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MARKET ANALYSIS OF SYNTHETIC DRUGS

Amphetamine-type stimulants, new psychoactive substances

WORLD DRUG REPORT 2017

4

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PREFACE

I am proud to say that this year we are marking 20 years of the *World Drug Report*.

Over the past two decades, the United Nations Office on Drugs and Crime (UNODC) has been at the forefront of global research into complex areas of drug use and supply, supporting international cooperation and informing policy choices with the latest estimates, information on trends and analysis.

This year we are launching a new format, with the report available as five separate booklets: the executive summary, together with the report's conclusions and policy implications; a global overview of drug use and supply; a market analysis of plant-based drugs; a market analysis of synthetic drugs; and a thematic booklet on the links between drugs and organized crime, illicit financial flows, corruption and terrorism. We have done this in response to readers' needs and to improve user-friendliness, while maintaining the rigorous standards expected from the Office's flagship publication.

The 2017 report comes at a time when the international community has acted decisively to achieve consensus on a way forward for joint action.

The outcome document unanimously adopted at last year's special session of the General Assembly on the world drug problem contains more than 100 concrete recommendations for implementing balanced, comprehensive and integrated approaches to effectively addressing and countering the world drug problem.

Moreover, at its sixtieth session, in March 2017, the Commission on Narcotic Drugs adopted resolution 60/1, reinforcing commitment to implementing the outcome document and charting a course to the 2019 target date of the 2009 Political Declaration and Plan of Action on the world drug problem, as well as strengthening action towards the Plan of Action's agreed goals and targets.

As the *World Drug Report 2017* clearly shows, there is much work to be done to confront the many harms inflicted by drugs, to health, development, peace and security, in all regions of the world.

Globally, there are an estimated minimum of 190,000 — in most cases avoidable — premature deaths from drugs, the majority attributable to the use of opioids.

The terrible impact of drug use on health can also be seen in related cases of HIV, hepatitis and tuberculosis.

Much more needs to be done to ensure affordable access to effective scientific evidence-based prevention, treatment and care for the people who desperately need them, including those in prison settings. As just one example, this year's report highlights the need to accelerate accessibility to the treatment of hepatitis C, a disease whose negative health impact on people who use drugs is far greater than that of HIV/AIDS.

Recent attention has focused on the threats posed by methamphetamine and new psychoactive substances (NPS). However, as the report shows, the manufacture of both cocaine and opioids is increasing. These drugs remain serious concerns, and the opioid crisis shows little sign of stopping.

The *World Drug Report 2017* further looks at the links with other forms of organized crime, illicit financial flows, corruption and terrorism. It draws on the best available evidence and, most of all, highlights the fact that much more research needs to be carried out in these areas.

Corruption is the great enabler of organized crime, and opportunities for corruption exist at every stage of the drug supply chain. However, too little is known about how different types of corruption interact with drug markets.

The outcome document of the special session of the General Assembly on the world drug problem and

Security Council resolutions express concern about terrorist groups profiting from drug trafficking, among other forms of transnational organized crime.

It is well established that there are terrorists and non-State armed groups profiting from the drug trade — by some estimates, up to 85 per cent of opium poppy cultivation in Afghanistan is in territory under influence of the Taliban.

However, evidence on the organized crime-terrorism nexus remains patchy at best. Moreover, these links are not static. Relations between organized crime and terrorists groups are always evolving, much like drug markets themselves.

As we have seen with the NPS market, drug use, supply, trafficking routes and the substances themselves continue to shift and diversify at alarming speed.

Drugs continue to represent a major source of revenue for organized crime networks, but business models are changing, with criminals exploiting new technologies, such as the darknet, that are altering the nature of the illicit drug trade and the types of players involved, with looser, horizontal networks and smaller groups becoming more significant. New ways of delivering drugs further point to the need to involve other sectors such as postal services in the fight against drug trafficking.

Clearly, countries must be able to act and react to an ever-changing and formidable array of threats and problems. UNODC is fully engaged in strengthening responses, working closely with our United Nations partners and in line with the international drug control conventions, human rights instruments and the 2030 Agenda for Sustainable Development, which are themselves complementary and mutually reinforcing.

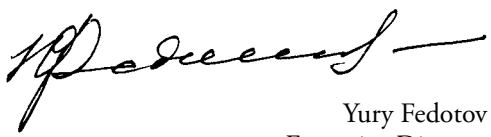
As the special session of the General Assembly and the recent session of the Commission on Narcotic Drugs have shown, the international community is equipped to respond swiftly and decisively to global drug-related challenges.

For example, in March, the Commission scheduled two precursors and an analogue to the scheduled drug fentanyl. This important step will make it harder for criminals to illicitly manufacture fentanyl and its analogues and, I hope, can help to stem the tragic increase in opioid overdoses in recent years.

However, there remains an enormous need for capacity-building and technical assistance, and funding continues to fall far short of political commitment. Further resources are urgently needed to help all Member States implement the recommendations contained in the outcome document of the special session of the General Assembly and achieve related targets under the Sustainable Development Goals.

The many evolving drug challenges also highlight the importance of prevention — science- and rights-based drug use prevention — but also prevention of crime, corruption, terrorism and violent extremism, in line with commitments under the conventions and United Nations standards and norms.

Finally, I ask all Governments to help us improve the evidence base for these reports. Areas such as the links between drugs, terrorism and insurgency clearly touch upon sensitive intelligence, and there are legitimate concerns about compromising sources, collection and operations. But if we want to effectively address drug challenges we need to strengthen international cooperation and information-sharing to the extent possible, to close the gaps and ensure that joint action is targeted, effective and timely.



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CONTENTS

Acknowledgements

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EXPLANATORY NOTES

The boundaries and names shown and the designations used on maps do not imply official endorsement or acceptance by the United Nations. A dotted line represents approximately the line of control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. Disputed boundaries (China/India) are represented by crosshatch owing to the difficulty of showing sufficient detail.

The designations employed and the presentation of the material in the *World Drug Report* do not imply the expression of any opinion whatsoever on the part of the Secretariat of the United Nations concerning the legal status of any country, territory, city or area, or of its authorities or concerning the delimitation of its frontiers or boundaries.

Countries and areas are referred to by the names that were in official use at the time the relevant data were collected.

All references to Kosovo in the *World Drug Report*, if any, should be understood to be in compliance with Security Council resolution 1244 (1999).

Since there is some scientific and legal ambiguity about the distinctions between "drug use", "drug misuse" and "drug abuse", the neutral terms "drug use" and "drug consumption" are used in the *World Drug Report.*

All uses of the word "drug" in the *World Drug Report* refer to substances under the control of the international drug control conventions.

All analysis contained in the *World Drug Report* is based on the official data submitted by Member States to the United Nations Office on Drugs and Crime through the annual report questionnaire unless indicated otherwise.

The data on population used in the *World Drug Report* are taken from: United Nations, Department of Economic and Social Affairs, Population Division, *World Population Prospects: The 2015 Revision.*

References to dollars ($) are to United States dollars, unless otherwise stated.

References to tons are to metric tons, unless otherwise stated. R stands for the correlation coefficient, used as measure of the strength of a statistical relationship between two or more variables, ranging from 0 to 1 in case of a positive correlation or from 0 to -1 in case of a negative correlation.

KEY FINDINGS

Expanding market for synthetic drugs

Unlike the manufacture of heroin and cocaine, the manufacture of synthetic drugs is not geographically constrained, as the process does not involve the extraction of active constituents from plants that have to be cultivated in certain conditions for them to grow. Yet any analysis of the synthetic drugs market is complicated by the fact that information on synthetic drug manufacture is limited, which prevents the estimation of the volume of such drugs being manufactured worldwide. Nevertheless, data on seizures and use suggest that the supply of synthetic drugs is expanding.

An increasing number of countries are reporting seizures of synthetic new psychoactive substances (NPS), with over 20 tons seized in 2015. Seizures of amphetamine-type stimulants (ATS) doubled in the five years prior to 2015, to reach 191 tons in 2015. This was a result of sharp increases in the amounts of amphetamines seized, of which methamphetamine accounted for some 61-80 per cent annually during that period.

Methamphetamine accounts for considerable harm

Disorders related to the use of amphetamines account for a considerable share of the global burden of disease attributable to drug use disorders, second only to those related to the use of opioids. Available data show that, among amphetamines, methamphetamine represents the greatest global health threat. Methamphetamine use is spreading and an increasing number of methamphetamine users are seeking treatment. In addition to the established and expanding market for methamphetamine in East and South-East Asia and Oceania, there are growing concerns about methamphetamine use in North America, South-West Asia and parts of Europe.

Geographical shift in the methamphetamine market

A major geographical shift appears to have occurred in the methamphetamine market in the last five years. In 2015, the quantity of methamphetamine intercepted in East and South-East Asia surpassed the quantity intercepted in North America for the first time, making East and South-East Asia the leading subregions for methamphetamine seizures worldwide. While this may be a reflection of an increase in the effectiveness of law enforcement in East and South-East Asia, methamphetamine trafficking routes appear to be increasingly connecting previously unconnected markets in various subregions. Of particular note is the large increase in methamphetamine seizures in China.

The expansion of the methamphetamine market in East and South-East Asia is visible in the, albeit scarce, information available on methamphetamine use and treatment. In 2015, experts in several countries in the subregion reported a perceived increase in the use of both crystalline methamphetamine and methamphetamine tablets. They also considered methamphetamine to be the most commonly used drug in some of those countries. In the same year, people receiving treatment for methamphetamine use accounted for the largest share of people treated for drug use in the majority of countries and territories in East and South-East Asia that reported on that indicator.

In Oceania, there has been an increase in both the quantities of methamphetamine seized and the prevalence of its use.

Amphetamine trafficking expanding in Asia and Central America

In contrast to methamphetamine, amphetamine has been confined to fewer subregions, such as the Near and Middle East and Western and Central Europe. The quantities of amphetamine seized in 2015 point to a possible recent expansion of the amphetamine market in South-Eastern Europe, but this may be simply related to the large amphetamine market in the neighbouring Near and Middle East. Quantities of amphetamine seized also sharply increased in Central America and South-West Asia.

"Ecstasy" market becoming increasingly multifaceted

While smaller than the market for methamphetamine, the "ecstasy" market has grown in complexity and the variety of "ecstasy" products available to drug users has increased. The three main types are: (a) "ecstasy" tablets containing little or no MDMA

(3,4-methylenedioxymethamphetamine); (b) "ecstasy" tablets with an extremely high content of MDMA; and (c) "ecstasy" sold in powder or crystal form, under different street names. "Ecstasy" tablets with a high MDMA content are of particular concern in Europe, where law enforcement entities have also discovered industrial-scale MDMA manufacturing facilities.

New psychoactive substances potentially more lethal than other drugs, but market still relatively small

Despite the large number of NPS present in drug markets, the overall size of the market for such substances is still relatively small when compared with other drug markets. However, one of the most troubling aspects of NPS is that users are unaware of the content and the dosage of the psychoactive substances contained in some NPS. This potentially exposes users of NPS to additional serious health risks. Little or no scientific information is available to determine the effects that these products may have and how best to counteract them.

A number of NPS have been implicated in fatalities, while the injecting of NPS with stimulant effects has been reported among high-risk groups of people who use drugs, further aggravating the health risks to which people in those groups are exposed.

New psychoactive substances continue to evolve, diversify and grow

The NPS market continues to be very dynamic and is characterized by the emergence of large numbers of new substances belonging to diverse chemical groups. Between 2009 and 2016, 106 countries and territories reported the emergence of 739 different NPS to UNODC.

Marketed in many different ways and forms, new substances often emerge quickly and disappear again, while some become used regularly among a small group of users. Several countries have reported NPS being sold under the name of controlled drugs such as "LSD" and "ecstasy". Often used for reasons similar to those for the use of traditional drugs, their easy availability and low prices have made certain NPS highly attractive to some groups of drug users. A market for some NPS in their own right now appears to have been established.

A core group of over 80 NPS were reported every year during the period 2009-2015 and appear to have become established on the global market; a number of them have been placed under international control. On the other hand, about 60 NPS seem to have disappeared from the market since 2013. Problems in identifying them in a laboratory may be a factor, however, in the low level of reporting of these lesser-known substances.

Use of synthetic cannabinoid products associated with severe health risks

Synthetic cannabinoids are not simply synthetic versions of the substances occurring in herbal cannabis, as street names such as "synthetic cannabis" or "synthetic marijuana" may suggest. They are a diverse group of potent psychoactive compounds that are designed to mimic the desired effects of cannabis, of which there are also many new products on the market. Despite the predominance of synthetic cannabinoids on the spectrum of NPS, users of cannabis have reported that they prefer natural cannabis to synthetic cannabinoids.

There is growing recognition of the harm associated with intoxication resulting from the use of synthetic cannabinoids. While, in general, these health harms are not dissimilar to the intoxication caused by natural cannabis, the use of products containing certain synthetic cannabinoids has been associated with severe adverse health events including hospitalisations and fatalities. It cannot be concluded, however, that the untoward or undesirable effects of synthetic cannabinoids will limit their uptake or use.

Opioid market in a constant state of change

The opioid market is becoming more diversified: this is illustrated by the example of the United States, where the opioid market comprises a combination of internationally controlled substances, particularly heroin, and prescription medicines that are either diverted from the legal market or produced as counterfeit medicines on a large scale. These counterfeit medicines are made to look like pharmaceutical products while actually containing fentanyl and fentanyl analogues, as well as non-opioid substances such as derivatives of benzodiazepine and methylphenidate.

INTRODUCTION

Although presented as a stand-alone publication, this booklet constitutes the fourth part of the *World Drug Report 2017*. The *World Drug Report* is aimed at improving the understanding of the world drug problem and contributing to fostering greater international cooperation for countering its impact on health, governance and security. The present booklet provides an extended analysis of the global synthetic drugs market, including of amphetamine-type stimulants (ATS) such as amphetamine, methamphetamine and "ecstasy", and of new psychoactive substances (NPS), as well as of GHB.

This booklet also contains the bulk of the analysis for the triennial global synthetic drugs assessment. With the emergence of NPS in traditional markets, the triennial assessment has analysed trends and significant developments in both the ATS market and emerging markets. An important aspect of the assessment is to highlight the links between the traditional ATS markets and emerging NPS markets.

* *Excludes GBL, ketamine and other medicines.*

A. AMPHETAMINE-TYPE STIMULANTS

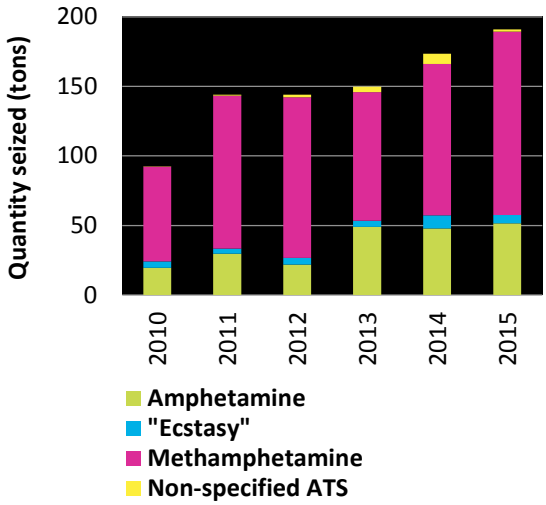
A.1. Amphetamine-type stimulants: market developments

Amphetamine-type stimulants (ATS) feature prominently in drug markets worldwide, with global patterns of supply and demand, particularly for methamphetamine, becoming increasingly interconnected and complex. In addition to the established and expanding market for methamphetamine in East and South-East Asia, there are growing concerns about methamphetamine in North America, South-West Asia and in parts of Europe. Amphetamine continues to feature prominently in synthetic drug markets in the Near and Middle East and in Western and Central Europe, and increasing seizures have recently been reported in parts of Central America, South-Eastern Europe and South-Western Asia. As ATS become increasingly available, concerns about the problems and health threats associated with ATS use are heightened, yet the quality of data and information on some aspects of the ATS market remains limited. In particular, information on ATS manufacture and demand-related data on the extent of ATS use remain scarce, which hinders estimates of the size of the ATS market.

Seizures of amphetamine-type stimulants continue to increase

Seizure data suggest that ATS markets continued to increase globally from 2010 to 2015. Methamphetamine dominates the global ATS market, while amphetamine is the main substance in ATS markets only in selected subregions, particularly the Near and Middle East and West and Central Europe, and "ecstasy" accounts for a relatively small portion of the global ATS market. Overall, global quantities of ATS seized doubled from 93 tons in 2010 to 191 tons in 2015, of which methamphetamine accounted for 61-80 per cent annually. With the exception of 2012, global amphetamine seizures annually accounted for 20-32 per cent of global ATS seizures between 2010 and 2015, whereas "ecstasy" seizures annually accounted for less than 5 per cent of global ATS seizures over the same period.

FIG. 1 Quantities of amphetamine-type stimulants seized worldwide, by type, 2010-2015



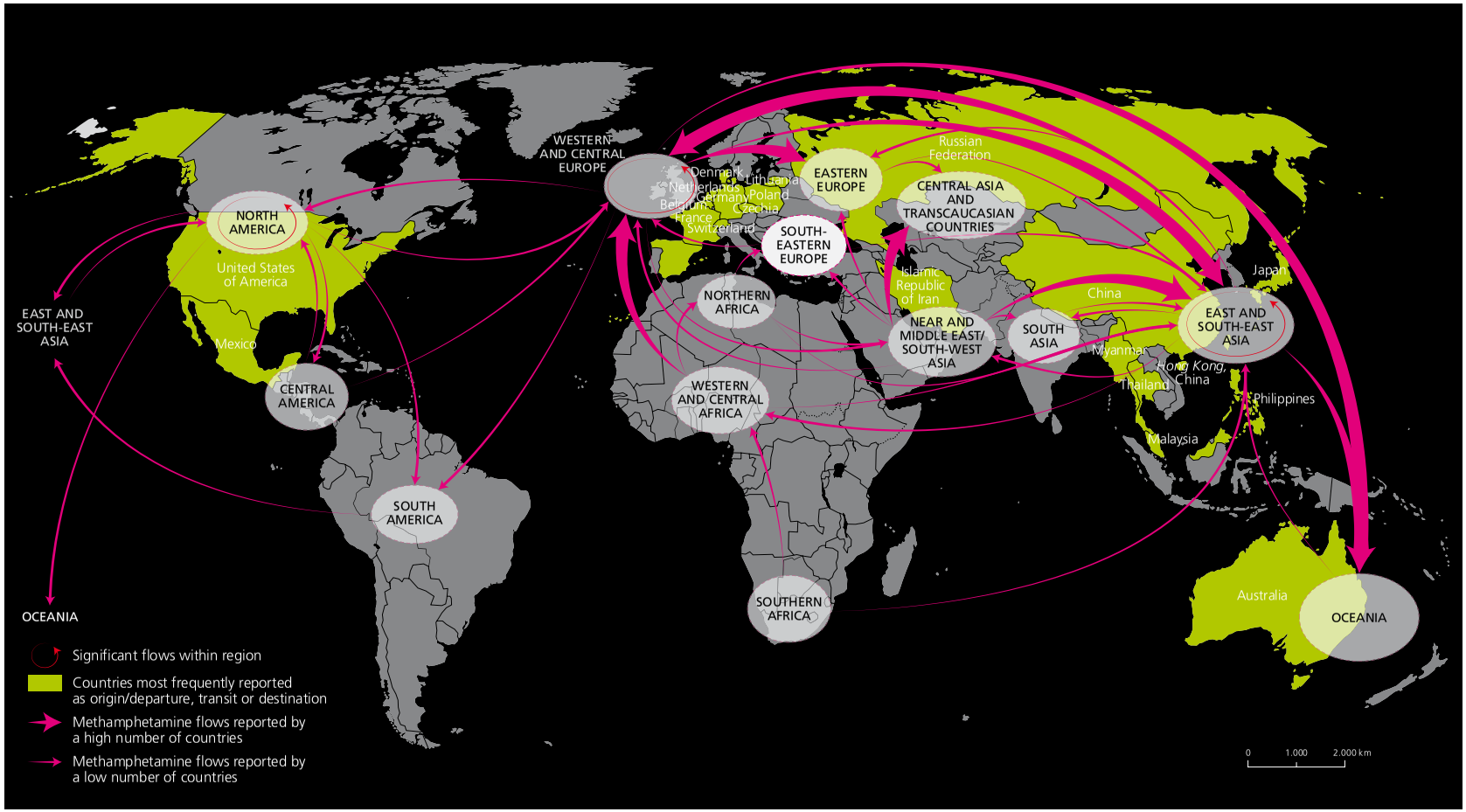
Source: UNODC, responses to annual report questionnaire, 2010-2015.

A.2. Methamphetamine: a dynamic global market

The transnational nature of global ATS trafficking routes has expanded, and they now connect subregions that previously had independent markets, a trend that has been particularly evident in reports concerning methamphetamine.[1] Between 2012 and 2015, methamphetamine was reported to have been smuggled from a number of subregions, including Western and Central Africa, North Africa, North America, East and South-East Asia, the Near and Middle East/South-West Asia and Western and Central Europe. East and South-East Asia and Oceania continue to be the main recipients of the methamphetamine trafficked worldwide, whereas the Near and Middle East, South-West Asia and Western and Central Europe appear to function primarily as transit points for global methamphetamine trafficking flows. In addition, there is a significant degree of intraregional methamphetamine trafficking occurring in North America, Western and Central Europe and East and South-East Asia.

1 UNODC, "Methamphetamine manufacture: global patterns and regional differences", *Global SMART Update 2014*, vol. 12 (September 2014).

MAP 1 | Interregional trafficking flows of methamphetamine, 2012-2015



Source: UNODC, responses to annual report questionnaire, 2012-2015.

Note: The origins of the flow arrows do not necessarily indicate the source/manufacture of methamphetamine. Flow arrows represent the direction of methamphetamine trafficking and are not an indication of the quantity trafficked. The boundaries shown on this map do not imply official endorsement or acceptance by the United Nations. Dashed lines represent undetermined boundaries. The dotted line represents approximately the Line of Control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. The final boundary between the Sudan and South Sudan has not yet been determined.

Diverse forms of amphetamine-type stimulants

Methamphetamine, amphetamine and "ecstasy" are sold in illegal drug markets in a variety of forms. In East and South-East Asia, South-West Asia and North America, methamphetamine appears in two main forms: methamphetamine tablets and crystalline methamphetamine. Methamphetamine tablets, commonly known as "yaba" in East and South-East Asia, are small tablets of low purity that are available in many different shapes and colours and are commonly ingested or smoked after being crushed. Crystalline methamphetamine, also called "crystal meth", "ice" or "shabu" (in East and South-East Asia), consists of (crushed) colourless crystals of various sizes and is usually of a much higher purity than the tablet form. In the case of crystalline methamphetamine, smoking, nasal insufflation and injecting are typical forms of use.[a]

In the Near and Middle East, amphetamine tablets are typically labelled with the brand name "captagon". Originally, "captagon" was the trade name of a pharmaceutical preparation containing fenetylline, a synthetic stimulant. However, in the past few years, most tablets seized as "captagon" essentially contained amphetamine, in combination with caffeine and occasionally with other adulterants.[b]

In the Americas, Europe, East and South-East Asia and Oceania, "ecstasy" is mainly available in tablet form. In addition, a niche market appears to have recently emerged for powder or crystalline MDMA[c] in some countries in Europe, North America and Oceania. In Australia, for example, the Ecstasy and Related Drugs Reporting System found that in 2015 more than half of the "ecstasy" users in that country had used "ecstasy" in the form of capsules containing powder or crystalline MDMA (60 per cent of users) or in the form of MDMA "crystal/rock" (57 per cent of users: an 18 per cent increase from the 2013 level), while tablets remained the form used by the vast majority of "ecstasy" users (82 per cent).[d]

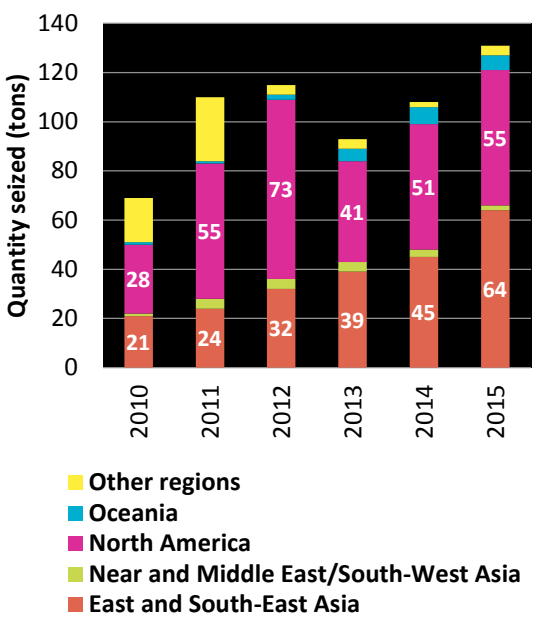
[a] *Terminology and Information on Drugs* (United Nations publication, Sales No. E.03.XI.14); *Recommended Methods for the Identification and Analysis of Amphetamine, Methamphetamine and Their Ring-Substituted Analogues in Seized Materials: Manual for Use by National Drug Testing Laboratories* (United Nations publication, Sales No. E.06.XI.1).

[b] *World Drug Report 2010* (United Nations publication, Sales No. E.10.XI.13), p. 114.

[c] MDMA (3,4-methylenedioxymethamphetamine) belongs to the "ecstasy"-group substances. It was placed under international control in 1986 (Schedule I of the Convention on Psychotropic Substances of 1971).

[d] Jennifer Stafford and others, "The 2016 EDRS key findings: a survey of people who regularly use psychostimulant drugs", *EDRS Drug Trends Bulletin* (Sydney, University of New South Wales, National Drug and Alcohol Research Centre, October 2016).

FIG. 2 Quantities of methamphetamine seized worldwide, by region, 2010-2015



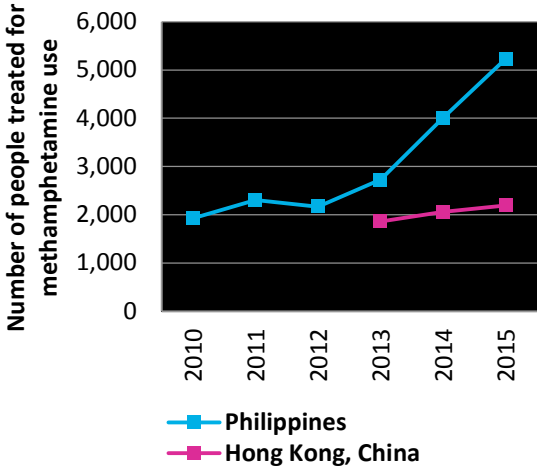
Source: UNODC, responses to annual report questionnaire, 2010-2015.

Seizure data for the period 2010-2015 signalled a geographical shift, with 2015 seizures in East and South-East Asia accounting for the highest percentage of global seizures of methamphetamine and surpassing seizures in North America for the first time. The recent predominance of East and South-East Asia in global seizures is possibly the result of two trends: methamphetamine markets expanding in Asia more than they are elsewhere, and an improved capacity of law enforcement authorities to detect methamphetamine, which is now recognized as one of the major drug threats in the region. Of particular note is the large increase in methamphetamine seizures in China, which reached 37 tons in 2015. Other countries in East and South-East Asia, such as Myanmar and Thailand, have also seen a steady increase in annual seizure quantities, although their seizure levels remain lower than those of China.

Methamphetamine use is widespread and treatment demand is growing

The expansion of the methamphetamine market in East and South-East Asia is visible in the — albeit

FIG. 3 Number of persons treated for methamphetamine use in the Philippines (2010-2015) and Hong Kong, China (2013-2015)



Sources: UNODC, responses to annual report questionnaire, 2010-2015; Narcotics Division, Security Bureau, of Hong Kong, China. (See "Newly/previously reported drug abusers by age group by common type of drugs abused (table 3)". Available at www.nd.gov.hk/en/statistics_list.htm).

scarce — information available on its use and treatment. Experts in six countries in the subregion reported a perceived increase in the use in 2015[2] of both crystalline methamphetamine and methamphetamine tablets. In that same year, national experts considered methamphetamine to be the most used drug in China and Macao, China; Japan; the Philippines; and Singapore.[3]

In 2015, people receiving treatment for methamphetamine use accounted for the largest share of people treated for drug use in five of the seven countries and territories[4] in East and South-East Asia that reported this indicator.[5] In both the Philippines and Hong Kong, China, the number of people receiving treatment for methamphetamine use has increased in recent years.[6, 7] Although the share of people treated for crystalline methamphetamine use in Indonesia in 2014 was, at around 30 per cent, far smaller than in other countries in the subregion, this still signifies an increase of almost 20 per cent from the previous year. Moreover, in Malaysia, crystalline methamphetamine users accounted for 80 per cent of ATS users receiving treatment in 2015, while the total number of ATS users receiving treatment represented a 47 per cent increase since 2014.[8]

In Oceania, quantities of methamphetamine seized increased in New Zealand from 15 kg in 2013 to 0.4 tons in 2015 and in Australia from 2.3 tons to 5.4 tons over the same period. Methamphetamine continues to be a drug of major concern in both countries. In Australia, data suggest that methamphetamine consumption has been increasing strongly in recent years,[9] triggering a comprehensive government response.[10]

In North America, the current heroin and opioid epidemic may dominate the national drug threat, but the threat posed by methamphetamine remains a key concern. The results of the National Drug Threat Survey, conducted by the Drug Enforcement Administration (DEA) of the United States of America, in 2016, show that 31.8 per cent of responding law enforcement agencies in the United States identified methamphetamine as the greatest drug threat in their areas, meaning that methamphetamine is perceived to be the second greatest drug threat after heroin in that country. Moreover, the percentage of responding United States law enforcement agencies reporting high availability of methamphetamine has increased annually, from 39.5 per cent in 2013 to

2 These countries included Cambodia, China, Lao People's Democratic Republic, Myanmar, Singapore and Viet Nam.

3 Drug Abuse Information Network for Asia and the Pacific.

4 These countries included Brunei Darussalam, the Lao People's Democratic Republic, the Philippines, Singapore and Thailand.

5 The Drug Abuse Information Network for Asia and the Pacific.

6 UNODC annual report questionnaire, replies submitted by the Philippines for 2010 to 2015.

7 Narcotics Division, Security Bureau, of Hong Kong, China, CRDA and Drug Statistics, 23 March 2017, "Newly/previously reported drug abusers by age group by common type of drugs abused (table 3)". Available at www.nd.gov.hk/en/statistics_list.htm.

8 The Drug Abuse Information Network for Asia and the Pacific.

9 Australian Criminal Intelligence Commission, *National Wastewater Drug Monitoring Program Report* (Canberra, March 2017).

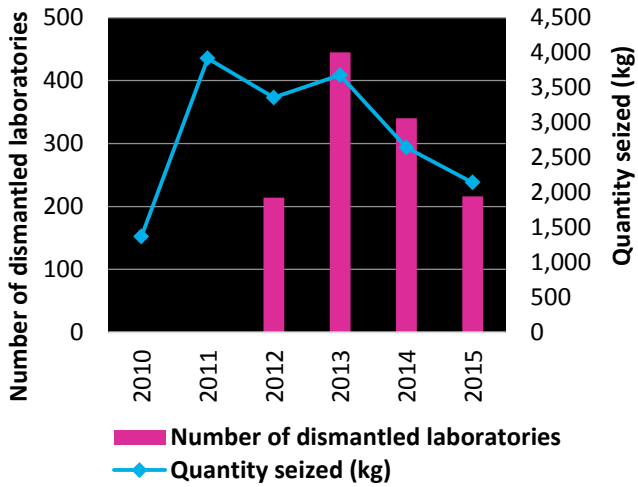
10 Australia, Department of the Prime Minister and Cabinet, *Final Report of the National Ice Taskforce 2015* (Canberra, 2015).

45.4 per cent in 2016.[11] Indeed, methamphetamine use in the United States continues to increase, with the annual prevalence of methamphetamine use among the general population aged 15-64 years rising from 0.5 per cent in 2012 to 0.8 per cent in 2015.

As well as persisting in regions such as Europe, where it has become consolidated in the past decades, the methamphetamine market is expanding into new geographical areas. Methamphetamine trafficking and use have emerged in Afghanistan, where, according to the records of the Ministry of Public Health, 908 methamphetamine users were registered at government treatment centres in Farah, Jawzjan, Kunduz and Nimroz provinces in the period 2011-2012.[12] In 2016, law enforcement agencies, health-care providers and treatment centres in certain parts of Afghanistan also perceived an increase in synthetic drug use, most of which was probably due to opiate users who also used methamphetamine. While the total annual quantity of methamphetamine seized in Afghanistan has, at less than 16 kg, remained quite small, the number of methamphetamine seizure reports in Afghanistan has increased. There are indications that some of the seized substance might have been manufactured domestically: a clandestine methamphetamine laboratory was detected in Nimroz Province in 2013. However, there continue to be significant gaps in the information and data relating to synthetic drugs in Afghanistan, and overall treatment figures and the prevalence of methamphetamine use among the general population are not well understood.[13]

In other parts of South-West Asia, such as the Islamic Republic of Iran, the methamphetamine market has a longer history, and, as in Afghanistan, there are indications that methamphetamine is used among opioid users.[14] In the Islamic Republic of Iran, both

FIG. 4 Quantity of methamphetamine seized and number of dismantled laboratories in the Islamic Republic of Iran, 2010-2015



Source: UNODC, responses to the annual report questionnaire from the Islamic Republic of Iran, 2010-2015.

methamphetamine seizure quantities and seizures of clandestine methamphetamine laboratories have declined since 2013. A large increase in methamphetamine use was perceived in that country in 2013; however, there is no recent information on prevalence of use trends, and it is not clear if and to what extent seizure trends reflect market developments.

Methamphetamine: trends in manufacture and precursors

Ephedrine and pseudoephedrine are two of the main precursors used in the manufacture of methamphetamine. Both chemicals have widespread legitimate use in the pharmaceutical industry, in bulk form and in the form of pharmaceutical preparations.[15] Historically, both ephedrine and pseudoephedrine in bulk form were the preferred precursors; however, because of increasingly strict controls in many countries, drug traffickers have diversified their approach and also diverted pharmaceutical preparations

11 United States, Drug Enforcement Administration, *2016 National Drug Threat Assessment Summary* (November 2016).

12 Afghanistan, Ministry of Public Health, Drug Demand Reduction Department, "Monthly treatment records", Hijri years 1390-1391 of the Islamic lunar calendar; Afghanistan, Ministry of Counter Narcotics, *Afghanistan Drug Report 2013,* (December 2014).

13 UNODC, "Afghanistan synthetic drugs situation assessment" (Vienna, January 2017).

14 Zahra Alam Mehrjerdi and Alireza Noroozi, "An emerging trend of methamphetamine injection in Iran: a critical target for research on blood-borne infection diseases", *Hepatitis Monthly,* vol. 13, No. 2. (2013).

15 *Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances: Report of the International Narcotics Control Board for 2014 on the Implementation of Article 12 of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988* (E/INCB/2014/4).

containing ephedrine or pseudoephedrine. As demonstrated in seizure data, 43 tons of the two precursors, in bulk form and 1 million tablets, were seized in 2013, with Australia, China, India, Mexico, Ukraine, the United Kingdom of Great Britain and Northern Ireland and the United States each reporting seizures greater than 1 ton. China alone reported a combined 16.7 tons of the two precursors seized in bulk form in 2013, 31.5 tons of bulk ephedrine in 2014 and 23.5 tons of that same precursor in 2015. India also reported seizures of more than 10 tons of ephedrine and 8.5 tons of pseudoephedrine in 2016.[16] Other notable seizures of pharmaceutical preparations in South-East Asia include seizures totalling 3.5 tons of pharmaceutical preparations of pseudoephedrine in Myanmar in 2013. The trend is not always towards the use of pharmaceutical preparations. Indeed, in recent years Australia and New Zealand have reported decreasing seizure quantities of preparations and increasing seizure quantities of ephedrine or pseudoephedrine in bulk form.[17, 18, 19, 20]

In order to circumvent controls on ephedrine and pseudoephedrine, traffickers started to use 1-phenyl-2-propanone (P-2-P) as their most common alternative. The first country where this shift became apparent was Mexico, where traffickers shifted their manufacturing to the use of P-2-P, as well as to the pre-precursor phenylacetic acid, a precursor of P-2-P, and its derivatives. From 2009 to 2012, when Mexico still reported large seizures of P-2-P, profiling data on methamphetamine from Mexico seized in the United States revealed that traffickers were already mainly using phenylacetic acid and its esters in the manufacture of methamphetamine. In 2013, multi-ton seizures of phenylacetic acid were reported by China (6.5 tons) and Mexico (3.3 tons). The use of P-2-P-based methods seems to have expanded beyond Mexico, with seizures of P-2-P reported by Bulgaria in 2013[21] and Myanmar in 2014. Large seizures of P-2-P were also reported in 2014 by Mexico, China, Poland, Lithuania and the Netherlands (in descending order of seizure amounts), and, similarly, seizures were reported in 2015, with Mexico (more than 16,500 litres), Poland (almost 7,000 litres) and China (almost 5,500 litres) being the most predominant. Notable seizure amounts were also reported that year by Myanmar[22] (seizures of P-2-P) and Lebanon (16 tons of phenylacetic acid).[23]

Seizure data indicate that other chemicals that are not under international control may be used to manufacture methamphetamine and its precursors. Mexico has reported large seizures of ethyl phenylacetate: 520 kg and 12,000 litres in 2013 and 63 tons in 2014. Notable seizures of other pre-precursors included 8 tons of 2-phenylacetamide in Mexico and 10 tons of benzaldehyde in Australia in 2013/14, although methamphetamine produced in Australia is primarily manufactured from ephedrine and pseudoephedrine.[24] In 2015, Mexico also reported seizing more than 4,000 litres of benzaldehyde and almost 5,500 litres of 1-phenyl-2-nitropropene (the product resulting from the reaction of benzaldehyde and nitroethane).[25] Profiling of methamphetamine seized in the United States in 2014-2015 reflected this by showing a significant increase in the use of benzaldehyde and nitroethane in the manufacture of P-2-P, which illustrates once again how drug trafficking organizations have adapted their approach in accordance with the availability of precursor chemicals.[26]

16 *Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances: Report of the International Narcotics Control Board for 2016 on the Implementation of Article 12 of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988* (E/INCB/2016/4).

17 *Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances: Report of the International Narcotics Control Board for 2015 on the Implementation of Article 12 of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988* (E/INCB/2015/4).

18 Australian Crime Commission, *Illicit Drug Data Report 2012-13* (Canberra, April 2014).

19 Ibid., *Illicit Drug Data Report 2013-14* (Canberra, May 2015).

20 Ibid., *Illicit Drug Data Report 2014-15* (Canberra, May 2016).

21 E/INCB/2014/4.

22 Asia and Pacific Amphetamine-type Information Centre (APAIC), Synthetic drugs trends, National trends: Myanmar, 14 February 2017. Available at www.apaic.org.

23 E/INCB/2016/4.

24 *Illicit Drug Data Report 2012-13, Illicit Drug Data Report 2013-14* and *Illicit Drug Data Report 2014-15.*

25 E/INCB/2016/4.

26 Ibid.; United States, Drug Enforcement Administration,

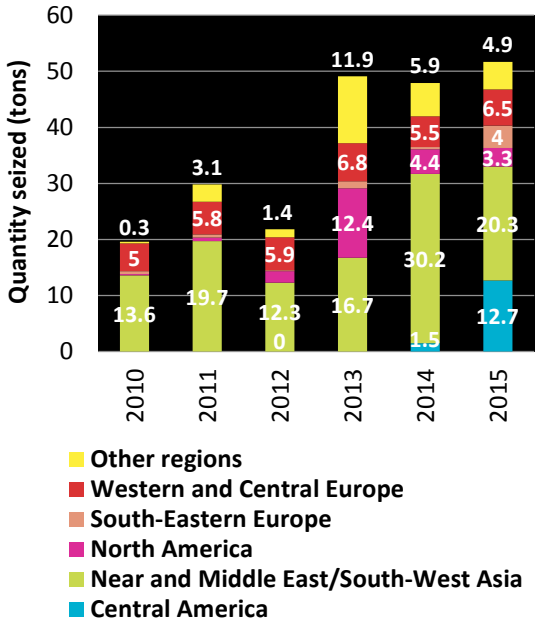
A.3. Amphetamine trafficking is spreading

In contrast to methamphetamine, amphetamine has been confined to fewer subregions, and seizures show stabilizing trends at the global level. Amphetamine has long been a prominent feature of synthetic drug markets in the Near and Middle East and Western and Central Europe, but there are signs of increasing seizures in South-Eastern Europe, which is mainly related to the large amphetamine market in the neighbouring Near and Middle East. From very low levels, quantities of amphetamine seized in Central America have increased greatly since 2014, but the reasons for this development remain unclear.

In the Near and Middle East, amphetamine continues to be extensively trafficked on an intraregional basis. In 2013 and 2014, amphetamine was primarily reported to have been trafficked within the subregion from Jordan, Lebanon and the Syrian Arab Republic to countries such as Israel, Jordan, Qatar, Saudi Arabia and the United Arab Emirates. However, recent seizure reports indicate that countries outside the region are also feeding the amphetamine market in the Near and Middle East.[27] It remains to be seen whether these new reports of amphetamine trafficking from outside the subregion indicate the development of new routes.

Recently, a large increase in amphetamine seizures has been reported in South-Eastern Europe, which may be related to the expansion of amphetamine trafficked in the neighbouring Near and Middle East. In 2015, the amount of amphetamine seized in South-Eastern Europe accounted for an 8 per cent share of global amphetamine seizures, increasing from less than 0.5 tons of amphetamine seized in 2014 to almost 4 tons in 2015. The increase in amphetamine seizures in South-Eastern Europe is primarily due to the increase in seizures reported in Turkey, which went up from 0.2 tons in 2014 to 3.8 tons in 2015. Although further information on the amphetamine situation in Turkey is not available for those years, earlier reports from the national authorities in 2013 point to an expansion in the trafficking of amphetamine tablets labelled with the brand name "captagon".[28] According to the Turkish National Police, "captagon" seizures in 2013 mostly occurred in Turkish provinces such as Hatay and Gaziantep, located along the border with the Syrian Arab Republic. Turkish authorities suspect that amphetamine seizures in the country are linked to "captagon" trafficking in the Near and Middle East, for which Turkey functions as both a transit and destination country. For instance, in 2013, Turkish authorities found that a consignment of "captagon" seized in Hatay Province had been manufactured in the Syrian Arab Republic and was destined for the Arabian Peninsula, with Turkey as a transit country.[29]

FIG. 5 Quantities of amphetamine seized worldwide, by region, 2010-2015



Source: UNODC, responses to annual report questionnaire, 2010-2015.

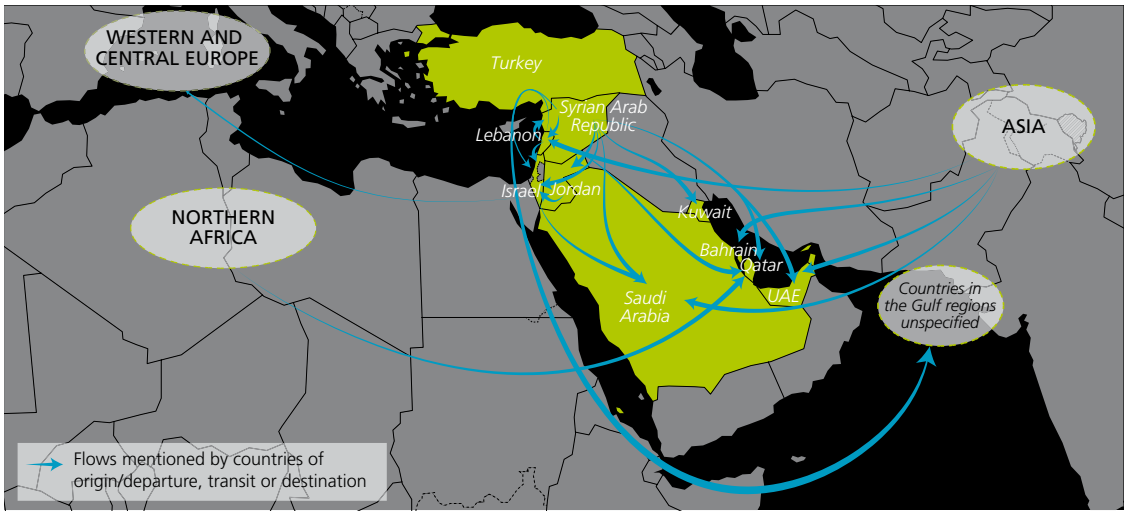
2016 National Drug Threat Assessment Summary.

27 Individual drug seizures reported to UNODC for the period 2014-2015 and drug seizures reported in the media from March 2014 to November 2015.

28 See box on page 15.

29 European Monitoring Centre for Drugs and Drug Addiction, *2014 National Report (2013 Data) to the EMCDDA by the Reitox National Focal Point: Turkey – New Development, Trends and In-Depth Information on Selected Issues* (Ankara, Turkish Monitoring Centre for Drugs and Drug Addiction, 2014).

MAP 2 | Amphetamine and "captagon" trafficking flows with countries in the Near and Middle East reported as provenance or destination, 2014-2015



Source: UNODC, responses to annual report questionnaire, 2014-2015, and official communication.

Note: The origins of the flow arrows do not necessarily indicate the source/manufacture of amphetamine/"captagon". Flow arrows represent the direction of trafficking and are not an indicator of the quantity trafficked. The boundaries shown on this map do not imply official endorsement or acceptance by the United Nations. Dashed lines represent undetermined boundaries. The dotted line represents approximately the Line of Control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. The final boundary between the Sudan and South Sudan has not yet been determined.

The manufacture and trafficking of amphetamine in Western and Central Europe is intraregional and amphetamine constitutes the most important ATS in terms of quantities seized. In 2015, countries in that subregion identified only countries within the same subregion as the origin of their amphetamine seizures, with six countries reporting the Netherlands as a country of origin and five reporting Poland.[30]

Amphetamine manufacture has been reported in a number of countries in Europe. In the period 2014-2015, amphetamine laboratories were discovered in Austria, Belgium, Germany, Hungary, Latvia, the Netherlands, Poland, Spain and Sweden. The largest number of amphetamine laboratories dismantled was in Belgium (14) and in Germany (13), but the Netherlands also reported a large number of laboratories dismantled.[31] Most amphetamine laboratories discovered in Western and Central Europe in the period 2014-2015 were small-scale, with the exception of those in Belgium, Poland and Sweden, where some were also medium-sized. P-2-P is the primary precursor used for the manufacture of amphetamine in Europe, and in recent years the emergence of a pre-precursor to P-2-P, namely *alpha*-phenylacetoacetonitrile (APAAN), has been seen in a number of countries. Since its international scheduling in 2013, increased seizures of APAAN have been reported, including 5.4 tons in Belgium, more than 1 ton in Estonia and 180 kg in Lithuania. A total of 43.5 tons were seized in 2013, and while seizures decreased in 2014, 11 tons of the substance were seized, including 5.1 tons seized in Germany, 3 tons seized in the Netherlands and 2 tons seized in Bulgaria. Seizures of APAAN continued to decrease in 2015, with slightly more than 1.5 tons in total being reported by five countries.[32]

There has been a recent surge in amphetamine seizures in Central America. In 2015, around 25 per cent of global amphetamine seizures were in that region, increasing from 1.5 tons in 2014 to 12.7 tons in 2015. This large increase in amphetamine seizures is almost entirely attributable to the increase

30 These countries include Austria, Czechia, Denmark, Poland and Sweden.

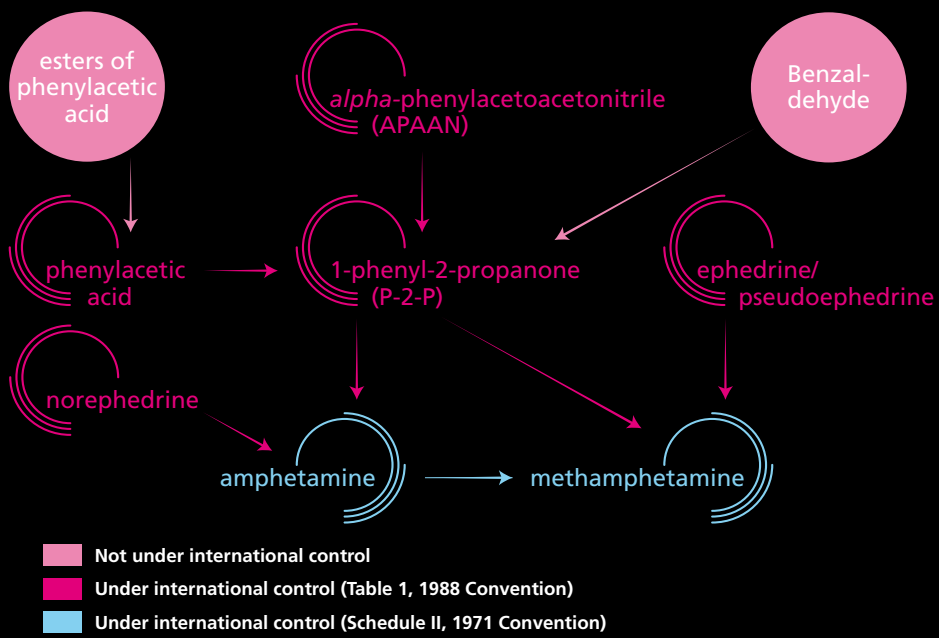
31 The Netherlands reported the dismantling of a total of 59 "ecstasy"/amphetamine laboratories in 2015. Disaggregated figures by manufactured drug were not available.

32 E/INCB/2015/4.

Amphetamine and methamphetamine: trends in manufacture

The illicit production of synthetic drugs, by nature, requires the use of precursor chemicals. In general, the clandestine manufacture and production of such substances is highly flexible, and a wide range of precursor chemicals can be used. Detected trends in the precursor chemicals used in the illicit manufacture of synthetic drugs provide important information that contributes to a more comprehensive understanding of synthetic drug markets, particularly for law enforcement authorities, forensic scientists and customs personnel in their respective roles in tackling the global trade in illicit drugs. The figure below shows the different substances that are typically used to manufacture amphetamine and methamphetamine, differentiating those that are not under international control. This helps understanding of how drug trafficking organizations attempt to modify their approaches and alter their manufacturing methods in response to national/international control and the efforts of law enforcement and industry in targeting and preventing the diversion of chemicals.

Precursors for amphetamine and methamphetamine



Source: UNODC, Laboratory and Scientific Section.

reported in Guatemala, where national authorities have reported amphetamine manufacture. Between 2013 and 2015, Guatemala reported having dismantled four or five amphetamine laboratories annually. However, the trafficking routes for the amphetamine manufactured in Central America remain unclear. In 2014 and 2015, Guatemala perceived Honduras and El Salvador to be the provenance of the amphetamine seized domestically, yet there are no indications of an expanding domestic market for amphetamine in Guatemala. Although large amounts of amphetamine have also been seized in North America, there are no clear indications that amphetamine seized in Central America is significantly connected to the North American amphetamine market. For example, Mexico has identified El Salvador only once as a departure country for amphetamine seized — in 2013.

A.4. "Ecstasy"

"Ecstasy" products are increasingly diversified

"Ecstasy" is a term that has traditionally been used to describe tablets containing 3,4-methylenedioxymethamphetamine (MDMA). In the past decade, however, the "ecstasy" market has undergone major

changes and has grown in complexity. Available products branded as "ecstasy" are now increasingly diversified, the three main types being "ecstasy" tablets containing little or no MDMA, "ecstasy" tablets with an extremely high content of high-purity MDMA, and "ecstasy" sold in powder/crystal form, under different street names.

Sales of tablets branded as "ecstasy" containing little or no MDMA have surged worldwide since a global plunge in MDMA supply towards the end of the previous decade following large seizures of precursors. These tablets often contain adulterants/substitutes, including a range of NPS, some of which have proved dangerous (see box). The reaction of consumers to the sale of adulterated/substituted "ecstasy" tablets has possibly led to the creation of a market niche for "ecstasy" in powder/crystal form, which is considered by users to contain MDMA of high purity (although powder is actually easier to adulterate than other forms and nowadays often contains NPS).[33, 34] User preference for powder or crystalline MDMA remains a regional phenomenon, but it is particularly prominent in North America, Western and Central Europe and Oceania.

In recent years, the market has seen the emergence of "ecstasy" tablets with a much higher content of MDMA than in the past, which tend to have very distinct shapes, colours and logos, most likely for branding purposes. This phenomenon has been linked to the apparent recovery of the "ecstasy" market (in terms of increased supply, use and improved quality of available products) seen in recent years, particularly in Europe.[35]

Manufacture and trafficking of "ecstasy" are spreading to other regions

According to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and the European Police Office (Europol), the Netherlands and Belgium are the most important areas for MDMA manufacture in Europe, where the professionalism of manufacturing facilities is increasing.[36] The manufacture of "ecstasy" is also occurring in other regions and subregions, including Asia, North America, Oceania and South America.

Annual "ecstasy" seizures have averaged around 4-5 tons since 2010, except for a peak in 2014 when they reached 9 tons. The 2014 peak can be explained by unusually large seizures in Australia, which exceeded 4 tons, as well as the more than 700 kg of

PMMA sold as "ecstasy", with deadly consequences

One example of adulterated "ecstasy" are tablets containing para-methoxymethamphetamine (PMMA), an MDMA substitute with a slower onset of action than other forms, which does not produce the same euphoric/empathogenic effects. Unsuspecting users ingesting PMMA-adulterated tablets may assume that the dose is too low and take greater amounts, which may lead to intoxication. PMMA has been associated with fatalities in several European countries, the first of which occurred in Spain in 1993,[a] and later in Canada.[b] Since 2009, the sale of PMMA-adulterated "ecstasy" tablets has intensified and seems to endure (PMMA has been reported in Australia, Belgium, Brunei Darussalam, Bulgaria, Colombia, Croatia, Estonia, Finland, France, Greece, Indonesia, Ireland, Israel, Italy, Japan, the Netherlands, Norway, Poland, the Republic of Korea, Romania, the Russian Federation, Singapore, Slovakia and Spain, and Hong Kong, China).[c] In 2016, PMMA was linked with five deaths in Argentina, and the Trimbos Institute issued a red alert after pink "Superman" pills containing PMMA reappeared in the Netherlands.[d]

a EMCDDA, *Report on the Risk Assessment of PMMA in the Framework of the Joint Action on New Synthetic Drugs* (Luxembourg, Publications Office of the European Union, 2003).

b Jennifer J. E. Nicol and others, "Deaths from exposure to paramethoxymethamphetamine in Alberta and British Columbia, Canada: a case series", *CMAJ Open*, vol. 3, No. 1 (2015), pp. E83-E90.

c UNODC early warning advisory on new psychoactive substances.

d For further information, see www.trimbos.nl.

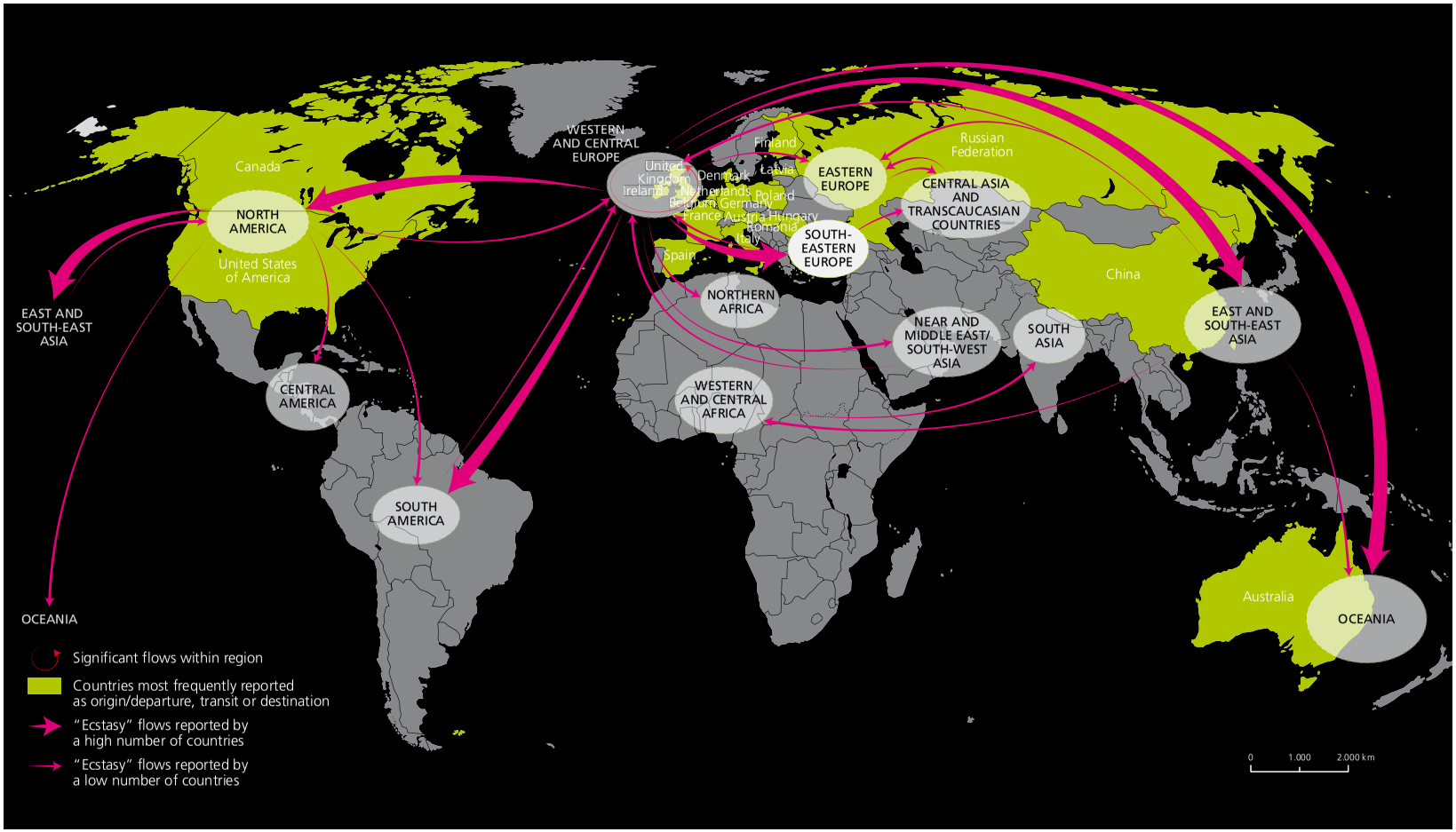
33 Joseph J. Palamar, "There's something about Molly: the underresearched yet popular powder form of ecstasy in the United States", *Substance Abuse,* vol. 38, No. 1 (2017).

34 Claudio Vidal Giné and others, "Crystals and tablets in the Spanish ecstasy market 2000-2014: are they the same or different in terms of purity and adulteration? *Forensic Science International,* vol. 263 (2016), pp. 164-168.

35 EMCDDA, *Recent Changes in Europe's MDMA/Ecstasy Market: Results from an EMCDDA Trendspotter Study,* EMCDDA Rapid Communication Series (Luxembourg, Publications Office of the European Union, 2016).

36 EMCDDA and Europol, *EU Drug Markets Report: In-Depth Analysis,* Joint Publications Series (Luxembourg, Publications Office of the European Union, 2016).

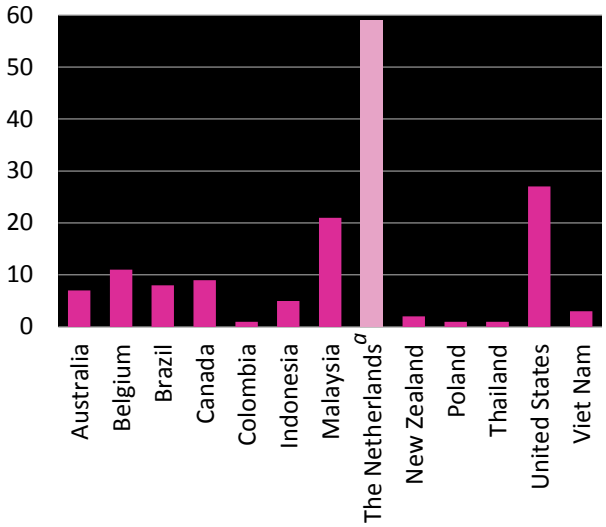
MAP 3 | Interregional trafficking flows of "ecstasy", 2012-2015



Source: UNODC, responses to annual report questionnaire, 2012-2015.

Note: The origins of the flow arrows do not necessarily indicate the source/manufacture of "ecstasy". Flow arrows represent the direction of "ecstasy" trafficking and are not an indication of the quantity trafficked. The boundaries shown on this map do not imply official endorsement or acceptance by the United Nations. Dashed lines represent undetermined boundaries. The dotted line represents approximately the Line of Control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. The final boundary between the Sudan and South Sudan has not yet been determined.

FIG. 6 Number of seized facilities related to the manufacture of "ecstasy", 2013-2015



Source: UNODC, responses to annual report questionnaire, 2013-2015.

Note: Data consist mostly of dismantled manufacturing sites; a small number of storage facilities and dumping sites were also reported and included in the figure.

[a] *The Netherlands reported the seizure of a total of 59 "ecstasy"/amphetamine laboratories in 2015. Disaggregated figures by manufactured drug were not available.*

"ecstasy" pills seized in Myanmar that same year. In 2015, quantities of "ecstasy" intercepted fell to 6 tons, with Europe accounting for almost 4 tons and Asia, the Americas and Oceania each accounting for less than 1 ton.

Data on dismantled facilities manufacturing "ecstasy", together with seizure statistics, suggest trafficking dynamics that originate mainly in Western and Central Europe. East and South-East Asia is a major destination for consignments originating in Europe or North America, with certain countries appearing to be important transit points. Oceania is on the receiving end of extensive "ecstasy" trafficking from Europe, either directly or through East and South-East Asia. The Americas are an important destination for consignments from Europe, with North America also being the origin of shipments destined for East and South-East Asia (see map 3). Further insight into MDMA trafficking flows in North America has been provided by a recent study that used wholesale prices of MDMA in 59 cities in the United States to infer trafficking patterns. The analysis identified low prices in cities adjacent to the Canadian and Mexican borders, indicating the hub-like or source-like status of those cities.[37]

Developments in regional "ecstasy" markets

The European "ecstasy" market seems to be expanding. Evidence of this are the industrial-scale MDMA manufacturing facilities being encountered by law enforcement agencies, increasing quantities of "ecstasy" being seized, increasing trends in the use of "ecstasy", aggressive marketing and branding, and growing concerns over "ecstasy" tablets with high MDMA content. The market for "ecstasy" in Europe is estimated to be worth at least 0.67 billion euros per annum.[38] European "ecstasy" seizures increased from 2013 to 2015, reaching almost 4 tons, while recent surveys indicate an overall increase in the use of "ecstasy" in Europe.[39]

"Ecstasy" has a strong presence in the North American market. While use is stable, increasing MDMA purity in "ecstasy" products is an indication that the market is recovering. In recent years, several facilities manufacturing MDMA have been dismantled in Canada and the United States. Canada has reported a large increase in "ecstasy" use, with the estimated number of users rising from about 100,000 in 2014 to over 200,000 in 2015. The prevalence of "ecstasy" use in the United States seems, however, to have remained stable between 2013 and 2015, with the number of users estimated at around 2.5 million. Data collected on the composition of street "ecstasy" tablets in the United States indicate a strong decrease in "ecstasy" tablet adulteration between 2009 and 2016, with MDMA being the only psychoactive component in almost half of "ecstasy" tablets tested in 2016 (a dramatic increase in MDMA content compared with the corresponding figure of 8.7 per cent in 2009).[40] In particular, there has been a dramatic drop in the number of tablets containing stimulant adulterants.

37 Siddharth Chandra, Yan-Liang Yu and Vinay Bihani, "How MDMA flows across the USA: evidence from price data", *Global Crime,* vol. 18, No. 2 (2016).

38 EMCDDA and Europol, *EU Drug Markets Report: In-Depth Analysis.*

39 EMCDDA, *European Drug Report: Trends and Developments 2016.* (Luxembourg, Publications Office of the European Union, 2016).

40 For further information, see www.ecstasydata.org/stats.php.

The trafficking of "ecstasy" to North America appears to be on the increase. In 2015, the number of seizures of MDMA trafficked to Canada increased by 109 per cent from the previous year, and the quantities increased by 513 per cent (throughout 2015, trafficking activities targeting Canada from the Netherlands increased significantly). Canada is known as a source and transit country for MDMA destined for the United States and other international markets, and Asian organized criminal groups are active in the cross-border smuggling of large quantities of MDMA between Canada and the United States as well as in the importation of precursor chemicals from source countries such as China, India and Viet Nam.

Data on the development of the "ecstasy" market in Latin America remain limited. According to the Inter-American Drug Abuse Control Commission (CICAD), "ecstasy" is the most widely used ATS in Latin America (and in the Americas as a whole), although its market share still seems to be relatively low compared with that of other drugs under international control. In some countries there is great concern over the use of "ecstasy" at a very young age, among secondary school students.[41] A study on the composition of "ecstasy" tablets in Brazil, conducted on samples from 150 different seizures made by Sao Paulo State Police (from August 2011 to July 2012) documented a strong trend in tablet adulteration; one particularly surprising result was the presence of methamphetamine in 22 per cent of the tablets analysed.[42] Seizures of "ecstasy"-type substances are generally low in Latin America. However, Brazil reported considerable amounts seized in 2014 (238 kg) and 2015 (153 kg). In Argentina, a record amount (180 kg) of "ecstasy" was seized in 2014, compared with only 20 kg in 2015. Chile and Colombia reported "ecstasy" seizures exceeding 30 kg, which was a dramatic increase from 2014, when only 2 kg were seized in Chile and 5 kg were seized in Colombia.

Oceania is an increasingly important market for "ecstasy". In Australia, according to the Ecstasy and Related Drugs Reporting System, pills remain the most popular form of "ecstasy" consumed regularly. However, the trend in the use of MDMA crystal (also known in Australia under the street name "rock"), first recorded in 2013, continues to increase. This form of MDMA is perceived to be more pure and potent than pills, powder and capsules, as reported by 54 per cent of MDMA crystal users. All forms of "ecstasy" were reported as being "easy" to "very easy" to obtain, and prices remained stable at about 25 Australian dollars per pill, 30 Australian dollars per capsule and 200 Australian dollars per gram of crystal MDMA.[43] Australia reported record "ecstasy" seizures in 2014, which exceeded 4 tons; however, seizures reported in 2015 amounted to less than 700 kg. Another recent development is the trafficking of MDMA in masked form as N-tert-butoxycarbonyl-MDMA. In September 2015, 80 litres of this substance were seized by the Australian Border Force.[44] In New Zealand, yearly seizures of "ecstasy" have been fluctuating between 5 and 50 kg since 2010.

In East and South-East Asia, many countries report seizures and use of "ecstasy"; however, pills sold as "ecstasy" in these areas may contain substances other than MDMA. Singapore reported an "ecstasy" purity of 36 per cent in 2015, a significant increase compared with the figures reported in the five preceding years (a range of 15.7-24.2 per cent). The retail price of "ecstasy" in Singapore has remained stable over the past five years at between approximately $18 and $22 per pill.[45] Further research is required to understand whether that steep increase in purity while prices remained stable indicates a greater availability of MDMA, as observed in other subregions.

41 Inter-American Drug Abuse Control Commission of the Organization of American States, *Report on Drug Use in the Americas*, *2015* (Washington D.C., 2015).

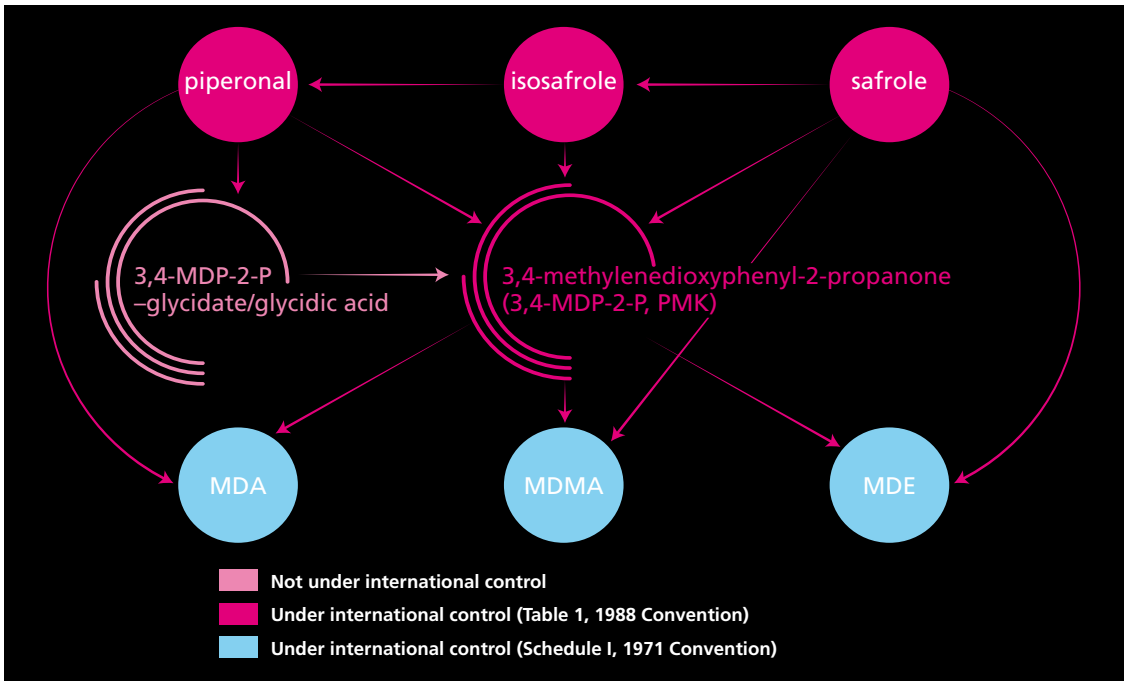
42 Loraine R.Togni and others, "The variability of ecstasy tablets composition in Brazil", *Journal of Forensic Sciences,* vol. 60, No. 1 (2015), pp.147-151.

43 Jennifer Stafford and others, "The 2016 EDRS key findings: a survey of people who regularly use psychostimulant drugs", *EDRS Drug Trends Bulletin* (Sydney, University of New South Wales, National Drug and Alcohol Research Centre, October 2016).

44 Michael Collins and others, "Identification and characterization of N-*tert*-butoxycarbonyl-MDMA: a new MDMA precursor", *Drug Testing and Analysis,* vol. 9, No. 3 (2016).

45 APAIC, Synthetic drug trends, National trends: Singapore, 1 December 2014. Available at www.apaic.org.

FIG. 7 | Precursors for "ecstasy"-type substances



Source: UNODC, Laboratory and Scientific Section.

Certain countries in the subregion seem to be involved in the trafficking of "ecstasy" or MDMA precursors. The large "ecstasy" seizure made in Myanmar in 2014 raised questions about the level of trafficking in that country and its role as a transit point. Before and after 2014, Myanmar reported insignificant quantities of "ecstasy" seized, but in 2014 itself a total of nearly 2.4 million "ecstasy" pills containing MDMA were seized in one single case, off the coast of Tanintharyi.[46] The seized pills were destined for Malaysia, which has been perceived to be a transit country for "ecstasy" by several countries, including Brunei Darussalam, New Zealand and Singapore, in recent years. Large quantities of "ecstasy" pills have also been seized in Malaysia in recent years, with some 408,000 "ecstasy" pills being seized in the country in 2015. Transnational drug trafficking groups are increasingly targeting Malaysia as both a destination and transit country for methamphetamine and other illicit drugs, as well as for the manufacture of MDMA to produce "ecstasy" pills.[47] Indonesia reported significant annual seizure amounts in the period 2010-2015, which oscillated between 0.1 tons and 1.3 tons. In Cambodia, the national authorities have made several significant seizures of precursor chemicals related to ATS manufacture in recent years. In particular, safrole-rich oils, one of the key precursor chemicals used in the manufacture of "ecstasy", continue to be produced in the country and trafficked to other countries and regions, including Europe. For instance, in August 2014, approximately 5,220 kg of safrole-rich oils was found by the police buried underground in Pursat Province, near the Gulf of Thailand in the western part of the country. A further 110 litres of safrole-rich oils were reported seized in the same province in May 2016.[48]

Recent trends in "ecstasy" precursors

A number of precursor chemicals are commonly used for the manufacture of "ecstasy"-group

46 APAIC, Synthetic drug trends, National trends: Myanmar, 14 February 2017. Available at www.apaic.org.

47 APAIC, Synthetic drug trends, National trends: Malaysia, 14 February 2017. Available at www.apaic.org.

48 APAIC, Synthetic drug trends, National trends: Cambodia, 14 February 2017. Available at www.apaic.org.

substances, which are controlled under the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988. Of these, piperonal, safrole (including in the form of safrole-rich oils) and isosafrole are used in the chemical and pharmaceutical industries and are thus susceptible to diversion from licit trade. The other most common precursor is 3,4-methylenedioxyphenyl-2-propanone (3,4-MDP-2-P or PMK), which itself has little or no legitimate use. Seizures of these precursors have fluctuated in recent years, with seizures of 3,4-MDP-2-P reported by Belgium (2,700 litres) and Slovenia (900 litres), and the Netherlands reporting the seizure of 14,000 litres of safrole-rich oils, in 2013. By contrast, significantly smaller seizures were reported later in the period 2014-2015, although notable amounts were seized by Namibia (2,100 litres of isosafrole) and Canada (1,500 litres of safrole-rich oils).[49, 50, 51]

The most notable development in the area of precursors for "ecstasy"-group substances in recent years parallels the situation with methamphetamine manufacture, in that drug traffickers appear to be using increasing amounts of non-controlled pre-precursor chemicals. In particular, the methyl glycidate ester and sodium glycidic salt of 3,4-MDP-2-P have been reported by a number of countries in the last two to three years. The identification of 3,4-MDP-2-P methyl glycidate in the clandestine manufacture of "ecstasy"-group substances was first identified in the Netherlands in 2010.[52] In recent years, large amounts of variants of 3,4-MDP-2-P methyl glycidate have been seized, with Slovenia (1.2 tons) and China (1.5 tons) reporting seizures of 3,4-MDP-2-P glycidic acid in 2013. Seizures of the methyl ester or sodium salt of 3,4-MDP-2-P totalling an equivalent of 1 ton or more were reported by Belgium, Bulgaria,[53] Germany, the Netherlands, Romania and Spain in 2014-16 (INCB).[54, 55, 56] Given that 3,4-MDP-2-P methyl glycidate can be manufactured from piperonal,[57] it is likely that this transformation is being carried out by drug trafficking organizations to mask controlled precursors and bypass national and international controls.

B. NEW PSYCHOACTIVE SUBSTANCES AND OTHER SYNTHETIC DRUGS

B.1. New psychoactive substances: market developments

New psychoactive substances (NPS) are substances of abuse that have similar effects to drugs under international control such as cannabis, cocaine, heroin, (+)-lysergide (LSD), MDMA ("ecstasy") and methamphetamine. A phenomenon reported by an increasing number of countries from 2009 onwards, this has since become a truly global issue, with over 100 countries and territories in all regions having reported the emergence of NPS.

Indeed, NPS are proliferating at an unprecedented rate and pose a significant risk to public health and a challenge to drug policy. More information on the prevalence of use of NPS has become available in recent years, ranging from representative population-based surveys among the general population or youth to qualitative, small-scale studies among specific user groups such as homeless persons or persons in prison settings. While the availability of more information on the prevalence of NPS use suggests that NPS use could be spreading, the increase may be partly due to improved survey instruments, which capture NPS use better than before, and increased research interest in the topic. That said, an overall assessment of NPS use and use trends remains difficult. More evidence continues to emerge about the harmful effects of NPS use, some of which is presented in this report (see the chapter on synthetic

49 E/INCB/2014/4.

50 E/INCB/2015/4.

51 E/INCB/2016/4.

52 *Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances: Report of the International Narcotics Control Board for 2011 on the Implementation of Article 12 of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988* (E/INCB/2011/4).

53 E/INCB/2016/4.

54 E/INCB/2014/4.

55 E/INCB/2015/4.

56 E/INCB/2016/4.

57 Michael Collins and others, "Methyl 3-[3',4'-(methylenedioxy)phenyl]-2-methyl glycidate: an ecstasy precursor seized in Sydney, Australia", *Journal of Forensic Science,* vol. 52, No. 4 (2007), pp. 898-903.

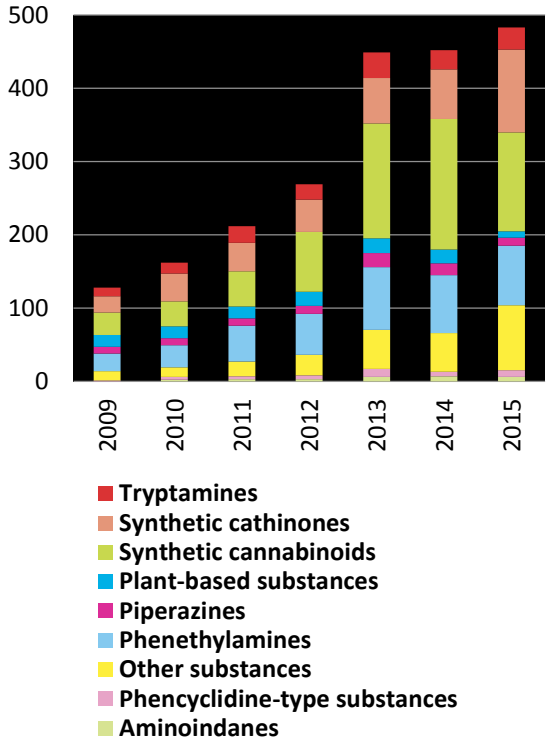
cannabinoids and synthetic opioids). Data on toxicity, the long-term effects and risk of use remain limited for many NPS.

For the purpose of this report, NPS are defined as substances, whether in a pure form or a preparation, which are not controlled by the international drug control conventions but which may pose a public health threat. In that context, the term "new" does not necessarily refer to new inventions but to substances that have recently become available.[58] The global analysis of NPS includes ketamine, which differs from other NPS in that it is widely used in human and veterinary medicine, while most NPS have little or no history of medical use. A number of NPS have been placed under international control since 2015 and are thus, by definition, no longer NPS. However, as this report also covers years when they were not yet under international control, and the granularity of the data does not always allow a separate analysis, they have been included in the NPS analysis unless otherwise indicated. When individual NPS are discussed, their control status (to date) with respect to the international drug control conventions is indicated in a footnote. NPS can be categorized in terms of similarity in chemical structure (for example, phenethylamines, tryptamines) and/or by their major pharmacological effects (for example, cannabinoid receptor agonists). Similarity in chemical structure does not always reflect identical pharmacological effects and a known pharmacological effect can be produced by NPS of dissimilar chemical structure. For the purpose of this report, NPS data are presented in eight categories. A final category labelled "others" covers substances of poorly understood pharmacological effects and/or miscellaneous chemical structures.

New psychoactive substances continue to spread

The global NPS market continues to be characterized by the emergence of large numbers of new substances belonging to diverse chemical groups. From 2009 and 2016, 106 countries and territories reported the emergence of a cumulative total of 739 different NPS to UNODC. Not all NPS are reported every single year, but an increasing number is being reported. Since the start of monitoring by UNODC, the number of different NPS reported each year has increased year on year, reaching almost 500 different substances in 2015.

FIG. 8 Number of different new psychoactive substances reported each year, 2009-2015



Source: UNODC, early warning advisory on new psychoactive substances.

Undergoing periods of both innovation and stagnation, the NPS market continues to be very dynamic. New substances continue to emerge; some NPS have been in the market for years, and others disappear over time. Data collection for 2016 is still ongoing, but in 2015, 100 NPS were reported globally for the first time, a two-thirds increase on the 66 NPS reported for the first time in 2014. However, at the time of writing, over 70 NPS never previously reported were registered by UNODC for 2016, which seems to indicate that "innovation" continues to be an important element of the NPS market. Yet there is a core group of over 80 NPS that show resilience in the global market, having been reported every year from 2009 to 2015. This group includes several synthetic cannabinoids of the JWH series,

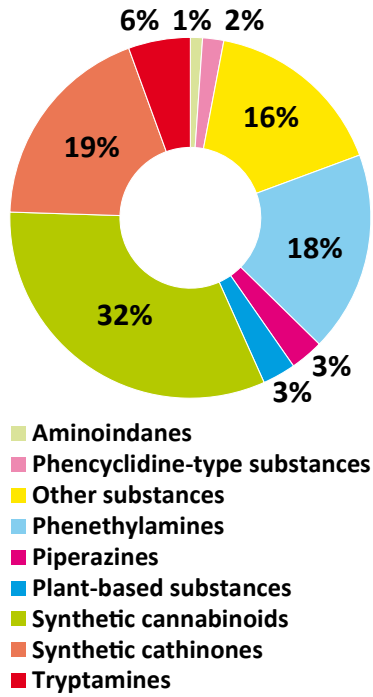
58 UNODC, *The Challenge of New Psychoactive Substances*, (Vienna, March 2013).

mephedrone and derivatives, several amphetamine analogues and piperazines, as well as a number of tryptamines and 2C-B analogues. A number of these persistent NPS were placed under international control in 2015 and 2016, including *alpha*-PVP, BZP, JWH-018, MDPV, mephedrone, methylone and PMMA.[59] While this persistence at the global level does not necessarily indicate widespread use, it suggests that some NPS have a longer "shelf-life" than others. On the other hand, about 60 NPS left the market after 2013, although it is more challenging to determine the group of NPS that have "disappeared" as a lack of reports may also be due to problems identifying these lesser known substances in the laboratory.

Among all the NPS reported to UNODC by the end of 2016, synthetic cannabinoids constitute the largest category in terms of the number of different substances reported, followed by synthetic cathinones and phenethylamines. Only a comparatively small number of tryptamines, piperazines, aminoindanes and plant-based NPS are reported annually, and those categories constitute only a small proportion of the total number of NPS. The number of NPS per category does not necessarily correspond to market share or prevalence of use. More evidence has become available on the severe adverse health consequences associated with the use of NPS, for example, synthetic cannabinoids (see chapters B.4 and B.5, below).

The category of "other substances", which combines structurally diverse substances, has experienced considerable growth since 2013 in terms of the number of substances reported. This is mainly down to the emergence of NPS-derivatives of prescription medicines, including 18 fentanyl analogues as well as derivatives of benzodiazepine and methylphenidate.[60] The emergence of fentanyl analogues, in particular, has been associated with rising numbers of overdose events among opioid users, including fatal intoxications (see chapter B.7, below; and booklet 2).

FIG. 9 Proportion of new psychoactive substances, by substance category, December 2016



Source: UNODC, early warning advisory on new psychoactive substances. Based on the analysis of 739 NPS.

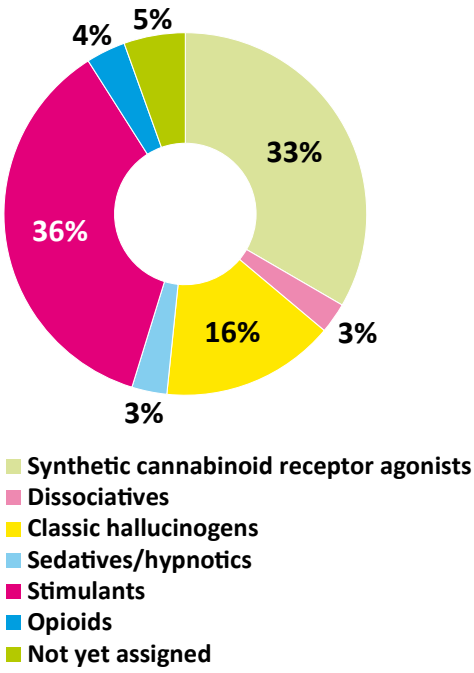
The proportion of new psychoactive substances with stimulant effects is on the increase

Notwithstanding the definition of NPS, those sold on drug markets may or may not have effects and profiles similar to those of the substances under international control that they are designed to mimic. Analysis of the pharmacological effects of NPS reported up to December 2016 revealed that the majority of the substances were stimulants, synthetic cannabinoid receptor agonists and classic hallucinogens. The number and proportion of NPS with stimulant properties has increased in recent years, whereas the proportion of synthetic cannabinoid receptor agonists, despite growth in numbers

59 *alpha*-Pyrrolidinovalerophenone (*alpha*-PVP) was placed under international control in 2016 (Schedule II of the 1971 Convention). *N*-benzylpiperazine (BZP), (1-pentyl-1*H*-indol-3-yl)-1-naphthalenyl-methanone (JWH-018), 3,4-methylenedioxypyrovalerone (MDPV), mephedrone and methylone were placed under international control in 2015 (Schedule II of the 1971 Convention). *Para*-methoxymethylamphetamine (PMMA) was placed under international control in 2016 (Schedule I of the 1971 Convention).

60 Methylphenidate was placed under international control in 1971 (original list, Schedule II of the 1971 Convention).

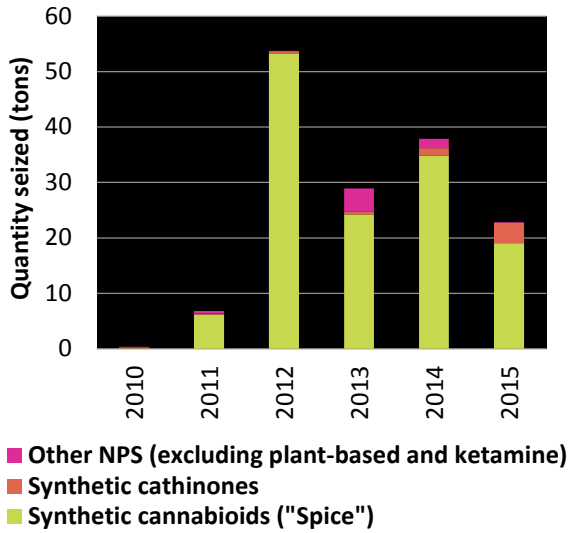
FIG. 10 Proportion of new psychoactive substances, by pharmacological effect, December 2016



Source: UNODC, early warning advisory on new psychoactive substances. Based on the analysis of 717 NPS.

Note: The analysis of the pharmacological effects comprises NPS registered up to December 2016. Plant-based substances were excluded from the analysis as they usually contain a large number of different substances some of which may not have been known and whose effects and interactions are not fully understood.

FIG. 11 Annual amounts of synthetic new psychoactive substances seized globally, 2010-2015



Source: UNODC, responses to annual report questionnaire, 2010-2015.

Note: Figures exclude plant-based NPS and ketamine.

in absolute terms, has decreased relative to other effect groups. Although still small by comparison, the largest percentage increase was observed in the group of synthetic opioids, which represented 4 per cent of all NPS at the end of December 2016 as opposed to only 2 per cent at the end of 2014.[61]

New psychoactive substances seizures and manufacture

The analysis of NPS seizures is limited by the fact that most substances are not under international control and thus may not be seized and reported to UNODC as part of the regular data collection mechanisms. Often NPS seizures are reported only under a product name or at the substance group level, which does not make it possible for data to be linked to a specific substance. While in 2010 hardly any seizures of synthetic NPS were reported, annual amounts have been in the range of 23-54 tons.[62] Seizures of synthetic cannabinoids have dominated global seizure amounts since 2011 but recently, the amount of synthetic cathinones seized has increased considerably.

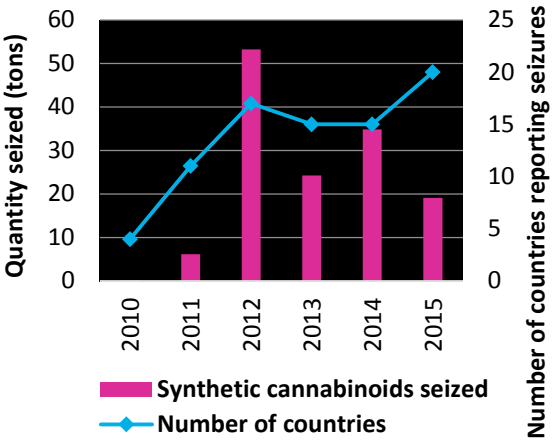
While the quantities of synthetic cannabinoids reported since 2010 have shown strong year-on-year variations, the number of countries reporting seizures of synthetic cannabinoids has shown an upward trend, reaching 18 countries in 2015. Seizure data reported to the EU Early Warning System in 2014 revealed that of the 50,000 seizures of NPS, synthetic cannabinoids comprised the majority of cases, with approximately 30,000 seizures amounting to more than 1.3 tons.[63] This may be an indication that law enforcement is prioritizing synthetic cannabinoids or the fact that those substances

61 UNODC early warning system on new psychoactive substances, 2008-2016.

62 For the purpose of this report, synthetic new psychoactive substances exclude plant-based new psychoactive substances and ketamine.

63 EMCDDA, *European Drug Report: Trends and Developments 2016.*

FIG. 12 Global quantities seized and number of countries and territories reporting seizures of synthetic cannabinoids, 2010-2015



Source: UNODC, responses to annual report questionnaire, 2010-2015.

Note: Contains seizures in the form of herbal material, as well as powder and liquids.

take a larger share of the NPS market than other substance groups, or a combination of both.

B.2. Characteristics of new psychoactive substances users and trends in new psychoactive substances use

The availability of data on the prevalence of use of NPS has improved in recent years but the data are still much more limited than data on traditional drugs, particularly with respect to trends. Although some drug use survey tools have been amended to capture NPS use better, the limited knowledge of NPS users about the substances they actually use continues to pose a challenge, as users may know only a brand or street names, which does not necessarily make it possible to identify the substances consumed. Thus, NPS use data are often limited to specific substances and subpopulations. Another key challenge for understanding NPS prevalence of use is the varying definitions of which substances are considered to be NPS. As that varies from survey to survey and may also vary from one respondent to another, the notion of NPS used by different prevalence surveys may not completely align with the group of substances defined as NPS by UNODC.

How widely are new psychoactive substances used?

Carried out in 2014, the Eurobarometer survey showed 8 per cent lifetime prevalence and 3 per cent past-year prevalence of use of NPS among young adults (aged 15-24 years) in Europe. Most of the respondents who had used NPS in the previous 12 months obtained them from a friend (68 per cent), while about a third bought them from a drug dealer (27 per cent).[64] Estimates in 2015 among young adults aged 15-16 years in the European School Survey Project on Alcohol and Other Drugs[65] showed a lower lifetime prevalence of 4 per cent and a past-year prevalence of 3 per cent. Information from epidemiological surveys on the prevalence of use of NPS among the general population is still very scarce, one of the few recent examples being Germany, where, in 2015, past-year prevalence of NPS was at 0.9 per cent among the population aged 18-64.[66]

Trend data on NPS prevalence are still very limited. A general problem in understanding NPS use is that users often do not know which substance they have taken or which substance(s) the product they consume contains. That may partly explain why some surveys show an increase while others show stable or decreasing trends, at least for specific population groups or substances.

For example, data from a survey of households in Ireland and in Northern Ireland showed a decrease in the past-year use of NPS. In Ireland and Northern Ireland, NPS use among persons aged 15-64 years dropped significantly between 2010/11 and 2014/15. Specifically, past-year mephedrone[67] use was reported to have decreased in Northern Ireland from 1.1 per cent in 2010/11 to 0.5 per cent in

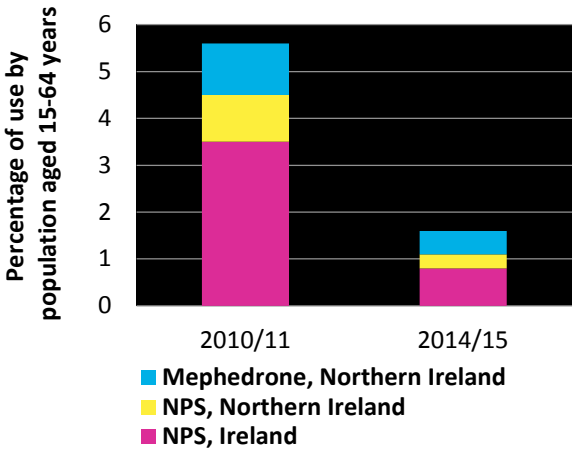
64 European Commission, *Young People and Drugs*, Flash Eurobarometer series No. 401 (August 2014).

65 EMCDDA and European School Survey Project on Alcohol and Other Drugs, *ESPAD Report 2015: Results from the European School Survey Project on Alcohol and Other Drugs* (Luxembourg, Publication Office of the European Union, 2016).

66 Elena Gomes de Matos and others, "Substanzkonsum in der Allgemeinbevölkerung in Deutschland: Ergebnisse des Epidemiologischen Suchtsurveys 2015", *SUCHT*, vol. 62, No. 5 (2016), pp. 271-281.

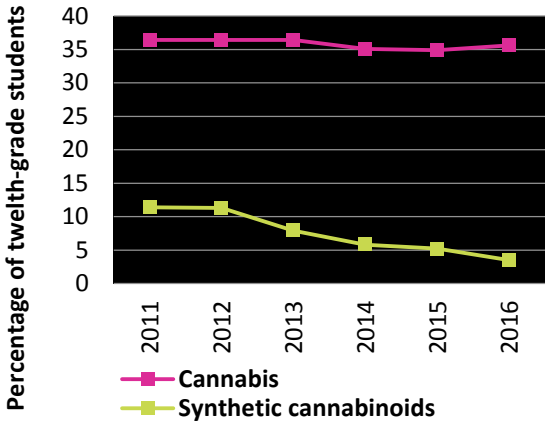
67 Mephedrone has been under international control as of November 2015.

FIG. 13 Past-year prevalence of use of new psychoactive substances and mephedrone in Ireland and Northern Ireland, 2010/11 and 2014/15



Source: National Advisory Committee on Drugs and Alcohol, *Prevalence of Drug Use and Gambling in Ireland and Drug Use in Northern Ireland*, Bulletin No. 1 (Dublin, 2016).

FIG. 14 Past-year prevalence of cannabis and synthetic cannabinoids ("Spice") use among twelfth-grade students, United States, 2011-2016



Source: United States National Institute on Drug Abuse, *Monitoring the Future Survey: National Survey Results on Drug Use 1975-2016.*

2014/15.[68] While no clear link has been established, government activities aimed at raising awareness among drug users about the health risks associated with NPS and the introduction of national controls took place over the same period.

The past-year prevalence of use of NPS with stimulant effects (reported as "bath salts") among secondary school students in the United States has, at 1.3 per cent or less in all grades, remained quite low since this category was first included in the Monitoring the Future Survey, in 2012. However, there has been a statistically significant increase in use by eighth graders, from 0.4 per cent in 2015 to 0.9 per cent in 2016, although annual prevalence remains at a low level, with no evidence of a progressive increase.[69]

In recent years, there has been a decrease in the use of synthetic cannabinoids among secondary school students in the United States: the prevalence of past-year use of synthetic cannabinoids among twelfth-grade students has decreased by more than two thirds from 11.4 per cent in 2011 to 3.5 per cent in 2016. At the same time, twelfth graders have been showing an increased awareness of the dangers associated with the use of synthetic cannabinoids. Perhaps access to NPS in the United States has been reduced by recent legal steps taken to outlaw their sale through retail outlets.[70]

Characteristics and patterns associated with new psychoactive substances use

Some of the characteristics associated with NPS use resemble those of traditional drugs, but others are specific to NPS. Similar to the recreational use of conventional drugs, motivations for NPS use reported by users include the search for an experience involving the paradigm of "modifying perceptions", curiosity, sociability and the search for energy or other functional expectations.[71] Other factors mentioned as driving initial experimentation and continued use include boredom and peer socialization.[72] Features specific to NPS include their

68 National Advisory Committee on Drugs and Alcohol, *Prevalence of Drug Use and Gambling in Ireland and Drug Use in Northern Ireland*, Bulletin No. 1 (Dublin, 2016).

69 Lloyd D. Johnston and others, *Monitoring the Future National Survey Results on Drug Use, 1975-2015: 2015 Overview – Key Findings on Adolescent Drug Use* (Ann Arbor, Michigan, University of Michigan, 2016).

70 Ibid.

71 Agnès Cadet-Taïrou, "New psychoactive substances: user profiles and practices", *Tendances,* No. 108 (April 2016).

72 Marie Claire Van Hout and Evelyn Hearne, "A community-based study of synthetic cannabinoid use in Co. Monaghan, Ireland" (July 2015).

easier availability, lower price and (assumed) better quality compared with traditional drugs. For user groups subject to drug screening, such as prisoners, their assumed non-detectability in tests is an important factor.

Specific social settings have a link to the use of NPS in some countries. In England and Wales, for example, visits to a bar, pub or a nightclub in the past month have been associated with past-year NPS use.[73] According to the Eurobarometer survey, most of the respondents who have used these new substances in the past 12 months did so at a party or event (65 per cent) or with friends (60 per cent), although 9 per cent used them during normal daily activities.[74] Daily use of NPS has also been reported in English prisons.[75] In New Zealand, in 2015, approximately 17 per cent of police detainees, in four central city police watch houses, reported having used synthetic cannabinoids for the first time, the equal highest proportion of all drugs reported, as 17 per cent also reported the use of methamphetamine.[76]

A study in France pointed to a strong link between the use of NPS belonging to the phenethylamines substance category and the "electro" music scene.[77] Several other factors also played a key role in determining if NPS were used in a recreational nightlife setting. For example, the younger the respondents and the lower their education level, the more likely NPS use was at the user's home or a friend's home (private context), and the less likely it was at a party or event (public context). There were also variations according to the occupational status of the respondents and whether they were the primary household earner.[78]

Recent data collected from wastewater analyses can provide deeper insight into local patterns of drug use and temporal trends, supplementing existing data mechanisms, such as household surveys or other epidemiological studies, which do not often cover NPS use at the substance level. A study conducted in Adelaide, Australia, between 2011 and 2015, detected several NPS, namely BZP, TFMPP,[79] mephedrone, methylone, *alpha*-PVP and MDPV, in wastewater samples. The study revealed that *alpha*-PVP, BZP, mephedrone and methylone were mostly used at weekends, similarly to the pattern reported for cocaine and MDMA. Whereas more established drugs such as methamphetamine, MDMA or heroin showed relatively regular trends in the observation period, NPS trends were characterized by pronounced but short-term peaks in particular months. Although the relationship between wastewater analysis results and drug use is complex, this pattern could indicate that the availability and/or usage of the NPS investigated was less stable than that of established drugs.[80]

Although not limited to NPS use, polydrug use seems to be one of the features of NPS use. In England and Wales, several factors were associated with past-year NPS use, including consumption of alcohol in the past month and use of another drug in the past year.[81] Among participants aged 16-59 years who had used an NPS in the past year, a total of 84.9 per cent also reported having used another drug.[82] In 2015, among European students who used NPS, around three quarters used cannabis, about a quarter used inhalants and tranquilizers/sedatives, and less than a quarter used a substance in the group of LSD/other hallucinogens and "ecstasy".[83] There are insufficient data on NPS as a contributing or main factor in the cause of death in overdose cases, partly because the pharmacological and toxicological properties of many NPS are not

73 Deborah Lader, ed., *Drug misuse: Findings from the 2015/16 Crime Survey for England and Wales,* 2nd ed., Statistical Bulletin 07/16 (London, Home Office, July 2016).

74 European Commission, *Young People and Drugs.*

75 Rob Ralphs and others, "Adding spice to the porridge: the development of a synthetic cannabinoid market in an English prison", *International Journal of Drug Policy*, vol. 40 (2016).

76 Chris Wilkins and others, *New Zealand Arrestee Drug Use Monitoring: 2010-2015 Report* (Auckland, SHORE and Whariki Research Centre, College of Health, Massey University, 2016.

77 Cadet-Taïrou, "New psychoactive substances: user profiles and practices".

78 European Commission, *Young People and Drugs*.

79 1-(3-Trifluoromethylphenyl)piperazine (TFMPP) is not under international control.

80 Benjamin J. Tscharke and others, "Temporal trends in drug use in Adelaide, South Australia by wastewater analysis", *Science of The Total Environment,* vol. 565 (2016), pp. 384-391.

81 Lader, ed., *Drug Misuse: Findings from the 2015/16 Crime Survey for England and Wales.*

82 Ibid.

83 EMCDDA and European School Survey Project on Alcohol and Other Drugs, *ESPAD Report 2015.*

yet fully understood, and overdose cases often involve polydrug use.

New psychoactive substances use among vulnerable and high-risk groups

Some studies have shown that selected groups, such as young people, people in contact with mental health services, people affected by homelessness, people who inject drugs (PWID) and men who have sex with men (MSM), are particularly vulnerable to NPS. In a survey among such vulnerable groups in Scotland, 59 per cent of respondents reported having used an NPS, most of them in the past six months. The most commonly used NPS were synthetic cannabinoids (41 per cent), followed by NPS with stimulant effects (21 per cent) and mephedrone (19 per cent).[84] As some NPS are more affordable than traditional drugs with similar effects, the homeless and marginalized people in general are more prone to NPS use. For example, a*lpha*-PVP is sold in the United States in quantities as small as one tenth of a gram, for as little as $3-5, a price affordable among population groups with little disposable income, including young or socially disadvantaged people. There are also reports of these substances being actively sold to, and by, homeless persons.[85, 86]

As traditional drugs, NPS have a higher use among youth. Surveys in European countries indicate that NPS use is often concentrated among those around 20 years of age. The Crime Survey for England and Wales for the reporting year 2015/16 estimated that 0.7 per cent of adults aged 16 to 59 years (around 244,000 people) had used an NPS in the past year, with prevalence of use highest among young adults aged 16 to 24 years, at 2.6 per cent. A survey of NPS users conducted in 2014 in Czechia, France, the Netherlands and Poland also showed that the majority of users were young adults, with almost half of them being under 25 years of age, 13 per cent being under 20 years of age and 3 per cent of respondents being minors,[87] although some respondents were over 50 years of age.[88, 89]

Gender differences in new psychoactive substances use

Gender differences in the prevalence of use of NPS vary greatly between countries but may be less pronounced in that of traditional drugs. In Europe, gender differences in NPS use in 2015 were small at the aggregated regional level but patterns were different at the country level. Significantly more boys than girls reported the use of NPS at the country level in Albania, Cyprus, Georgia, Greece, Montenegro, the Netherlands and the Republic of Moldova, while significantly more girls than boys reported the use of NPS in Czechia and Iceland.[90] No significant gender differences in NPS past-year prevalence were confirmed in an epidemiological survey in Germany among the general population in 2015.[91] However, in the Crime Survey for England and Wales in 2015/16, of the general population, men (1.1 per cent) were, statistically, significantly more likely to have used an NPS in the past year than had women (0.4 per cent), and a similar gender difference was found among participants aged 16-24 years.[92]

New psychoactive substances and traditional drug markets

The initial expansion of the NPS market may have happened at the expense of use of traditional drugs because of the comparative advantage of NPS in terms of low prices and quasi legal status, yet more recent studies are providing evidence that some NPS have now established a market in their own right.

84 Katy MacLeod and others, *Understanding the Patterns of Use, Motives, and Harms of New Psychoactive Substances in Scotland,* Social Research Series (Edinburgh, November 2016). Mephedrone was not included into the new psychoactive substances category in this study.

85 National Drug Early Warning System (NDEWS) Coordinating Center, *Southeastern Florida (Maimi Area), Sentinel Community Site, Drug Use Patterns and Trends* (2016). Available at http://miamicoalition.org/doc/florida_scs_drug_use_patterns_and_trends_2016.pdf.

86 MacLeod and others, *Understanding the Patterns of Use, Motives, and Harms of New Psychoactive Substances in Scotland.*

87 I-TREND (Internet tools for research in Europe for new drugs) project, which was co-funded by the European Commission.

88 Cadet-Taïrou "New psychoactive substances: user profiles and practices".

89 American Association of Poison Control Centers, Alerts, Synthetic cannabinoids. Available at www.aapcc.org/alerts/synthetic-cannabinoids/.

90 *ESPAD Report 2015.*

91 Gomes de Matos and others, "Substanzkonsum in der Allgemeinbevölkerung in Deutschland".

92 Lader, ed,. *Drug misuse: Findings from the 2015/16 Crime Survey for England and Wales.*

Studies showing a replacement effect for NPS include a wastewater analysis in South Australia, in which the average weekly use of certain NPS (i.e., BZP, mephedrone, MDPV, and TFMPP) increased when MDMA became less available in 2010 to 2011, while the use of those NPS decreased once MDMA became available again. The study suggested that changes in the use of those NPS might be driven by irregular supply rather than by changes in demand.[93] Meanwhile, in a community study in Ireland, easy availability of NPS also appeared first and foremost as driver for introduction and use.[94]

In prisons in the United Kingdom and the United States, synthetic cannabinoids seem to be used as a replacement for cannabis, possibly because they may remain undetected in mandatory drug screens.[95, 96] Moreover, synthetic cannabinoids were reported to be used among United States military personnel, probably to evade detection, as current workplace drug tests can only detect some but not all synthetic cannabinoids in use.[97] Similarly, in Scotland, some youth offenders and individuals in treatment programmes have switched to mephedrone in the belief that it will not be picked up by tests to detect drug use.[98] In France, in a drug user survey, the main reason reported for choosing the last substance that the respondent used was "curiosity" (50 per cent), while the perceived danger to health of a substance, the control status and its perceived non-detectability in urine or saliva drug tests were criteria that seem to have played a secondary role in the choice of substance.[99]

93 Tscharke and others, "Temporal trends in drug use in Adelaide, South Australia by wastewater analysis". In this study, use was expressed as average weekly use (doses/week/1,000 people or mg excreted/week/1,000 people).

94 Van Hout and Hearne, "A community-based study of synthetic cannabinoid use in Co. Monaghan, Ireland".

95 Nicola J. Kalk and others, "Spice and all things nasty: the challenge of synthetic cannabinoids", *British Medical Journal,* vol. 355 (2016).

96 E. D. Wish, A. S. Billing and E. E. Artigiani, *Community Drug Early Warning System: The CDEWS-2 Replication Study* (Washington, D. C., Office of National Drug Control Policy, Executive Office of the President, 2015).

97 United States, Drug Enforcement Administration, *2016 National Drug Threat Assessment Summary.*

98 Alex Chadd, "Mephedrone emergence in southern Wales" (2013), presentation.

99 Cadet-Taïrou, "New psychoactive substances: user profiles and practices".

The fact that NPS have now become drugs of choice for certain user groups or in certain settings is visible in other studies, including the Global Drug Survey, although the comparability of different years is limited and the change in motivational factors for the use of NPS should be interpreted with caution. While the primary reason for NPS use reported four years ago was the non-availability and the poor quality of traditional drugs, in 2015 and 2016, NPS were reportedly used instead for their perceived value for money and ease of access, specifically via online services.[100] In another study in Scotland, only a very small number of study participants (3-6 per cent) who had used NPS equivalents to "traditional" drugs in the past 6 months did so because they thought they would be safer.[101]

B.3. How well-informed are users of new psychoactive substances and how concerned are they about what they are using?

The purity and composition of products containing NPS are often unknown, and safety data on the toxicity of many NPS, as well as information on the long-term adverse effects and risks, are unavailable or are very limited, which places users at high risk. The great lack of awareness and knowledge about the risks and harms related to dosages and the use of NPS is demonstrated by studies among men who have sex with men (MSM), night clubbers, prisoners, and by poison centre records. Younger, potentially new users seem to be less aware and informed about the drugs they take, while experienced drug users appear to be more aware and careful about the composition, effects and dosages of drugs they take.

In a survey of MSM in Scotland, 54 per cent reported lifetime use of NPS and almost a quarter of synthetic cannabinoid users reported first using synthetic cannabinoids without knowing that they were taking a substance from that group.[102] A study conducted to assess NPS and drug use among 679 nightclub/festival-attending young adults (aged

100 Global Drug Survey 2016 findings. Available at www.globaldrugsurvey.com.

101 MacLeod and others, *Understanding the Patterns of Use, Motives, and Harms of New Psychoactive Substances in Scotland.*

102 Ibid.

18-25 years) in New York City revealed that of those respondents who reported no lifetime use of stimulant NPS, unknown pills or powders, 41.2 per cent tested positive for NPS with stimulant effect. Results suggest that many "ecstasy"-using nightclub/festival attendees may be unintentionally using "bath salts" or other products containing NPS.[103]

Callers to poison centres in the United Kingdom reported the specific chemical involved in branded products in only 8 of the 108 telephone enquiries (7.4 per cent) relating to synthetic cannabinoids.[104] In France, about 64 per cent of users indicated that they did not have enough information on the NPS they were using. However, more than two thirds of NPS users reported the purchase of NPS mainly from websites where they are sold under their chemical names, rather than from websites that display brand names and colourful packaging, without giving specific chemical information.[105]

Risk perception and harms reported by new psychoactive substances users

There is a severe lack of information on the risks of NPS use, particularly when (unknown) combinations of substances are consumed. For example, prisoners who use NPS stated that they had no idea what "Spice" contained and what it might do to their bodies, and that they only had personal and others' experiences to draw upon, suggesting that potential physical harm does not deter prisoners from continued use.[106] As reported by the Eurobarometer survey, however, a large majority of all respondents considered regular use of NPS to carry a high risk to health, although they believed that using these new substances only once or twice carries less risk.[107]

103 Joseph J. Palamar and others, "Detection of "bath salts" and other novel psychoactive substances in hair samples of ecstasy/MDMA/"Molly" users, *Drug and Alcohol Dependence*, vol. 161 (2016), pp. 200-205.

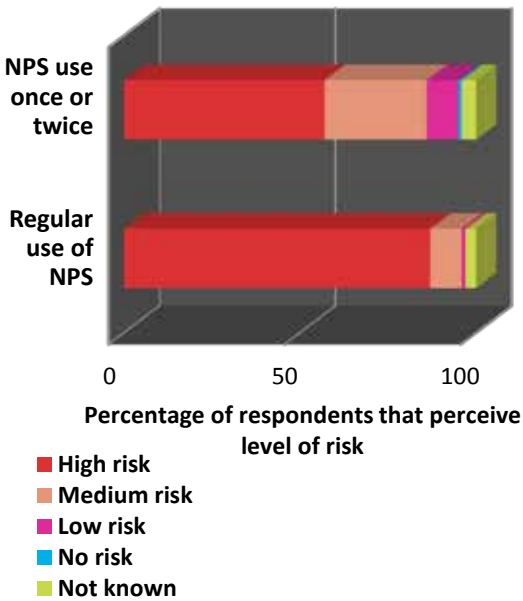
104 United Kingdom, Public Health England, *National Poisons Information Service Report 2015/2016* (September 2016).

105 Cadet-Taïrou, "New psychoactive substances: user profiles and practices".

106 User Voice, "Spice: the bird killer — what prisoners think about the use of spice and other legal highs in prison" (May, 2016).

107 European Commission, *Young People and Drugs*.

FIG. 15 Extent of perceived risk to a person's health posed by the use of new psychoactive substances, Europe, 2014



Source: European Commission, *Young People and Drugs*, Flash Eurobarometer series No. 401, (August 2014).

According to the Global Drug Survey 2017, the overall risk of seeking emergency medical treatment was highest for the use of synthetic cannabinoids among NPS.[108] One likely reason is that different substances are sprayed in varying proportions and dosages on the herbal material of NPS products of the same brand, which increases the risk of adverse health consequences for users.[109]

A study in Ireland on the profile of NPS users investigated the risk awareness and dependence potential of synthetic cannabinoids. The study interviewed only dependent user participants who described their intention to stop using the substances, although unpleasant physical and mental withdrawal symptoms prevented them from doing so. The fear of stopping use was also grounded in youth psychotic behaviours, suicidal ideation and suicide attempts when in withdrawal. However, user

108 The definition of NPS used in the Global Drug Survey is not comparable to the definition used by the UNODC.

109 Global Drug Survey 2017, detailed findings on drug cryptomarkets. Available from Dr. Monica Barratt, National Drug and Alcohol Research Centre, Australia.

awareness about the dangers of smoking synthetic cannabinoid products was low.[110]

Concerning the harms associated with NPS use, respondents to a survey in Scotland in 2016 who had used an NPS in the previous six months reported anxiety, paranoia and depression. Moreover, the majority of respondents reported negative effects on their family relationships relating to NPS use. The key reasons for stopping the use of NPS were related to "not liking it" or to specific harms that individuals had experienced, such as a negative impact on mental or physical health.[111]

B.4. Health risks of new psychoactive substances with stimulant effects

NPS can be grouped into six pharmacological effect groups, one of them being NPS with stimulant effects. This group consists of structurally diverse substances including aminoindanes, synthetic cathinones, piperazines and phenethylamines, which act as stimulants of the central nervous system by mediating the actions of dopamine, norepinephrine and serotonin. Accounting for 36 per cent of all substances reported to UNODC up to December 2016, NPS with stimulant effects have a mechanism of action similar to traditional drugs such as cocaine, amphetamine, methamphetamine and "ecstasy". The reported health risks and harm associated with the use of NPS with stimulant effects, particularly their injecting use, gives great cause for concern as it has been associated with increasing rates of HIV infection.

High-risk groups injecting new psychoactive substances with stimulant effects

The injecting use of NPS with stimulant effects has been reported among high-risk drug user groups, further aggravating the health risks that persons in this group are particularly exposed to.[112] The injecting use of stimulants increases the health risks of users as they are prone to inject at a more frequent rate than other PWID and are more likely to share needles and other contaminated injecting paraphernalia.[113] Users at risk include young people, subgroups of MSM, long-term abstinent former opiate users, people who inject other drugs such as heroin and amphetamines, people who switch to injecting synthetic cathinones and people who have switched from snorting to injecting. This points to the growing interplay between NPS and traditional illicit drug markets, with specifically synthetic cathinones, e.g., mephedrone, MDPV and pentedrone being used by PWID.[114]

In an analysis conducted in Paris in 2012 on the residual content of 3,489 used syringes collected from 17 automatic injection kit dispensers, opiate substitutes and new compounds including the synthetic cathinone 4-MEC[115] were found at all sites. Heroin was detected in 42 per cent of cases, followed by cocaine in 41 per cent of cases, buprenorphine in 29 per cent of cases, and 4-MEC in 23 per cent of cases. Over the course of 2012, 4-MEC was detected in an increasing number of syringes between the summer and the winter months, pointing to an increase in the use of the substance at a time when cocaine consumption decreased.

National data on PWID attending syringe exchange programmes in Hungary from 2011 to 2015 has shown a transition from injecting use of amphetamine and heroin to NPS. Over a five-year period, there was a significant decrease in the percentage of PWID reporting amphetamine as the primary injected drug, as well as heroin and an increase in injecting use of NPS, which more than tripled in the same period.[116]

110 Van Hout and Hearne, "A community-based study of synthetic cannabinoid use in Co. Monaghan, Ireland".

111 MacLeod and others, *Understanding the Patterns of Use, Motives, and Harms of New Psychoactive Substances in Scotland.*

112 High-risk drug users are defined as people who inject drugs, people who use drugs on a daily basis and/or people diagnosed as drug-dependent.

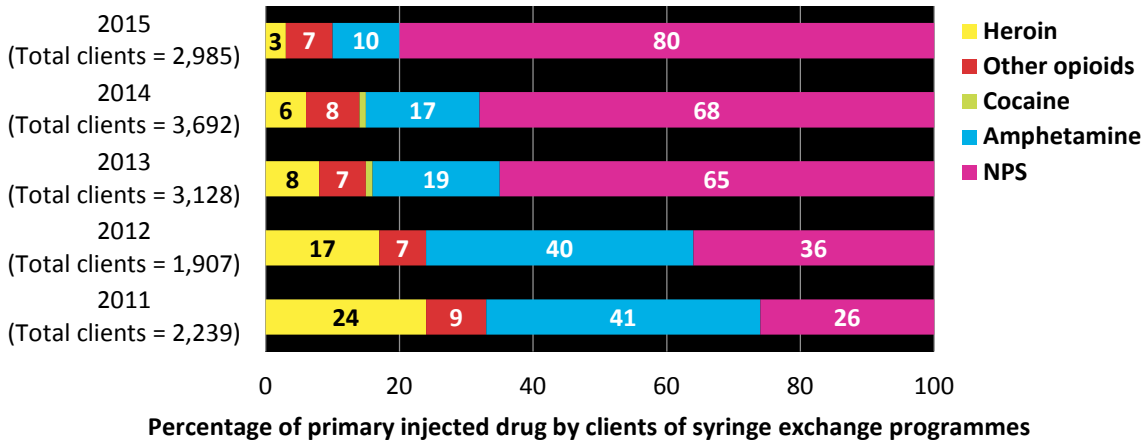
113 Andrea Fischer and others, *The Link between Amphetamine-Type Stimulant Use and the Transmission of HIV and other Blood-borne Viruses in the Southeast Asia Region,* ANCD Research Paper No. 25 (Melbourne, National Drug Research Institute, Australian National Council on Drugs, 2013).

114 Mephedrone and MDPV were placed under international control, in Schedule II of the 1971 Convention in 2015. In March 2017, the Commission on Narcotic Drugs decided to add pentedrone to the same Schedule.

115 In March 2017, the Commission on Narcotic Drugs decided to place 4-methylethcathinone (4-MEC) under international control (Schedule II of the 1971 Convention).

116 Anna Tarján and others, "HCV prevalence and risk behaviours among injectors of new psychoactive substances in a risk environment in Hungary: an expanding public health burden", *International Journal of Drug Policy,* vol. 41

FIG. 16 | Breakdown of clients of syringe exchange programmes, by primary injected drug, Hungary, 2011-2015



Source: Hungary, syringe distribution and client data from national syringe exchange programmes, 2011-2015.

By mid-2010, needle and syringe programmes in Hungary reported a sharp increase in the injecting use of mephedrone, with participants reportedly seeking the euphoric effects in the early stages after injection. The stimulating effect of mephedrone enabled previous heroin users to take part in collective use, rather than earlier individual use, and that factor played an important role in the quick spread of mephedrone use.[117] In 2011, MDPV became the main substance injected by PWID, with injecting use of mephedrone and 4-MEC reported at a lower rate. By 2012, the synthetic cathinone pentedrone had become the predominant substance injected by PWID, accounting for about 43 per cent of active substances detected in the residual contents of injecting equipment, a trend that continued until 2013.[118] In 2014, *alpha*-PVP was the most detected substance in the residual contents of syringes, at 40 per cent, while pentedrone had decreased to 9.5 per cent.[119] In 2015, *alpha*-PHP[120] became the most frequently detected cathinone derivative at 26 per cent. However, in the majority of cases of the analysis of the residual content of injecting equipment in 2015, the identity of the active substance was not confirmed.[121]

In the United Kingdom, there have also been reports of injecting use of mephedrone, methamphetamine and GHB immediately before or during sex in groups of MSM in the past year. Commonly referred to as "slamming", careful injecting use with clean needles was reported, with no sharing of needles between sexual partners at "chemsex" parties[122] (more information on GHB can be found in chapter B.7, below). There are also concerns about the injection of mephedrone and other drugs among some subgroups of MSM during sex, who often share injecting equipment and engage in unprotected sex.[123]

(2017), pp. 1-7.

117 József Rácz, Róbert Csák and Sándor Lisznyai, "Transition from "old" injected drugs to mephedrone in an urban micro segregate in Budapest, Hungary: a qualitative analysis", *Journal of Substance Use,* vol. 20. No. 3 (2015), pp. 178-186.

118 Anna Péterfi and others,"Changes in patterns of injecting drug use in Hungary: a shift to synthetic cathinones", *Drug Testing and Analysis,* vol. 6, Nos.7 and 8 (2014), pp. 825-831.

119 EMCDDA, *2015 National Report to the EMCDDA by the Reitox National Focal Point: Hungary* (Budapest, 2015).

120 *Alpha*-pyrrolidinohexanophenone (*alpha*-PHP) is not under international control.

121 EMCDDA, *2015 National Report to the EMCDDA by the Reitox National Focal Point: Hungary.*

122 Adam Bourne and others, ""Chemsex" and harm reduction need among gay men in South London", *International Journal of Drug Policy*, vol. 26, No. 12 (2015), pp. 1171-1176.

123 Adam Bourne and others, *The Chemsex Study: Drug Use in Sexual Settings Among Gay and Bisexual Men in Lambeth, Southwark and Lewisham* (London, Sigma Research, London School of Hygiene and Tropical Medicine, 2014); Victoria L. Gilbart and others, "High-risk drug practices in men who have sex with men", *The Lancet*, vol. 381, No. 9875 (2013), pp. 1358 and1359; and David Stuart, *"Sexualised drug use by MSM: background, current status and*

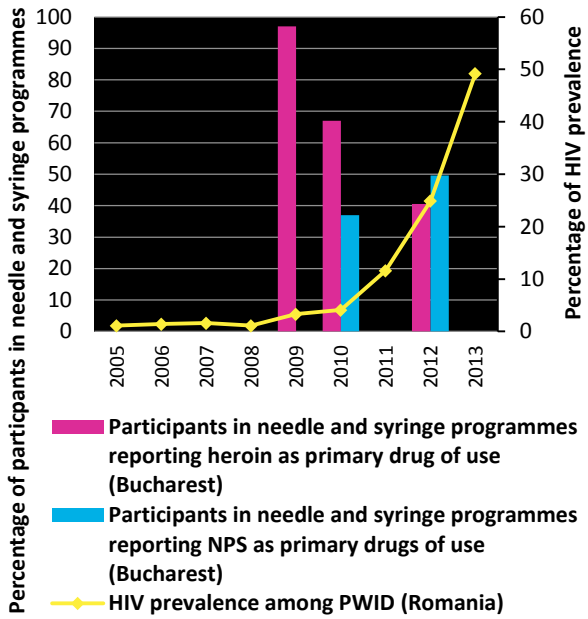
Increase in HIV and hepatitis C infections associated with injecting stimulant new psychoactive substances

Synthetic cathinones, alone or in combination with other stimulants (e.g., methamphetamine and cocaine) are injected to enhance sexual experiences, and users report compulsive re-injecting because of the substances' relatively short duration of action. Thus, people who inject synthetic cathinones may be at a higher risk of acquiring and transmitting HIV than NPS users who do not inject and people who inject other drugs. Risky sexual behaviour such as unprotected sex, to which the stimulant and euphoric effects of such substances may contribute, can also be an important factor in acquiring or transmitting HIV, as well as hepatitis C to some extent.

A study conducted in 2012 and 2013 on the epidemiology of synthetic drug use among a cohort of PWID in San Diego, California, showed that a considerable proportion of PWID use synthetic drugs and experience harms associated with their use. Of the 485 respondents, 31 PWID (7 per cent) reported lifetime use of synthetic cathinones such as mephedrone, MDPV and methylone. Injecting was reported as the most common route of administration (48 per cent) among PWID, followed by snorting (36 per cent) and smoking (23 per cent). Compared with PWID who did not report synthetic cathinone use, people who inject synthetic cathinones were more likely to have initiated injecting drug use with stimulants and less likely to have initiated injecting drug use with heroin, were significantly younger (34 years old on average versus 45 years old) and were more likely to be HIV-positive. Moreover, rates for receptive syringe sharing, hospitalization and the use of other drugs in the previous six months were higher for those who injected synthetic cathinones than for those who did not.[124]

In Romania, data from a needle and syringe programme in Bucharest showed that HIV infections through injecting drug use have increased since 2009 and that the primary type of drug injected among

FIG. 17 HIV prevalence among people who inject drugs and primary drugs used among participants in needle and syringe programmes, Romania, 2005-2013



Source: Romania, National Anti-drug Agency.
The prevalence of HIV refers to tested PWID in treatment services.

PWID has become NPS (97 per cent) in place of heroin.[125] This might suggest that NPS injecting is related to a higher rate of HIV-positive cases among injecting drug users.

In Ireland, an unexpected increase in the number of acute HIV infection cases among PWID might be linked to an increase in injecting use of the synthetic cathinone, *alpha*-PVP, among the homeless population.[126] Injecting was reported to occur multiple times a day, with users often reusing syringes and sharing filters. All users that reported injecting methamphetamine also reported injecting *alpha*-PVP.

Public Health England pointed to an increase in the

response", HIV Nursing, vol. 13, No. 1 (2013), pp. 6-10.

124 Karla D. Wagner and others, "Use of synthetic cathinones and cannabimimetics among injection drug users in San Diego, California" *Drug and Alcohol Dependence,* vol. 141 (2014), pp. 99-106.

125 European Centre for Disease Prevention and Control/ WHO Regional Office for Europe, *HIV/AIDS Surveillance in Europe, 2015* (Stockholm, 2016).

126 C. Giese and others, "Injection of new psychoactive substance snow blow associated with recently acquired HIV infections among homeless people who inject drugs in Dublin, Ireland, 2015", Eurosurveillance, vol. 20, No. 40 (2015), pp. 1-6.

number of people injecting stimulants, with concern being expressed about the fact that within five years of the first appearance of mephedrone, around 1 in 10 PWID reported its injecting use. Among the population surveyed in England, Wales and Northern Ireland, injecting use of mephedrone during the preceding month was reported by 5.9 per cent (92 out of 1,554) of PWID in 2014. Mephedrone injecting occurred mainly among people who had previously injected other drugs, people who had switched from snorting mephedrone and among younger people. Those who reported that they had injected mephedrone during the preceding year were more likely to have reported HIV infection, antibodies to the hepatitis C virus and injection site infections.[127]

Lack of knowledge of the substance regarding purity, dosing, effects and health consequences, as well more frequent injecting practices, increases the risks related to synthetic cathinone use. The health harms associated with injecting use of pentedrone were shown in a study on HIV among PWID in Hungary. Some 92 out of 167 PWID tested positive for HIV, with the most common drug injected being pentedrone.[128] Furthermore, hepatitis C infection was reported to be more prevalent among people who inject NPS with stimulant effects, since the short duration of action from injecting use of some synthetic drugs leads to a high-frequency use pattern.[129] The prevalence of hepatitis C infection among PWID in Budapest increased from 41 per cent in 2013 to 60 per cent in 2014, indicating that factors favouring the spread of injecting related infections were present among PWID.[130] Among persons injecting NPS, prevalence of hepatitis C infection, sharing syringes and sharing any injecting equipment (past month), roughly doubled from 2011 to 2014, significantly exceeding prevalence in other PWID groups. Among young adults up to 25 years of age, prevalence of hepatitis C infection increased about sixfold. At the same time, the estimated number of syringes distributed per PWID nationally fell from 114 in 2011 to 28 in 2015.[131] A slight increase in the injecting use of synthetic cathinones was reported by needle and syringe programme clients in 2015.

Other adverse health events of stimulant new psychoactive substances use

In early 2014, Scotland experienced a large outbreak of soft-tissue infections among people who inject drugs[132] during the period when the injecting of ethylphenidate, mainly by previous injecting users of heroin, suddenly increased. The use of this relatively short-acting stimulant is known to increase injection frequency and thus the associated risks.[133] Consequently, ethylphenidate, which had significant adverse effects on physical and mental health, including hospitalization and death,[134] was placed under temporary control in the United Kingdom in April 2015.[135] Based on the analysis of needle exchange data from the NHS, people that reported current injecting use of NPS (exclusively stimulant NPS) indicated that the average frequency of injecting was five times per day. In addition, they reported incidences of equipment sharing and poor injecting technique, which can lead to health complications.[136]

127 United Kingdom, Public Health England, Health Protection Scotland, Public Health Wales, and Public. Health Agency Northern Ireland, "Shooting up: infections among people who inject drugs in the United Kingdom" (London, November 2015).

128 József Rácz, V. Anna Gyarmathy and Róbert Csák, "New cases of HIV among people who inject drugs in Hungary: false alarm or early warning?, *International Journal of Drug Policy,* vol. 27 (2016), pp. 13-16.

129 "Injecting of new psychoactive substances and related risks in Hungary." PDU annual expert meeting, EMCDDA, Lisbon, 27 September 2013. Gergely Horvath, Hungarian national focal point.

130 József Rácz, V. Anna Gyarmathy and Róbert Csák, "New cases of HIV among people who inject drugs in Hungary: false alarm or early warning?".

131 Tarján and others, "HCV prevalence and risk behaviours among injectors of new psychoactive substances in a risk environment in Hungary".

132 Health Protection Scotland, HPS eWeekly Report, "Outbreak of soft tissue infections: injected 'legal highs'", 31 March 2015. Available at www.hps.scot.nhs.uk/documents/ewr/pdf2015/1513.pdf.

133 Con Lafferty and others, "The experience of an increase in the injection of ethylphenidate in Lothian April 2014-March 2015", *Scottish Medical Journal,* vol. 61, No. 2 (2016).

134 "Ethylphenidate (EPH): critical review report" (report of the World Health Organization Expert Committee on Drug Dependence, Thirty-eighth Meeting, 14-18 November 2016).

135 In March 2017, the Commission on Narcotic Drugs decided to place ethylphenidate under international control (Schedule II of the 1971 Convention).

136 MacLeod and others, *Understanding the Patterns of Use, Motives, and Harms of New Psychoactive Substances in Scotland.*

In the United States, increased reports of *alpha*-PVP, allegedly used as an alternative to cocaine, were observed from 2011 to 2015. Among impaired drivers tested in the State of Maine, 6 per cent of urinalyses tested positive for *alpha*-PVP and MDPV in 2012; the proportion decreased to 2 per cent in 2013. In 2012, two deaths were caused by *alpha*-PVP.[137] In Florida, an outbreak of *alpha*-PVP use was observed, which led to the substance being linked to 80 deaths and thousands of hospital emergency cases, many from excited delirium syndrome, from September 2014 to December 2015.[138] Excited delirium involves hyperstimulation, paranoia and hallucinations that can lead to violent aggression and self-injury. In 2015, *alpha*-PVP was linked to 63 deaths and more than 1,800 hospital emergency cases in one county alone in south-east Florida.[139]

B.5. Synthetic cannabinoids: toxicity and fatalities

Synthetic cannabinoid receptor agonists, also known as synthetic cannabinoids, are man-made substances designed to mimic the desired effects of cannabis. Their potency may, however, vary significantly from that of cannabis, although extremely potent synthetic cannabinoid receptor agonists produce effects, such as agitation, that are similar to intoxication by the major psychoactive component of cannabis, *delta*-9-tetrahydrocannabinol (THC), a partial agonist[140] of the cannabinoid receptors. Synthetic cannabinoid receptor agonists constitute the largest NPS group in the drug market in terms of the number of different substances reported. Many of the substances in this structurally diverse group were initially designed for pharmacological research and none are currently licensed for medical use.[141]

137 Marcella H. Sorg, "Drug abuse patterns and trends in Maine", update: January 2014. Available at www.drugabuse.gov.

138 "Southeastern Florida (Miami Area), Sentinel community site, drug use patterns and trends (2016)", NDEWS Coordinating Center.

139 Ibid.

140 An agonist is a substance that acts on a receptor to produce effects. A partial agonist is a substance that produces a reduced response as it is unable to elicit the maximum effect or response. For more information, see *Terminology and Information on Drugs* (United Nations publication, Sales No. E.16.XI.8).

141 *Terminology and Information on Drugs* (United Nations publication, Sales No. E.16.XI.8).

Typically, one or several synthetic cannabinoids are soaked in or sprayed onto plant material, which itself does not contain substances with psychoactive effects. Synthetic cannabinoids are also sold in liquid form and, more recently, have been presented in the United States in the form of pills, as counterfeit prescription drugs.[142] Products containing synthetic cannabinoids are often highly variable both in the quantity of active ingredients and number of different synthetic cannabinoids present, and thus pose a public health risk.

Between 2008 and 2016, over 240 different synthetic cannabinoids were reported to UNODC by 65 Member States, with year-on-year figures showing significant increases in substances reported, up to 2014, while the figures for 2015 showed a slight decrease from 2014. Although not all the substances identified to date have been present every single year, the number of different synthetic cannabinoids constitutes a challenge for forensic laboratories and emergency services.[143]

Evolution of synthetic cannabinoids

Since the discovery of the cannabinoid receptors in the 1980s and the ensuing research for potential therapeutic agents,[144] the development of synthetic cannabinoids has experienced continued growth, with the evolution of a series of different structural classes. Products containing synthetic cannabinoids first appeared in the mid-2000s, which were sold as smokable "herbal blends" and "legal highs" under a variety of brand names such as "Spice", "K2", "Kronic" and labelled "not for human consumption". A post-2008 phenomenon occurred as successive structural modifications were introduced to keep synthetic cannabinoids in an ambiguous legal status.[145] For instance, the emergence of the first wave of naphthoylindoles (for example, JWH-018) developed into naphthoylindazoles such as THJ-018, indazole carboxamides such as AKB-48, and

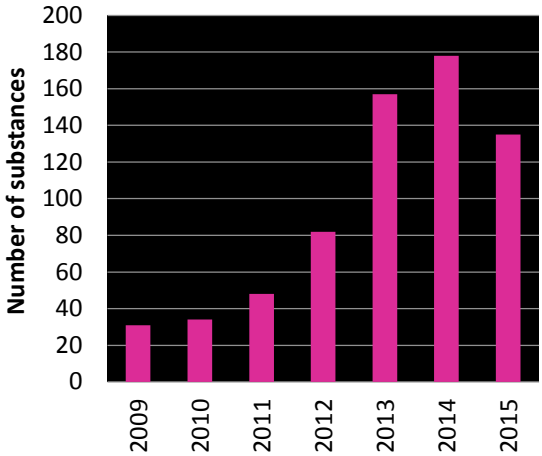
142 *2016 National Drug Threat Assessment Summary.*

143 UNODC early warning advisory on new psychoactive substances, 2016.

144 Leslie Iversen, "Cannabis and the brain", *Brain,* vol. 126, No. 6 (2003), pp. 1252-1270.

145 Ruri Kikura-Hanajiri and others, "Changes in the prevalence of new psychoactive substances before and after the introduction of the generic scheduling of synthetic cannabinoids in Japan", *Drug Testing and Analysis,* vol. 6, Nos. 7 and 8 (2014), pp. 832-839.

FIG. 18 Number of synthetic cannabinoids reported yearly to the UNODC early warning advisory from 2009 to 2015



Source: UNODC early warning advisory on new psychoactive substances.

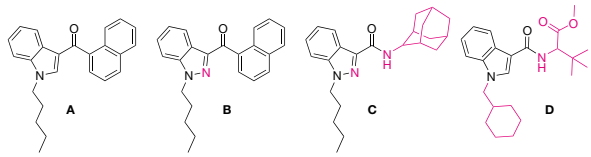
indole carboxamides such as MDMB-CHMICA, which have emerged more recently.[146] New derivatives of synthetic cannabinoids that have emerged in the drug market have generated more potent and dangerous substances with detrimental effects on humans.

Composition of cannabis and synthetic cannabinoids

Synthetic cannabinoids are not simply synthetic versions of the substances occurring in herbal cannabis, as street names such as "synthetic cannabis" and "synthetic marijuana" might suggest. Rather, based on the reported differences in potency, toxicity, duration of effects and pharmacology, synthetic cannabinoids could be described as a group of substances with both similarities to cannabis, such as acting on the same receptors, and significant differences, such as lacking the effects of other components of herbal cannabis, including cannabidiol (CBD). Although not psychoactive, CBD contributes to the

146 THJ-018 (1-naphthalenyl-(1-pentyl-1*H*-indazol-3-yl)-methanone) and 5F-AKB-48 (also known as 5F-APINACA or N-(adamantan-1-yl)-1-(5-fluoropentyl)-1*H*-indazole-3-carboxamide) are not under international control. In March 2017, the Commission on Narcotic Drugs decided to place MDMB-CHMICA (methyl 2-(1-(cyclohexylmethyl)-1*H*-indole-3-carboxamido)-3,3-dimethylbutanoate) under international control (Schedule II of the 1971 Convention).

FIG. 19 Examples of chemical modifications leading to new synthetic cannabinoids



(A) The naphthoylindole, JWH-018, (B) The naphthoylindazole THJ-018, (C) the indazole carboxamide AKB-48, also known as "APINACA", and the indole carboxamide (D) MDMB-CHMICA. The areas of the structures marked in red show the chemical modifications.

overall effects of cannabis, including its anxiolytic properties. Synthetic cannabinoids pose a considerable risk to public health for a number of reasons, and many of those that appear in different products can be much more potent than THC.[147]

Public health harms and risks associated with the use of synthetic cannabinoids

Synthetic cannabinoids have structural features that allow binding to the cannabinoid receptors within the body. Many synthetic cannabinoids, such as JWH-018 and AM-2201,[148] are more potent than THC[149, 150] and are associated with increased severe adverse events and greater toxicity.[151] A number of toxic effects have been reported by users of synthetic cannabinoids, including seizures, loss of consciousness, psychosis, vomiting, drowsiness, chest pain, agitation, hot flushes, dilation of pupils and a dry mouth. Evidence also suggests that tolerance or withdrawal symptoms may occur when use is discontinued following regular chronic use.[152]

147 *Terminology and Information on Drugs* (United Nations publication, Sales No. E.16.XI.8).

148 AM-2201 [1-(5-fluoropentyl)-1*H*-indol-3-yl]-1-naphthalenylmethanone has been under international control since 2015 (Schedule II of the 1971 Convention).

149 G S. M. R. Gurney and others, "Pharmacology, toxicology, and adverse effects of synthetic cannabinoid drugs", *Forensic Science Review,* vol. 26, No. 1 (2014), pp. 53-78.

150 Ziva D. Cooper, "Adverse effects of synthetic cannabinoids: management of acute toxicity and withdrawal", *Current Psychiatry Reports,* vol. 18, No. 5 (2016).

151 Robert Kronstrand and others, "Toxicological findings of synthetic cannabinoids in recreational users", *Journal of Analytical Toxicology,* vol. 37, No. 8 (2013), pp. 534-541.

152 "Critical review of psychoactive substances: JWH-018 and AM-2201 in *WHO Expert Committee on Drug Dependence: Thirty-sixth Report,* WHO Technical Report Series, No. 991 (Geneva, World Health Organization, 2014).

The high potency and associated toxicity of some synthetic cannabinoids have led to severe adverse effects, including fatalities. Acute synthetic cannabinoid intoxications greatly increased in the United States between January 2010 and November 2015.[153] Those intoxication events were often confined to specific areas and time periods, and the exact synthetic cannabinoids (or combination of cannabinoids) causing the intoxications could not always be established. For example, cases of exposure to synthetic cannabinoids reported to poison centres in the Unites States showed a stark but short-lived increase in April 2015. The largest increase in acute intoxication cases was reported in the north-east area of the country, predominantly driven by growing reports in New York, where an increase in cannabinoid-related emergency department visits was recorded.[154] Among those patient cases, the majority (83.1 per cent) were male, with three deaths reported. A similar outbreak of intoxications was also reported in New York in 2016, when 33 cases of AMB-FUBINACA[155] intoxications were recorded.[156]

In addition, several fatal intoxications associated with the use of synthetic cannabinoids have been reported in Europe. Twenty-nine deaths were associated with MDMB-CHMICA, a synthetic cannabinoid of a higher potency than THC, and potentially also JWH-018,[157] in 2014 and 2015.[158]

153 Anne M. Riederer and others, "Acute poisonings from synthetic cannabinoids: 50 U.S. toxicology investigators consortium registry sites, 2010-2015", *Morbidity and Mortality Weekly Report,* vol. 65, No. 27 (2016), pp. 692-695.

154 Michelle L. Nolan and others, "A public health approach to increased synthetic cannabinoid-related morbidity among New York City residents, 2014-2015", *International Journal of Drug Policy*, vol. 34 (2016), pp. 101-103.

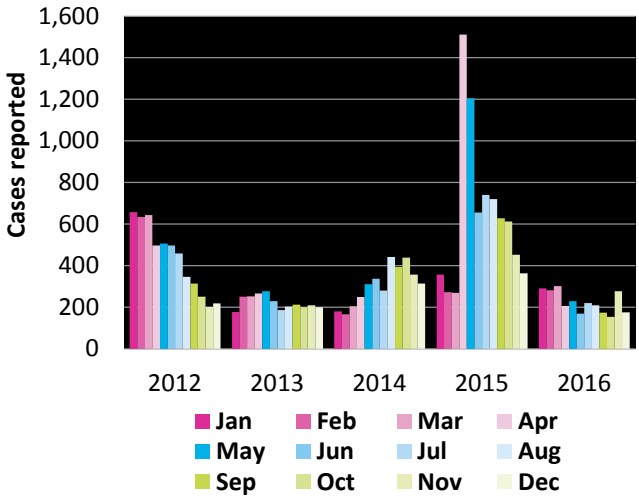
155 AMB-FUBINACA (methyl (1-(4-fluorobenzyl)-1*H*-indazole-3-carbonyl)valinate) is not under international control.

156 Alex J. Adams and others, "'Zombie' outbreak caused by the synthetic cannabinoid AMB-FUBINACA in New York", *New England Journal of Medicine*, vol. 376, No. 3 (2017), pp. 235-242.

157 WHO Expert Committee on Drug Dependence, "MDMB-CHMICA: critical review report-thirty-eighth meeting" (Geneva, World Health Organization, 2016).

158 EMCDDA, *EMCDDA-Europol Joint Report on a New Psychoactive Substance: Methyl 2-[[1-(cyclohexylmethyl) indole-3-carbonyl]amino]-3,3-dimethylbutanoate (MDMB-CHMICA),* Joint Reports Series (Luxembourg, Publications Office of the European Union, 2016).

FIG. 20 Exposure to synthetic cannabinoids reported to poison centres, United States, 2012-2016



Source: American Association of Poison Control Centers.

In Poland, a large outbreak of several hundred intoxications was registered in 2015, including at least three fatal cases, caused by the use of an NPS product known as "Mocarz" (Strongman), which contained a mixture of synthetic cannabinoids.[159] The presence of MDMB-CHMICA was recorded and reports suggested that even low doses of the substance could have fatal consequences. More intoxications and fatal cases associated with the use of synthetic cannabinoids may have remained undetected because of knowledge gaps in toxicology, particularly of newly emerging substances, and the interaction between synthetic cannabinoids and other drugs.[160]

Violence in prisons associated with synthetic cannabinoid use

The use of synthetic cannabinoids in prisons is becoming an increasingly pronounced issue in the United Kingdom, where reports associate prison violence and adverse health effects with the use of

159 Piotr Adamowicz, "Fatal intoxication with synthetic cannabinoid MDMB-CHMICA", *Forensic Science International,* vol. 261 (2016), pp. e5-e10.

160 Laura M. Labay and others, "Synthetic cannabinoid drug use as a cause or contributory cause of death", *Forensic Science International,* vol. 260 (2016), pp.31-39.

Use of synthetic cannabinoids in prison settings

The use of synthetic cannabinoids seems to be increasing in prison settings, probably due to the challenge of detecting and identifying them. Up to a third of prisoners in the United Kingdom use synthetic cannabinoids, potentially as a replacement for cannabis. Consequently, positive drug tests for cannabis have decreased by 59 per cent over the past decade, while the detection of synthetic cannabinoids has increased in the same period.[a] In New Zealand in 2015, 60 per cent of police detainees had tried synthetic cannabinoids at some point in their lives, an increase from the 54 per cent recorded in 2013, while 27 per cent had used them in the past 12 months and 12 per cent had used them in the past month. These proportions are relatively high compared to the corresponding prevalence of use in the general population, indicating the popularity of synthetic cannabinoids among persons who have come into formal contact with police.[b]

A recent report indicated that in the United States, synthetic cannabinoids are possibly used by inmates because they are not detected in mandatory drug screens or by trained narcotics sniffer dogs.[c] For example, to avoid controls and smuggle the substances into correctional facilities, liquid forms of synthetic cannabinoids are sprayed onto paper products, such as greeting cards, letters and coffee filters, dried and then mailed to inmates, who may then chew or smoke them. A study in the United States, which re-tested biological specimens from probationers, found metabolites of synthetic cannabinoids in samples that originally tested negative for drugs in general tests which did not include substances from this group.[d] Indeed, synthetic cannabinoids pose significant challenges not only to health care and detection techniques but also to the management of offenders in prison settings.

[a] Kalk and others, "Spice and all things nasty: the challenge of synthetic cannabinoids".

[b] Wilkins and others, *New Zealand Arrestee Drug Use Monitoring 2010-2015 Report*.

[c] United States, Drug Enforcement Administration, *2016 National Drug Threat Assessment Summary*.

[d] Wish, Billing and Artigiani, *Community Drug Early Warning System: The CDEWS-2 Replication Study*.

synthetic cannabinoids by inmates. In 2015, synthetic cannabinoids were reported to be particularly linked to destabilizing effects in prisons, exacerbating issues of bullying, debt, riots, self-harm, self-inflicted death, serious illnesses and violence amongst prisoners and against staff.[161] Staff and prisoners of a prison in Kent witnessed an increase in inmates collapsing, seizures and hospitalizations from the use of synthetic cannabinoids, despite inmates being aware of the potential risks of NPS use.[162] In addition, the quantities of synthetic cannabinoids (973 grams) seized in an English prison surveyed during the first three months of 2015 vastly outweighed the quantities of cannabis (15 grams) and heroin (3 grams) seized.[163]

In a survey conducted in nine prisons in England in the first half of 2016, the self-reported past-month use of synthetic cannabinoids was reported by a third of respondents, with almost half of them using the substances daily. Responses implied the use of synthetic cannabinoids in acts of bullying in which vulnerable mentally ill prisoners were given high doses of synthetic cannabinoids for the purpose of entertaining others, relieving boredom and expressing dominance.[164] A study of nine different English prisons recorded 54 serious incidents over a three-month period (April to June) in 2015 in which synthetic cannabinoids were implicated: 44 per cent of the prisoners involved required hospital admission for toxicity, 19 per cent of incidents involved violence, and 9 per cent involved self-harm.[165]

Challenges for legislative responses

The structural diversity and rapid development of new derivatives of synthetic cannabinoids pose challenges to legislative control. A wide range of legislative responses have been adopted by Member States at the national level to control synthetic cannabinoids, including individual listings and generic or analogue controls to tackle the increase of new compounds. In principle, generic legislation can be used to control any group of substances with structural similarities, which is what has occurred in the

161 United Kingdom, Her Majesty's Inspectorate of Prisons, *Changing Patterns of Substance Misuse in Adult Prisons and Service Responses* (London, 2015).

162 Shane Blackman and Rick Bradley, "From niche to stigma – headshops to prison: exploring the rise and fall of synthetic cannabinoid use among young adults", *International Journal of Drug Policy*, vol. 40 (2016), pp. 70-77.

163 Ralphs and others, "Adding spice to the porridge: the development of a synthetic cannabinoid market in an English prison".

164 User Voice, "Spice: the bird killer – what prisoners think about the use of spice and other legal highs in prison" (May, 2016).

165 Rehabilitation for Addicted Persons Trust, "Tackling the issue of new psychoactive substances in prisons", RAPt Research and Policy Briefing Series No. 4 (London, September 2015).

case of synthetic cannabinoids as a result of the sheer number emerging within a relatively short timeframe in some countries. Generic legislation defines a core molecular structure and specifies particular variations of the structure that fall under its control.[166] The intended advantage of generic legislation is the simultaneous control of large groups of substances without the need to list them individually. This includes substances that have not yet been reported, potentially preventing their emergence. However, the interaction between the generic control of synthetic cannabinoids and market developments has proved to be complex.[167] In some cases, the definitions of generic legislation have had to be amended or extended to include new classes of synthetic cannabinoids, whose design was not envisaged under the original law.[168] Of the 59 countries for which information is available on the UNODC early warning advisory on new psychoactive substances, 19 countries in Asia, Europe and North America have adopted the generic legislation approach.

B.6. Use of hallucinogenic new psychoactive substances is increasing in South America

As a diverse group of both naturally occurring plant-based and synthetic substances, hallucinogens induce distorted states of consciousness, perception, thinking and feeling, accompanied by different degrees of auditory or visual hallucinations.[169] Synthetic substances, possessing similar effects to potent hallucinogens under international control, such as LSD and 2C-B, have emerged recently.[170] These NPS with hallucinogenic effects constitute roughly 16 per cent (as of December 2016) of all substances in the UNODC early warning advisory on new psychoactive substances and have been reported by 55 Member States.[171] These substances are chemically diverse and include phenethylamines, in particular derivatives of the psychedelic 2C-B series of compounds, such as NBOMe compounds, and tryptamines (e.g., *alpha*-methyltryptamine (AMT)).[172]

The emergence of these substances has been associated with severe intoxications, including fatalities. Several countries have reported substances belonging to the NBOMe series that were either sold, or referred to, as LSD, "synthetic LSD"[173] or "ecstasy". As with LSD, NBOMe compounds are often sold on blotter paper which has been soaked with a solution of the substance. However, users may not be aware that they are consuming NBOMe compounds[174] and, as NBOMe compounds vary in potency and toxicity, even small differences in dosage may lead to overdoses with potentially fatal consequences.[175]

Following their emergence in East Asia, Europe, North America and Oceania,[176] NBOMe compounds have also been reported in South America. The emergence of NPS with hallucinogenic effects in South America is noteworthy, as other NPS

166 UNODC, "Synthetic cannabinoids: key facts about the largest and most dynamic group of NPS", *Global SMART Update 2015*, vol. 13 (March 2015).

167 Kikura-Hanajiri and others, "Changes in the prevalence of new psychoactive substances before and after the introduction of the generic scheduling of synthetic cannabinoids in Japan".

168 See, for example, United Kingdom, Misuse of Drugs Act 1971 (Amendment) Order 2009. A large group of synthetic cannabinoids was first controlled in 2009. Owing to new variations of synthetic cannabinoids appearing in the market, the generic definition was further revised in 2012. However, there are now more "third generation" synthetic cannabinoids in the United Kingdom market that do not fall under the control of the Misuse of Drugs Act 1971 (see *New Psychoactive Substances Review: Report of the Expert Panel* (London, September 2014)).

169 *Terminology and Information on Drugs* (United Nations publication, Sales No. E.16.XI.8).

170 (+)-Lysergide (LSD) has been under international control since 1971 (original list, Schedule I of the 1971 Convention), and 2C-B was placed under international control in 2001 (Schedule II of the 1971 Convention.

171 UNODC early warning advisory on new psychoactive substances.

172 Several NBOMe compounds were placed under international control in 2015 (25B-NBOMe, 25C-NBOMe and 25I-NBOMe). *alpha*-methyltryptamine (AMT) is not under international control.

173 Will Lawn and others, "The NBOMe hallucinogenic drug series: patterns of use, characteristics of users and self-reported effects in a large international sample", *Journal of Psychopharmacology,* vol. 28, No. 8 (2014), pp. 780-788.

174 Juji Suzuki and others, "Toxicities associated with NBOMe ingestion: a novel class of potent hallucinogens–a review of the literature", *Psychosomatics*, vol. 56, No. 2 (2015), pp. 129-139.

175 "Critical review of psychoactive substances: 25B-NBOMe, 25C-NBOMe and 25I-NBOMe in *WHO Expert Committee on Drug Dependence: Thirty-sixth Report.*

176 David M. Wood and others, "Prevalence of use and acute toxicity associated with the use of NBOMe drugs", *Clinical Toxicology,* vol. 53, No. 2 (2015), pp. 85-92; UNODC early warning advisory on new psychoactive substances.

groups, such as synthetic cannabinoids, are much less prominent in that subregion than in North America or Europe. An explanation for this regional peculiarity could be that hallucinogenic NPS are emerging onto an existing and possibly growing market for hallucinogens such as LSD. Indeed, seizures of NBOMe compounds have increased in South America and recent surveys show increases in the prevalence of use of LSD. In Chile, several NBOMe compounds sold as LSD were seized by law enforcement authorities or identified in connection with emergency room admissions.[177] Moreover, in Chile, the past-year prevalence of use of LSD among the general population increased from 0.2 per cent in 2012 to 0.5 per cent in 2014. By comparison, the number of doses of NBOMe compounds seized in Chile increased exponentially, from 2,245 in 2013 to 41,762 in 2015.[178]

In Colombia, there was a significant increase in the lifetime prevalence of LSD use among the general population, from 0.05 per cent in 2008 to 0.73 per cent in 2013,[179] similar to the trend in Chile. However, a number of emergency room cases documented that users, wrongly believing to have consumed LSD, had actually taken 25B-NBOMe and 25C-NBOMe. Similarly, shipments of "ecstasy" and "LSD" containing NPS have been reported being sent from Western and Central Europe to South America. In 2013, the National Police of Chile seized a shipment of 800 stamps, originating in Spain, that supposedly contained LSD but which actually consisted of 25I-NBOMe.[180] Given the presence of hallucinogenic NPS in South America, documented in seizure data and emergency room reports, it is possible that a potentially growing market for hallucinogens, indicated by increases in prevalence of use, has opened up opportunities for traffickers to sell NPS with hallucinogenic effects.

Countries in South America have already reacted to the emergence of hallucinogenic NPS, including by setting up early warning systems, issuing alerts and introducing new legislation. For example, the early warning system in Colombia, established in 2013, issued alerts on NPS sold as LSD that were made available online to the general population.[181] In Chile, meanwhile, a total of 100 NPS, including several NBOMe compounds, were included in the national lists of controlled psychoactive substances in 2014 and 2015.[182] A similar approach was adopted in Brazil in May 2016, when the Brazilian Health Regulatory Agency (ANVISA) approved a resolution to add 11 different NBOMe compounds to the national list of controlled substances.[183] At the international level, three NBOMe compounds, namely 25B-NBOMe, 25C-NBOMe and 25I-NBOMe, were placed under international control in 2015.

B.7. Synthetic opioids: the resurgence of fentanyl and its analogues

Synthetic opioids are narcotic analgesics that generate effects similar to those caused by natural opioids. Although some of them have remarkable pain-relieving properties and are widely used in human therapy, they are also liable to abuse and may produce dependence. In North America, the non-medical use of synthetic opioids and the use of heroin have escalated into a crisis of overdose deaths, and evidence of mounting overdoses has been registered in other regions (for more information, see booklet 2 of the present report).

The growing supply and use of illicitly manufactured synthetic opioids such as fentanyl and fentanyl analogues is particularly alarming and present a complex challenge. Fentanyl itself is a powerful analgesic with

177 UNODC, "Global SMART programme Latin America", Information Bulletin No. 1 (June 2016).

178 Chile, Ministry of the Interior and Public Security, "NSP y precursors", pp. 14-16; (Spanish only) available from www.interior.gob.cl.

179 Observatorio de Drogas de Colombia, *Estudio Nacional de Consumo de Sustancias Psicoactivas en Colombia—2013* (Bogotá, June 2014). Additional information to the final report, drawn from the database of the study, available from www.unodc.org.

180 Inter-American Drug Abuse Control Commission of the Organization of American States, *Report on Drug Use in the Americas,* 2015, p. 154.

181 UNODC, "Global SMART programme Latin America", Information Bulletin No.º 2 (September 2016).

182 Chile, Ministry of the Interior and Public Security, *Official Journal of the Republic of Chile, No. 41120* (Santiago, 30 March 2015); and Chile, Ministry of the Interior and Public Security, National Committee on New Psychoactive Substances, Inter-agency coordination, collection and analysis of available information to update drug lists", Report No. 1 (Santiago, September 2015), pp. 5-9.

183 Brazil, Brazilian Health Regulatory Agency, Resolution No. 79 (23 May 2016).

an established place in medicine, but it is also known for its potential for abuse and dependence. Heroin containing, or substituted with, fentanyl or fentanyl analogues originally appeared on the illicit drug market in the 1970s and 1980s under names like "China White", "Tango and Cash" or "synthetic heroin", products that became notorious for accidental overdoses.[184] A similar situation seems to have been developing since around 2014, when fentanyl originating mainly from clandestine manufacturing rather than from diversion of pharmaceutical products containing fentanyl was identified on the opioid market. That situation has been aggravated by the rapid appearance of novel fentanyl analogues and other synthetic opioids that have not been approved for medical use. In recent years, several emergent opioids have been associated with increasing numbers of serious adverse events and deaths.[185] The pills and powders containing synthetic opioids sold on the illicit market pose a threat to public health because of the variable quantity and potency of their active components, which in extreme cases, such as carfentanil,[186] may be 10,000 times more potent than morphine. Such products can prove particularly dangerous when sold as street heroin or as counterfeit prescription drugs without the user's knowledge.

Medical use and adverse effects of synthetic opioids

Fentanyl, which has about 100 times the potency of morphine, is the strongest opioid available for use in humans. Its powerful analgesic and sedative effects mean that it is widely used in the management of severe pain and in anaesthesia. The three fentanyl analogues approved for pharmaceutical use, sufentanil, alfentanil and remifentanil,[187] have very short onset and duration of action, and their medical use is limited to intravenous anesthesia. Carfentanil is intended only for veterinary use on large animals and is not approved for human use.[188]

Synthetic opioids have a well-documented potential for abuse and dependence, which is reflected in international legislative responses. First synthesized in 1959, fentanyl was placed under international control as a Schedule I substance in 1964 under the Single Convention on Narcotic Drugs of 1961. In the ensuing decades, the list of scheduled substances grew to include all fentanyl analogues approved for medical use in humans, and several analogues that were not developed into pharmaceutical products were placed under international control between 1988 and 1990.[189] More recently, acetylfentanyl and butyrfentanyl were placed under international control.[190] Carfentanil, which was first synthesized in 1974 and remains the most potent commercially available opioid in the world, is not under international control.

Within the past five years, more than a dozen additional synthetic opioids have entered the illicit opioid market, some of which have been rediscovered by traffickers in research done between the 1960s and 1990s, when they were described in scientific literature but never developed into pharmaceutical products. Examples include several fentanyl analogues developed between the 1960s and 1990s, such as acetylfentanyl, butyrfentanyl, furanylfentanyl and ocfentanil.[191] Novel fentanyl analogues such as acrylfentanyl and *para*-fluoroisobutyrfentanyl continue to appear.[192] A number of newly marketed synthetic opioids have structures distinct from those used in medical practice, including AH-7921 (a benzoamide), MT-45 (a piperazine) and U-47700 (a compound closely related to AH-7921), all of which were first synthesized in the

184 G.L. Henderson, "Fentanyl-related deaths: demographics, circumstances, and toxicology of 112 cases", *Journal of Forensic Sciences,* vol. 36, No. 2 (March 1991), pp. 422-433.

185 UNODC early warning advisory on new psychoactive substances, "Deaths associated with use of emerging synthetic opioids", November 2016. Available at www.unodc.org.

186 Carfentanil is not under international control.

187 Sufentanil, alfentanil and remifentanil have been under international control since 1980, 1984 and 1999, respectively, and are listed in Schedule I of the 1961 Convention.

188 P. A. J. Janssen, "Potent, new analgesics, tailor-made for different purposes", *Acta Anaesthesiologica Scandinavica,* vol. 26, No. 3 (June 1982), pp. 262-268.

189 UNODC, "Fentanyl and its analogues: 50 years on", *Global SMART Update 2017*, vol. 17 (Vienna, March 2017).

190 Acetylfentanyl was placed under international control in 2016 (Schedules I and IV of the 1961 Convention) and butyrfentanyl in 2017 (Schedule I of the 1961 Convention).

191 Furanylfentanyl and ocfentanil are not under international control.

192 Acrylfentanyl and *para*-fluoroisobutyrfentanyl are not under international control.

1970s.[193] Fourteen fentanyl analogues and three synthetic opioids belonging to other structural groups were reported to the UNODC early warning advisory on new psychoactive substances between 2012 and 2016 by countries in East Asia, Europe and North America. The countless possibilities for creating new compounds by making minor changes in chemical structures pose a growing challenge to legislative controls.

Risks associated with the use of, or exposure to, synthetic opioids

The non-medical use of synthetic opioids can have severe health consequences. Tolerance and dependence develop very quickly and may reach extreme levels. Above all, each episode of non-medical use carries a high risk of overdose and death as a result of respiratory depression, a common side effect of opioids. Overdoses can be effectively reversed by naloxone, a μ-opioid receptor antagonist but, importantly, reversing overdoses of fentanyl or its analogues often requires very high doses of naloxone. In response to the growing need for overdose treatment, some countries have made efforts to increase the availability of naloxone, including Australia,[194] Canada,[195] Italy[196] and the United States.[197]

The recreational use of pharmaceutical products containing fentanyl can easily prove fatal if users increase the dose or change the route of administration. The use of illicitly manufactured synthetic opioids increases the danger because they lack quality control, are typically not portioned in precise doses and can be deadly in minuscule amounts because of their extreme potency. Users experimenting with new synthetic opioids, whose levels of potency are not well-defined, increase the odds of making a fatal mistake.

An overdose can also be caused by handling strong synthetic opioids without the precautions that prevent the substance from being inhaled or absorbed through the skin or mucous membranes. Contact with fentanyl or its analogues is so hazardous that both Canada and the United States have recorded incidents of hospitalization of law enforcement officers who carried out seizures of such chemicals. The Drug Enforcement Administration of the United States has recently released safety alerts for fentanyl and carfentanil, advising what steps to follow in situations where such drugs might be present, including the immediate application of naloxone in case of exposure.[198]

Manufacturing and trafficking of synthetic opioids

According to the Drug Enforcement Administration, the current fentanyl crisis in the United States is largely fuelled by illicitly manufactured fentanyl and its analogues,[199] which are either illegally imported as such or synthesized from imported precursors. The materials and apparatus used in fentanyl synthesis and tableting are inexpensive and easy to obtain from online vendors, and the synthesis does not require sophisticated laboratory skills, which facilitates small-scale manufacturing by minor drug trafficking organizations. Most of the fentanyl recently seized in the United States has been of non-pharmaceutical origin and synthesized using the so-called "Siegfried route", which was first described in the 1980s and is relatively easy to perform.

Precursor chemicals used in this route are *N*-phenethyl-4-piperidone (NPP) or its derivative, 4-anilino-*N*-phenethylpiperidine (ANPP). The majority of fentanyl analogues reported to UNODC in recent years, including acetylfentanyl, butyrfentanyl and furanylfentanyl, can be synthesized from

193 AH-7921, MT-45 and U-47700 have been under international control since 2015, 2016 and 2017, respectively, listed in Schedule 1 of the 1961 Convention.

194 Australia, Department of Health, Therapeutic Goods Administration, "Final decisions and reasons for decisions by a delegate of the Secretary to the Department of Health" (Canberra, 2015).

195 Canada, Health Canada, "Availability of Naloxone Hydrochloride Nasal Spray (NARCAN®) in Canada", 6 July 2016. Available from www.hc-sc.gc.ca.

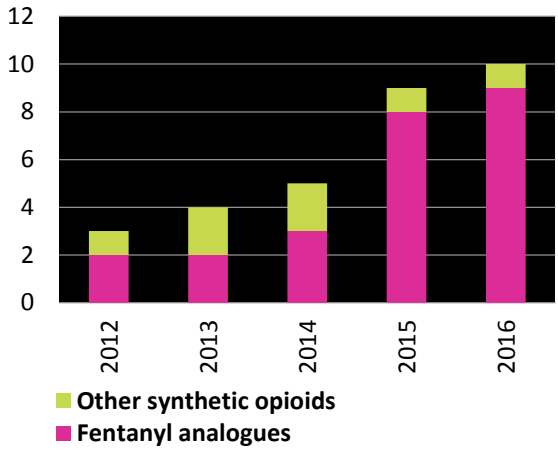
196 Simon R. Lenton and Kim M. Hargreaves, "Should we conduct a trial of distributing naloxone to heroin users for peer administration to prevent fatal overdose?" *Medical Journal of Australia,* vol. 173, No. 5 (September 2000), pp. 260-263.

197 US Department of Health and Human Services, The Opioid Epidemic: By the Numbers, June 2016.

198 US Drug Enforcement Administration, DEA Officer Safety Alert, Fentanyl – A Real Threat to Law Enforcement. Available at www.dea.gov/video_clips/Fentanyl%20Roll%20Call%20Video.mp4.

199 United States, Drug Enforcement Administration, "Counterfeit prescription pills containing fentanyls: a global threat". DEA Intelligence Brief. DEA-DCT-DIB-021-16 (2016).

FIG. 21 Annual number of synthetic opioids reported to UNODC, 2012-2016



Source: UNODC early warning advisory on new psychoactive substances. Includes only synthetic opioids reported as NPS (i.e., with no current approved medical use). Data for 2016 are preliminary.

NPP or ANPP. These two precursors were placed under international control in March 2017. However, a large group of long-known fentanyl analogues that were put under international control between the 1960s and the 1990s, and which do not appear to be linked to the current opioid crisis in the United States, cannot be produced from NPP or ANPP.

Data reported to UNODC on dismantled laboratories that had been used for manufacturing fentanyl include three cases in Canada (one kitchen laboratory and one industrial-scale facility in 2011, and one medium-to-large-scale facility in 2012), one kitchen laboratory in Germany (2015), one kitchen laboratory in Slovakia (2011), one case of manufacturing 3-methylfentanyl[200] in the Russian Federation (2014) and three kitchen laboratories in the United States (one in 2013 and two in 2015).

Sources of synthetic opioids sold on illicit markets are often specific to a given subregion or country. In North America, for example, synthetic opioids are most commonly sold as adulterated/substituted heroin or counterfeit pharmaceuticals resembling prescription pills. In Australia and Germany, fentanyl diverted from pharmaceutical products is the main synthetic opioid liable to non-medical use. In Estonia, clandestinely produced fentanyl or its analogues are sold as the drug of choice.

Owing to their extreme potencies, synthetic opioids are often present in trace amounts in the products available, be it as pharmaceuticals, illicitly manufactured material or in admixture with, for example, heroin. This makes detection of these substances extremely challenging in the forensic laboratory and could lead to underreporting of the extent to which they appear on the market.

B.8. GBL: a ready source of GHB?

Gamma-hydroxybutyrate (GHB) is used in medicine as an adjunct in surgical anaesthesia and as an aid in alcohol or opiate withdrawal. The depressant effect of GHB on the central nervous system produces relaxation, reduced inhibition, euphoria and mild hallucinations — factors that have driven the recreational use of the substance. On the illicit drugs market, GHB is known under street names such as "G", "liquid ecstasy", "Georgia Home Boy" and "Grievous Bodily Harm" and has been associated with drug-facilitated sexual assault.[201] Chronic use of GHB, which was placed under international control in 2001, results in the development of physiological and physical dependence and withdrawal syndromes. GHB is particularly dangerous when ingested together with alcohol or other sedatives, and overdosing on GHB can lead to coma, respiratory depression and death.

GHB has been implicated in a rising number of fatalities, particularly in developed subregions, including North America, Western and Central Europe and Australasia. A recent European study found that GHB was ranked as the fourth most commonly reported drug for hospital emergency cases and was on an upward trend.[202] In 2015, a substantial increase in deaths associated with GHB was registered in London, of which 25 per cent of case history records indicated an association with

200 3-Methylfentanyl was placed under international control in 1988 (in Schedules I and IV of the 1961 Convention).

201 See also *Guidelines for the Forensic Analysis of Drugs Facilitating Sexual Assault and Other Criminal Acts* (ST/NAR/45).

202 EMCDDA, *Hospital Emergency Presentations and Acute Drug Toxicity in Europe: Update from the Euro-DEN Plus Research Group and the EMCDDA*, Rapid Comunication Series (Luxembourg, Publications Office of the European Union, August 2016).

so-called "chemsex" events.[203] However, fatal cases are likely to be underreported because the drug is often not included in a routine analysis and has a short half-life, which limits toxicological detection.

While GHB is controlled under the 1971 Convention, the closely related chemical *gamma*-butyrolactone (GBL),[204] which is an important solvent and reagent in industry, is not under international control. GBL has widespread legitimate use in industry, with global requirements being in the region of hundreds of thousands of tons and single consignments reaching up to 500 tons.[205] GBL also serves as a prodrug of GHB, being readily converted to the latter after ingestion and producing the full spectrum of effects. Furthermore, GBL provides a ready source as an immediate precursor for the clandestine manufacture of GHB.

It is difficult to assess to what extent GBL is traded for non-industrial purposes such as direct human consumption or illicit conversion to GHB. However, recent reports by EMCDDA and Europol about the European GBL market indicate that large-scale manufacturing for the drug market seems to be concentrated in the Netherlands, and it occasionally occurs in the same place as the manufacturing of other illicitly used synthetic drugs such as MDMA or amphetamine.[206] This provides a link between GBL and the clandestine manufacture and trafficking of illicit drugs.

The use of GBL as a prodrug for GHB may actually be more prevalent than assumed, with small-scale studies indicating that users may be mistakenly self-reporting ingestion of GHB when they have in fact ingested GBL. In Europe, Oceania and North America, in countries where GBL is under national control, significant amounts of GBL were seized from January 2015 to December 2016, including several shipments exceeding 100 kg and one exceptionally large seizure of 15 tons of GBL in Poland in March 2016, which was destined for the Netherlands. Ordering such large amounts, breaking them down into smaller shipments and successfully distributing them requires a certain degree of organization and a correspondingly large consumer base. Indeed, a 2013 study combining Internet-monitoring processes, packaging and isotopic analyses concluded that the GBL market was organized into three levels: a manufacturing stage located mainly in China and Germany; an intermediary online distribution level hosted mainly in the Netherlands; and customers who order online.[207]

In view of the large-scale shipments of GBL seized in 2015 and 2016, it seems plausible that organized criminal groups are trying to increase the availability of GBL. However, because of the rapid conversion of GBL to GHB upon ingestion, it is challenging, from the forensic perspective, to determine from human fluids which of the two substances was ingested initially. It thus remains uncertain to what extent GBL is used as a precursor for GHB or consumed directly.

B.9. Ketamine supply is increasing in South-East Asia

A widely used human and veterinary anaesthetic, ketamine is listed as an essential medicine by the World Health Organization (WHO).[208] Increasing presence on illicit drug markets led to the scheduling of ketamine as a controlled substance in 70 out of 100 countries[209] that responded to a WHO survey in 2015. For non-medical use, ketamine is typically presented in the form of a powder, although it may be available as pills, and is sold on illicit

203 Joanna Hockenhull, Kevin G. Murphy and Sue Paterson, "An observed rise in γ-hydroxybutyrate-associated deaths in London: evidence to suggest a possible link with concomitant rise in chemsex", *Forensic Science International,* vol. 270, No. 1 (January 2017), pp. 93-97.

204 Another substance closely related to GHB is 1,4-butanediol (1,4-BD; BDO), a substance widely used in industry. It can be easily converted into GHB by chemical synthesis or, in principle, also in the human body. However, direct consumption of 1,4-BD for recreational purposes is rarely reported. 1,4-BD is not under international control.

205 "Critical review of psychoactive substances: gamma-butyrolactone (GBL)" in *WHO Expert Committee on Drug Dependence: Thirty-sixth Report.*

206 EMCDDA and Europol, *EU Drug Markets Report: In-Depth Analysis.*

207 Diego Pazos and others, "Combining Internet monitoring processes, packaging and isotopic analyses to determine the market structure: example of gamma butyrolactone", *Forensic Science International,* vol. 230, Nos. 1-3 (2013), pp. 29-36.

208 WHO, *Model List of Essential Medicines: 19th List (*April 2015) (amended November 2015).

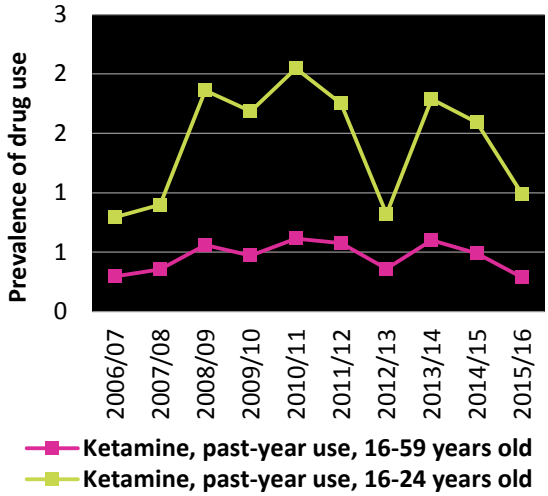
209 "Ketamine (INN): questionnaire report", presented to the WHO Expert Committee on Drug Dependence at its thirty-seventh meeting, held in Geneva from 16 to 20 November 2015.

markets under different street names such as "K" and as established products such as "ecstasy" or methamphetamine pills (Thailand, Indonesia),[210] sometimes to unwitting users. In 2014, China requested consideration for the scheduling of ketamine under the international drug control conventions to curb its abuse,[211] but WHO recommended against international control of ketamine on the basis that this might affect its availability for medical use.[212]

In a 2015 WHO survey, the use of ketamine for non-medical purposes was reported by 32 countries, of which 10 identified specific subpopulations that use ketamine: youth, males (aged 16-24 years), prison population, medical staff, night clubbers, pub or party goers and recreational drug users.[213] The non-medical use of ketamine is indicated to have increased in each of the past six years in (mainland) China but seems to be on decline in Hong Kong, China, where — based on drug-user registration data — the number of reported ketamine users decreased by 46 per cent over the past five years, from 3,600 in 2011 to 1,974 in 2015. In the United States, past-year use among twelfth graders remained without significant year-on-year changes over the period 2013 and 2016, ranging between 1.2 per cent and 1.5 per cent.[214] In England and Wales, after a peak in 2010/11, the past-year prevalence of use of ketamine seemed to be on the decrease, with 2015/16 drug-use survey prevalence figures back to the baseline levels first recorded in 2006/07.[215]

While the ketamine sold on drug markets in the past tended to have been diverted from the pharmaceutical sector, clandestine manufacture has emerged in recent years as a significant source, particularly in East and South-East Asia. In China, 89 illicit ketamine laboratories were dismantled in 2014 and 118 in 2013, while in Malaysia, national authorities dismantled the first ever ketamine manufacturing facility in the country in 2016. Other countries that have reported ketamine labs since 2010 include Canada (1 in 2013), India (1 in 2012) and the United States (1 in 2013).

FIG. 22 Prevalence of use of ketamine in England and Wales, United Kingdom, 2006/07-2015/16



Source: Home Office of the United Kingdom, "Drug misuse: findings from the 2015 to 2016 CSEW", data tables, 2nd edition.

The average number of countries/territories reporting ketamine seizures increased from 21 over the period 2010-2012, to 27 over the period 2013-2015. In addition, significant increases in the quantities of ketamine seized globally have been reported since 2012, which have mainly been driven by increases in seizures in China. In 2015, global ketamine seizures amounted to 23 tons, the largest amount recorded since the start of systematic monitoring by UNODC in 1999.

The proportion of ketamine seized in different subregions has varied considerably since 2010. East and South-East Asia accounted for 65 per cent of the amount seized globally in 2010, while Europe and South Asia accounted for 6 per cent (800 kg) and 10 per cent (1 ton) respectively. By 2015, East and

210 APAIC, Synthetic drug trends, National trends: Indonesia (1 December 2014) and Thailand (14 February 2017). Available at www.apaic.org.

211 Note by the Secretariat on the changes in the scope of control of substances (E/CN.7/2015/7).

212 *WHO Expert Committee on Drug Dependence Thirty-seventh Report*, WHO Technical Report Series, No. 998 (Geneva, World Health Organization, 2015).

213 "Ketamine (INN): questionnaire report", presented to the WHO Expert Committee on Drug Dependence at its thirty-seventh meeting.

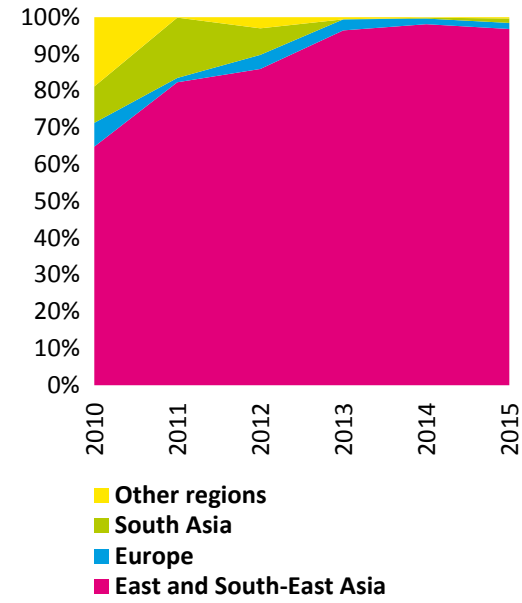
214 United States, National Institute on Drug Abuse, "Monitoring the future study: trends in prevalence of various drugs". Available at www.drugabuse.gov.

215 Ketamine was first controlled in the United Kingdom as a class C drug in 2006, and moved to the stricter class B schedule in 2014.

FIG. 23 Quantities of ketamine seized globally, 2010-2015

Source: UNODC, responses to annual report questionnaire, 2010-2015.

FIG. 24 Proportion of quantity of ketamine seized, by subregion/region, 2010-2015



Source: UNODC, responses to annual report questionnaire, 2010-2015.

South-East Asia accounted for 97 per cent of the total quantity of ketamine seized worldwide that year, which took place primarily in China (19.6 tons), including Taiwan Province of China (1.8 tons) and Hong Kong, China (0.5 tons).

The amount of ketamine seized in East and South-East Asia is also significant in comparison with that of other major drugs of abuse in the subregion. For example, the quantity of ketamine seized in 2015 was twice that of heroin (11 tons).

While ketamine manufactured in clandestine laboratories in mainland China is believed to mainly be consumed locally, there is trafficking to the Macao, China; Hong Kong, China; and other countries. Hong Kong, China, was perceived to be a transshipment location for ketamine from mainland China en route to other countries.[216]

216 APAIC, Synthetic drug trends, National trends: Hong Kong, China, and Thailand, 14 February 2017.

Annual prevalence of the use of amphetamines[a] and "ecstasy", by region and globally, 2015

Region or subregion	Amphetamines and prescription stimulants						"Ecstasy"					
	Number (thousands)			Prevalence (percentage)			Number (thousands)			Prevalence (percentage)		
	Best estimate	Lower	Upper	Best estimate	Lower	Upper	Best estimate	Lower	Upper	Best estimate	Lower	Upper
Africa	**5,900**	**1,520**	**10,150**	**0.90**	**0.23**	**1.54**	**1,430**	**390**	**2,160**	**0.22**	**0.06**	**0.33**
East Africa	-	-	-	-	-	-	-	-	-	-	-	-
North Africa	860	290	1,430	0.58	0.20	0.98	-	-	-	-	-	-
Southern Africa	-	-	-	-	-	-	-	-	-	-	-	-
West and Central Africa	-	-	-	-	-	-	-	-	-	-	-	-
Americas	**7,500**	**6,270**	**8,800**	**1.13**	**0.95**	**1.33**	**3,370**	**3,280**	**3,510**	**0.51**	**0.50**	**0.53**
Caribbean	240	10	540	0.86	0.05	1.91	40	10	130	0.16	0.03	0.47
Central America	200	150	270	0.71	0.52	0.95	20	10	30	0.06	0.03	0.11
North America	6,340	5,430	7,260	1.97	1.69	2.26	2,860	2,860	2,860	0.89	0.89	0.89
South America	700	680	730	0.25	0.24	0.26	440	400	490	0.16	0.14	0.17
Asia	**20,690**	**4,400**	**36,980**	**0.70**	**0.15**	**1.26**	**12,490**	**1,880**	**23,100**	**0.43**	**0.06**	**0.79**
Central Asia	-	-	-	-	-	-	-	-	-	-	-	-
East and South-East Asia	-	-	-	-	-	-	-	-	-	-	-	-
Near and Middle East/ South-West Asia	890	580	1,580	0.31	0.20	0.55	-	-	-	-	-	-
South Asia	-	-	-	-	-	-	-	-	-	-	-	-
Europe	**2,460**	**1,940**	**3,250**	**0.45**	**0.36**	**0.59**	**3,750**	**3,200**	**4,700**	**0.69**	**0.59**	**0.86**
Eastern and South-Eastern Europe	720	410	1,260	0.32	0.18	0.56	1,340	900	2,070	0.59	0.40	0.91
Western and Central Europe	1,740	1,540	1,980	0.55	0.48	0.62	2,400	2,290	2,640	0.75	0.72	0.83
Oceania	**480**	**380**	**530**	**1.91**	**1.51**	**2.08**	**610**	**560**	**630**	**2.42**	**2.22**	**2.49**
Global estimate	**37,030**	**14,520**	**59,700**	**0.77**	**0.30**	**1.24**	**21,650**	**9,310**	**34,110**	**0.45**	**0.19**	**0.71**

Source: UNODC estimates based on annual report questionnaire data and other official sources.

[a] *Amphetamines include both amphetamine and methamphetamine.*

GLOSSARY

amphetamine-type stimulants — a group of substances composed of synthetic stimulants that were placed under international control in the Convention on Psychotropic Substances of 1971 and are from the group of substances called amphetamines, which includes amphetamine, methamphetamine, methcathinone and the "ecstasy"-group substances (3,4-methylenedioxymethamphetamine (MDMA) and its analogues).

amphetamines — a group of amphetamine-type stimulants that includes amphetamine and methamphetamine.

annual prevalence — the total number of people of a given age range who have used a given drug at least once in the past year, divided by the number of people of the given age range, and expressed as a percentage.

coca paste (or coca base) — an extract of the leaves of the coca bush. Purification of coca paste yields cocaine (base and hydrochloride).

"crack" cocaine — cocaine base obtained from cocaine hydrochloride through conversion processes to make it suitable for smoking.

cocaine salt — cocaine hydrochloride.

new psychoactive substances — substances of abuse, either in a pure form or a preparation, that are not controlled under the Single Convention on Narcotic Drugs of 1961 or the 1971 Convention, but that may pose a public health threat. In this context, the term "new" does not necessarily refer to new inventions but to substances that have recently become available.

opiates — a subset of opioids comprising the various products derived from the opium poppy plant, including opium, morphine and heroin.

opioids — a generic term applied to alkaloids from opium poppy (opiates), their synthetic analogues (mainly prescription or pharmaceutical opioids) and compounds synthesized in the body.

problem drug users — people who engage in the high-risk consumption of drugs; for example, people who inject drugs, people who use drugs on a daily basis and/or people diagnosed with drug use disorders (harmful use or drug dependence), based on clinical criteria as contained in the Diagnostic and Statistical Manual of Mental Disorders (fifth edition) of the American Psychiatric Association, or the International Classification of Diseases (tenth revision) of the World Health Organization.

people who suffer from drug use disorders/people with drug use disorders — a subset of people who use drugs. People with drug use disorders need treatment, health and social care and rehabilitation. Dependence is a drug use disorder.

prevention of drug use and treatment of drug use disorders — the aim of "prevention of drug use" is to prevent or delay the initiation of drug use, as well as the transition to drug use disorders. Once there is a drug use disorder, treatment, care and rehabilitation are needed.

REGIONAL GROUPINGS

The World Drug Report uses a number of regional and subregional designations. These are not official designations, and are defined as follows:

- East Africa: Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Mauritius, Rwanda, Seychelles, Somalia, Uganda and United Republic of Tanzania
- North Africa: Algeria, Egypt, Libya, Morocco, South Sudan, Sudan and Tunisia
- Southern Africa: Angola, Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Zambia and Zimbabwe
- West and Central Africa: Benin, Burkina Faso, Cameroon, Cabo Verde, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome and Principe, Senegal, Sierra Leone and Togo
- Caribbean: Antigua and Barbuda, Bahamas, Barbados, Bermuda, Cuba, Dominica, Dominican Republic, Grenada, Haiti, Jamaica, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines and Trinidad and Tobago
- Central America: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama
- North America: Canada, Mexico and United States of America
- South America: Argentina, Bolivia (Plurinational State of), Brazil, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Suriname, Uruguay and Venezuela (Bolivarian Republic of)
- Central Asia and Transcaucasia: Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan
- East and South-East Asia: Brunei Darussalam, Cambodia, China, Democratic People's Republic of Korea, Indonesia, Japan, Lao People's Democratic Republic, Malaysia, Mongolia, Myanmar, Philippines, Republic of Korea, Singapore, Thailand, Timor-Leste and Viet Nam
- South-West Asia: Afghanistan, Iran (Islamic Republic of) and Pakistan
- Near and Middle East: Bahrain, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, State of Palestine, Syrian Arab Republic, United Arab Emirates and Yemen
- South Asia: Bangladesh, Bhutan, India, Maldives, Nepal and Sri Lanka
- Eastern Europe: Belarus, Republic of Moldova, Russian Federation and Ukraine
- South-Eastern Europe: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Montenegro, Romania, Serbia, the former Yugoslav Republic of Macedonia and Turkey
- Western and Central Europe: Andorra, Austria, Belgium, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Monaco, Netherlands, Norway, Poland, Portugal, San Marino, Slovakia, Slovenia, Spain, Sweden, Switzerland and United Kingdom of Great Britain and Northern Ireland
- Oceania: Australia, Fiji, Kiribati, Marshall Islands, Micronesia (Federated States of), Nauru, New Zealand, Palau, Papua New Guinea, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu and small island territories

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To celebrate 20 years since its inception, the *World Drug Report 2017* is presented in a new five-booklet format designed to improve reader friendliness while maintaining the wealth of information contained within.

Booklet 1 summarizes the content of the four subsequent substantive booklets and presents policy implications drawn from their findings. Booklet 2 deals with the supply, use and health consequences of drugs. Booklet 3 focuses on the cultivation, production and consumption of the three plant-based drugs (cocaine, opiates and cannabis) and on the impact of new cannabis policies. Booklet 4 provides an extended analysis of the global synthetic drugs market and contains the bulk of the analysis for the triennial global synthetic drugs assessment. Finally, Booklet 5 contains a discussion on the nexus between the drug problem, organized crime, illicit financial flows, corruption and terrorism.

Enhanced by this new format, the *World Drug Report 2017* is, as ever, aimed at improving the understanding of the world drug problem and contributing towards fostering greater international cooperation for countering its impact on health and security.

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