Quest Diagnostics®

Summary: Assessing the presence of novel psychoactive substances in patients

Q1 update, January – March 2025

Novel psychoactive substances (NPS) are a rapidly evolving drug market that require frequent analyses to ensure accurate representations of what patients may be taking. Use of NPS agents, also referred to as "synthetic drugs" or "designer drugs," is meant to circumvent current national and international drug laws, while obtaining effects similar to or even more potent than those associated with controlled substances.[1,2] Monitoring for such drug use is critical since NPS use can be more difficult to detect than traditional illicit drugs and has been increasingly implicated in poisoning and overdose events.[3]

To meet these challenges, Quest Diagnostics launched our **Drug Monitoring, Novel Psychoactive Substances (NPS), Qualitative, Urine panel** in November 2023. We continue to update our assay, performing monthly analyses of our total results. Our previous update, "Summary: Assessing the presence of novel psychoactive substances in patients, November 2023 – December 2024," included the addition of 25 new analytes.

In this update, we report on the results of Quest's NPS testing in the first quarter of 2025. Patient specimens analyzed include those from pain clinics, treatment centers, rehabilitation facilities, and doctors' offices, including from situations in which clinicians believe that their patients may be demonstrating abnormal behaviors or symptoms. Our first quarter 2025 summary reports results in 6 different NPS drug classes, including the following:

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

In the first quarter of 2025, 2,988 specimens analyzed using the Quest Diagnostics NPS assay were positive. Xylazine continued to be the most common analyte seen (see page 3). However, designer fentanyl analogs were the most frequently reported class (see page 4).

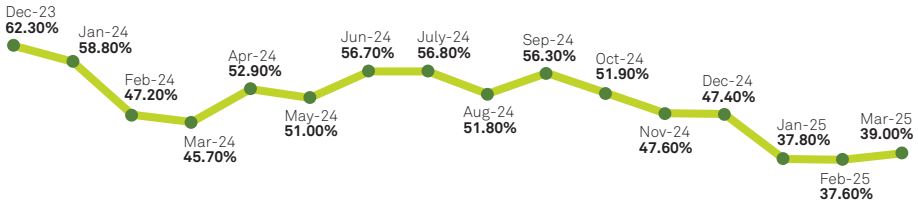
Quest Diagnostics®

Other illicit additives (OI)

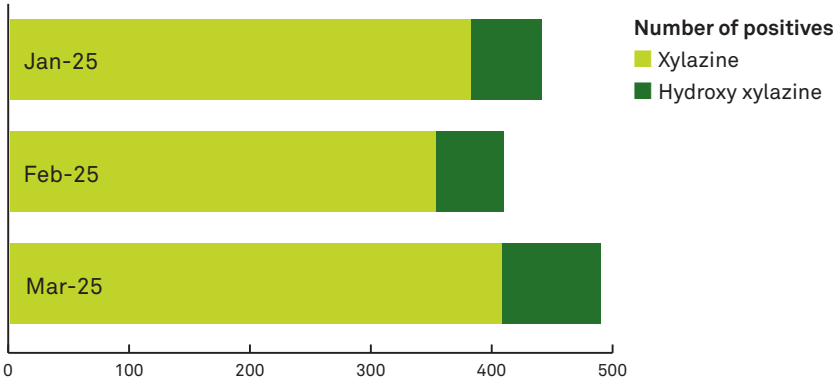
Of the specimens analyzed in the first quarter of 2025, 2,988 were positive for at least 1 NPS. Xylazine was the most common single analyte seen, being positive in 1,140 specimens.

While illicit xylazine use remains a concern across the country, the percentage of positive specimens that contain xylazine has decreased steadily over the past 6 months. When the Quest Diagnostics NPS test was first launched in November 2023, greater than 60% of all positive specimens contained xylazine. In January 2025, that percentage dropped to less than 40% of all positive specimens. While xylazine use is still a major issue, it is not the only NPS of concern.[4]

Xylazine positivity among patient samples

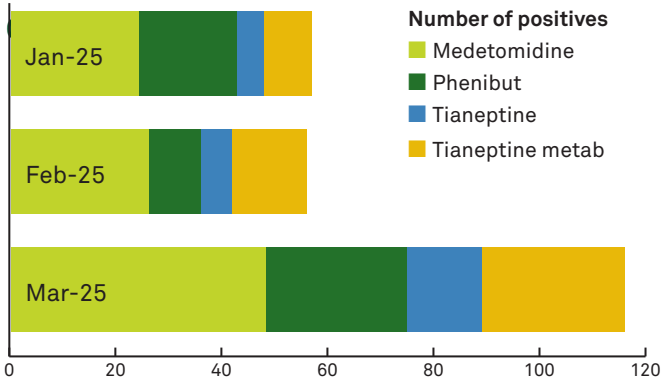


Over 350 patient specimens were positive for xylazine each month in the first quarter of 2025. Xylazine's metabolite, hydroxy xylazine, was positive in at least 58 patients each month and was only seen in combination with xylazine.



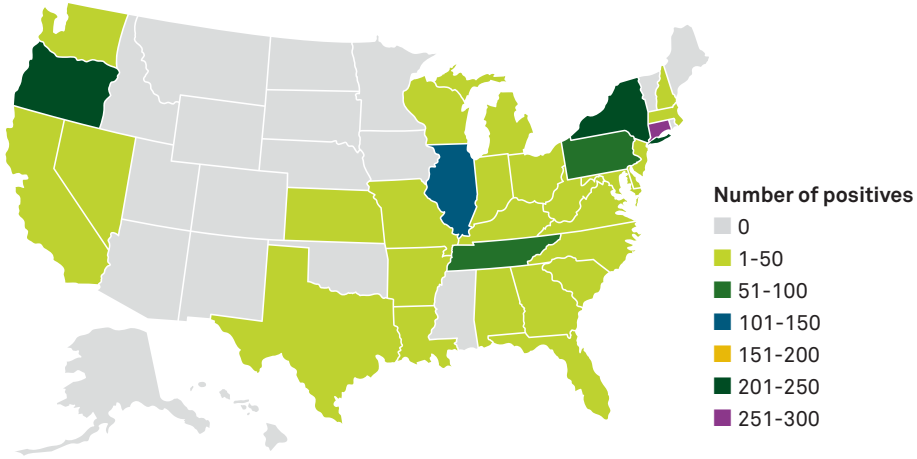
Xylazine and hydroxy xylazine positivity

All other compounds in the OI class also saw positivity in the first quarter, the most prevalent being medetomidine. Like xylazine, medetomidine is also a veterinary tranquilizer that has emerged as an adulterant in purchased drugs.[5]



OI class number of positives by state January-March 2025

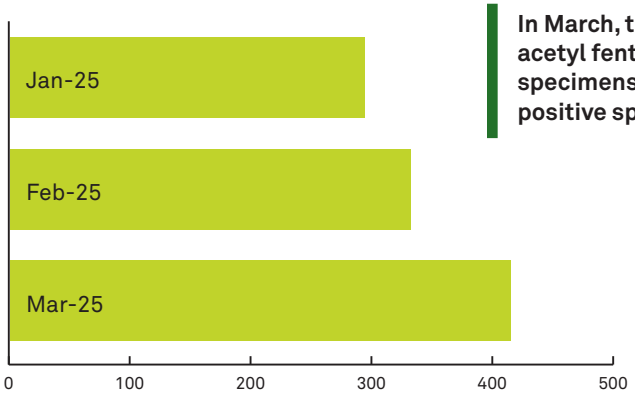
Connecticut was the state with the highest number of positives from the OI class.



Designer fentanyl analogs (FA)

The NPS designer fentanyl analogs (FA) class was the most positive in the first quarter of 2025. The most-seen FA compound was acetyl fentanyl.

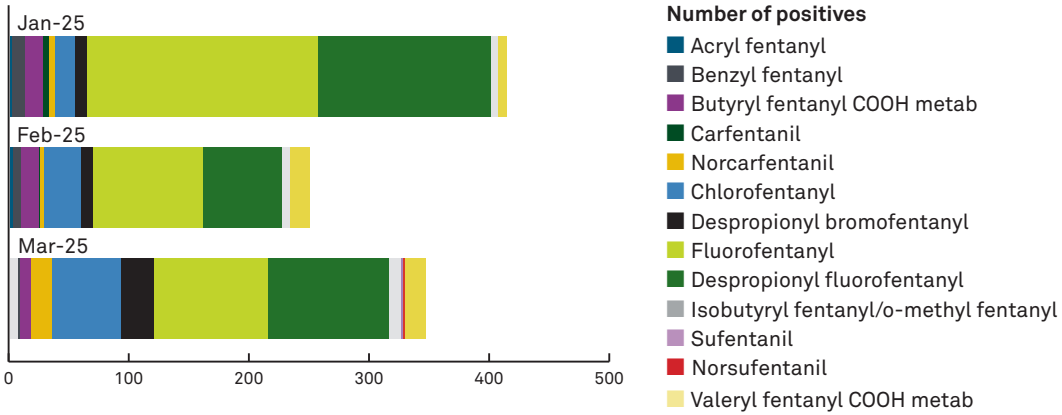
Acetyl fentanyl positivity



In March, there were more acetyl fentanyl–positive specimens than xylazine–positive specimens.

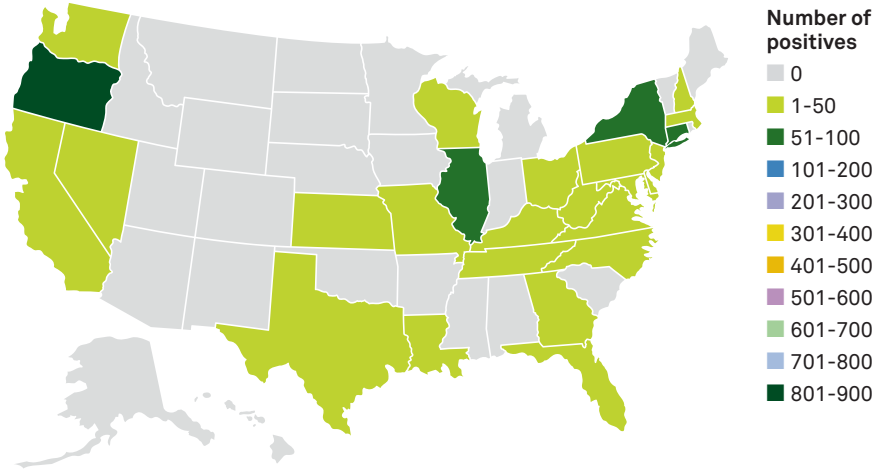
Thirteen additional fentanyl analogs were positive in the first quarter of 2025. Fluorofentanyl and its precursor, despropionyl fluorofentanyl, were the second and third most positive FAs. Carfentanil continues to be of concern and was present in 28 specimens in the first quarter.

FA class number of positives



FA class number of positives by state January-March 2025

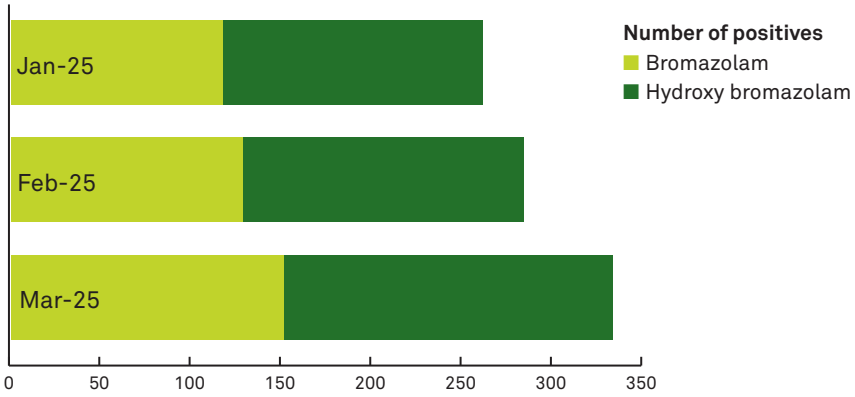
Oregon continued to have the highest number of specimens positive for fentanyl analogs. Outside of Oregon, there was a relatively equal distribution of positives from the East Coast to the West Coast.



Designer benzodiazepines (DB)

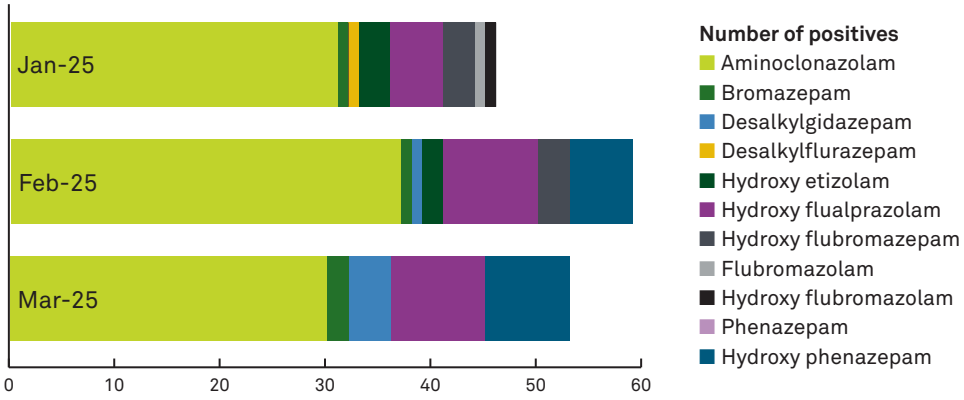
In the first quarter, bromazolam and its metabolite, hydroxy bromazolam, continued to be the most positive in the designer benzodiazepine (DB) class and were frequently seen together.

Bromazolam and hydroxy bromazolam positivity



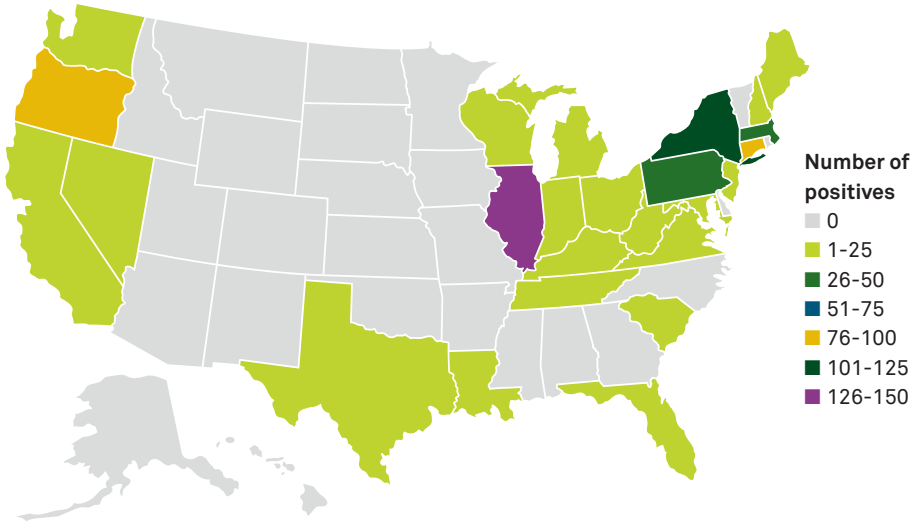
DB positivity

Eleven other DBs were seen in specimens from the first quarter, with aminoclonazolam being the second most positive. Aminoclonazolam was frequently seen in combination with xylazine, various fentanyl analogs, and some designer opioids.



DB class number of positives by state January-March 2025

Illinois was the state with the highest number of positive specimens for DBs, closely followed by New York and Oregon.

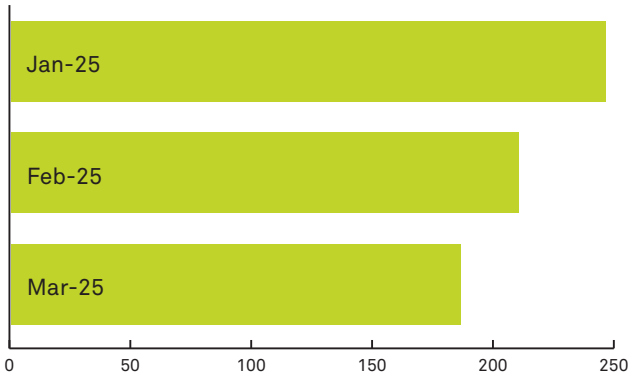


Quest Diagnostics®

Synthetic cannabinoids (SC)

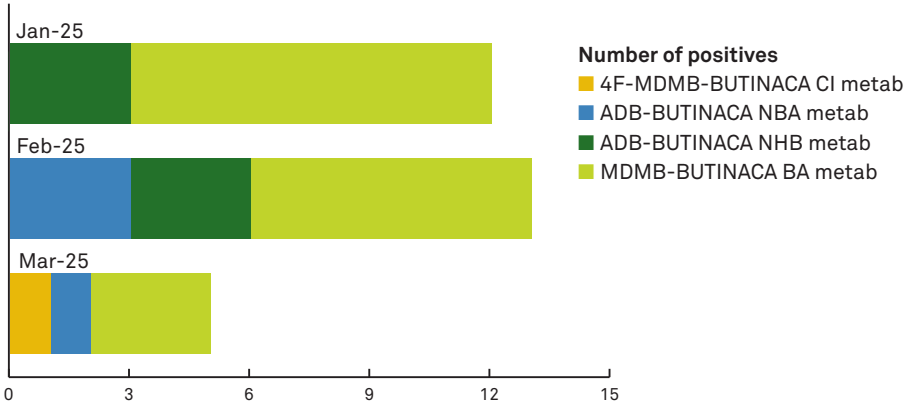
In the synthetic cannabinoid (SC) class, the butanoic acid metabolite for MDMB-4en-PINACA continued to be the most positive compound and was seen in 21% of positive specimens. This compound was most frequently seen by itself but was also found with xylazine in some patient specimens.

MDMB-4en-PINACA BA metabolite positivity



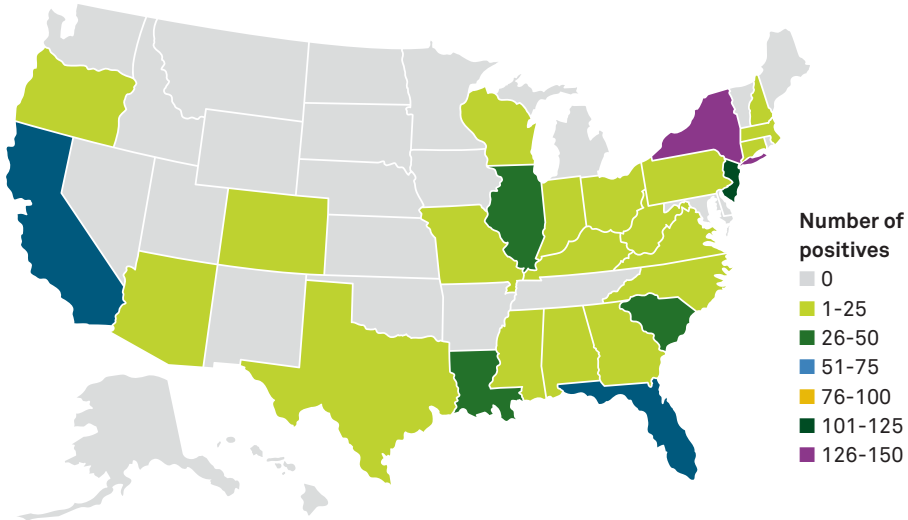
Synthetic cannabinoid positivity

Other synthetic cannabinoids were not frequently detected during the first quarter. However, those that were seen were mixed with the MDMB-4en-PINACA metabolite.



SC class number of positives by state January-March 2025

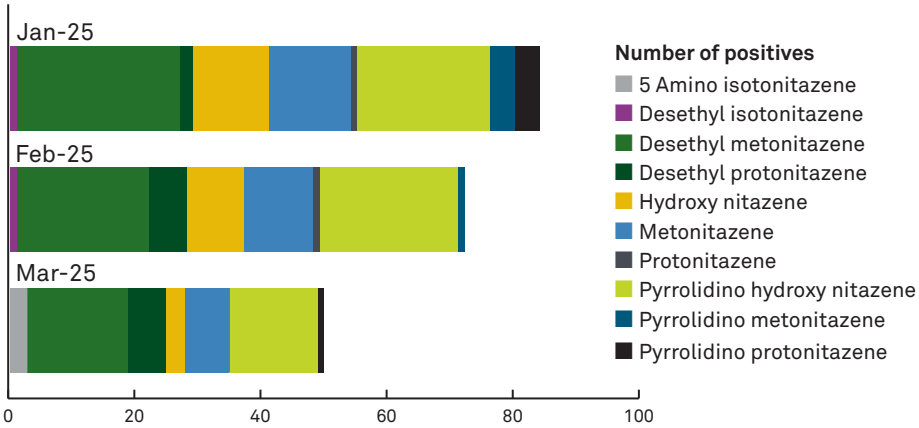
Synthetic cannabinoids were found in positive specimens from across the US.



Designer opioids (DO)

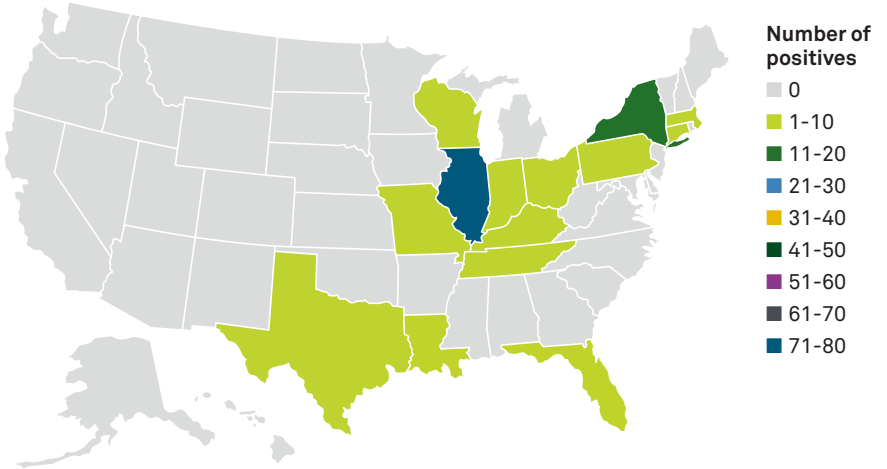
The NPS designer opioid (DO) class continued to have lower positivity than other classes, with such compounds being present in only 3.5% of positive specimens. The most frequently seen designer opioid continued to be pyrrolidino hydroxy nitazene, a metabolite for several designer opioids. Desethyl metonitazene was the next most positive designer opioid and is thought to be both a parent compound as well as a metabolite of another designer opioid.[6]

DO positivity



DO class number of positives by state January-March 2025

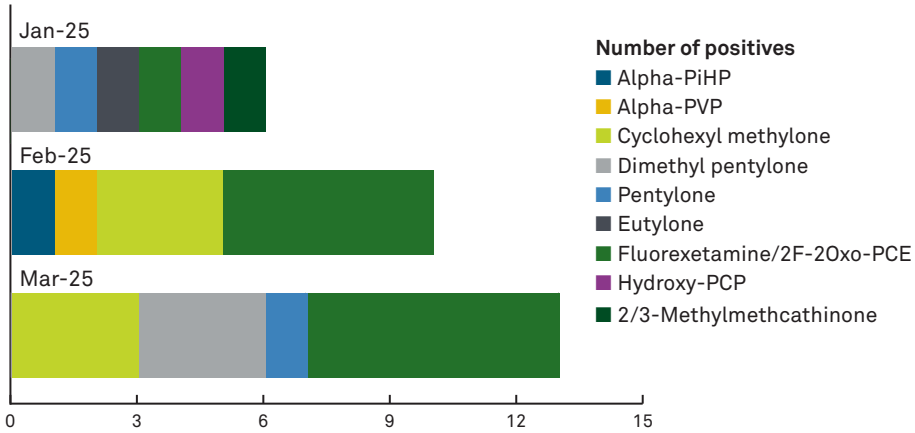
In the first quarter of 2025, most positive specimens containing DOs came from Illinois. All positive specimens from this class came from the eastern half of the US.



Designer stimulants (DS)

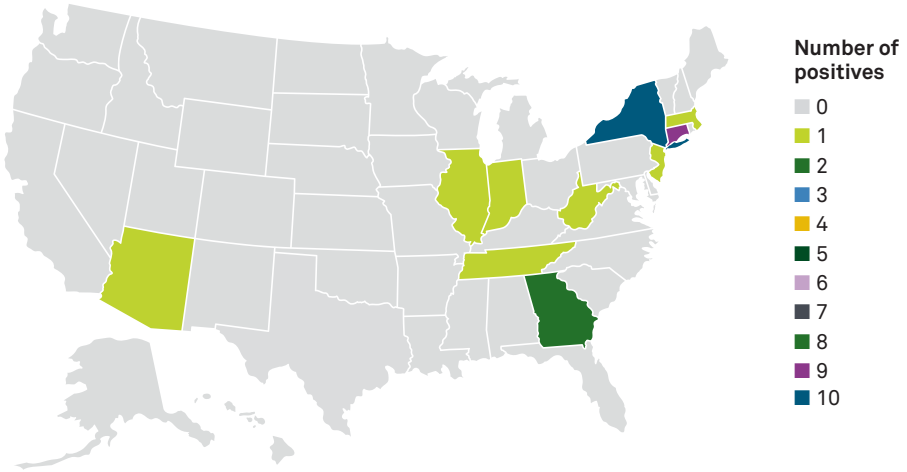
The NPS designer stimulant (DS) class saw the least number of positive specimens in the first quarter, with less than 1% of positive specimens. The isomers fluorexetamine and 2-fluoro 2-oxo PCE were seen the most frequently.

DS positivity



DS class number of positives by state January-March 2025

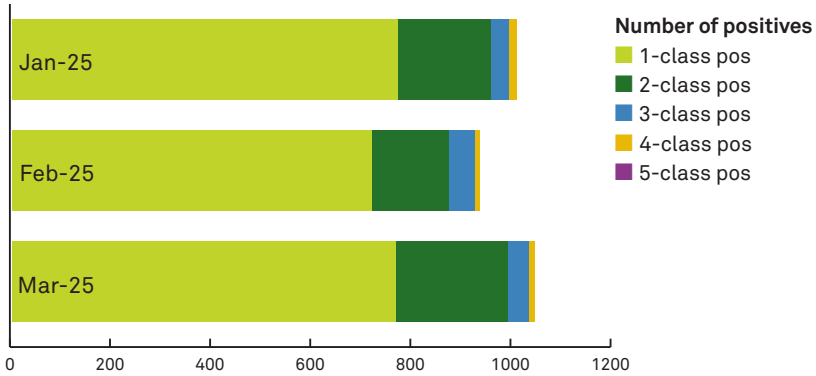
Most DS positive specimens came from the eastern part of the US, with most being from New York.



In conclusion

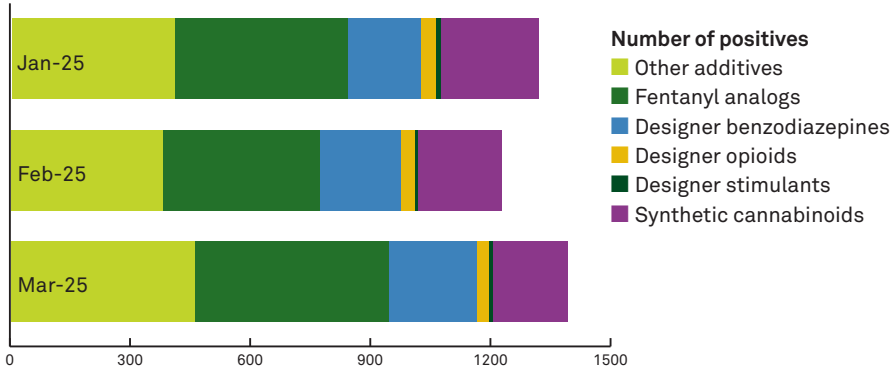
During the first quarter of 2025, a total of 2,988 patient specimens were positive for NPS compounds, and 57 different NPS compounds were observed. Although most specimens (75%) were positive for only 1 NPS class, 1 patient specimen was positive for 5 of the 6 NPS classes (with the exception being the synthetic cannabinoid class).

NPS positivity

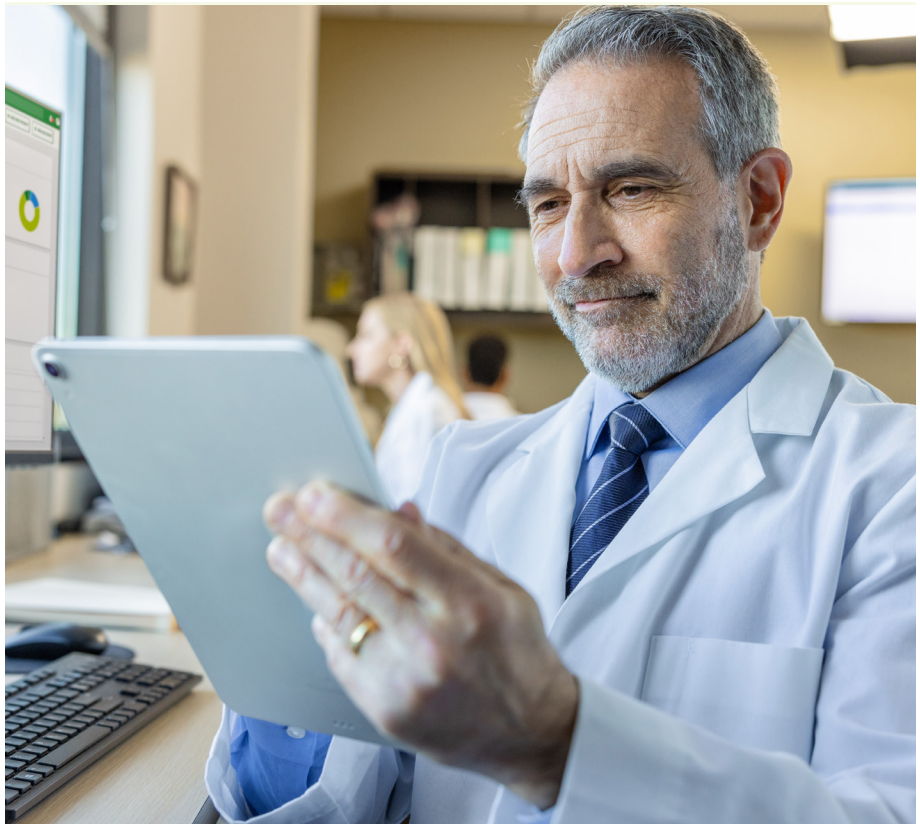


The OI and FA classes saw the most positivity in the first quarter and were frequently seen together in patient specimens. The DO and DS classes had the lowest positivity among positive specimens.

Positivity by NPS class



NPS positivity in clinical specimens continues to be of great concern for clinicians and laboratory analysts. The different NPS classes seen in analyzed specimens can be vast and unexpected. Therefore, if such drug use is suspected, it is imperative to test with a full NPS panel that includes all classes to ensure proper detection and appropriate treatment.



References

1. Peacock A, Bruno R, Gisev N, et al. New psychoactive substances: challenges for drug surveillance, control, and public health responses. *Lancet*. 2019;394(10209):1668-1684. doi:10.1016/ s0140-6736(19)32231-7

2. Mohr ALA, Logan BK, Fogarty MF, et al. Reports of adverse events associated with use of novel psychoactive substances, 2017–2020: a review. *J Anal Toxicol.* 2022;46(6):e116-e185. doi: 10.1093/jat/bkac023

3. Iwersen-Bergmann S, Lehmann S, Heinemann A, et al. Mass poisoning with NPS: 2C-E and Bromo-DragonFly. *Int J Legal Med.* 2019;133(1):123-129. doi:10.1007/s00414-018-1882-9

4. Centers for Disease Control and Prevention. Overdose prevention: what you should know about xylazine. Updated May 16, 2024. Accessed February 21, 2025. https://www.cdc.gov/overdose-prevention/about/what-you-should-know-about-xylazine.html

5. The Center for Forensic Science Research & Education. Medetomidine. NPS discovery - new drug monograph. [Report]. November 27, 2023. Accessed June 6, 2025. https://www.cfsre.org/images/monographs/Medetomidine-New-Drug-Monograph-NPS-Discovery-112723.pdf

6. Federal Register, Food and Drug Administration, HHS. International drug scheduling; Single convention on narcotic drugs; Convention on psychotropic substances; hexahydrocannabinol; N-pyrrolidino protonitazene (protonitazepyne); N-pyrrolidino metonitazene (metonitazepyne); N-piperidinyl etonitazene (etonitazepipne); N-desethyl-isotonitazene; 3-hydroxy-phencyclidine; N-ethylheptedrone; carisoprodol; Request for comments. Published Document: 2024-18045 (89 FR 66117). August 14, 2024. Accessed June 6, 2025. https://www.federalregister.gov/documents/2024/08/14/2024-18045/international-drug-scheduling-single-convention-on-narcotic-drugs-convention-on-psychotropic#citation-1-p66119

Image content features models and is intended for illustrative purposes only.

QuestDiagnostics.com

Quest Diagnostics®