



Summary: Assessing the presence of novel psychoactive substances in patients

November 2023 - December 2024



In November 2023, Quest Diagnostics launched the **Drug Monitoring, Novel Psychoactive Substances (NPS), Qualitative, Urine panel**. Also known as designer or synthetic drugs, NPS agents are intended to mimic the effects of controlled substances while circumventing national and international drug laws.^{1,2} Over the last several years, NPS use has risen significantly, and these agents have been increasingly implicated in overdose and poisoning events.³ Obtained primarily online and from street retailers, NPS can be more difficult to detect than “traditional” drugs.^{1,3}

In the first year of testing, 8,384 specimens evaluated using this panel were positive for NPS. Patient specimens for this assay include those from pain clinics, treatment centers, rehabilitation facilities, and doctors’ offices as well as from circumstances in which a clinician thinks a patient may be exhibiting abnormal behaviors or symptoms. The Quest NPS test reports results in 6 different NPS drug classes, including the following:

- Designer benzodiazepines (DB)
- Designer fentanyl analogs (FA)
- Designer opioids (DO)
- Designer stimulants (DS)
- Synthetic cannabinoids (SC)
- Other illicit additives (OI)

Quest’s NPS assay will be updated annually to keep current with emerging drug trends. The first update (Generation 2 or NPS Gen2) was launched in December 2024 with the addition of 25 new analytes. These analytes are indicated below with a double asterisk (**) if there were positive specimens within the first month of analysis.



Other illicit additives (OI)

In 2024, the most frequently reported NPS class was OI, with 52.9% of all positives containing a compound from this category. The most-seen compound in all specimens—as well as the most-seen compound in the OI category—was xylazine, which was present in 52.0% of all positive specimens.

What is xylazine, and why is it so dangerous?

Xylazine, also called “tranq” or “tranq dope,” is a powerful veterinary sedative, analgesic, and muscle relaxant that is not currently approved for human consumption. Often taken unknowingly and found in combination with other drugs, most frequently fentanyl, use of xylazine may slow a person’s breathing and cause bradycardia and hypotension, increasing the risk of a fatal drug poisoning. The effects of opioids, like fentanyl, can be reversed using naloxone (Narcan®), a common and effective treatment in case of overdose. However, xylazine is not an opioid, so its effects cannot be reversed by naloxone. The absence of a treatment to reverse overdose makes xylazine more dangerous and overdosing more deadly.

Xylazine is inexpensive, thought to enhance the effects of other drugs of abuse like fentanyl, and is often added to other recreational drugs to raise street value.⁴ Some media outlets have referred to xylazine as a “zombie drug,” since those who inject xylazine are at risk of heavy sedation and skin ulcerations, rotting of tissue, and potential limb amputations.^{5,6}

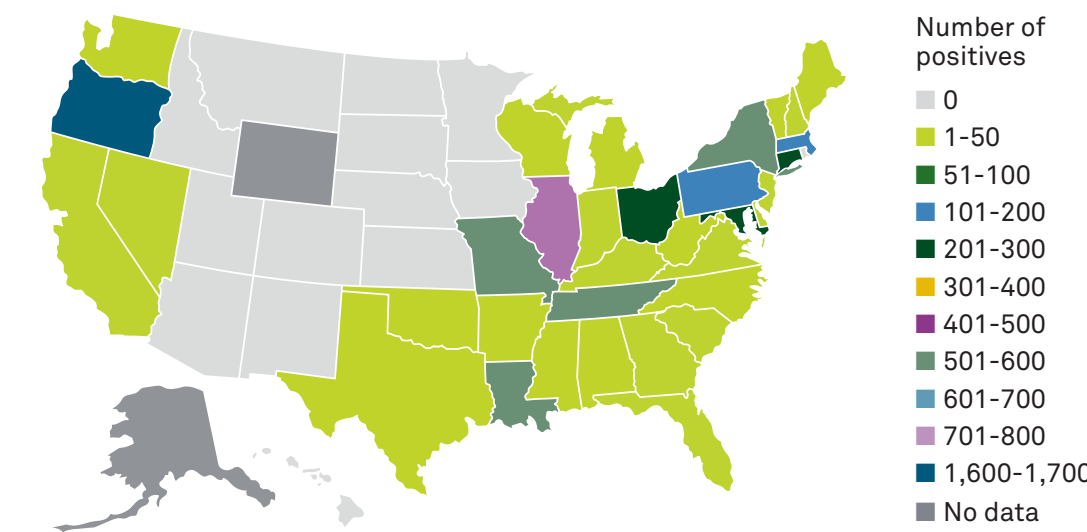
Other compounds in the OI class were also seen in 2024. Hydroxy xylazine was detected in 9.7% of positive specimens, and tianeptine was found in 0.8% of positive specimens. Hydroxy xylazine, a metabolite of xylazine, was never observed alone; rather, it was always detected with xylazine. With the launch of NPS Gen2, 3 new analytes were added for the OI class, all of which were seen in samples in December 2024. They included medetomidine, phenibut, and the tianeptine metabolite.

OI class number of positives November 2023 - December 2024

Compound	Number of positive specimens			
Xylazine	4,360			
Hydroxy xylazine	816			
Tianeptine	66			
Medetomidine**	7			
Phenibut**	9			
Tianeptine metab**	9			

OI class number of positives by state November 2023 - December 2024

Most positive specimens from the OI class were from the East, the Midwest, and the state of Oregon, confirming that these compounds are being used across the US.



Designer fentanyl analogs (FA)

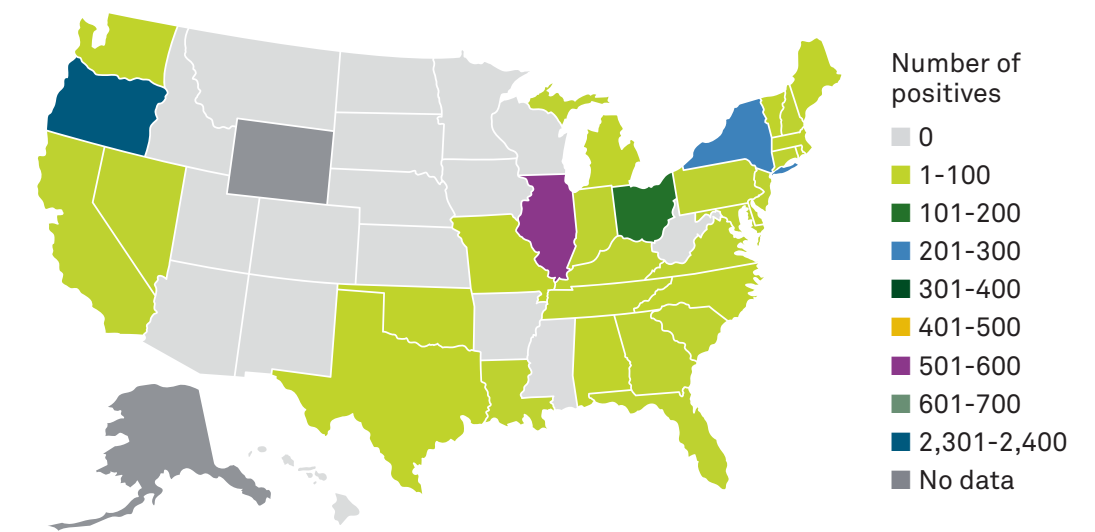
The NPS designer fentanyl analogs (FA) class was detected in 44.3% of positive specimens. The most-seen FA compounds were acetyl fentanyl (27.3% of positive specimens) and fluorofentanyl (29.3% of positive specimens), both of which are potent synthetic opioid analgesics and fentanyl analogs. Carfentanil, also a fentanyl analog, was detected in 47 specimens. The most potent opioid used commercially, carfentanil is intended as a general anesthetic for large animals since its extreme potency makes its use inappropriate for humans. It is 100 times more potent than fentanyl and 10,000 times more potent than morphine.⁷

FA class number of positives November 2023 - December 2024

Compound	Number of positive specimens			
Acetyl fentanyl				2,286
Acryl fentanyl	15			
Butyryl/Isobutyryl fentanyl	2			
Carfentanil	47			
Fluorofentanyl				2,458
Furanyl fentanyl	1			
o-chlorofentanyl	10			
p-chlorofentanyl	51			
Sufentanil	4			
Tetrahydrofuranyl fentanyl	5			
Valeryl fentanyl	5			
Benzyl fentanyl**	10			
Butyryl fentanyl COOH metab**	38			
Norcarfentanil**	2			
Chlorofentanyl**	15			
Despropionyl bromofentanyl**	17			
Despropionyl fluorofentanyl**	88			
Valeryl fentanyl COOH metab**	7			

FA number of positives by state November 2023 - December 2024

Compounds from the FA class have also been seen in specimens from across the US.



Designer benzodiazepines (DB)

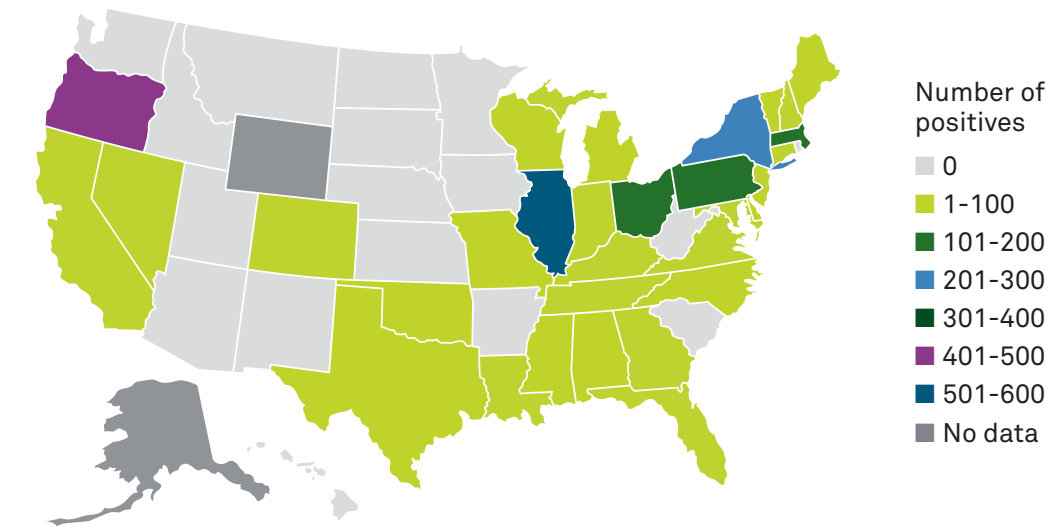
The NPS designer benzodiazepines (DB) class was detected in 21.5% of positive specimens. The most-seen DB compounds were bromazolam and hydroxy bromazolam, which is a bromazolam metabolite. Bromazolam, a synthetic benzodiazepine, was initially seen in the recreational drug supply in 2019 and has never been approved for therapeutic use in the US.⁸ It has sedative, hypnotic, and anxiolytic effects and may be highly potent at low doses. Considered a designer counterpart to alprazolam (Xanax),⁹ bromazolam has commonly been paired with opioids (known as “benzo-dope”) such as fentanyl and is associated with hospitalization and death.⁸

DB class number of positives November 2023 - December 2024

Compound	Number of positive specimens			
Aminoclonazepam	413			
Clonazepam	32			
Bromazolam	1,027			
Hydroxy bromazolam	1,364			
Desalkylflurazepam	8			
Etizolam	9			
Flualprazolam	38			
Hydroxy flualprazolam	69			
Flubromazolam	4			
Hydroxy flubromazolam	7			
Bromazepam**	2			
Hydroxy etizolam**	1			
Hydroxy flubromazepam**	2			
Hydroxy phenazepam**	2			

DB class number of positives by state November 2023 - December 2024

The DB compounds have been seen across the US, with a large number coming from the Northeast and the Midwest.



Designer opioids (DO)

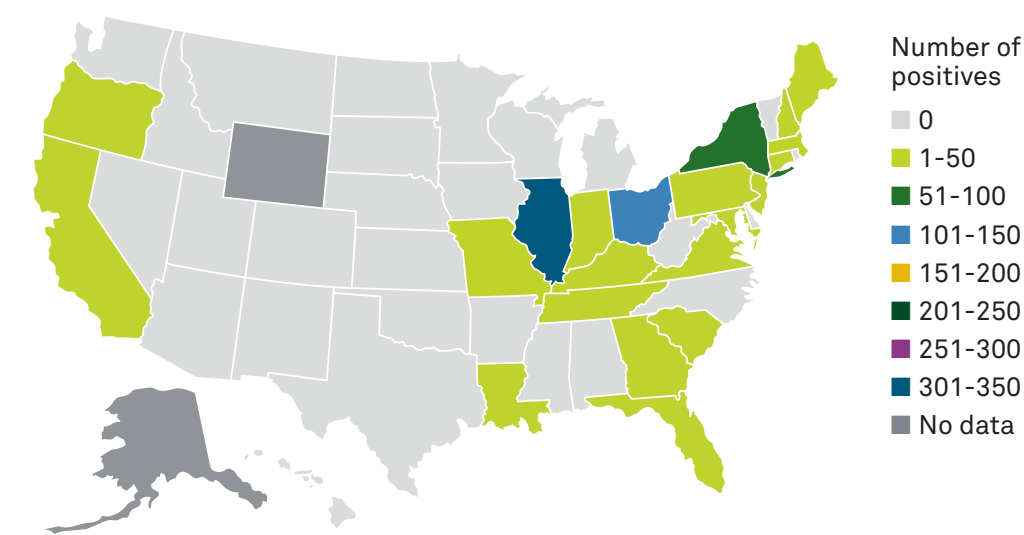
The NPS designer opioids (DO) class was detected in 6.6% of positive specimens. The most-seen DO compounds were hydroxy nitazene and pyrrolidino hydroxy nitazene, both metabolites of nitazene compounds. Developed in the 1950s as opioid analgesics, nitazenes have not been approved for use in the US. They have extremely high potency, reportedly being **tenfold more potent than fentanyl and hundreds- to thousands-fold more potent than other opioids,** including morphine. The nitazenes are often mixed with fentanyl and other agents in the illicit drug supply. In the last several years, their use has been associated with fatal overdose, but because the nitazenes are largely unknown other than within research labs, their inclusion with other drugs is not always disclosed to those who purchase them.¹⁰

DO class number of positives November 2023 - December 2024

Compound	Number of positive specimens			
2-methyl AP-237	2			
5-amino isotonitazene	1			
Brorphine	21			
Desethyl isotonitazene	14			
Hydroxy nitazene		228		
Metonitazene		113		
Protonitazene	12			
Pyrrolidino etonitazene	52			
Pyrrolidino hydroxy nitazene			441	
Pyrrolidino metonitazene	41			
Pyrrolidino protonitazene	19			
Desethyl metonitazene**	16			
Desethyl protonitazene**	2			

DO class number of positives by state November 2023 - December 2024

Compounds from the DO class were primarily observed in the East and Midwest regions.



Designer stimulants (DS)

The NPS designer stimulants (DS) class was detected in 4.0% of positive specimens. The most-seen compounds were dimethyl pentylone and its metabolite, pentylone.

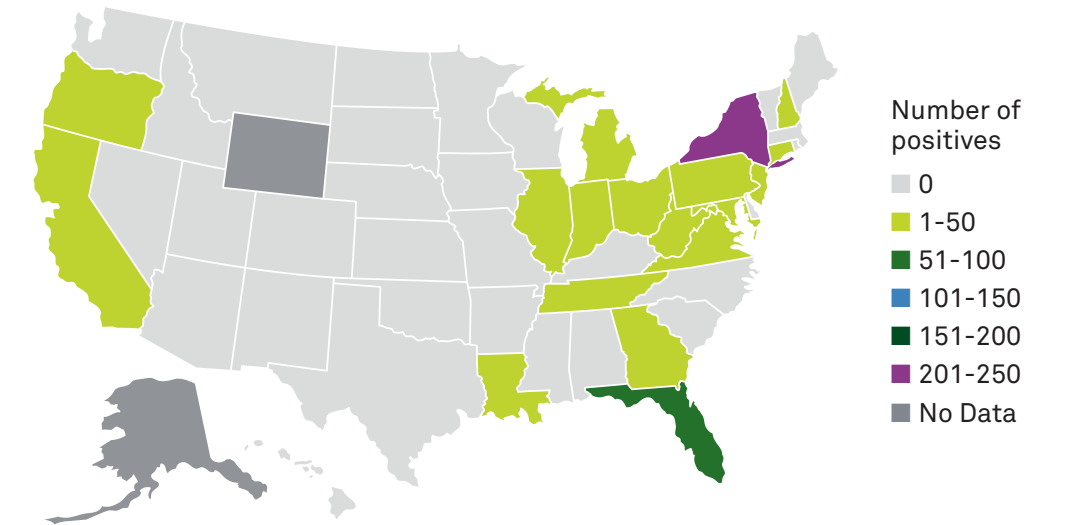
Since eutylone (also known as “ecstasy” or “Molly”) was recommended for international control in September 2021, the synthetic stimulant market has shifted from illicit use of eutylone to dimethyl pentylone and its more potent metabolite, pentylone. Using these agents, which are often mixed with other illicit drugs, may result in cardiovascular and neuropsychiatric symptoms, including arrhythmias, an elevated pulse, hallucinations, agitation, and serotonin syndrome, and has been associated with fatal poisoning.^{11,12}

DS class number of positives November 2023 - December 2024

Compound	Number of positive specimens			
2F-deschloroketamine	4			
Alpha-PHP/PIHP	27			
Alpha-PVP	1			
Cyclohexyl butylone	14			
Cyclohexyl methylone	62			
Dimethyl pentylone				215
Pentylone			178	
Eutylone	19			
Fluorexetamine	1			
Hydroxy PCP	22			
Methylmethcathinone	2			
Propyl butylone	3			

DS class number of positives by state November 2023 - December 2024

Compounds from the DS class have been detected on the East Coast and in the Midwest, with most positive specimens coming from the states of New York and Florida.



Synthetic cannabinoids (SC)

The NPS synthetic cannabinoids (SC) class was detected in 17.6% of positive specimens. The most-seen compound was the metabolite of MDMB-4en-PINACA. Synthetic cannabinoids, known by multiple names including “K2” and “spice,” are designed to mimic the effects of tetrahydrocannabinol (THC), which is the primary psychoactive component in marijuana. However, synthetic cannabinoids are much more potent than marijuana and can cause elevated blood pressure, rapid heart rate, tremors, seizures, unconsciousness, hallucinations, agitation, and other symptoms and result in accidental toxicity with associated mortality.^{13,14}

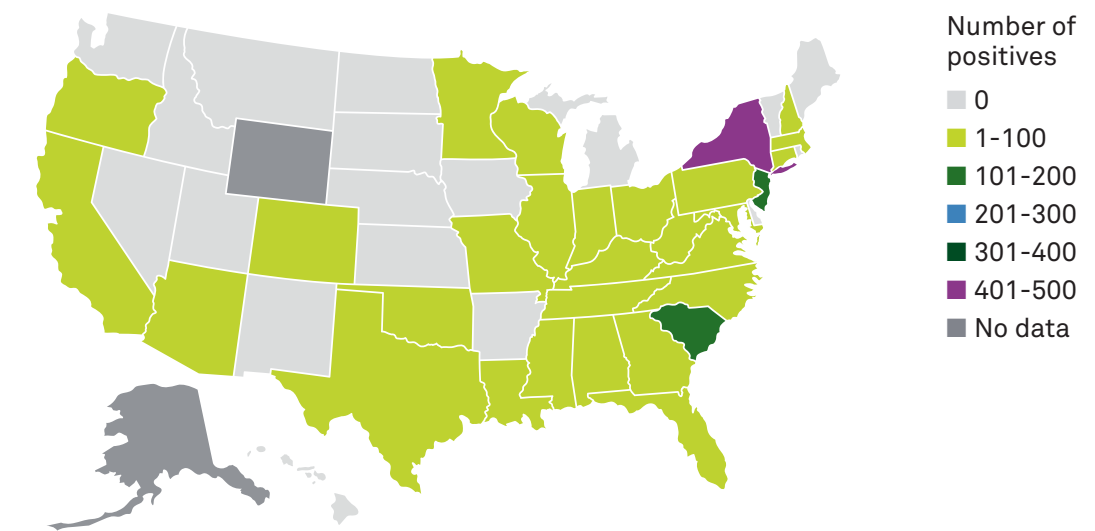
Synthetic cannabinoids, frequently marketed as “potpourri” or “herbal incense,” are often mixed with plant material or paper and smoked. In addition, liquid cannabinoids are designed to be vaporized through electronic cigarettes.¹³

SC class number of positives November 2023 - December 2024

Compound	Number of positive specimens			
5F-MDMB-PICA metab7	4			
ADB-BINACA	3			
ADB-BUTINACA	3			
ADB-BUTINACA COOH metab	48			
ADB-BUTINACA OH metab	18			
ADB-FUBIATA	1			
MDMB-4en-PINACA	6			
MDMB-4en-PINACA COOH metab				1,445
MDMB-BUTINACA BA metab**	14			

SC class number of positives by state November 2023 - December 2024

Compounds from the SC class have been seen across the US, with most positive specimens coming from the state of New York.



Summary

The prevalence of illicit drug use within different NPS classes changes over time and differs throughout the various geographic locations in the US. Although xylazine was the most-seen analyte in this report and its use reflects an alarming trend, it only tells half of the NPS story—since it was identified in little more than half (52%) of the analyzed specimens.

To understand what a patient may have taken, it's important that clinicians analyze for all NPS classes vs just 1 or 2 NPS classes. For example, when a patient is illicitly obtaining fentanyl or trying what they think may be a synthetic cannabinoid, they are usually unaware of what other compounds may be present. **While 64.7% of positive specimens were positive for 1 NPS class, 35.3% of positive specimens contained compounds from 2 or more NPS classes.** Six specimens in 2024 contained compounds from 5 of the 6 NPS classes: ie, OI, FA, DB, DO, and DS.

2024 multiple NPS class positivity summary		
Number of classes positive	Number of positives	Percent of positives
1	5,428	64.7%
2	2,196	26.2%
3	553	6.6%
4	200	2.4%
5	6	0.1%
6	0	0.0%

Accordingly, if there is any concern that a patient may have taken a particular NPS, the specimen should be analyzed by a full NPS panel that includes all classes to ensure proper NPS detection and appropriate treatment.



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