

New psychoactive substances

Ten-year overview of the situation in France

Magali
Martinez,
Thomas
Néfau,
Agnès
Cadet-Taïrou

In France, although some synthetic psychoactive substances have been circulating occasionally since the 1990s, signs of consumption of a wide variety of new synthetic compounds started to emerge at the end of the '00s. None of these substances were included on the list of narcotics issued by the international conventions, and were thus originally referred to as legal highs. After the first reports in France of "Spice"¹ and mephedrone², the term "new psychoactive substances (NPS)" [1] was used to describe a vast group of compounds imitating chemical structures and the effects of traditional illegal drugs such as cannabis, MDMA or cocaine. While this phenomenon was becoming increasingly apparent in mainland France, a rapidly growing number of these substances were identified in Europe³, representing a challenge for all public stakeholders (Figure 2).

The emergence of these new drugs, which received extensive media coverage from the outset, was favoured by a combination of several factors. In addition to the gap in the legislation on these substances, their novelty compared to traditional illegal drugs, perceived as "poor quality" by many users, prompted some users to try them. As regards dealers, the creativity of chemists led to a wide range of compounds being produced, while the Internet, via online retail sites (e-shops), opened up simple distribution channels. Lastly, the Internet also led to the revival on the market of a number of substances already manufactured by the pharmaceutical industry, but abandoned owing to their inefficacy or toxicity.

In this context, in order to improve knowledge of users and supply modes, and to identify the risks arising from these unknown substances more clearly, the OFDT developed specific Internet monitoring tools (monitoring of user forums, analysis of supply and substances, online survey) concerning NPS (I-TREND European project⁴).

Ten years after the emergence of NPS, the available data reveal lower detection rates for new substances [2], and their use is still somewhat limited in France. This has not prevented these substances from

The emergence of NPS represents a major development in the field of drugs, despite their limited use in France. Overview of the phenomenon.



gaining a foothold in certain user circles and occasionally being sought after by a wider audience.

Supply and dynamics of the phenomenon, substances used, user profiles, health consequences: this issue of Tendances covers the overall developments observed concerning these drugs, originally analysed by the OFDT in 2013 [1]. This is based on the knowledge developed by the OFDT via its TREND scheme, SINTES, the I-TREND project, and all information sources used by the French Monitoring Centre (see box on p. 2). For greater reading clarity, these are not reported in detail in the text.

■ Access to NPS

Growth in supply somewhat losing momentum

The NPS market has long been characterised by dynamic supply. Despite a few substances detected between 2000 and 2008, the 2008–2014 period showed the

1. 'Spice' is the commercial name for a herbal blend which may contain one or more synthetic cannabinoids.

2. This cathinone remained relatively under the radar in seizures up to 2010, the year in which it was allegedly implicated in deaths in the UK.

3. The European definition of new psychoactive substances is, however, broader and can include certain hallucinogenic plants for instance.

4. Internet Tools for Research in Europe on New Drugs <http://www.i-trend.eu/>, European project JUST/2012/DPIP/AG/3641, with funding support from the European Union "Drugs, prevention and information" programme (DPIP).

greatest increase in the annual identification rate⁵, with 56 reports maximum in France, in 2014. This exponential growth, both in France and Europe, led to fear of an uncontrollable increase in use.

As regards the class of substances⁶, up to 2011, most new identified cases in France concerned phenethylamines, particularly categories of hallucinogenic compounds: DOx, 2C-x and 25x-NBOMe. A larger number of synthetic cannabinoids (SC) and cathinones then began emerge, constantly increasing up to 2016. More unusual compounds also emerged. These originated from the arylcyclohexylamines class with dissociative⁷ or psychedelic⁸ effects, notably with methoxetamine (a ketamine derivative) and PCP analogues, or the arylalkylamines class with the x-APB. Synthetic opioids were the last to appear.

In 2018, approximately 650 substances in total were recorded in Europe, and slightly over 300 in France, spread between 11 chemical categories (Figure 1).

The number of cases detected has declined in recent years: 53 in 2015, 44 in 2016, and 15 in 2017 (Figure 2). Only 3 new compounds were identified in the first semester of 2018. This decline does not appear to be related to customs and law enforcement service activities, which have reported an increasing number of seizures each year: nearly 900 in 2015, over 2,000 in 2017. This decline can be explained by several hypotheses. Firstly, following the creation of a large number of substances, there are fewer possibilities for manufacturing new ones. Furthermore, the measures taken by authorities in producer countries, together with the international control of precursors⁹ may have hindered NPS production. Lastly, it is likely that manufacturers ultimately focus on the production of the substances most sought by users: in 2013, the e-shops monitored as part of the I-TREND project only sold approximately 30% of the compounds already identified in Europe [6].

5. Mainly based on customs activities.

6. The classes of NPS are shown on the OFDT website <https://www.ofdt.fr/produits-et-addictions/de-nouveaux-produits-de-synthese/> [in French] and in the Théma NBOMe publication <https://en.ofdt.fr/BDD/publications/docs/epfammx6.pdf> for hallucinogens in particular.

7. Feeling of dissociation between physical sensations and the mind.

8. Psychedelic molecules, a subcategory of hallucinogens, are characterised by hallucinations (visual, audible, etc.), by changes in the perception of self and of the world, or by introspective experiences.

9. A chemical precursor is a compound which takes part in a chemical reaction producing one or more compounds. Chemical precursors are essential to the production of synthetic drugs.

Measuring NPS supply and use

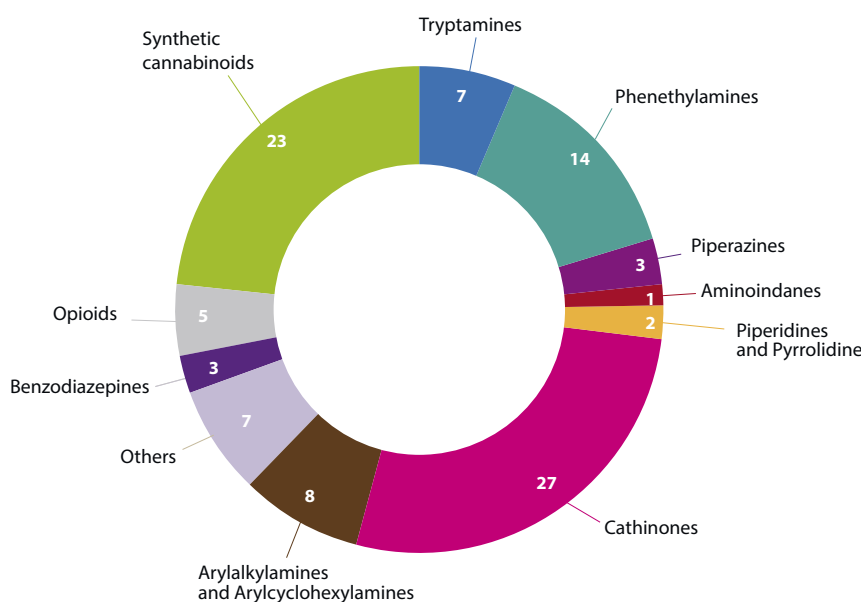
In view of its complexity, in order to monitor the NPS phenomenon, a combination of different sources is essential.

As regards NPS supply, I-TREND monitors e-shops; however, customs seizures are still the main source of information. If a compound is on sale on several websites or identified in a seizure, this does not necessarily mean that it is sought after and consumed. NPS are also difficult to detect, due to being shipped via postal freight. In France, substances seized and identified at Charles-de-Gaulle airport in Paris account for the majority of new reports, but are usually in transit to other destinations. Owing to its central position, this Paris airport is one of the largest postal hubs in Europe, with large quantities of letters and small parcels passing through in transit. Hence, annual variations in the identification rates mainly reported by customs and law enforcement services only partly reflect the prevalence of NPS use in France. According to customs and law enforcement service data, out of all NPS already identified in France, it was estimated that less than half are observed each year in seizures or SINTES collections, and only 10% are observed more than 5 times.

Estimation of the prevalence of use is equally complex. Relatively limited, this concerns substances which are available under a wide variety of names, with which users are often unfamiliar. Users do not always understand the generic terms (Research Chemicals or RC, NPS or synthetic cannabis), which limits the measurement of substance use in surveys, among the general population, and among drug users. Furthermore, reports of acute health problems (intoxication, at-risk behaviour) or chronic health problems (addiction, psychiatric consequences), recorded by the French addiction monitoring network, may be used as indirect indicators of NPS use [3]. However, owing to the very limited recourse to medical care among drug users [4], the diversity of NPS, obstacles to their identification in biological samples, and, lastly, the difficulties encountered by medical staff in reporting cases, it is likely that the numbers of fatal or nonfatal cases of intoxication are underestimated [5].

To supplement these sources of information on demand, on a national scale, the OFDT relies on its observation and qualitative monitoring network (TREND/SINTES) and the online forum monitoring software introduced as part of the I-TREND project. Lastly, exchanges with international institutions, such as the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in the context of the European Early-Warning System (EWS), and the United Nations Office on Drugs and Crime (UNODC) shed light on the French situation compared to other countries.

Figure 1. Number of NPS identified in France between 2008 and April 2017 according to chemical class (%)



Source: SCL, INPS, IRCqN, SINTES (OFDT)

Recent changes in the digital market

Since the beginning of NPS trade, the surface web¹⁰ has been the main supply channel.

Two types¹¹ of e-shops exist in parallel: colourful, attractive “commercial sites”, offering substances with invented names (Spice, Buddha Blue, etc.), and more austere “specialist sites”. These only display the name of the active substance (3-MMC, 5F-AKB-48, 25I-NBOME, etc.) and claim to commonly sell research substances, hence the name Research Chemicals (RC), a term preferred by users instead of NPS [1].

In France, in contrast to the findings in other countries¹², “commercial sites” tend to be more widespread (two-thirds of sites listed in 2014) compared to specialist sites [6]. The main shopfront for these commercial sites predominantly corresponds to the sale of natural products: seeds, hallucinogenic mushrooms and plants, and, more recently, substances containing cannabidiol (CBD)¹³. They also often sell paraphernalia for cannabis use.

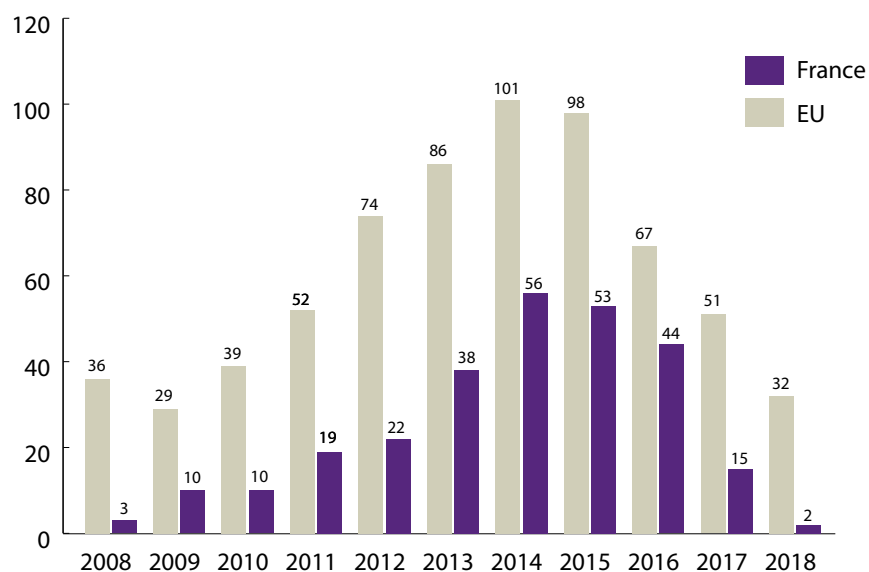
There have been several developments since 2013. Commercial e-shops now ship substances in neutral packaging, and no longer with recognisable graphics, which makes them harder for customs and law enforcement services to detect. Moreover, the possibilities of establishing a link between the chemical composition of a seized substance and the commercial name under which it was purchased are limited.

The other new development corresponds to payment methods. Since 2016, most sites now only offer two payment options, money transfer or cryptocurrency¹⁴ (i.e., bitcoin). Use of the latter aims to prevent transactions being traced.

Lastly, in 2016, the vote on the Psychoactive Substances Act in the United Kingdom, aiming to ban the production, sale, and delivery of NPS renewed digital supply, after resulting in the closure of several highly visible e-shops on the surface web.

On the darknet¹⁵, French-language distribution platforms could represent another pathway to NPS; however, these mainly offer conventional illegal drugs (cannabis, cocaine, MDMA, heroin, and amphetamines) [7]. Slower to emerge compared to their English-speaking counterparts, these platforms were first identified through user accounts in the context of the TREND scheme and monitoring of darknet forums in the summer of 2013. In 2017, 2 out of the 4 sites identified at the time were still active.

Figure 2. Number of NPS identified per year, in the EU and in France



Sources: EMCDDA and SINTES, OFDT schemes

Despite regular mentions in the media, the darknet, access to which requires a certain level of knowledge, particularly in terms of payment (cryptocurrency), is a space rarely frequented by drug users. The generation gap also seems to be a factor, with twice as many purchases being made by under 25s compared to older users [4]. These findings are also corroborated by direct observations alongside users.

Extremely limited supply on conventional markets

NPS are rarely found on conventional markets (sales on the streets, housing estates, festive scenes). They mainly circulate among users via their immediate social circles. As for drugs in general, most users do not purchase their own substances. The 2014 online survey showed that one in two users found themselves in this situation [4]. This usually involves gifts, sharing, joint purchases, or dealing within a network of friends or acquaintances. This social supply method concerns specific user groups and the most well-known NPS (see below). Internet purchases are made by the person most familiar with this process: this person purchases varying large quantities, so as to reduce costs, and then sells them on, with or without a profit margin.

No organised networks trading NPS online exist in mainland France, although a few TREND sites are reporting accounts of street deals (synthetic cannabinoids and cathinones) or deals in the festive scene (synthetic halluci-

nogens) by isolated drug dealers. For example, the limited uptake of synthetic cannabinoids in this territory is consistent with the geographical position of France relative to cannabis trafficking routes destined for Europe, in addition to growing domestic production. The presence of NPS is, in fact, influenced by pre-existing demand for the imitated drug (cannabis, MDMA), but also by the availability or quality of these substances [8; 9].

The other major aspect of NPS supply on conventional markets corresponds to drug rip-off, when NPS are sold instead of conventional drugs, unbeknown to the purchaser. This process currently appears to diminish, but has led to numerous cases of intoxication each time a new substance is brought to the conventional market. The majority of NPS require specific knowledge of potency, owing to the higher risks of toxicity compared to conventional drugs.

10. The surface web is the openly accessible internet indexed by standard search engines.

11. At the beginning of the '10s, substances could also be purchased via classified advertisements, now used to a much lesser extent than in the past.

12. Those taking part in the I-TREND project: the Netherlands, Poland, the Czech Republic and the United Kingdom.

13. A cannabinoid found in cannabis, mainly claimed to have analgesic, anxiolytic, sedative, anti-inflammatory, and antiemetic properties.

14. Cryptocurrency is a unit of value stored on electronic media, managed by the user community rather than by a financial institution. Records of exchanges, together with the identity of the creditor and debtor are encrypted, preventing users from being identified.

15. The darknet is the part of the deep web, the part of the Internet not indexed by search engines, dedicated to illegal activities.

■ Main groups of compounds used

NPS with established visibility in the territory, beyond being merely identified, can be divided into 5 main groups, representing the effects of the most widely known substances (cannabis, MDMA, LSD and ketamine, heroin, and amphetamines). In 2018, all those NPS were banned, at least in France, and some also in Europe or worldwide (see box on p. 6).

Synthetic cannabinoids: a variety of forms

Synthetic cannabinoids are sold in powder form, under their chemical names, or presented in more familiar forms (herbal or resin form). In this case, powdered synthetic cannabinoids are blended with a paste imitating resin, but with an unknown composition, or sprayed onto a herbal mixture. These forms of synthetic cannabinoids, mainly used by younger populations (2015 ESPAD data), tend to have invented brand names. They may also be sold as e-liquids (see box on p. 4), used with e-cigarettes.

In 2016 and 2017, the synthetic cannabinoids appearing in seizures and on forums were 5F-AKB-48, AB-FUBINACA, MDMB-CHMICA, and 5F-MDMB-PINACA, driven by interest in e-liquid forms. This form can be taken by vaping, which is considered more discreet, from both a visual and olfactory perspective, compared to conventional joints (see box hereafter).

Changes in preferences for synthetic cannabinoid use, based on forum monitoring

In 2017 (cut-off date: April 30), less than 12% of synthetic cannabinoids already identified in Europe were the subject of discussions on user forums. Qualitative monitoring of conversations since 2008 has made it possible to observe changes in interest in synthetic cannabinoids (Figure 3). The average number of daily views, calculated each month, shows how certain synthetic cannabinoids or certain topics (e-liquids) are enthusiastically received among Internet users or, on the contrary, abruptly rejected.

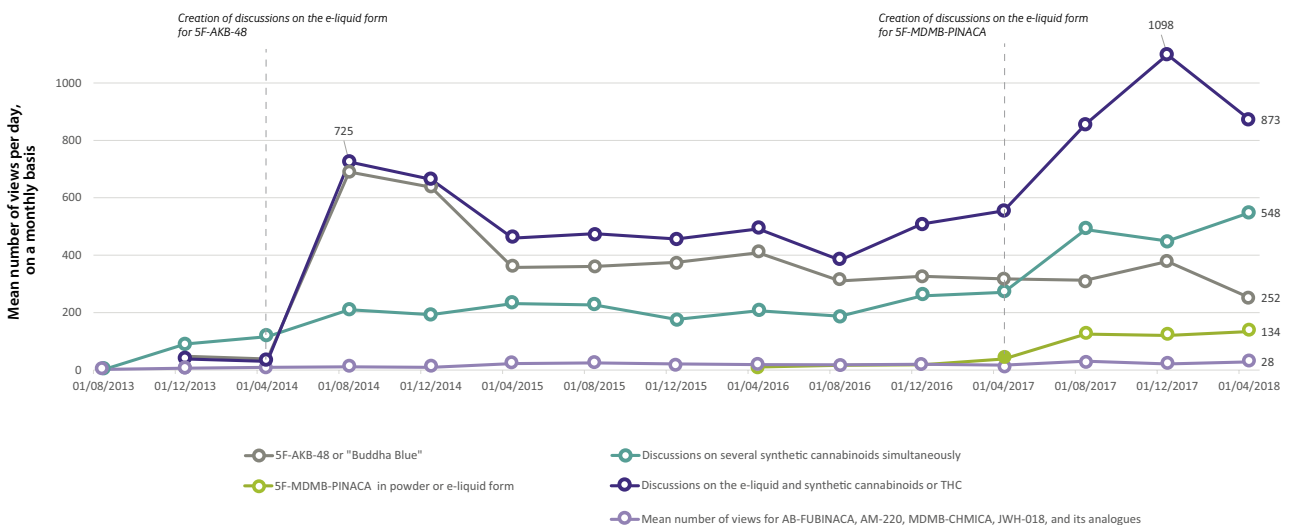
Initially, conversations mainly focused on the preparation of synthetic cannabinoids belonging to the "JWH"^a class, before use. This interest then gradually weakened, switching to the subject of adverse effects and, after JWH was banned, other synthetic cannabinoids such as AM-2201 and UR-144 were also shown to benefit. In February 2013, following the publication of a press article on the immunosuppressant potential of certain synthetic cannabinoids, online forum users clearly distanced themselves from these compounds as a whole. That same month, AM-2201 and UR-144 were classed as narcotics in Britain, affecting their online availability.

Although new variants emerged over the next few months, renewed interest in synthetic cannabinoids was not observed in French-language forums until the summer of 2014. This is evidenced by the strong rise in forum visits, from 230 to 1,000 views/day, evenly matched between cathinones and phenethylamines, which had received the most views until that point.

This trend was sparked by a specific discussion thread, on the sale of 5F-AKB-48 in e-liquid form, "Buddha Blue". Since 2015, several other threads on the e-liquid form have appeared, illustrating the intensified interest in this form, particularly concerning 5F-MDMB-PINACA. Lastly, in 2017, views were fuelled by messages on THC extraction from cannabis and the production of liquid for e-cigarettes. Current forum conversations on synthetic cannabinoids practically only concern the e-liquid form, and, by way of comparison, threads on conventional use as joints or with the powder form are now hardly ever viewed.

^aThe acronym for the names of compounds often corresponds to the name of their inventor or the laboratory where they were produced. This refers to John William Hufmann, whose research paved the way for initial studies on synthetic cannabinoids.

Figure 3. Audiences of discussion threads relating to a synthetic cannabinoid or topic on three French-language forums



Sources: Psychoactif.org, Psychonaut.com and Lucid-State forums (exclusively over the period 2013-2015)

Since 2011, 11 cases of health care related to synthetic cannabinoid use (i.e., 13% of cases relating to NPS use – figures as of 30 April 2017) have been reported to the OFDT. These exclusively concern non-fatal acute intoxications, although deaths have been reported in the European Union (EU) and in the United States. Furthermore, problem synthetic cannabinoid use has developed in a population of young users in Mayotte [10]. The clinical presentation of cases reported in the scientific literature is not particularly specific to synthetic cannabinoids: neurological, psychiatric, and cardiovascular disorders, along with pulmonary, gastrointestinal, and even renal disorders [11]. Occasional violent psychotic episodes, and seizures appear to be more common after synthetic cannabinoid use compared to natural cannabis. Withdrawal syndrome may develop after long-term use [11]. Lastly, follow-up of regular users and animal studies suggest long-term toxicity of synthetic cannabinoids on the nervous system, with persistent cognitive disorders [12].

Cathinones, highly problematic NPS

Often referred to as “bath salts”, these stimulant, but also empathogen-entactogen compounds¹⁶ have limited visibility in public spaces in France, contrary to the situation observed in several European countries [2]. They are sometimes mentioned in the media, with some exaggeration¹⁷. They are often seized in postal freight (approximately 40% of annual NPS seizures), increasingly in the context of micro trafficking or bulk purchases, than for personal use. Apart from a few former polydrug users, or men who have sex with men (MSM) taking these substances in a sexual context, use was observed to be limited [13].

Cathinones are usually snorted, but are also injected by a minority of users, confirmed by analysing the contents of syringes collected in Paris [14]. Like numerous stimulants, these give rise to tolerance and compulsion to use, leading to a substantial increase in the doses used. Furthermore, owing to the quantities used, cathinones could become not simply the most widespread NPS category, but, in quantitative terms, the most widely used NPS category in France.

Since mephedrone was classed as a controlled substance in 2010¹⁸, and its gradual disappearance from e-shops up to 2014, 3-MMC and 4-MEC, according to the information sources used, have been and continue to be the substances with the strongest presence on the market. Moreover, users often generally adopt the names of these key compounds when describing their

cathinones of choice, which can also be supplied in the form of blends.

Cathinones, particularly alpha-PVP and MDPV, are NPS responsible for the highest number of acute intoxications and deaths in the EU¹⁹. In France, 142 health cases were reported between 2009 and 2014, involving 17 different compounds [15]. Like cocaine, amphetamines, or even MDMA, cathinones act on the dopaminergic, adrenergic, and serotonergic systems [16]. The symptoms reported for acute intoxication are diverse and unspecific, as for synthetic cannabinoids. More severe cases of intoxication cause symptoms such as hyperthermia, intense and sometimes aggressive agitation, delirium, visual and auditory hallucinations, and sometimes muscle and renal impairment [16].

Psychedelic and dissociative substances, niche user substances

Hallucinogenic, psychedelic or dissociative NPS belong to 4 different classes of NPS (phenethylamines, arylalkylamines, arylcyclohexylamines, and tryptamines) and are mainly used in private settings and alternative festive scenes (free parties, multi-sound parties, festival “off zones”). Compared to other countries, French users and “e-psychonauts” in particular show strong interest in these substances (see section below).

25x-NBOMe and methoxetamine (MXE) are the most iconic compounds in this group. At one time, their arrival on the market offset the fluctuating supply of LSD and ketamine, respectively [17]. Then sold as substitutes, these substances were responsible for extensive drug rip-offs in the festive scene, i.e., when a user believes they have purchased and used one substance instead of another, sometimes with serious health consequences owing to the difference in the toxicity of the substances. This was notably the case for 25x-NBOMe, between 2013 and 2016, the toxic doses of which are lower than for LSD. At present, these NPS may be marginally sought after for themselves, and no longer used as substitutes.

The marked consumption of longer-standing psychedelic NPS, such as 2C-B, DOC, and dimethyltryptamine (DMT) is also observed [17]. The latter has a consumption pattern characteristic of numerous NPS. Reported by TREND back in 1999, it was then symbolic of these new substances reserved for circles of experienced users. Following a period of lesser visibility, it resurfaced in 2015 in the alternative festive scene, benefiting from the development in supply and shared knowledge on the Internet concerning its patterns of use and effects.

The available health data on this type of compound are highly disparate. Between 2014 and 2016, 14 medical cases were reported to the OFDT for 25x-NBOMe. In June 2017, the first case of death following the intake of a blend of NBOMe assumed to be cocaine received extensive media coverage²⁰.

Synthetic opioids: a potential threat

Synthetic opioids (SO), having recently emerged on the market, developed later than the other classes of NPS in France. These notably arrived on the market via fentanyl analogues. Since 2013, 10 SO have been identified out of the 21 compounds listed by the EMCDDA. These compounds are always seized in small quantities, and are in very limited circulation.

When the first non-medicinal SO appeared in France (AH-7921, MT-45, and U47-700), forum members (see below) showed little interest, highlighting the dangers of these substances which are difficult to control and toxic at very low doses. From 2015, an increase in SINTES collections and medical reports on fentanyl analogues was observed, despite only involving limited cases of intoxication. Between 2012 and 2017, the French addiction monitoring network recorded 8 cases of intoxication related to non-medicinal fentanyl use, ofentanyl (5 overdoses including 2 deaths), carfentanyl (2 cases), and butyrylfentanyl (1 case) [18]. These predominantly reflected intentional use, suggesting isolated experimentations, among males. However, these substances could also be used as heroin cutting agents, giving rise to a high risk of overdose. Some fentanyl analogues, 1,000 times more potent than morphine, are causing numerous cases of fatal and nonfatal intoxication in the United States and Northern Europe. In contrast, their presence in France is still rare. The availability and accessibility of opiate substitutes in France [19] more than likely limits diversion towards SO among users. These are nonetheless still a cause for concern, and are the subject of surveillance by the health authorities.

16. Neologisms used to describe the effects specific to a compound, respectively meaning that it incites empathy for others and increases the sense of touch.

17. https://www.lemonde.fr/les-decodeurs/article/2017/11/20/cannibalisme-et-hallucinations-les-intox-de-la-droque-zombie_5217652_4355770.html

18. Decree of 7 June 2010 (NOR SASP1014839A).

19. For MDPV, 108 direct or indirect deaths and 525 nonfatal cases of intoxication, between 2009 and 2013 (Council decision 2014/688). For Alpha-PVP, 115 direct or indirect deaths and 191 nonfatal cases of intoxication, between 2011 and 2015 (Council decision 2016/1070).

20. https://www.francetvinfo.fr/societe/droque/la-nouvelle-droque-nbome-provoque-une-premiere-mort-en-france_2231699.html

“Functional” stimulants

The term “functional” in this case denotes the reasons for substance use, which relates to doping, or self-medication, for stimulation purposes. These NPS reflect the way in which some substances, driven by commercial supply, are spreading towards larger, more diverse and dispersed audiences. Less visible compared to other substances in specific NPS user groups, consumption has been steadily rising. However, reports on these substances in information sources have remained recurrent and stable over the years.

The most popular substances in this category is ethylphenidate, a compound similar to methylphenidate, the active substance of Ritalin®, a medication notably dispensed for attention deficit-hyperactivity disorder. Misuse of this medication, mainly located in the Mediterranean region, enables vulnerable populations to stay awake to withstand the conditions of life on the streets [20]. Ethylphenidate use is observed among more socially integrated individuals. Since its emergence on the market, at the end of 2011, this substance has been identified by French-speaking forums as a stimulant which does not cause significant craving²¹. Its persistence in 2018, reflected by its wide popularity since 2013 (between 150 and 200 views/days in forums) and numerous regional seizures, indicates its ability to fulfil user expectations.

Another example, methiopropamine (MPA), which appeared on the Internet in 2010–2011 under the name “synthacaine”, was soon rejected by forum users due to its random composition and minor effects. However, it resurfaced in 2013–2014 among more diffuse, socially integrated or vulnerable user groups, probably less tolerant to stimulants compared to forum users. The similarity of its commercial name to cocaine undoubtedly prompted this new consumption.

Alpha-PVP, known as “Flakka” across the Atlantic, was also soon abandoned by forum users after it emerged on the market in 2011. In 2015, following its production by sites normally reserved for the usual stimulants, mainly in Poland, it resurfaced on conventional markets, attracting a few disadvantaged users. This situation led to visible renewed interest on French-speaking forums.

Since 2008, five emergency medical care signals have been reported to the OFDT related to alpha-PVP or a similar compound, including two deaths. Intoxication seems to be characterised by major psychiatric symptoms, confirmed

Limits of classification of controlled drugs

Inclusion of NPS on the list of narcotics remains the main method for legislative control. In France, this list was laid down by the decree of 1990^a, drawn up based on the international conventions on narcotics and psychotropics of 1961 and 1971. It has been regularly updated since the emergence of NPS. The decree of 27 July 2012, banning several cathinones, represented the first ban, in France, based on a “generic” classification, i.e., concerning a group of compounds rather than individual substances [21]. Since then, another three decrees of this type have been issued^b.

NPS may also be classified on a European scale, further to a decision by the Council of Europe. The procedure for collecting information from Member States and evaluation by the EMCDDA scientific committee was overhauled in 2017, in order to speed up the process^c. Lastly, NPS may also be subject to international classification by the United Nations. Between January 2013 and March 2018, 42 of these substances were placed under control, an unprecedented number since the first substances were classified in the 1970s.

However, the change in the status of a compound has little bearing on the motivation of users to procure these substances. Forum accounts and the findings of the online survey on NPS [4] show that regular users are prepared to take risks to procure the substance, regardless of its legal status. Ultimately, illegality is less of a decisive factor for users than the desire to discover new sensations or find substitutes for conventional substance use. It should also be noted that NPS in established use in France have been banned. Hence, 3-MMC and 4-MEC, the two most widely seized NPS in France in 2017, are cathinones which were classified in 2012.

^a Decree of 22 February 1990 laying down the list of substances classified as narcotics (NOR SP5M9000498A).

^b First- and second-generation synthetic cannabinoids according to the decree of 19 May 2015 (NOR AFSP1511929A), NBO/Me compounds and their derivatives according to the decree of 6 November 2015 (NOR AFSP1526800A) and third-generation synthetic cannabinoids according to the decree of 31 March 2017 (NOR AFSP1710288A).

^c Regulation (EU) 2017/2101 of the European Parliament and of the Council of 15 November 2017 amending Regulation (EC) No 1920/2006 as regards information exchange on, and an early warning system and risk assessment procedure for, new psychoactive substances.

by accounts reported via TREND or SINTES. The “coming down”²² phase after use is difficult, characterised by fits of violence and paranoid-type disorders. On a European level, 115 deaths have been attributed to alpha-PVP, due to direct intoxication or related to the behavioural effects of the substance.

■ **Use and users in France**

Demand still marginal, but involving acute health problems

Despite the difficulties encountered when estimating levels of use (see box on p. 2), the overall quantitative and qualitative data reflect moderate substance use which is gaining a foothold.

Synthetic cannabinoids represent the only class for which data estimating the prevalence of use are available. In 2014, lifetime use in the general population for synthetic cannabinoids only was estimated at 1.7% among 18–64 year-olds, admittedly a low level, but which remains negligible, similar to heroin (1.5%), and amphetamines (2.3%) (2014 Health Barometer Survey). In 2017, nearly 4% of 17 year-olds claimed to have “already

taken a substance imitating the effects of a drug” (ESCAPAD 2017), synthetic cannabinoids in the vast majority of cases. In 2015, the European School Survey on Alcohol and other Drugs (ESPAD) ranked France within the European average, by estimating that 5% of high school students aged 16 years had already tried an NPS. No strictly comparable data are currently available for the general population in France and other EU Member States for other NPS classes or wider age groups, for instance, 15–34 year-olds. The findings of these surveys on NPS as a whole should, moreover, be interpreted with caution, owing to numerous potential biases (see box on p. 2).

Aside from a few exceptions (some local situations, due to an NPS dealer moving into the area), French psychoactive substance users seem to have rarely turned to NPS. Beyond a possible curious phase, on the whole, users only, in fact, show interest in a handful of substances.

21. An irrepresible desire to use.

22. Phase occurring when the effects of a drug subside, which may present as varying degrees of intense fatigue, sometimes accompanied by depression and pain. The intensity and duration of the coming down phase vary and depend on the individual, the substance, and the dose used.

User profiles and contexts of use

The different sources available show that NPS mainly attract individuals who use psychotropic substances, mainly relatively young, urban, qualified adult males (under 30 in the large majority of cases) [4].

E-psychonauts or forum members (forumers)

The term “e-psychonauts” refers to the combination of psychonautics²³ and Internet use. It describes a core of users considered as “experienced” [22]. Their substance use predominantly centres on psychedelic or dissociative NPS. Due to the way in which their knowledge and expertise are specifically structured around NPS, these users tend to seek experiences and attempt to create contexts of use which reduce harm so as to limit health problems as far as possible. The online community is an essential space of sociability for these specialised online discussion adepts. Substance experimentation often takes place in a private context, alone or with a few friends, or in somewhat alternative festive scenes.

Users in the alternative electro festive scene

Observed in 2002, new synthetic substances were first used in the alternative electro festive scene, but also by the forerunners of e-psychonauts and pioneers of online purchases. In this setting, with frequent polydrug use, characterised by the key role of psychedelic substances, interest in hallucinogens has notably encouraged the consumption of methoxetamine (MXE) and 25x-NBOMe [17]. After an initial curious phase, alternative users have remained “conservative” in terms of their choices and image with regard to substances. “Good quality” products are, in fact, expected to be expensive and often “natural”. They can, moreover, be deterred by the complexity of the subject, and the hazards of new substances.

Users in the commercial dance-event setting

In the commercial setting (paying events, bars, clubs, and discotheques), use of stimulant substances is observed in particular, either with empathogen effects, such as 3-MMC and 4-MEC, or functional effects, such as alpha-PVP. In contrast to the findings in the alternative festive scene, here, users more readily accept that substances can be sold at relatively low prices, while being claimed to have higher purity than substances circulating on the conventional market. However, once again, interest in NPS is tending to wane, due to the combined

effect of increased cocaine potency, the quantities of MDMA detected in ecstasy tablets, and the rising online prices of NPS.

Chemsex adepts or people who use drugs in the sex context

At the end of the '00s, the emergence, of NPS – mainly cathinones – revived chemsex practices, mainly among a group of men who have sex with men (MSM), which led to the first visible health consequences of this type of substance use [13]. This form of cathinone use in a private context aims to increase libido, pleasure, and stamina, allowing MSM to maintain sexual activity for several hours. Despite already being “conventional” drug users in general, they are often relatively unaware of harm reduction measures, and regularly combine these products with other substances such as cocaine, MDMA, GHB/GBL or even medications for erectile dysfunction, which increases the risk of cardiovascular events. When cathinones are injected (a practice known as *slamming*), the intensity and short-lived nature of the effects encourage repeated use, sometimes up to fifteen to twenty times in the same session.

“Long-standing” drug users engaged in polydrug use

This group concerns heroin users from the 80s-90s, now on opioid substitution treatment (OST), or slightly younger individuals having mainly used stimulants (cocaine and MDMA) in the 90s-00s. These users distanced themselves from distribution networks and sites as they grew older, or due to changes in their socio-economic status. With the arrival of NPS, they now have access to a whole new range of substances, particularly stimulants which earned visibility due to the creation of a section dedicated to NPS on the Psychoactif.org forum, in 2013. Former heroin addicts in particular, affected by the AIDS epidemic, are immersed in the harm reduction culture. This “cultural baggage” has allowed them to quickly assimilate certain codes specific to e-psychonauts. NPS may incite curiosity and desire in this group, owing to visibly easy access or, indeed, the hope of rediscovering sensations which once no longer seemed possible due to their acquired tolerance to conventional substances, with the risk of falling back into uncontrolled use.

Long-term cannabis users

“Synthetic cannabis” is attracting interest among a group of long-term cannabis users. This is primarily observed among young people since

two-thirds of 17 year-olds interviewed in 2017 (2017 ESCAPAD) having used synthetic cannabinoids had also smoked cannabis on more than 10 occasions in the past month. This is also observed among “heavy smokers”, less attached to the natural characteristics of the herbal form. Hence, in 2017 and 2018, the TREND scheme has observed the spreading of synthetic cannabinoid use to older (above 35) heavy cannabis users, treated for addiction. While curiosity seems to be their main motive, some users are tending to seek out a substitute to reduce their cannabis use, or to replace cannabis when in scarce supply, or to avoid urine tests further to drug treatment orders.

■ Conclusion

The NPS phenomenon represents a decisive development in the field of drugs over the past decade. The nature of supply has been transformed, owing to the number of substances and variety of effects, but also because they are difficult to detect. Unlike conventional drugs, their synthetic nature enables production which does not entail cultivation, thus reducing costs and, consequently, the sale price, which can be low. Trade in these substances has also shown that the Internet could be a mechanism for drug supply in general. With the Internet, psychotropic substances are more accessible, the market is more dispersed, and allows greater discretion.

The new structure of the drug market has not only led to changes in legislative procedures on narcotics control, but has also led to significant developments in the resources and methods used by the law-enforcement services for online investigations²⁴. However, NPS do not appear to have had a profound impact on psychoactive substance use in France, only appealing to a fairly limited audience. Unlike certain countries (Poland, Ireland, Sweden, etc.), only very limited circulation of these substances has been observed on conventional markets in France, particularly for synthetic cannabinoids [23]. The country has not faced a large-scale health crisis [24; 25], and use is mainly limited to individuals who tend to be well socially integrated [23].

23. This was a counterculture trend in the 1960s which developed in music and the graphic arts. The use of psychoactive substances was particularly perceived as a way of discovering and learning about oneself.

24. Law no. 2016-731 adopted on 3 June 2016 strengthening the Fight against Organised Crime, Terrorism and their Financing, and Improving Efficiency and Guarantees of Criminal Procedure, NORJUSD1532276L.

Two aspects specific to France may explain the limited impact of NPS. Firstly, there are no physical smartshops²⁵ in France. In countries where such stores existed, having since been banned in some countries (Poland, Ireland), their presence facilitated access to NPS, particularly among younger age groups. The absence of such stores in France has slowed NPS consumption, particularly for brand-name substances. This partly explains why serious, but isolated individual health situations have mainly been reported in France.

Furthermore, although the French-language digital market has numerous "commercial" e-shops, the editorial policy of French-speaking online discussion forums also plays a protective role. In contrast to English-language forums or central European countries, members are requested to only use the chemical names of the substances. They also prohibit any mention of e-shops, and refuse advertising or dedicated spaces for dealers. This limits the visibility and appeal of substances for young users, along with the spread of inaccurate information.

Fear of a "tidal wave" of new drugs is waning, as identification rates fall and the large majority of French users still focus on "conventional" drugs. However, a small number of substances have been adopted by certain user profiles, more than likely associated with acute intoxication and as yet unclear long-term physical or psychological risks.

Are pathologies potentially affecting these users likely to differ considerably from those caused by conventional drug use? Questions posed by the lack of knowledge on NPS pharmacology and

toxicology could be answered through further researches, and this is the first challenge which needs to be addressed. The second challenge is to provide all hospital departments with resources for identifying these substances and/or their metabolites in biological samples, so as to improve screening for problem use, and also to document the risks associated with NPS use more effectively. Providing information on substances, prevention, harm reduction measures, and training on how to manage effects, aimed at both potential users and professionals working in the field, are key challenges.

The slow emergence of new substances on the market, and the fact that these practices are limited to an audience with a very specific profile should not cause us to lose sight of this very recent NPS phenomenon. While these substances have gained a poor reputation among psychotropic substance enthusiasts for the time being, due to the extent of unexpected, adverse effects, this perception could change with time, according to the state of the conventional drug market and how consumers get to familiarise themselves with these substances.

25. Stores similar to the commercial online e-shops described above: these sell natural products, vitamins and food supplements, together with paraphernalia for cannabis use and hallucinogenic mushrooms.

Bibliography

1. Lahaie E. et al., [New psychoactive substances and the Internet: current situations and issues](#), Tendances, OFDT (84), 2013, 8 p.
2. EMCDDA, [European Drug Report 2017: Trends and Developments](#), 2017, 90 p.
3. Jouanjus E. et al., « Comment identifier un signal en addictovigilance ? », *Thérapie*, 70(2), 2015, p. 113-122.
4. Cadet-Tairou A., [New psychoactive substances: user profiles and practices](#), Tendances, OFDT (108), 2016, 8 p.
5. Gaulier J.-M., « Chemobyl syndrome ? », *Toxicologie Analytique et Clinique*, 29(1), 2017, p. 3.
6. Martinez M. et al., "A method for exploring the number of online shops selling new psychoactive substances: initial I-TREND project results", In: EMCDDA (Dir.), [The Internet and drug markets](#), 2016, p. 97-104.
7. EMCDDA, Europol, [Drugs and the darknet: perspectives for enforcement, research and policy](#), 2017, 90 p.
8. Winstock A., Wilkins C. Legal highs: The challenge of new psychoactive substances. Amsterdam, TNI, 2011, 16 p.
9. Wersé B., Morgenstern C., "How to handle legal highs? Findings from a German online survey and considerations on drug policy issues", *Drugs and Alcohol Today*, 12(4), 2012, p. 222-231.
10. Cadet-Tairou A., Gandilhon M. [L'Offre, l'usage et l'impact des consommations de « chimique » à Mayotte : une étude qualitative](#). Saint-Denis, OFDT, 2018, 80 p.
11. Pélassier-Alicot A.-L., « Les cannabinoïdes de synthèse : épidémiologie, modalités de consommations et effets cliniques », *Toxicologie analytique et clinique*, 27(1), 2015, p. 33-40.
12. Compton D.M. et al., "Adolescent exposure of JWH-018 "Spice" produces subtle effects on learning and memory performance in adulthood", *Journal of Behavioral and Brain Science*, 2(2), 2012, p. 146-155.
13. Milhet M., Néfau T. [Chemsex, slam. Renouveau des usages de drogues en contextes sexuels parmi les HSH](#). Saint-Denis, OFDT, 2017, 32 p.
14. Néfau T. et al., "Drug analysis of residual content of used syringes: A new approach for improving knowledge of injected drugs and drug user practices", *Int. J. Drug Pol.*, 26(4), 2015, p. 412-419.
15. ANSM. Commission des stupéfiants et psychotropes - Séance n° 3. Compte rendu de la séance du 12 janvier 2017, 2017, 21 p.
16. Coppola M., Mondola R., Synthetic cathinones: chemistry, pharmacology and toxicology of a new class of designer drugs of abuse marketed as "bath salts" or "plant food", *Toxicology Letters*, 211(2), 2012, p. 144-149.
17. Martinez M. et al., ["25x-NBOMe" type molécules - Available information on the diffusion of a class of NPS in France](#). Saint-Denis, OFDT, 2017, 30 p.
18. CEIP-A de Paris, « Nouveaux produits de synthèse : zoom sur les fentanylloïdes », *Addictovigilance*, (5), 2017, 2 p.
19. Milhet M. et al., [Usages de BHD non conformes au cadre médical. De la buprénorphine au « Subu » : observations récentes du dispositif TREND](#). Saint-Denis, OFDT, 2017, 30 p.
20. Frauger E. et al., "Patterns of methylphenidate use and assessment of its abuse among the general population and individuals with drug dependence", *European Addiction Research*, 22(5), 2016, p. 119-126.
21. Martinez M., « Contrôler les NPS : du classement comme stupéfiant à l'utilisation d'autres réglementations », *Actal*, (13), 2013, p. 62-66.
22. Martinez M., « [Les e-psychoautes, des usagers sous influence numérique](#) », In: Beck F. (Dir.), *Jeunes et addictions*, Saint-Denis, OFDT, 2016, p. 70-73.
23. EMCDDA et al., [High-risk drug use and new psychoactive substances. Results from an EMCDDA trendspotter study](#), 2017, 21 p.
24. Heame E. et al., Country report on New Psychoactive Substances in Ireland. NPS-transnational Project, 2017, 24 p.
25. Brodziak A., Wiczorek L., "Mysterious wave of severe poisonings in Poland by new psychoactive substances", *J. Gerontol. Geriatric Res.*, 5(269), 2016.

tendances

Director of publication
Julien Morel d'Arleux

Editorial Committee
Christian Ben Lakhdar, Bruno Falissard, Virginie Gautron,
Emmanuelle Godeau, Aurélie Mayet, Frank Zobel

Editor in chief : Julie-Émilie Adès

Graphic designer : Frédérique Million

Documentation : Isabelle Michot

French Monitoring Centre for Drugs and Drug Addiction

3, avenue du Stade-de-France
93218 Saint-Denis La Plaine cedex

Tel. : (+ 33) 1 41 62 77 16

Fax : (+ 33) 1 41 62 77 00

e-mail : ofdt@ofdt.fr



www.ofdt.fr

Acknowledgment

Review credits: Anne de l'Épervier, Maitena Milhet, Ivana Obradovic, Christophe Palle, Antoine Philippon.

We would also like to thank the current and former Psychoactif.org, Psychonaut.com and Lucid-State forums.