Sistema Nacional de Políticas Públicas sobre Drogas | MINISTÉRIO DA CIDADANIA | MINISTÉRIO DA ECONOMIA | MINISTÉRIO DA SAÚDE | MINISTÉRIO DA JUSTIÇA E SEGURANÇA PÚBLICA | PÁTRIA AMADA BRASIL GOVERNO FEDERAL

CdE | UNODC Escritório das Nações Unidas sobre Drogas e Crime | PNUD

First Report of the Early Warning Subsystem on Drugs (EWS)

Overview of the use of psychoactive substances

According to estimates by the United Nations Office on Drugs and Crime (UNODC), 5.4% of the world population between 15 to 64 years old used some kind of psychoactive substance in 2019, corresponding to 275 million people. Cannabis was the most used drug (4%) followed by opioids (including opiates, 1.2%), amphetamine-type stimulants (0.5%) and cocaine (0.4%)[1]. Although illicit drugs produced from natural sources (e.g. cocaine, heroin, marijuana etc.) consistently exhibit the highest population prevalence, synthetic substances have drawn the attention of both health and law enforcement authorities worldwide during the last decade.

The term New Psychoactive Substances (NPS) refers to substances (mostly synthetic drugs) which are not subject to international legislation, such as the Single Convention on Narcotic Drugs (1961) and the Convention on Psychotropic Substances (1971) but pose a public health risk comparable to those already under control[2]. As of August 2021, 1,049 NPS have been identified and reported to the UNODC by 133 countries[3]. Particularly, in the decade ranging from 2009 (131 reports) to 2019 (542 reports) an increase above 300% in the number of new substances has been observed.[4].

Starting in 2015, for the first time, the total number of reported NPS has stabilized and even decreased in a few years. However, there is a growing concern about its use among high-risk users, such as marginalized, vulnerable, or socially disadvantaged groups, including homeless people, prisoners, the unemployed and people with mental health disorders[5]. Although less extensive as in other regions, the available data on NPS for Latin America and the Caribbean show the predominance of stimulants and hallucinogens among substances reported for the first time[4].

New Psychoactive Substances (NPS)

Heterogeneous group of substances, often divided into groups according to their chemical structure, such as: synthetic cannabinoids, synthetic cathinones, tryptamines, piperazines and phenethylaminess. NPS are also referred to by the following names:

- *Designer drugs*
- *Research chemicals*
- *Legal highs*

Little is known about their health risks, body effects and social harm which poses a serious challenge to effective prevention programs and public safety.

Globally, for the first time, the annual number of **NPS** reported has stabilized and even decreased in some years; however, there is growing concern about their use among high-risk users.

Strategies for controlling NPS

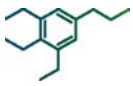
The NPS problem is directly related to international drug control and regulation. However, in addition to international efforts, individual country policies and legislation play a vital role in the matter.

In general, countries with a limited number of new psychoactive substances casework tend to control each substance individually through the inclusion of its name on a **nominal** list, often before it is controlled internationally. It is not uncommon that the inclusion of a substance on the nominal list goes through a lengthy legislative process, or it takes place by quick procedures or temporary controls.

First Report of the Early Warning Subsystem on Drugs (EWS)

On the other hand, countries facing relevant NPS occurrence tend to act beyond nominal control, applying, for example, generic or analog-based substance controls. **Generic controls** target the core molecular structure and allow for legislation to detail acceptable variations in structure, especially substituent groups at specific positions in the molecule.

In Brazil, to keep up with the increasing emergence of NPS, **nominal list** control had to be updated and complemented with the inclusion of structural chemical classes (**generic controls**).



In Brazil, the original nominal list had to be complemented with the inclusion of control by structural chemical classes (generic controls), to keep up with the increasing emergence of NPS.

As a supporting tool for government decision and policy making regarding the NPS issue, including which form of control is the most appropriate for each country, it is essential to have information on the presence of these drugs in each region. One of the main tools used internationally for this purpose is known as the Early Warning System (EWS).

The primary role of the Early Warning System is to exchange information about NPS and, through monitoring, to detect, assess and respond to social and public health threats. This includes threats that may not be caused directly by a new psychoactive substance, but due to other hazards associated with its use. Examples include harmful adulterants, diluents, impurities, and synthesis-related contaminants, among others. In addition to this function, the EWS can also be used to exchange information on new trends in the use of existing psychoactive substances or new combinations of psychoactive substances that pose a potential risk, as well as information on possible measures related to public health[2].

The different types of actions taken based on EWS information depend on the substance of interest, the type and level of threat, the individuals who are at risk, as well as the role of the organization and the responding people. Actions can be taken at the level of public security (such as police investigations), public policy (such as investments in public health and safety) and research (such as data collection on NPS use in Brazil).

Therefore, the overall objective of an EWS is to maintain a surveillance system using information from sources such as epidemiological, public health and safety data, as well as information on NPS and other emerging drug phenomena, in order to support the development of fast interventions by public authorities.

The EWS is a multidisciplinary, interagency network managed by key stakeholders that generate and exchange information for the purpose of identifying NPS, other emerging substances, and other drug-related events that pose a public health threat; assessing the risks related to its use; and sending quick alerts for working on responses. In addition, the EWS also contributes to improving communication and the flow of information between the institutions involved.

The overall purpose of an Early Warning System is to maintain a surveillance system using information from a variety of sources, such as data on NPS and other emerging drug phenomena, in order to support the development of fast interventions.

First Report of the Early Warning Subsystem on Drugs (EWS)

Even before the implementation of an EWS, Brazil had already implemented actions aimed at identifying NPS in its territory.

The Ministry of Justice and Public Security (MJSP) through its National Secretariat for Drug Policy and Asset Management (SENAD), together with the National Secretariat for Public Security (SENASP), the Secretary for Management and Education in Public Security (SEGEN) and the Federal Police (FP) have created a project for training criminal experts in the identification of NPS, called the "Minerva Project".

Brazilian Early Warning Subsystem on Drugs

The creation of an EWS is essential to quickly and correctly face the threats posed by NPS and other emerging drug phenomena. Many governments have already established national systems and some already integrate wider regional mechanisms, as in the case of the European Union's EWS, the Americas Region's EWS (*Sistema de Alerta Temprana de las Américas* – SATA), and the UNODC's EWS at the global level[6].

In Brazil, the National Drug Policy, approved by Decree No. 9,761 of 2019, within the scope of the National Drug Policy System (SISNAD), provided for the structuring of an early warning system on new drugs, in addition to stimulating the production of knowledge by universities and research institutions on NPS regarding their composition, potential action and toxicity, among other related issues.

In 2021, the SISNAD's Early Warning Subsystem on Drugs has been established by Resolution No. 6 of August 30. Initially, it was created on an experimental basis, but further it will be associated with the Unified Public Security System (SUSP) and the Unified Health System (SUS). The Brazilian EWS intends to become a strategic tool for the country, anticipating adverse events arising from the entry of NPS in Brazil.

Minerva Project

Created in 2019, the project aims to reinforce and update the technical background of forensic chemistry and toxicology experts in order to provide rapid detection of new substances and reduce the supply of illicit drugs. Among the project's goals are training strategies to state and district experts in NPS identification, forensic toxicology, and preventive maintenance of equipment. Courses are taught by federal criminal experts and other specialists, which include both theoretical and practical laboratory classes. In addition to expert training, the project supports the elaboration of technical recommendations, the acquisition of analytical standards and the evaluation of proficiency tests.

Minerva Project strengthens the National Drug Policy System (SISNAD) and the Brazilian Early Warning Subsystem, disseminating knowledge, techniques, and technologies for the identification of new drugs in the country. In addition, the project may be included in the National Plan for Drug Policies (PLANAD), with qualification targets for most experts from all Brazilian states in the areas of Chemistry and Toxicology until 2026.

First Report of the Early Warning Subsystem on Drugs (EWS)

The structuring of the EWS enables the exchange of information between federative units, generating a risk assessment and developing legal control through cooperation at both national and international levels.

The EWS, whose coordination will be the responsibility of SENAD, is formed by different state and federal agencies in the scope of public safety, health, and research (Figure 1). It is also composed of a Technical Committee with the objective of defining the criteria for entering information in the Subsystem database, being composed of members of the following bodies:

- National Secretariat for Drug Policy and Asset Management (SENAD);
- National Secretariat for Drug Care and Prevention (SENAPRED);
- National Secretariat for Public Security (SENASP);
- Federal Police (FP);
- Federal Revenue (RFB);
- National Health Surveillance Agency (ANVISA);
- Ministry of Health.

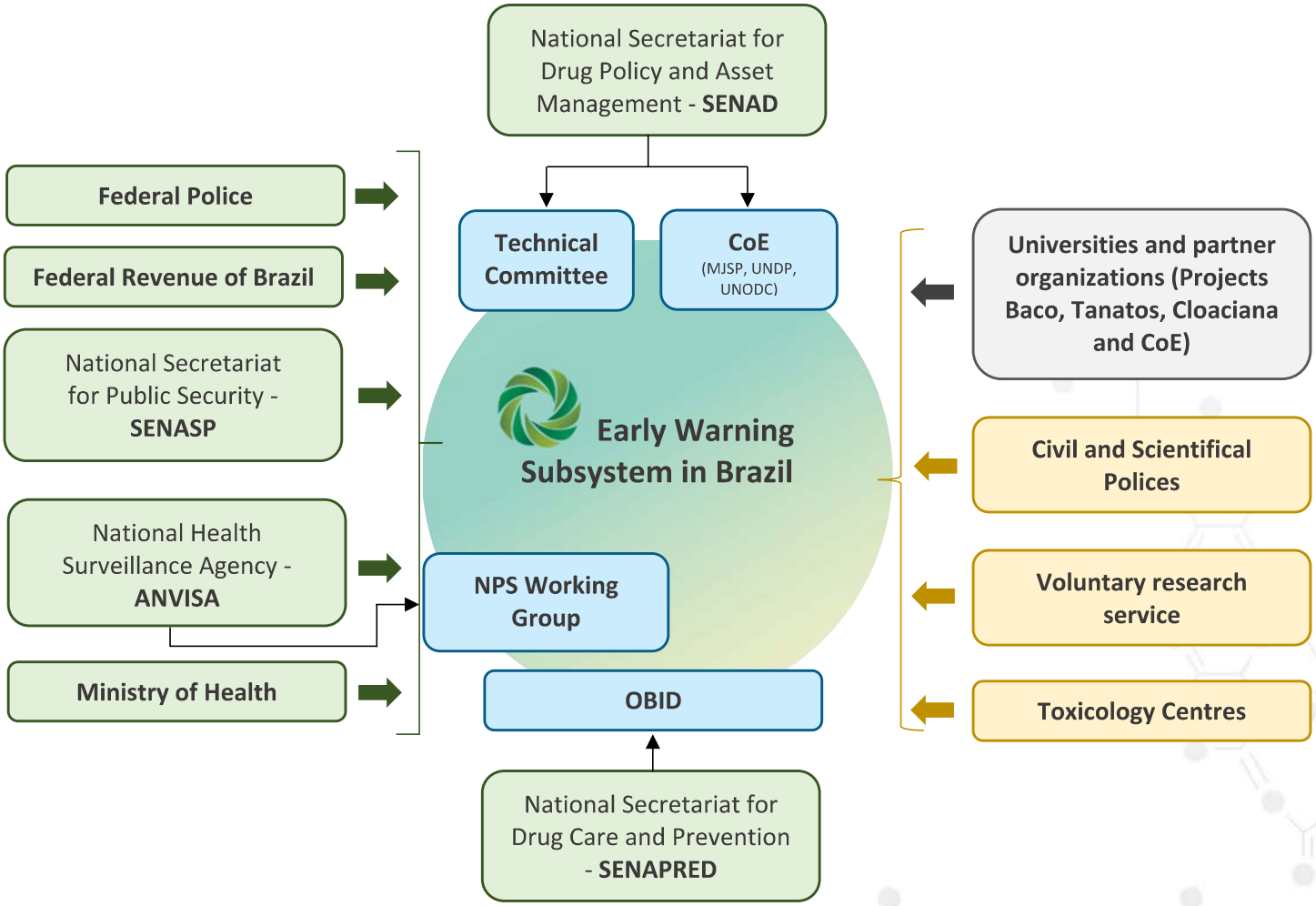


Figure 1. Organizational Chart of the Early Warning Subsystem on Drugs in Brazil

First Report of the Early Warning Subsystem on Drugs (EWS)

Classification of New Psychoactive Substances

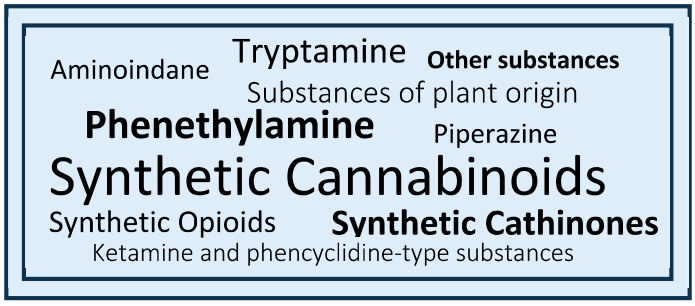
NPS may be grouped in different categories according to specific purposes. Therefore, each area of activity (medical, legal, laboratory, among others) can choose a type of classification depending on its purpose.

Among the types of drug classifications focused on NPS, are those based on its effects (such as hallucinogens, stimulants or depressants), origin (natural, synthetic or semi-synthetic), and chemical structure groups.

There are several proposals for grouping the chemical structures of NPS found in the scientific literature, health reports and several international institutions related to drug control and monitoring[2, 7, 8]. In Brazil, the classification of NPS adopted in the "Synthetic Drugs Report" produced by the Federal Police is based on 10 groups.

In Brazil, the classification of NPS adopted by the Federal Police is based on groups of chemical structures, presenting 10 groups of substances.

Among the NPS groups, synthetic cannabinoids, phenethylamines and synthetic cathinones deserve special attention.



Synthetic cannabinoids

Synthetic cannabinoids, also known as synthetic cannabinoid receptor agonists, are a group of substances that mimic the effects of Δ9-tetrahydrocannabinol (THC), the active ingredient in marijuana, by binding themselves to cannabinoid receptors located in the central nervous system (CNS) and in other body organs. They were originally developed for the study of the endocannabinoid system and to aid in the process of understanding diseases and developing of medicine. In the early 2000s, in Europe, synthetic cannabinoids began to be marketed as "legal" substitutes for cannabis (legal highs), being called *spice*[9].

As these substances activate the same receptors as THC, the effects resulting from its use include relaxation, euphoria, lethargy, distorted temporal perception, decreased motor coordination, hallucinations, paranoia, dry mouth, red eyes, tachycardia, nausea, and vomiting. Despite their similarities, synthetic cannabinoids can cause deeper intoxications when compared to THC. Poisonings and deaths resulting from the use of these substances are commonly informed[10, 11].

Little is known about the toxic effects of these substances on the body, but episodes of cardiovascular toxicity, loss of consciousness and coma, respiratory depression, convulsions, hyperemesis, delirium, psychosis, and aggressive behavior have already been reported. On the one hand, these effects may be related to unintentional high doses to which users are exposed. On the other hand, studies have already shown that synthetic cannabinoids are much more potent than THC, acting as a full agonist of cannabinoid receptors, whereas THC is a partial agonist. This means that, even at low doses, synthetic cannabinoids can activate cannabinoid receptors with greater potency than THC.

First Report of the Early Warning Subsystem on Drugs (EWS)

Phenethylamines

Phenethylamines are a group of synthetic substances with psychoactive and stimulant actions, which include both amphetamines and substances with chemical modifications in the chemical structure ring. Some examples of these substances are the "2C series", "D series", benzodifurans, p-methoxymethamphetamine (PMMA), NBOMes (N-benzylphenethylamines), among others[11].

Most phenethylamines act as CNS stimulants or hallucinogens. Stimulants act through dopamine, norepinephrine and/or serotonin, mimicking the effects of "classic" drugs such as cocaine, amphetamine, methamphetamine, and ecstasy. Classic hallucinogens mediate specific actions of serotonin receptors, producing hallucinations. Substances from this group mimic the effects of LSD (lysergic acid diethylamide) and may also have a residual stimulant effect[11].

Although the origin of the induced toxicity of NBOMes is not yet fully understood, there are several cases in which the recreational use of NBOMes caused severe toxic effects. These compounds vary in their potency, pharmacological effects, and toxicity, such that dosage overshoots may have fatal consequences for the users. As an example, fatalities associated with the use of these substances have already been reported in Brazil and Colombia[12].

Symptoms of acute NBOMes poisoning include tachycardia, hypertension, agitation/aggressiveness, hyperthermia, and seizures. In addition, their use can cause acute liver damage. These symptoms indicate that NBOMes are associated with both serotonin syndrome and sympathomimetic toxicity similar to what occurs with amphetamine and mephedrone ingestion[13].

Synthetic cathinones

Synthetic cathinones are a group of NPS belonging to the phenethylamines group, having chemical similarity to amphetamines. Synthetic cathinones derive from cathinone, an active ingredient found in the leaves of the *Catha eduli* plant (known as khat)[11].

As a cultural habit, indigenous people from the Middle East chew this plant's leaves for stimulant effects. The laboratory synthesis of cathinone began in the 1920s, the main substance of this group being mephedrone, synthesized in 1929[14].

The first synthetic cathinone police seizures took place in the mid-2000s in Europe. Methylone (a substance analogous to MDMA) was the first synthetic cathinone reported to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in 2005. Synthetic cathinones are known as *bath salts* in the illicit market and can be found in the form of powder, pills, or tablets, often sold as ecstasy[11].

These substances have stimulant effects on the CNS, mediated by the action of dopamine, norepinephrine, and serotonin, mimicking the effects of more "traditional" stimulant drugs. Some users have reported that they look for the following effects when using synthetic cathinones: increased disposition, empathy, and libido. However, adverse effects may occur such as palpitation, abdominal pain, nausea, vomiting, erectile dysfunction, muscle tension, aggression, headache, blurred vision, hallucination, and paranoia[15].

Sistema Nacional de Políticas Públicas sobre Drogas | MINISTÉRIO DA CIDADANIA | MINISTÉRIO DA ECONOMIA | MINISTÉRIO DA SAÚDE | MINISTÉRIO DA JUSTIÇA E SEGURANÇA PÚBLICA | PÁTRIA AMADA BRASIL GOVERNO FEDERAL

CdE | UNODC Escritório das Nações Unidas sobre Drogas e Crime | PNUD

First Report of the Early Warning Subsystem on Drugs (EWS)

Report classifications

This document will follow the classifications adopted by the Federal Police and by the Narcotics Testing Centre (NEE) of the Institute of Criminalistics from the Superintendence of the Technical and Scientific Police of the State of São Paulo.

As a result of the increasing number of synthetic drug seizures, the Brazilian Federal Police has expanded its monitoring system, which was previously focused only on NPS, to also include synthetic drugs in general, especially those commonly used in the context of parties.

For this reason, the category "classical drugs" was created, referring to synthetic substances controlled by the 1961 and 1971 Conventions up to 2014. Some examples of compounds that fall into this group are methamphetamine, 3,4-methylenedioxymethamphetamine – MDMA, lysergic acid diethylamide – LSD, among others.

Data from the NEE, in addition to information on NPS, also provide information on the group "amphetamine-type stimulants". In this group, information on amphetamine and its derivatives (methamphetamine, MDMA, 3,4-methylenedioxyamphetamine – MDA, 3,4-methylenedioxyethylamphetamine – MDEA, fenproporex, methylphenidate, ephedrine) was gathered. In the FP report, some of these substances fall into the "classic drugs" category and others fall into the "medications" category.

This report was prepared with the contribution of the **Federal Police** (FP), through the Synthetic Drugs Report, and the **Narcotics Testing Centre** (NEE) of the Institute of Criminalistics from the Superintendence of the Technical and Scientific Police of the State of São Paulo, in collaboration with the **Centre of Excellence for Illicit Drug Supply Reduction** (CoE).

First Report of the Early Warning Subsystem on Drugs (EWS)

Substances detected in the Brazilian territory - Federal Police

Due to its seizures in all Brazilian States, its well-equipped laboratories and highly trained forensic chemistry experts, the Federal Police (FP) play an important role in the systematic collection and data analysis on illicit psychoactive substances.

To build knowledge in the field, the FP has periodically gathered information on synthetic drugs examined by its forensic laboratories. The data presented in this report were taken from the 2020 Report: Synthetic Drugs[16], produced by the Forensic Laboratory Service (SEPLAB/DPER/INC/DITEC/FP) and prepared based on information contained in the reports issued by the Federal Police in 2020.

The procedures and methods used by the FP forensic laboratories have been standardized since 2006, based on international recommendations from the UNODC and the Standard Working Group for Drugs (SWGDRUG). In addition, SEPLAB is the only forensic chemistry laboratory in the country with accreditation in the ABNT NBR ISO/IEC 17025:2005 standard.

According to data provided by the FP, in the year 2020, 594 synthetic drug forensic reports were produced, equivalent to 677 entries, according to the adopted definition. When compared to the previous year, there was a reduction in the number of cases involving synthetic drugs, probably due to the COVID-19 pandemic (Figure 2). In Brazil, the use of synthetic drugs is more common in the context of parties, which were drastically reduced with the social distancing measures implemented.

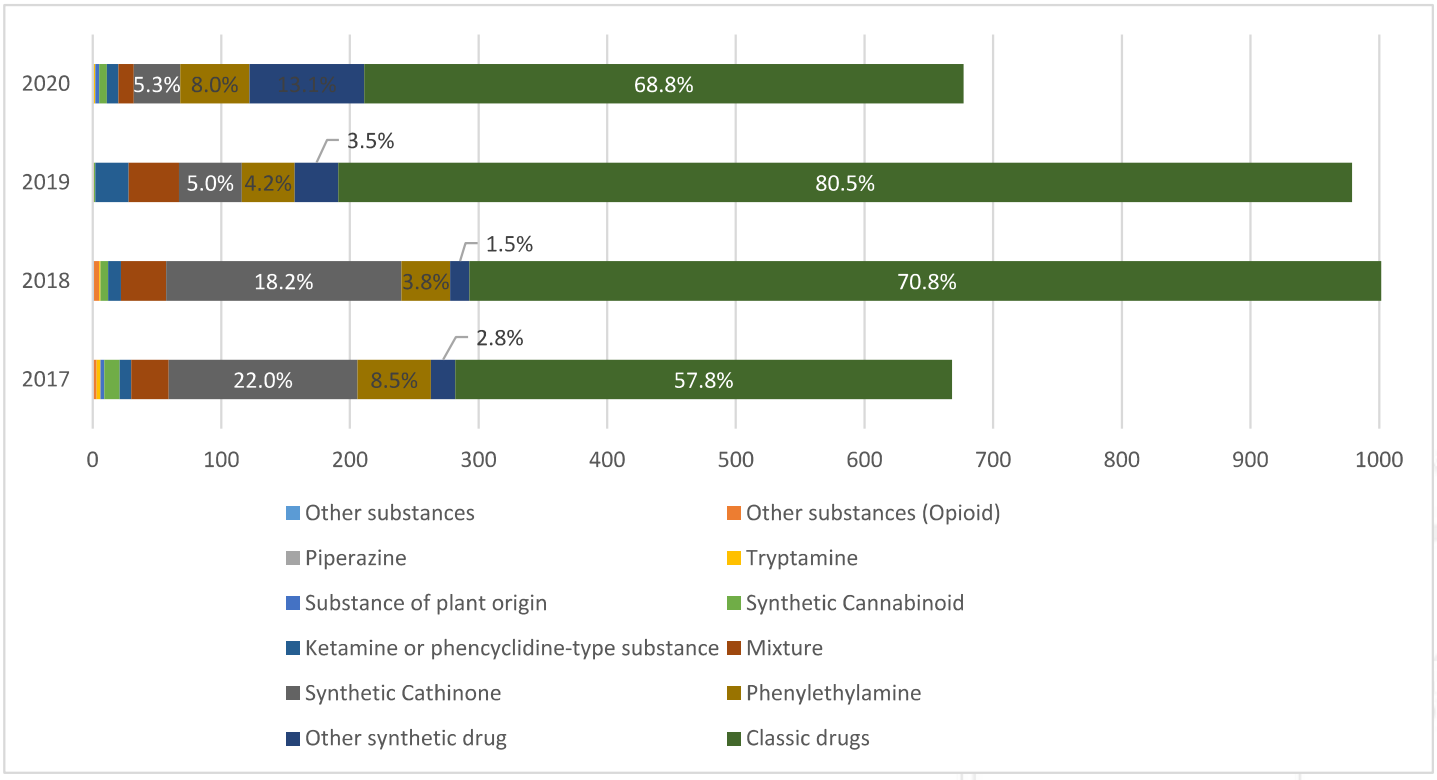


Figure 2. Number of reports on synthetic drugs produced per year by the Federal Police

First Report of the Early Warning Subsystem on Drugs (EWS)

Regarding NPS, 33 substances have been identified (in the previous year there were 28), with 10 of them identified for the first time. These data are presented in Table 1.

Table 1. New Psychoactive Substances identified by the Federal Police in 2019 and 2020. In red, those identified for the 1st time each year.

2019	2020
3-Fluorophenmetrazine	2-fluoro-dechlorocetamide
5F-MDMB-PINACA	MD-PV8
N-butylpentylone	3-CDC
25B-NBOH	4F-MDMB-BINACA
25C-NBOH	5-MeO-DMT
25C-NBOMe	Bufotenin
25E-NBOH	6-Br-DMPEA
25I-NBOH	N,N-Diethylpentylone
25I-NBOMe	N-butilhexedrone
2C-E	N-Ethylheptedrone
2C-I	25B-NBOH
4-CDC	25B-NBOMe
4-CEC	25C-NBOH
4-chloro-PVP	25E-NBOH
4-CMC	25I-NBOH
5-APDB	25I-NBOMe
ADB-FUBINACA	2C-C
MMMP (Caccure 907)	2C-E
Ketamine	4-CDC
Dibutylone	5F-MDMB-PICA
DOC	5-MeO-DMT
Eutylone	BMDP
Furanylfentanyl	Ketamine
MDPV	DOET
3-MeO-PCP	DOI
N-ethylhexedrone	Ethylone
N-ethylpentylone	Eutylone
U-47700	N-butylpentylone
	Kratom
	MMMP (Caccure 907)
	tBuONE
	N-ethylpentylone
	TFMPP

Traditional synthetic drugs

As already classified in previous reports by the FP, the terms “classic” or “traditional” synthetic drugs refer to those drugs that are internationally controlled until 2014.

Among seized “traditional” synthetic drugs, MDMA, MDA and LSD stand out, occupying, for the second year in a row, the first three places among the most reported ones in forensic reports in this category. These three drugs are used primarily in the context of parties. Figure 3 shows the synthetic substances most identified by the Federal Police in 2020 and a comparison of the number of reports produced in the last 4 years.

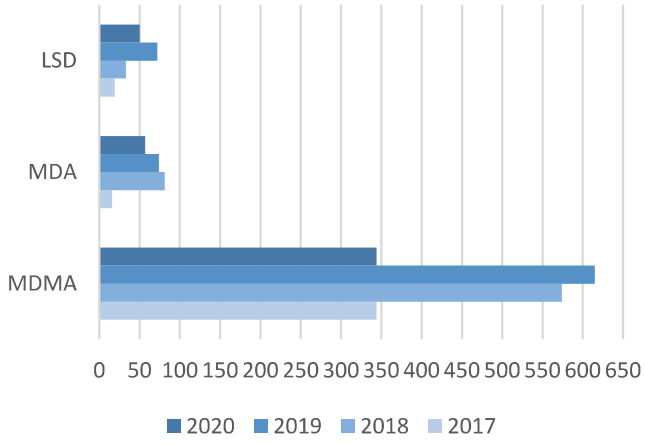


Figure 3. Number of reports produced per year by the Federal Police on the most detected synthetic drugs in 2020

With respect to MDMA, a substance found in “ecstasy-type pills” or in the form of crystals, it is worth mentioning that there was a large reduction in the number of forensic reports and in the amount of seized material[17]. Possible factors causing this reduction may be related to pandemic limitations on social events and restricting travelling conditions from Europe (an important worldwide MDMA producing region) to Brazil.

First Report of the Early Warning Subsystem on Drugs (EWS)

In the case of MDA, another substance commonly found in "ecstasy-type pills", although the number of reports in which the substance was identified also decreased, it has been observed that the reduction occurred to a lesser extent than in the case of MDMA (-23% for MDA and -44% for MDMA). In recent years, the production of MDA in Brazil from helional, a precursor rarely used internationally for this type of synthesis, has been reported[18, 19]. This may mean that the difficulties faced in the trafficking of drugs used in parties that came from Europe at the beginning of the pandemic, were surpassed by the consolidation of a national production of MDA.

Phenethylamines

Phenethylamines are seized primarily in the form of "LSD-type blotter paper" by the FP. The most detected substances in blotter papers are NBOMe type (25B-, 25C- and 25I-NBOMe) and NBOH type (25B-, 25C-, 25E- and 25I - NBOH). Over a 5-year FP monitoring period, Figure 4 demonstrates the replacement of NBOMes by NBOHs. It should be noted that the substances 25B-, 25C- and 25I-NBOMe begun to be internationally controlled by 2015, and the gradual decrease in their presence in the Brazilian drug market could be explained by this. NBOH-type substances, on the other hand, are not internationally controlled and have been banned in Brazil since 2016 (25I-NBOH as of 2016; 25B-, 25C-, 25E- and 25H-NBOH as of 2018).

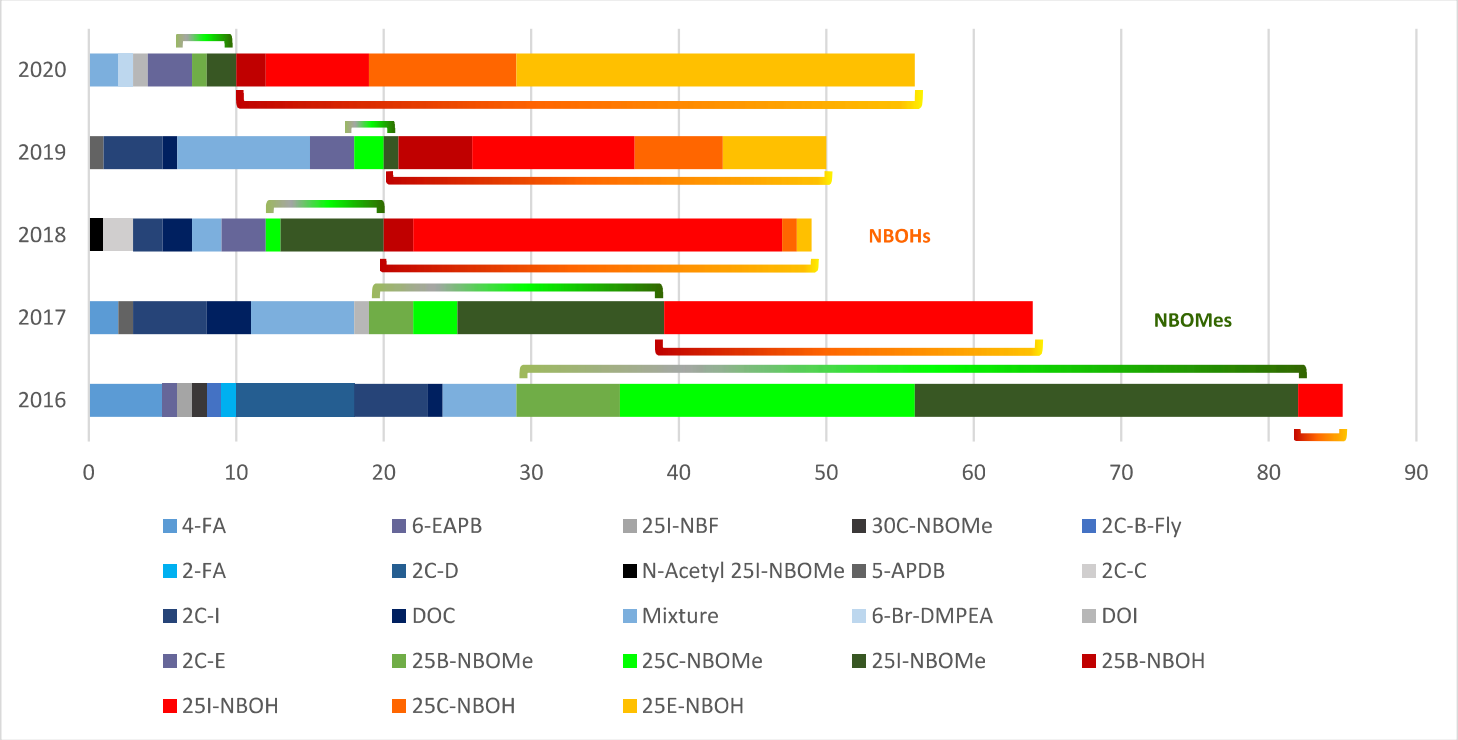


Figure 4. Number of reports on phenethylamines produced per year by the Federal Police

First Report of the Early Warning Subsystem on Drugs (EWS)

In 2020, a phenethylamine never analyzed by the FP was identified: 6-Br-DMPEA.

Synthetic cathinones

Synthetic cathinones are often found in "ecstasy-type pills" or as crystals, simulating the presentation of the substance MDMA. Since 2019, a sharp drop has been observed in both the number of reports and seizures of synthetic cathinones, as can be seen in Figure 5.

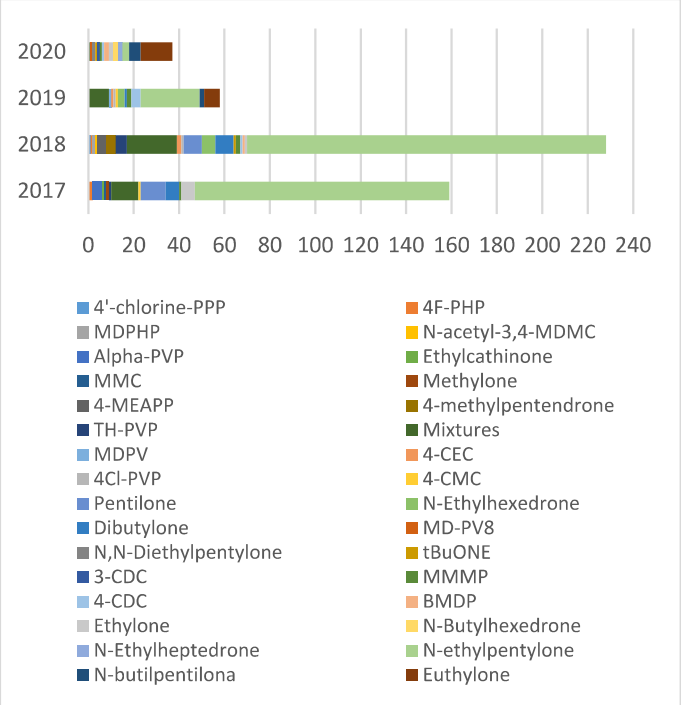


Figure 5. Reports on synthetic cathinones produced per year by the Federal Police

In 2020, the category presented six substances never analyzed by the FP: 3-CDC; MD-PV8; N,N-Diethylpentylone; tBuONE; N-Butylhexedrone and N-Ethylheptedrone.

Synthetic cannabinoids

Since 2014, the Federal Police has been warning mainly ANVISA about the presence of synthetic cannabinoids in the country.

Until 2016, synthetic cannabinoids seized by the Federal Police were usually found impregnated in dry herbs, to be smoked. From that year on, they began to appear impregnated in papers.

It is worth emphasizing the warnings made in the Reports for the years 2017 and 2018[20, 21], in which synthetic cannabinoids continued to appear on LSD-type blotter papers.

In prisons, this new form of presentation was named "K4" (Figure 6). There are other remarks in the literature of synthetic cannabinoids impregnated in papers found in prisons in Europe and in the United States[22, 23, 24, 25].

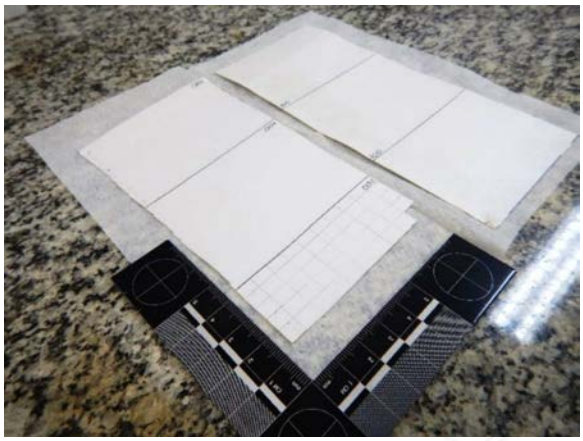


Figure 6. Papers containing 4F-MDMB-BINACA seized in a prison in Mato Grosso do Sul. Source: Federal Police.

In Brazilian prisons, there are data on an increase in the identification of synthetic cannabinoids in papers, especially those found in penitentiaries[26]. The various health restrictions in prisons that occurred during the COVID-19 pandemic may have stimulated the sending of synthetic cannabinoids impregnated in papers via postal packages.

Only two synthetic cannabinoids were identified by the FP in 2020: 4F-MDMB-BINACA and 5F-MDMB-PICA.

First Report of the Early Warning Subsystem on Drugs (EWS)

Synthetic substances detected in the Brazilian territory - State of São Paulo

The Narcotics Testing Centre (NEE) of the Institute of Criminalistics from the Superintendence of the Technical and Scientific Police of the State of São Paulo is responsible for carrying out identification, verification and proof tests for toxic substances and other drugs classified as causing physical or psychological dependence[27]. The NEE meets both demands arising from the capital of São Paulo and offers support to some cases from the Centres in the interior of the State. Since October 2020, NEE has started to provide analytical standards for certain substances for the Centres in the interior of the state, making them autonomous for analysis involving these substances.

All analysis carried out at the NEE follow the international recommendations of the SWGDRUG for the identification of seized materials. Drugs seized are analyzed by gas chromatography coupled to mass spectrometry (GC-MS), and for those substances that require structural elucidation, the analysis is performed by Fourier-transform infrared spectroscopy (FTIR)[28].

According to data provided by NEE, analysis requests for seized synthetic materials increased from 783 in the second half of 2020 to 1,274 during the first half of 2021. In addition to the increase in the number of occurrences, there was also an increase in the diversity of substances detected: from 22 in the second half of 2020 to 29 in the first half of 2021. Of the 1,274 analysis involving synthetic substances, 42% corresponded to synthetic cannabinoids, the most prevalent group of NPS in the State of São Paulo (Figure 7). Furthermore, the identification of the substance ADB-BUTINACA has increased by more than 50 times from 2020 to 2021.

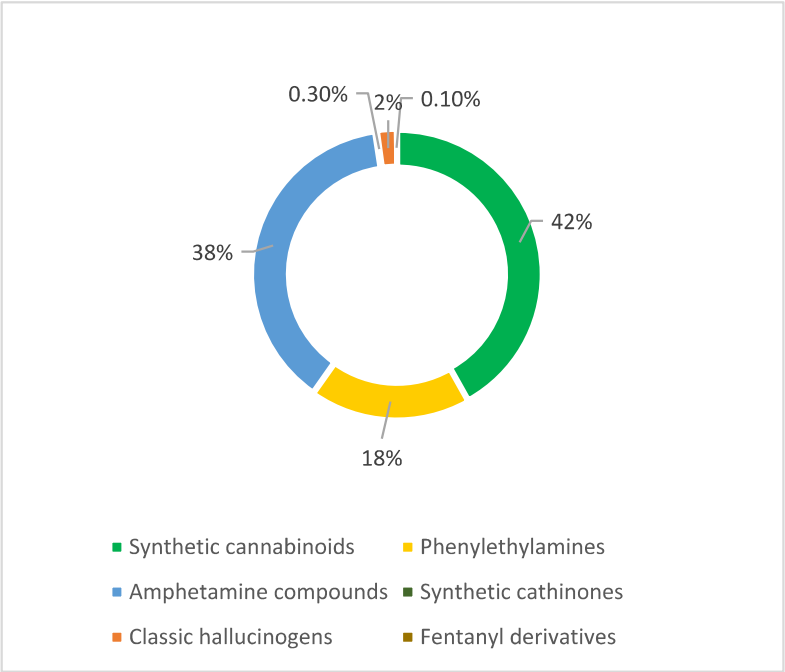


Figure 7. Proportion of detected synthetic substances groups by the Narcotics Testing Centre of the Technical and Scientific Police of the State of Sao Paulo from January to June 2021 (n = 1,274).

On the other hand, in the city of São Paulo, the number of analyses more than doubled between the second half of 2020 and the first six months of 2021. During this entire period (from August 2020 to June 2021), 818 analysis were performed, with amphetamine-type stimulants being the main group of synthetic substances detected followed by synthetic cannabinoids (Figure 8).

Both the **quantity** and **diversity** of synthetic drugs have increased between 2020 and 2021 in the State of São Paulo

First Report of the Early Warning Subsystem on Drugs (EWS)

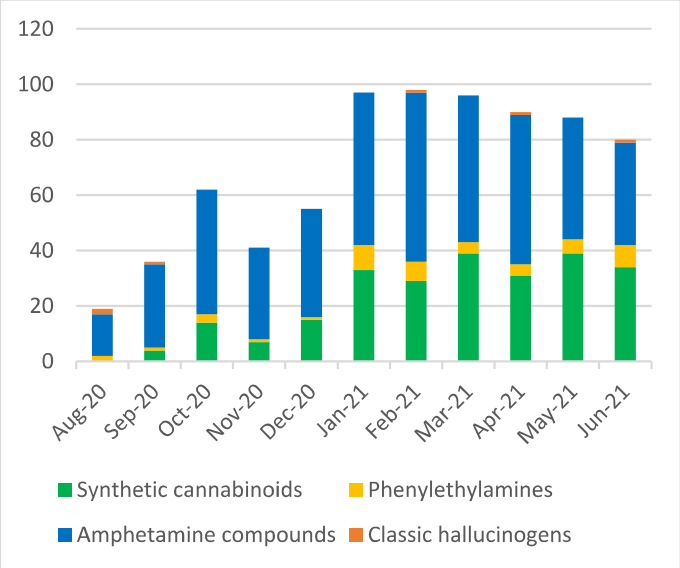


Figure 8. Number of analyzes (n = 818) by group of synthetic substances seized in the city of São Paulo between August 2020 and June 2021.

Synthetic cannabinoids

Synthetic cannabinoids come mainly in four forms: tobacco mixes (mixes of herbs that receive the popular names of spice, K2, K4, among others), liquids for electronic cigarettes, blotter papers or infused in paper.

This last form has been frequently detected in Brazil. A recent study pointed out the presence of seven different synthetic cannabinoids, in combination or not, infused in papers seized in prisons in the State of São Paulo between 2016 and 2020[26].

In the state of São Paulo, between 2020 and 2021, the following synthetic cannabinoids have been identified:

- 4-Fluoro-MDMB-BICA
- 4-Fluoro-MDMB-BINACA
- 5F-EDMB-PICA
- 5F-MDMB-PICA
- 5F-EMB-PICA
- ADB-BUTINACA*
- ADB-FUBINACA
- MDMB-4en-PINACA*

* most prevalent substances

Nomenclature of synthetic cannabinoids

The nomenclature of most synthetic cannabinoids is associated with their discovery. In some cases, the names are derived from the initials of the scientists who synthesized them, for instance, JWH compounds from John W. Huffman. In other cases, the names come from the institution or company that synthesized them, as is the case of the "CP" named by Carls Pfizer.

Currently, synthetic cannabinoids are named by codes derived from the designation of their chemical structures, such as APICA [N-(1-adamantyl)-1-pentyl-1H-indazole-3-carboxamide].

The structure of synthetic cannabinoids can be categorized into four components: tail, core, linker and linked group. By associating a code for each component, it is possible for the cannabinoid to be identified without using the nomenclature of the chemical structure, using the following syntax structure:

Linked group – TailCoreLinker

In cases where a tail substituent is present (e.g., 5F), it is placed at the beginning of the name; linked group substituent is added prior to its nomenclature, and core substituent is added to the end of the cannabinoid name.

Source: https://www.emcdda.europa.eu/topics/pods/synthetic-cannabinoids

Phenethylamines

In Brazil, the main classes of phenethylamines found are NBOMes (N-benzylphenethylamines) and NOBHs. In the case of NBOMes, the codes that precede the nomenclature "NBOMe" refer to the position and identity of the substituents in the substance molecule (e.g., 25B-NBOMe: existence of a methoxy group in positions 2- and 5- and a bromine group in position 4-). The NB code refers to N-benzyl and OMe refers to the methoxy substituent in the ortho position of the benzyl structure[29].

NBOHs, on the other hand, are N-benzylhydroxyl compounds derived from hallucinogens of the 2C family. NBOHs have been developed as a "legal" alternative after the detection and prohibition of NBOMEs. Its physiological and toxicological properties are not yet fully described. NBOHs are potent serotonin receptor agonists, being responsible for important behavioral changes. NBOHs, as they are derived from the "2C" series of compounds, have a very similar chemical structure, making their correct identification difficult[30].

In the state of São Paulo, the following compounds have been identified between 2020 and 2021, mainly in the form of papers and blotter papers (Table 2):

Table 2. Substances from the group of phenethylamines seized in the State of São Paulo between August 2020 and June 2021 and the number of identifications made for each compound

Compound	Number of identifications
25B-NBOH	73
25B-NBOMe	5
25C-NBOH	17
25C-NBOMe	11
25E-NBOH	65
25E-NBOMe	1
25H-NBOH	9
25H-NBOMe	1
25I-NBOH	18
25I-NBOMe	1
2C-B	16
2C-C	4
2C-E	10

Amphetamine-type stimulants

Despite being considered "classic drugs", they are synthetic compounds belonging to the phenethylamine class. It is a group composed of amphetamine and its derivatives (methamphetamine, 3,4-methylenedioxymethamphetamine – MDMA, 3,4-methylenedioxyamphetamine – MDA, 3,4-methylenedioxyethylamphetamine – MDEA, fenproporex, methylphenidate, ephedrine). They are CNS stimulants, acting as sympathomimetic amines that interact by competitive antagonism with pre-synaptic α and β-adrenergic receptors, causing the release of dopamine, epinephrine, and norepinephrine. The stimulant effects of amphetamines result from the structural similarity with dopamine and norepinephrine, thus functioning as a false neurotransmitter, mimicking its effects on the sympathetic nervous system[31]. In addition, amphetamines are inhibitors of monoamine oxidase (MAO), an enzyme responsible for oxidation of norepinephrine, serotonin, and dopamine.

In Brazil, the use of amphetamine-type stimulants occurred mainly through ecstasy pills and as appetite suppressant drugs, whose active ingredient is bio-transformed into amphetamine in the body. Truck drivers used these medications to inhibit fatigue and sleepiness during long-distance freight. Furthermore, over a period of 8 years, a change in the pattern of use of stimulant substances by truck drivers in the State of São Paulo was detected[32]. Amphetamine used to be the most used

stimulant by this group; however, as of 2011, cocaine use has become more prevalent. Currently, the production and sale of drugs containing sibutramine, amfepramone, fenproporex and mazindol is prohibited according to recent understanding of the Supreme Federal Court (STF).

Data from NEE show an increase in the seizure of materials containing amphetamine compounds. In 2020, from August to December, these substances were identified in 291 occasions. In 2021, from January to June, 485 detections were recorded, being seized mainly in the form of pills, crystal, paper, and rock.

Synthetic cathinones

In the State of São Paulo, despite not being a group of NPS with high prevalence, the frequency of identifications has been increasing. In 2020, only one case was identified, resulting from the seizure of pills containing the substance N-ethylpentylone. As early as 2021, until June, synthetic cathinones were identified on four occasions. In addition, a new structure was also detected, N-butylpentylone.

Referências

[1] UNITED NATIONS OFFICE on DRUGS and CRIME – UNODC. **World Drug Report 2021**, Vienna, 2021.
[2] EUROPEAN MONITORING CENTRE FOR DRUGS AND DRUG ADDICTION – EMCDDA. **EMCDDA operating guidelines for the European Union Early Warning System on new psychoactive substances**. 2019. Retrieved from https://www.emcdda.europa.eu/publications/guidelines/operating-guidelines-for-the-european-union-early-warning-system-on-new-psychoactive-substances_en.
[3] UNITED NATIONS OFFICE on DRUGS and CRIME – UNODC. **Data from the UNODC Early Warning Advisory on New Psychoactive Substances**. 2021. Retrieved from https://www.unodc.org/unodc/en/scientists/ewa/data.html
[4] UNITED NATIONS OFFICE on DRUGS and CRIME – UNODC. **Global SMART Update**. Regional diversity and the impact of scheduling on NPS trends. V 25, 2021.
[5] EUROPEAN MONITORING CENTRE FOR DRUGS AND DRUG ADDICTION – EMCDDA. **High-risk drug use and new psychoactive substances**, EMCDDA Rapid Communication, Publications Office of the European Union, Luxembourg .2017. Retrieved from https://www.emcdda.europa.eu/system/files/publications/4540/TD0217575ENN.pdf
[6] UNITED NATIONS OFFICE on DRUGS and CRIME – UNODC. **The role of drug analysis laboratories in Early Warning Systems**. 2020, Retrieved from https://www.unodc.org/documents/scientific/Drug-Analysis-Systems_EWS_EN.pdf
[7] ZAPATA et al. Chemical classification of new psychoactive substances (NPS). **Microchemical Journal**, v. 163, Apr. 2021.
[8] DEA. **NFLIS - Drug 2019 Annual Report**. Drug Enforcement Administration - Diversion Control Division. 2020.
[9] EUROPEAN MONITORING CENTRE FOR DRUGS AND DRUG ADDICTION – EMCDDA. **Technical Report – Synthetic cannabinoids in Europe – a review**. Lisboa, 2021.
[10] ALON, M.H., SAINT-FLEUR, M. O. Synthetic cannabinoid induced acute respiratory depression: case series and literature review. **Respir Med Case Rep**. p. 137-141, Jul-2017.
[11] UNITED NATIONS OFFICE on DRUGS and CRIME – UNODC. **UNODC Early Warning Advisory on New Psychoactive Substances**. Retrieved from https://www.unodc.org/LSS/SubstanceGroup/GroupsDashboard?testType=NPS
[12] UNITED NATIONS OFFICE on DRUGS and CRIME – UNODC. **Synthetic Drugs and New Psychoactive Substances in Latin America and the Caribbean 2021**. Vienna, 2021.
[13] WOOD D. M. et al. Prevalence of Use and acute toxicity associated with the use of NBOMe drugs. **Clin. Toxicol**. p. 85-92, 2015.
[14] PIEPRZCA E. et al. Synthetic cathinones – from natural plant stimulant to drug of abuse. **Eur J Pharmacol**. 173012, 2020.
[15] PROSSER J. M. & NELSON L. S. The toxicology of bath salts: a review of synthetic canthinones. **J Med Toxicol**. p. 33-42, 202.
[16] MINISTÉRIO DA JUSTIÇA E SEGURANÇA PÚBLICA. POLÍCIA FEDERAL. **Relatório 2020: Drogas Sintéticas**. Brasília. 2021.
[17] EUROPEAN MONITORING CENTRE FOR DRUGS AND DRUG ADDICTION – EMCDDA. **European Drug Report 2019**: Trends

and Developments. 2019. Retrieved from https://www.emcdda.europa.eu/system/files/publications/11364/20191724_TDAT19001ENN_PDF.pdf

[18] INTERNATIONAL NARCOTICS CONTROL BOARD – INCB. **Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances**. 2020. Retrieved from https://www.incb.org/documents/PRECURSORS/TECHNICAL_REPORTS/2020/AR_with_Annexes/Precursors_with_annex_E_eBook_final_rev.pdf

[19] MINISTÉRIO DA JUSTIÇA E SEGURANÇA PÚBLICA. POLÍCIA FEDERAL. **Relatório 2019: Drogas Sintéticas**. Brasília, 2020.

[20] MINISTÉRIO DA JUSTIÇA E SEGURANÇA PÚBLICA. POLÍCIA FEDERAL. **Relatório 2017: Drogas Sintéticas**. Brasília, 2018.

[21] MINISTÉRIO DA JUSTIÇA E SEGURANÇA PÚBLICA. POLÍCIA FEDERAL. **Relatório 2018: Drogas Sintéticas**. Brasília, 2019.

[22] EUROPEAN MONITORING CENTRE FOR DRUGS AND DRUG ADDICTION - EMCDDA. **New psychoactive substances in prison**. Luxembourg. 2018.

[23] FORD, L. T.; BERG, J. D. Analytical evidence to show letters impregnated with novel psychoactive substances (NPS) are a means of getting drugs within the UK prison service. **Annals of Clinical Biochemistry**, 55, 2018.

[24] NORMAN, C. et al. Detection and quantitation of synthetic cannabinoid receptor agonists in infused papers from prisons in a constantly evolving illicit market. **Drug Testing and Analysis**. Drug Testing and Analysis, 12, 2020. 538-554.

[25] NORMAN, C, Halter, S, Haschimi, B, et al. A transnational perspective on the evolution of the synthetic cannabinoid receptor agonists market: Comparing prison and general populations. **Drug Test Anal**. 2021; 13: 841– 852. https://doi.org/10.1002/dta.3002

[26] RODRIGUES, T. B. et al. Synthetic cannabinoid receptor agonists profile in infused papers seized in Brazilian prisons. **Forensic Toxicology**. 2021.

[27] SÃO PAULO. **Decreto nº 48.009**, de 11 de agosto de 2003.

[28] SCIENTIFIC WORKING GROUP FOR THE ANALYSIS OF SEIZED DRUGS (SWGDRUG) **Recommendations**. Edition 8.0, 2019. Retrieved from https://www.swgdrug.org/Documents/SWGDRUG%20Recommendations%20Version%208_FINAL_ForPosting_092919.pdf

[29] POULIE, C. B. M. et al. DARK Classic in Chemical Neuroscience: NBOMes. **ACS Chem. Neurosci**. p. 3860-3869, 2020.

[30] ARANTES L. C. et al. 25I-NBOH: a new potent serotonina 5-HT2A receptor agonist identified in blotter paper seizures in Brazil. **Forensic Toxicol**. p. 408-414, 2017.

[31] LOGAN B. K. Methamphetamine – Effects on Human Performance and Behavior. **Forensic Sci Rev**. p. 133-151, 2002.

[32] LEYTON V. et al. Trends in the use of psychoactive substances by truck drivers in São Paulo State, Brazil: A time-series cross sectional roadside survey (2009-2016). **Traffic Inj Prev**. p. 122-127, 2019.