UNODC
United Nations Office on Drugs and Crime

Current NPS Threats

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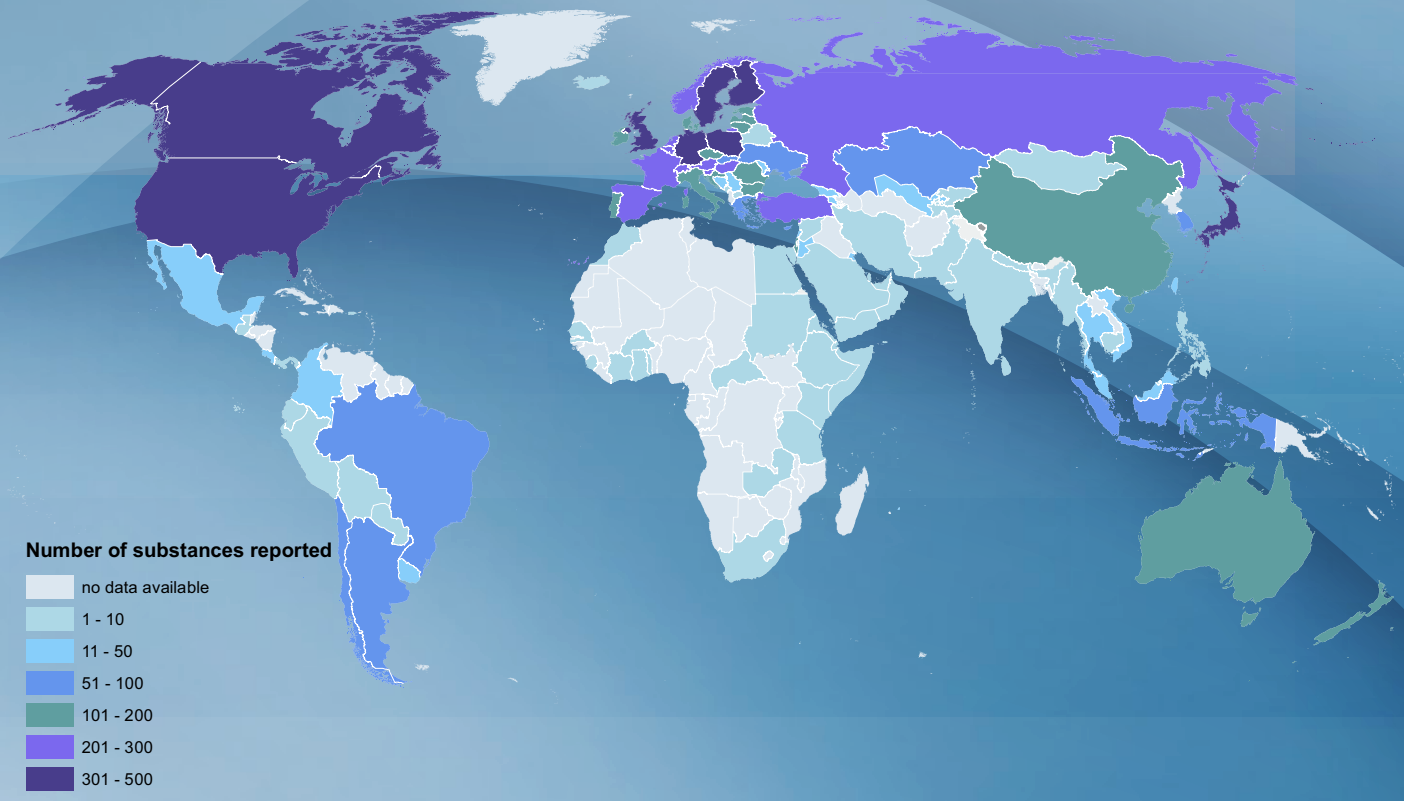


Figure 1: UNODC Early Warning Advisory NPS Portal database
*Data: Number of NPS reported by country/territory, January 2020**

UNODC Early Warning Advisory Toxicology Highlights

- **Poly-drug use continues to feature highly in cases of fatalities associated with NPS.**
- **Benzodiazepine-type NPS are increasingly reported in cases of driving under the influence of drugs in some countries.**
- **Incidents of kratom identification in poly-drug use cases are increasingly reported in a number of countries**

2020

Introduction - What is the UNODC Early Warning Advisory

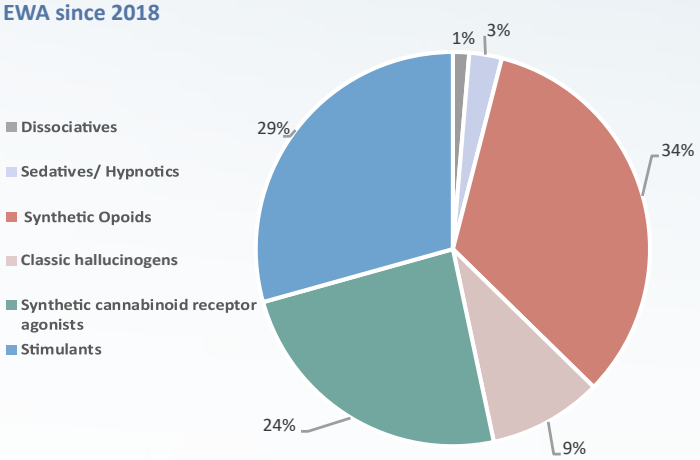
The UNODC Early Warning Advisory (EWA) on new psychoactive substances (NPS) was established in 2013 following a resolution passed by Member States at the Commission on Narcotic Drugs as a response to the emergence of NPS at the global level. The EWA aims to monitor, analyse and report trends on NPS, as a basis for effective evidence-based policy responses. The EWA provides access to information on NPS in a range of subject areas including NPS emergence and global monitoring, risk communication, chemical identification and analysis, toxicology, pharmacology, and national legislative responses by Member States.

The EWA thus serves as a repository for information on NPS leading to an improved understanding of their distribution and use at the global level and offers a platform for the provision of technical assistance to Member States. In order to identify the most harmful, persistent and prevalent NPS and assist in their prioritization for international control, the EWA was expanded in 2018 to collect toxicology data in post-mortem, clinical and other casework. This allows for the first time, the collection of data on harms associated with the use of NPS at a global level.

NPS reported by Member States

As of January 2020, 120 countries and territories have reported to UNODC the emergence of a cumulative total of 950 individual new psychoactive substances belonging primarily to six groups based on their mode of action, i.e. classic hallucinogens, dissociatives, sedatives/hypnotics, stimulants, synthetic cannabinoid receptor agonists and synthetic opioids. The NPS situation globally has a marked heterogeneity as 85 countries and territories have reported the emergence of less than 100 NPS and only 8 countries have reported more than 300 substances (figure 1). As a consequence, many Member States face challenges of differing scale and complexity. Information on the emergence of NPS by effect group over the period 2009-2018 are illustrated in figure 2. The largest group of substances that have been reported to UNODC are stimulants at 35%, (primarily phenethylamines and synthetic cathinones), while the second largest group at 30%, are synthetic cannabinoid receptor agonists (SCRAs). Figure 2 shows that year on year, there are fluctuations in the number and type of substances that are reported due to the dynamic nature of the NPS market. However, the initial rapid increase in substances seems to be levelling off somewhat in recent years. The changes in the market can be exemplified if we look at the substances that have been reported for the first time since the beginning of 2018. Figure 3 shows that the largest group of new substances during this period were synthetic opioids (34%) with 19 countries reporting their identification. While the data on NPS emergence and related trends show a dynamic market, it is necessary to examine the cases submitted by toxicology laboratories to shed light on substances with the greatest potential to cause harm.

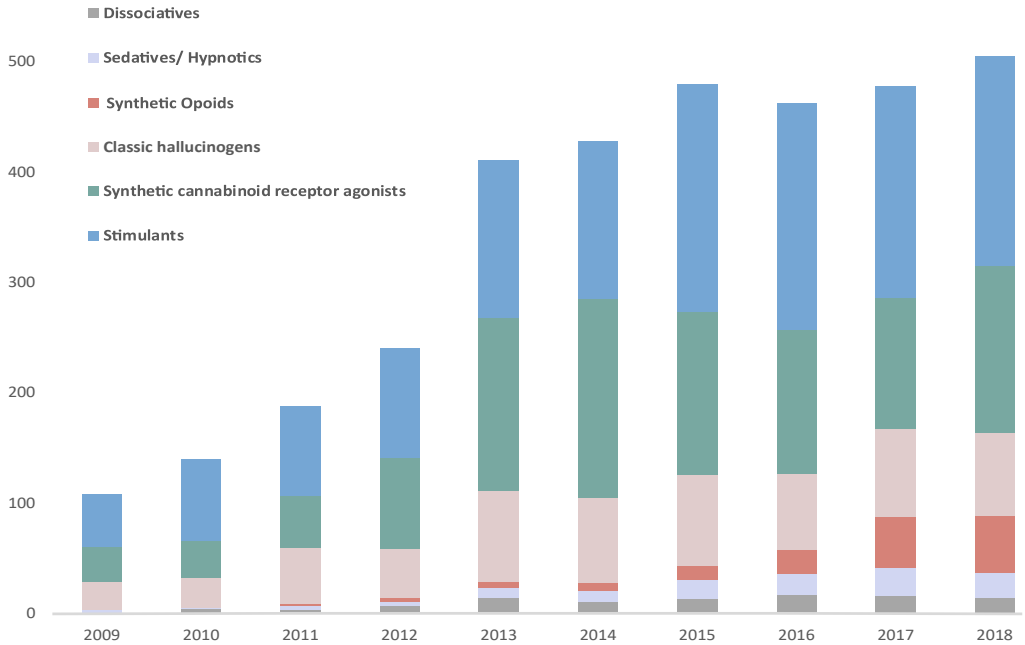
Figure 3: Distribution of new substances reported to the UNODC EWA since 2018



NPS toxicology case reports

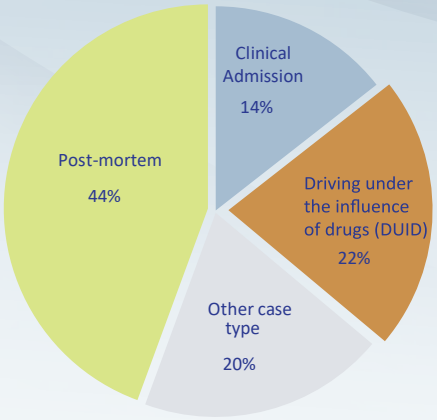
In the first volume of Current NPS Threats published in March 2019 looking at toxicology cases submitted between 2016-2018, just over half of all NPS cases reported involved synthetic opioids (particularly U-47700 and fentanyl analogues) or SCRAs. The most recent information from 2019 indicates that while SCRAs continue to persist, the group of sedative/hypnotic

Figure 2: Emergence of NPS by effect group reported to the UNODC EWA 2009-2018



benzodiazepine-type NPS now account for the majority of cases reported. Overall, 44% of cases reported in 2019 were post-mortem, 22% were driving under the influence of drugs (DUID), 20% were other case types (e.g. cases of drug facilitated sexual assault) and 14% were clinical admissions (figure 4). Toxicology cases with controlled substances (e.g. heroin, cannabis, fentanyl) and prescription opioids (e.g., tramadol) were not collected, unless reported in polydrug use cases with NPS.

Figure 4: Types of toxicology cases reported to the UNODC EWA in 2019



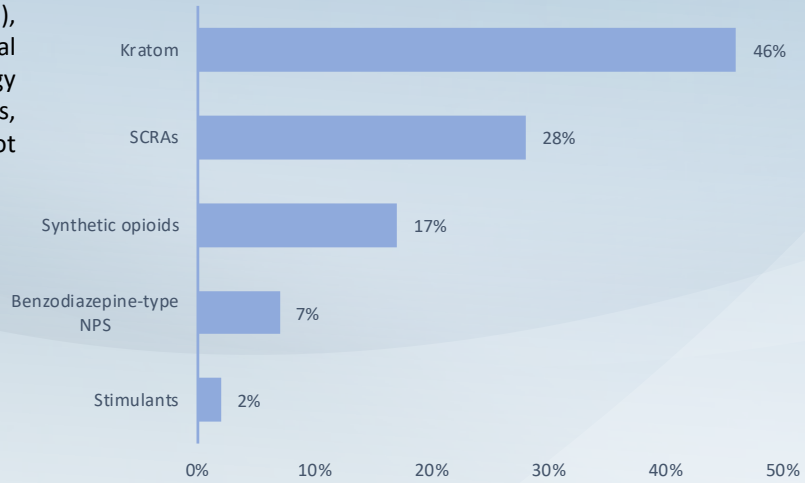
Post mortem cases:

Other drugs were detected in virtually every case demonstrating a continued feature of poly drug use within the NPS setting as outlined in the first volume of Current NPS Threats. In ascending order, stimulants accounted for 2% of the NPS identified in fatalities (only α-pyrrolidinovalerophenone (α-PVP)), followed by benzodiazepine-type NPS (7%), with synthetic opioids accounting for 17% and SCRAs representing 28% of all NPS cases (figure 5). The remaining cases (46%) predominantly involved kratom. Note that identfication of an NPS does not necessarily mean it was causal to the outcome of the case.

Of the SCRAs detected in fatalities in 2019, 5F-MDMB-PICA and AMB-FUBINACA (FUB-AMB) predominated with some detections of 5F-MDMB-PINACA (5F-ADB) and ADB-FUBINACA. Whilst other drugs were detected in nearly all cases, the SCRAs were assessed to have contributed to death in the majority of cases. In the data pertaining to synthetic opioids, all cases of fatalities were reported from the United States and also involved fentanyl itself in addition to other drugs. However, the fentanyl analogues (acetylfentanyl, butyrfentanyl or cyclopropylfentanyl) were assessed as having contributed to death in the majority of fatalities in which they were detected. With regard to benzodiazepine-type NPS reported in post-mortem cases in 2019, both etizolam and flualprazolam were detected. Other drugs were detected in all cases and the benzodiazepines were not deemed to be contributory to death except for the one case that involved flualprazolam.

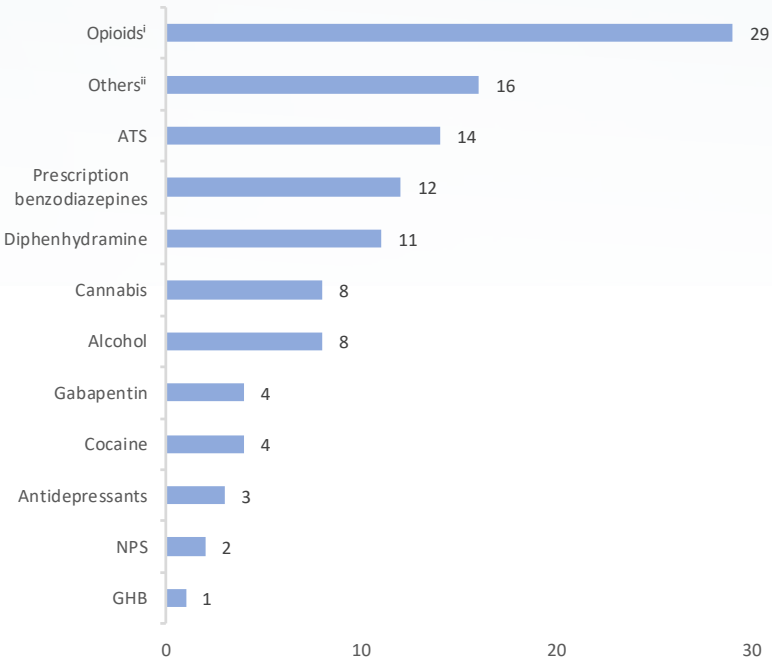
A high proportion of reported NPS fatalities in 2019 involved kratom, the colloquial name of the plant Mitragyna speciosa which has some opioid and stimulant properties, containing pharmacologically active alkaloids especially mitragynine and 7-hydroxymitragynine. Forty-seven instances were reported to the Toxicology Portal between 2017 and 2019 from the United States and Thailand, with 1 report in 2017 increasing to 16 in 2018 and 30 reports in 2019.

Figure 5: NPS detected in fatalities reported to the UNODC EWA in 2019



Overall, where information regarding the circumstances was known, there were 29 deaths, 16 instances of DUID, 1 sexual assault and 1 individual being under the influence in public. In the fatalities where blood concentrations had been determined, peripheral post-mortem mitragynine concentrations of between 48 and 380 ng/mL (n=6) were reported. In cases where heart/ cardiac blood was analysed, concentrations between 10.6 and 1200 ng/mL were found (n=6).

Figure 6: Frequency of other substances reported together with kratom



Opioids[i] : including morphine, heroin, fentanyl and prescription opioids. Others[ii] :methorphans, ondansetron, carisoprodol, LSD, lignocaine, doxylamine, cyclobenzoprine, methocarbamol, phenobarbital, piroxicam, chlorphenamine, hydroxyzine, quetiapine. ATS: Amphetamine-type stimulants.

For some comparison, blood mitragynine concentrations found in in cases of driving or being under the influence of drugs, were between 13.2 and 410 ng/mL with a median concentration of 45.25 ng/mL (n=17). The limited data provided for concentrations indicates a potential overlap between mitragynine blood concentrations found in non-fatal and fatal cases, which is not uncommon within post-mortem toxicology and especially relates to drugs where tolerance may be a factor.

In the deaths where causality could be assessed, kratom (as mitragynine or 7-hydroxymitragynine) was determined to be non-contributory (low) or of medium contribution to death in all the fatalities. There were no cases in which kratom was deemed to have caused or have significantly contributed to death. This was due to the circumstances and/or the presence of other drugs of potentially greater toxicological significance, such as opiates or opioids (morphine/heroin, codeine, oxycodone, buprenorphine, methadone).

For all cases in which kratom featured (figure 6), other drugs or alcohol were reported to have been detected, except for one case of DUID with an associated mitragynine blood concentration of 46.3 ng/mL. The antihistamine, diphenhydramine, was frequently detected (in addition to a few instances of chlorphenamine) purportedly due to relieving symptoms of itching following use of kratom but also as diphenhydramine may potentiate the effects of kratom. The most common classes of other drugs (across all case types) were opioids (including morphine, heroin, fentanyl and prescription opioids), amphetamine-type stimulants and benzodiazepines.

Driving under the influence of Drugs (DUID):

In 2018 and 2019, toxicology cases submitted to the EWA indicated the appearance of Benzodiazepine-type NPS associated with driving under the influence of drugs (DUID) cases with 44 cases in 2018 which increased to 89 cases in 2019. Etizolam, flualprazolam and flubromazolam were the benzodiazepine-type NPS most often reported during this time period (figure 7).

The increasing reports of instances of sedative/hypnotic NPS in recent DUID data highlights an ongoing concern pertaining to this class of NPS. However it should be noted that the reports are not global as a large percentage of these case reports were submitted by United States and Canada with some data from France, Germany and the United Kingdom. In DUID cases reported across 2018 and 2019, other drugs were detected in virtually all instances, especially cannabis, cocaine, MDMA, amphetamine, methamphetamine, and prescription benzodiazepines (e.g. alprazolam, clonazepam, diazepam, lorazepam) all of which are commonly associated with DUID in forensic toxicology casework.

Given the sedative/hypnotic nature of the benzodiazepines-type NPS identified, their use in combination with additional drugs could impair driving capabilities. Therefore, the increasing reports of instances of sedative/hypnotic NPS in the recent DUID data highlights an ongoing concern, especially within a drug driving context. As outlined elsewhere, in addition to being detected in fatalities, kratom was also detected in instances of DUID across 2018 and 2019. All instances except one also involved other drugs and the additional drugs involved all have the potential to exacerbate the impairing effects of kratom. This includes stimulants and central nervous system depressants, such as opioids/opiates and benzodiazepines, but also antihistamines – including diphenhydramine.

Synthetic Cannabinoid Receptor Agonists:

280 individual SCRAs have been reported to the UNODC early warning advisory from 90 different countries by 2019. While the number of new substances emerging within this group seems to be decreasing, their continued persistence, prevalence and harm was noted in Current NPS Threats volume I. In 2019, 5F-MDMB-PINACA (5F-ADB), 5F-MDMB-PICA and AMB-FUBINACA (FUB-AMB) were the SCRAs most frequently reported and featured in fatalities as well as clinical admissions. Instances of other SCRAs reported in toxicology cases in 2019 involved substances such as 4F-MDMB-BINACA, CUMYL-4CNBINACA, 5F-CUMYL-PeGACLONE and CUMYL-5F-PICA.

Figure 7: Most reported NPS in DUID cases in 2018 and 2019, illustrated by relative size of substance name displayed in relation to number of reports.

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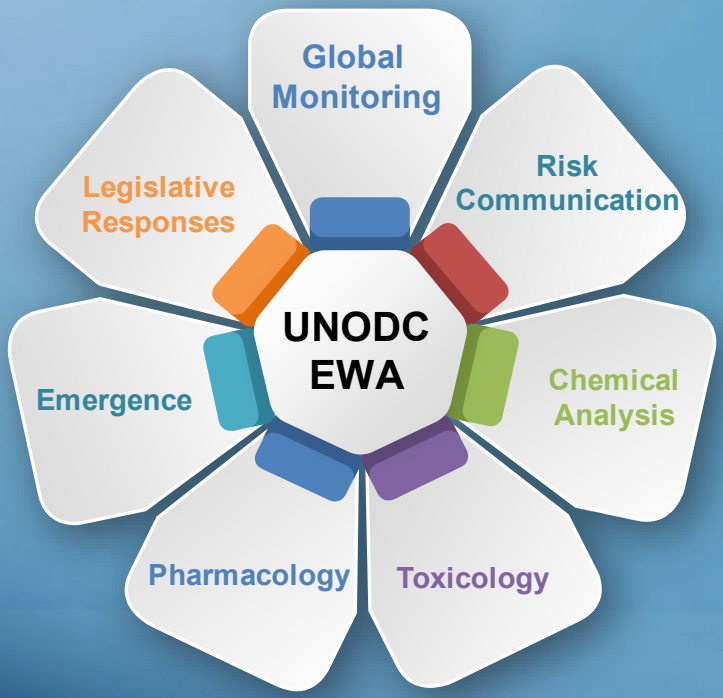

Acknowledgments

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*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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