



Novel Psychoactive Substances (NPS): Up-To-Date Emerging Drug Trends

Alex J Krotulski, PhD – Associate Director (CFSRE)

*The Tail Wagging the Dog - Staying on Top of Emerging Drug Trends / Sunday August 15, 2021, 1:00-2:00 PM
2021 IACP Training Conference on Drugs, Alcohol, and Impaired Driving (DAID)*

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.



Background

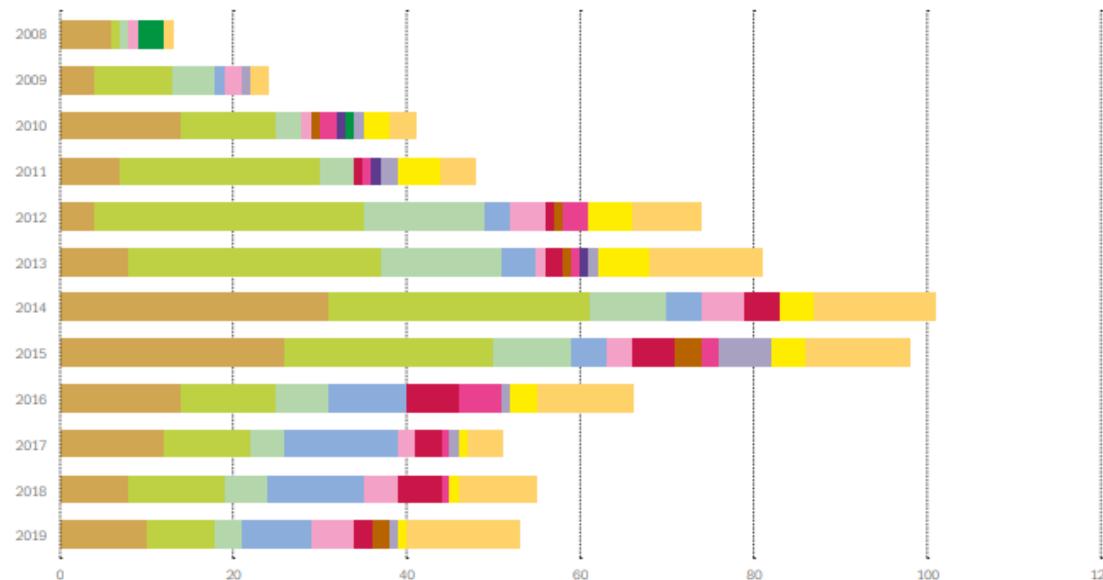
Novel Psychoactive Substances (NPS)

- Can be a **natural, synthetic, or semi-synthetic substance** in pure form, mixture, or preparation:
 - A. Discovered or synthesized for the first time since the mid-2000's (*Example: MDMB-4en-PINACA*)
 - B. Previously discovered, synthesized, or reported but has now been observed for the first time in more than 10 years (*Example: Isotonitazene*)
 - C. Used in a novel way or differing manner from its original intended us (*Example: Fentanyl*)
 - D. Not-well described or studied but now presents significant challenges or threats due to an altered toxicological effect profile (*Example: Mitragynine*)

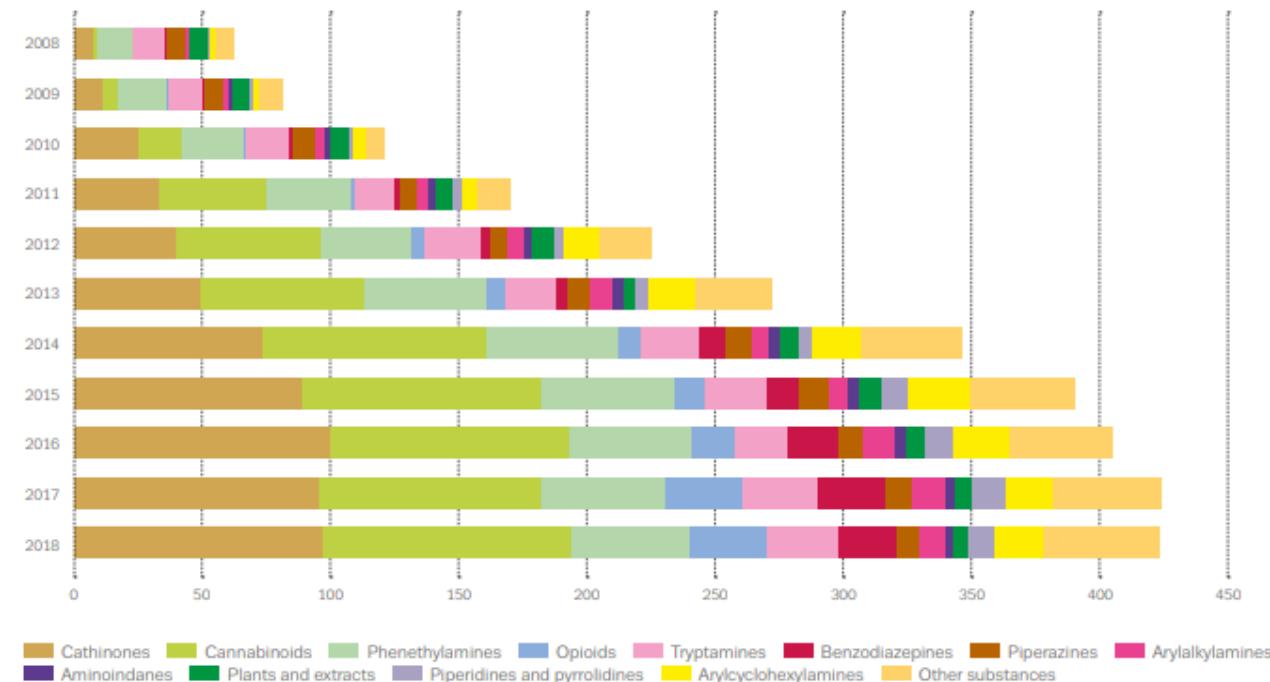


The Vast Universe of NPS

NUMBER AND CATEGORIES OF NEW PSYCHOACTIVE SUBSTANCES REPORTED TO THE EU EARLY WARNING SYSTEM FOR THE FIRST TIME, 2008-19

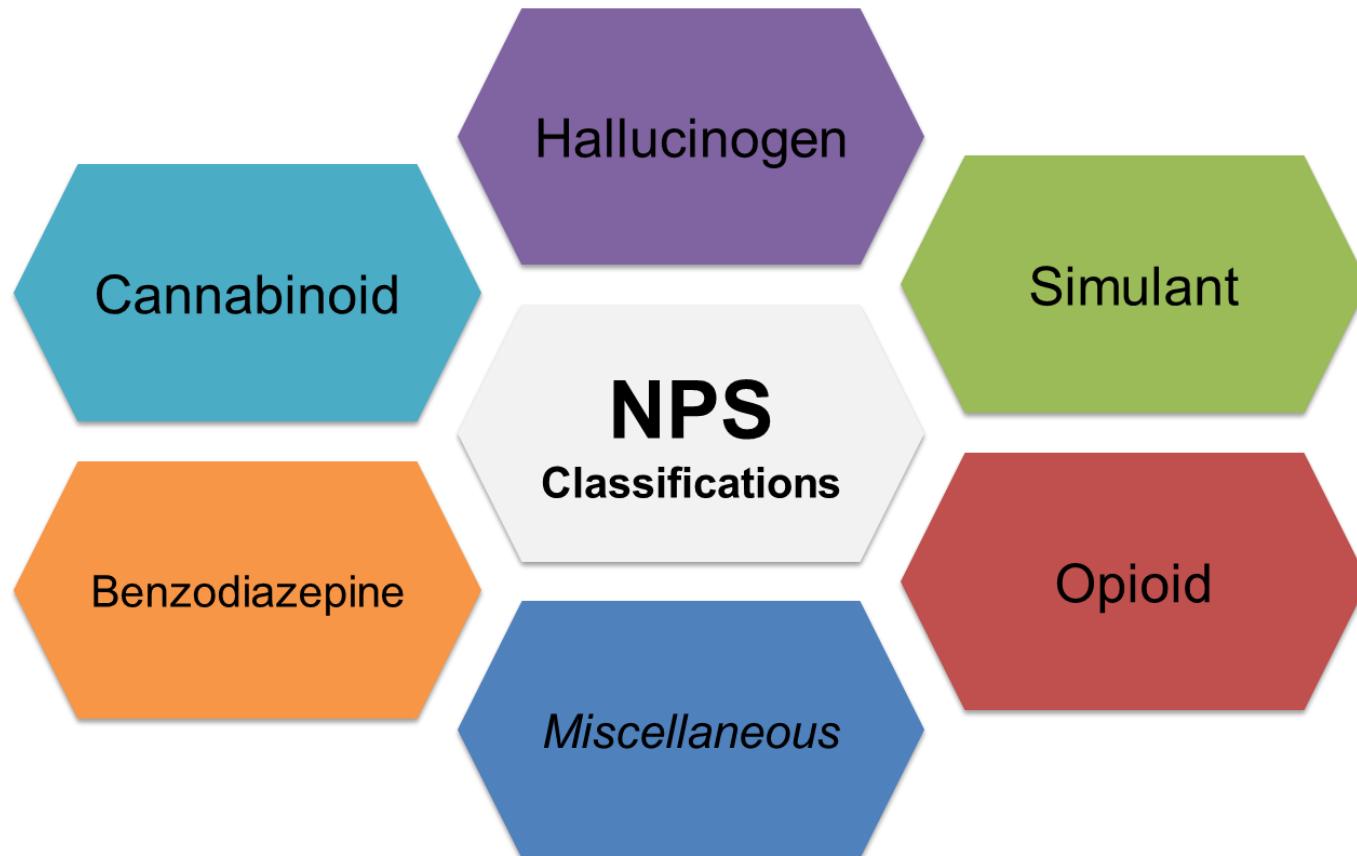


NUMBER AND CATEGORIES OF SUBSTANCES DETECTED EACH YEAR, FOLLOWING THEIR FIRST DETECTION, 2008-18



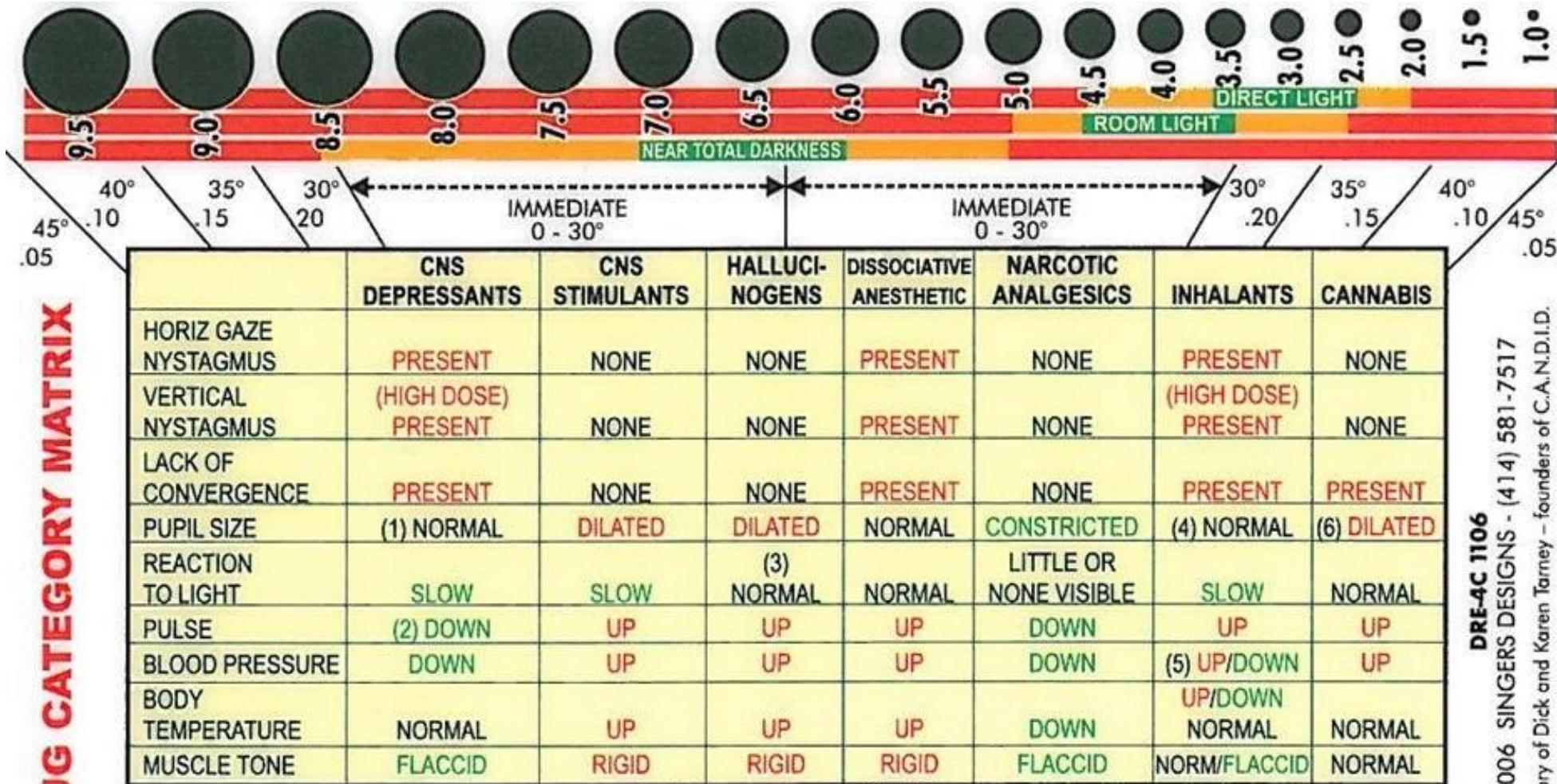
Source: www.emcdda.europa.eu

NPS Classes and Sub-Classes



- **NPS Opioids:**
 - Fentanyl Analogues
 - Carfentanil
 - Diaminocyclohexane Benzamides
 - U-47700
 - Benzimidazoles
 - Isotonitazene
 - Cinnamylpiperazines
 - 2-Methyl AP-237
 - Thiambutenes
 - Piperidylthiambutene
 - Piperidine Benzimidazolones
 - Brorphine
 - Etc.

DRUG CATEGORY MATRIX



(1) Soma & Quaaludes usually dilate.

(2) Quaaludes & alcohol may elevate.

(3) Certain psychedelic amphetamines cause slowing.

(4) Normal but may be dilated.

B.A.C =
50 minus
ANGLE OF ONSET

(5) Down with anesthetic gases - up with volatile solvents & aerosols.

(6) Possibly normal.

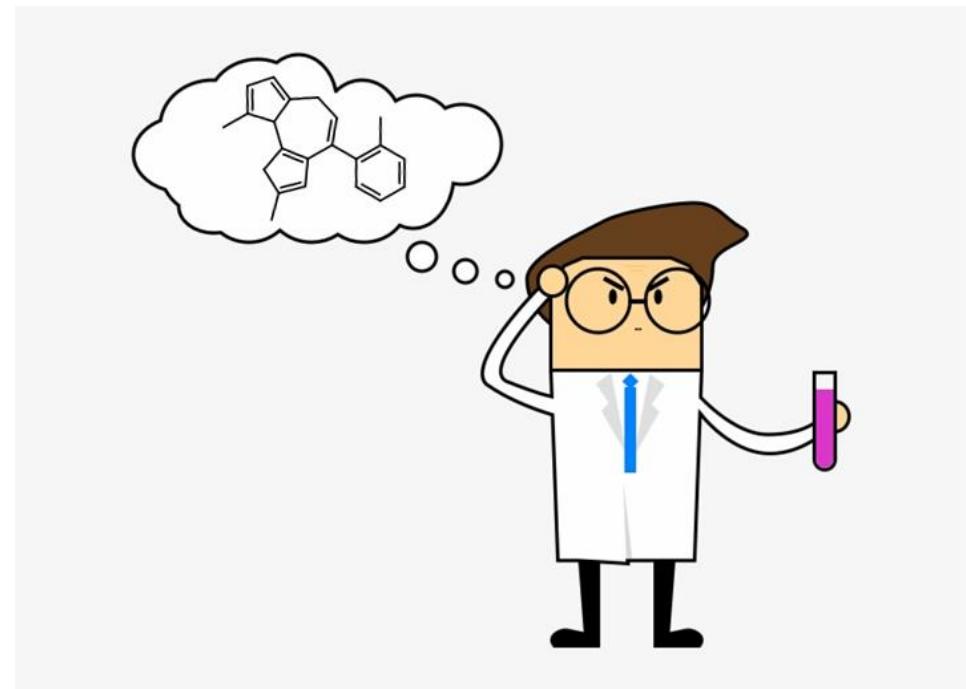
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In Memory of Dick and Karen Tarney - founders of C.A.N.D.I.D.



NPS Challenges

- Synthetic drugs present in forensically relevant samples often remain **unidentified** due to scope of analysis and analyst experience/expertise
 - But... what do you do with a positive finding?
- First identification are often **lagging or delayed**
 - Analytical capabilities, testing performed
 - Standard reference material
- Historically, there had been **no centralized reporting system** within the United States



Resources For Emerging Drug Information

- NPS Discovery
 - www.npsdiscovery.org
- Cayman Chemical
 - www.caymancell.com
- Drug Enforcement Administration
 - www.dea.gov
 - www.nflis.deadiversion.usdoj.gov
- EMCDDA
 - www.emcdda.europa.eu
- UNDOC
 - www.unodc.org/LSS/Home/NPS
- World Health Organization
 - www.who.int

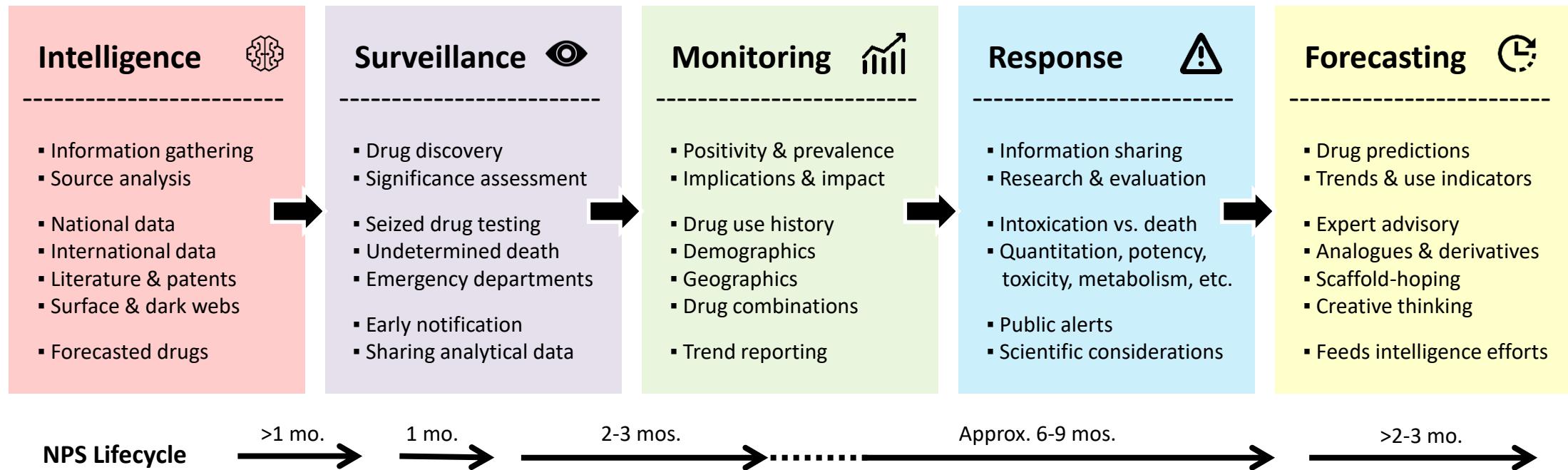
NPS Discovery

NPS Discovery

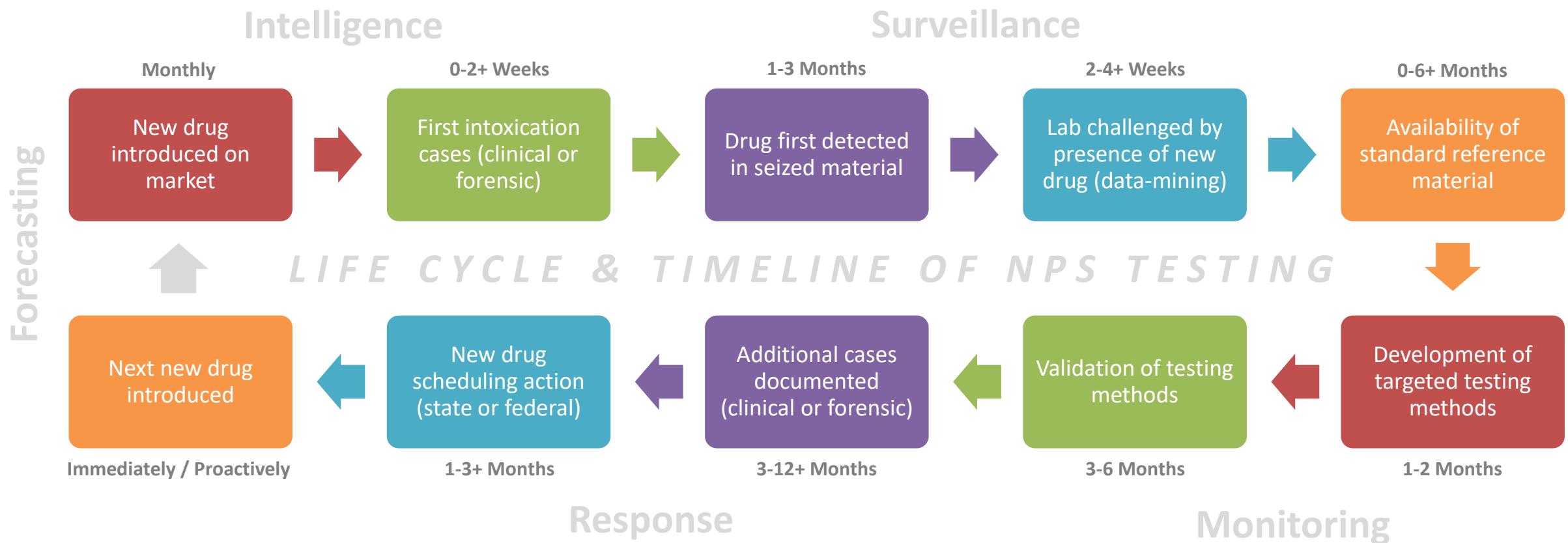
- Open-access drug early warning system with a national perspective



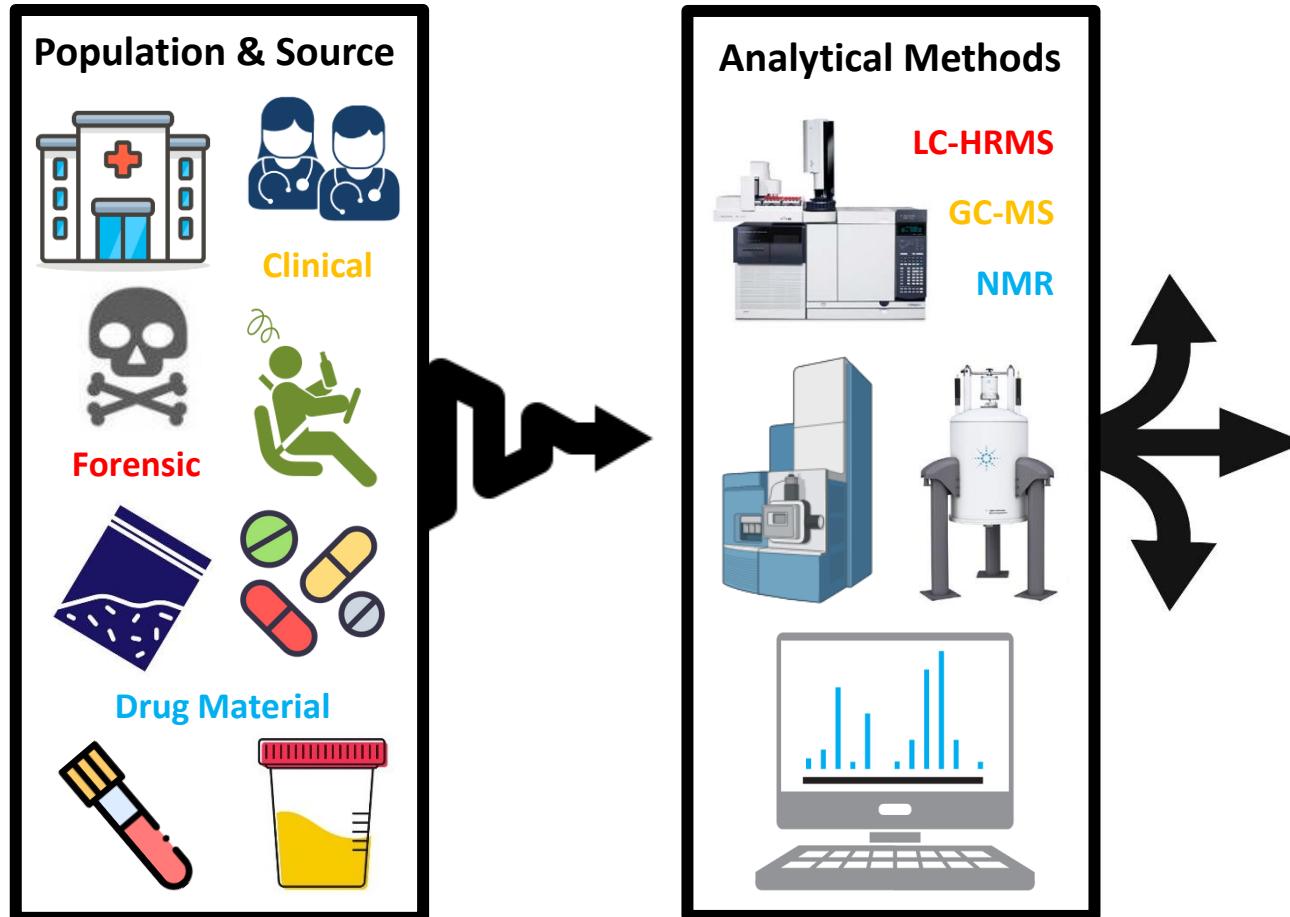
NPS Discovery Initiatives



Timeline for an Emerging NPS



Testing Workflows for NPS

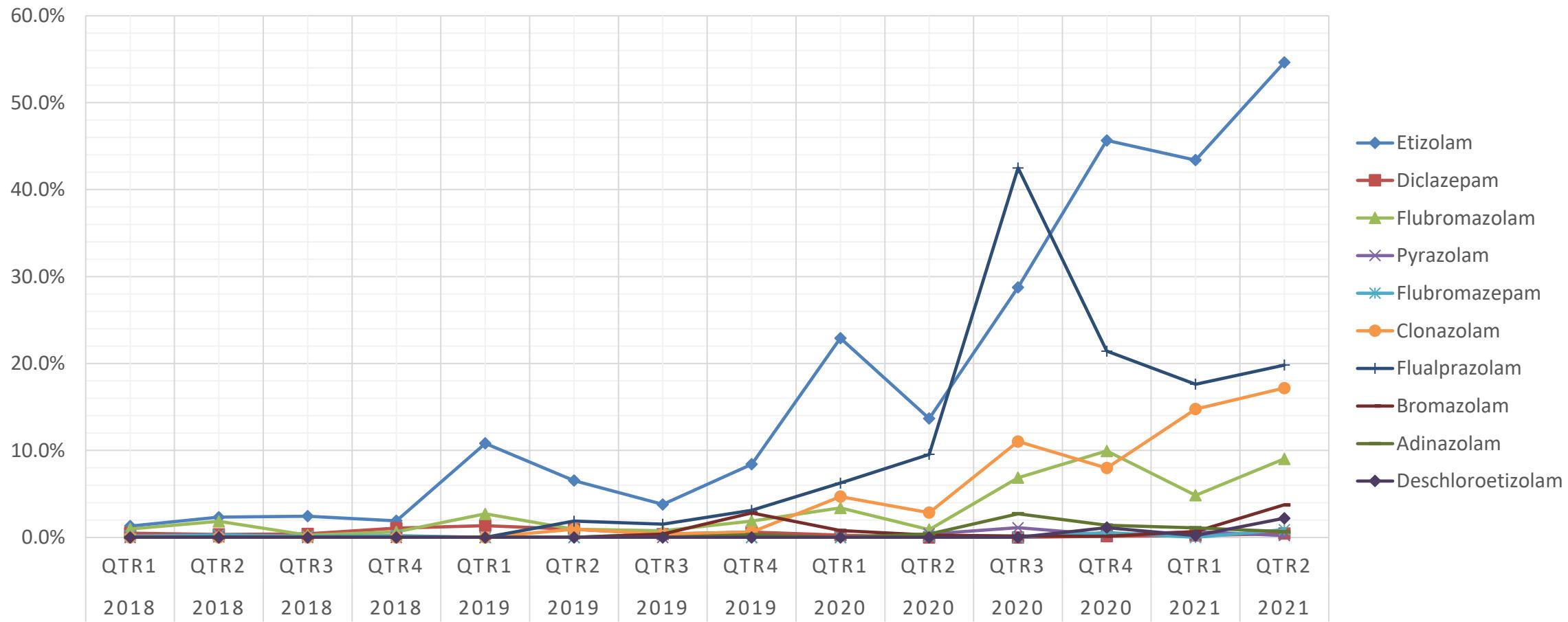


- **Model Scenarios:**

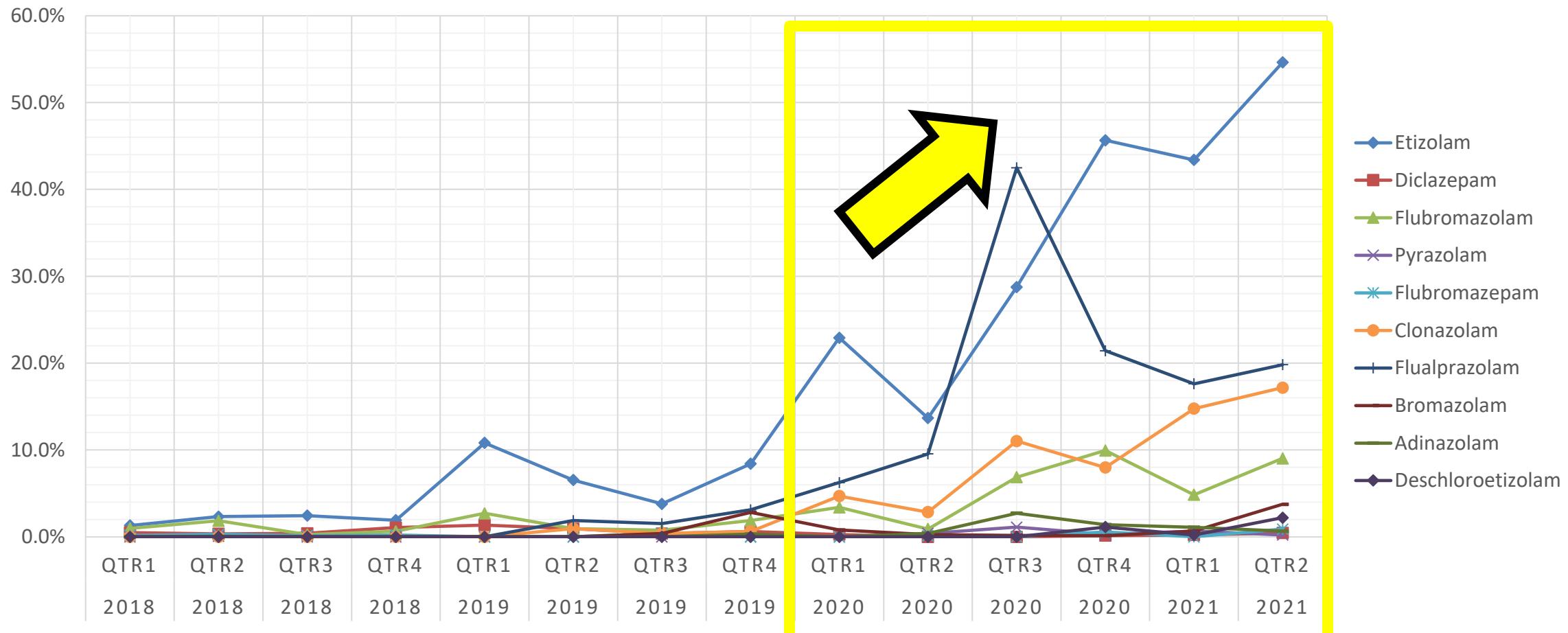
- Unknown powder found near decedent
- Suspected drugs overdose with no identifiable cause of death
- Individuals acting / driving erratically with negative toxicology
- Patients presenting to emergency department with adverse effects

Current NPS Trends (*UPDATED*)

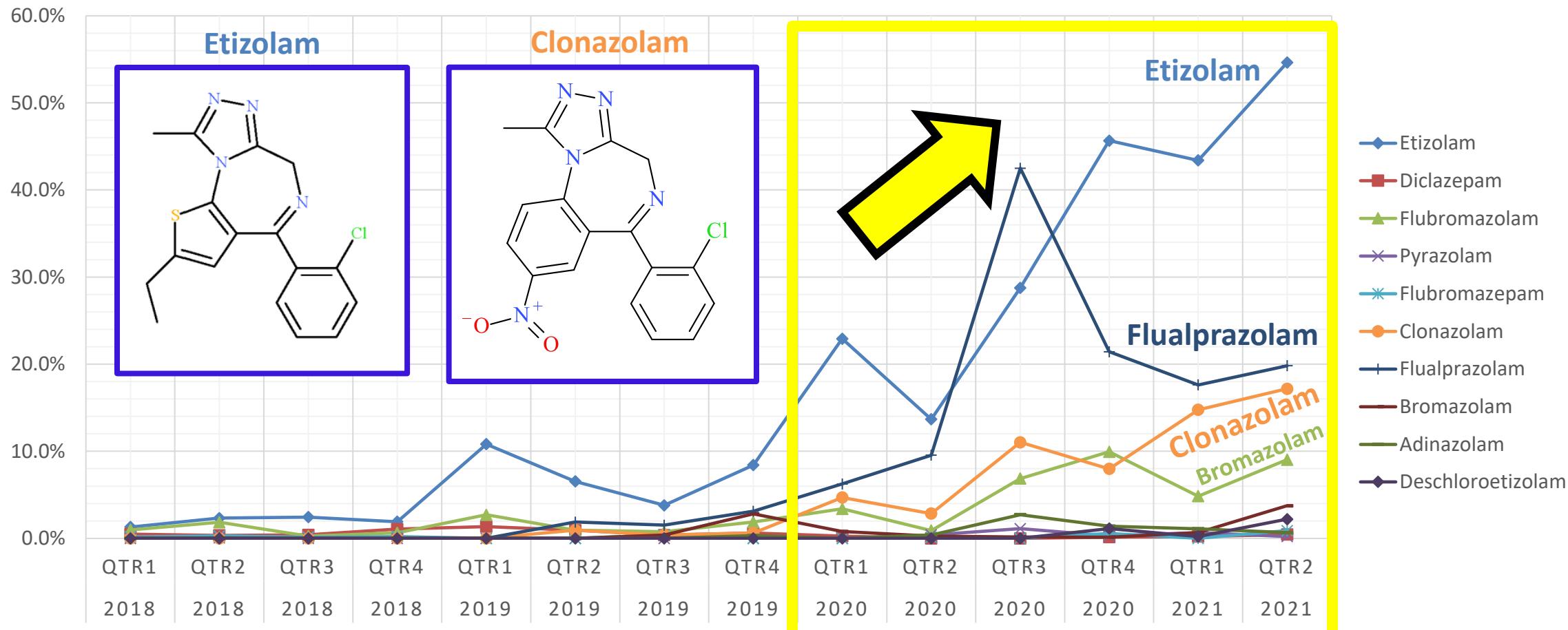
NPS Benzodiazepines



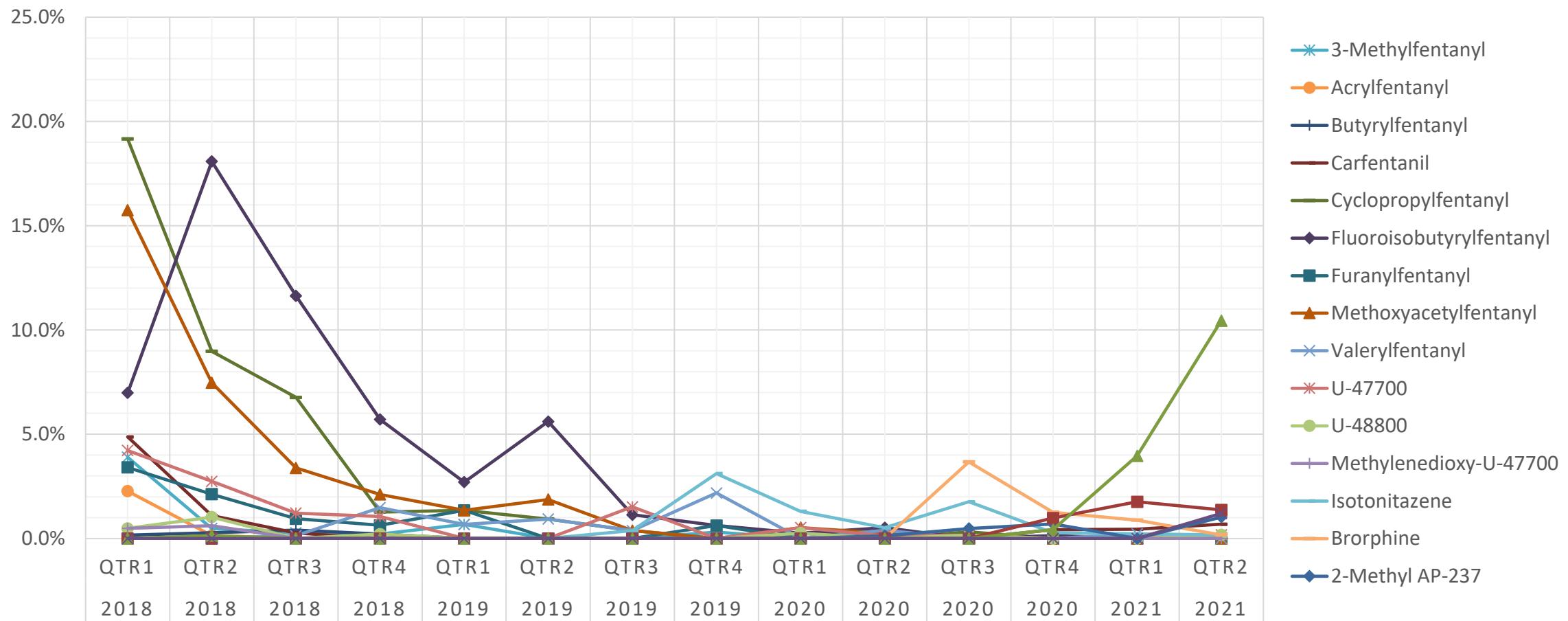
NPS Benzodiazepines



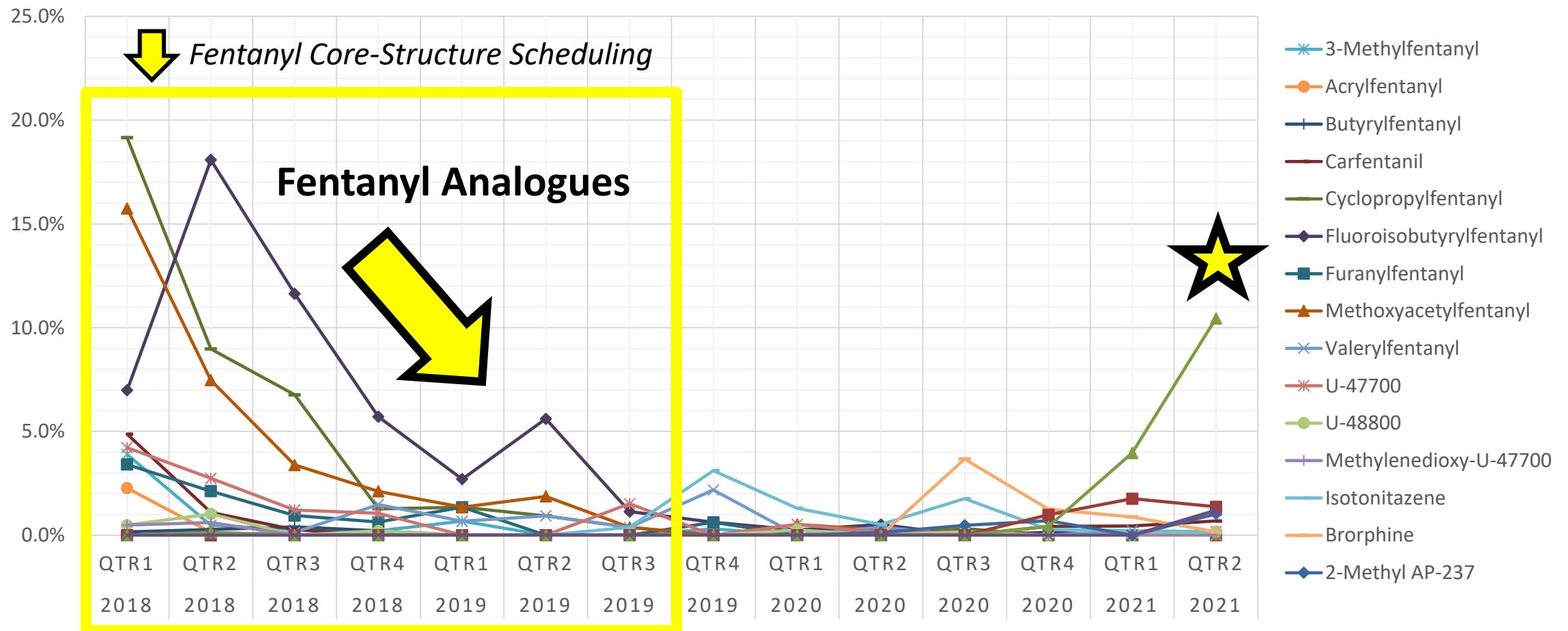
NPS Benzodiazepines



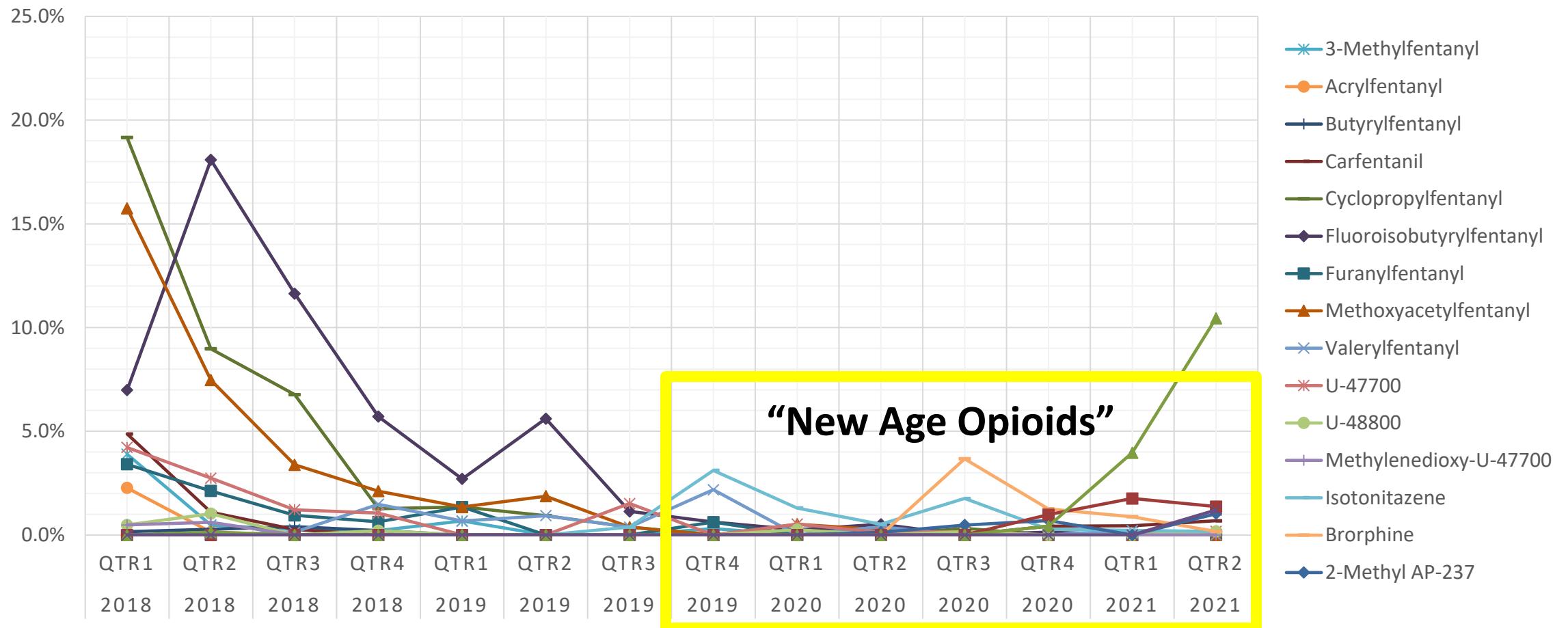
NPS Opioids



NPS Opioids

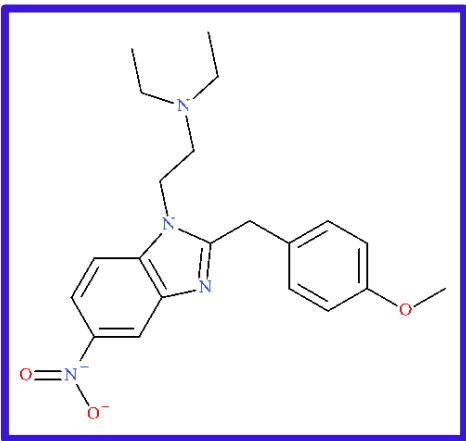


NPS Opioids

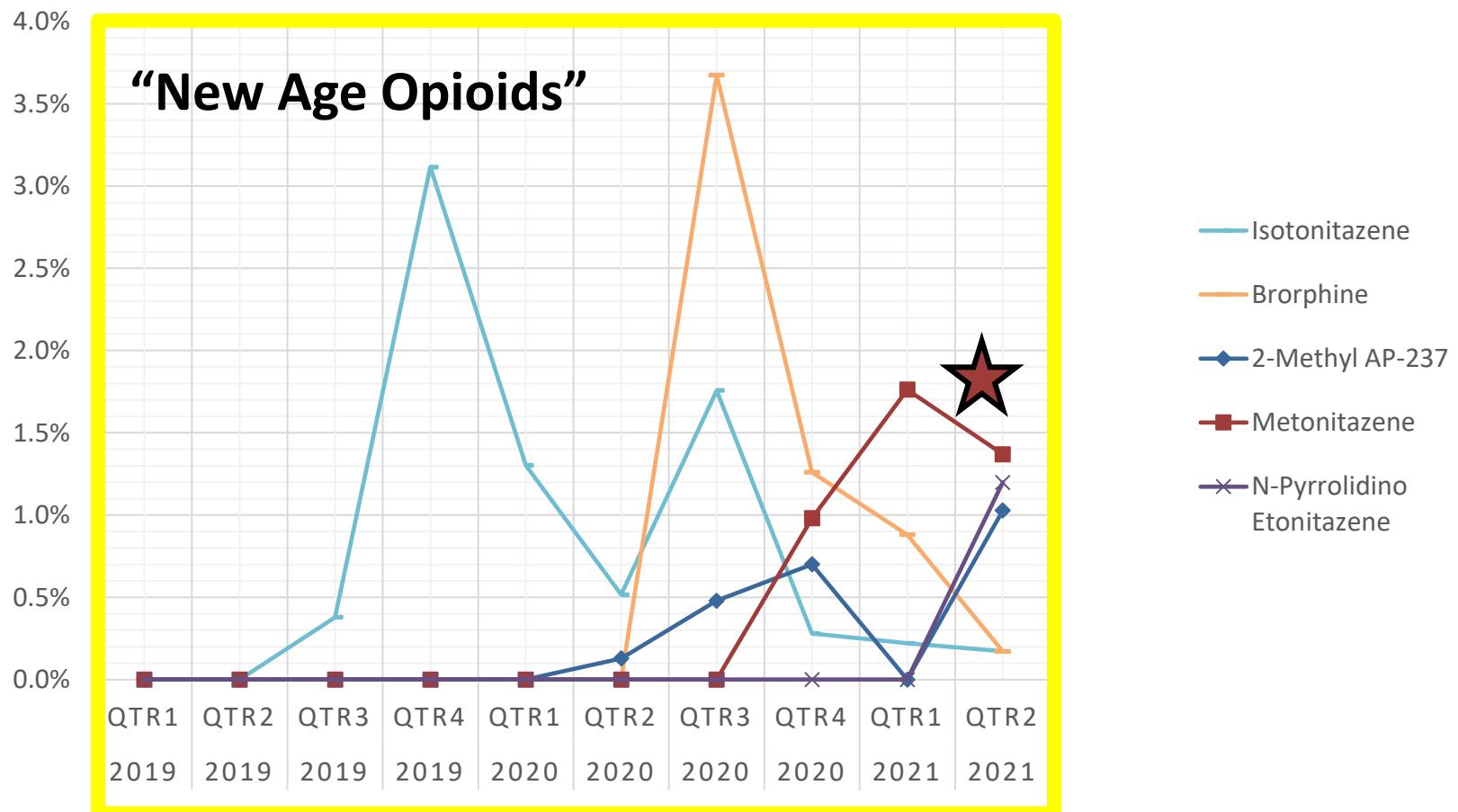
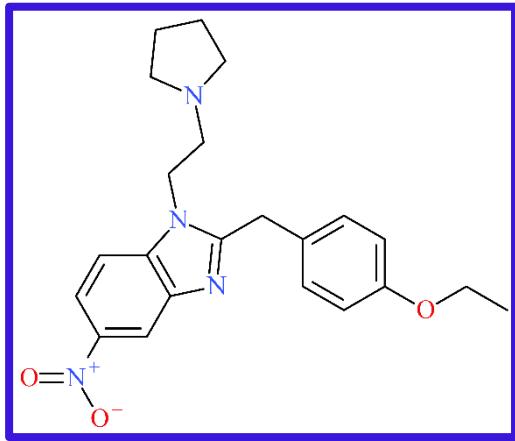


NPS Opioids

Metonitazene



N-Pyrrolidino Etonitazene



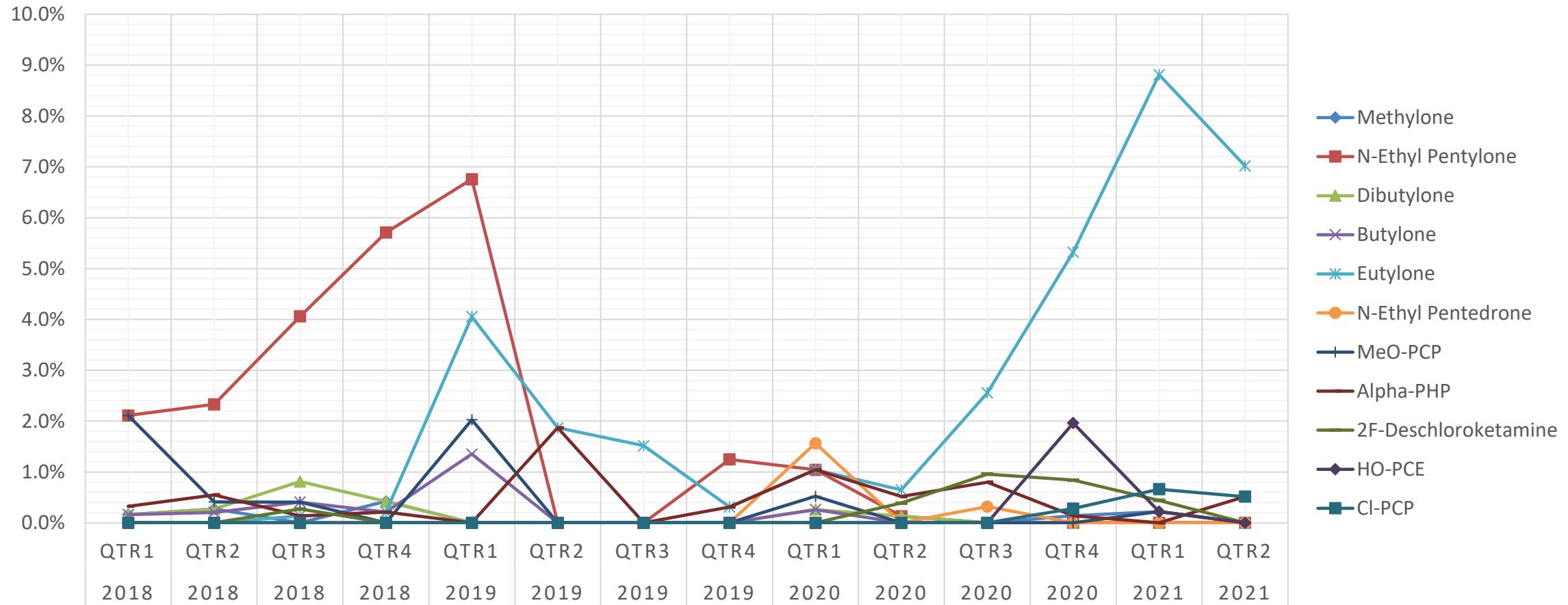
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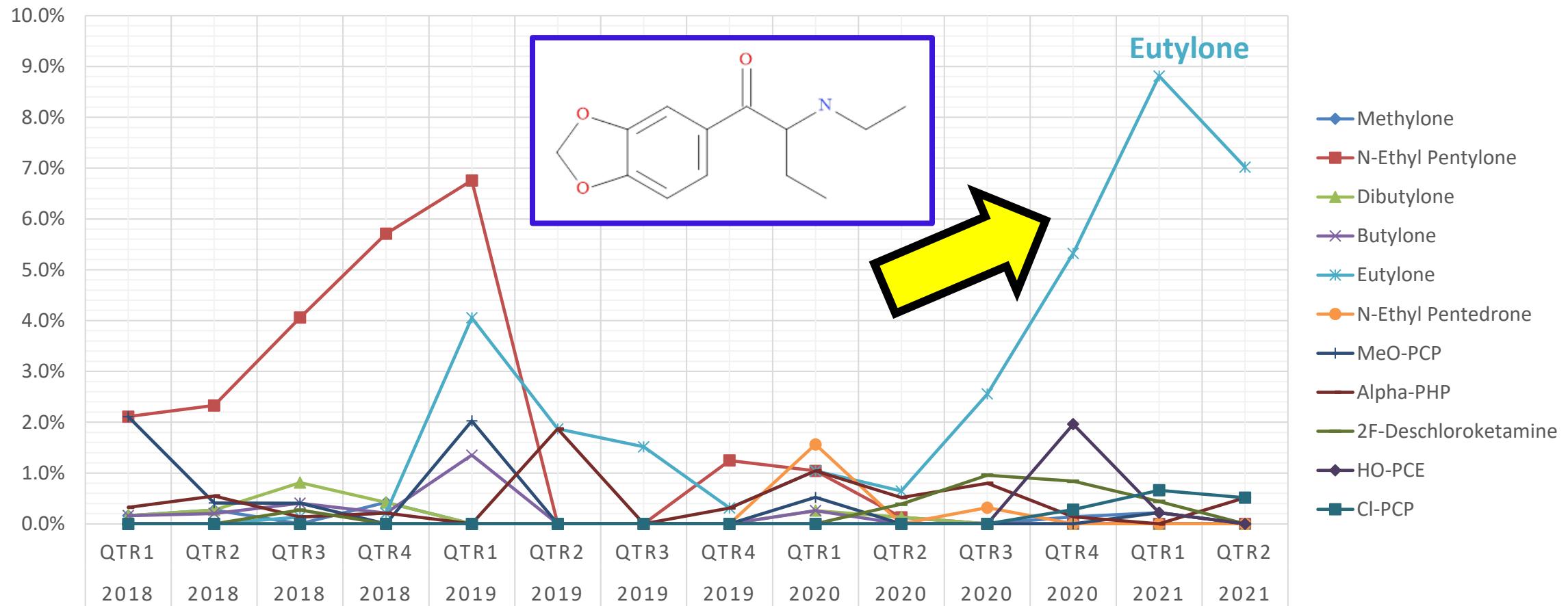
NPS DISCOVERY

*Rapid Turnover

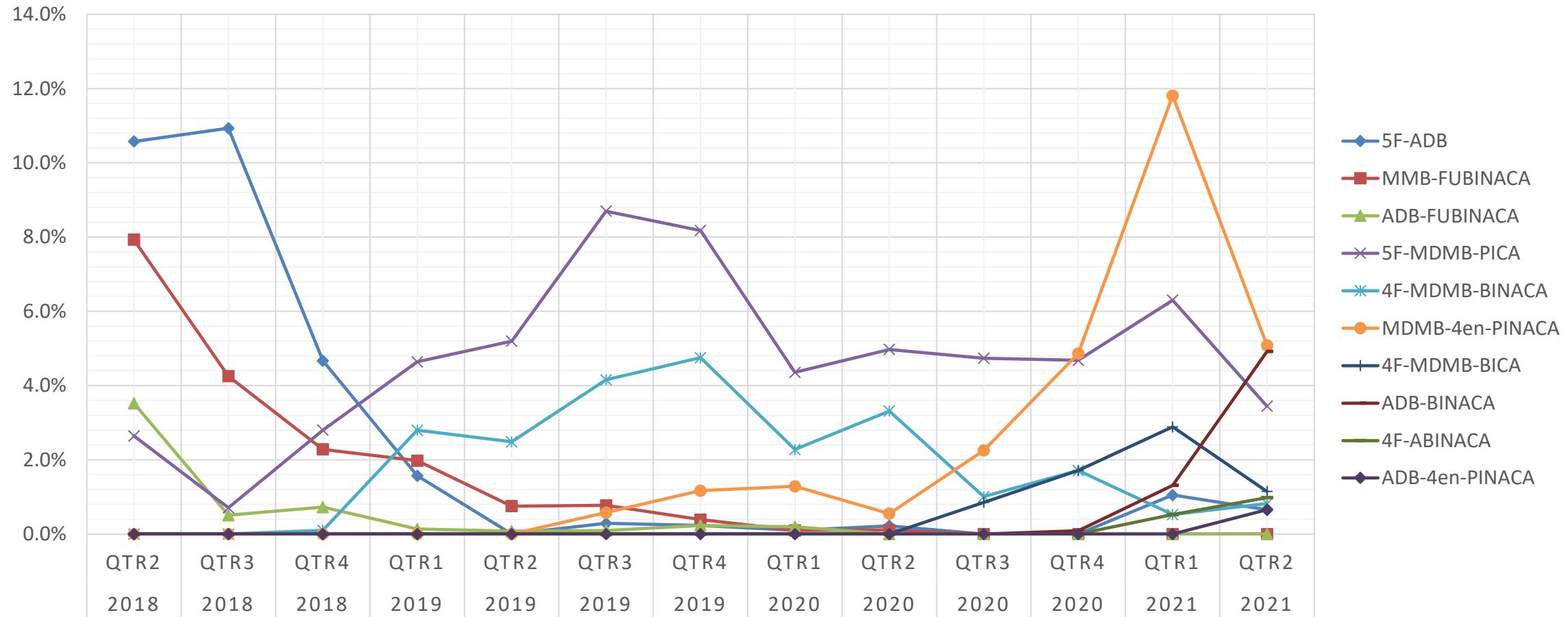
NPS Stimulants and Hallucinogens



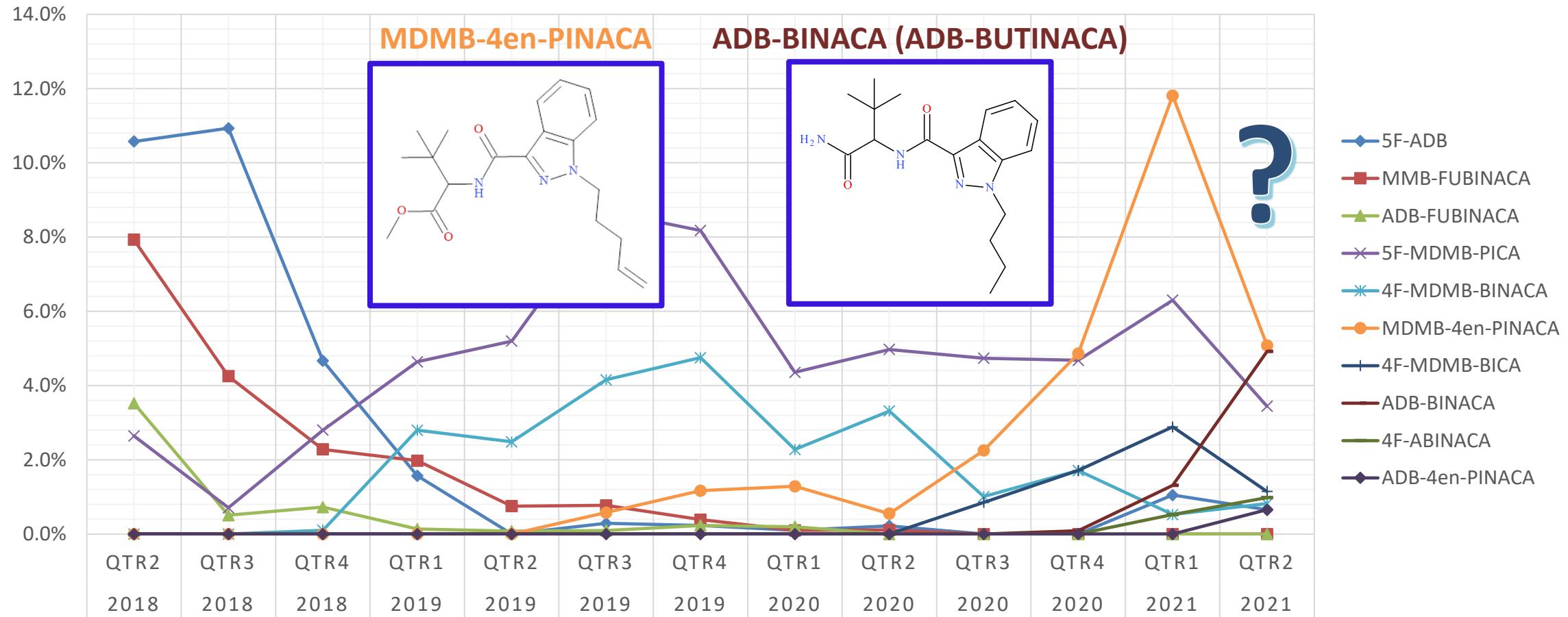
NPS Stimulants and Hallucinogens



Synthetic Cannabinoids



Synthetic Cannabinoids



Emerging Market Trends

- **NPS Benzodiazepines**
 - New drugs continue to appear, more so than in previous years
 - Retain simple chemistry but can vary in potency and effects
 - “-lams” are most common (etizolam)
- **NPS Stimulants and Hallucinogens**
 - Same stimulant, little turnover
 - New hallucinogens
 - PCP and ketamine analogues
- **NPS Opioids**
 - Increased potency → challenging
 - Rapid emergence and turnover
 - Increased sub-class variety
 - “Nitazene” analogues and AP series
- **Synthetic Cannabinoids**
 - Less structural variety in recent years***
 - Retaining high potency
 - More “ADB-” variants emerging

NPS Discovery Reports → www.npsdiscovery.org

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N-Pyrrolidino Etonitazene

Sample Type: Biological Fluid

Latest Revision: May 13, 2021
Date of Report: May 13, 2021

Trend Report: Q2 2020

NPS Stimulants & Hallucinogens in the United States

Purpose: This report provides up-to-date information regarding NPS stimulant & NPS hallucinogen prevalence and positivity within the United States.

Overview: Novel psychoactive substances (NPS), including NPS stimulants and NPS hallucinogens, continue to pose great challenges for forensic science, clinicians, and public health safety personnel. Both NPS stimulants and NPS hallucinogens have been implicated in emergency room admissions, poisonings, and other medical emergencies, often with night clubs and music festivals. Maintaining a current scope of analysis can be challenging, requiring comprehensive analytical methodologies and reference materials for identification.

Objective: Our laboratory employs novel approaches for the analysis of drugs in biological samples and seized materials using comprehensive non-targeted data acquisition by gas chromatography mass spectrometry (GC-MS) and liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The laboratory has developed a novel approach for screening and identification of NPS stimulants and hallucinogens, including red-line identification of emerging stimulants and hallucinogens, and further data analysis of important trends. This project was conducted in collaboration with the toxicology and stimulants laboratories of NMS Labs. Forensic case types linked to these results include illicit drug investigations, toxicology cases, and controlled substance analyses. The following tables and figures present the data. The numbers presented represent the total number of NPS identifications at CFSRE during this quarter, including those from sample-testing, drug-testing, and/or casework testing.

Important Notes: All data presented here is preliminary and subject to change in comparison to analysis.

Prepared By: Alex J. R. Fogarty, MSFS, D-A

1. GENERAL INFO

IUPAC Name: N-Ethyl Pentone

InChI String: CC(C)C

CFR: None

CAS#: None

Synonyms: None

Source: CFSRE

Notes: None

Important Notes: All data presented here is preliminary and subject to change in comparison to analysis.

Prepared By: Alex J. R. Fogarty, MSFS, D-A

Sample Type: Biological Fluid

Latest Revision: May 13, 2021
Date of Report: May 13, 2021

Chemical Structure: CN1CC=CC=C1Cc2ccccc2OCC(=O)N3CCC4=C(C=C3)C=C4

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Date of Report: May 13, 2021

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January 2019

New Synthetic Cannabinoid: 4F-MDMB-BINACA

Purpose: The objective of this public announcement is to notify public health and public safety, law enforcement, clinicians, medical examiners and coroner, laboratory personnel, and all other related communities about new information surrounding the emerging synthetic cannabinoid 4F-MDMB-BINACA.

Summary: 4F-MDMB-BINACA, first identified in seized drug casework in the United States in December of 2018, has been identified in eight blood specimens associated with post-mortem death investigations and driving under the influence of drugs (DUID) investigations. 4F-MDMB-BINACA is very similar in structure to the popular synthetic cannabinoid 5F-ADB (5F-MDMB-PINACA), differing by the removal of one carbon ($-CH_2-$) linkage from the carbon chain (or tail) portion of the molecule. 5F-ADB has been associated with a large number of adverse events, including death. The pharmacology and toxicity of 4F-MDMB-BINACA have not been explicitly studied, but its relation to 5F-ADB and association with drug user deaths lead professionals to believe this new synthetic cannabinoid would be an active novel psychoactive substance (NPS) and retain the potential to cause adverse events.

Background: Synthetic cannabinoids ("Spice" or "K2") are chemically manufactured drugs, often associated with unknown biological effects and health risks, a dangerous combination for any recreational drug user. Synthetic cannabinoids can be prepared (e.g. plant material, powder) and packaged (e.g. foil packaging) in a variety of forms. Recently, synthetic cannabinoids have been identified in combination with more traditional drug supplies, including the heroin supply in Philadelphia, PA; a circumstance that lead to more the 160 drug overdoses in the city over one year and 15 deaths.

Adverse Events: Adverse events associated with 4F-MDMB-BINACA include (e.g., psychosis, agitation, irritability, paranoid delusions, self-harm, etc.), other physical ailments (tachycardia, gastrointestinal distress, acute kidney injury, etc.) and death.

Recommendations for Clinicians: Be familiar with the signs and symptoms of synthetic cannabinoid use; can range from mild and agitated delirium to sedation, drowsiness, and bradycardia; always alert to the fact that clinical conditions may be rapidly and unpredictably.

Conclusion: If illicit drugs are of quality control, containing adulterants, and causing the tested clinical effects or findings, alert about the dangers of synthetic cannabinoid products and other drugs.

Recommendations for M/F's & Coroners:

- Utilize analytical data available for identification of 4F-MDMB-BINACA synthetic cannabinoids if not available to your laboratory.
- Develop screening and up-to-date protocols for synthetic cannabinoids if instances result in an unspecified drug test.
- Prioritize analytical testing of samples taken from drug overdose investigations.
- Share data on synthetic cannabinoids with local health departments, examiners, and coroners.

Recommendations for Laboratories:

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New Discoveries in Q2 2020

Chemical Structures:

Learn More About NPS Discovery:

Get Involved:

Get Involved:

Learn More About NPS Discovery:

Opioid Overdoses from the Toxicology Investigators Consortium (ToxIC) Fentanyl Study Group

Q2 2021

Sample Source: Patients presented to emergency departments within ACMT - Toxicology Investigators Consortium (ToxCi) experiencing a suspected opioid overdose. Baseline discarded biological samples were obtained for testing against an extensive library of drugs and other substances. Our findings provide a new real-time assessment of the drug market and allow to resulting implications on clinical institutions.

Testing: Analysis was performed via liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The scope of testing targeted more than 900 drugs, including a vast majority of NPS and metabolites. Drug classes included opioids, stimulants, cannabinoids, and benzodiazepines, among others.

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Location: Bethlehem, PA
Key Findings:

- > 1000 of samples were positive for at least one opioid
- Fentanyl (94%) was very commonly detected, followed by propoxyphene (45%), tramadol (12%), and oxymorphone (8%)
- 2-Xylazine was observed alongside fentanyl (20%)
- Combined opioid and stimulant was the most common combination and was observed alongside fentanyl and zolamadol

Comparison to Key Findings in Q1 2021:

- Fentanyl remains the most commonly encountered synthetic opioid in eastern Pennsylvania
- The percentage of novel synthetic opioid is increasing
- Opioid and stimulant co-occurrence remained common and increased from 50% to 60%

Drug Supply Assessment: Q2 2021

Philadelphia, Pennsylvania, USA

Purpose: This report provides up-to-date information regarding the drug supply in Philadelphia, Pennsylvania, United States.

Overview: Traditional drugs (e.g., cocaine, methamphetamine, etc.) identified among seized samples in Philadelphia, Pennsylvania, are the most commonly identified drugs. However, new drugs, such as fentanyl, are appearing in the drug market and are being used in combination with traditional drugs or added to traditional drug preparations. The drug supply in Philadelphia, Pennsylvania, is dynamic and changing rapidly. The following tables and figures present the data. The numbers presented represent the total number of samples reported between February and April 2021.

Summary and Key Findings:

- > 91 samples were reported between February and April 2021
- Most "heroin" samples contained fentanyl (or) with zylactone, which was identified in a few samples
- Cocaine and methamphetamine are still the most commonly identified drugs in Philadelphia, Pennsylvania, but were not adulterated with other uncapping drugs, but fentanyl contamination was observed and determined to be insignificant
- pseudo-Fluorofentanyl is increasing in prevalence and was identified as the primary opioid in some "heroin" samples

Heroin / Dope (n=61)

Methamphetamine

PCP

Oxycodeone

2

2f-Tetrahydronaphthalene (2f-TDN)

2

2f-Tetrahydronaphthalene (2f-TDN)

8

Other (e.g. 4f-PCP, Fluorofentanyl)



Acknowledgements

- **Center for Forensic Science Research & Education (CFSRE)**

- Barry Logan
- Mandi Mohr
- Melissa Fogarty
- Judith Rodriguez-Salas
- Sara Walton

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- Donna Papsun
- Sherri Kacinko





Thank You!

Contact Information:

Alex J Krotulski, PhD

alex.krotulski@cfsre.org

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