



# An Open Access Drug Early Warning System – Tracking Trends and Prevalence in the United States

NADDI Webinar Learning Series – Thursday July 13, 2023, from 1:00 to 2:00 PM ET

**Alex J. Krotulski, Ph.D.** – Center for Forensic Science Research and Education (CFSRE)



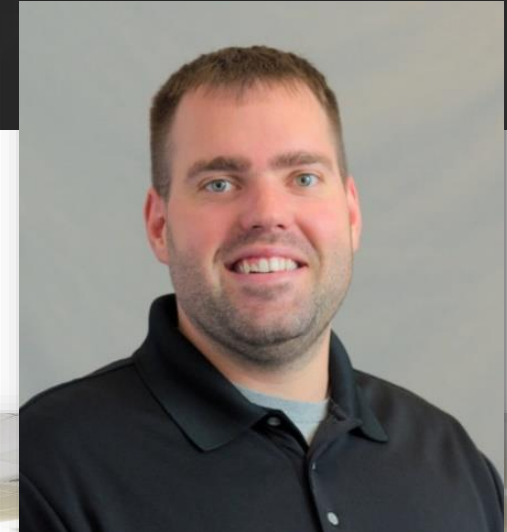
# INTRODUCTION

- **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



# 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-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.

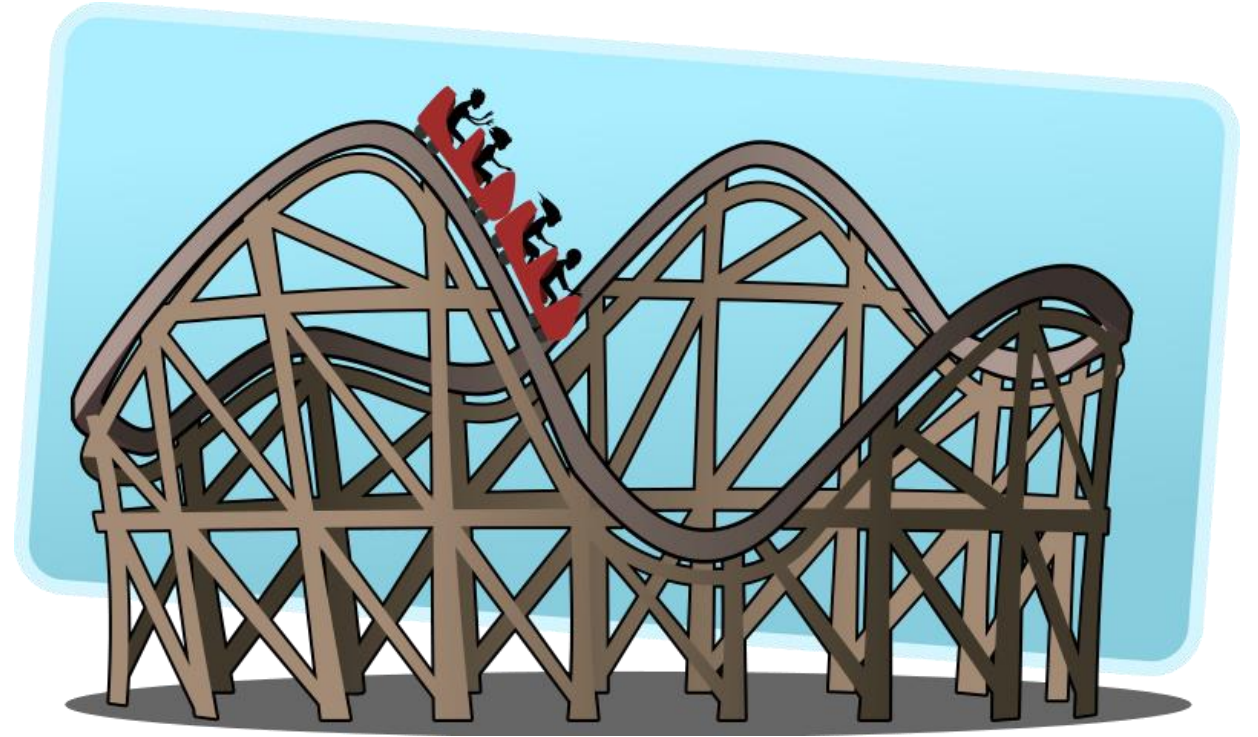


**NIJ** | *National Institute  
of Justice*

STRENGTHEN SCIENCE. ADVANCE JUSTICE.

# PRESENTATION OUTLINE

- The CFSRE and NPS Discovery
  - Analytical Workflows and Our Approach
- NPS Trends, Positivity, and Prevalence
- Impacts, Outcomes, and Reporting
  - NPS Opioids
  - Synthetic Cannabinoids
  - Xylazine
  - Drug Checking Surveillance (*if time*)
- Where To Find Us !!





# THE CFSRE & NPS DISCOVERY



# THE CFSRE & OUR LAB

- The Center for Forensic Science Research and Education (CFSRE)
  - 501(c)(3) non-profit research and educational facility
  - Home to *NPS Discovery* and other programs



Waters Xevo® G2-S LC-QTOF-MS



Sciex X500R LC-TOF-MS



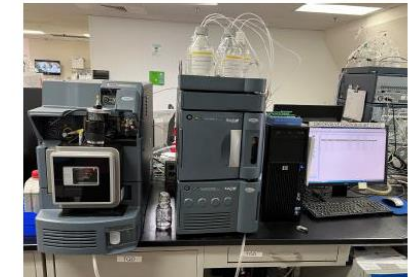
Sciex TripleTOF® 5600+ LC-TOF-MS



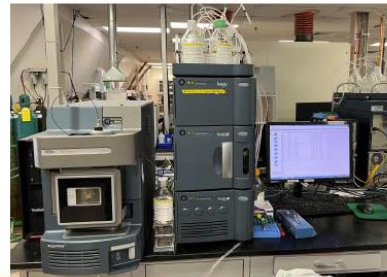
Agilent 6495 LC-QQQ-MS



Agilent 6430 LC-QQQ-MS



Waters TQS LC-QQQ-MS



Waters TQD LC-QQQ-MS



Agilent 5975 GC-MS



Agilent 5975 GC-MS

# EXAMPLES OF SAMPLE “POPULATIONS”

- **Important → Right populations paired with good intelligence**
- **Toxicology Specimens:**
  - Collaborations with medical examiner and coroner offices, other toxicology labs, clinical partners, and other
  - Example: Initial toxicology testing negative but “suspected overdose”
- **Drug Materials:**
  - Collaborations with crime labs, law enforcement agencies public health partners, and others
  - Routine analysis vs. chemical characterization (structural elucidation)
- **Intelligence & Surveillance:**
  - Monitor online surface web gray market sites, drug use forums, etc.
  - Some correlation between sites and drug markets but delayed



# ANALYTICAL WORKFLOWS & STRATEGIES

## ▪ Sample-Mining (Prospective):

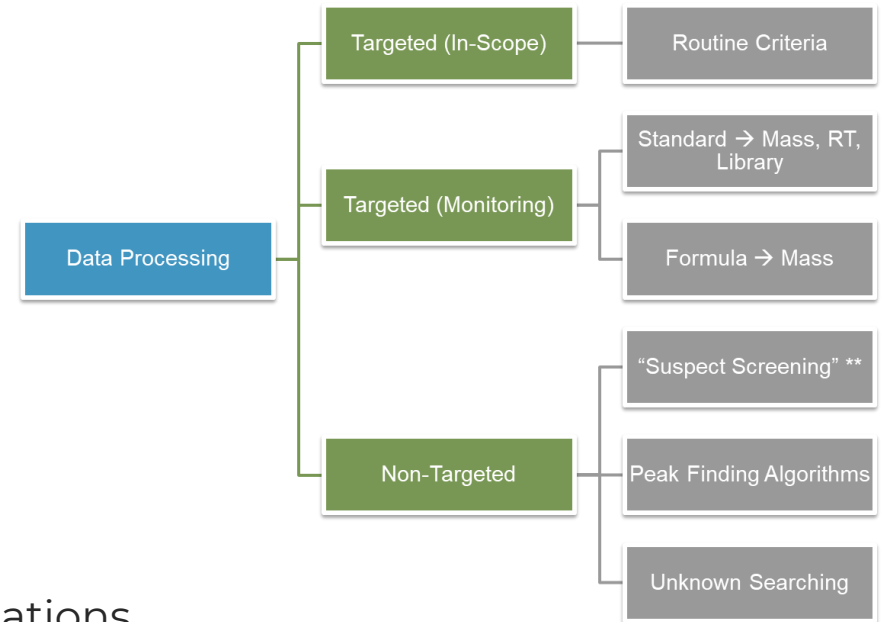
- Use of discarded authentic sample extract vials
- High-*ish* volume, higher rate of incidence
- Best for trend data (consistency)

## ▪ Data-Mining (Retrospective):

- Use of electronic datafiles
- Gives historical perspective
- Not ideal way to discover NPS

## ▪ Real-Time Surveillance / Case Analysis:

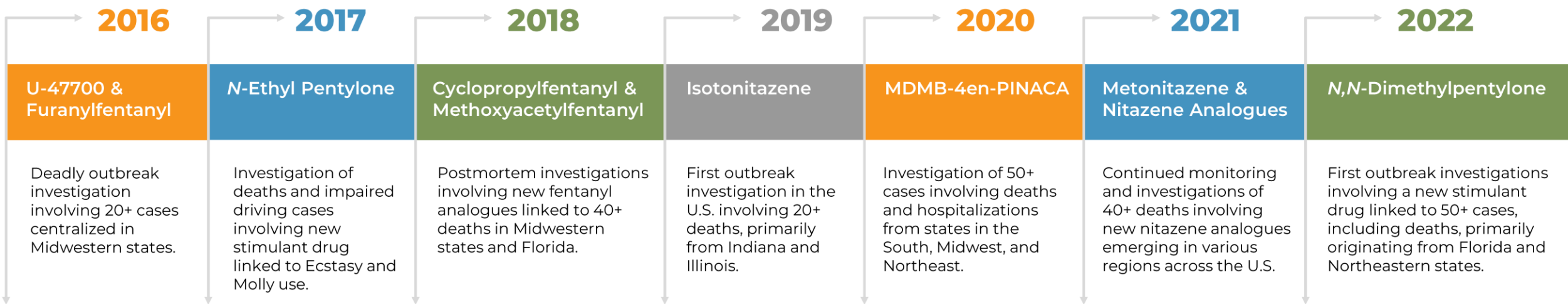
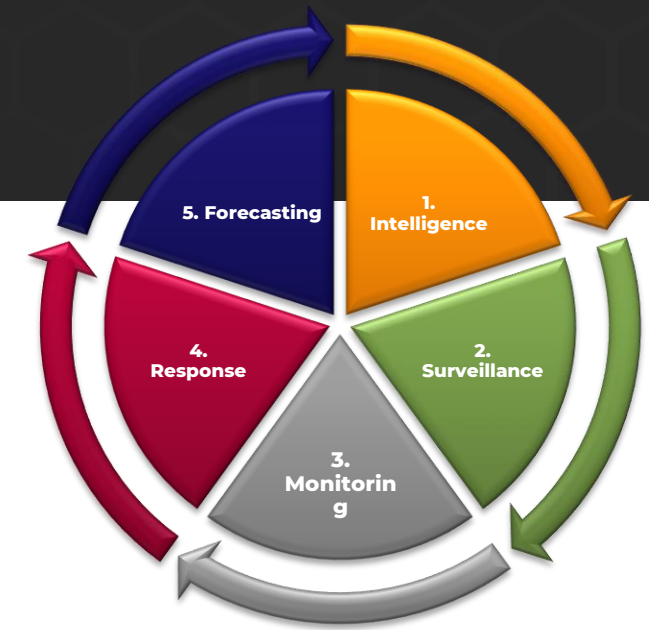
- Analysis of toxicology/chemistry samples from forensic investigations
- Individual case basis but often can give insights into trending information





# NPS DISCOVERY – THE CFSRE’S EWS

- Open-access drug early warning system (EWS)
  - Combine aspects of research & authentic cases
  - Analyze samples and generate data in-house
  - Develop a panel of high impact reports
  - Disseminate results and reports widely to stakeholders



# NECESSARY COMPONENTS OF A DRUG EARLY WARNING SYSTEM

- **Access to sample populations & data sources**

- Toxicology samples – forensic and clinical
- Drug materials – various distribution points
- Surveys and drug use information
- Online sources – drug fora, gray market sites, etc.

- **Framework that defines drugs of interest**

- NPS vs. traditional drugs vs. adulterants, etc.

- **Uniform reporting format and structure**

- **Research initiatives / research programs**



- **Dissemination avenues**

- Scientific community
- Public health and public safety
- Drug consuming populations and general public

- **Scientific and health expertise**

- Pharmacology
- Toxicology
- Medical treatment

- **Collaborations, cooperation, information sharing, and plan for action**

- Drug control and scheduling actions



# BRIEF HISTORY & TIMELINE

- 2017**
  - Development of LC-QTOF-MS assay for >400 drugs (including many NPS)
  - Began charactering NPS using GC-MS, LC-QTOF-MS, and/or NMR workflows
- 2018**
  - Development and dissemination of first new drug monograph for NPS
  - Formally launched our NPS Discovery program
- 2019**
  - Launched first NPS Discovery website pages to archive reports and data
  - Began issuing *Public Alerts* to scientific stakeholders and practitioners
- 2020**
  - Expanded *Trend Reporting* to include all five major subclasses of NPS
  - Continued data collections through onset of COVID-19 pandemic
- 2021**
  - Greatly expanding program outputs (including several new report types)
  - Library database expanded to encompass >950 drugs and NPS
- 2022**
  - Advancements in *Drug Checking* initiatives (e.g., purity testing, potency index)
  - Expansion of drug checking and clinical monitoring with new collaborators
- 2023**
  - Continued expansion of *Clinical/NPS* investigations (database >1,100 drugs)
  - Launch of *NPS Discovery Quarterly Webinar Series*



**NEW POTENT SYNTHETIC OPIOID—N-DESETHYL ISOTONITAZENE—PROLIFERATING AMONG RECREATIONAL DRUG SUPPLY IN USA**

**PURPOSE:** The objective of this announcement is to notify public health and safety law enforcement, first responders, clinicians, medical examiners and coroners, forensic and clinical laboratory personnel, and all other related construction about new information surrounding the emergent synthetic opioid **N-Desethyl Isotonitazene**.

**BACKGROUND:** Synthetic opioids (e.g., heroin, fentanyl) and other synthetic substances have caused a significant increase in overdose deaths and other adverse effects in the United States. Synthetic opioids are frequently mixed with more traditional opioids (e.g., heroin) and other drugs (e.g., benzodiazepines, alcohol, and stimulants) and are often sold in combination with other substances. Synthetic opioids may be distributed in multiple ways, including in the United States (U.S.), an increasing number of countries in North America, and other regions.

**SUMMARY:** N-Desethyl Isotonitazene is a new synthetic opioid having structural resemblance to Suboxone and recently emergent synthetic analogues. N-Desethyl Isotonitazene is classified as chemical structure to be tested for the synthetic opioid commonly encountered, but this subclass of new opioids is not presently in the table of identifying fentanyl analogues. N-Desethyl Isotonitazene is a known metabolite of Isotonitazene. However, it has now emerged as a primary drug in its own right. Most laboratory samples encountered have contained Isotonitazene and generic analogs in a greater than 100:1 ratio. **PHARMACOLOGICAL DATA:** Isotonitazene and N-Desethyl Isotonitazene are active opioid agonists with approximately 200 times greater analgesic activity in September 2022. N-Desethyl Isotonitazene was first identified by NPS Discovery Florida. However, first identification was obtained in early September 2022. To date, seven drug material samples ("drug") samples collected from the following drug supply have been reported for N-Desethyl Isotonitazene in December 2022 by the Pennsylvania Department of Health. Health alert on drug regarding the discovery of this new synthetic analogue in the U.S. drug supply. The toxicity of N-Desethyl Isotonitazene has not been confirmed in reported but recent association with overdose among persons who use drug. Health professionals should be alerted to monitor for use from and test for high-potency opioids.

**TIMELINE — N-DESETHYL ISOTONITAZENE ...**

Identified in urine specimen from a drug treatment program in PA, USA (September 2022)

Identified in oral fluid specimen collected from a person who uses drugs (October 2022)

Identified in a commercial "NPS" (November 2022)

Identified in "street" samples containing N-Desethyl Isotonitazene (December 2022)

Confirmed to be identified in "street" samples among Pennsylvania drug supply (January 2023)

**LOCATION PENNSYLVANIA, PA, USA**

**FLORIDA - PENNSYLVANIA**

**RECOMMENDATIONS FOR PUBLIC HEALTH:**

- Law enforcement should be alerted to monitor for use from and test for high-potency opioids.
- First responders should be alerted to monitor for use from and test for high-potency opioids.
- Clinicians should be alerted to monitor for use from and test for high-potency opioids.
- Medical examiners and coroners should be alerted to monitor for use from and test for high-potency opioids.
- Forensic and clinical laboratory personnel should be alerted to monitor for use from and test for high-potency opioids.
- All other related construction should be alerted to monitor for use from and test for high-potency opioids.

**RECOMMENDATIONS FOR LABORATORIES:**

- Law enforcement should be alerted to monitor for use from and test for high-potency opioids.
- First responders should be alerted to monitor for use from and test for high-potency opioids.
- Clinicians should be alerted to monitor for use from and test for high-potency opioids.
- Medical examiners and coroners should be alerted to monitor for use from and test for high-potency opioids.
- Forensic and clinical laboratory personnel should be alerted to monitor for use from and test for high-potency opioids.
- All other related construction should be alerted to monitor for use from and test for high-potency opioids.

**RECOMMENDATIONS FOR MEDICAL CONSUMERS:**

- Law enforcement should be alerted to monitor for use from and test for high-potency opioids.
- First responders should be alerted to monitor for use from and test for high-potency opioids.
- Clinicians should be alerted to monitor for use from and test for high-potency opioids.
- Medical examiners and coroners should be alerted to monitor for use from and test for high-potency opioids.
- Forensic and clinical laboratory personnel should be alerted to monitor for use from and test for high-potency opioids.
- All other related construction should be alerted to monitor for use from and test for high-potency opioids.

**NPS Discovery — New Drug Monograph** 2023

**ADB-5'Br-PINACA**

**NPS SUBCLASS**  
Synthetic Cannabinoid

**REPORT DATE**  
May 1, 2023

**SAMPLE RECEIVED**  
March 3, 2023

**SAMPLE TYPE**  
Drug Material

**Preferred Name** ADB-5'Br-PINACA

**Synonyms** ADB-P-5Br-INACA, ADB-P-5Br-INACA, 5'Br-ADB-PINACA, ADB-5'Br-PINACA

**Formal Name** 5-bromo-N-[2-carbamoyl-2-(dimethyl-propyl)-1-pentyl-indazole-3-carboxamide]

**InChI Key** CUV9BTCKLMBRLT LHMFFACVSA-N

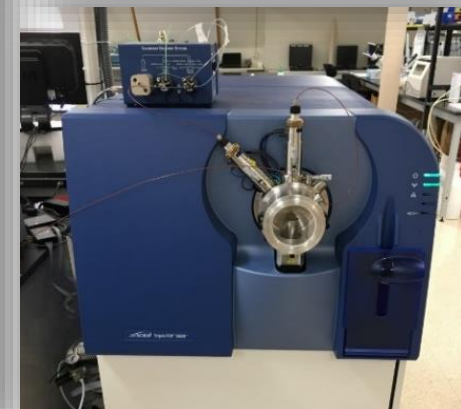
**CAS Number** Not Available

**Chemical Formula** C<sub>24</sub>H<sub>38</sub>BrN<sub>2</sub>O<sub>2</sub>

**Molecular Weight** 423.35

**Molecular Ion [M]** 422

**Exact Mass [M+H]<sup>+</sup>** 423.1390



# NPS DISCOVERY REPORTS

### NPS Discovery — New Drug Monograph 2023

#### ADB-5r-B-PINACA

**NPS SUBCLASS**  
Synthetic Cannabinoid

**REPORT DATE**  
May 1, 2023

**SAMPLE RECEIVED**  
March 3, 2023

**SAMPLE TYPE**  
Drug Material

Preferred Name	ADB-5r-B-PINACA
Synonyms	ADB-P-5r-B-PINACA, ADB-P-5r-B-PINACA, 5r-B-ADB-PINACA, ADB-5r-B-PINACA
Formal Name	5-Torono-N-[1-carbamoyl-2-(2-dimethylpropyl)propyl]-pentyl-indole-3-carboxamide
ICHI Key	OUVETBZMLBTLAFYACRYADYN
CAS Number	Not Available
Chemical Formula	C <sub>24</sub> H <sub>34</sub> N <sub>2</sub> O <sub>2</sub>
Molecular Weight	413.56
Molecular Ion (M <sup>+</sup> )	422
Exact Mass [M+H] <sup>+</sup>	413.190

### NPS Benzodiazepines in the United States

**PURPOSE:** This report provides up-to-date information regarding the status of NPS benzodiazepine prevalence and positivity within the United States.

**OVERVIEW:** Most synthetic benzodiazepines (NPS) are not included in the United States Drug Schedules, and their use is not regulated. However, they are often used to treat anxiety, insomnia, and pain. They are also used in the treatment of alcohol withdrawal and seizure disorders. They are often used in combination with opioids, increasing the risk of overdose and death. This report provides information on the prevalence and positivity of NPS benzodiazepines in the United States.

**OBJECTIVE:** Our laboratory utilizes a novel approach for the analysis of drugs in forensic samples and applied materials using comprehensive non-targeted MS/MS detection for gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS/MS). This approach allows for the identification of new benzodiazepines and further data analysis of important trends. This project was completed in collaboration with the toxicology and confirmation laboratories of H&M Labs. Forensic case files linked to these results include illicit drug investigations, investigation of death investigations, and/or during the course of drug (DUI) investigations. The results of this report represent the total number of NPS benzodiazepines identified in the United States during the quarter, including those from sample mining, data mining, and/or generic testing.

**TREND REPORT**

**Q4 2022**

**NPS in Q4 2022:**

- Opioids: 32%
- Benzodiazepines: 33%
- Stimulants & Hallucinogens: 27%
- Synthetic Cannabinoids: 9%

#### NPS BENZODIAZEPINES IDENTIFIED

Substance	Toxicology	Drug Material
Phenazepam	2	0
Desethylfurazepam	2	0
Flumazenil	3	0
Desethylclonazepam	3	0
4-CI-Deschlorazepam	3	0
Flutazolam	5	0
Clonazepam	6	0
Flurazepam	9	0
Etizolam	16	0
Bromazolam	39	0

#### SELECT POSITIVITY: Q4 2019 to Q4 2022

### Synthetic Stimulant Market Rapidly Changing as N,N-Dimethylpiperone Replaces Bupropion in Drug Supply

**Purpose:** The objective of this assessment is to identify public health and safety, law enforcement, and regulatory, clinical, and consumer risks associated with the rapid change in the synthetic stimulant market. This report provides information on the prevalence and positivity of N,N-Dimethylpiperone in the United States.

**Background:** Synthetic stimulants are chemically synthesized drugs that act on the central nervous system. They are often used to treat attention deficit hyperactivity disorder (ADHD) and depression. They are also used in the treatment of chronic pain and as a performance enhancer. They are often used in combination with opioids, increasing the risk of overdose and death. This report provides information on the prevalence and positivity of N,N-Dimethylpiperone in the United States.

**Summary:** In 2022 and 2021, the substituted cathinone class has the most recent reported incidents related to the use of synthetic stimulants. In 2022, the most common synthetic stimulant identified in the United States was N,N-Dimethylpiperone. In 2021, the most common synthetic stimulant identified in the United States was Bupropion. This report provides information on the prevalence and positivity of N,N-Dimethylpiperone in the United States.

### Recommended Scope for NPS Testing in the United States

**PURPOSE:** The objective of this report is to provide updated guidance in developing an appropriate analytical scope of testing for most psychotropic substances (NPS) in the United States based on current trends and emerging drug supply, prevalence, and manufacturing. To meet this need, this report provides information on the prevalence and positivity of NPS in the United States.

**Background:** The NPS market is rapidly changing, and new substances are being introduced into the market. This report provides information on the prevalence and positivity of NPS in the United States.

Substance	Prevalence	Positivity	Notes
Benzodiazepines	33%	15%	High prevalence, low positivity
Opioids	32%	25%	High prevalence, moderate positivity
Stimulants & Hallucinogens	27%	10%	High prevalence, low positivity
Synthetic Cannabinoids	9%	5%	Low prevalence, low positivity

### Toxic Fentanyl Study Group — Quarterly NPS Report

**CLINICAL**

**Q3 2022**

**PITTSBURGH, PA**

- 70% positive for at least one opioid
- Fentanyl (90%) commonly detected, followed by Heroin (20%) and Tramadol (20%)
- Opioid and stimulant use commonly detected (20%)
- NPS in Fluorazepam (20%), Clonazepam

**BETHLEHEM, PA**

- 70% positive for at least one opioid
- Fentanyl (80%) commonly detected, followed by Heroin (20%) and Tramadol (20%)
- Opioid and stimulant use commonly detected (20%)
- NPS in Fluorazepam (20%), Clonazepam

**NEW YORK, NY**

- 80% positive for at least one opioid
- Fentanyl (90%) commonly detected, followed by Heroin (20%) and Tramadol (20%)
- Opioid and stimulant use commonly detected (20%)
- NPS in Fluorazepam (20%), Clonazepam

**NEWARK, NJ**

- 80% positive for at least one opioid
- Fentanyl (90%) commonly detected, followed by Heroin (20%) and Tramadol (20%)
- Opioid and stimulant use commonly detected (20%)
- NPS in Fluorazepam (20%), Clonazepam

**ST. LOUIS, MO**

- 70% positive for at least one opioid
- Fentanyl (80%) commonly detected, followed by Heroin (20%) and Tramadol (20%)
- Opioid and stimulant use commonly detected (20%)
- NPS in Fluorazepam (20%), Clonazepam

**LOS ANGELES, CA**

- 70% positive for at least one opioid
- Fentanyl (90%) commonly detected, followed by Heroin (20%) and Tramadol (20%)
- Opioid and stimulant use commonly detected (20%)
- NPS in Fluorazepam (20%), Clonazepam

**GRAND RAPIDS, MI**

- 70% positive for at least one opioid
- Fentanyl (90%) commonly detected, followed by Heroin (20%) and Tramadol (20%)
- Opioid and stimulant use commonly detected (20%)
- NPS in Fluorazepam (20%), Clonazepam

### QUARTERLY REPORT — PHILADELPHIA, PA

**DRUG CHECKING**

**Q3 2022**

**136** samples checked

**49** positive for at least one opioid

**10** positive for at least one stimulant

**24** positive for at least one synthetic cannabinoid

### Fentanyl Purity, Potency, & Synthesis

**Real-Time Testing of Opioid Drug Products in the United States**

**WHAT IS FENTANYL?**

**WHAT ARE FENTANYL PRECURSORS, INTERMEDIATES, AND BYPRODUCTS?**

**WHAT ARE PURITY AND POTENCY?**

**HOW IS PURITY DETERMINED?**

**HOW DOES PURITY TESTING SUPPORT HARM REDUCTION?**

### NPS Discovery Toolkit

**N-Pyrrolidino Etizolam**

**Stamp™**

**Stamp™** is a rapid, accurate, and easy-to-use method for the detection and identification of NPS in forensic samples. It is a colorimetric assay that can be used to detect a wide range of NPS, including opioids, stimulants, and synthetic cannabinoids. The Stamp™ assay is easy to perform and can be used in a variety of settings, including law enforcement, forensic laboratories, and harm reduction programs.

### YEAR IN REVIEW 2022

**Since 2016, NPS Discovery has reported 137 newly discovered NPS in the United States (Figure 1). NPS opioids remain the largest subclass (Figure 2). In 2022, NPS Discovery reported the discovery of 21 NPS for the first time.**

**Since 2016, NPS Discovery has identified 338 NPS in forensic samples (Figure 3). NPS opioids, stimulants, and cannabinoids represent the largest subclasses observed in 2022. 76 total NPS were detected (Figure 4).**

**In 2022, NPS Discovery observed more than 2,200 total NPS detections within examined sample populations (Figure 5). A portion of more than 10,000 total NPS detections since our program launched in 2016 (Figure 6).**



# YEAR IN REVIEW ▶

## YEAR IN REVIEW 2022

**Purpose:** This report provides cumulative and updated statistics about the emergence and landscape of novel psychoactive substances (NPS) in the United States based on data developed by NPS Discovery at the CFSRE — a premier open-access drug early warning system utilizing an evidence-based approach to disseminate information for real-time public health and safety actions.

Since 2018, NPS Discovery has reported **137** newly discovered NPS in the United States (Figure 1). **NPS opioids** remain the largest subclass (Figure 2). In 2022, NPS Discovery reported the discovery of **21** NPS for the first time.

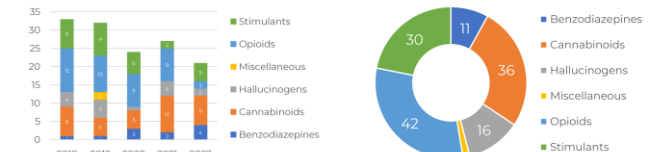


Figure 1: Newly discovered NPS reported for the first time since 2018.

Figure 2: Breakdown by subclass of newly discovered NPS, 2018-2022.

Since 2018, NPS Discovery has identified **218** NPS in forensic samples (Figure 3). **NPS opioids, stimulants, and cannabinoids** represent the largest subclasses observed. In 2022, **76** total NPS were detected (Figure 4).



Figure 3: Breakdown by subclass of individual NPS detected, 2018-2022.

Figure 4: Individual NPS detected each year, cumulative since 2018.

In 2022, NPS Discovery observed more than **2,200** total NPS detections within examined sample populations (Figure 5), a portion of more than **10,000** total NPS detections since our program launched in 2018 (Figure 6).

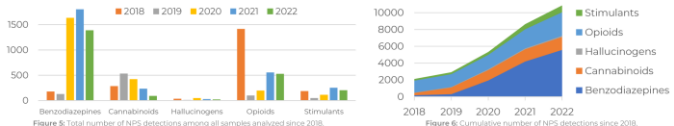


Figure 5: Total number of NPS detections among all samples analyzed since 2018.

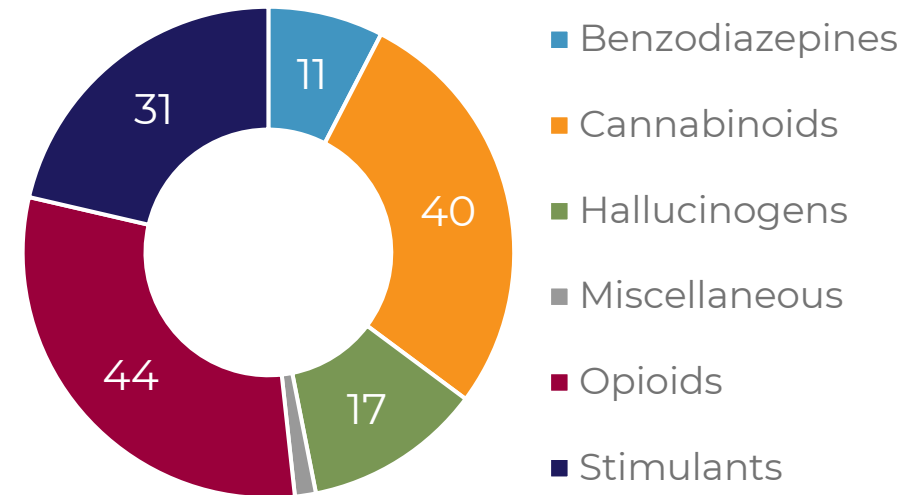
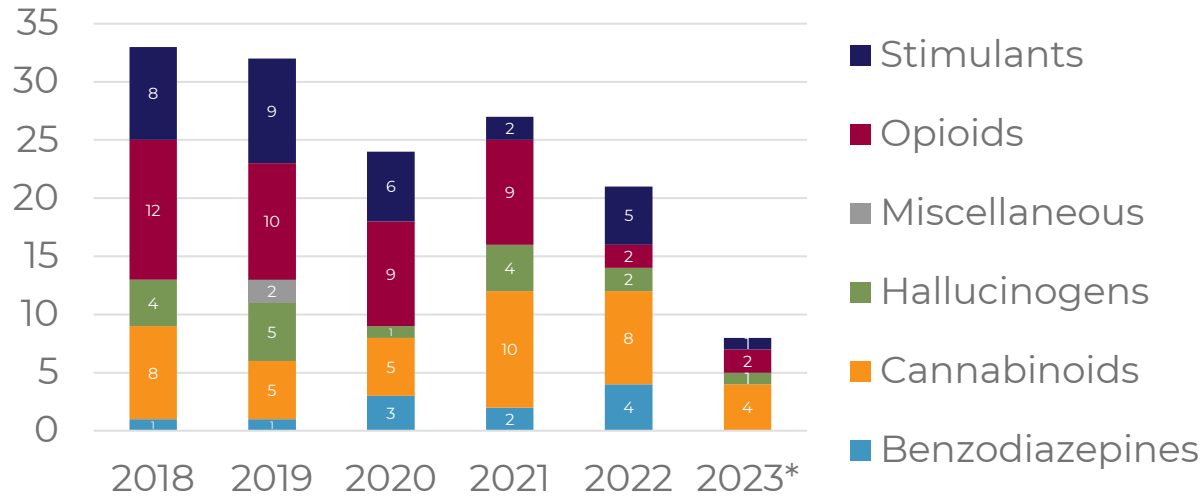
Figure 6: Cumulative number of NPS detections since 2018.

**ACKNOWLEDGMENTS:** The report was prepared by the Center for Forensic Science Research and Education (CFSRE) at the University of New Hampshire. CFSRE is supported in part by the National Institute of Justice, Office of Justice Programs, U.S. Department of Justice, and the U.S. Department of Health and Human Services, Office of the Inspector General. The authors acknowledge the support of the CFSRE for their contributions to this report.

**DISCLAIMER:** NPS Discovery is a service provided by the U.S. Department of Justice, Office of Justice Programs, U.S. Department of Health and Human Services, Office of the Inspector General. The information contained herein is for informational purposes only and does not constitute an offer of any product or service. The information is not intended to be used for any purpose other than that for which it was provided. The information is not intended to be used for any purpose other than that for which it was provided. The information is not intended to be used for any purpose other than that for which it was provided.

# EMERGENCE OF NPS IN THE U.S.

- Since 2018, NPS Discovery has reported **145** newly discovered NPS (and counting)
- **NPS opioids** remain the largest subclass of newly emerging drugs encountered
- As of June 2023, NPS Discovery has reported **8** NPS for the first time this year



# NEW DRUG MONOGRAPHS – 2023

Date	NPS Class	Drug Name	Formula	[M+]	[M+H] <sup>+</sup>
06/28/2023	Cannabinoid	<b>CHO-4'Me-5'Br-FUBOXPYRA</b>	C <sub>20</sub> H <sub>22</sub> BrFN <sub>2</sub> O <sub>2</sub>	420	421.0921
06/27/2023	Cannabinoid	<b>MDMB-BINACA</b>	C <sub>19</sub> H <sub>27</sub> N <sub>3</sub> O <sub>3</sub>	345	346.2125
06/26/2023	Cannabinoid	<b>MDMB-INACA</b>	C <sub>15</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub>	289	290.1499
06/23/2023	Opioid	<b>N-Pyrrolidino Metonitazene</b>	C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> O <sub>3</sub>	380	381.1921
06/22/2023	Opioid	<b>N-Pyrrolidino Protonitazene</b>	C <sub>23</sub> H <sub>28</sub> N <sub>4</sub> O <sub>3</sub>	408	409.2234
06/21/2023	Hallucinogen	<b>25B-NBOH</b>	C <sub>17</sub> H <sub>20</sub> BrNO <sub>3</sub>	365	366.0699
06/20/2023	Stimulant	<b>4-Methylmethylphenidate</b>	C <sub>15</sub> H <sub>21</sub> NO <sub>2</sub>	247	248.1645
05/01/2023	Cannabinoid	<b>ADB-5'Br-PINACA</b>	C <sub>19</sub> H <sub>27</sub> BrN <sub>4</sub> O <sub>2</sub>	422	423.1390

# LANDSCAPE OF NPS IN THE U.S.

- Since 2018, NPS Discovery has identified **more than 225** NPS in forensic samples
- **NPS opioids**, **stimulants**, and **cannabinoids** represent the largest subclasses observed

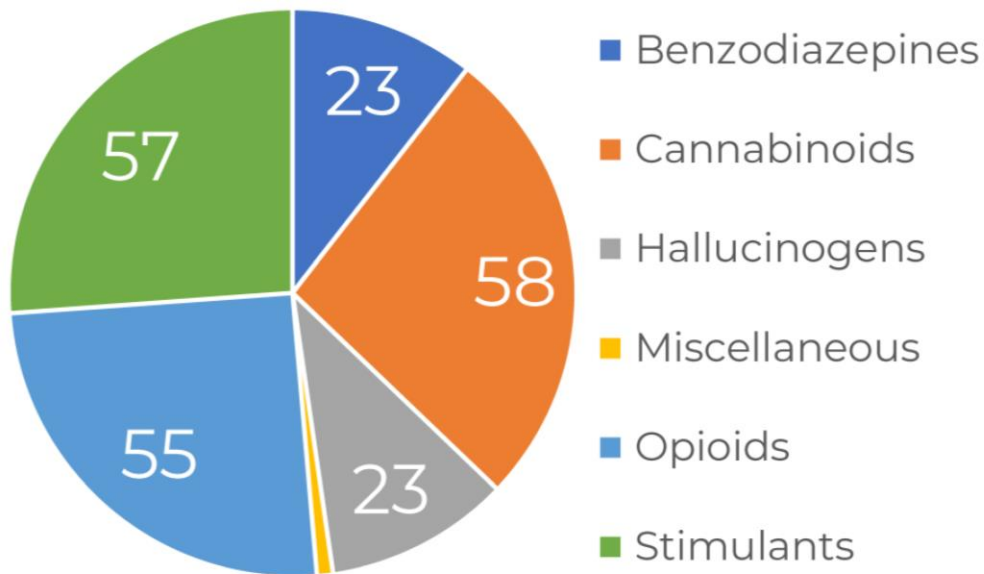


Figure 3: Breakdown by subclass of individual NPS detected, 2018-2022.

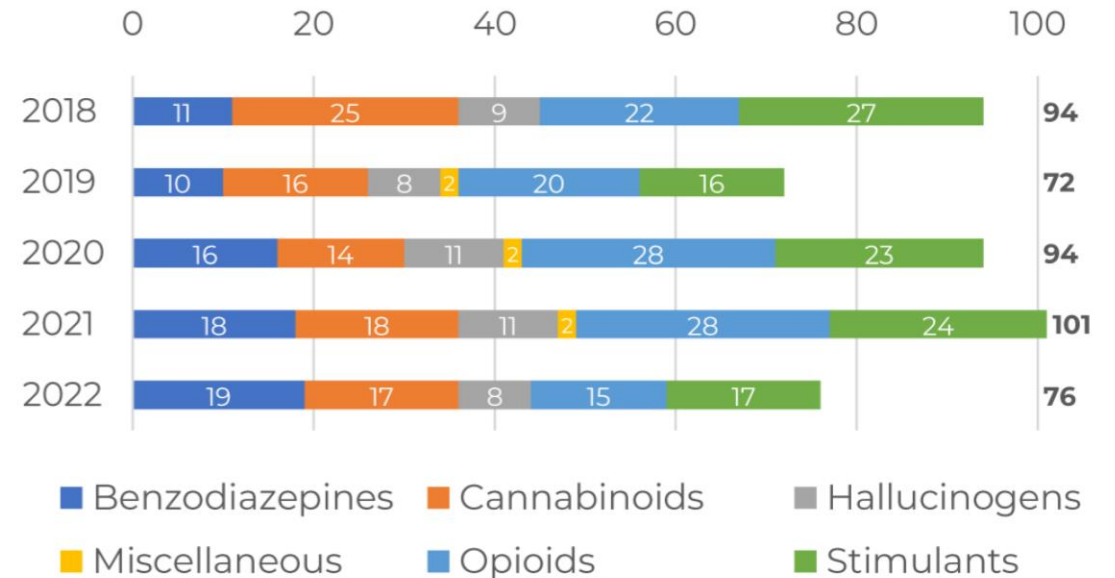


Figure 4: Individual NPS detected each year, cumulative since 2018.



# PROLIFERATION OF NPS IN THE U.S.

- In 2022, NPS Discovery observed more than **2,200** total NPS detections
- A portion of more than **10,000** total NPS detections since 2018

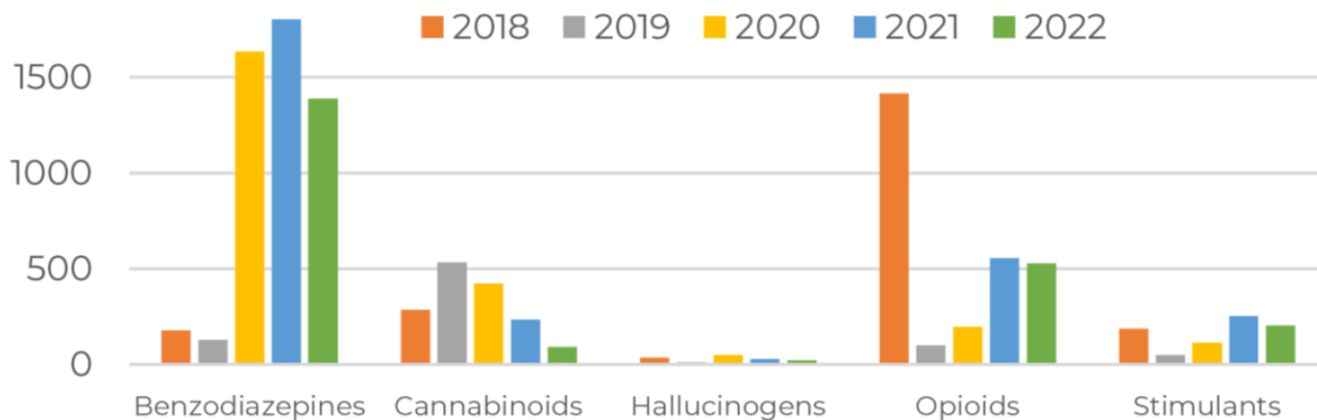


Figure 5: Total number of NPS detections among all samples analyzed since 2018.

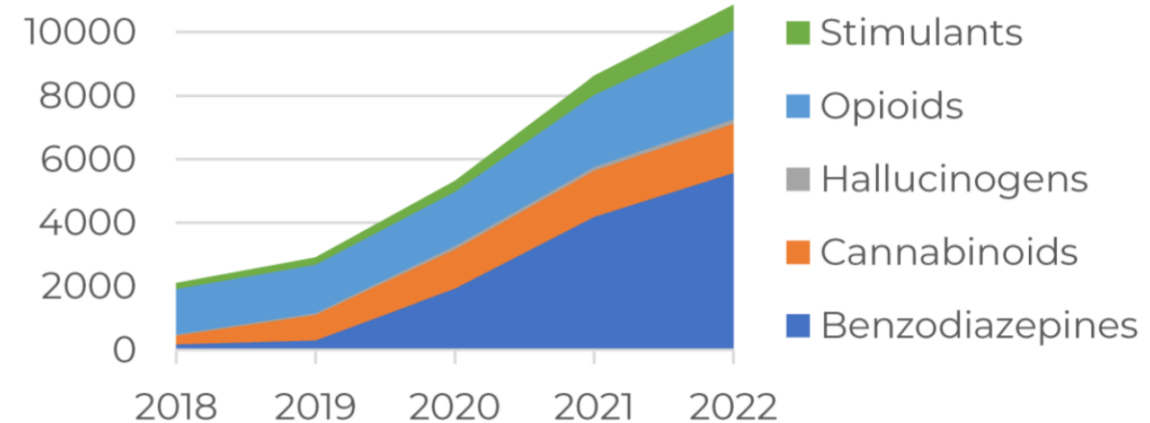


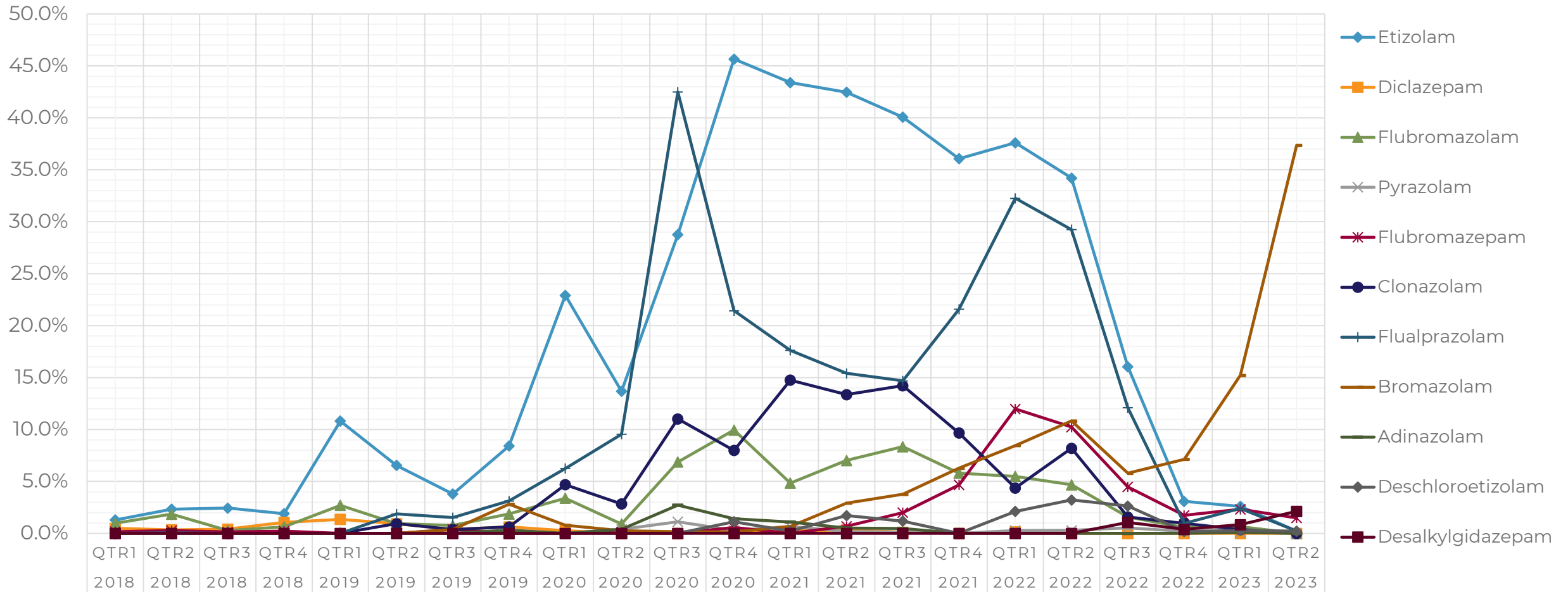
Figure 6: Cumulative number of NPS detections since 2018.



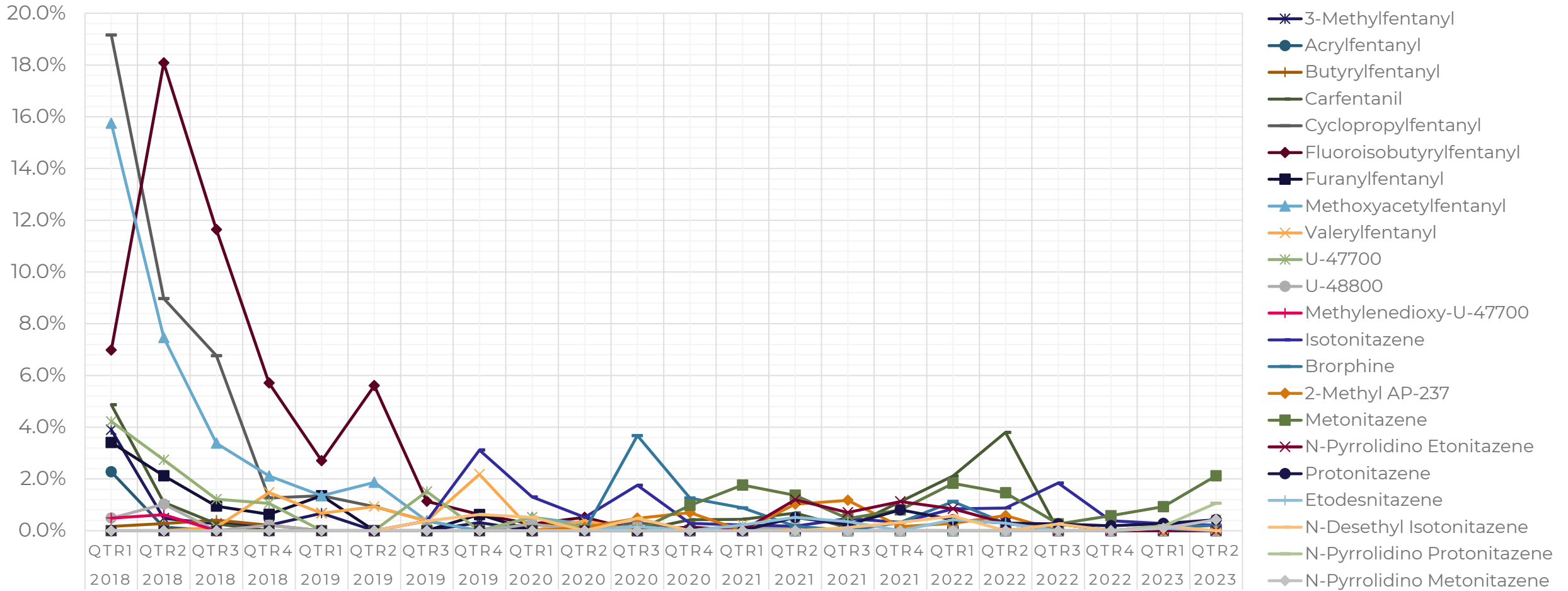
# POSITIVITY PLOTS SINCE 2018



# POSITIVITY PLOTS – NPS BENZODIAZEPINES

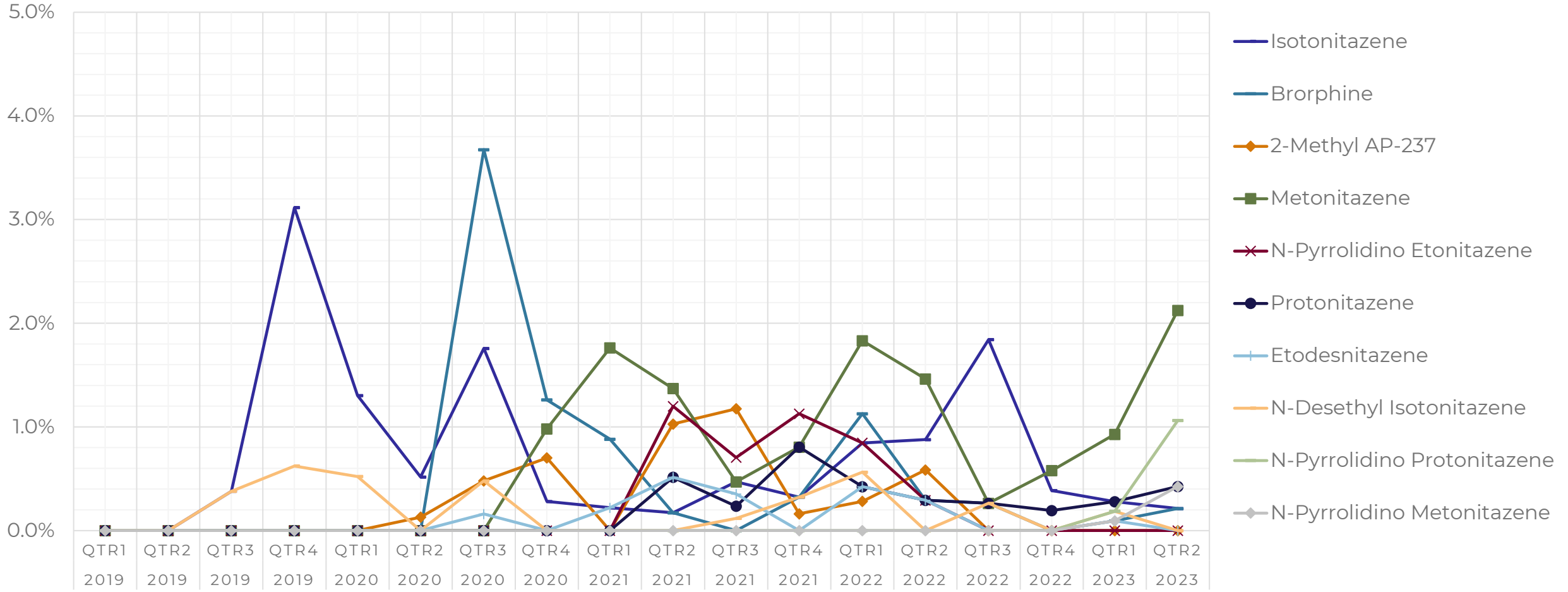


# POSITIVITY PLOTS – NPS OPIOIDS

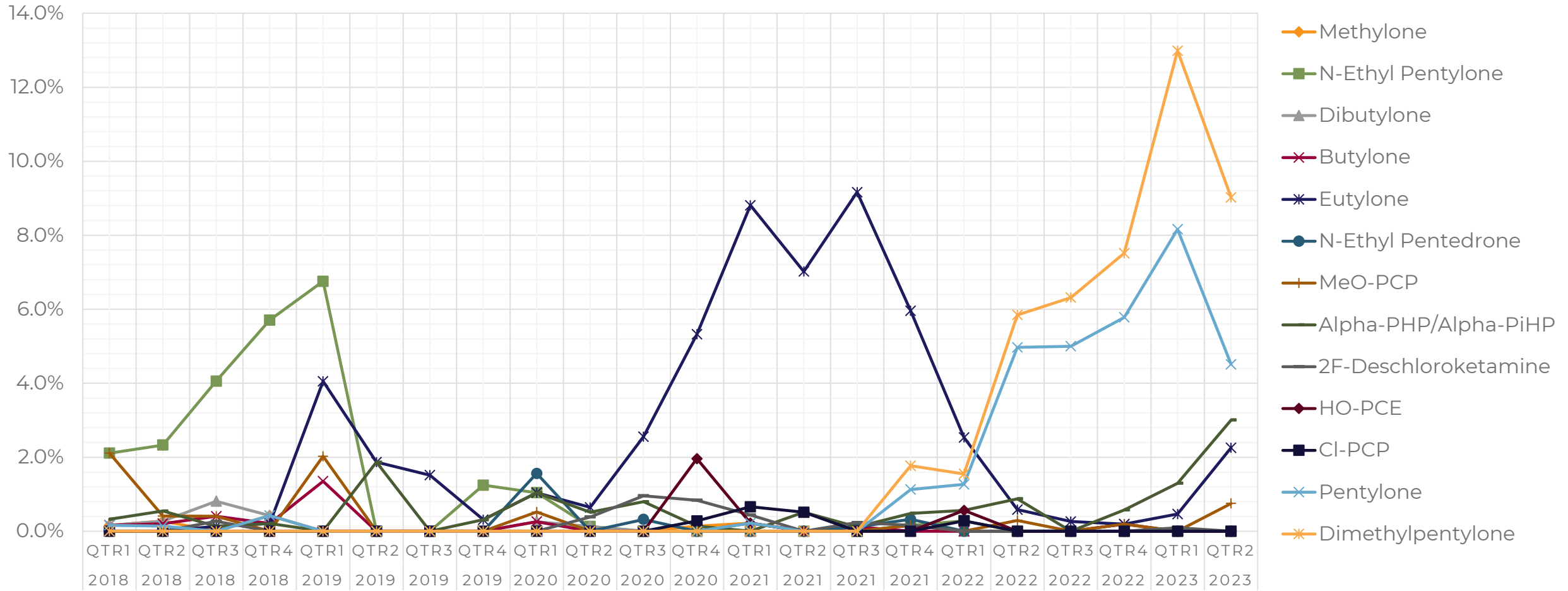


Note: Fluorofentanyl Excluded

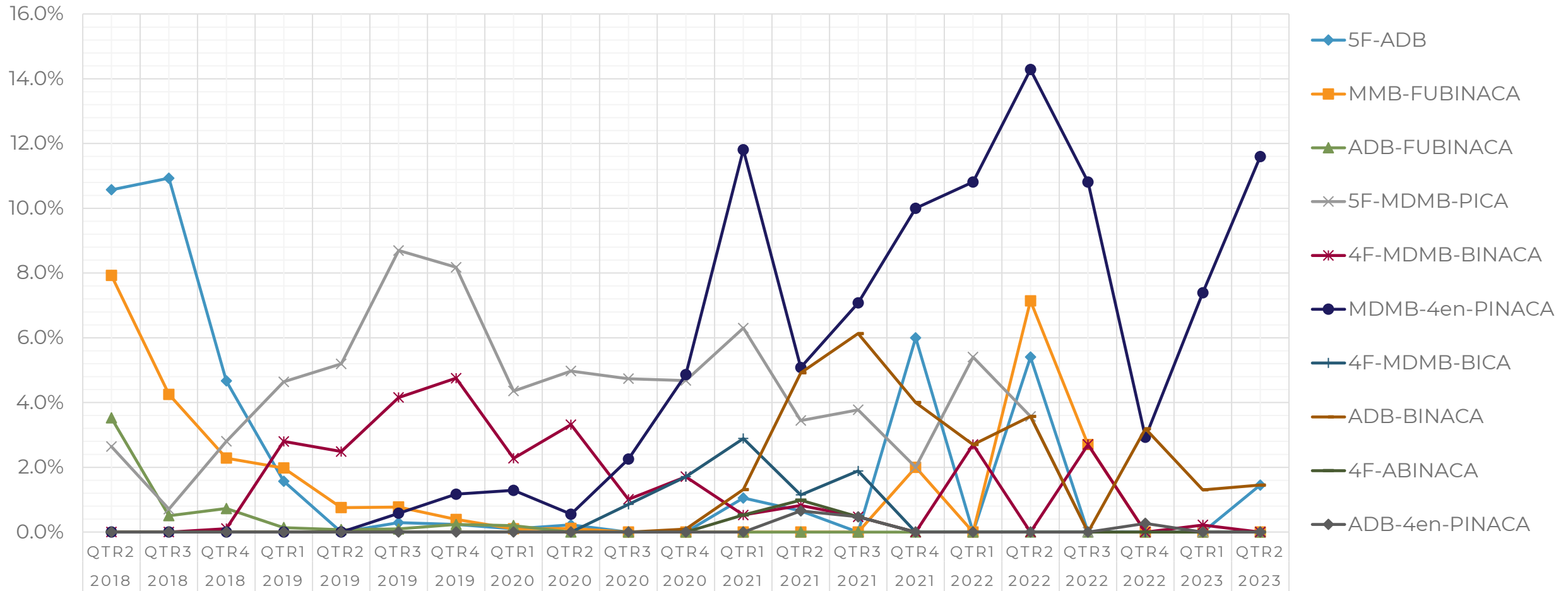
# POSITIVITY PLOTS – NPS OPIOIDS (NEW GENERATION ONLY)



# POSITIVITY PLOTS – NPS STIMULANTS & HALLUCINOGENS

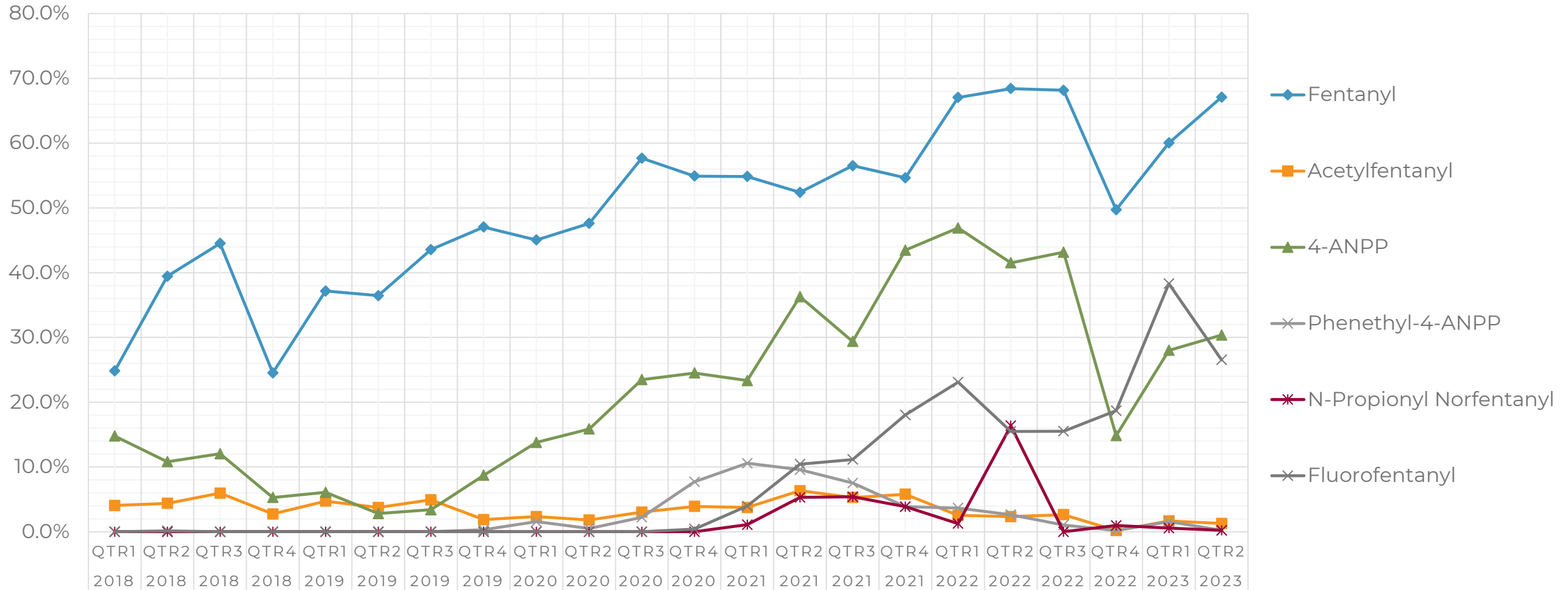


# POSITIVITY PLOTS – SYNTHETIC CANNABINOIDS



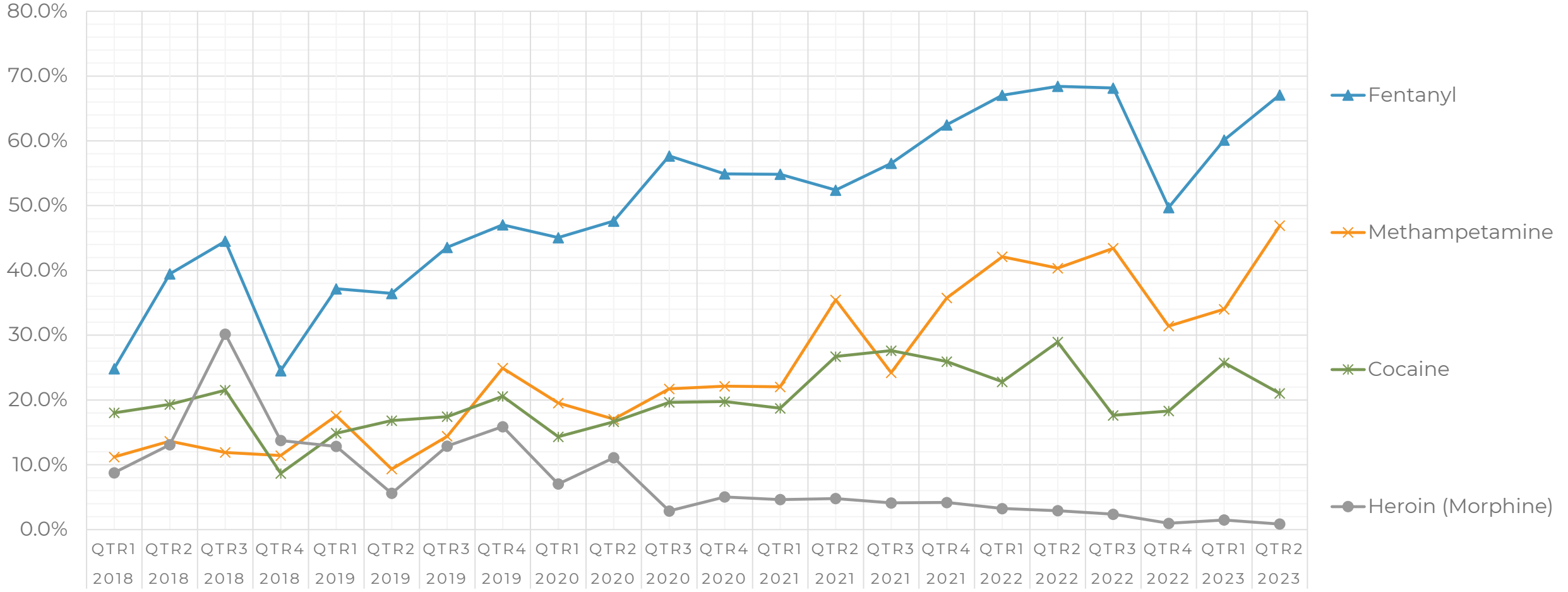
Note: Some quarters may be skewed due to low sample volume

# POSITIVITY PLOTS – FENTANYL & FLUOROFENTANYL

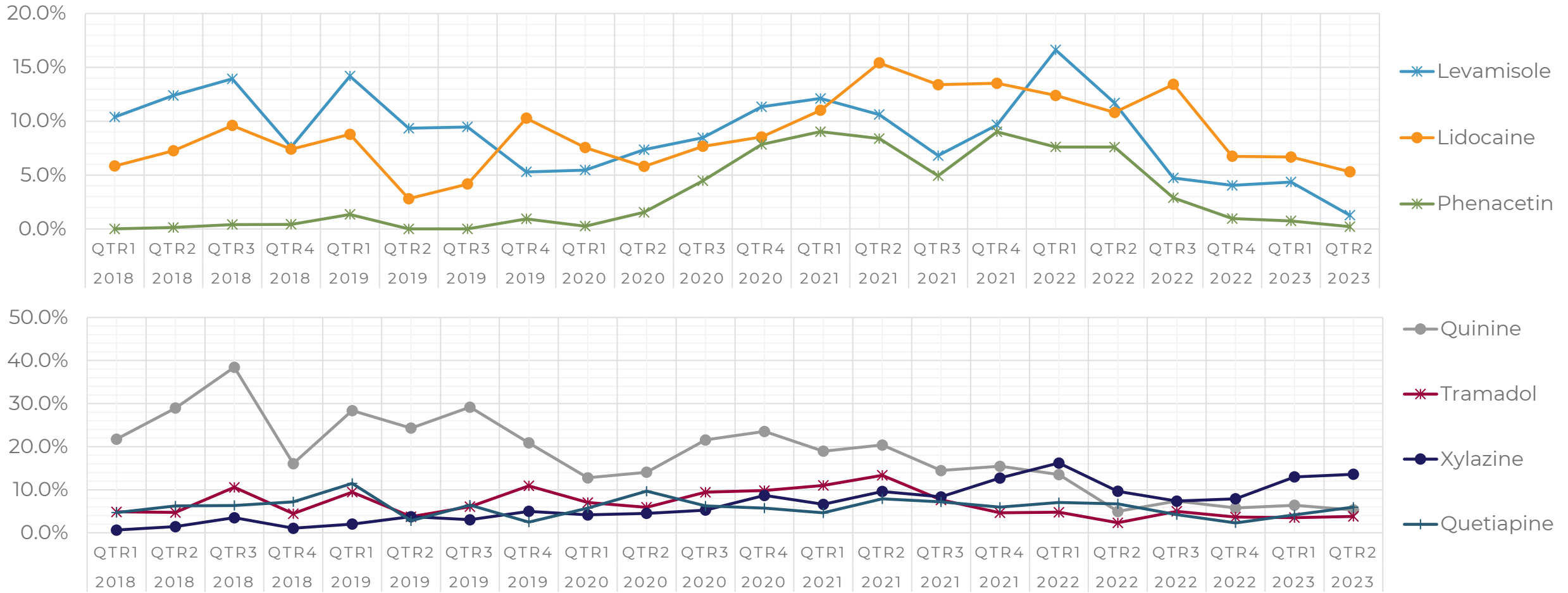




# POSITIVITY PLOTS – TRADITIONAL DRUGS

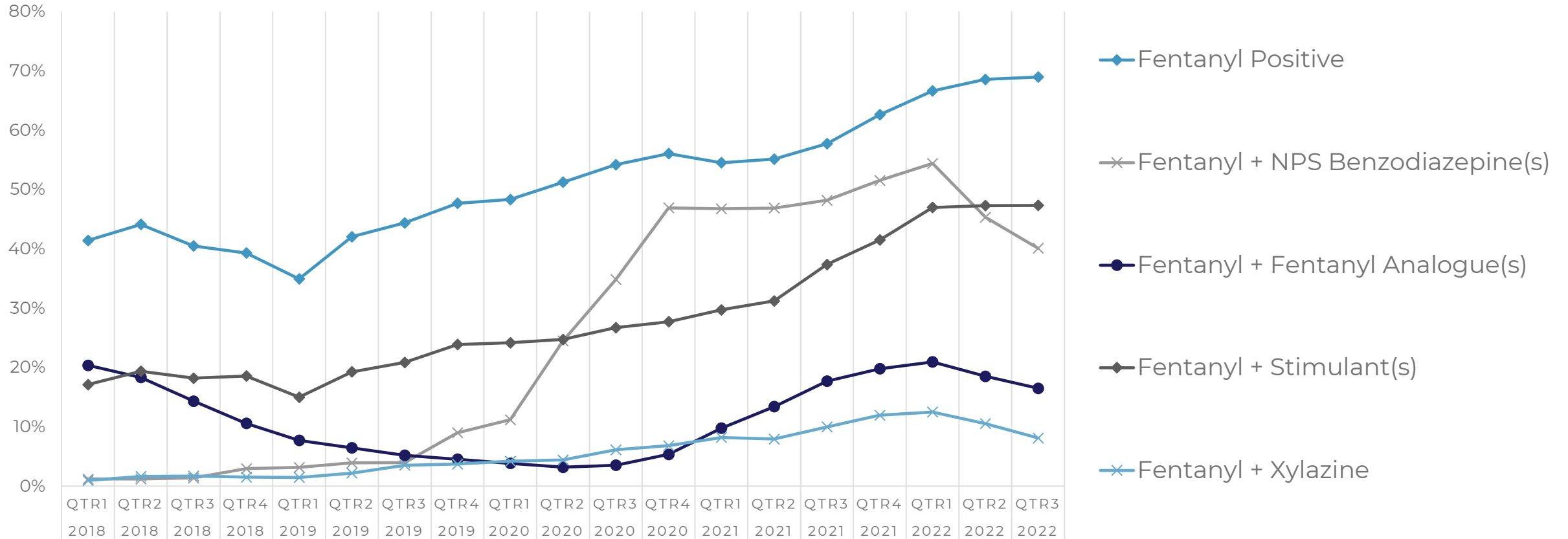


# POSITIVITY PLOTS – ADULTERANTS



# ENTERING THE POLYDRUG STAGE OF OPIOID EPIDEMIC

Fentanyl Co-Positivity – the “Nested Waves” Underlying Positivity and Prevalence



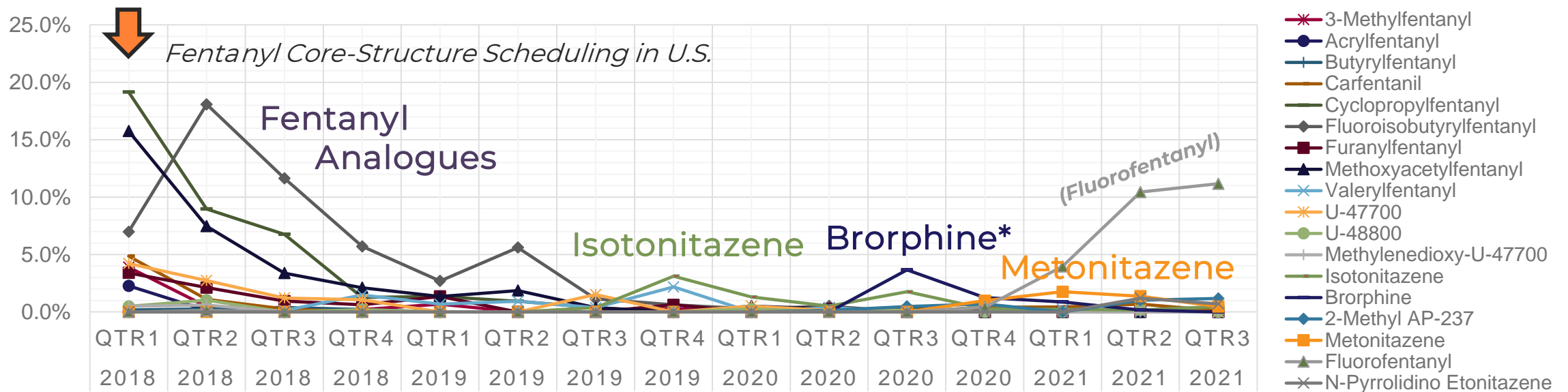


# NPS OPIOIDS



# FENTANYL ANALOGUES → “NITAZENE ANALOGUES”

- In 2018, the DEA placed all **fentanyl-related substances** in Schedule I
  - Role of EWS → track what the impact of this scheduling action might be
- Between 2019 and 2021, NPS Discovery observed the **emergence of “nitazene analogues”**
  - And this has continued into 2023



\*Not a “nitazene” analogue

# NPS OPIOID DISCOVERIES SINCE 2018

2018

- MD-U-47700
- Phenylfentanyl
  - U-47931E

2019

- Fluorofuranylfentanyl
  - p-MeO-Fu-Fentanyl
  - 2',5'-DiMeO-Fentanyl
- 2-Methyl AP-237
  - AP-237
- Piperidylthiambutene
  - 2F-Viminol
- **Isotonitazene**
  - N-Methyl U-47931E
  - p-Me-Cpr-Fentanyl

2020

- 3,4-Difluoro-U-47700
- N-Ethyl-U-47700
- para-Methyl AP-237
  - Brorphine
- **Metonitazene**
  - AP-238
- Fluorofentanyl
- Chlorofentanyl
- Bromofentanyl

2021

- **Butonitazene**
- **Etodesnitazene**
  - Flunitazene
- **N-Pyrrolidino Etonitazene**
- **Protonitazene**
- Metodesnitazene
- **N-Piperidinyl Etonitazene**

2022

- Dipyanone
- **N-Desethyl Isotonitazene**

2023

- **N-Pyrrolidino Metonitazene**
- **N-Pyrrolidino Protonitazene**

# EWS IMPACT – NITAZENE ANALOGUE TIMELINES



# EWS IMPACT – NITAZENE ANALOGUE TIMELINES



**First brorphine case**  
based on testing at CFSRE  
(Toxicology, June 2020)

**Public alert issued**  
for brorphine (CFSRE)  
(July 2020)



**Notice of intent**  
to schedule (DEA)  
(Dec. 2020)

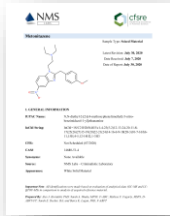


**Brorphine waning**  
in positivity (CFSRE)  
(Q4 2020)

6 7 8 9 10 11 12 2020 1 2 3 4 5 6 7 8 9 10 11 12 2021 1 2 3 4 5 6 7 8



# EWS IMPACT – NITAZENE ANALOGUE TIMELINES



**First metonitazene case**  
based on testing at CFSRE  
(Drug material, July 2020)

**Public alert issued**  
for metonitazene (CFSRE)  
(Jan. 2021)



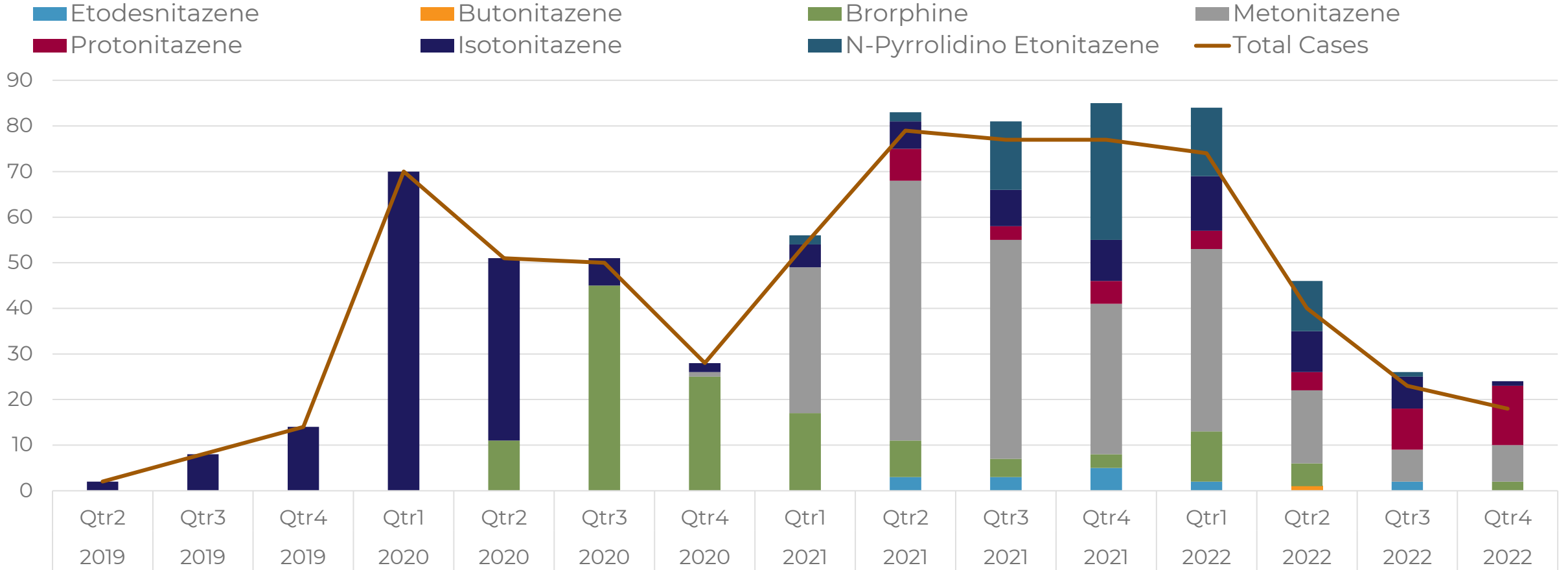
**Notice of intent**  
to schedule (DEA)  
(Dec. 2021)



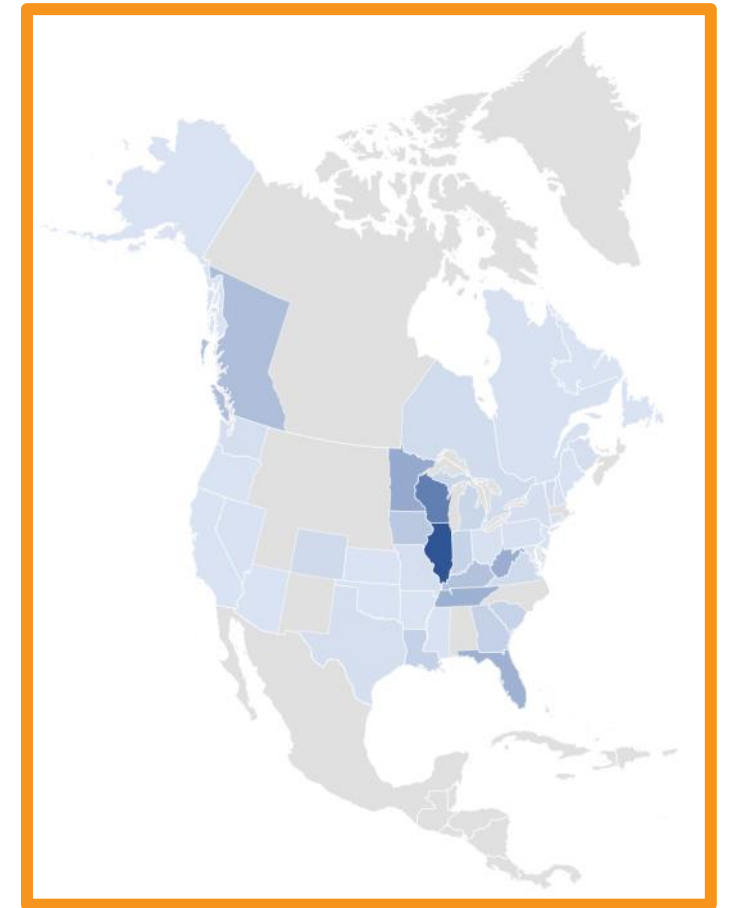
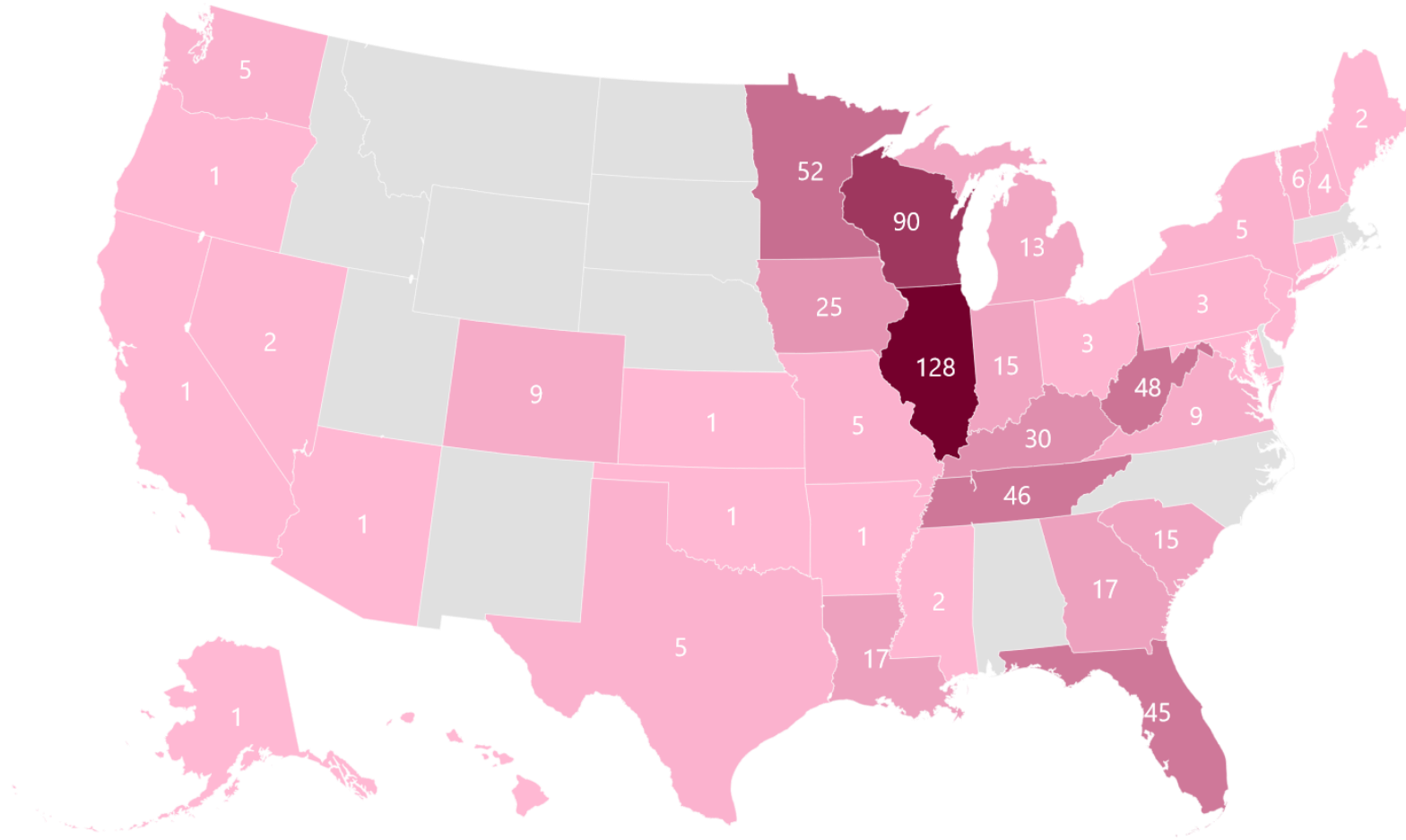
**Metonitazene waning**  
in positivity (CFSRE)  
(Q3/Q4 2021)

2020 1 2 3 4 5 6 7 8 9 10 11 12 2021 1 2 3 4 5 6 7 8 9 10 11 12 2022

# DIVERSIFICATION OF NITAZENE ANALOGUES



# PROLIFERATION OF NITAZENE ANALOGUES



*\*Forensic toxicology cases. Data from NMS Labs representing cumulative identifications.*

*\*Includes: isotonitazene, brorphine, metonitazene, N-pyrrolidino etonitazene, protonitazene*

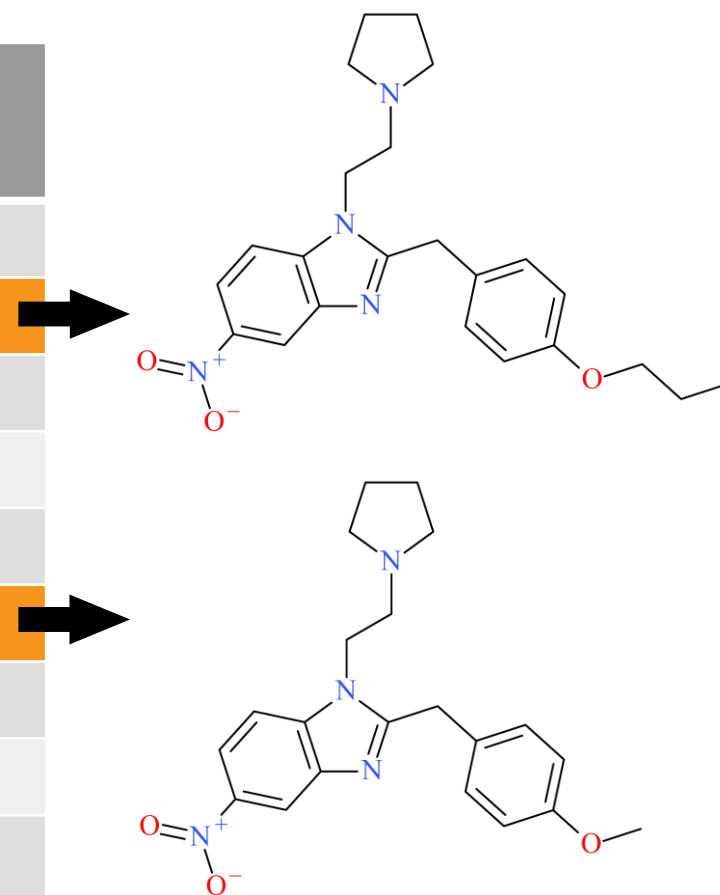
# IN COMBINATION WITH OTHER DRUGS

Analogue	% Co-Positivity of Nitazene Analogue with...				
	Fentanyl	NPS Benzo.	Methamp.	Cocaine	Xylazine
Isotonitazene	57%	89%	30%	32%	11%
Brorphine	84%	100%	43%	29%	10%
Metonitazene	51%	94%	37%	16%	20%
N-Pyrro. Eto.	59%	89%	48%	37%	15%
Protonitazene	60%	87%	87%	13%	0%
Etodesnitazene	50%	92%	58%	17%	17%

*\*Forensic toxicology cases. Data from the CFSRE.*

# THE NEWEST ANALOGUES

Analogue	CFSRE Cases	Estimated Potency Compared to Fentanyl
<i>N</i> -Pyrrolidino Etonitazene	15	43x more
<b><i>N</i>-Pyrrolidino Protonitazene</b>	<b>9</b>	<b>25x more</b>
Isotonitazene	69	9x more
Protonitazene	3	4x more
Metonitazene	18	2x more
<b><i>N</i>-Pyrrolidino Metonitazene</b>	<b>5</b>	<b>2x more</b>
<i>Fentanyl</i>	-	-
Butonitazene	1	2x less
Etodesnitazene	15	4x less



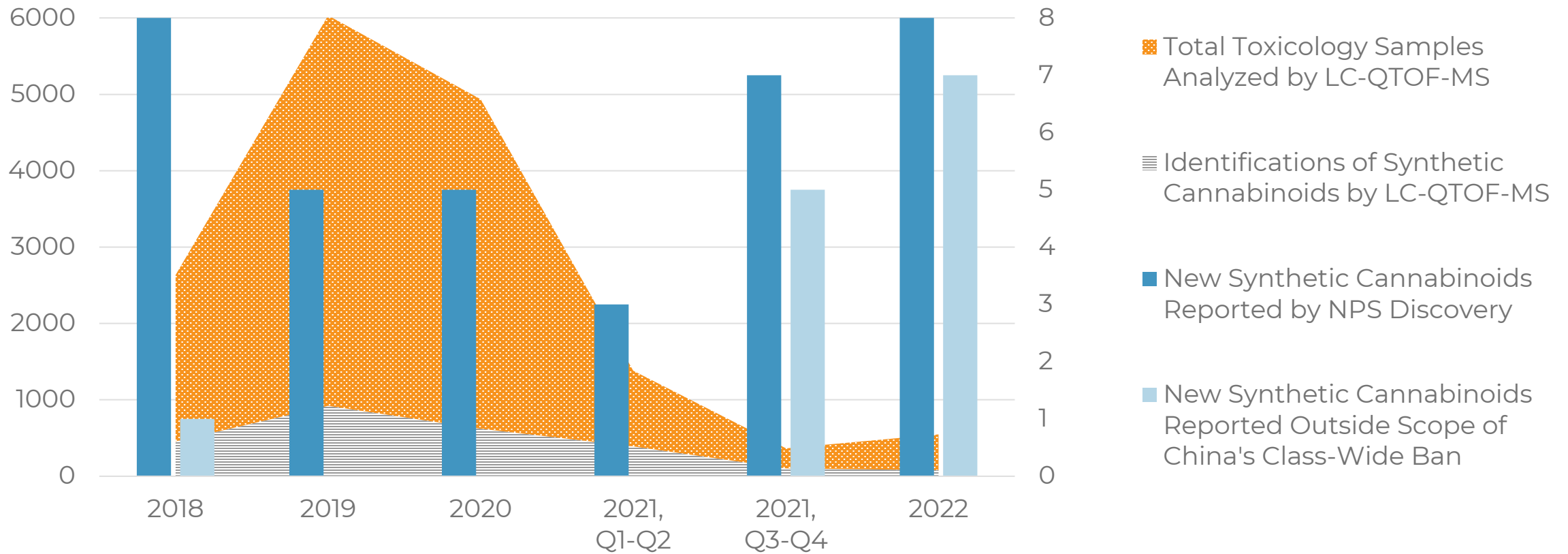


# SYNTHETIC CANNABINOIDS



# WHAT'S HAPPENING WITH SYNTHETIC CANNABINOIDS?

- Dramatic change in the landscape of synthetic cannabinoids (nationally and internationally)



# CHINA IMPOSES CLASS-WIDE BAN



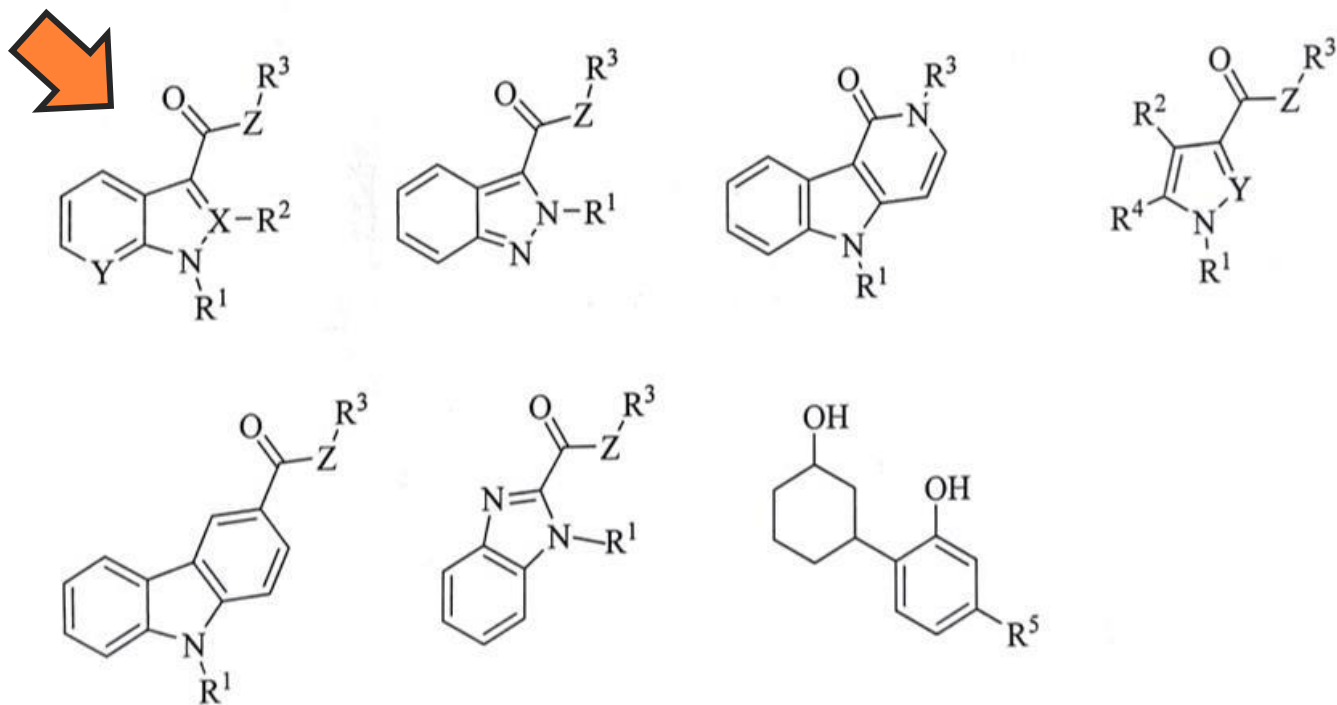
## *The Questions:*

1. How did this come about?
2. What is a “total ban”?
3. Is this even possible?

**Effective: July 2021**



# QUICK REVIEW OF THE LEGISLATION

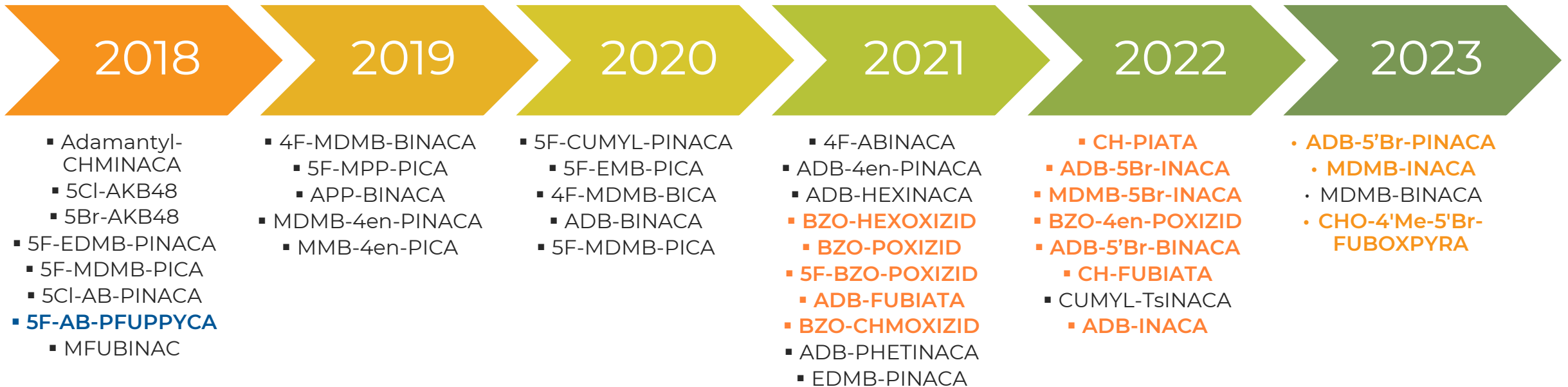


- **Summary – This included previously prevalent indoles (-ICA's) and indazoles (-INACA's)**

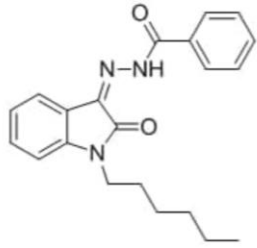
- R1 represents substituted or unsubstituted C3-C8 **alkyl** group; substituted or unsubstituted heterocyclic group containing 1-3 heteroatoms; substituted or unsubstituted methyl or ethyl group substituted by heterocyclic group containing 1-3 heteroatoms.
- R2 represents hydrogen or methyl or no atom.
- R3 represents substituted or unsubstituted C6-C10 aryl group; substituted or unsubstituted C3-C10 **alkyl** group; substituted or unsubstituted heterocyclic group containing 1-3 heteroatoms; substituted or unsubstituted methyl or ethyl group substituted by heterocyclic group containing 1-3 heteroatoms.
- R4 represents hydrogen; substituted or unsubstituted phenyl group; substituted or unsubstituted benzyl group.
- R5 represents substituted or unsubstituted C3-C10 hydroxy group.
- X represents N or C.
- Y represents N or CH.
- Z represents O or NH or no atom.

# SYNTHETIC CANNABINOID DISCOVERIES SINCE 2018

- NPS Discovery now (almost exclusively) sees new synthetic cannabinoids that fall **outside** the scope of the 2021 Chinese class-wide ban; however, expectations remain (as with all NPS).



# MONITORING GRAY MARKET SITES



MDA-19

MDA-19 is a drug that acts as a potent and selective agonist for the cannabinoid receptor 1 (CB1R).

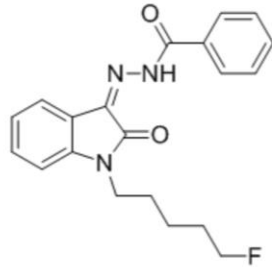
\$1.70



4C-ADB

4C-ADB is the best analog of 5F-ADB...

\$28.00



5F-MDA-19

5F-MDA-19 is a drug that acts as a potent and selective agonist for the cannabinoid receptor 1 (CB1R).

\$1.70

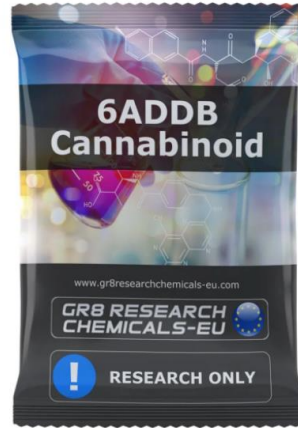


7-ADD

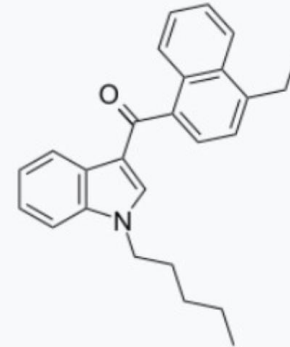
On 19.10.2021 By ADMIN

Cannabinoids New Chemicals

7-ADD is a new synthetic cannabinoid, synthesized as one of...



NEW



JWH-210



ADB-Butinaca, ADBB

On 05.06.2021 By ADMIN

Cannabinoids New Chemicals

ADB-Butinaca or ADBB synthetic is a designer cannabinoid created on...



5F-MDA-19

On 05.06.2021 By ADMIN

Cannabinoids New Chemicals

5F-MDA-19 is a cannabinoid drug, a structural analog of MDA-19



AZ-037 (5F-AB-FUPPYCA)

On 20.05.2021 By ADMIN

Cannabinoids New Chemicals

AZ-037 or 5F-AB-FUBINACA is a new designer cannabinoid based on...



5F-MDA-19 (new legal noid!)

5F-MDA-19 is a drug that acts as a potent and selective agonist for the cannabinoid receptor 1 (CB1R).

\$30.00

# DIY SYNTHETIC CANNABINOIDS???

Home \ Cannabinoids \ ADB-BUTINACA PRECURSOR (SEMI-FINISHED)



## ADB-BUTINACA PRECURSOR (SEMI-FINISHED)

\$2,400.00 – \$15,000.00

Since the finished product is already illegal in China, the laboratories there have found a solution and can provide us with a precursor to the good old adb butinaca.

### Quantity

Choose an option

1

Add to cart

SKU: N/A

Category: Cannabinoids

### You need:

1kg ADB-BUTINACA PRECURSOR (SEMI-FINISHED) – 3500\$

3L DMF (CAS 68-12-2)

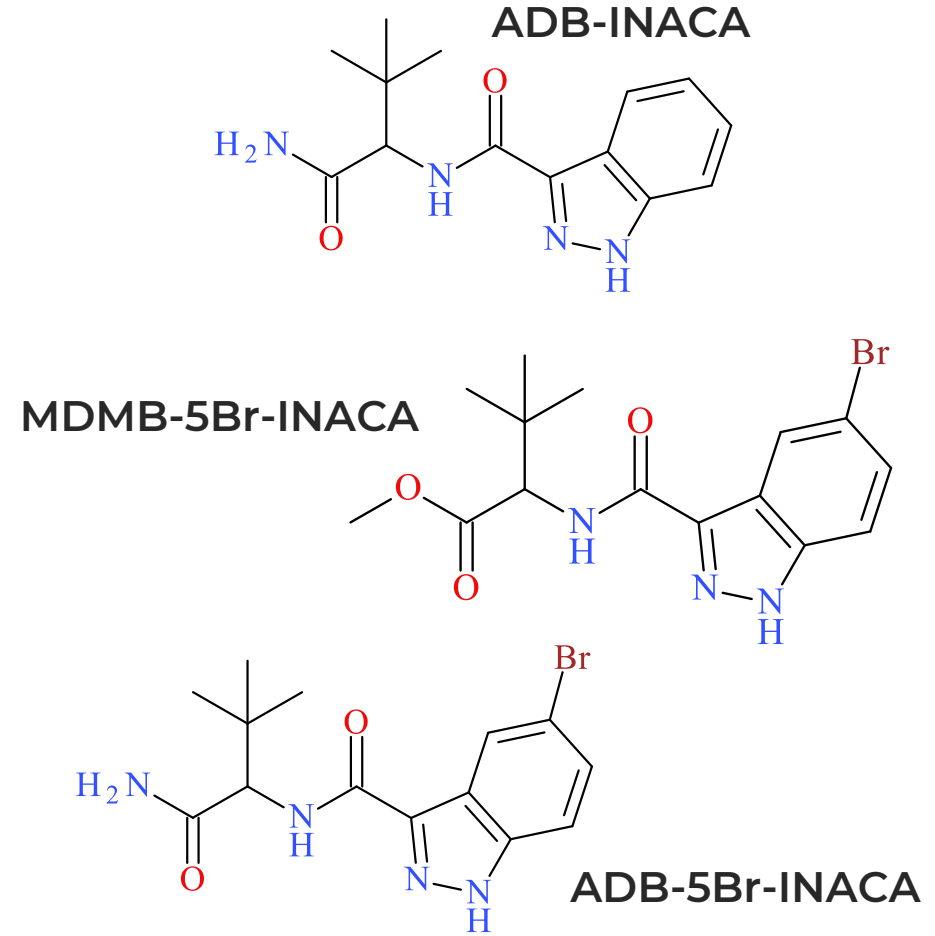
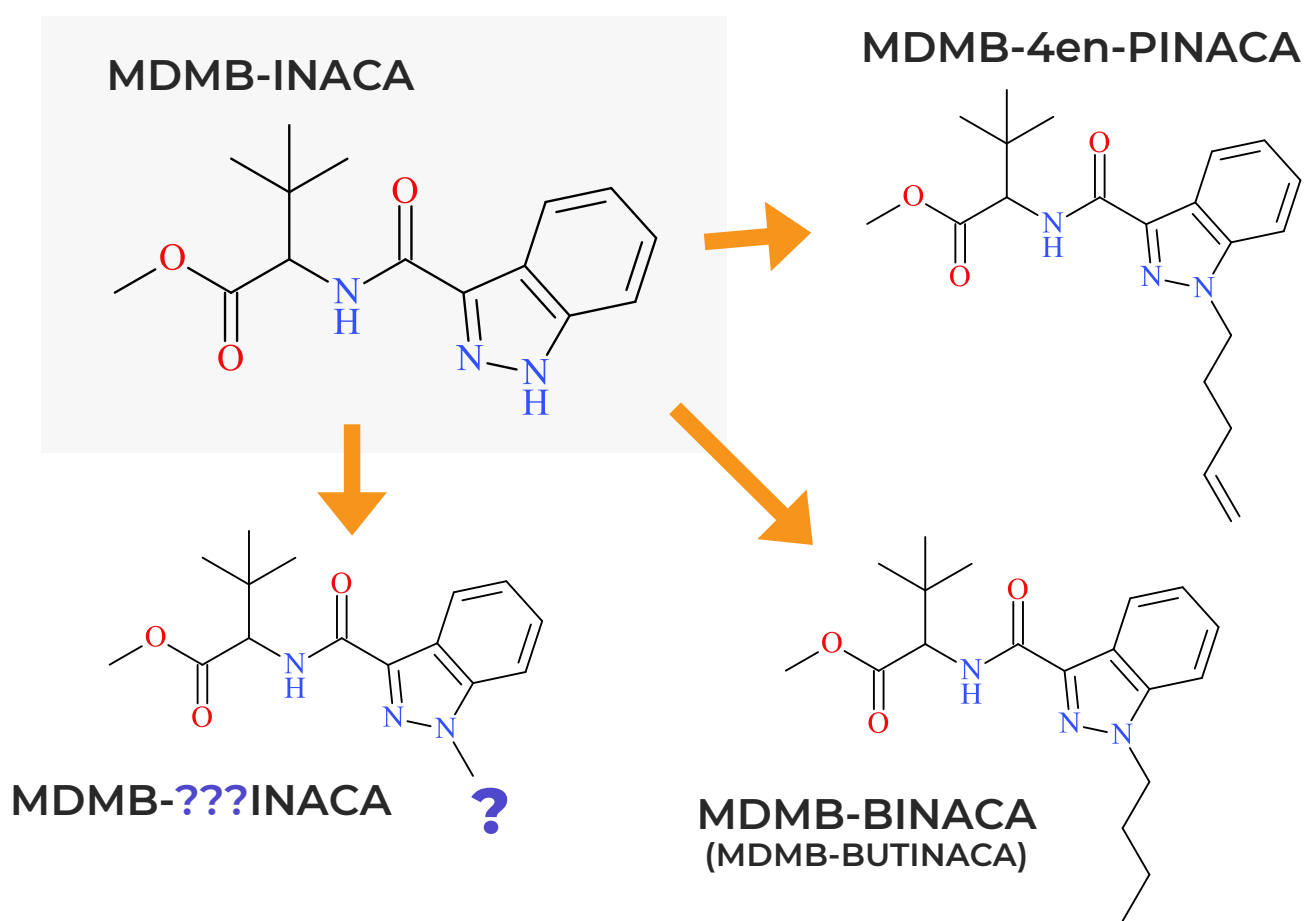
850g anhydrous potassium carbonate (CAS: 584-08-7)

680g of bromobutane (CAS: 109-65-9)

### Instructions:

1. They were successively added into the reaction bottle;
2. The temperature was raised to 70-80°C for 5h; after the reaction, it was cooled to room temperature.
3. Prepare a bucket in advance and add 15L water;
4. Then pour the reaction solution into the bucket, cool to room temperature, filter the solid, wash the solid to neutral and dry.

# SYNTHETIC CANNABINOIDS PRECURSORS

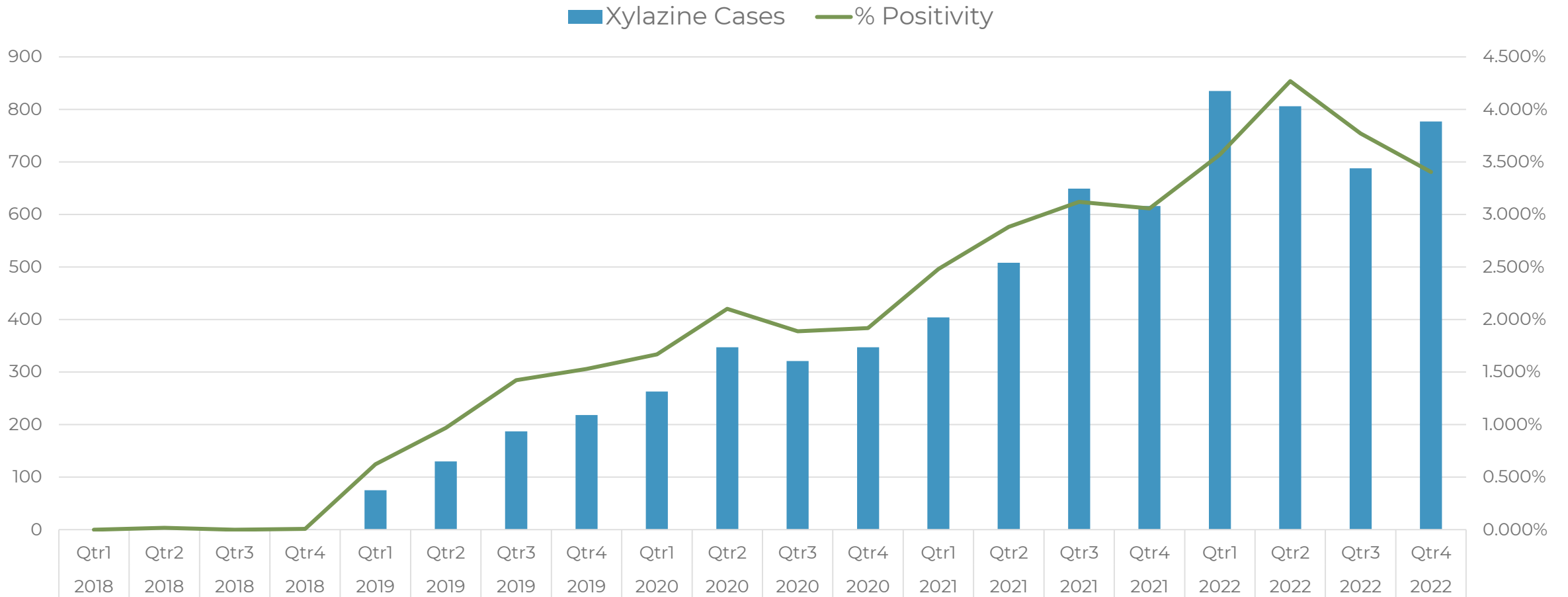




XYLAZINE

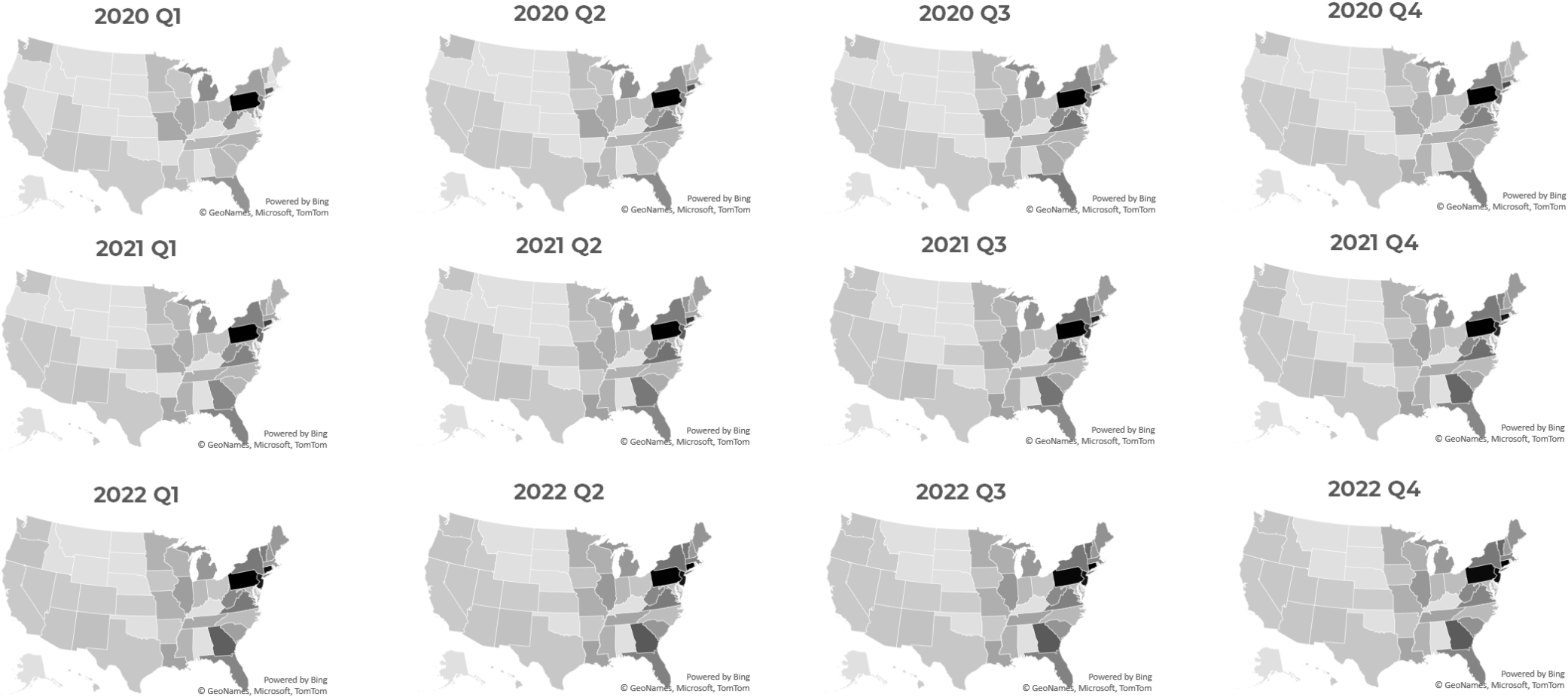


# PREVALENCE OF XYLAZINE IN THE U.S.



*\*Data from NMS Labs / Not final numbers*

# SPREAD OF XYLAZINE ACROSS THE U.S.



*\*Data from NMS Labs / Crude analysis with other necessary caveats*





# DRUG CHECKING SURVEILLANCE



# DRUG CHECKING RESULTS

			
Clonazolam	Etizolam	Etizolam	Desalkylflurazepam
			
Fentanyl, Gabapentin	<i>para</i> -Fluorofentanyl, Gabapentin	Methamphetamine	
			
Cocaine, Lidocaine	Cocaine, Lidocaine	Methamphetamine, Caffeine	Methamphetamine



1  
Methamphetamine



3  
ADB-5'Br-IANCA



2  
Methamphetamine



4  
ADB-5'Br-IANCA



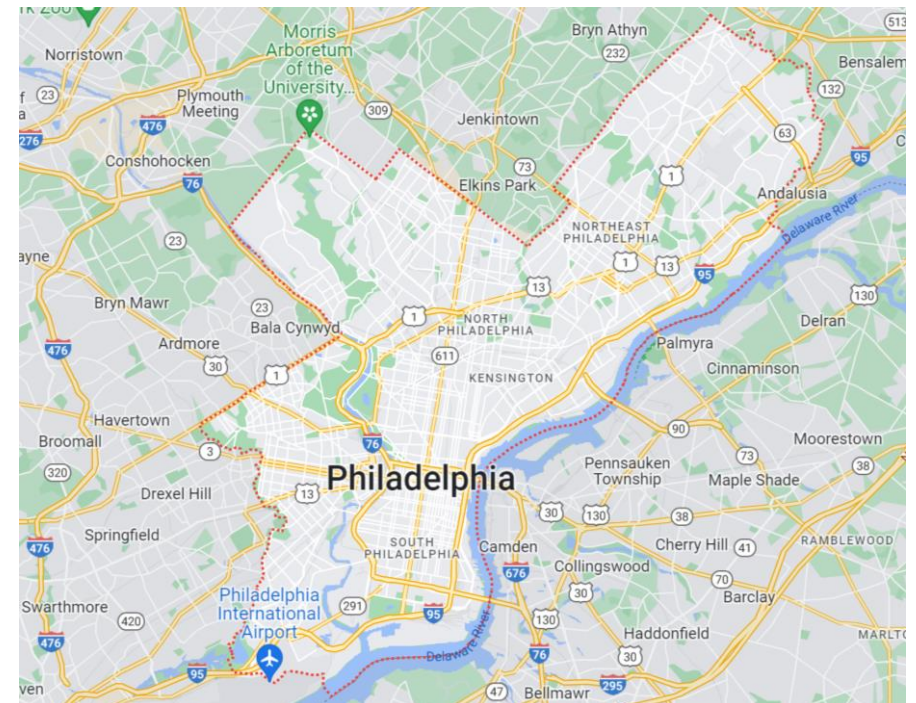
ADB-BINACA



ADB-BINACA

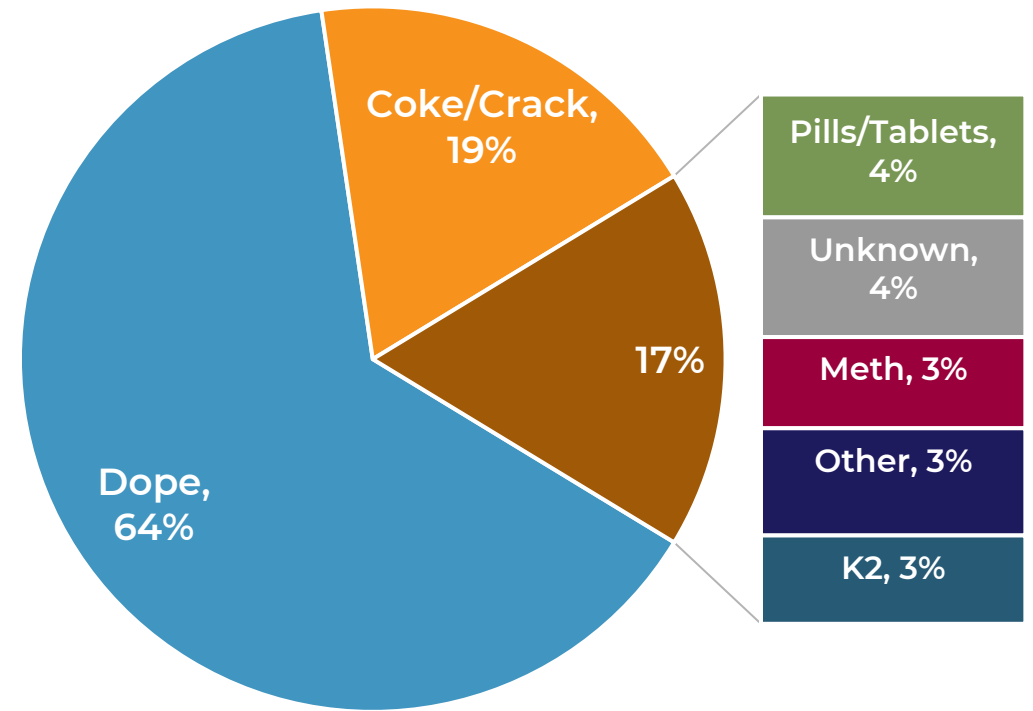
# PHILADELPHIA & ITS DRUG SUPPLY

- Nestled in the center of the larger mid-Atlantic metropolitan region (“Northeast Corridor”)
  - 6<sup>th</sup> largest city by population and 7<sup>th</sup> largest metro area
- **“Open air drug market”** (Kensington neighborhood)
- Drug markets → dope, crack/coke, meth, K2, etc.
- Continually changing and diverse drug environment
- Collaboration between the **CFSRE** and the **Philadelphia Department of Public Health (PDPH)**

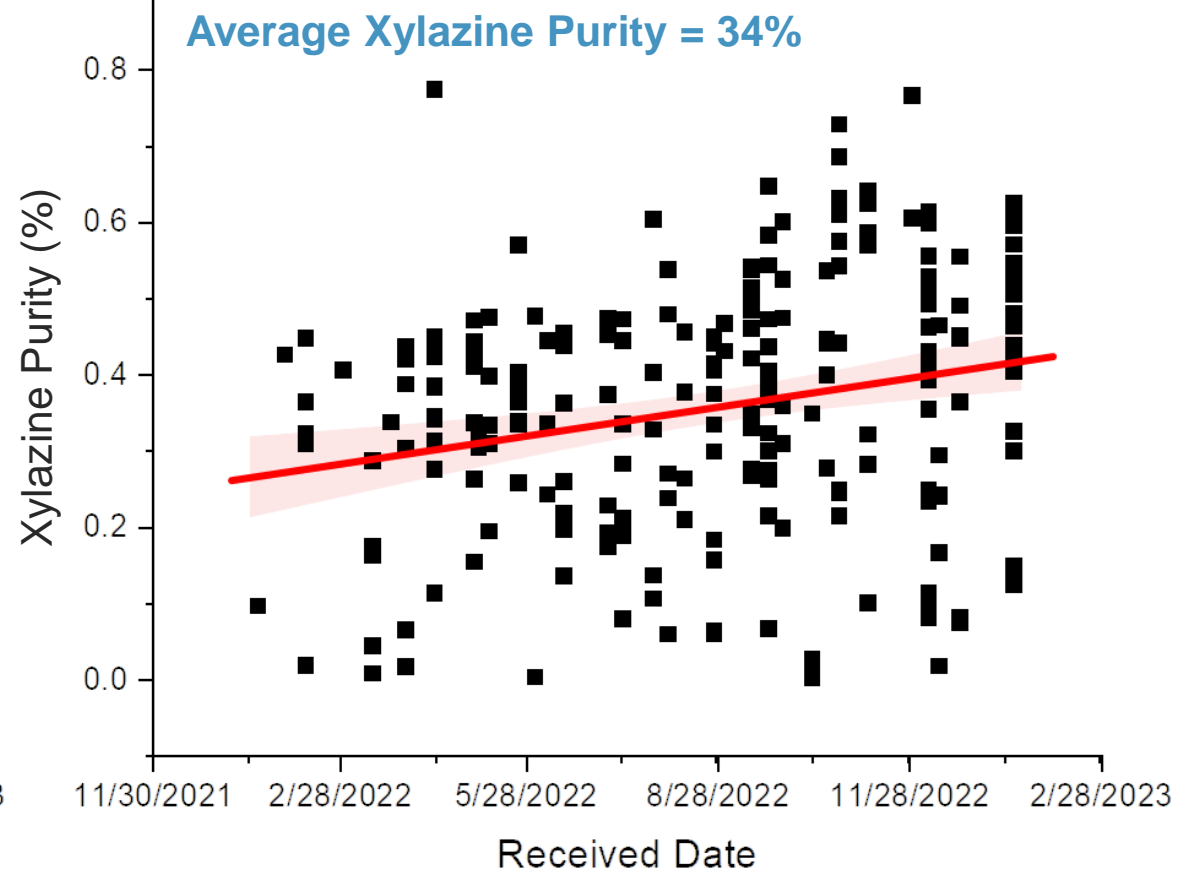
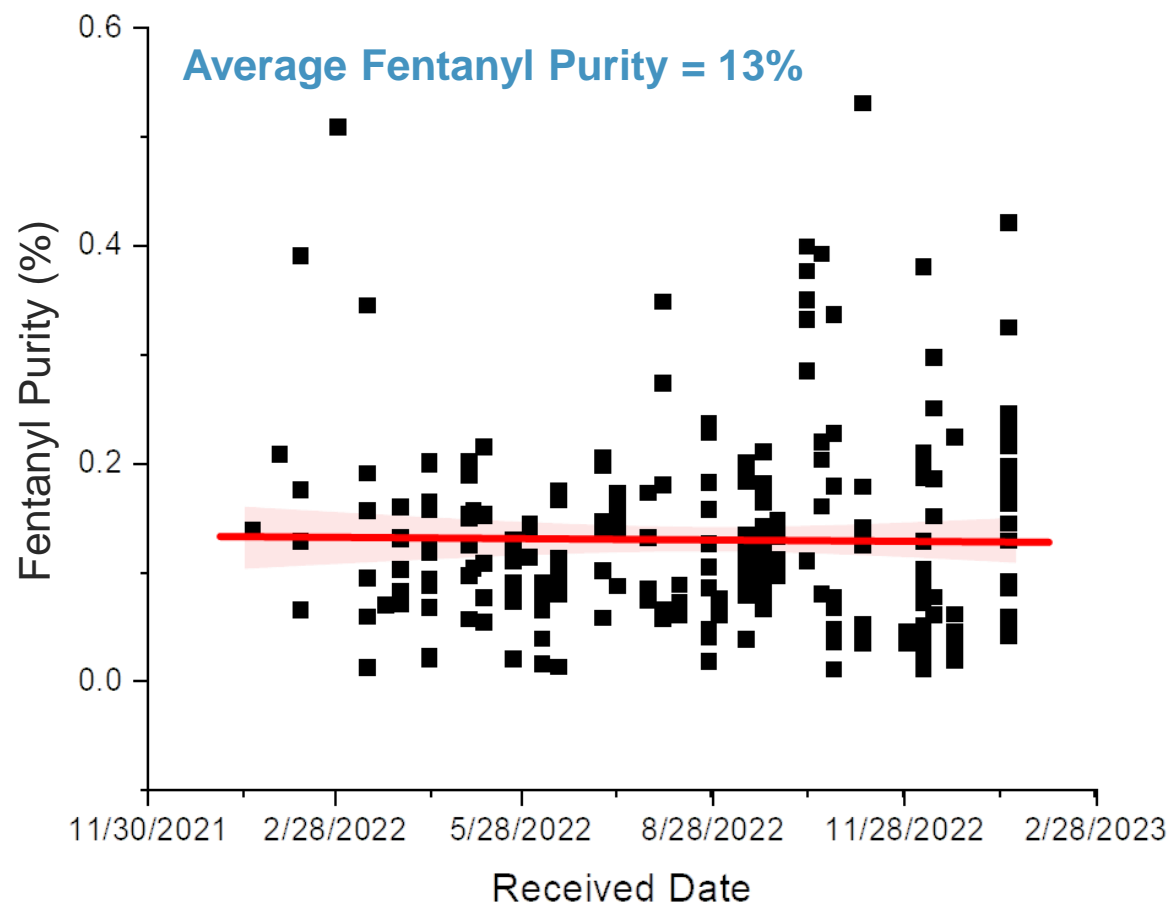


# PDPH/CFSRE DRUG CHECKING

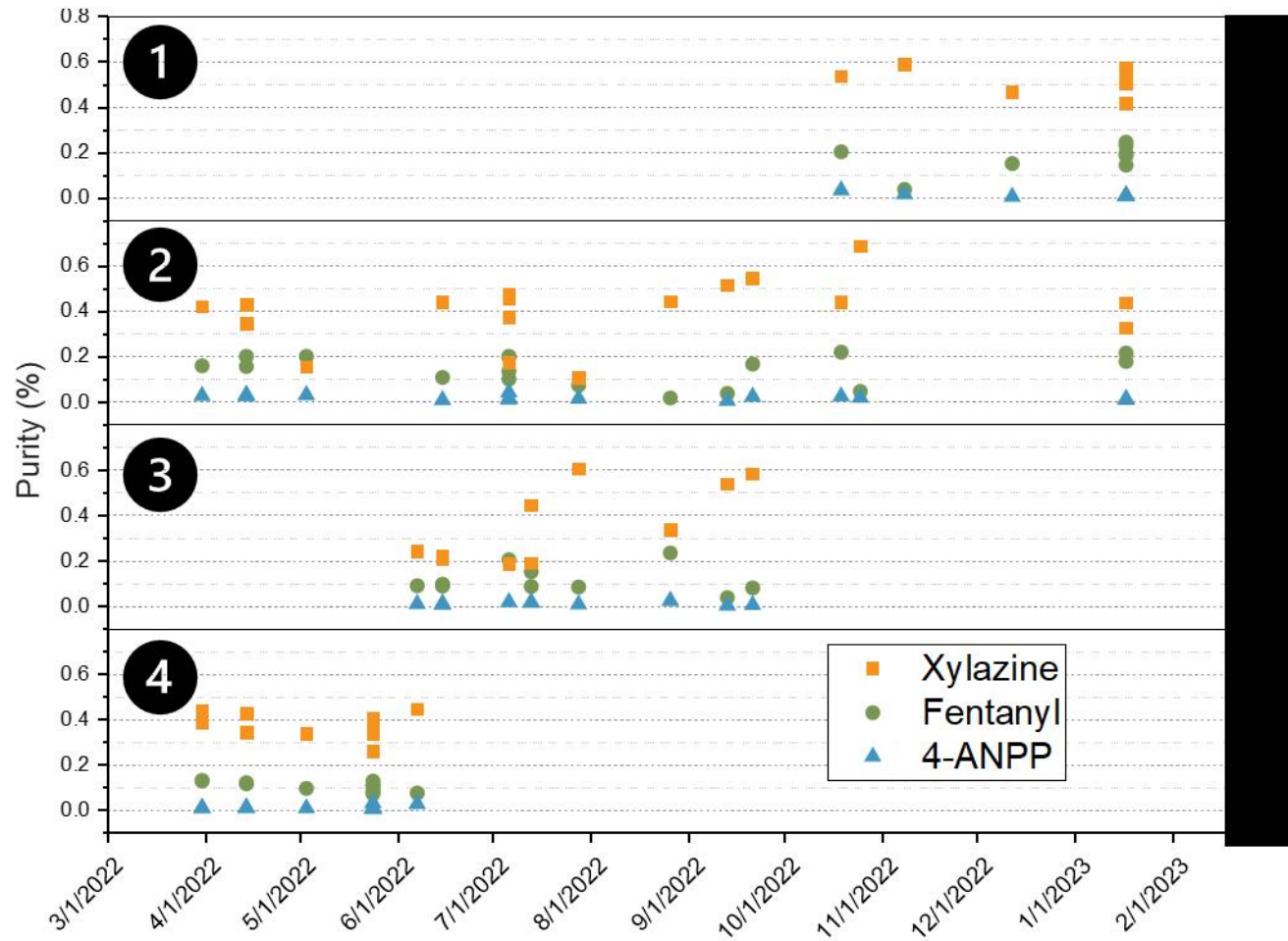
- **2020** → Partnership formally launched
- **Sample Analyzed**
  - 950+ samples received since 2020
  - Variety of sample types (suspected contents) →
  - Paired FTIR and test strip results\*\*\*
- **Key Findings**
  - “Dope”: 99% contain fentanyl and ~90% contain xylazine
  - Methamphetamine – rarely adulterated or substituted
  - Cocaine – “coke” samples sometimes test positive for trace fentanyl
  - K2 – revolving door of synthetic cannabinoids



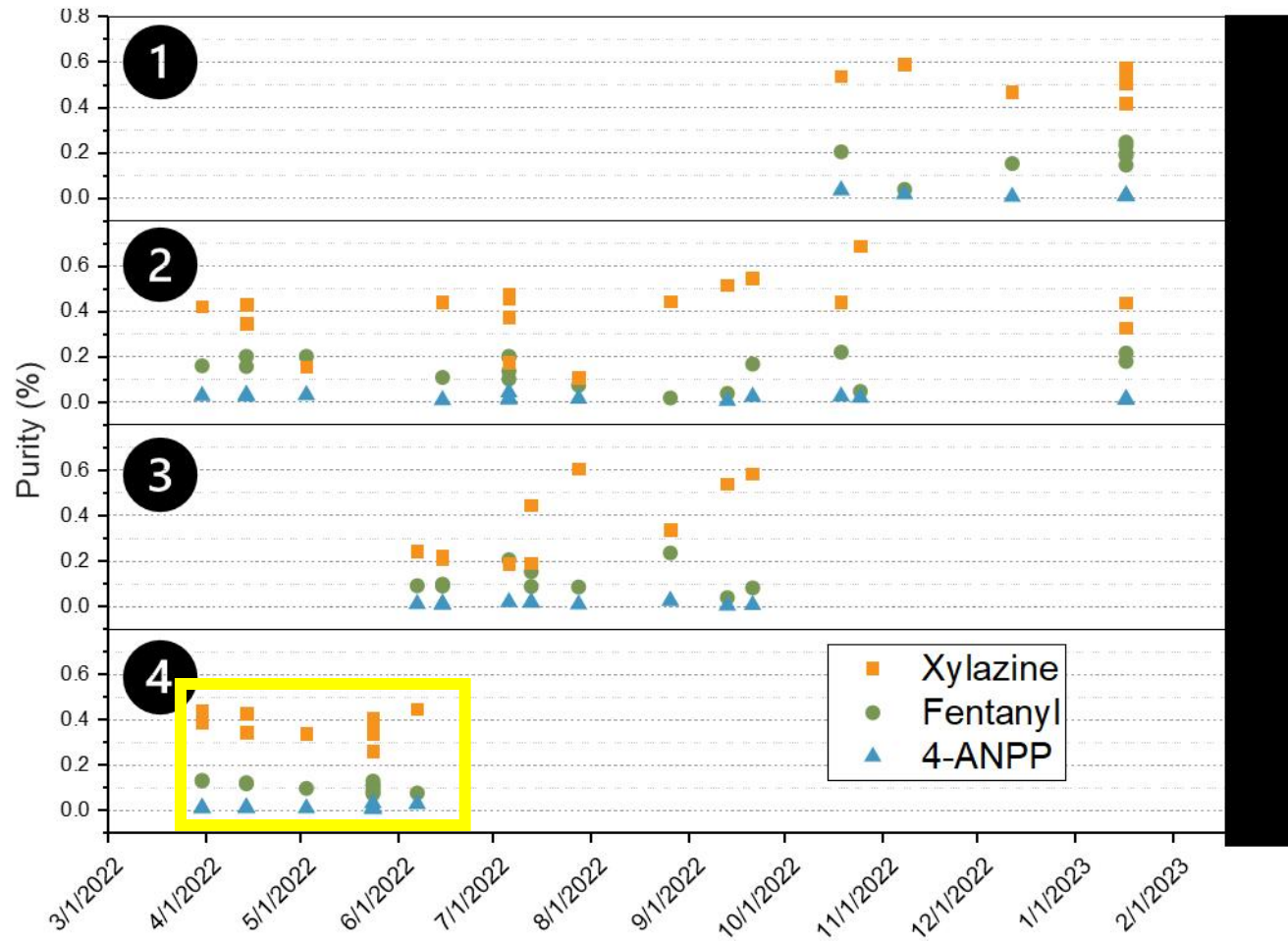
# TEMPORAL CHANGES IN PURITY (2022)



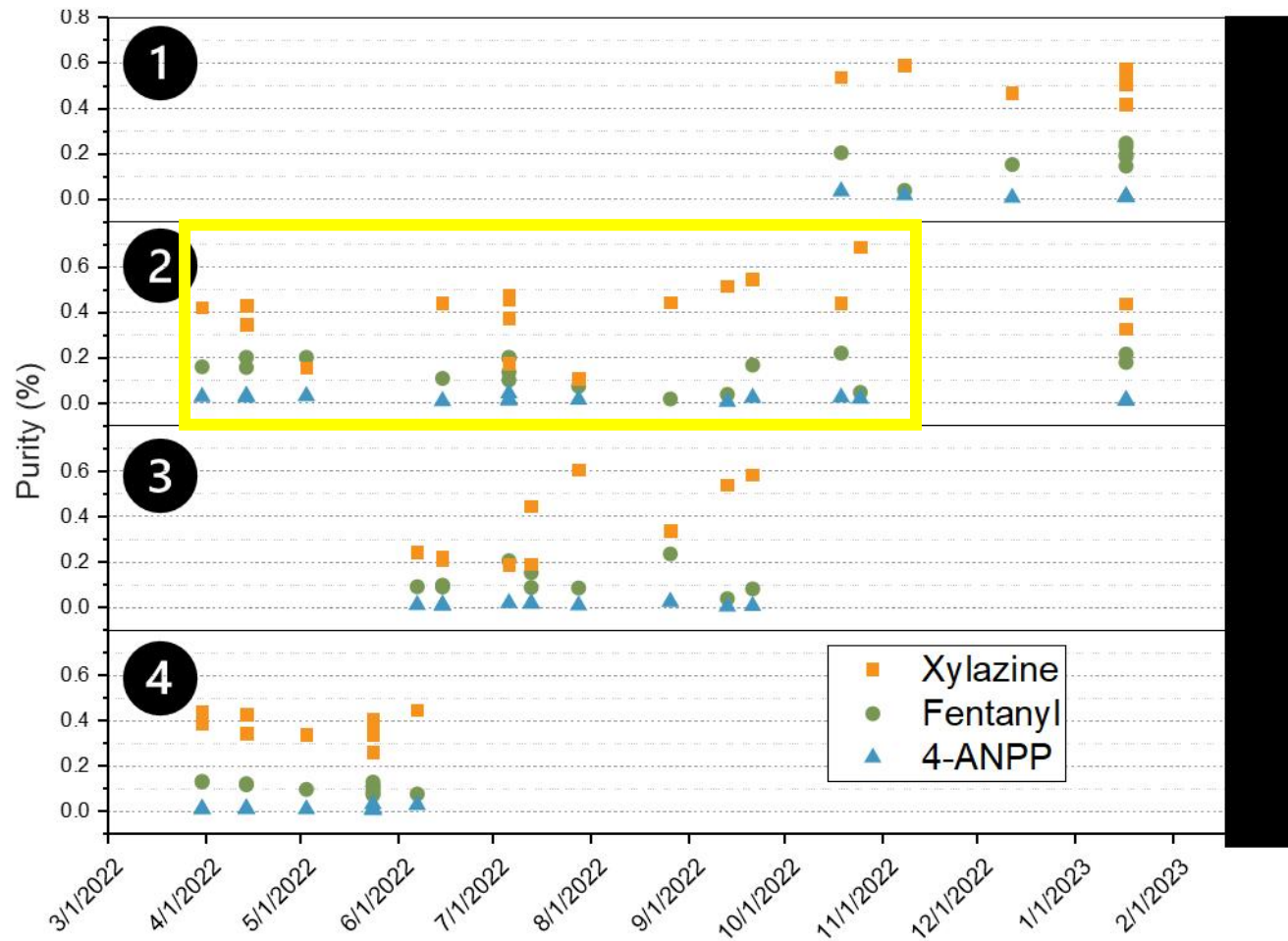
# LONGITUDINAL ASSESSMENT OF DRUG PRODUCTS



# LONGITUDINAL ASSESSMENT OF DRUG PRODUCTS

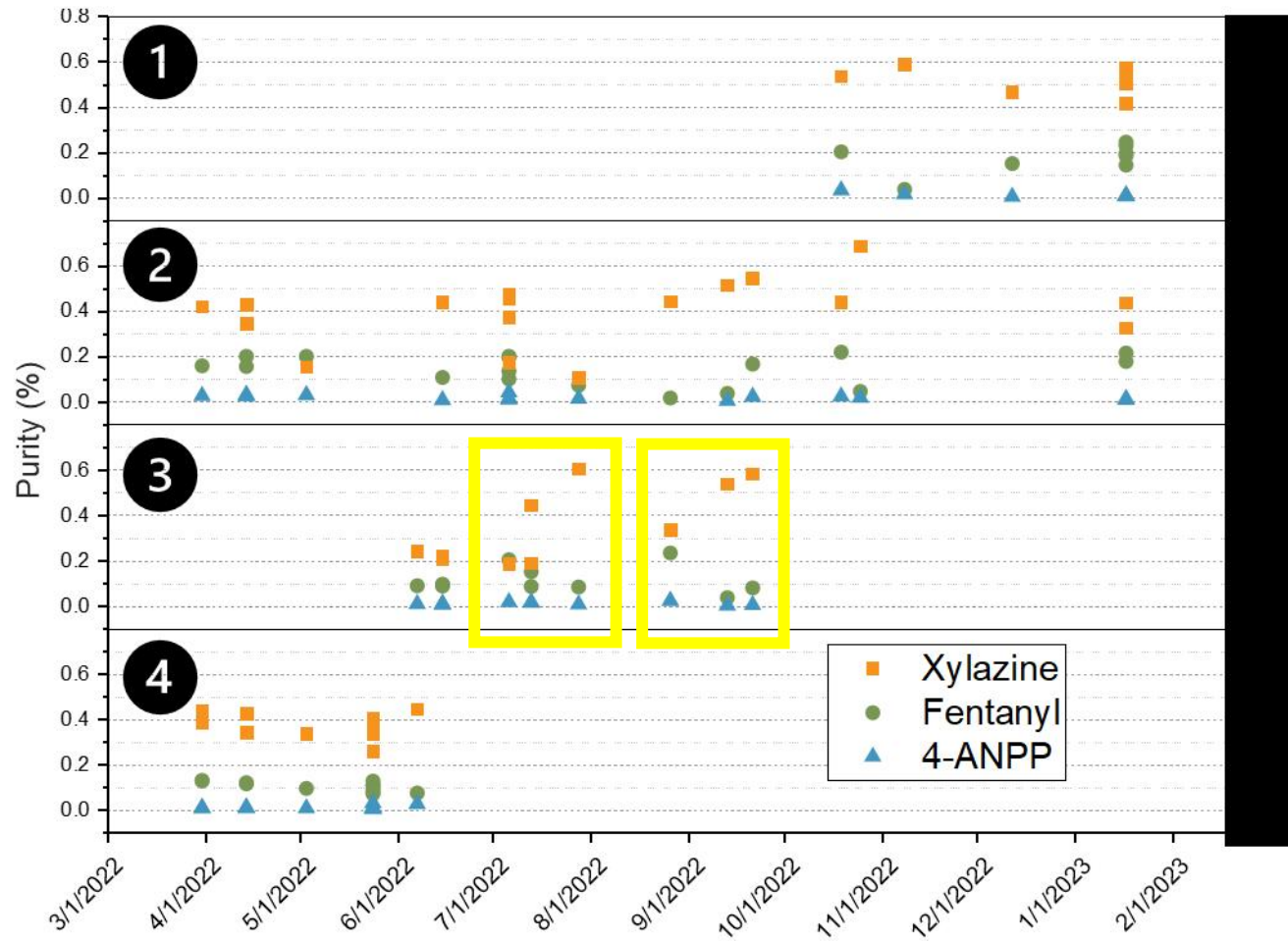


# LONGITUDINAL ASSESSMENT OF DRUG PRODUCTS





# LONGITUDINAL ASSESSMENT OF DRUG PRODUCTS





**ACCESS NPS DISCOVERY & JOIN LISTSERV**



# WEBSITE ► [WWW.NPSDISCOVERY.ORG](http://WWW.NPSDISCOVERY.ORG)



The screenshot shows the homepage of the NPS Discovery website. At the top, there is a navigation bar with links for RESOURCES, ABOUT, OUR LAB, CONTACT, and a DONATE button. The main header features the cfsre logo and the text "The Center for Forensic Science Research & Education" and "A PROGRAM OF THE FREDRIC RIEDERS FAMILY FOUNDATION". Below the navigation bar, there are tabs for EDUCATION, RESEARCH, and NPS DISCOVERY, along with a SEARCH button. The main content area has a large image of a laboratory with the text "NPS DISCOVERY" overlaid. Below this, there is a sub-header "NPS DISCOVERY" and a paragraph describing the program as an open-access drug early warning system (EWS) operating in the United States. A second paragraph explains the program's goal to identify emerging drugs (NPS) and disseminate information. A final paragraph mentions an email listserve for stakeholders.

RESOURCES ABOUT OUR LAB CONTACT DONATE

cfsre The Center for Forensic Science Research & Education

A PROGRAM OF THE FREDRIC RIEDERS FAMILY FOUNDATION

EDUCATION RESEARCH NPS DISCOVERY SEARCH

## NPS DISCOVERY

### NPS DISCOVERY

The CFSRE's NPS Discovery program is an open-access drug early warning system (EWS) operating in the United States. Our evidence-based approach leads the development of high impact reports for real-time action among public health and safety stakeholders.

We are working in collaboration with forensic science, public health, emergency medicine, and criminal justice agencies to rapidly identify emerging drugs, also known as Novel Psychoactive Substances (NPS), associated with intoxications and adverse events. Our data and results are consolidated into reports and resources to allow for the rapid dissemination of information to colleagues and affected communities.

Stakeholders interested in receiving up-to-date information and notifications can join our [email listserve](#) (be sure to select the NPS Discovery check box at the bottom).




# JOIN OUR LISTSERV & NEWSLETTER



DON'T MISS THE LATEST FROM NPS DISCOVERY SUBSCRIBE TO OUR E-NEWSLETTER TODAY

SUBSCRIBE NOW



The Center for Forensic Science Research & Education

### Sign Up for Our Newsletter

Subscribe to our Newsletter!

Take future action with a single click. Log in or sign up for FastAction

[fastaction](#)

#### Contact Information

I'm signing up on behalf of a company or organization

First Name  Last Name

Email

Remember me so that I can use FastAction next time.

#### Profession

Please choose the closest match, so we can keep you up to date on relevant content from the CFSRE!

- Crime Lab Directors
- Forensic Biology
- Forensic Chemistry
- Forensic Toxicology
- Law Enforcement
- Legal Professional
- Medical Professional
- Student

What Newsletter would you like to sign up for?

- CFSRE Weekly Newsletter
- NPS Discovery Newsletter

# DOWNLOAD MORE PRESENTATIONS FROM THE CFSRE

The screenshot shows the CFSRE website interface. At the top, the navigation bar includes 'RESOURCES', 'ABOUT', 'OUR LAB', 'CONTACT', and a 'DONATE' button. Below this is a secondary navigation bar with 'EDUCATION', 'RESEARCH', and 'NPS DISCOVERY' dropdown menus, along with a search icon. The main content area is titled 'Presentations' and features a list of items. The first item is 'Quarterly NPS Discovery Webinar Series – July 2023' by Logan BK, Krotulski AJ, Papsun DM, and Walton SE. A 'READ MORE' button is located below this entry. To the right, a sidebar contains links for 'News', 'Publications', and 'Presentations'. The 'Presentations' link is highlighted with a red circle and the number '2'.

▪ Visit [www.cfsre.org](http://www.cfsre.org)

1 Select → *Resources*

2 Select → *Presentations*

3 Browse & Download



# COLLABORATE WITH CFSRE & NPS DISCOVERY

- We accept toxicology samples and drug materials for NPS testing
- Contact Alex Krotulski for more information ► [alex.krotulski@cfsre.org](mailto:alex.krotulski@cfsre.org)

## BENEFITS OF TOXICOLOGY TESTING AT THE CFSRE:

- ☠ Perform routine testing for all NPS subclasses, including opioids, benzodiazepines, stimulants, hallucinogens, and cannabinoids.
- ☠ Assist medical examiners and coroners with determining cause of death when prior toxicology testing is negative or inconclusive.
- ☠ Analysis by state-of-the-art instrumentation and methodologies.
- ☠ Regularly updated, comprehensive in-house library database containing more than 1,000 drugs.
- ☠ Sample handling and analysis performed under chain of custody.
- ☠ Forensic quality data and individual reports generated per case.
- ☠ World-leading forensic toxicologists, chemists, and scientists.
- ☠ Laboratory follows forensic toxicology industry best practices.

## TESTING CATALOG

### NPS Opioids

Fentanyl Analogues, Nitazene Analogues, U-Series, AP-Series, Other Novel Opioids

### NPS Benzodiazepines

Etizolam, Flualprazolam, Flubromazepam, Clonazolam, Bromazolam, Flubromazolam

### NPS Stimulants

Empathogens, Cathinones, Amphetamines, Phenethylamines, Pyrrolidines

### NPS Hallucinogens

Psychedelics, Dissociatives, PCP Analogues, Ketamine Analogues, LSD Analogues

### Synthetic Cannabinoids

Classical, Indoles, Indazoles, Miscellaneous, Newly Emergent, & Many More!

# ACKNOWLEDGEMENTS

- **CFSRE Team**

- Barry Logan
- Alex Krotulski
- Sara Walton
- Josh DeBord
- Mandi Mohr
- Melissa Fogarty
- Alyssa Reyes
- Brianna Stang
- Lindsey Domonoski
- Natasha Cunningham
- Many others!

- **NMS Labs**

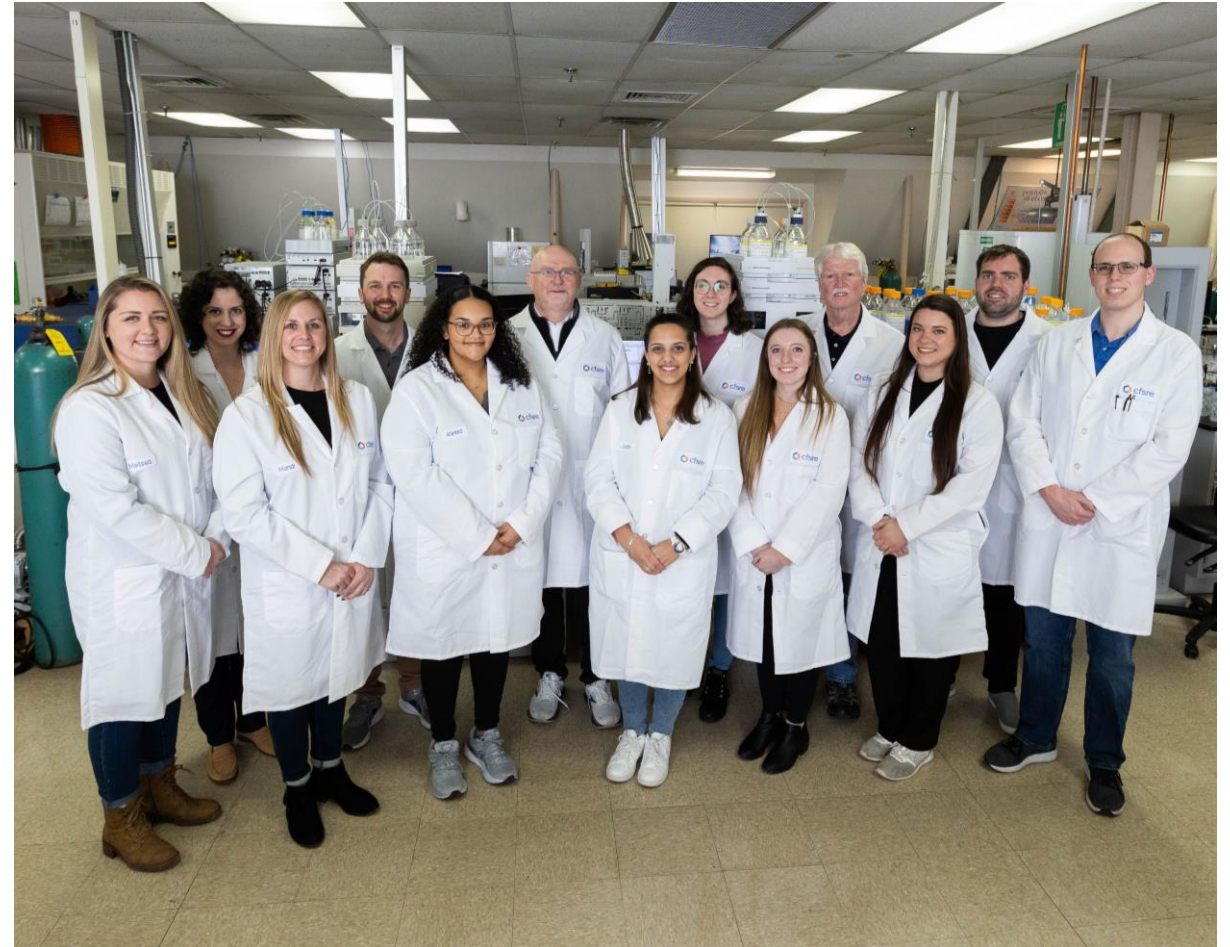
- Donna Papsun

- **Funding Agencies**

- NIJ, CDC, NIH, etc.

- **Collaborators & Partners**

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





**THANK YOU!**      **QUESTIONS?**



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