UNODC
United Nations Office on Drugs and Crime

Current NPS Threats

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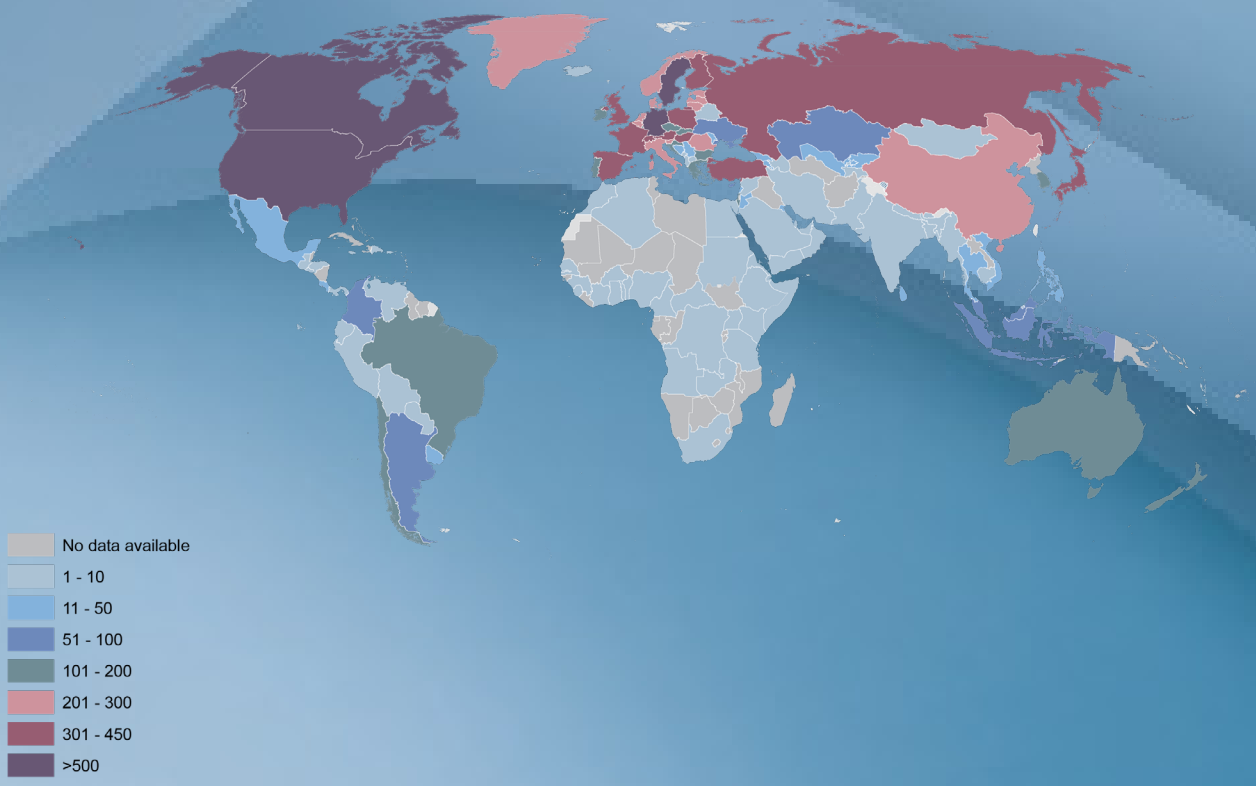


Figure 1: UNODC Early Warning Advisory (EWA) on New Psychoactive Substances (NPS). Number of NPS reported by country/territory up to 2024

UNODC Early Warning Advisory Toxicology Highlights

- **Over 1,200 individual NPS have been reported to the UNODC Early Warning Advisory on New Psychoactive Substances (NPS) by 142 countries and territories worldwide.**
- **Continuous prevalence of benzodiazepine-type NPS in toxicology casework, particularly bromazolam, across driving under the influence of drugs (DUID), clinical admissions, and post-mortem cases.**
- **Polysubstance use is a significant concern with numerous cases involving the combination of multiple NPS but also of NPS with synthetic opioids such as fentanyl and other controlled substances.**

2024

What is the UNODC Early Warning Advisory?

Established in 2013 under the United Nations Commission on Narcotic Drugs Resolution 56/4 (2013), the UNODC Early Warning Advisory (EWA) was the first global monitoring system on new psychoactive substances (NPS). Managed by the UNODC Laboratory and Scientific Service's SMART Forensics, EWA serves as a tool for effective, evidence-based policy responses by monitoring, analysing, and reporting global and regional trends on NPS. Since its inception, UNODC EWA has served as a voluntary online data system that gathers and consolidates both regular and ad-hoc submissions from forensic drug testing laboratories, Member States, and partner organisations on NPS found in seized materials and toxicology cases.

This information contributes to the identification of the most persistent, prevalent, and harmful NPS which pose the greatest threat to public health, thus, assisting in the prioritisation of substances for placement under international control, as well as legislative responses at the national level. Since 2015, 80 NPS have been placed under international control and these substances continue to be included in the EWA to assist in and monitor the implementation of international scheduling decisions.

The following report presents the latest information on NPS that has been reported to UNODC and an analysis of over 2,800 cases submitted from toxicology laboratories within 11 Member States from the Americas, Europe, Asia and Oceania in 2023. Although the analysis allows for a broader understanding of the associated harm of NPS, it is not an exhaustive representation of the variety and toxicity of NPS present globally.

Trend analysis of NPS reported by Member States

Currently, 1,245 individual NPS have been reported to UNODC by 142 countries and territories worldwide. As highlighted in previous reports, the global NPS landscape continues to be marked by significant diversity. While 15 countries have identified over 300 substances, 93 countries have reported fewer than 50 substances. This variation in the number of identified NPS across countries reflects not only the diverse challenges faced by each country but also the complexity of addressing the NPS phenomenon on a global scale (Figure 1).

Based on their mode of action, NPS can broadly be classified into six effect groups and the number of reports of substances within each of these groups from 2012 to 2023 is shown in Figure 2. Since reporting began in 2008, stimulants and synthetic cannabinoid receptor agonists (SCRAs) have been the two largest groups of NPS, collectively representing 61% of all reported NPS. While the data submission for 2023 is currently ongoing, previous year-to-year reporting has shown fluctuations within individual substance groups. Nonetheless, the total number of NPS reported annually from 2013 onwards has consistently ranged between 400 and 500 substances each year.

In recent years, the number of new substances that have emerged has dropped significantly with 44 new substances in 2022 and 31 in 2023. With regard to the new substances that have emerged in 2023, the most prominent group was synthetic opioids (36%) with stimulants, primarily synthetic cathinones, and SCRAs each accounting for 24% (Figure 3).

Figure 3: New Substances reported to UNODC EWA in 2023

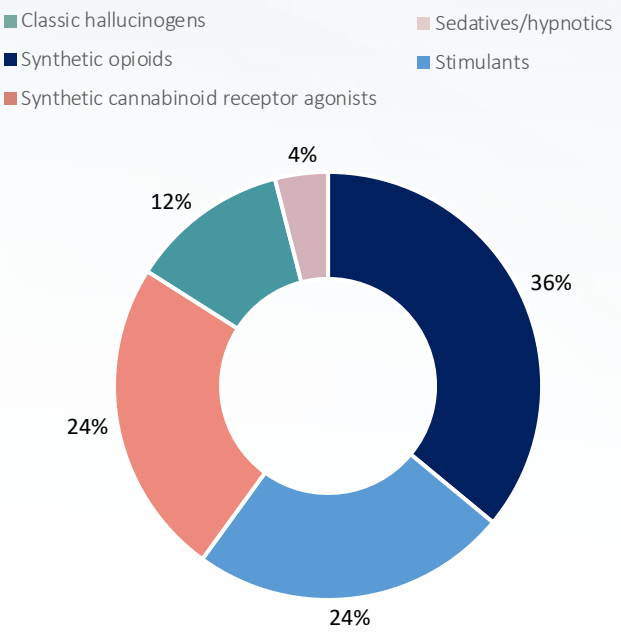
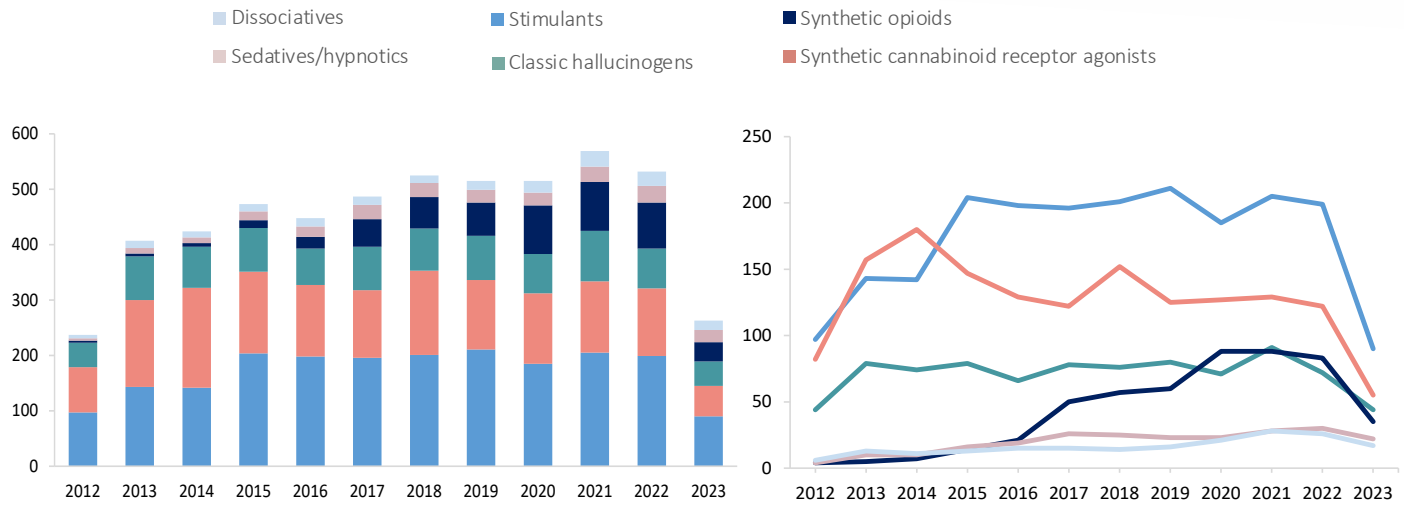


Figure 2: Emergence of NPS by effect group reported to the UNODC EWA 2012-2023*

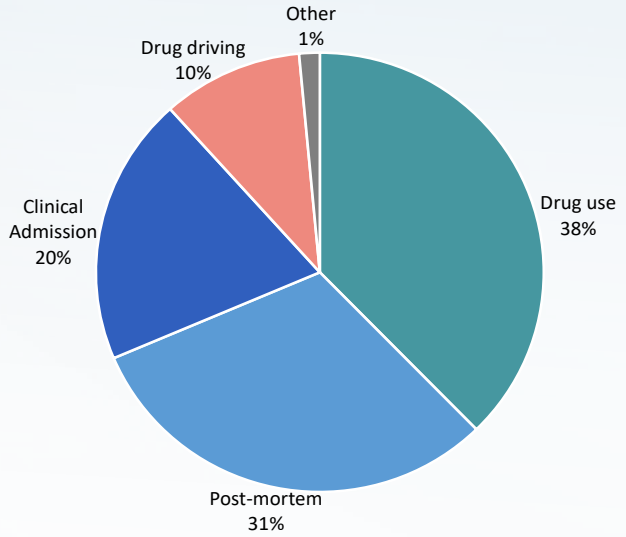


*Data for 2023 are not yet finalized

NPS toxicology case reports

The UNODC EWA Tox-portal contains over 8100 toxicology cases reported from 31 countries. In the data collection period covered by this report, 2,801 reports of NPS in a total of 1,955 toxicology cases (21% female, 58% male, 21% unknown/not reported, <1% other) were reviewed, identifying more than 100 individual NPS. As shown in Figure 4, 38% of the cases related to drug use and 31% were post-mortem cases. The increase in post-mortem cases compared to the previous volume of the Current NPS Threats, is primarily related to a greater number of case submissions from North America. Among the remaining case types, there were 639 reports of NPS in clinical admissions (20%), 240 reports in cases related to driving under the influence of drugs (DUID) (10%), and 46 reports of NPS categorized as other case types, including reports in drug facilitated sexual assault (1%) (Figure 4).

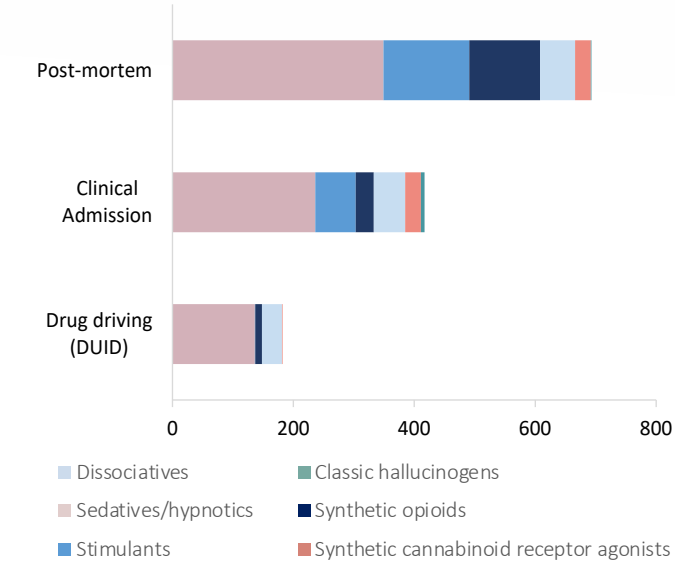
Figure 4: Types of toxicology cases reported (n=1,955)



Note: Drug use cases refer to instances of drug use within a criminal context that are not included in the other categories displayed.

The majority of reported NPS across the three main toxicology case types of post-mortem, drug driving incidents, and clinical admissions were benzodiazepine-type substances, followed by substances with stimulant effects and then synthetic opioid NPS (Figure 5).

Figure 5: Substance groups reported across main toxicology case types



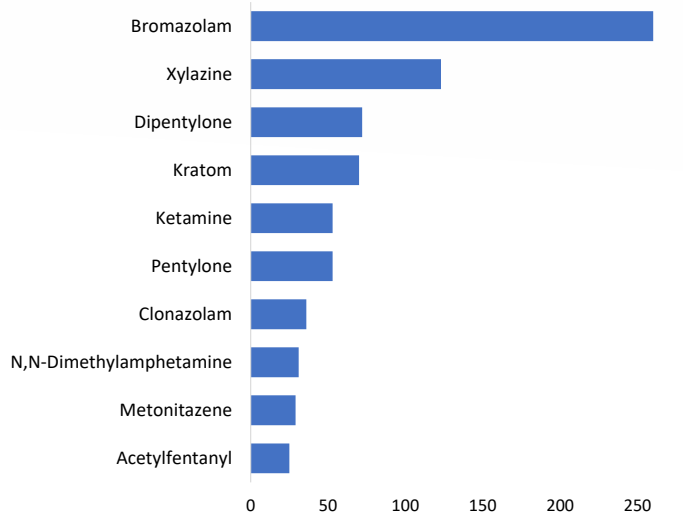
Post-mortem (PM) cases

A total of 605 post-mortem cases were analysed, in which there were 1,014 reports of 61 individual NPS. Post-mortem cases were provided from toxicology laboratories in five countries, while 88% of cases were submitted from North America. The primary substance reported in post-mortem cases was fentanyl, identified in 55% (n=333) of the cases. These fentanyl cases (blood concnetration range; 0.29-463 ng/mL, 15 ng/mL median) primarily involved polysubstance use, in which fentanyl was identified together with a range of controlled substances and medications as well as NPS spanning several different groups.

Benzodiazepine-type substances, particularly bromazolam[1] and clonazolam, were among the top ten reported NPS in post-mortem cases, with bromazolam being the most commonly identified substance (n=260, Figure 6). Fentanyl was found in 62% of case reports in which bromazolam was also identified, and in 56% of post-mortem cases involving clonazolam. Benzodiazepine-type NPS such as etizolam, flualprazolam or flubromazolam highlighted in the previous Current NPS Threats Report remained present but less frequently detected in this case type across the reporting period.

In addition, a number of NPS with stimulant effects were also identified in PM cases. Among the most commonly identified stimulants were the synthetic cathinones dipentylone (n=72) and pentylone (n=53) and the phenethylamine N,N-dimethylamphetamine (n=31) (Figure 6). When interpreting such case information. it should be considerd that pentylone is also a metabolite of dipentylone. A similar pattern of polydrug use involving the aforementioned stimulants and fentanyl was observed in 71% of the cases with stimulant-type NPS present. Xylazine, a veterinary sedative, has emerged in recent years as a substance of considerable concern as it has been commonly found in combination with fentanyl. Both drugs can cause sedation and respiratory depression which increases the likelihood of fatal overdoses. In case of an overdose, administration of the opioid antagonist naloxone (Narcan) can reverse the effects of fentanyl, but it will not affect the non-opioid substance xylazine.[2] Within the current data set for PM cases, xylazine was identified in 123 cases (Figure 6), with fentanyl being identified in 87% of these cases, and methamphetamine in 49% of them.

Figure 6: Substances most often reported in post-mortem (PM) cases



[1] Bromazolam was one of 5 NPS placed under International control at the 67th Commission on Narcotic Drugs in March 2024. The other substances include butonitazene, 3-chloromethcathinone, dipentylone and 2-fluorodeschloroketamine.

Within PM cases, involving NPS opioids, eight individual nitazenes, primarily metonitazene, protnitazene and N-desethyl isotonitazene were reported in 58% (n=80) of cases, while fentanyl analogues, primarily acetylfentanyl were identified in 40% of cases. Ketamine was identified in 53 PM cases and synthetic cannabinoid receptor agonists (primarily MDMB-4en-PINACA) were reported in 30 post-mortem cases mainly from Southeast Asia.

Regarding the relative contribution of the NPS identified in PM cases to the outcome of the event, this remained undetermined in 85% of all PM cases. In instances where the NPS was deemed causal to the outcome of the event (n=21), 76% of cases showed combined consumption of bromazolam with other opioids or stimulants such as methamphetamine. Xylazine, kratom, and clonazolam each had a contributory role in a small number of post-mortem events (n=3). Ketamine and acetylfentanyl contributed to a fatal outcome in n=2 cases each.

Clinical Admission (CA) cases

Clinical admissions represented the second largest group of toxicology cases during the current reporting period (n=386) involving 639 reports of NPS (Figure 5). The two most commonly reported NPS groups within this case type were benzodiazepines, accounting for 355 reports, followed by 100 reports of stimulants. Bromazolam (n=203), clonazolam (n=39), and desalkylgidazepam (n=36) comprised the top three identified NPS in over 40% of clinical case reports. The concentrations of bromazolam and clonazolam observed in toxicology casework, as presented in Table 1 and Figure 7, provide forensic toxicology laboratories with an anticipated range for each drug.

In 115 clinical admissions involving bromazolam, no other NPS were reported. For the remainder of cases, 43% (n=88) included the identification of other NPS primarily desalkylgidazepam, clonazolam, and flubromazepam and fentanyl was identified in 20 cases. Patients who consumed bromazolam presented clinically in several cases with symptoms such as an altered mental state (e.g., confusion), respiratory and/or cardiovascular complications which manifested in hypoxia, tachycardia and hypotension. Clinical cases involving clonazolam showed that this substance was mainly consumed alongside other benzodiazepine-type NPS of which bromazolam was found in 23 cases. With regard to cases involving desalkylgidazepam (n =36), bromazolam was also identified in all cases.

All clinical cases linked to xylazine (n=16) were associated with polydrug use. Patients typically consumed a mixture of multiple other NPS and illicit substances, including fentanyl, which manifested in symptoms characteristic of an overdose (e.g., respiratory depression and unresponsiveness). Additional case information disclosed that naloxone was commonly administered, yet patients exhibited either no or only a partial response to this treatment ultimately requiring more intense medical intervention.

Of 100 admissions associated with the consumption of stimulant-type NPS, dipentylone (n=21), pentylone (n=21), or 3,4-methylenedioxy-*alpha*-pyrrolidinohexanophenone (MDPHP) (n=16) accounted for most of the instances. The latter was frequently observed to cause symptoms of severe agitation alongside hypertension and tachycardia (n=9 cases). In 60 clinical cases dissociatives were identified, with ketamine occurring in 32 of them. In 35 clinical admissions in which NPS with opioid effects were reported, 77% of the reports detected protonitazene or metonitazene. Patients admitted to the hospital for synthetic cannabinoid use from cases in the Americas and Oceania were most commonly associated with MDMB-4en-PINACA (n=17) and ADB-BUTINACA (n=16). Lastly, hallucinogenic substances of the NBOH series were identified in a number of clinical cases (n=14) from the Americas.

Figure 7: Bromazolam and clonazolam concentrations in post-mortem (PM) cases and clinical admissions (CA)

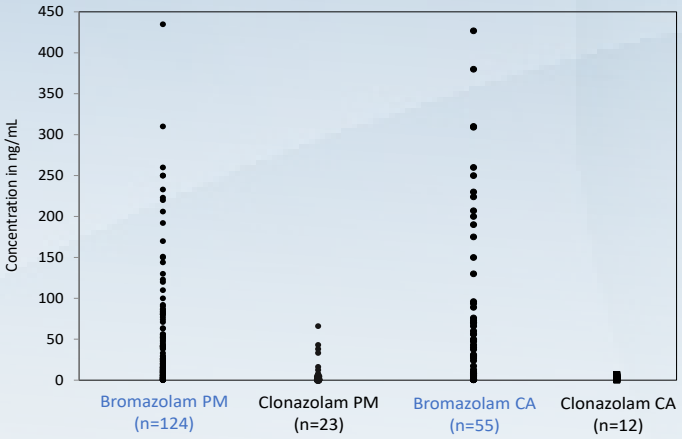


Table 1: Bromazolam and clonazolam concentration ranges (ng/mL) across toxicology case types

	Bromazolam			Clonazolam		
	PM (n=127)	**CA** (n=58)	**DUID** (n=6)	**PM** (n=23)	**CA** (n=12)	**DUID** (n=1)
Minimum (ng/mL)	0.016	0.5	29	0.15	0.1	
Median (ng/mL)	24	53.0	81.5	3.8	2.75	0.57
Maximum (ng/mL)	5800	1030	330	66	7	

Driving under the influence of drugs (DUID)

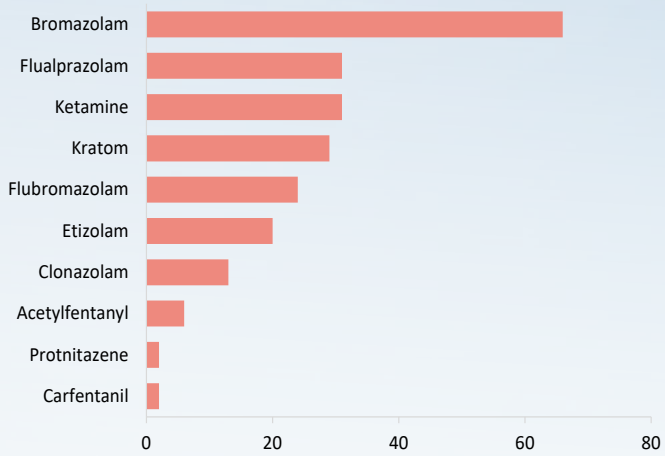
In cases related to driving under the influence of drugs (DUID) provided during the current reporting period, there were 191 case reports of NPS almost exclusively from North America with benzodiazepines being identified in 68% of cases. As with other case types, bromazolam emerged as the most commonly reported substance (n=66). Other frequently identified benzodiazepines included flualprazolam (n=31), flubromazolam (n=24), etizolam (n=20), and clonazolam (n=13) (Figure 8). Given that these substances were highlighted in previous NPS threats reports (link), this emphasizes the continued presence of benzodiazepine-type NPS in both drug-driving and PM cases and the potential threat they pose. Synthetic opioids (acetylfentanyl n=6, carfentanil n=2, protonitazene n=2) were identified in a small number of cases (Figure 8). Furthermore, the presence of kratom (n=29) and ketamine (n=31) was also evident in a number of cases.

With regard to instances of polysubstance use in DUID, two or more NPS were identified in 29 cases, primarily involving multiple benzodiazepine-type NPS. For instance, bromazolam was often found with etizolam (n=4), flubromazolam (n=4), and

[2] *Edinoff, Amber N., et al. "Xylazine: A Drug Adulterant of Clinical Concern." Current Pain and Headache Reports (2024): 1-10*

flulaprazolam (n=3). Flualprazolam and etizolam were jointly consumed in nine cases. When benzodiazepine-type NPS were used alongside synthetic opioids, fentanyl analogues like acetylfentanyl, carfentanil and acryloylfentanyl were among the most frequently identified substances. Ketamine was combined with other benzodiazepine-type NPS in 2 cases. Fentanyl was identified in 13% of DUID reports and the detection of cocaine alongside an NPS was present in 28%.

Figure 8: Substances most often reported in DUID cases



Other toxicology case types

Drug use cases constituted the largest portion of submitted toxicology cases with 863 identified NPS (Figure 4). Of these cases, almost 90% of case reports were from East Asia and 71% of these involved the use of ketamine. In 75% of cases from Southeast Asia, only ketamine and no other illicit substances were identified, while in 24% of cases, it was identified with stimulants such as 3,4-methylenedioxymethamphetamine (MDMA) and/or methamphetamine. A similar pattern related to case reports from East Asia was highlighted in the previous issue of the Current NPS Threats Report.

Lastly, a small number of reports (n=27) were drug-facilitated sexual assault cases (DFSA) which almost exclusively had more than one substance reported in addition to an NPS. The two synthetic cathinones pentylone and dipentylone were identified in over 67% of cases involving DFSA. Benzodiazepine-type NPS (flualprazolam, flubromazolam, bromazolam, xylazine) were reported in six cases.

Acknowledgments

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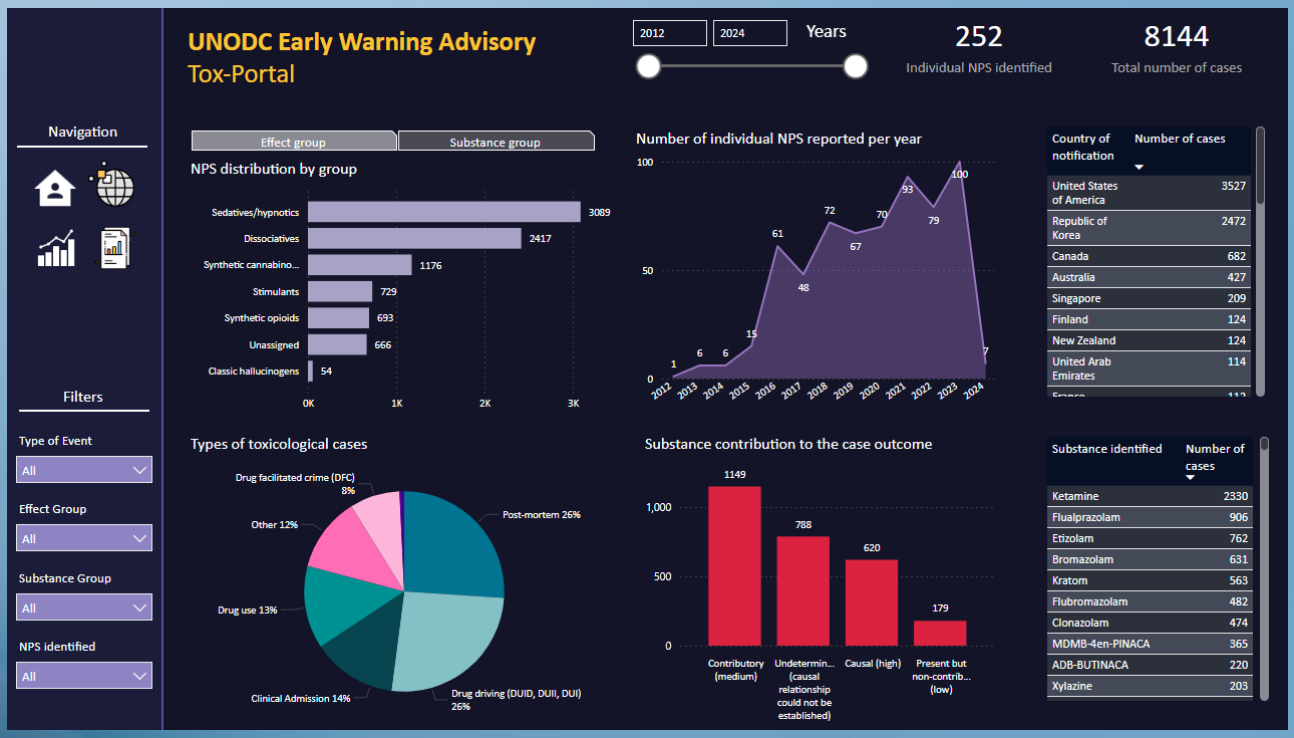
UNODC has introduced a new interactive feature of the Tox Portal, a Data Dashboard, which allows registered users to analyse and visualize submitted case information involving new psychoactive substances. The Data Dashboard can now be accessed after logging in with your user credentials at www.unodc.org/tox.



*Note: The boundaries and names shown and the designations in this document do not imply official endorsement or acceptance by the United Nations. Dashed lines represent undetermined boundaries. The dotted line represents approximately the Line of Control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. The final boundary between the Republic of Sudan and the Republic of South Sudan has not yet been determined. A dispute exists between the Governments of Argentina and the United Kingdom of Great Britain and Northern Ireland concerning sovereignty over the Falkland Islands (Malvinas).

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