Updated Trend Reports and Positivity Plots

NPS Discovery Webinar Series – Thursday October 12, 2023

Sara E. Walton, M.S. – Center for Forensic Science Research and Education (CFSRE)

FUNDING DISCLOSURE

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  - 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.

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Q3 2023 NPS TREND REPORTS

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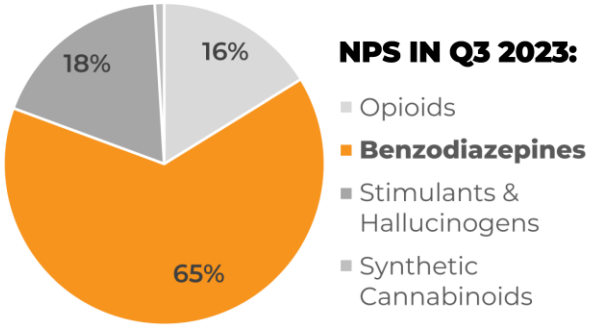
NPS Benzodiazepines in the United States

TREND REPORT | Q3 2023

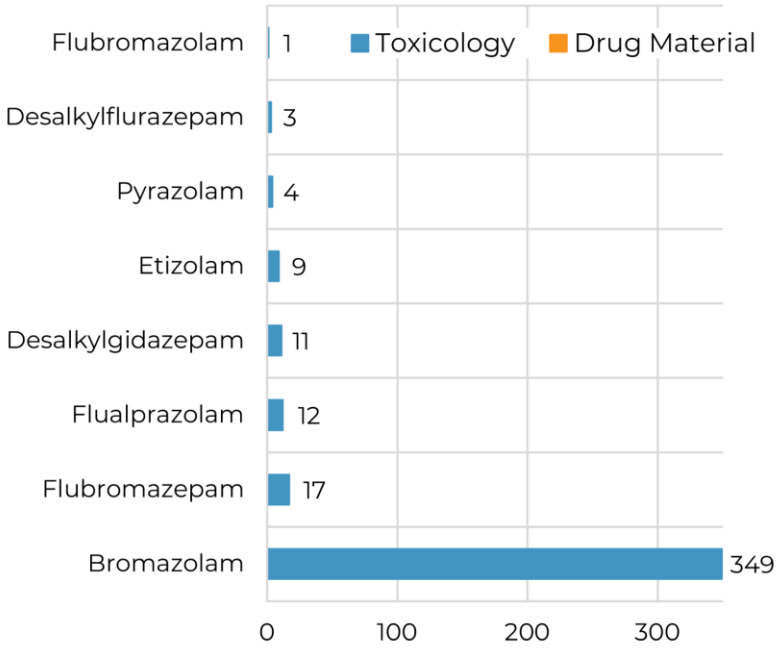
PURPOSE: This report provides up-to-date information regarding the status of NPS benzodiazepine prevalence and positivity in the United States.

OVERVIEW: Novel psychoactive substances (NPS), including NPS benzodiazepines, continue to pose great challenges for forensic scientists, clinicians, and public health and safety personnel. NPS benzodiazepines have been implicated in an increasing number of adverse health events, marked by emergency room admissions and death investigations, especially when ingested in combination with opioids. Maintaining a current scope of analysis can be challenging, requiring comprehensive analytical methodologies and reference materials for identification(s).

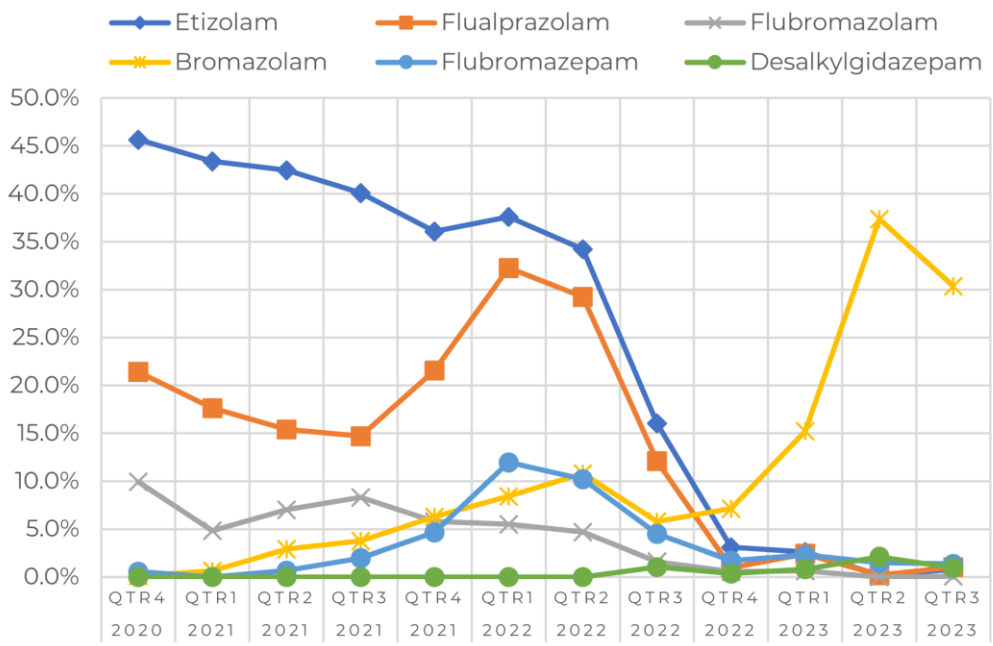
OBJECTIVE: Our laboratory utilizes novel approaches for the analysis of drugs in biological samples and seized materials using comprehensive non-targeted data acquisition by gas chromatography mass spectrometry (GC-MS) and liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The scope of analysis contains more than 1,100 drugs, including a vast majority of NPS and their metabolites. This approach allows for real-time identification of new benzodiazepines and further data analysis of important trends. This project was conducted in collaboration with the toxicology and criminalistics laboratories of NMS Labs. Forensic case types linked to these results include illicit drug investigations, medicolegal death investigations, and/or driving under the influence of drugs (DUID) investigations. The results in this report represent the total number of NPS identifications at the CFSRE during this quarter, including those from sample-mining, data-mining, and/or esoteric testing.



NPS BENZODIAZEPINES IDENTIFIED



SELECT POSITIVITY: Q4 2020 to Q3 2023



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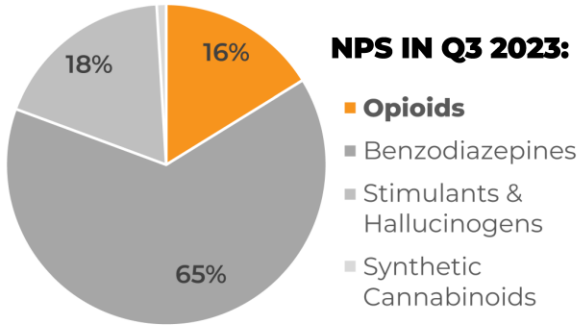
NPS Opioids in the United States

TREND REPORT | **Q3 2023**

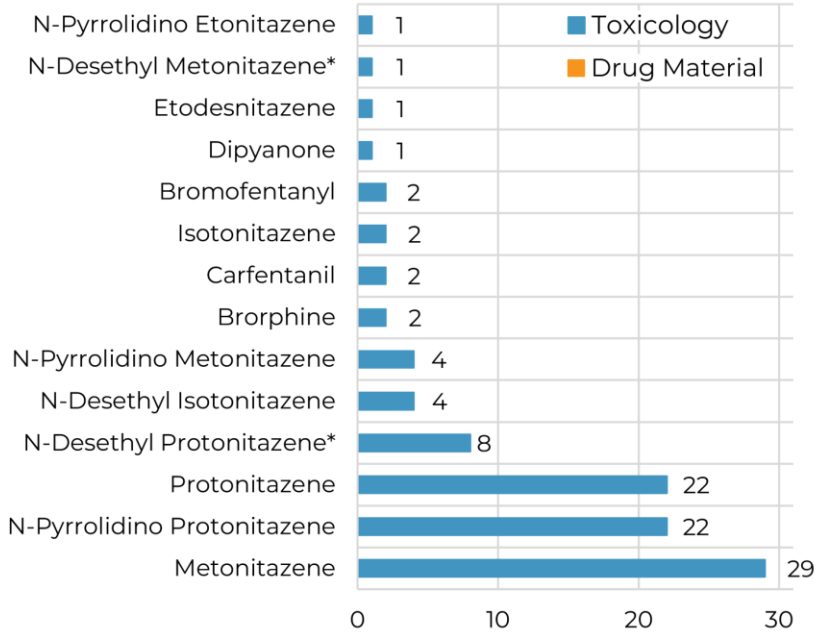
PURPOSE: This report provides up-to-date information regarding the status of NPS opioid prevalence and positivity in the United States.

OVERVIEW: Novel psychoactive substances (NPS), including NPS opioids, continue to pose great challenges for forensic scientists, clinicians, and public health and safety personnel. NPS opioids have been implicated in an increasing number of emergency room admissions, death investigations, and mass intoxication events, and often appear in combination with other illicit opioids (e.g. fentanyl, heroin). Maintaining a current scope of analysis can be challenging, requiring comprehensive analytical methodologies and reference materials for identification(s).

OBJECTIVE: Our laboratory utilizes 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 scope of analysis contains more than 1,100 drugs, including a vast majority of NPS and their metabolites. This approach allows for real-time identification of novel opioids and further data analysis of important trends. This project was conducted in collaboration with the toxicology and criminalistics laboratories of NMS Labs. Forensic case types linked to these results include illicit drug investigations, medicolegal death investigations, and/or driving under the influence of drugs (DUID) investigations. The results in this report represent the total number of NPS identifications at the CFSRE during this quarter, including those from sample-mining, data-mining, and/or esoteric testing.

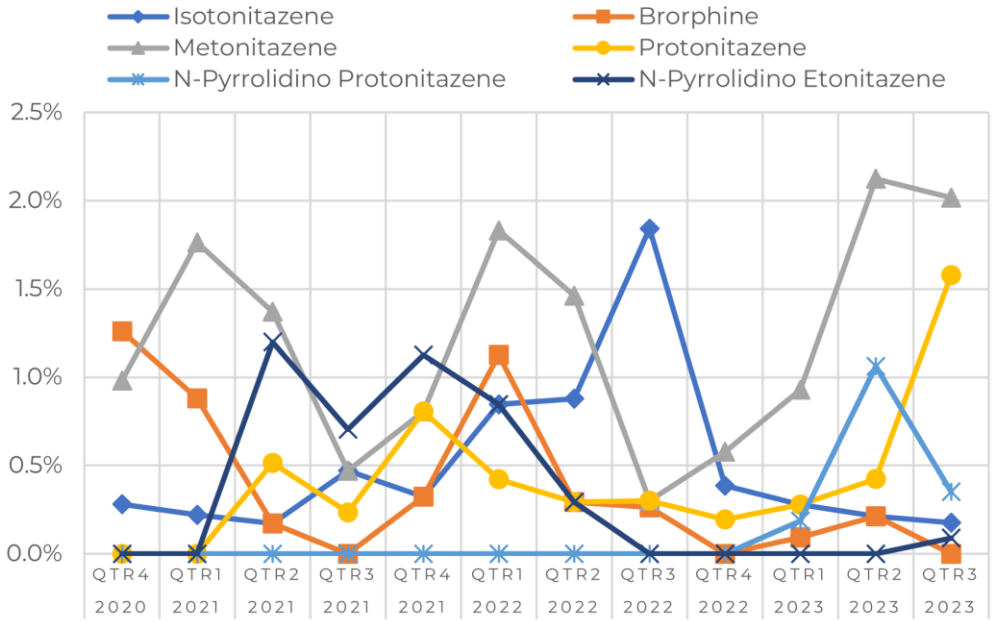


NPS OPIOIDS IDENTIFIED



*Detected only as metabolites to date. — For Reference: Fentanyl (n=699) & Fluorofentanyl (n=335) [Toxicology]

SELECT POSITIVITY: Q4 2020 to Q3 2023



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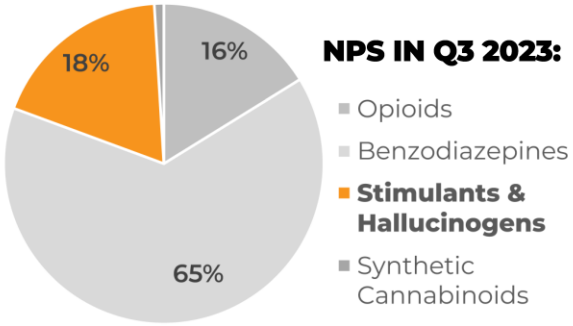
NPS Stimulants & Hallucinogens in the United States

TREND REPORT | **Q3 2023**

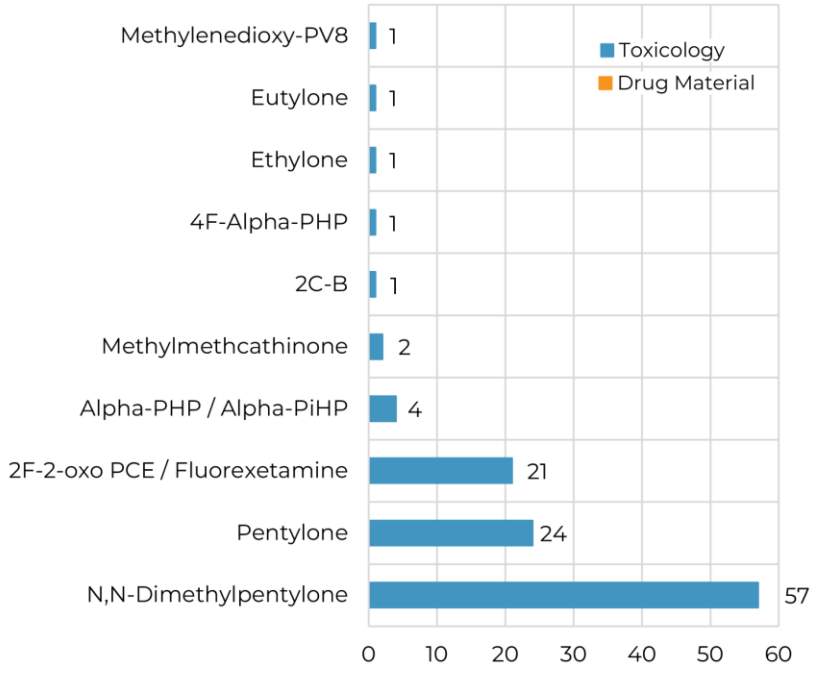
PURPOSE: This report provides up-to-date information regarding NPS stimulant & NPS hallucinogen prevalence and positivity in the United States.

OVERVIEW: Novel psychoactive substances (NPS), including NPS stimulants and NPS hallucinogens, continue to pose great challenges for forensic scientists, clinicians, and public health and safety personnel. Both NPS stimulants and NPS hallucinogens have been implicated in emergency room admissions, death investigations, and/or intoxication events associated with night clubs and music festivals. Maintaining a current scope of analysis can be challenging, requiring comprehensive analytical methodologies and reference materials for identification(s).

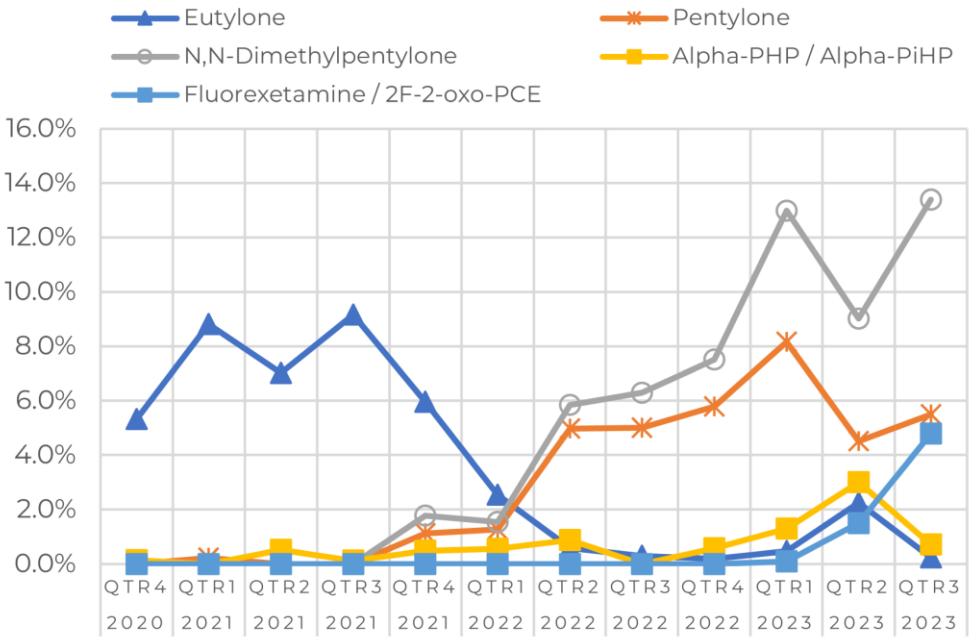
OBJECTIVE: Our laboratory utilizes novel approaches for the analysis of drugs in biological samples and seized materials using comprehensive non-targeted data acquisition by gas chromatography mass spectrometry (GC-MS) and liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The scope of analysis contains more than 1,100 drugs, including a vast majority of NPS and their metabolites. This approach allows for real-time identification of emerging stimulants and hallucinogens, and further data analysis of important trends. This project was conducted in collaboration with the toxicology and criminalistics laboratories of NMS Labs. Forensic case types linked to these results include illicit drug investigations, medicolegal death investigations, and/or driving under the influence of drugs (DUID) investigations. The results in this report represent the total number of NPS identifications at the CFSRE during this quarter, including those from sample-mining, data-mining, and/or esoteric testing.



NPS STIMULANTS & HALLUCINOGENS IDENTIFIED



SELECT POSITIVITY: Q4 2020 to Q3 2023



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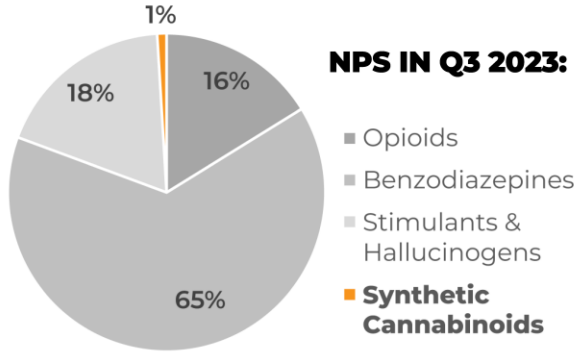
Synthetic Cannabinoids in the United States

TREND REPORT | **Q3 2023**

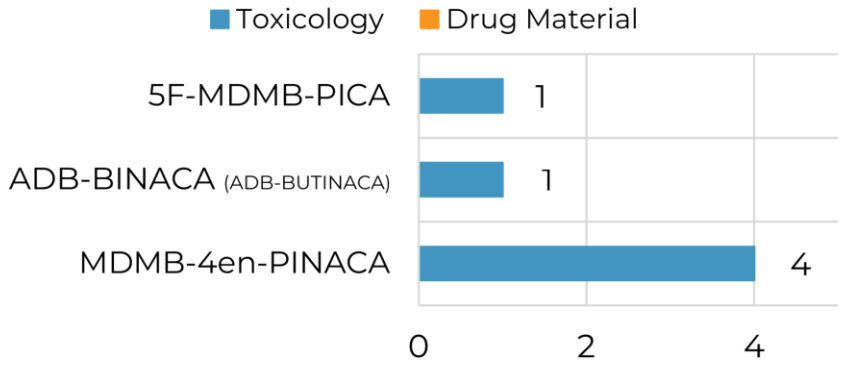
PURPOSE: This report provides up-to-date information regarding the status of synthetic cannabinoid prevalence and positivity in the United States.

OVERVIEW: Novel psychoactive substances (NPS), including synthetic cannabinoids, continue to pose great challenges for forensic scientists, clinicians, and public health and safety personnel. Synthetic cannabinoids have been implicated in an increasing number of emergency room admissions, death investigations, and intoxication events in corrections populations. Maintaining a current scope of analysis can be challenging, requiring comprehensive analytical methodologies and reference materials for identification(s).

OBJECTIVE: Our laboratory utilizes 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 scope of analysis contains more than 1,100 drugs, including a vast majority of NPS and their metabolites. This approach allows for real-time identification of novel synthetic cannabinoids and further data analysis of important trends. This project was conducted in collaboration with the toxicology and criminalistics laboratories of NMS Labs. Forensic case types linked to these results include illicit drug investigations, medicolegal death investigations, and/or driving under the influence of drugs (DUID) investigations. The results in this report represent the total number of NPS identifications at the CFSRE during this quarter, including those from sample-mining, data-mining, and/or esoteric testing.

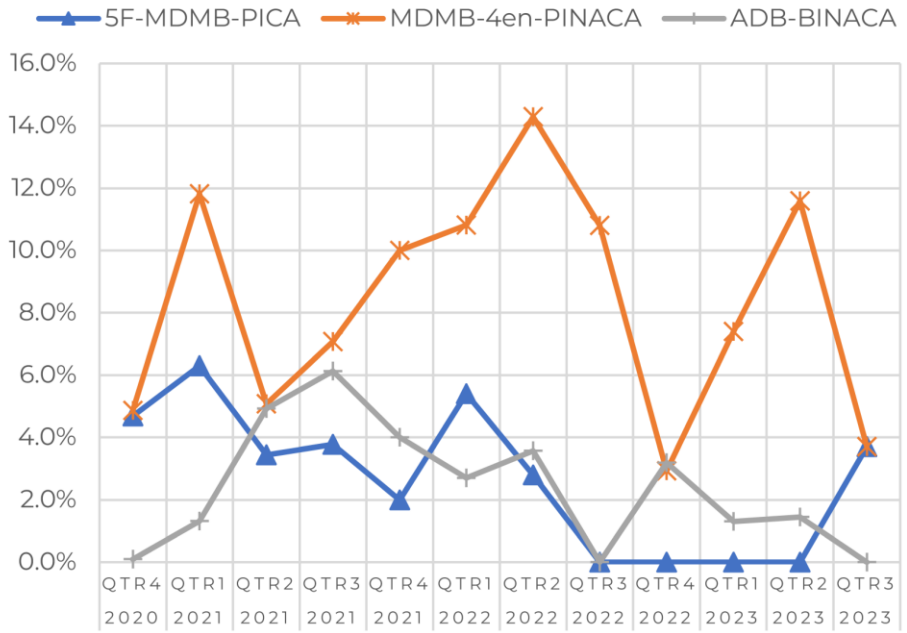


SYNTHETIC CANNABINOIDS IDENTIFIED



NOTABLE SYNTHETIC CANNABINOIDS TO MONITOR
MDMB-BINACA (MDMB-BUTINACA) + Metabolites
MDMB-PICA, MDMB-PINACA, + Others
MDMB-5'Me-INACA + Related Final Products (e.g., MDMB-5'Me-PINACA)

SELECT POSITIVITY: Q4 2020 to Q3 2023



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POSITIVITY PLOTS SINCE 2018

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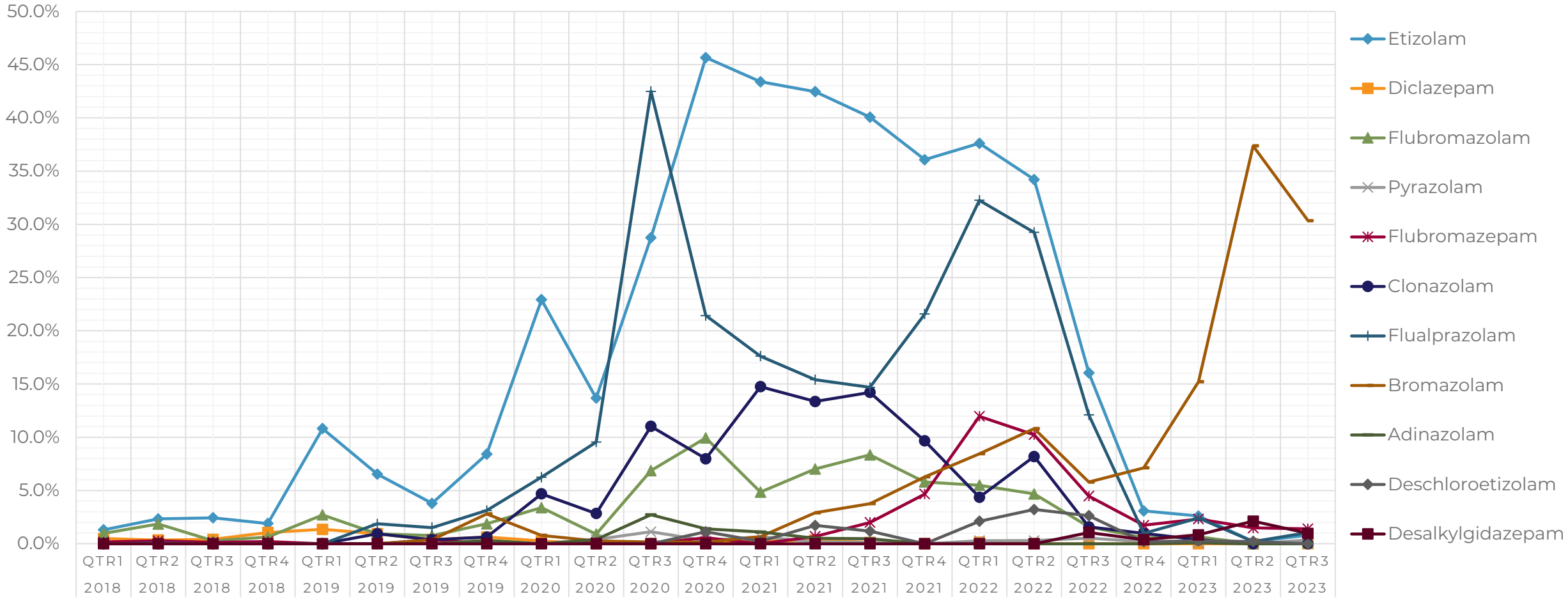
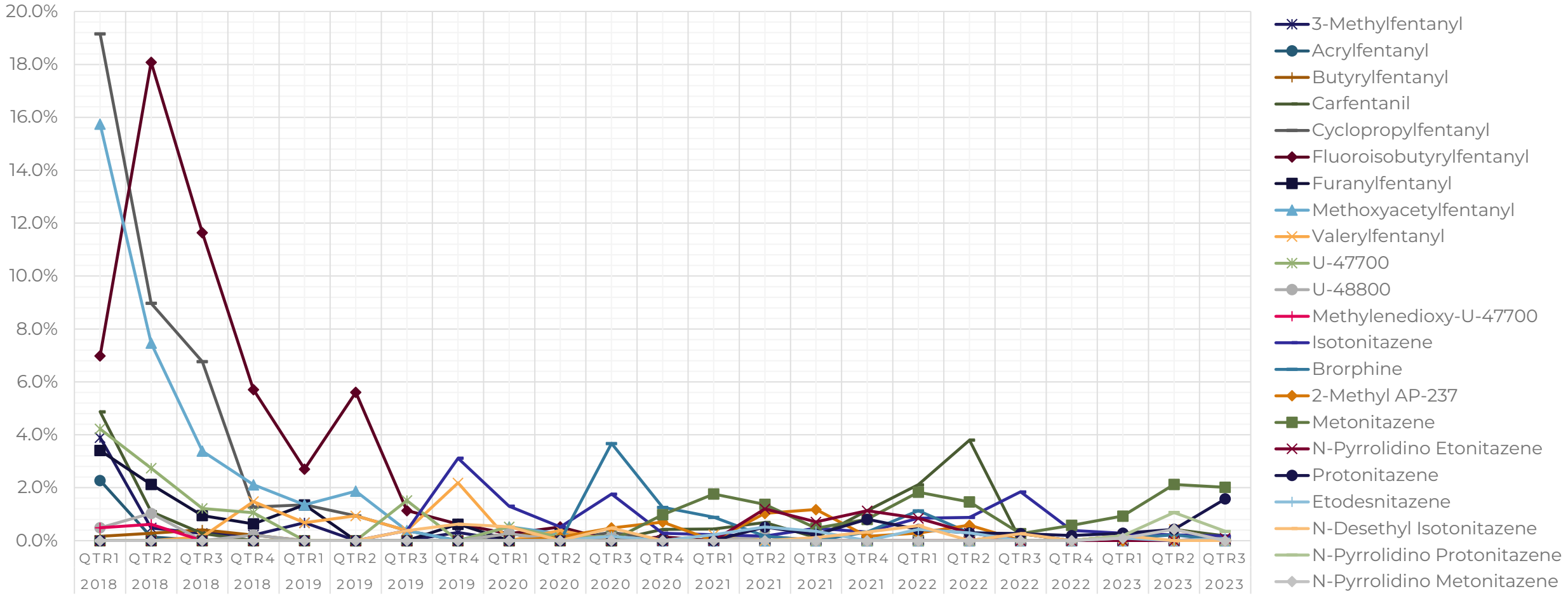
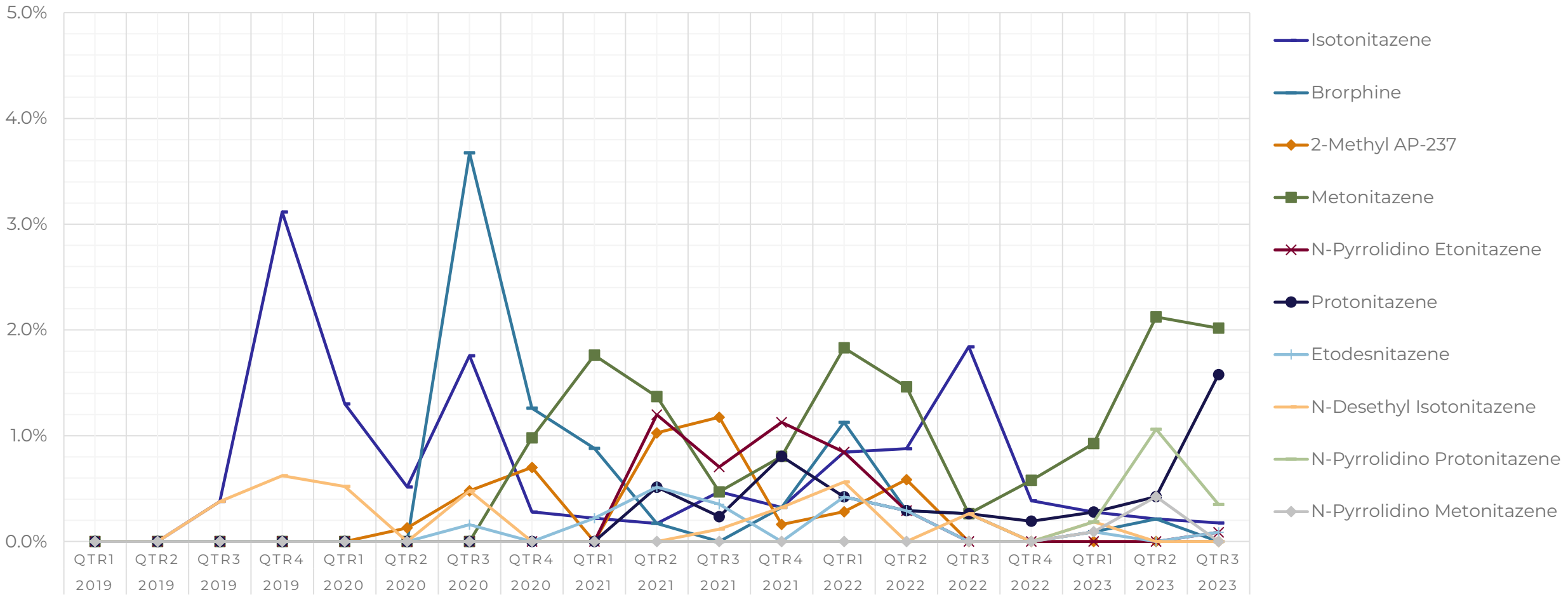
POSITIVITY PLOTS – NPS BENZODIAZEPINES



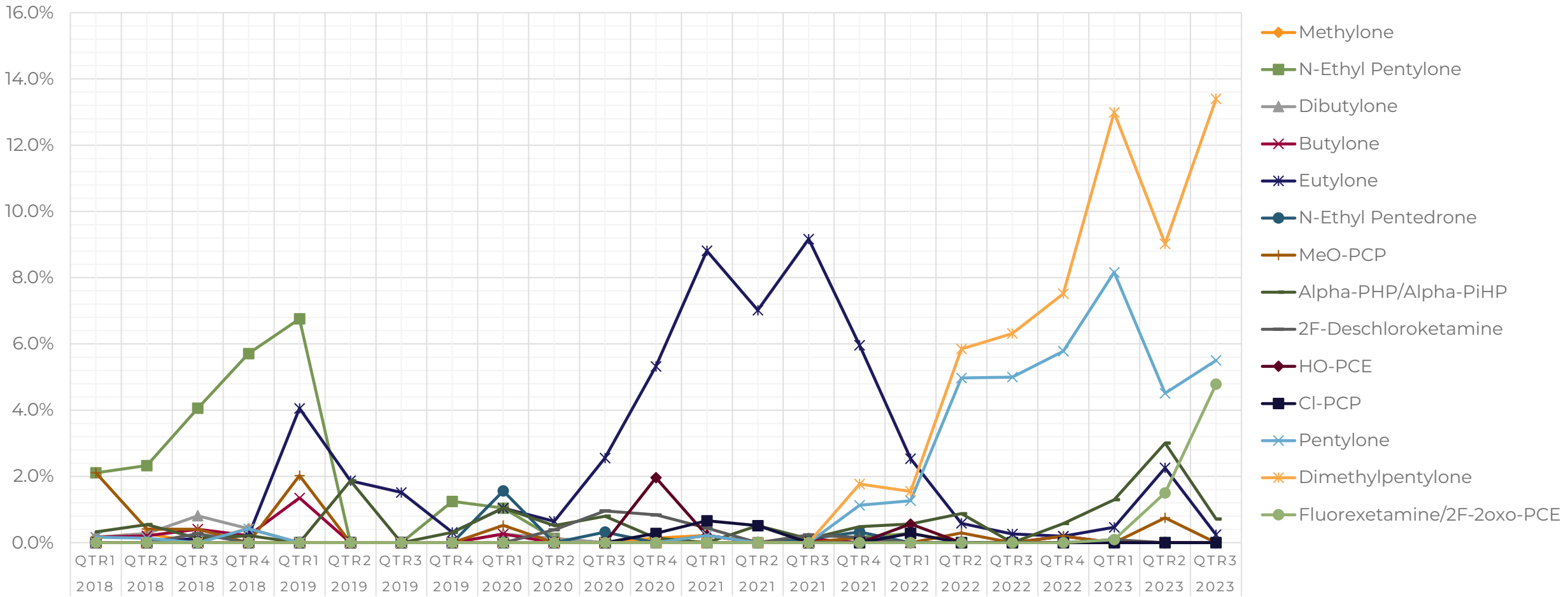
POSITIVITY PLOTS – NPS OPIOIDS



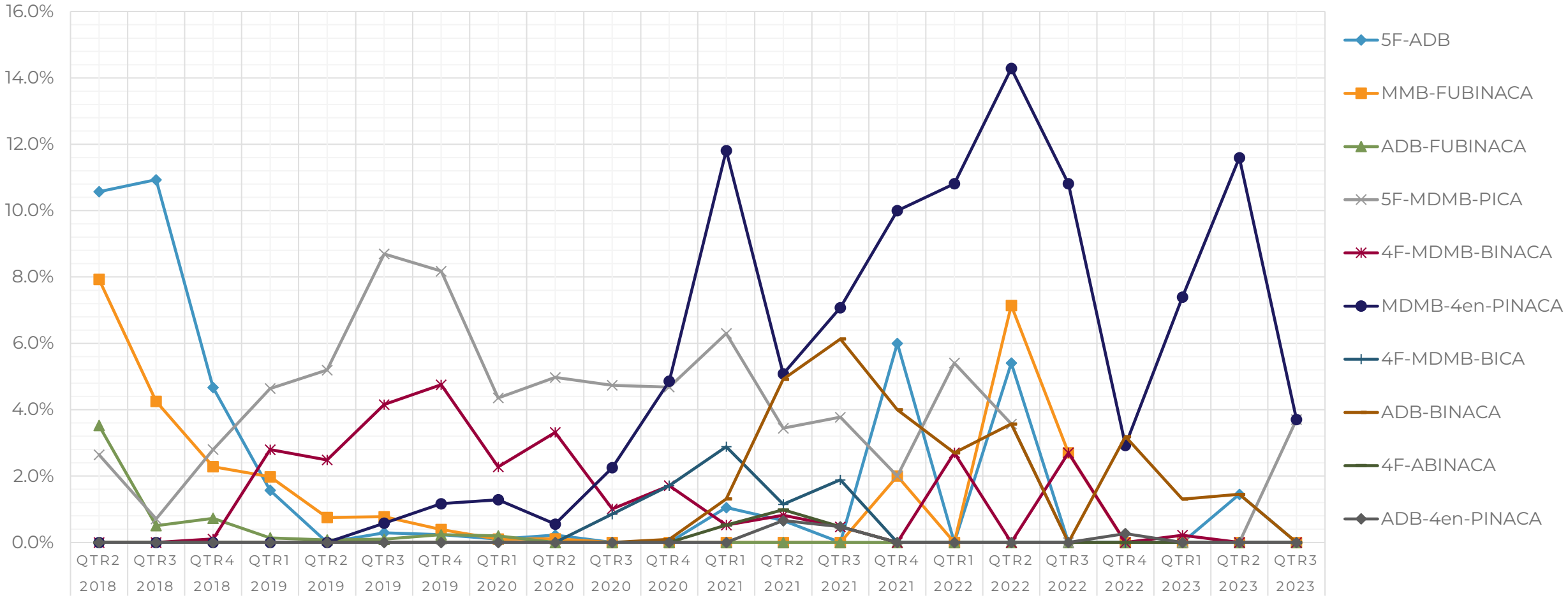
POSITIVITY PLOTS – NPS OPIOIDS (NEW GENERATION)



POSITIVITY PLOTS – NPS STIMULANTS & HALLUCINOGENS

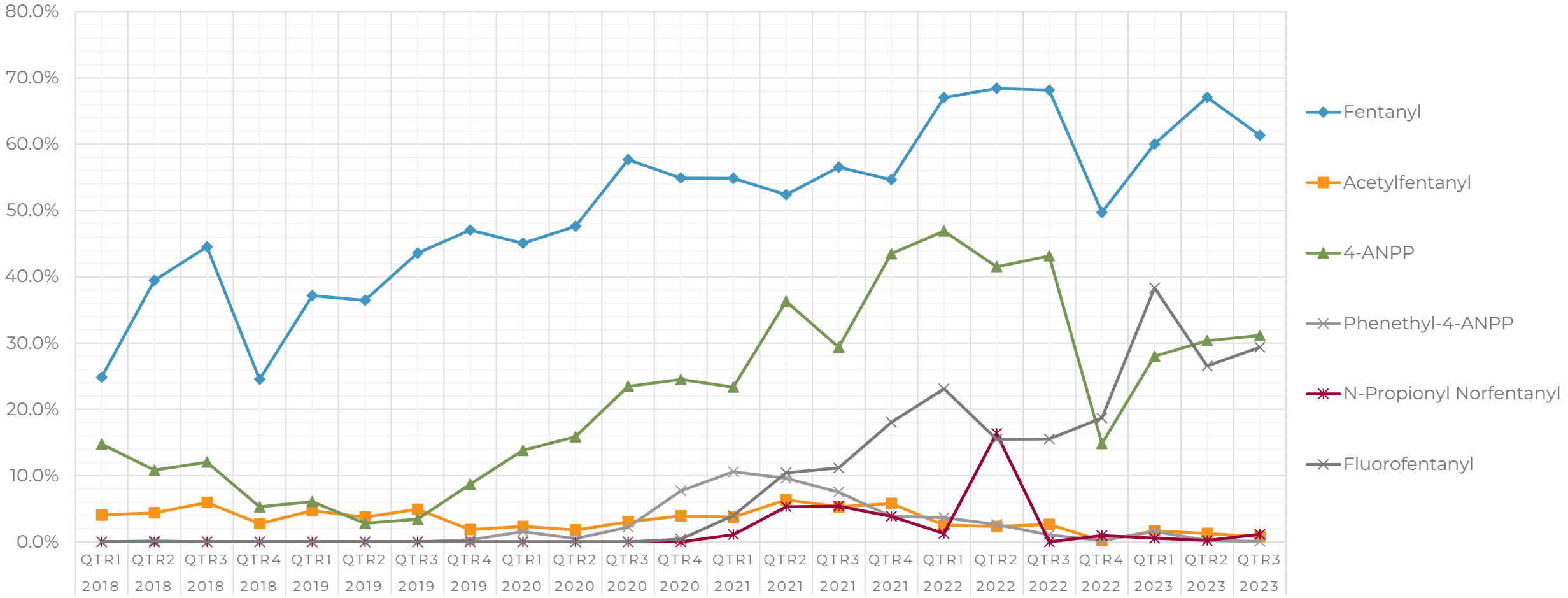


POSITIVITY PLOTS – SYNTHETIC CANNABINOIDS

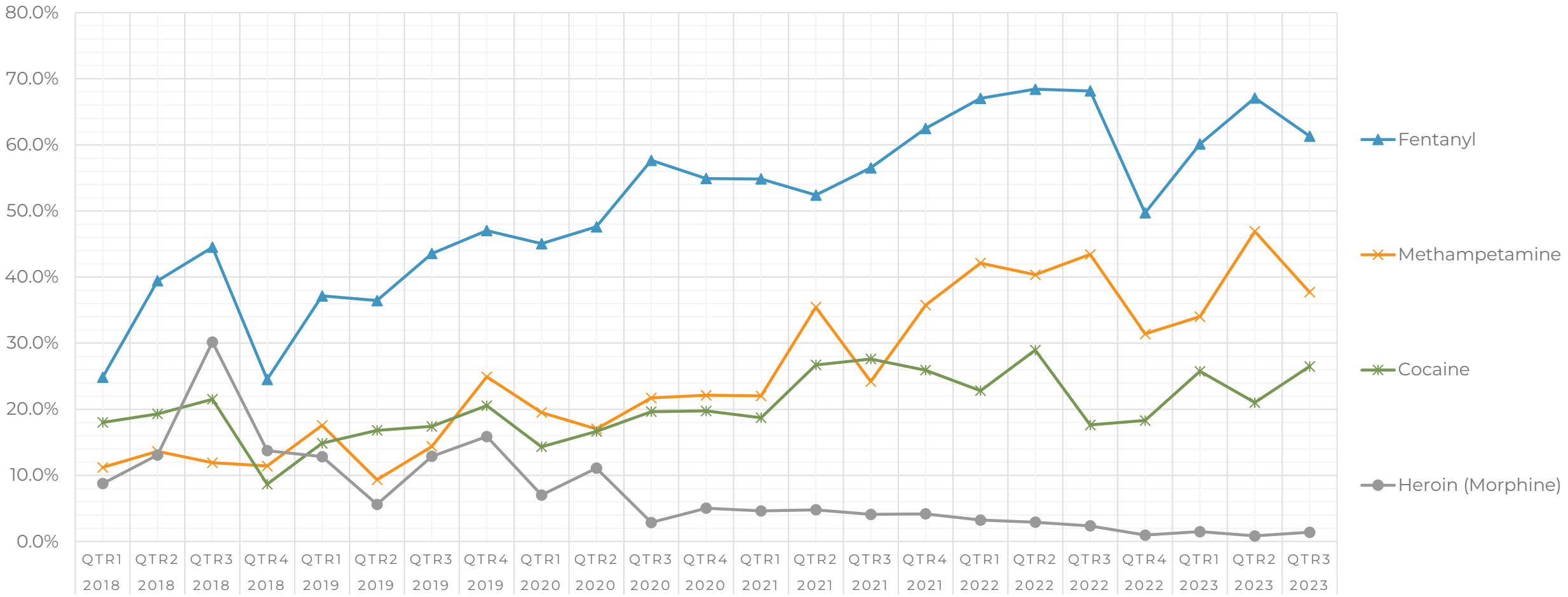


Note: Data is recent quarters is skewed due to low sample volume.

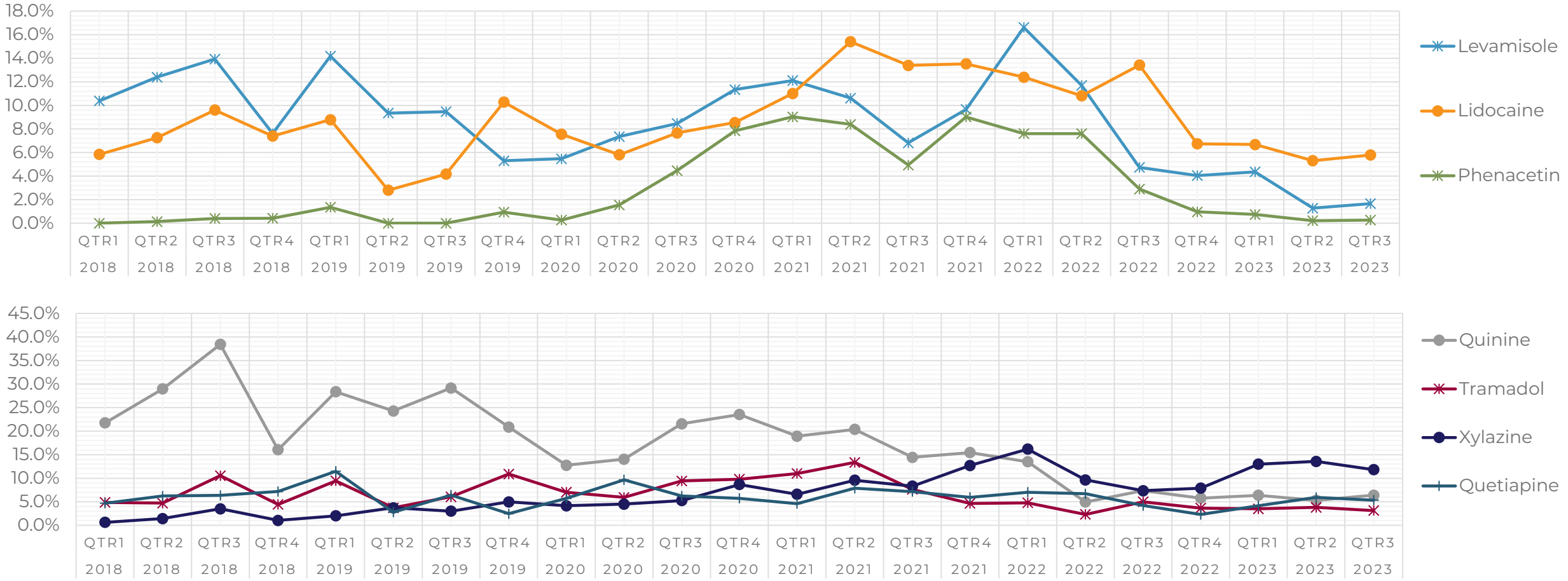
POSITIVITY PLOTS – FENTANYL, FLUOROFENTANYL, & MORE



POSITIVITY PLOTS – TRADITIONAL DRUGS



POSITIVITY PLOTS – ADULTERANTS



NEW REPORTS

NEW Drug Checking & Clinical Reports
COMING SOON!

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PUBLIC ALERT

AUG 2023

NEW NITAZENE ANALOGUE *N*-PYRROLIDINO PROTONITAZENE IMPACTING DRUG MARKETS IN NORTH AMERICA AND EUROPE

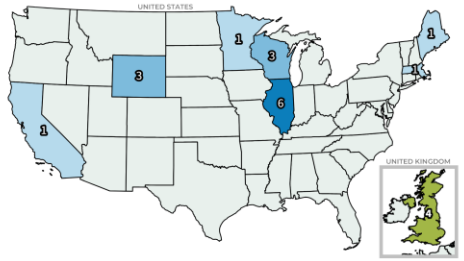
PURPOSE: The objective of this announcement is to notify public health and safety, law enforcement, first responders, clinicians, medical examiners and coroners, forensic and clinical laboratory personnel, and all other related communities about new information surrounding the emergent novel synthetic opioid ***N*-pyrrolidino protonitazene** (also referred to as "protonitazepyne").

BACKGROUND: Synthetic opioids (e.g., fentanyl analogues, nitazene analogues) are chemically manufactured drugs, often having unknown potency and adverse effects or health risks. Synthetic opioids are frequently mixed with more traditional opioids (e.g., fentanyl, heroin) and other drugs in unregulated drug markets creating additional risk and danger for people who use recreational drugs. Synthetic opioids may be distributed in powder or tablet form. In the United States, an alarming increase in the number of deaths linked to synthetic opioid use has been observed. Deaths involving synthetic opioids in Europe, Oceania, and other regions continue to increase as well. Primary adverse effects associated with synthetic opioid use are sedation and respiratory depression, leading to death.

SUMMARY: *N*-Pyrrolidino protonitazene is a new synthetic opioid and the latest to emerge among the nitazene analogue (or 2-benzyl benzimidazole) subclass. *N*-Pyrrolidino protonitazene bears structural resemblance to both **protonitazene** and ***N*-pyrrolidino etonitazene**, two previously encountered nitazene analogues. *N*-Pyrrolidino protonitazene is dissimilar in chemical structure to fentanyl. New synthetic opioids, namely the nitazene analogues, have sustained proliferation following the 2018 scheduling of fentanyl related substances. Most nitazene analogues encountered among the recreational drug supply retain opioid receptor activity and exhibit potency similar to or greater than that of fentanyl. Recently acquired *in vitro* pharmacological data show that *N*-pyrrolidino protonitazene is an active opioid with potency approximately 25 times greater than that of fentanyl *[source: L. De Vrieze and C. Stove, Ghent University]*.

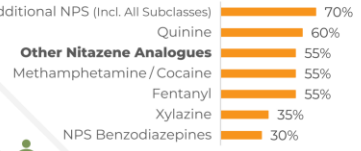
To date in August 2023, *N*-pyrrolidino protonitazene has been confirmed in 20 forensic toxicology cases, all of which were medicolegal death investigations. *N*-Pyrrolidino protonitazene was first reported by **CFSRE's NPS Discovery** in January 2023; however, the date of first sample collection was as early as December 2022. Cases originated from seven states across many regions within the United States, as well as the United Kingdom. Decedent age ranged from mid-20s to mid-70s (mean: 45 years, median: 44 years). Quantitative blood concentrations for *N*-pyrrolidino protonitazene ranged from 0.1 to 55 ng/mL (mean: 6.9 ng/mL, median: 1.1 ng/mL). The toxicity of *N*-pyrrolidino protonitazene has not been examined or reported but recent association with overdoses among people who use drugs leads professionals to believe that this synthetic opioid has the potential to cause harm and is of high public health concern globally.

GEOGRAPHICAL DISTRIBUTION OF CASES

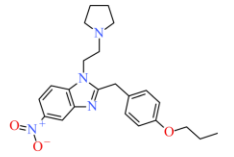


DRUG CO-POSITIVITY IN TOXICOLOGY SAMPLES

N-Pyrrolidino Protonitazene was found in combination with...



SEX OF DECEDENTS



***N*-PYRROLIDINO PROTONITAZENE**

RECOMMENDATIONS FOR CLINICIANS

- Become familiar with the signs and symptoms associated with synthetic opioid use (e.g., sedation, respiratory depression).
- Naloxone should be administered to reverse critical respiratory depression and repeated naloxone administration may be necessary. Be aware that clinical conditions may change rapidly and unpredictably after naloxone administration due to other drugs onboard or precipitation of withdrawal, which may be more severe with faster onset.
- Be mindful that drugs have limited quality control, containing undeclared substances that impact clinical effects or findings.
- Counsel about the harms and dangers of synthetic opioid products and other drugs.

RECOMMENDATIONS FOR PUBLIC HEALTH

- Implement surveillance for rapid identification of drug overdose outbreaks. Engage local poison centers and clinicians to assist with treatment of affected patients.
- Track and monitor geographical drug distribution and trends. Track demographics and known risk factors.
- Raise awareness about the risks, harms, and dangers associated with opioid use.
- Make naloxone available to people who use drugs. Notify personnel that naloxone remains effective at reversing opioid overdose caused by nitazene analogues.
- Be aware that FTIR and fentanyl test strips are not effective for detecting nitazene analogues.

RECOMMENDATIONS FOR LABORATORIES

- Utilize analytical data available publicly for the identification of ***N*-pyrrolidino protonitazene** if a reference standard is not immediately available.
- Utilize previously developed non-targeted testing protocols or develop sensitive and up-to-date testing procedures for synthetic opioids and novel drugs.
- Prioritize analytical testing of drug materials obtained from drug overdose scenes during death investigations.
- Share data on synthetic opioid drug seizures with local health departments, medical examiners, coroners, and related communities.

RECOMMENDATIONS FOR MEDICAL EXAMINERS & CORONERS

- Test for new synthetic opioids and their biomarkers (if known) in suspected opioid overdose cases.
- Be aware that ELISA screening for synthetic opioids is not specific or specialized for the newest generations of drugs — Mass spectrometry-based screening is necessary.
- Be aware that concentrations of synthetic opioids in biological specimens can vary and GC-MS sensitivity may not be adequate.
- Consult with forensic toxicologists about novel opioid activity, potency, and association with overdose and/or death.

ACKNOWLEDGEMENTS: This report was prepared by Alex J. Krotulski, Sara E. Walton, Donna M. Papsun, Joshua DeBord, Melissa F. Fogarty, and Barry K. Logan at the Center for Forensic Science Research and Education (CFSRE) at the Fredric Rieders Family Foundation. The authors acknowledge scientists and staff at the CFSRE and NMS Labs for their involvements and contributions. For more information, please contact CFSRE's NPS Discovery at npsdiscovery@cfsre.org or visit our website at www.npsdiscovery.org.

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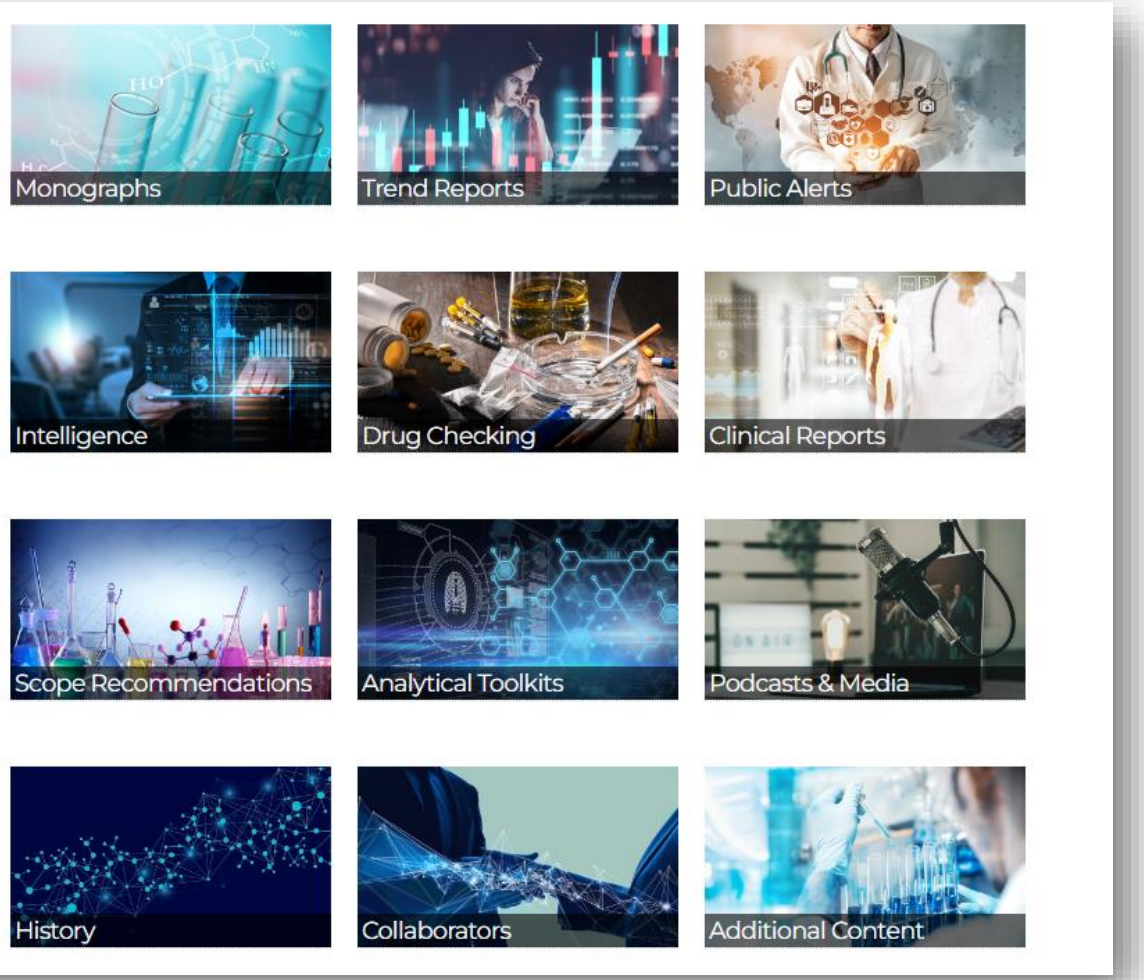

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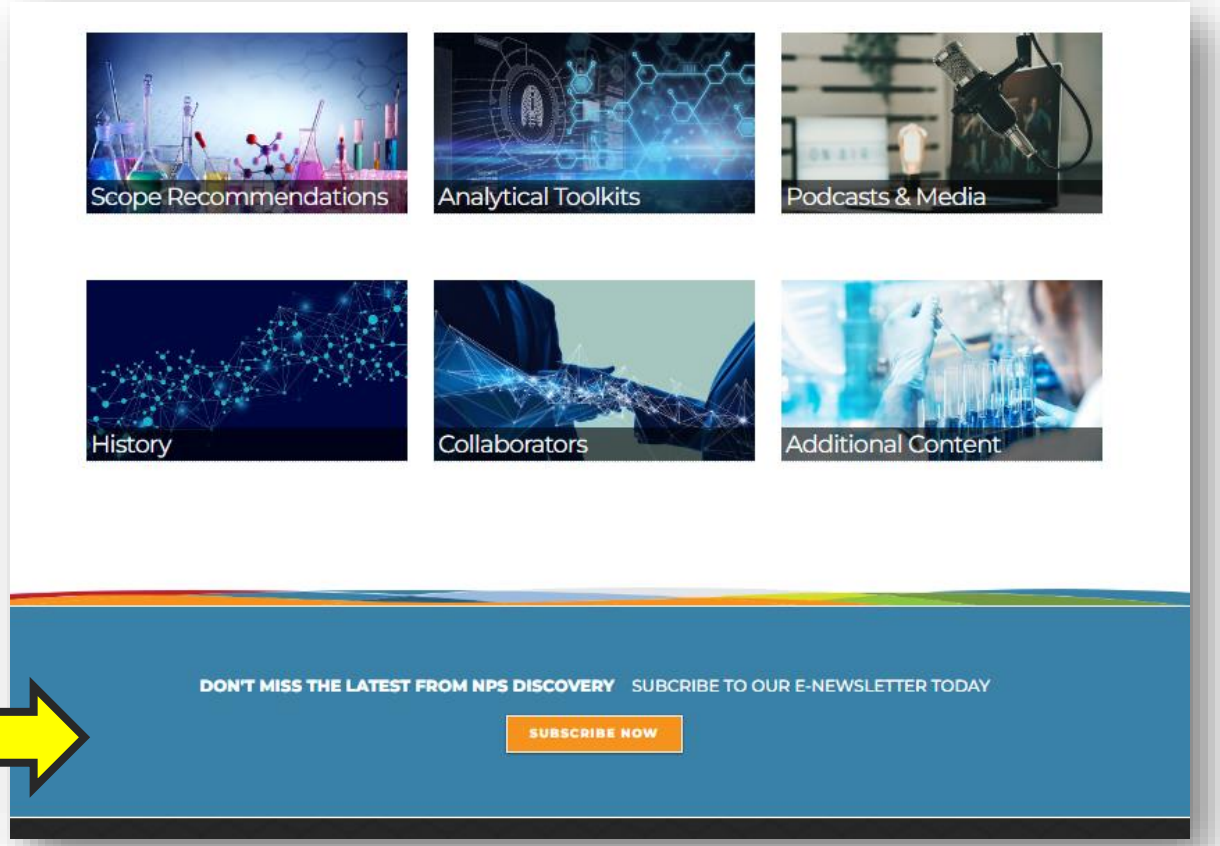

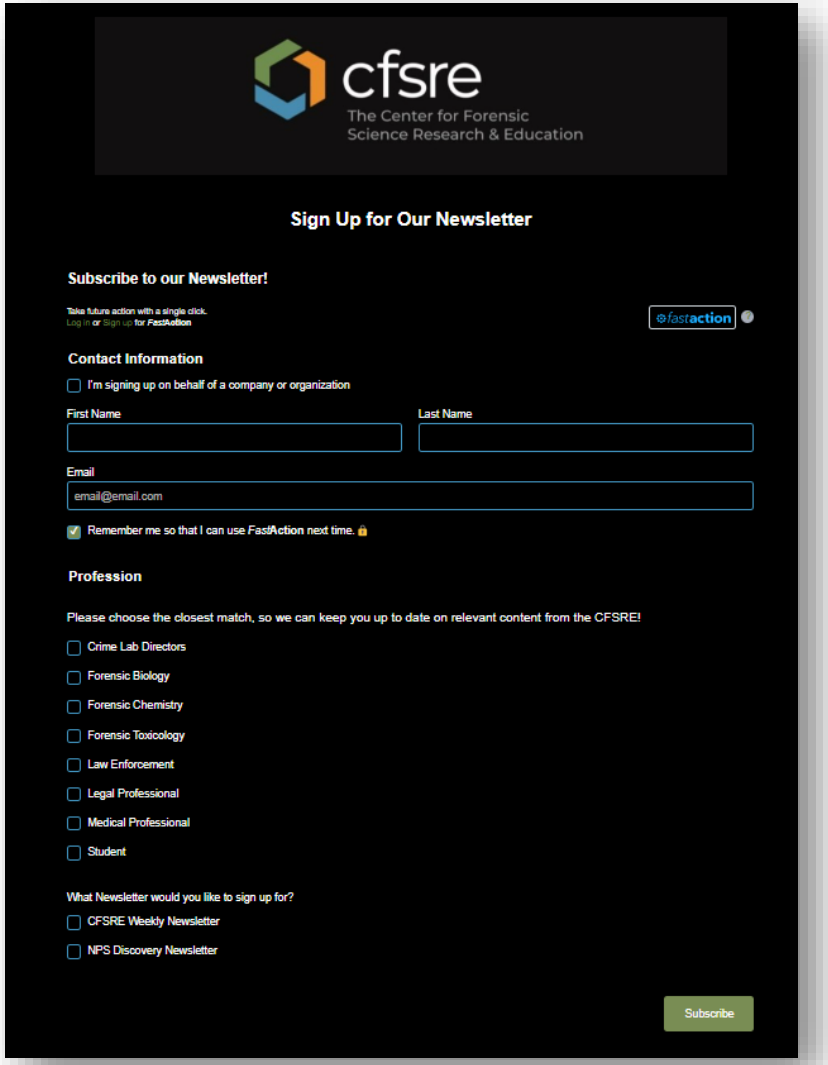

COLLABORATE WITH OUR TEAM

- We accept toxicology samples and drug materials for NPS testing
- Contact Alex Krotulski for more information ▸ 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!

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- **CFSRE Team**
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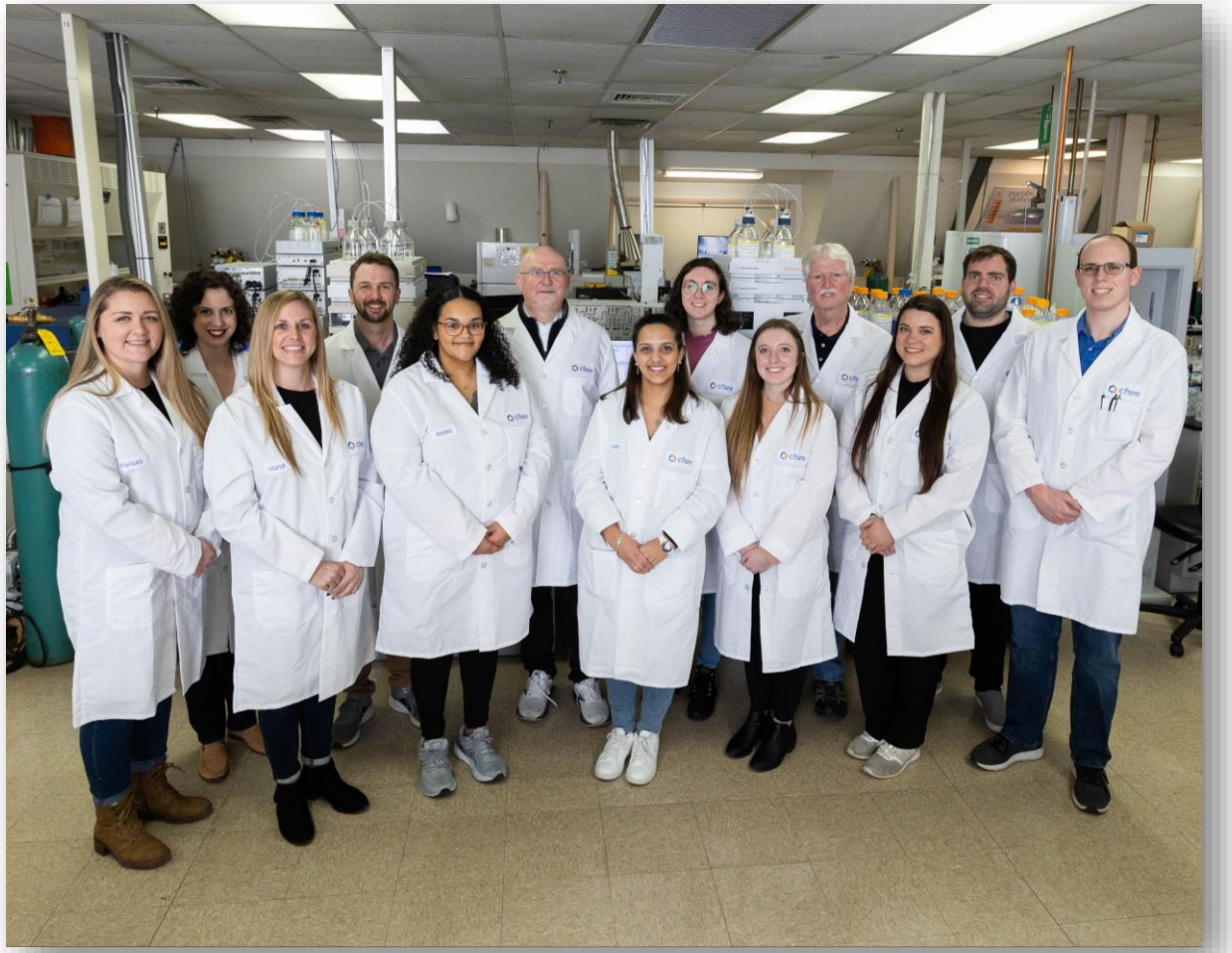
  - Alyssa Reyes
  - Brianna Stang
  - Alexis Quinter
  - Max Denn
  - Many others!
- **NMS Labs**
  - Donna Papsun
- **Funding Agencies**
  - National Institute of Justice (NIJ)
- **Collaborators & Partners**
  - Forensic
  - Clinical
  - Medical Examiner
  - Coroner
  - Crime Lab



NIJ | National Institute of Justice
STRENGTHEN SCIENCE. ADVANCE JUSTICE.

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THANK YOU! QUESTIONS?

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