** in 2024)
  - **NPS opioids**, **stimulants**, and **cannabinoids** represent the largest subclasses



cfsre | NPS DISCOVERY

NEW NPS DETECTED & REPORTED IN 2025

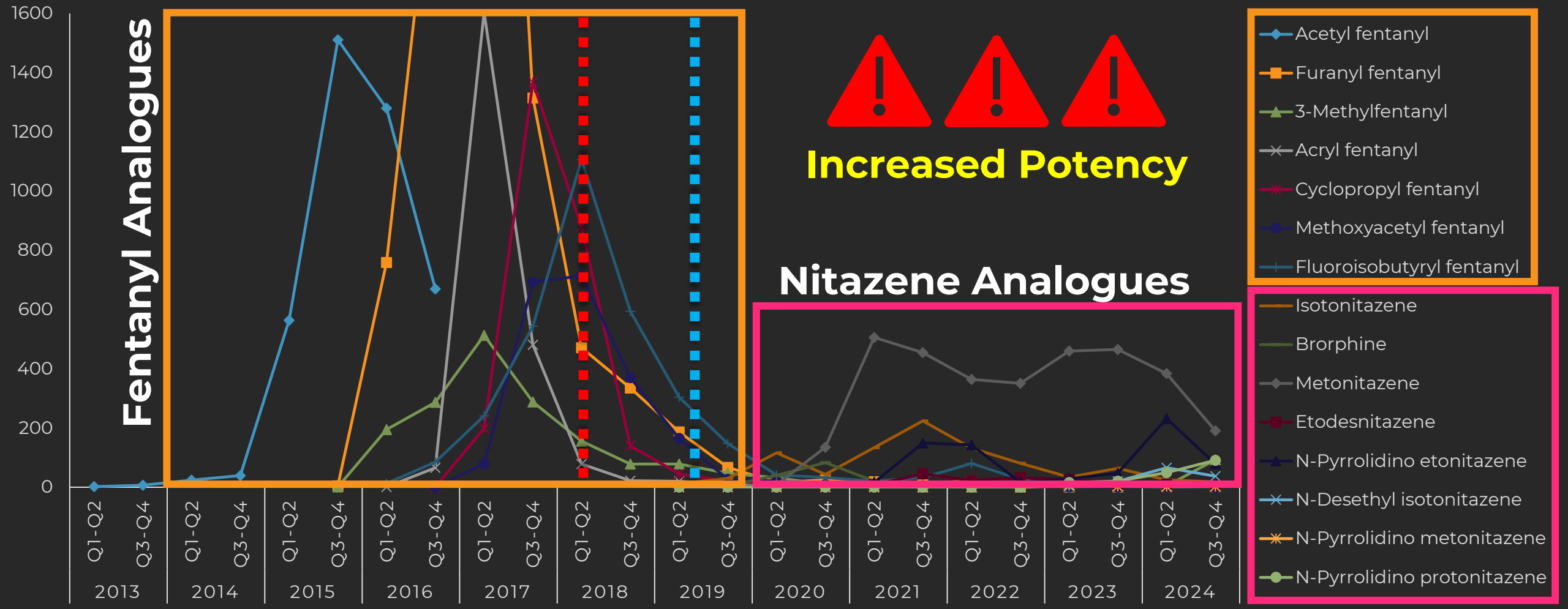


N-Desethyl Protonitazene	7-Hydroxy Mitragynine	Spirochlorphine	Mitragynine Pseudoindoxyl
Dicloqualone	2C-B-FLY	THCP	Dihydro-7-Hydroxy Mitragynine
4F-MBZP	N-Pyrrolidino Metodesnitazene	Tetramethylfentanyl	Etonitazene
HHCH	CUMYL-INACA	3C-P	AMB-4en-PINACA
AB-MDMSBA	Dipropyltryptamine (DPT)	Deoxymethoxetamine	MMB-PICA
Alpha-PiHpP	*N*-Pyrrolidino Ethylene Isotonitazene	Deschloroketamine	5,6-Dichloro Brorphine
4F-Alpha-PHP	Ethylbromazolam	Despentyl-UR-144	**Forthcoming:** DPP-26, Methidone, Avizafone, Methyl-K, PiPTentadol, LSM-75, Pynazolam, 2Me-PiHP, +++

NPS and related emerging drugs continue to appear at steady or increasing rates in the United States

NPS OPIOIDS

FRS Scheduling in U.S.	February 6, 2018
FRS Scheduling in China	May 1, 2019



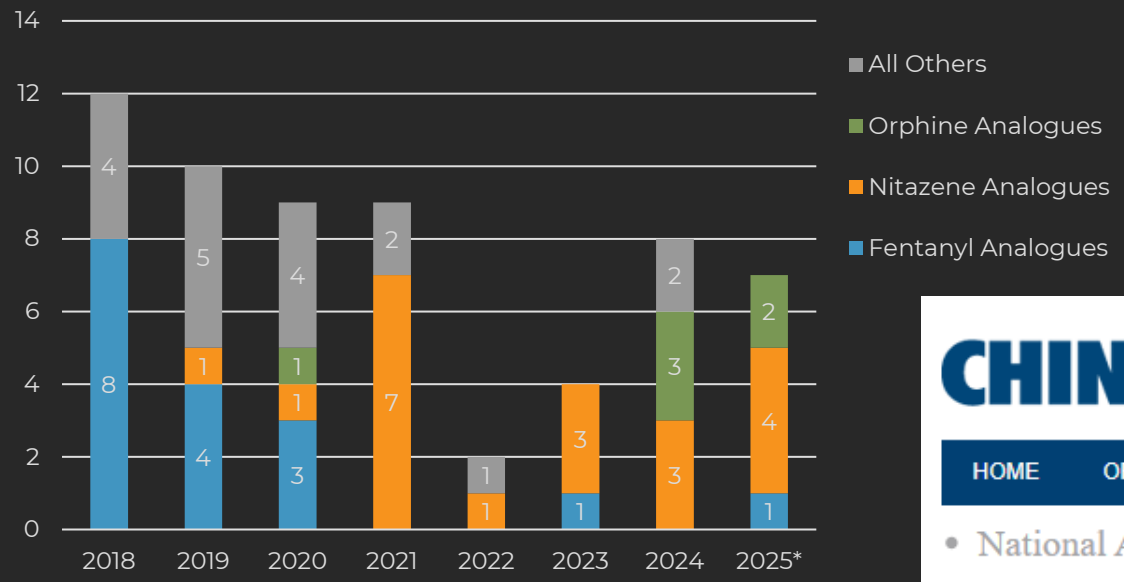
cfsre | NPS DISCOVERY

Source: DEA/NFLIS crime lab data.

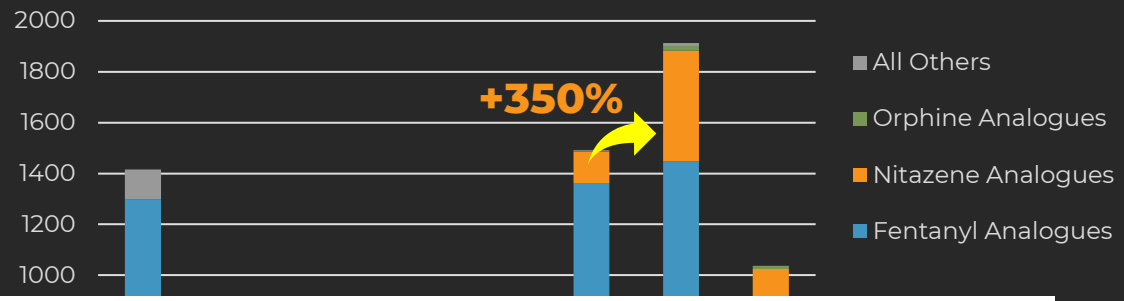
NPS OPIOIDS

- North America has experienced **continual shifts** amongst its **novel synthetic opioid (NSO)** market, often influenced by national and international efforts to **ban or illegalize** specific NSOs.

NEW NSOs DETECTED



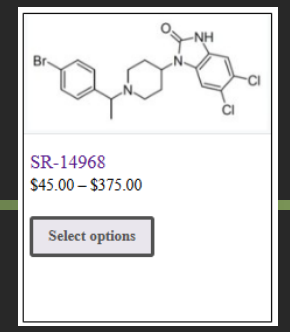
CUMULATIVE NSO DETECTIONS




CHINADAILY.COM.CN 中国日报网
Global Edition
Nov 19, 2025
HOME OPINION VIDEO WORLD CHINA TECHNOLOGY BUSINESS CULTURE TRAVEL
• National Affairs
China clamps down on nitazene-related substances

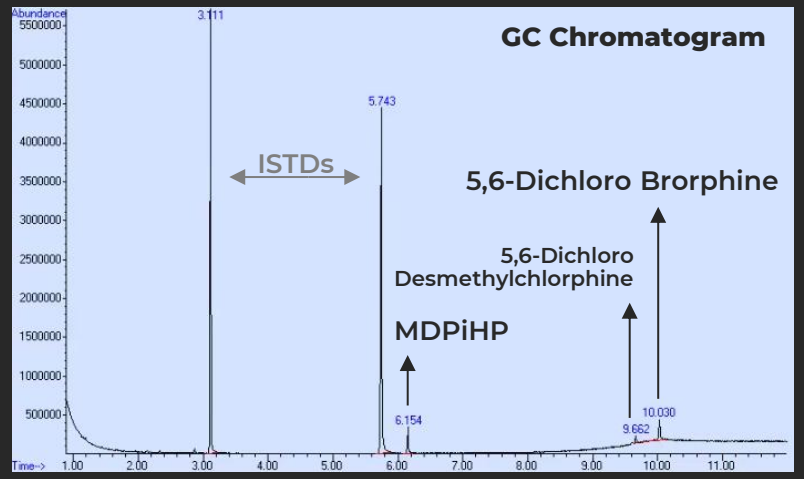
cfsre | NPS DISCOVERY

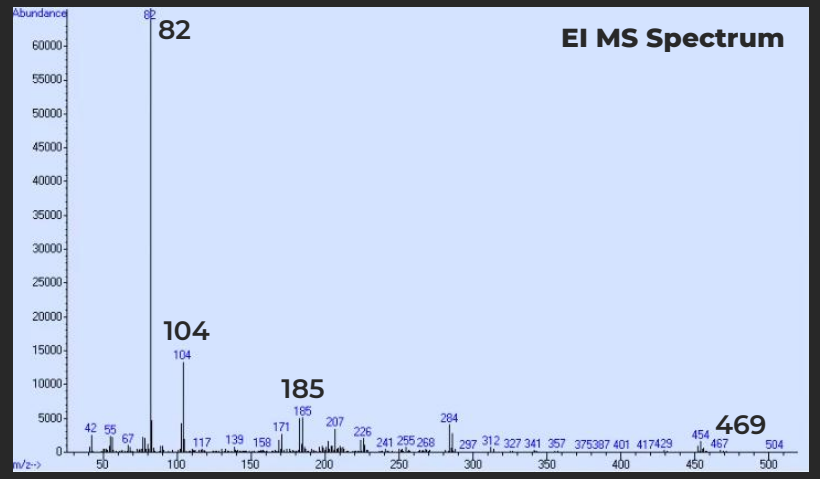
5,6-DICHLORO BRORPHINE (SR-14968)

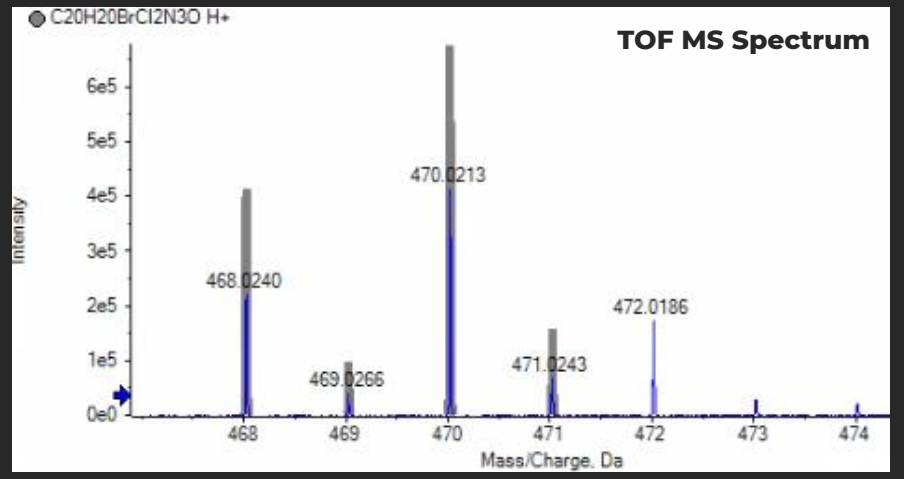


- Began appearing on gray market sites after nitazene analogue ban (China)
- **Two samples tested positive:**
  - November 5th – Received through drug checking (“unknown white powder”)
  - November 17th – Received test purchase

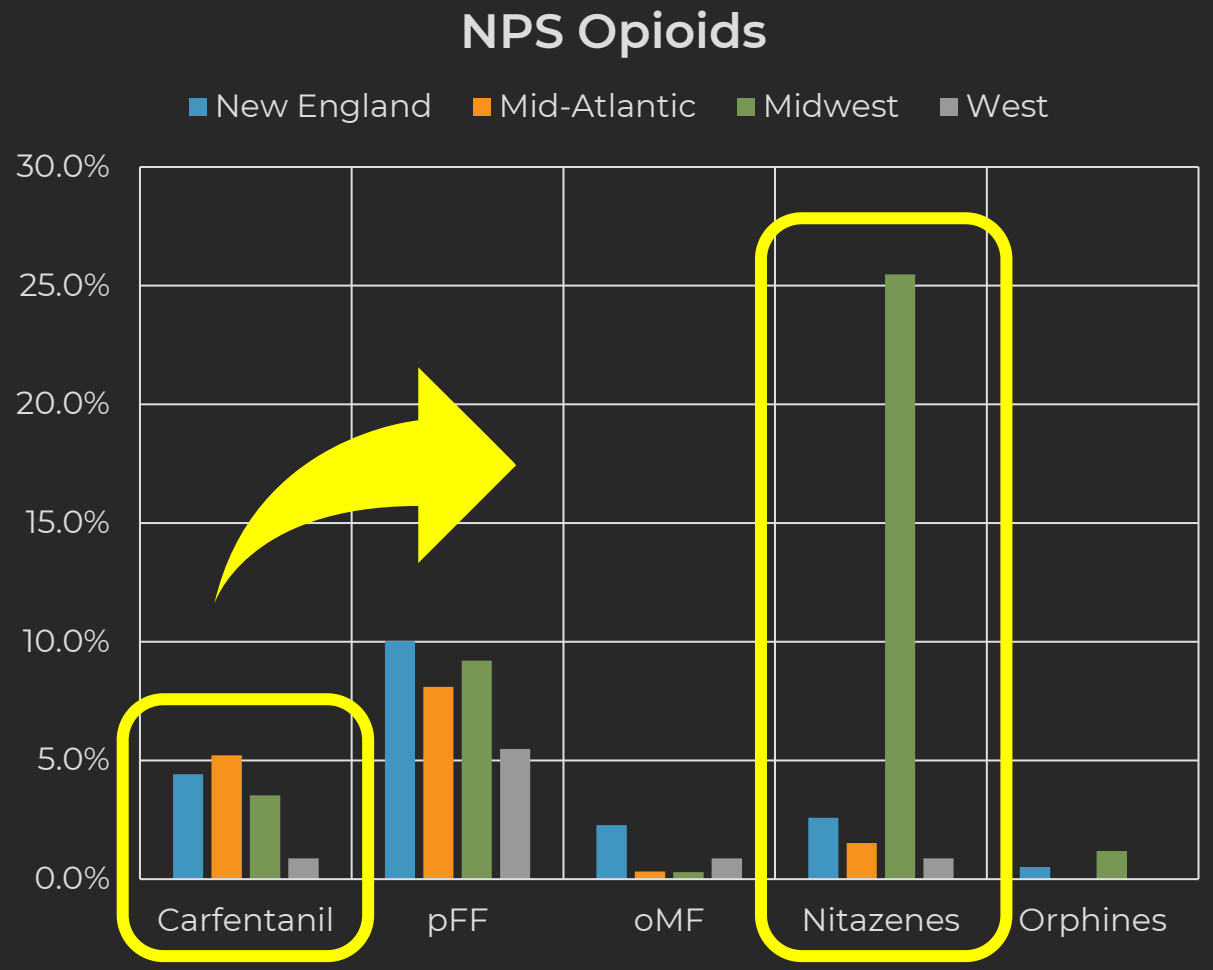
- **Analytical Data (Drug Checking):**

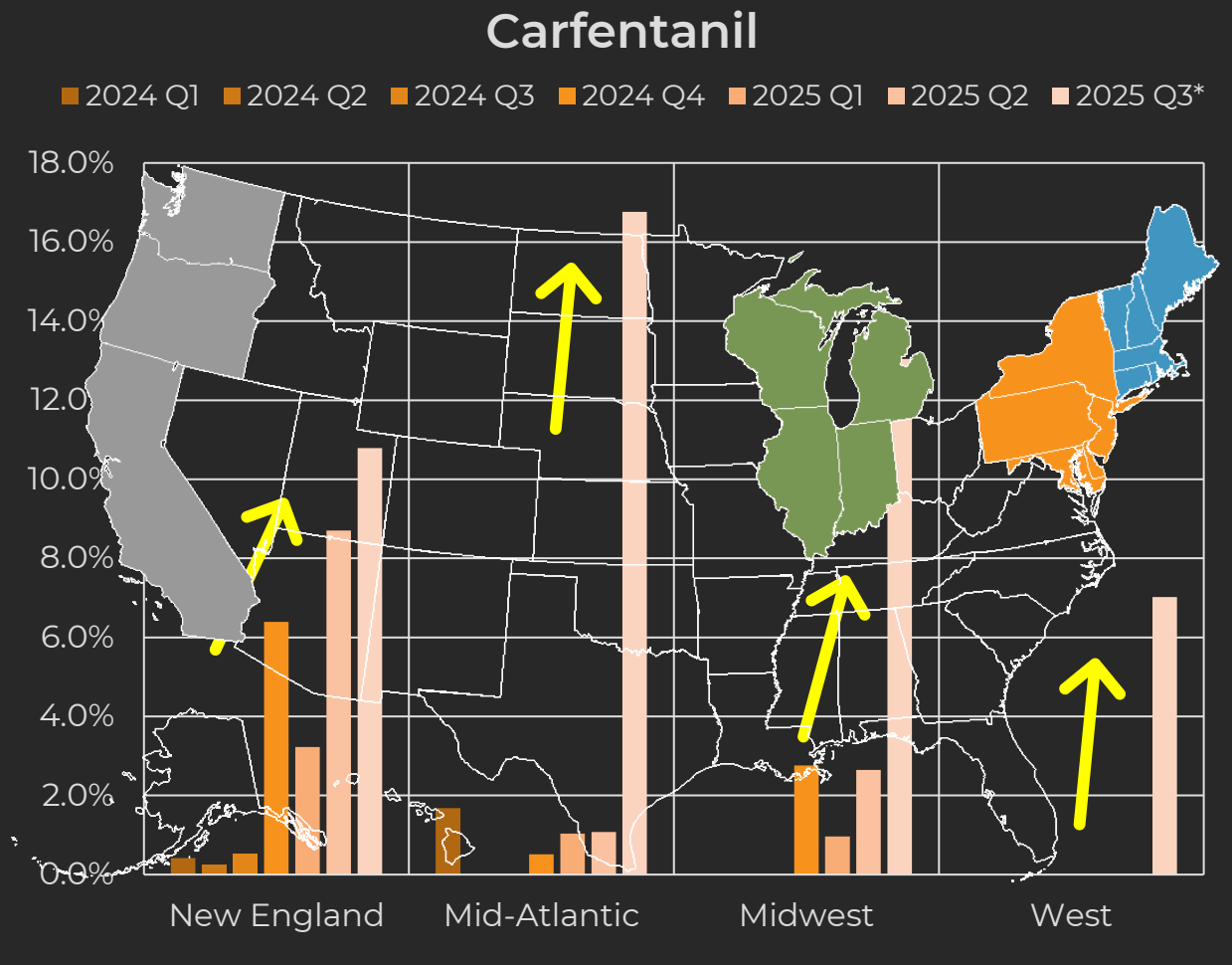






NITAZENES & CARFENTANIL



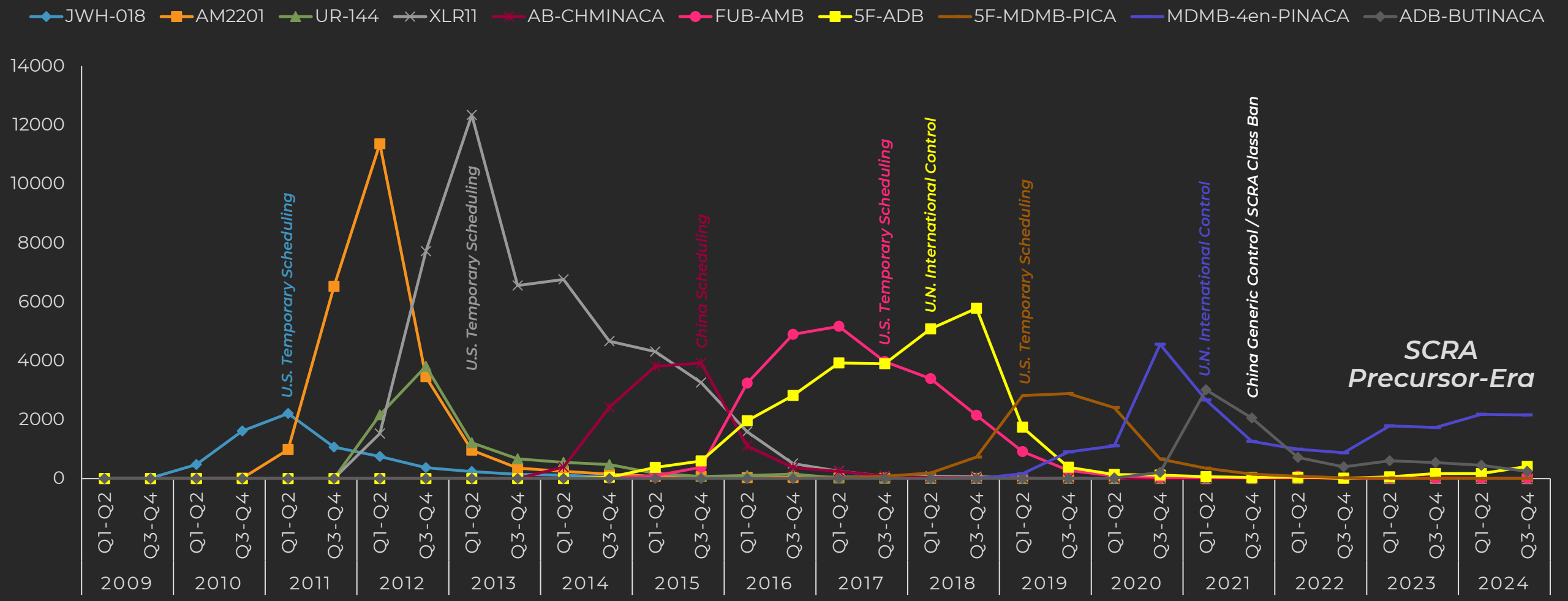


cfsre | NPS DISCOVERY

Source: CFSRE drug checking data.

The North American opioid crisis continues – fueled by fentanyl but exacerbated by potent novel synthetic opioids

SYNTHETIC CANNABINOIDS

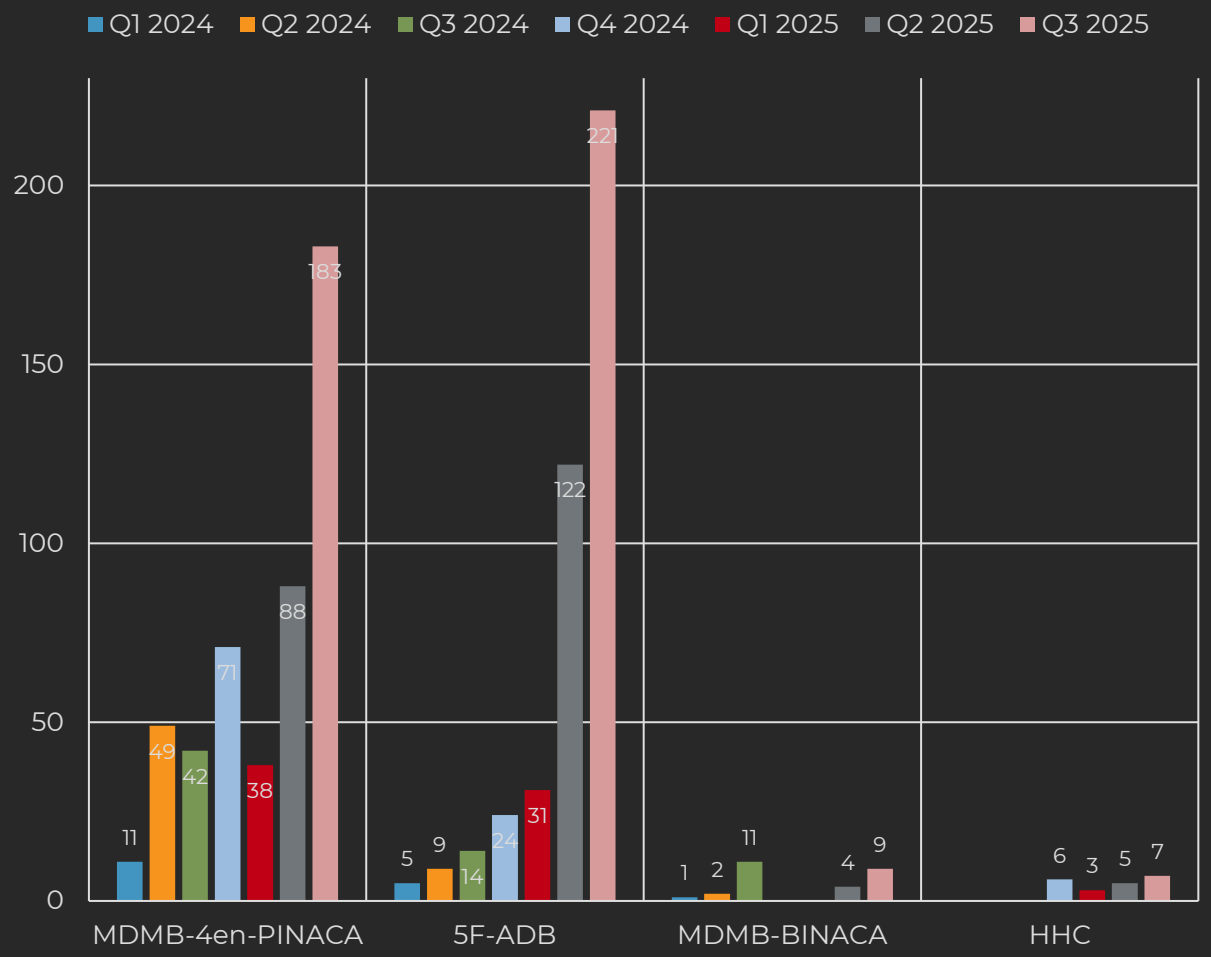


cfsre | NPS DISCOVERY

Source: DEA/NFLIS crime lab data.

JAIL & PRISON DEATHS INVOLVING SYN. CANN.

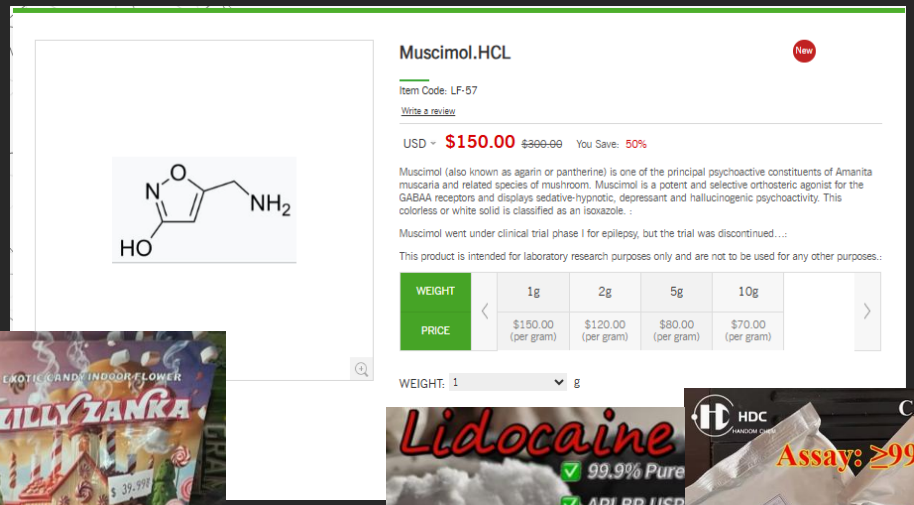
- **Increased number of deaths involving synthetic cannabinoids**
  - Fueled by use of precursors and (seemingly) domestic production
- **Cases analyzed in:**
  - 2023 = 7
  - 2024 = 30
  - 2025 (to date) = 40+
- **Able to provide answers for challenging or underdetermined death investigation cases**



The synthetic cannabinoid market is rebounding – contributing to increased jail and prison deaths

MISCELLANEOUS

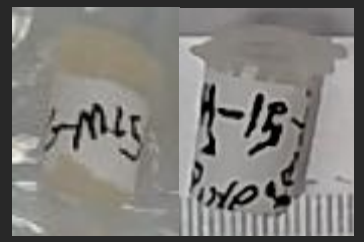
- **Plant-Based Substances**
  - Kratom alkaloids
  - Semi-synthetic cannabinoids
  - Kava alkaloids
- **Opioid Adulterants**
  - Medetomidine
  - Etomidate
  - Local Anesthetics
- **Edibles & Synthetics**
  - Psilocin & 4-AcO-DMT
  - Muscimol
  - Blue Lotus
- **Other Synthetic Drugs**
  - Dihydro-7-Hydroxy Mitragynine
  - Tianeptine
  - Phenibut
  - Nootropics

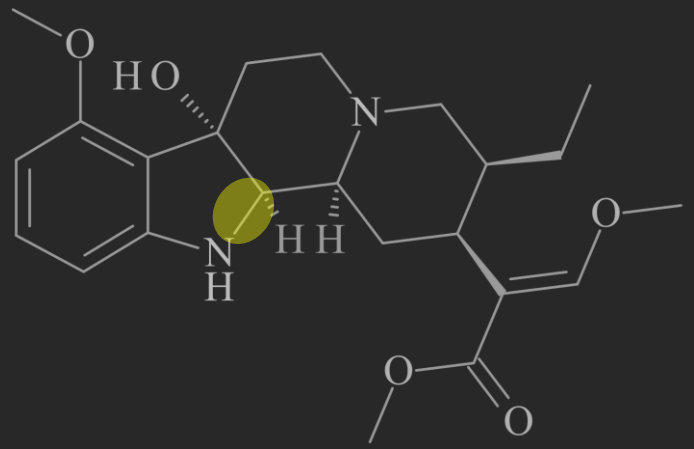


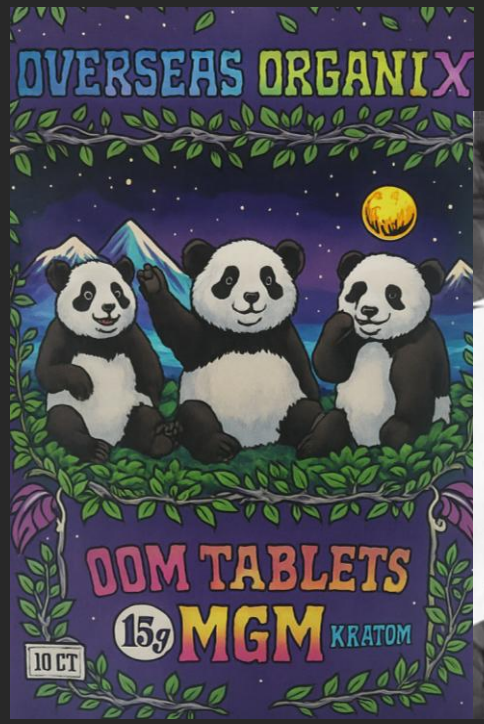
cfsre | NPS DISCOVERY

DIHYDRO-7OH MITRAGYNINE (MGM-15)

- Began hearing about “MGM-15” in August 2025
- **Two samples (drug checking):**
  - September 2nd – Plastic container labeled "MGM-15 RitPure“
  - September 2nd – Plastic container labeled "MG-M15"
- **Analytical Challenges:**
  - GC-MS: Conversion to mitragynine
  - LC-QTOF-MS: DH-7OH vs. 7OH M+2
- **First Fatal Intoxication:**
  - September 3rd, 2025 → New Jersey
  - History: Purchasing research chemicals
  - Results: DH-7OH (2,900 ng/mL), kratom, benzos

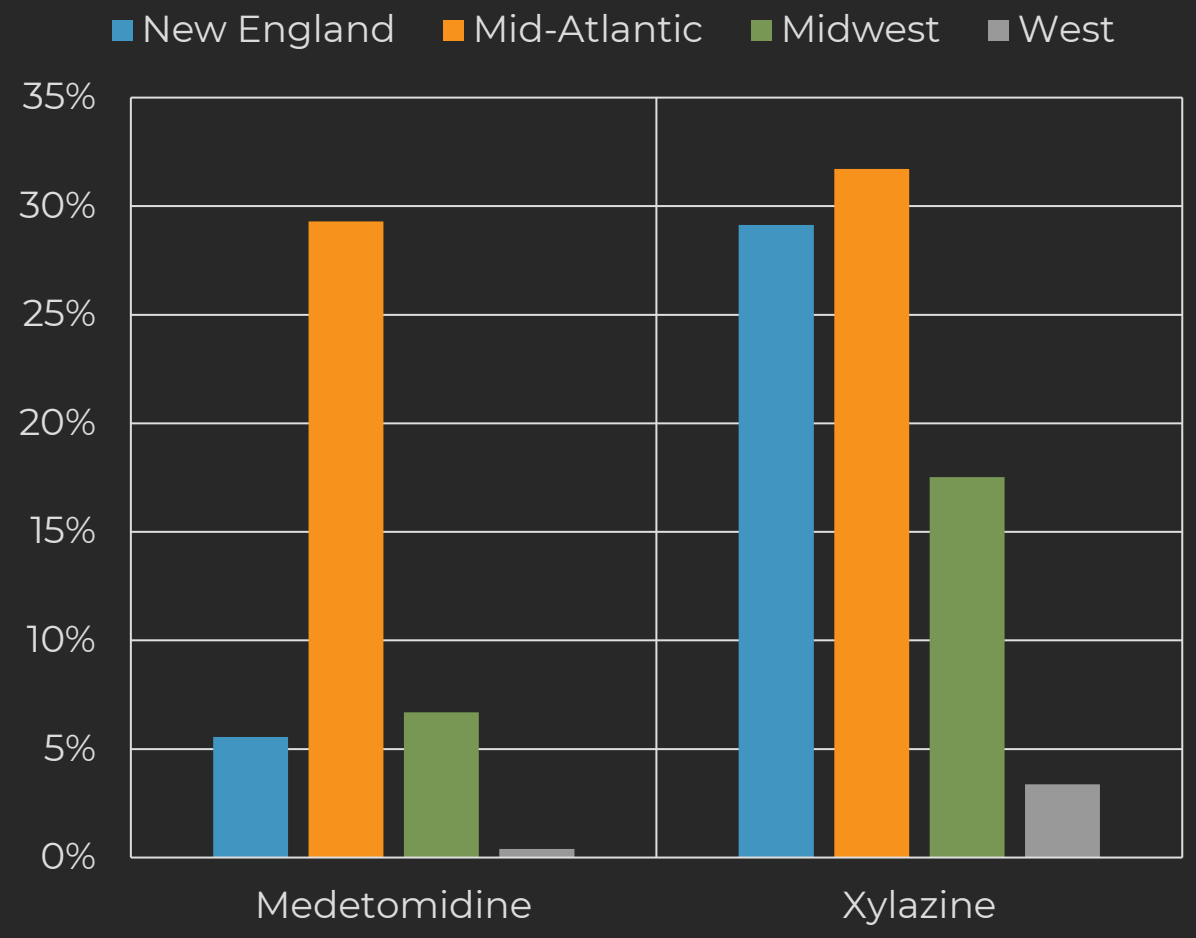


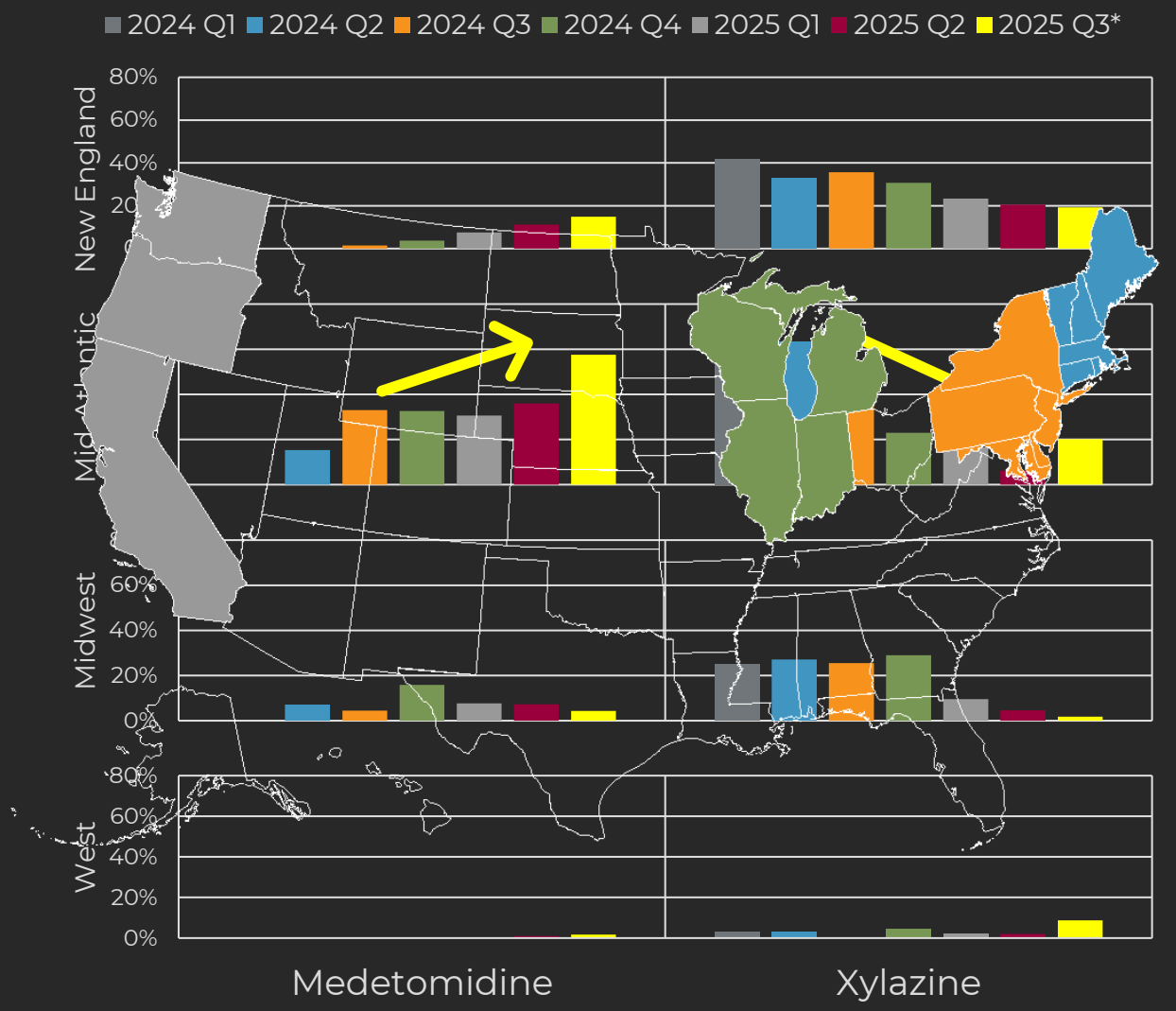




cfsre | NPS DISCOVERY

MEDETOMIDINE – TRENDS





MEDETOMIDINE – UNDERSTANDING ITS IMPACT

U.S. Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 74 / No. 15 May 1, 2025

Overdoses Involving Medetomidine Mixed with Opioids — Chicago, Illinois, May 2024

Amy Nham, PharmD[1,2,*]; John N. Le, PharmD[1,3,*]; Shawn A. Thomas, PhD[1,4]; Kimberly Gressick, MD[1,2]; Emily N. Ussery, PhD[5]; Jean Y. Ko, PhD[5]; R. Matt Gladden, PhD[5]; Christina A. Mikosz, MD[5]; Joshua G. Schier, MD[5]; Alana Vivolo-Kantor, PhD[5]; Maria Fiorillo, MPH[2]; McKenna McMaster, MPH[2]; Darlene Nolasco Magana, MBA, MPH[2]; Livia Verklan-McInnes[2]; Michael Wahl, MD[6]; Taylor Wood[7]; Axel Adams, MD[6,8]; Alex Krotulski, PhD[9]; Jordan Trecki, PhD[10]; Ross Ellison[11]; Roy Gerona, PhD[11]; Ponni Arunkumar, MD[12]; Mojde Mir, MS, MPH[12]; Leslie M. Wise, PhD[13]; Emma Betancourt, MPH[14]; Kathleen Monty[14]; Jhoanna Gulmatico, MSN[15]; Angie Pojas, MS, MBA[16]; Ruchi Fitzgerald, MD[17]; Miao Hua, MD, PhD[2]

Abstract

Medetomidine, a nonopioid sedative not approved for use in humans, has periodically been detected in illegally manufactured opioids across North America since 2022. On May 11, 2024, the Chicago Department of Public Health (CDPH) and the Illinois Department of Public Health were alerted by hospitals and the Illinois Poison Center to an increase in emergency medical services responses for suspected opioid-involved overdoses with atypical symptoms, mostly clustered on Chicago's West Side. CDPH and CDC investigated and identified 12 confirmed, 26 probable, and 140 suspected overdoses involving medetomidine mixed with opioids among patients treated at three hospitals in Chicago's West Side during May 11–17, 2024. Medetomidine had not been previously identified in Chicago's illegal drug supply. Fentanyl was identified in all drug samples and blood specimens containing medetomidine. Most patients were male, non-Hispanic Black or African American, and aged 45–64 years; most patients with confirmed cases experienced bradycardia and had no or only a partial response to naloxone. This cluster is the largest reported for confirmed medetomidine-involved overdoses. Multisector surveillance, including by health care providers, toxicology laboratories, and public health personnel, was essential for quickly identifying and responding to new adulterants in the illegal drug supply. Because all specimens and samples in this investigation that contained medetomidine also contained natural or synthetic opioids, administering naloxone for all suspected opioid-involved overdoses remains crucial.

* These authors contributed equally to this report.

Introduction

On May 11, 2024, the Chicago Department of Public Health (CDPH) and the Illinois Department of Public Health (IDPH) were alerted by the Overdose Detection Mapping Application Program† that 50 emergency medical services (EMS) responses for suspected opioid-involved overdoses occurred that day, a number more than two standard deviations above the 2023 daily average (27.4) in Chicago. Events were mostly clustered on Chicago's West Side. Area hospitals and the Illinois Poison Center (IPC) also notified CDPH of several patients observed with bradycardia and suspected opioid-involved overdose symptoms not fully reversed by naloxone during the weekend of May 11.

† The program, developed by the Office of National Drug Control Policy, links first responders and records management systems to a mapping tool to track overdoses and stimulate real-time response and strategic analysis across jurisdictions. ODMAP

Continuing Education examination available at https://www.cdc.gov/mmwr/mmwr_continuingEducation.html

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

CLINICAL TOXICOLOGY
https://doi.org/10.1080/15563650.2025.2500601
Taylor & Francis
SHORT COMMUNICATION

Clinical characteristics of patients exposed to medetomidine in the illicit opioid drug supply in Philadelphia – a case series

Lauren Murphy[a,b], Alex Krotulski[c,d], Brendan Hart[e], Matthew Wong[f], Rebeccah Overton[g] and Rita McKeever[a,b]

[a]Department of Emergency Medicine, Division of Medical Toxicology, Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA; [b]The Poison Control Center at Children's Hospital of Philadelphia, Philadelphia, PA, USA; [c]Center for Forensic Science Research and Education (CFSRE), Fredric Rieders Family Foundation, Horsham, PA, USA; [d]College of Life Sciences, Thomas Jefferson University, Philadelphia, PA, USA; [e]Department of Emergency Medicine, Division of Addiction Medicine, Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA; [f]Department of Emergency Medicine, Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA; [g]Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA

ABSTRACT

Introduction: Medetomidine is an emerging adulterant in the illicit opioid drug supply with minimal data regarding clinical effects or blood concentrations after uncontrolled exposures in humans.
Methods: A retrospective case series was performed of patients presenting to the emergency department after illicit opioid overdose with confirmed exposure to medetomidine. Patient outcomes and clinical data were summarized with descriptive statistics.
Results: Eleven patients were included in the series. Whole blood medetomidine concentrations ranged from 1.2 µg/L to 16 µg/L. Patients had sinus bradycardia for a median of 3.4 h, and hypotension was not common. Six cases were admitted to the hospital, one to the intensive care unit, and all survived. All cases tested positive for fentanyl and xylazine, and other adulterants were common.
Discussion: Sinus bradycardia was the most salient finding of patients with confirmed medetomidine exposure from the illicit opioid supply. Bradycardia resolved within the expected five half-lives determined by early drug studies, and no patient required atropine, electrical pacing, or vasopressors for hypotension. The duration and degree of bradycardia did not correlate well with medetomidine concentrations.
Conclusion: In this retrospective case series, patients who tested positive for medetomidine had sinus bradycardia and required prolonged monitoring.

ARTICLE HISTORY
Received 4 March 2025
Revised 14 April 2025
Accepted 27 April 2025

KEYWORDS
Drug overdose; drug toxicity; levomedetomidine; medetomidine; substance-related disorders

Introduction

Medetomidine was first detected as an adulterant in blood samples taken from suspected illicit opioid overdose patients in Missouri, Colorado, and Pennsylvania in August 2022 and rapidly proliferated in 2024 [1,2]. Medetomidine is the racemic mixture of the more familiar sedative dexmedetomidine and its enantiomer, levomedetomidine. It is an α_2-adrenergic receptor agonist used in veterinary medicine for sedation and anesthesia but is not approved for human use [3]. An alert issued by the Philadelphia Department of Public Health in May 2024 indicated medetomidine had been detected in the illicit opioid supply stating a concern that patients may be at risk for bradycardia, hypotension, and prolonged sedation [4].

The purpose of this paper is to describe the clinical characteristics of patients who tested positive for medetomidine after presenting to the emergency department after illicit opioid overdose.

Methods

As part of ongoing public health surveillance, de-identified, waste blood samples from patients presenting with atypical features after presumed opioid overdose within a single university health system are sent to a local forensic laboratory for testing on a continuous basis. Discarded blood samples are analyzed at the Center for Forensic Science Research and Education (Horsham, PA). Samples are first analyzed using non-targeted acquisition by liquid-chromatography quadrupole time-of-flight mass spectrometry against an in-house library database of more than 1,200 targets. Samples testing positive for substances of interest (e.g., fentanyl, xylazine, and novel agents) are secondarily analyzed by liquid chromatography tandem quadrupole mass spectrometry to determine concentration of drug.

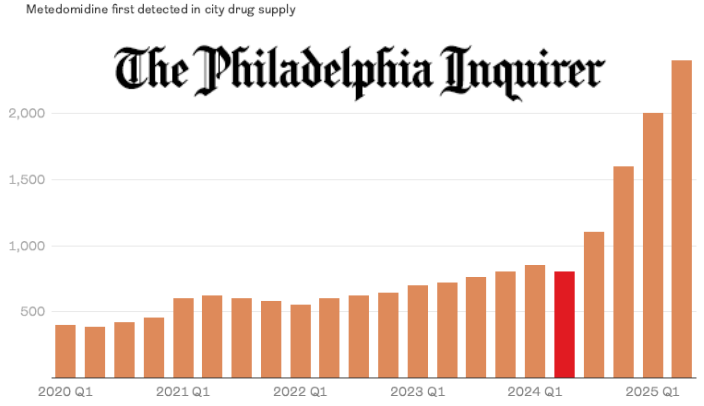
From April 29, 2024, to May 12, 2024, patients presenting to the emergency department with opioid overdose and bradycardia of 50 beats/min or less for at least one measurement,

CONTACT Lauren Murphy ltm8j@virginia.edu Department of Emergency Medicine, Division of Medical Toxicology, Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA.

Withdrawal Cases Soar in Hospitals, While Skin Damage Wanes

Over the last year, as medetomidine quickly replaced xylazine, also known as "tranq," in Philly's street drug supply, emergency rooms saw a stark shift. Cases where drug-addicted patients came in with soft-tissue damage — an injury widely linked to xylazine — dropped by more than half. But the number of patients being admitted for severe withdrawal more than tripled in the same period.

ER Visits for Drug-Related Withdrawal | ER Visits for Drug-Related Skin Damage



Note: Quarterly totals are rounded estimates based on data obtained through a Right-to-Know request.
Chart: Max Marin/Staff • Source: Philadelphia Department of Public Health

Philadelphia's rapidly changing and increasingly toxic drug supply often acts as a bellwether for other U.S. cities. The city was among the first to see overdose deaths spike after fentanyl, a potent synthetic opioid, emerged last decade, and has spent the last five years trying to respond to xylazine.

cfsre | NPS DISCOVERY

New subclasses of NPS are emerging – causing harm and mortality amongst knowing and naïve users

DEATH CASE INVOLVING NPS

cfsre | NPS DISCOVERY

DEATH CASE

CASE SYNOPSIS

- **20 y.o. male – college student**
  - History of purchasing drugs online
  - Purchased a variety of substance
  - Sell or distribute amongst friend and community
- **Intended to purchase "quaaludes"**
  - Schedules a time to try with his girlfriend
  - Snorted substance twice
  - Girlfriend decided not to use
  - [Gave some to a friend]
- **Next morning – found unresponsive in bed**

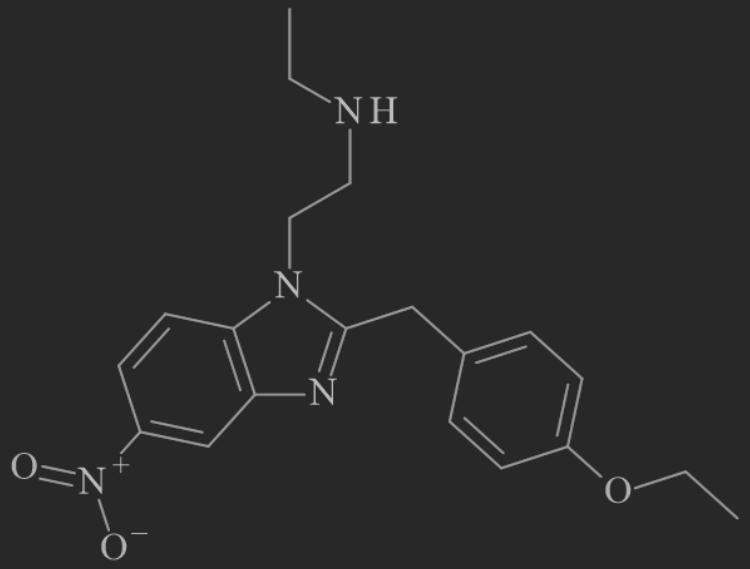
AUTOPSY FINDINGS

- No evidence of injury
- **Severe cerebral (brain) edema**
- **Severe pulmonary (lung) edema**
- Drugs and paraphernalia found at scene
  - History of drug use

CASE #3

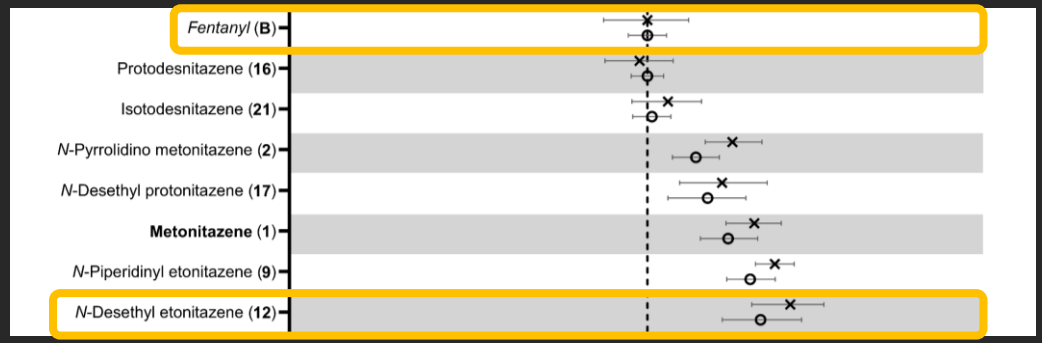
TOXICOLOGY RESULTS

- **Peripheral Blood:**
  - Methamphetamine (<10 ng/mL)
  - Ketamine (50 ng/mL) & Norketamine (43 ng/mL)
  - ***N*-Desethyl Etonitazene (est. ~10 ng/mL)**
  - 2F-2oxo-PCE
- **Urine:**
  - Methamphetamine
  - Ketamine + metabolite
  - ***N*-Desethyl Etonitazene**
  - 2F-2oxo-PCE



DEATH CERTIFICATION

- **Manner of Death:**
  - Accident
- **Cause of Death:**
  - *N*-Desethyl etonitazene and 2F-2oxo-PCE intoxication



doi.org/10.1007/s00204-024-03774-7

CONCLUDING REMARKS

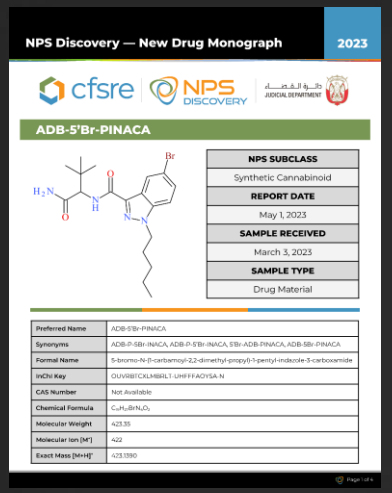
cfsre | NPS DISCOVERY

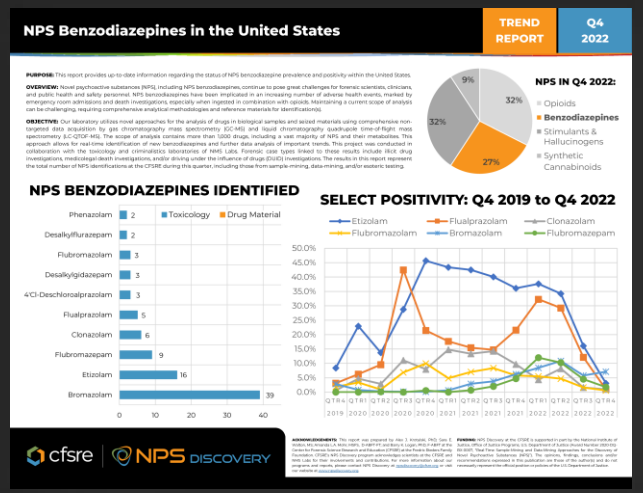
CONCLUDING REMARKS

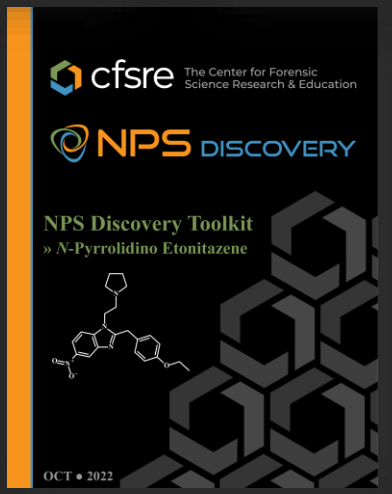
- The U.S. drug market remains **dynamic**, **geographically diverse**, and **variable over time**
  - **Converging trilogy:** Street drugs, smoke shop drugs, and online drugs
- **NPS** continue to emerge at a **steady rate**; however, major market influences are now common
  - **Opioids:** Fentanyls ▸ Nitazenes ▸ Orphine Analogues
  - **Cannabinoids:** MDMB-4en-PINACA, 5F-ADB
  - **Miscellaneous:** Mitragynine alkaloids, medetomidine
- Today, **single-drug intoxications** are rare for NPS in the U.S., especially as **co-occurrence** with other drugs and NPS increase
- **Collaboration, collaboration, collaboration**
  - **Forensic, public health, public safety, medicine, law, & others!**

NPS DISCOVERY REPORTS

WWW.NPSDISCOVERY.ORG

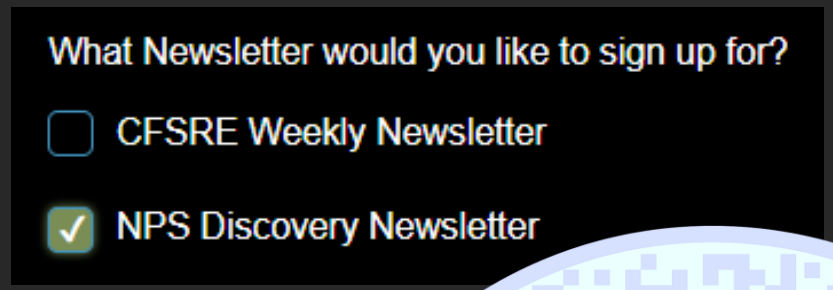






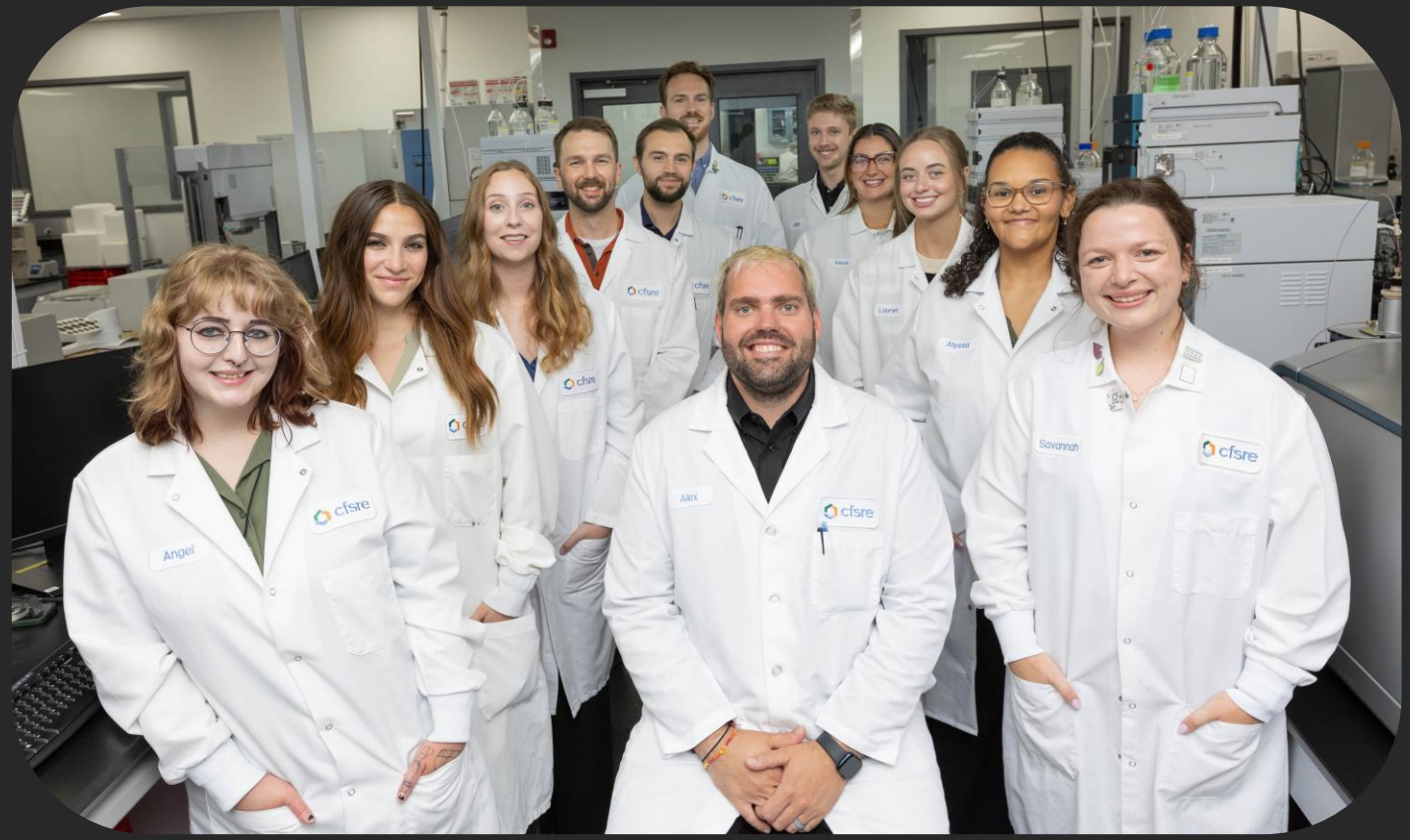
cfsre | NPS DISCOVERY

RECEIVE REAL-TIME UPDATES VIA EMAIL



ACKNOWLEDGEMENTS

- **CFSRE Toxicologists & Chemists**
  - Barry Logan, Sara Walton, Josh DeBord, Brianna Stang, Max Denn, & many others!
- **NMS Labs**
  - Donna Papsun & others
- **Funding Agencies**
  - National Institute of Justice (NIJ)
  - CDC, NIH, FDA, etc.
- **Collaborators & Partners**



NIJ | NATIONAL INSTITUTE OF JUSTICE
ADVANCING JUSTICE THROUGH SCIENCE

cfsre | NPS DISCOVERY

THANK YOU! QUESTIONS?

Alex J. Krotulski, Ph.D.
Director – Toxicology & Chemistry – CFSRE
Program Manager – NPS Discovery
alex.krotulski@cfsre.org