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An expanding synthetic drugs market – Implications for precursor control

EN



About the SMART Update

Synthetic drugs constitute one of the most significant drug problems worldwide. After cannabis and opioids, amphetamine-type stimulants (ATS) are the most widely used drugs across the globe, with use levels often exceeding those of heroin and/or cocaine. Along with ATS, the continued growth of the new psychoactive substances (NPS) market over the last years has become a policy challenge and a major international concern. A growing interplay between these new drugs and traditional illicit drug markets is being observed, and trends on the synthetic drugs market evolve quickly each year.

The UNODC Global Synthetics Monitoring: Analyses, Reporting and Trends (SMART) Programme enhances the capacity of Member States in priority regions to generate, manage, analyse, report and use synthetic drugs information to design effective policy and programme interventions. Launched in September 2008, the Global SMART Programme provides capacity building to laboratory personnel, law enforcement and research officers in the Pacific, East and South-East Asia, South Asia, the Middle East, Africa, Latin America and the Caribbean; and regularly reviews the global ATS and NPS situation. Its main products include online drug data collection, situation assessment reports, regional assessments and the UNODC Early Warning Advisory (EWA) on NPS. The EWA is a webportal that provides access to information on NPS in the range of subject area including global monitoring, risk communication, chemical analysis, toxicology, pharmacology, emergence and legislative response. (available at: www.unodc.org/nps and www.unodc.org/tox).

The Global SMART Update (GSU) series is published twice a year in English, Spanish and Russian. It provides information on emerging patterns and trends of the global synthetic drugs market in a concise format*. Past issues have covered topics such as the ATS market – 10 years after the 2009 Plan of Action, understanding the global opioid crisis, the dominance of methamphetamine in the synthetic drugs market, the role of NPS in the synthetic drugs market and non-medical use of benzodiazepines. Electronic copies of the Global SMART Updates and other publications are available at: www.unodc.org/unodc/en/scientists/publicationssmart.html.

* The information and data contained within this report are from the Annual Report Questionnaire (ARQ) submitted by Member States to UNODC, the UNODC Early Warning Advisory (EWA) on NPS, official Government reports, press releases, scientific journals or incidents confirmed by UNODC Field Offices. This report has not been formally edited. The contents of this publication do not necessarily reflect the views or policies of UNODC or contributory organizations and neither do they imply any endorsement. Suggested citation: United Nations Office on Drugs and Crime, 2019. An expanding synthetic drugs market – Implications for precursor control. *Global SMART Update*, Volume 23.

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An expanding synthetic drugs market – Implications for precursor control

A. INTRODUCTION

Within two short decades, the global synthetic drug market has gathered tremendous momentum all across the world. Over the period of 1998 to 2017, the growth in seizures of synthetic drugs have outpaced that of traditional plant-based substances with the biggest proportional increases seen in seizures of synthetic new psychoactive substances ('NPS'), followed by amphetamine-type stimulants ('ATS').¹ The estimated global number of ATS users has grown significantly from 30.2 million users in the 1990s to approximately 50 million users in 2017.² Regions such as North America, West, Central and North Africa are also experiencing on-going crises relating to the widespread non-medical use of pharmaceutical and illicitly-manufactured synthetic opioids.³

This expansion has radically transformed the drug market; from one that revolved around plant-based drugs to a multifaceted drug market posing new challenges to drug policy.

Analysis of the available information suggests that the current market expansion is largely supply driven. Rather than reacting to growing demand for drugs, traffickers seem to be able to produce large quantities of synthetic drugs with relatively low costs and ship large amounts within and across regions. In part, the unprecedented growth in the global synthetic drug market may have been fuelled by relatively low barriers of entry to illicit manufacture. Without geographic constraints such as the need to have access to suitable land and climate, clandestine manufacturing facilities for synthetic drugs of varying scales have spread to every region of the world.

However, this has been the case since the advent of synthetic drugs decades ago and does not provide sufficient explanation for the current rapid expansion. Because of their "chemical" origin, precursor chemicals⁴ are the key ingredients for synthetic drugs, and it seems obvious that changes in the way synthetic drugs are manufactured under clandestine conditions and the range of precursors used in that process deserve a closer look.

This issue of the Global SMART Update discusses the challenges for precursor control against the backdrop of the expanding global synthetic drug market. It presents key developments in precursor chemicals used in the clandestine manufacture of synthetic drugs and outlines possible approaches and response options which can enhance the present international and the individual states' precursor control regimes.

1 United Nations Office on Drugs and Crime (UNODC), *World Drug Report 2019: Global Overview of Drug Demand and Supply* (United Nations publication, Sales No. E.19.XI.8 (Booklet 2)), pp. 45-46.

2 *Ibid*, pp. 12-13; United Nations Office for Drug Control and Crime Prevention, *Global Illicit Drug Trends 1999* (United Nations publication, Sales No. E99.XI.16), pp. 95.

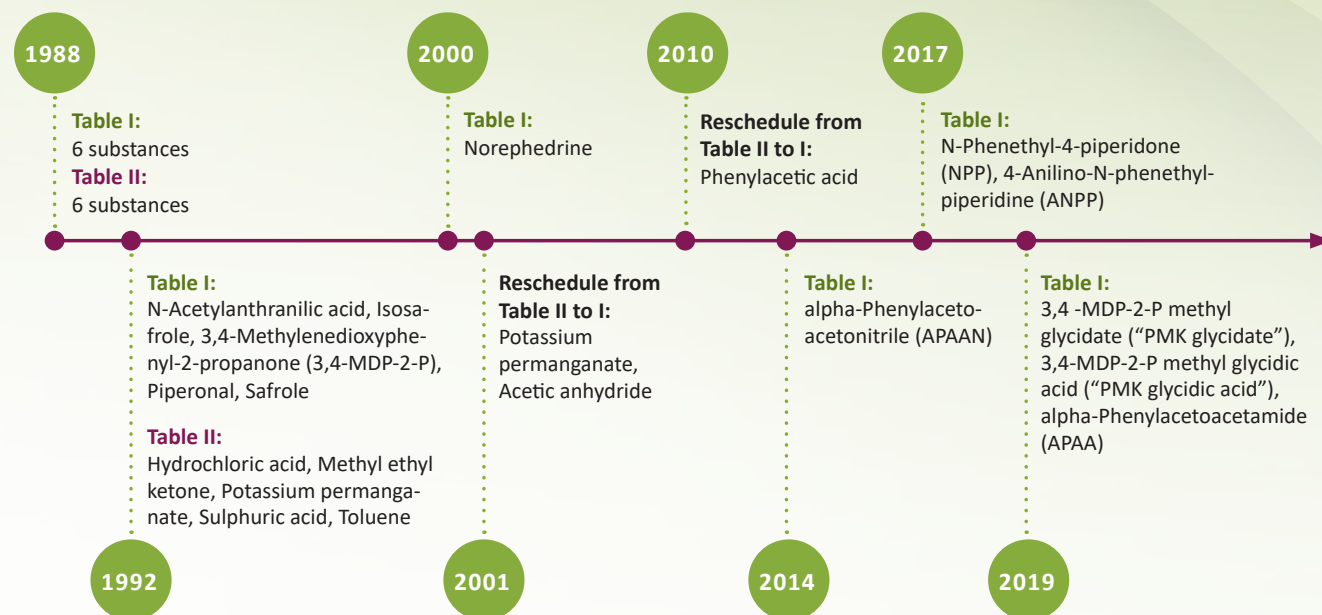
3 UNODC, *World Drug Report 2019: Depressants* (United Nations publication, Sales No. E.19.XI.8 (Booklet 3)), pp. 13-30.

4 The term "precursor" is used to indicate any of the substances listed in Table I or Table II of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988, except where the context requires a different expression. Such substances are often described as *precursors or essential chemicals*, depending on their principal chemical properties. The plenipotentiary conference that adopted the 1988 Convention did not use any one term to describe such substances. Instead, the expression "substances frequently used in the illicit manufacture of narcotic drugs or psychotropic substances" was introduced in the 1988 Convention. It has become common practice, however, to refer to all such substances simply as "precursors"; although that term is not technically correct, it is used in this publication for the sake of brevity.



B. KEY TRENDS AND DEVELOPMENTS IN PRECURSOR CHEMICALS

FIG. 1: Changes to Tables of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychoactive Substances of 1988 over time



Source: United Nations, *Tables of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988, as at 19 November 2019 and UNODC, Commissions Resolutions & Decisions Database*.⁵

In the Political Declaration and Plan of Action of 2009, the international community acknowledged that synthetic drugs pose a special problem due to the diversity and ease of substitution of precursor chemicals used in the manufacturing process.⁶ As if foreshadowing future developments, the world saw the proliferation of the use of non-scheduled precursor chemicals in the following decade alongside increased sophistica-

tion, diversification and scale in drug manufacturing operations.⁷ This proliferation in the use of non-scheduled precursor chemicals is reflected in the increasing pace and number of precursor chemicals that were scheduled in recent years after relative inactivity in the first two decades of the 1988 Convention (see Figure 1).

The use of non-scheduled and "designer" (pre-)precursors

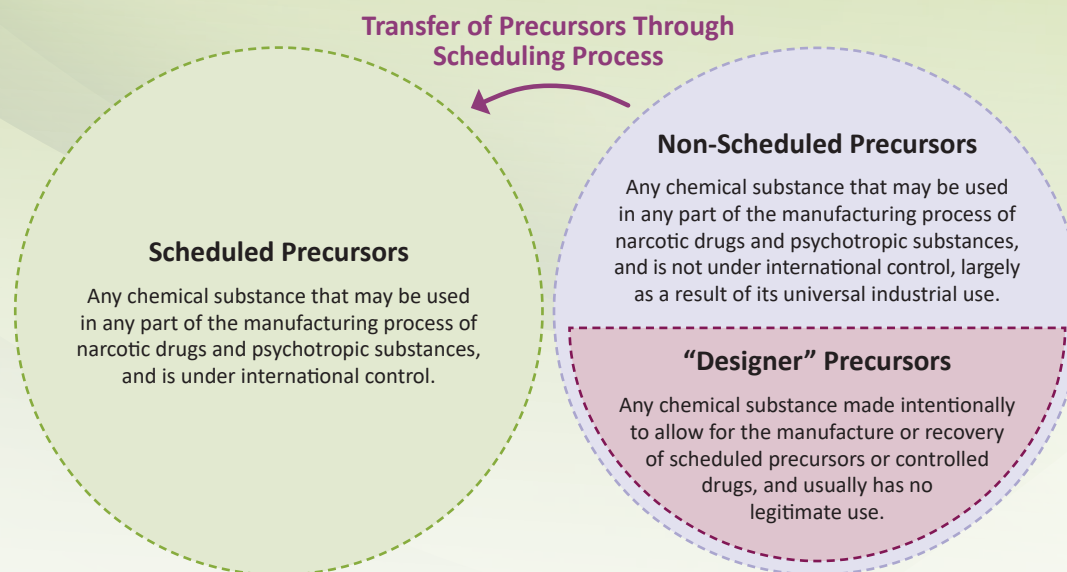
Following the adoption of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988, the use of precursor chemicals in

the illicit manufacture of narcotic drugs and psychotropic substances saw two significant overlapping developments: the switching from scheduled to non-scheduled precursors and the use of "designer" precursors (see Figure 2). Apart from international scheduling decisions, these developments are influenced by a multitude of factors including individual states' precursor legislation and enforcement capabilities, discrepancy between precursor controls across neighbouring states and the increasing versatility amongst illicit manufacturers in switching between alternate precursors and synthetic routes. These developments are not linear in nature and illicit manufacturers have switched back and forth between scheduled, non-scheduled and "designer" precursors. Whilst the use of non-scheduled precursors is not a recent development, it is the emergence of a large number of "designer" precursors in recent years that is of major concern to the international community.

⁵ United Nations, "Tables of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988, as at 19 November 2019," *The International Drug Conventions*, ST/CND/1/Add.3/Rev.3 (2019); UNODC, *Commissions Resolutions & Decisions Database*, <https://www.unodc.org/rddb/>.

⁶ UNODC, *Political Declaration and Plan of Action on International Cooperation towards an Integrated and Balanced Strategy to Counter the World Drug Problem*, High-level segment Commission on Narcotic Drugs, Vienna, 11-12 March 2009, pp. 35.

⁷ Statement by Dr. Viroj Sumyai, President, International Narcotics Control Board (INCB) on Item 9(b) Challenges and future work of the CND and WHO in the review of substances for possible scheduling recommendations, Sixty-second session of the Commission on Narcotic Drugs, Vienna, Austria, 18 March 2019.

FIG. 2: Difference between scheduled precursors, non-scheduled precursors and “designer” precursors

Source: Adapted from INCB, *Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances 2018* and UNODC, *Multilingual Dictionary of Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances under International Control*⁸.

Note: The definitions for non-scheduled and “designer” precursors are not mutually exclusive.

“Designer” precursors, broadly speaking, are chemicals made intentionally to allow for the manufacture or recovery of controlled precursors or drugs.⁹ For the purpose of this report, we have classified “designer” precursors, as either “masked” precursors or chemical intermediates. “Masked” precursors are chemical substances that are specifically designed to disguise scheduled precursors, and from which scheduled precursors can be easily obtained. They may include derivatives of

scheduled precursors of varying degrees of complexity. Examples include derivatives of phenylacetic acid and P-2-P such as methyl phenylacetate, P-2-P bisulfite adduct and P-2-P methyl glycidate. Chemical intermediates on the other hand are chemical substances that are produced during the manufacture of drugs from precursors but are not typically isolated. When isolated, these chemical substances can be considered as precursors. Examples of these substances include *alpha*-phenylacetoacetonitrile (APAAN)¹⁰, methyl *alpha*-phenylacetoacetate (MAPA)¹¹ and chloroephedrine.

Chemicals in both categories usually have few if any legitimate

use and were designed and manufactured specifically to circumvent existing legislation and or avoid detection and identification. This distinguishes “designer” precursors from those non-scheduled precursors which have industrial uses. “Designer” precursors, especially “masked” precursors, present a significant challenge to control measures as there is theoretically an almost infinite number of ways to “mask” or disguise scheduled precursors from existing control measures. An example of how “designer” precursors, which are used in the illicit manufacture of methamphetamine, falls into each of these defined categories is illustrated in Figure 3.

Precursor trends in the manufacture of amphetamine and methamphetamine

For the purpose of this section, precursor trends for amphetamine and methamphetamine are discussed together, as they are chemically related drugs and the range of precursors used for their manufacture overlaps to a large extent. The significant developments in precursor trends are evident in the

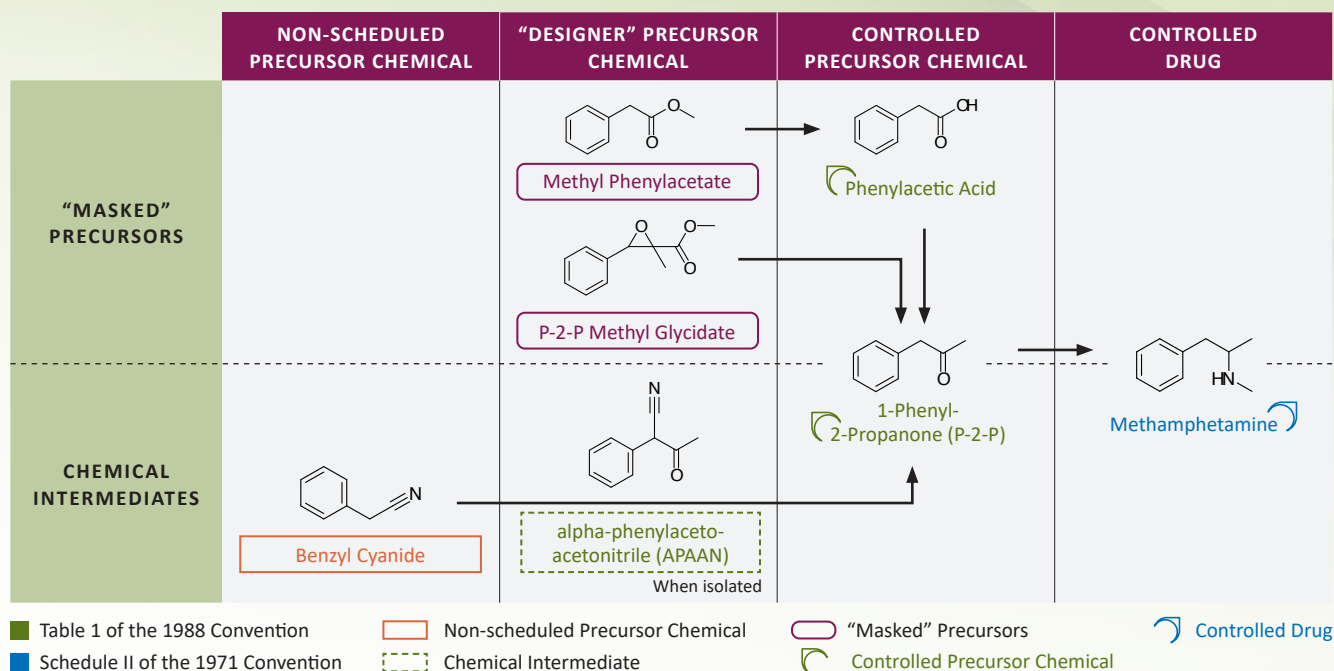
⁸ UNODC, *Multilingual Dictionary of Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances under International Control*, pp. viii, https://www.unodc.org/documents/scientific/MLD_Precursors_2015_Ebook.pdf.

⁹ INCB, *Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances 2018* (United Nations publication, Sales No. E.19.XI.6), pp. 38.

¹⁰ APAAN and its optical isomers have been included into Table I of the 1988 Convention during the 57th Commission on Narcotic Drugs in 2014; UNODC, Commission on Narcotic Drugs, “Decision 57/1: Inclusion of *alpha*-phenylacetoacetonitrile and its optical isomers in Table I of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988”, *Report on the fifty-seventh session (13 December 2013 and 13-21 March 2014)*, Economic and Social Council, Official Records, 2014, Supplement No. 8, pp. 49-50.

¹¹ The possible inclusion of MAPA in Table I of the 1988 Convention will be discussed and voted on at the upcoming 63rd Commission on Narcotic Drugs in 2020.

FIG. 3: Flowchart depicting the illicit manufacture of methamphetamine with precursors designated within each “designer” precursor category

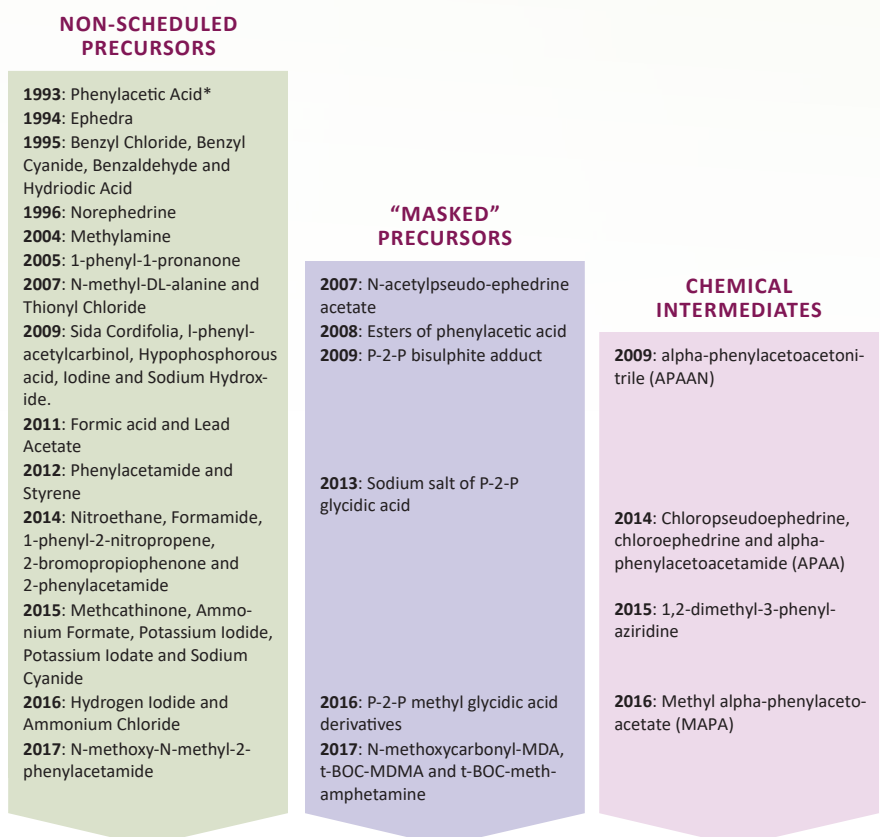


Source: UNODC elaboration based on INCB, *Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances 2014*.

FIG. 4: Evolution of the range of precursors and plants used in the illicit manufacture of amphetamine and methamphetamine

evolution of precursors used for the illicit manufacture of amphetamine and methamphetamine (see Figure 4). Since the 1990s, illicit manufacturers in various parts of the world have complemented the use of traditional precursors such as ephedrine, pseudoephedrine, and 1-phenyl-2-propanone (also known as “P-2-P”) with the use of non-scheduled precursors and “designer” precursor chemicals to circumvent national/international controls, and the efforts of law enforcement and industry in targeting and preventing the diversion of chemicals.¹²

Despite the overall precursor trends, there are distinct regional and country differences in precursors that are commonly used for domestic manufacture of methamphetamine and amphetamine.



* Common amphetamine/methamphetamine precursors including ephedrine, pseudoephedrine and 1-phenyl-2-propanone (P-2-P) were already listed in Table I, and phenylacetic acid in Table II of the 1988 Convention when it came into force on 11th November 1990.

Source: International Narcotics Control Board (INCB), *Various Yearly Reports on Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances*.

Note: The years indicate when a precursor was documented as a significant change or innovation, not necessarily when it was first used.

¹² INCB, Various yearly reports on Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances.

These distinct differences are likely a result of an interaction of factors such as the individual states' precursor control regime, the illicit manufacturers' capabilities and manufacturing costs. In East and South East Asia, ephedrine and pseudoephedrine are the predominant precursors used in the manufacture of methamphetamine.¹³ However, recent seizures of 2-bromopropiophenone¹⁴ (a non-scheduled precursor for ephedrine¹⁵), thionyl chloride¹⁶ (used for the manufacture of methamphetamine through the metal hydrogenation process using ephedrine and pseudoephedrine¹⁷) and P-2-P¹⁸ indicate possible shifts in the types of precursor chemicals and synthesis routes used in the manufacture of methamphetamine. The change in synthesis routes and additional levels of processing required for some of these new emerging precursors also suggest increased sophistication amongst illicit manufacturing facilities in the region.

In North America and Europe, P-2-P synthesis routes dominate the illicit manufacture of amphetamine and methamphetamine.¹⁹ In North America, illicit manufacturers in

Mexico were observed in recent years to have switched back-and-forth between phenylacetic acid (scheduled precursor) and its derivatives ("designer" precursors),²⁰ and benzaldehyde and nitroethane (general non-scheduled precursors)²¹ in the manufacture of P-2-P, possibly in response to the national bans on these substances.²² In Europe, the use of chemical intermediates such as *alpha*-phenylacetoacetonitrile (APAAN), *alpha*-phenylacetoacetamide (APAA), both of which have been placed under international control recently, and methyl *alpha*-phenylacetoacetate (MAPA) in the manufacture of P-2-P has intensified in recent years in order to circumvent controls on P-2-P, to lower costs of manufacturing and ensure business continuity in the illicit manufacturing trade.²³ To a smaller extent, ephedrine and pseudoephedrine were the predominant precursors used in domestic manufacture of methamphetamine in the United States, Czechia, Bulgaria, Germany, Poland and Slovakia.²⁴

Precursor trends in the manufacture of fentanyl

A similar worrying development of switching from scheduled to non-scheduled precursors is also beginning to surface in the illicit manufacture of fentanyl, whose non-medical use is associated with increasing numbers of overdose deaths, especially in North America.²⁵ In response to international regulations on *N*-phenethyl-4-piperidone (NPP) and 4-anilino-*N*-phenethylpiperidine (ANPP) in 2017²⁶, illicit fentanyl manufacturers have switched to other synthesis methods involving the use of non-scheduled precursor chemicals. Of particular concern is the emergence of *N*-(1-benzyl-4-piperidyl)-propionanilide (also known as benzylfentanyl) and 4-anilinopiperidine (also known as "4-AP"), which have recently been increasingly encountered in seizures and/or through drug profiling and are being considered by the US Drug Enforcement Administration (DEA) for control as List I chemicals²⁷ under the US Controlled Substances Act (CSA).²⁸

13 UNODC, *Synthetic Drugs in East and South-East Asia: Trends and Patterns of Amphetamine-type Stimulants and New Psychoactive Substances 2019*, pp. 9.

14 *Ibid.*, pp. 10.

15 Fourneau, E., *Process for the manufacture of phenyl-methyl-amino-propanol (synthetic ephedrine)*, Patent GB 302,940 (December 1928).

16 UNODC, *Transnational Organised Crime in Southeast Asia: Evolution, Growth and Impact 2019*, pp. 36-37.

17 Emde H., "Diastereoisomerism, III, Chloro- and bromo- ephedrine.", *Helvetica Chimica Acta*, Vol. 12, No. 1 (1929), pp. 384-399; Emde H., "Diastereoisomerism, I, Configuration of ephedrine.", *Helvetica Chimica Acta*, Vol. 12, No. 1 (1929), pp. 365-376.

18 UNODC, *Transnational Organised Crime in Southeast Asia: Evolution, Growth and Impact 2019*, pp. 36.

19 INCB, *Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances 2018* (United Nations publication, Sales No. E.19.XI.6), pp. 18-23.

20 UNODC, *Clandestine Manufacture of Substances under International Control*, pp. 164.

21 Gairaud C.B. and Lappin G.R., "The synthesis of ω -nitrostyrenes.", *Journal of Organic Chemistry*, Vol. 18, No. 1 (1953), pp. 1-3; Tindall J. B., *Process for preparing 1-aryl-2-oxoalkanes*, Patent US 2,427,822 (September 1947).

22 INCB, *Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances 2018* (United Nations publication, Sales No. E.19.XI.6), pp. 21-22; INCB, *Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances 2015* (United Nations publication, Sales No. E.16.XI.4), pp. 3; INCB, *Precursors and chemicals frequently used in the illicit manufacture of narcotic drugs and psychotropic substances 2012* (United Nations publication, Sales No. E.13.XI.4), pp. 18; U.S. Department of Justice, Drug Enforcement Administration, *2018 National Drug Threat Assessment*, pp. 67-68.

23 European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and Europol, *EU Drug Markets Report 2019*, Publications Office of the European Union, Luxembourg, pp. 159-161; EMCDDA (2019), *Drug precursor developments in the European Union*, EMCDDA Papers, Publications Office of the European Union, Luxembourg (2019), pp. 8-9.

24 EMCDDA and Europol, *EU Drug Markets Report 2019*, Publications Office of the

European Union, Luxembourg, pp. 158; EMCDDA, *Drug precursor developments in the European Union*, EMCDDA Papers, Publications Office of the European Union, Luxembourg (2019), pp. 7-8; INCB, *Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances 2018* (United Nations publication, Sales No. E.19.XI.6), pp. 17; U.S. Department of Justice, Drug Enforcement Administration, *2018 National Drug Threat Assessment*, pp. 65.

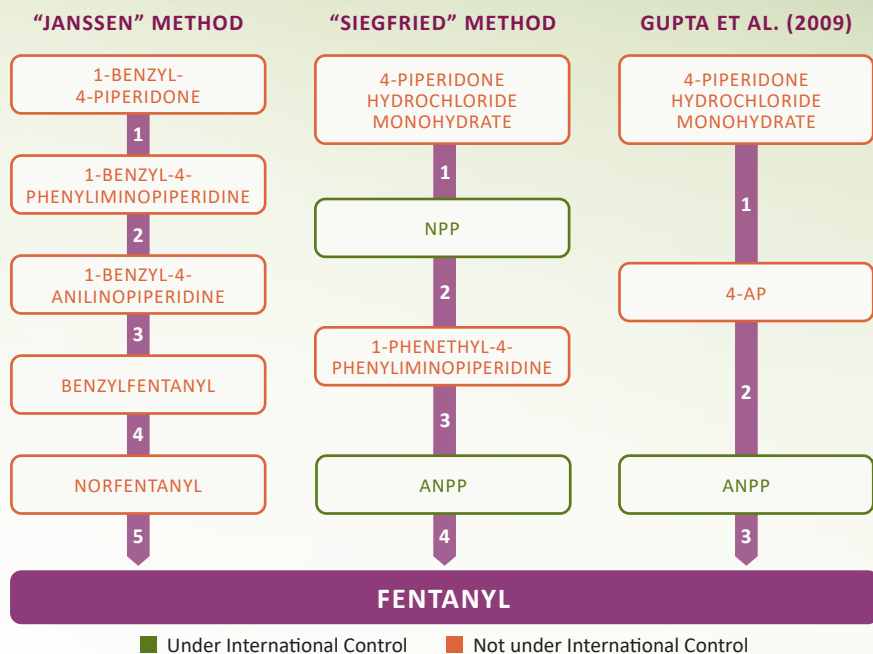
25 UNODC, *World Drug Report 2019: Depressants* (United Nations publication, Sales No. E.19.XI.8 (Booklet 3)), pp. 12.

26 UNODC, Commission on Narcotic Drugs, "Decision 60/12: Inclusion of 4-anilino-*N*-phenethylpiperidine (ANPP) in Table I of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988; Decision 60/13: Inclusion of *N*-phenethyl-4-piperidone (NPP) in Table I of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988", *Report on the sixtieth session (2 December 2016 and 13-17 March 2017)*, Economic and Social Council, Official Records, 2017, Supplement No. 8, pp. 39.

27 The control will also extend to the salts of benzylfentanyl and the amides, carbamates and salts of 4-AP.

28 Drug Enforcement Administration, "Desig-

FIG. 5: Selected methods for the synthesis of fentanyl



Source: UNODC, *Clandestine Manufacture of Substances under International Control*, Yadav et al., *Synthetic Methodology and Structure Activity Relationship Study of N-[1-(2-phenylethyl)-Piperidin-4-yl]-Propionamides* (2010) and Gupta et al., *A Method for the Preparation of Fentanyl* (2009)²⁹

In the early 2000s, the DEA reported two primary synthesis routes used in the illicit manufacture of fentanyl: the "Janssen" and "Siegfried" methods (see Figure 5).³⁰ The "Janssen" method³¹,

which was developed in the 1960s for the pharmaceutical manufacture of fentanyl, is considered to be the more difficult and time-consuming of these two methods due to the need for advanced chemical knowledge.³² The much simpler "Siegfried" method, first published online under a pseudonym in the 1990s which improved on alternative synthesis routes published in the 1980s, was the more preferred method amongst clandestine manufacturers.³³

However, with the introduction of international regulations on NPP and ANPP³⁴, the "Janssen" method has surged in popularity and illicit manufacturers have started to exploit benzylfentanyl, a non-internationally controlled substance, in the synthesis of norfentanyl³⁵ and subsequently fentanyl. DEA reported that, in 2018, 94% of 85 fentanyl exhibits and in 2019, 64% of 312 exhibits that were selected for drug profiling were manufactured using the "Janssen" method, far outstripping the number of exhibits manufactured with the "Siegfried" method.³⁶ Illicit manufacturers have also switched to the use of 4-AP as an alternative precursor chemical to NPP for the synthesis of ANPP (see Figure 5), using an alternative synthetic route developed more recently.³⁷ Unlike NPP where two chemical reactions are required for the synthesis for ANPP, 4-AP can be optimally converted into ANPP in a single step chemical reaction and then be synthesized into fentanyl.³⁸

... nation of Benzylfentanyl and 4-Anilinopiperidine, Precursor Chemicals Used in the Illicit Manufacture of Fentanyl, as List I Chemicals", *Federal Register*, Vol. 84, No. 178 (September 2019), pp. 48315-6.

29 UNODC, *Clandestine Manufacture of Substances under International Control*, pp. 208-9; Gupta P. K., Manral L., Ganesan K., Malhotra R. C. and Sekhar K., "A Method for the Preparation of Fentanyl", *European Patent 09721316.9*, European Patent Office (March 2009); Yadav P., Chauhan J. S., Ganesan K., Gupta P. K., Chauhan D., and Gokulan P. D., "Synthetic Methodology and Structure Activity Relationship Study of N-[1-(2-phenylethyl)-Piperidin-4-yl]-Propionamides." *Der Pharmacia Sinica*, Vol. 1, No. 3 (2010), pp. 133-134; Siegfried, "Synthesis of Fentanyl", Rhodium Chemistry Archive webpage, accessed on 17 December 2019, <https://erowid.org/archive/rhodium/chemistry/fentanyl.html>.

30 *Ibid.*

31 Janssen P. A., "Pirinitramide (R 3365), a Potent Analgesic with Unusual Chemical Structure.", *Journal of Pharmacy and Pharmacology*, Vol. 13, No. 1 (1961), pp. 513-530; Janssen P. A. and Nathan B. E., "Compounds Related to Pethidine-IV. New General Chemical Methods of Increasing the

... Analgesic Activity of Pethidine.", *Journal of Medicinal and Pharmaceutical Chemistry*, Vol. 2 (1960), pp. 31-45.

32 Drug Enforcement Administration, "Control of a Chemical Precursor Used in the Illicit Manufacture of Fentanyl as a List I Chemical.", *Federal Register*, Vol. 72, No. 77 (April 2007), pp. 20039; Yadav P., Chauhan J. S., Ganesan K., Gupta P. K., Chauhan D., and Gokulan P. D. "Synthetic Methodology and Structure Activity Relationship Study of N-[1-(2-phenylethyl)-piperidin-4-yl]-propionamides." *Der Pharmacia Sinica*, Vol. 1, No. 3 (2010), pp. 126-139.

33 *Ibid*; Pardo B., Taylor J., Caulkins J. P., Kilmer B., Reuter P. and Stein B. D., *The Future of Fentanyl and Other Synthetic Opioids*, Santa Monica, CA: RAND Corporation (2019), pp. 62; UNODC, *Clandestine Manufacture of Substances under International Control*, pp. 209; Siegfried, "Synthesis of Fentanyl", Rhodium Chemistry Archive webpage, accessed on 17 December 2019, <https://erowid.org/archive/rhodium/chemistry/fentanyl.html>.

... 34 UNODC, Commission on Narcotic Drugs, "Decision 60/12: Inclusion of 4-anilino-N-phenethylpiperidine (ANPP) in Table I of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988; Decision 60/13: Inclusion of N-phenethyl-4-piperidone (NPP) in Table I of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988", *Report on the sixtieth session (2 December 2016 and 13-17 March 2017)*, Economic and Social Council, Official Records, 2017, Supplement No. 8, pp. 39.

35 Norfentanyl, as an immediate precursor to fentanyl, is also being proposed by the DEA to be controlled as a schedule II substance under the CSA.

36 Drug Enforcement Administration, "Designation of Benzylfentanyl and 4-Anilinopiperidine, Precursor Chemicals Used in the Illicit Manufacture of Fentanyl, as List I Chemicals", *Federal Register*, Vol. 84, No. 178 (September 2019), pp. 48315-6; *Fentanyl Signature Profiling Program Report* (October 2019).

37 *Ibid*; Gupta P. K., Manral L., Ganesan K., Malhotra R. C. and Sekhar K., "A Method for the Preparation of Fentanyl.", *European Patent 09721316.9*, European Patent Office (March 2009)

38 *Ibid.*

These precursor developments, which are beginning to mirror those seen in the illicit manufacture of methamphetamine/amphetamine, underscore the risk that illicit fentanyl manufacture may shift to other non-scheduled precursors or even “designer” precursors to evade the international controls recently put in place.

Challenges and options for adapting precursor control regimes

The rapid shifts in precursors used in the manufacture of amphetamine, methamphetamine and fentanyl suggest that the effects of existing precursor regulations may be more transient and less disruptive to the global synthetic market than before.³⁹ New alternate precursors chemicals using similar or completely different synthetic routes are appearing pre-emptively or as soon as new precursor regulations come into force. Also, illicit manufacture can no longer be perceived as “primitive” given recent evidence of their abilities to increase the level of complexity in processing required for some of these alternate precursors⁴⁰ and adaptability and flexibility with regard to synthetic routes.

These developments, especially the emergence of “designer” precursors with no legitimate use in industry, present significant challenges to the existing international precursor control regime, which is geared at monitoring licit trade

flows of a limited number of key chemicals with legitimate uses and preventing their diversion for illicit purposes.⁴¹ These significant challenges include: the timely detection of, and agile response to, new developments in illicit manufacture; and identification of additional measures to complement and or enhance current control regimes to respond to new phenomena such as the emergence of designer precursors. Possible options which Member States may wish to consider in an effective response include: improving knowledge and understanding of clandestine manufacturing, including through drug profiling and forensic intelligence; undertaking new legal approaches; establishing public-private partnerships; and enhancing international cooperation.

C. ENHANCING PRECURSOR CONTROL – PRESENT REALITY

Understanding Clandestine Manufacture – Role of Drug Characterisation and Impurity Profiling

Drug characterisation and impurity profiling (or simply drug profiling) can be broadly defined as an analysis of a drug sample’s chemical and/or physical attributes, which not only supports the gathering of intelligence in the context of law enforcement but also facilitates the monitoring of developments on the illicit drug market to inform

drug/precursor control policies.⁴² Similar to the concept of how trace evidence occurs as a result of an event, samples of synthetic drugs often contain trace impurities of precursor chemicals essential to the drug manufacturing process and by-products resulting from side-reactions.⁴³ Through analysing the presence or absence of impurities in the samples and the variations in impurity profiles, forensic science can help identify the types of precursor chemicals and synthetic routes used in the manufacture of the sample.⁴⁴ With a systematic process of integrating and organising all of these drug profiles, a further analysis can be conducted on new and pre-existing data to draw intelligence of the present precursor situation and assist policy makers in making timely, critical decisions to address any new developments.⁴⁵ The iterative nature of this process allows policy makers to evaluate the effect of their policy decisions through

42 Esseiva P., Ioset S., Anglada F., Gaste´ L., Ribaux O., Margot P., Gallusser A., Biedermann A., Specht Y. and Ottinger E., “Forensic Drug Intelligence: An Important Tool in Law Enforcement.”, *Forensic Science International*, Vol. 167, No. 2-3 (2007), pp. 247-254.

43 UNODC, *Drug Characterization/Impurity Profiling: Background and Concepts*, pp. 7.

44 United Nations International Drug Control Programme, “Drug characterization/impurity profiling, with special focus on methamphetamine: recent work of the United Nations International Drug Control Programme.”, *Bulletin on Narcotics*, Volume LI, No. 1 and 2 (1999), pp. 103.

45 Ribaux O., Genessay T. and Margot P., “Les processus de veille opérationnelle et science forensique.”, in: Leman-Langlois S. (Ed.), *Sphères De Surveillance*, Presses de l’Université de Montréal, Montréal (2011), pp. 137-158 ; Morelato M., Beavis A., Tahtouh M., Ribaux O., Kirkbride P. and Roux C., “The use of forensic case data in intelligence-led policing: the example of drug profiling.”, *Forensic Science International*, Vol. 226, No. 1-3 (2013), pp. 5-6; Marclay F., Mangin P., Margot P. and Saugy M., “Perspectives for Forensic Intelligence in anti-doping: Thinking outside of the box.”, *Forensic Science International*, Vol. 229, No. 1-3 (2013), pp. 137-139; Morelato M., *Forensic drug profiling : a tool for intelligence-led policing* (2015), University of Technology, Sydney, PhD dissertation, Open Publications of UTS Scholars, pp. 46, <https://opus.lib.uts.edu.au/bitstream/10453/34517/2/02whole.pdf>.

39 Strang J., Babor T., Caulkins J., Fischer B., Foxcroft D. and Humphreys K., “Drug policy and the public good: evidence for effective interventions.”, *The Lancet*, Vol. 379, Issue 9810 (January 2012), pp. 73-74; Caulkins J. P. and Reuter P., “How Drug Enforcement Affects Drug Prices.”, *Crime and Justice*, Vol. 39, No. 1 (2010), pp. 213-271; Dobkin C. and Nicosia N., “The War on Drugs: Methamphetamine, Public Health and Crime.”, *American Economic Review*, Vol. 99, No. 1 (March 2009), pp. 324-49.

40 EMCDDA (2019), *Drug precursor developments in the European Union*, EMCDDA Papers, Publications Office of the European Union, Luxembourg (2019), pp. 9.

41 Statement by Dr. Viroj Sumyai, President, International Narcotics Control Board (INCB) on Item 9(b) Challenges and future work of the CND and WHO in the review of substances for possible scheduling recommendations, Sixty-second session of the Commission on Narcotic Drugs, Vienna, Austria, 18 March 2019.

continuous collection, analysis and interpretation of new drug profiles, and to make any policy adjustments if necessary.⁴⁶

It is important to recognise that drug profiling is not just a routine analytical technique. It requires a multi-disciplinary collaborative approach through the participation of forensic laboratories and law enforcement agencies to properly analyse, interpret and communicate the results.⁴⁷ It requires countries to put in place qualified personnel, dedicated equipment and databases for the feedback process to work soundly. If done correctly, the same process can also contribute valuable tactical and operation intelligence for its actors.⁴⁸ Practical examples of how drug profiling has shaped policy decisions include DEA's Fentanyl Signature Profiling Programme⁴⁹, and the Australian Illicit Drug Intelligence Program (AIDIP) and Enhanced National Intelligence Picture on Illicit Drugs (ENIPID).⁵⁰

New Legal Approaches to Precursor Controls

The rapid pace of developments in precursor trends requires a fundamental rethink on existing national legal approaches to precursors, building on the controls prescribed in the 1988 Convention. One practical approach is to proactively control known chemicals

which could be used in the manufacture of controlled precursors/drugs and have no known legitimate uses, even before their use becomes widespread practice in the illicit manufacture of drugs. This approach requires regular monitoring of precursor trends, extensive mapping of known synthesis routes and consultations with the chemical industries. Such an approach would pre-emptively deter illicit manufacturers from simply switching between known precursor chemicals and synthetic routes, and possibly prolong the market disruption effects of precursor regulations. A major limitation to this approach however is that whilst it addresses the use of non-scheduled precursors, it does not fully address the issue of "designer" precursors.

Despite the chemical complexity associated with "designer" precursors, the controls specified in the 1988 Convention and other national legislations that closely replicate it, extends to the salts of scheduled substances but not necessarily all other possible derivatives of these substances. A more extensive legislative approach would be to adopt national controls over generic groups of scheduled precursor chemicals ("generic controls"), which has defined structural similarities and could be easily converted to the parent compounds, to complement the provisions of the 1988 Convention. A similar but broader approach is to adopt analogue controls, which operate on more general aspects of similarity in chemical structure with the parent compounds and cover a wider range of substances. Whilst desirable as proactive mechanisms, the broadness of such approaches may have unintended negative consequences on limiting the accessibility to these chemicals for medical and/or research purposes and inevitably controlling present or future variations of

precursor chemicals which have legitimate uses. Effective enforcement of such controls also requires high-levels of scientific knowledge and forensic capabilities. Countries that have adopted a mixture of generic or analogue approaches to precursor chemicals include the US⁵¹ and Canada⁵².

With respect to the diversion of pharmaceutical preparations which can be used as precursors, national authorities could consider strengthening their medicines legislation, related monitoring systems as well as guidelines and capacity building towards rationale prescribing, to ensure that approved preparations, such as ephedrine and pseudoephedrine cold medications, are prescribed, sold and dispensed to legitimate end-users. Ultimately, there is a fine balance to strike between taking either one or more of these approaches to avoid under- or overregulation of precursor chemicals within each country's unique operating environment.

Expanding Partnerships with the Private Sector – Voluntary Public-Private Partnerships

Beyond policies and law enforcement actions, an effective precursor regime should be supplemented by strong partnerships and initiatives amongst the public and private sectors. Private industries, especially those involved in the production, distribution, trade, financing and shipping of precursor chemicals, wield great influence and potential in identifying vulnerabilities in their supply chains and preventing the diversion of their products into illicit channels. Apart from

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⁴⁶ *Ibid.*

⁴⁷ UNODC, *Drug Characterization/Impurity Profiling: Background and Concepts*, pp. 3.

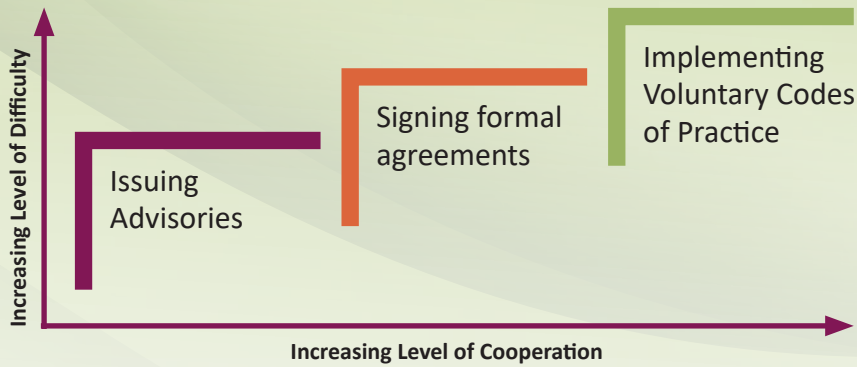
⁴⁸ *Ibid.*; Morelato M., Beavis A., Tahtouh M., Ribaux O., Kirkbride P. and Roux C., "The use of forensic case data in intelligence-led policing: The example of drug profiling.", *Forensic Science International*, Vol. 226, No. 1-3 (2013), pp. 1-9.

⁴⁹ Please refer to the earlier section on "Precursor trends in the manufacture of fentanyl".

⁵⁰ Collins M., "Illicit drug profiling: the Australian experience – revisited.", *Australian Journal of Forensic Sciences*, Vol. 49, No. 6 (2017), pp. 591-604; Morelato M., Beavis A., Tahtouh M., Ribaux O., Kirkbride P. and Roux C., "The use of forensic case data in intelligence-led policing: The example of drug profiling.", *Forensic Science International*, Vol. 226, No. 1-3 (2013), pp. 6.

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⁵¹ United States, Congress, House, United States Code, Title 21 – Food and Drugs, Chapter 13 – Drug Abuse Prevention and Control, Subchapter I – Control and Enforcement, Part A – Introductory Provisions, Section 34.

⁵² Controlled Drugs and Substances Act, Precursor Control Regulations, Schedule, SOR/2002-359, *Statutes of Canada*.

FIG. 6: Mechanism of establishing public-private partnerships

Source: UNODC elaboration.

achieving profitability, it is also their interest to avoid exposure to legal, financial and reputational risks and losses for being associated with criminal activities.⁵³ This presents an opportunity for collaborative arrangements between the public and private sectors to align their interests and achieve greater collective outcomes through compliance measures such as information sharing, initiating good business practices and even voluntary self-regulation.⁵⁴ Three primary mechanisms for doing such include issuing advisories, entering into formal agreements and implementing voluntary codes of practice, which entails varying levels of cooperation and difficulties in implementation (see Fig. 6).

One mechanism is to issue advisories to relevant private industries to raise their awareness on the existing precursor situation and eventually initiate public-private cooperation through informal/formal working relationships. Recent examples include the series of private sector advisories issued

by the US Office of National Drug Control Policy, intended to engage the private sector in curbing the production and sale of illicit synthetic opioids.⁵⁵ These advisories provide private businesses a summary of the existing situation, typologies and red flags associated with criminal activities that are specific to their industries. In addition, it includes case studies illustrating the commitment of the government in combating the threat, specific regulatory obligations of various industries and reporting information to the relevant government authorities.

Another mechanism is to formalise public-private partnerships through agreements such as memorandum of understandings (MOUs). An example was the signing of a MOU between Hong Kong Customs and five private transnational express couriers to enhance cooperation and facilitate exchange of expertise, information and intelligence on suspicious cargoes.⁵⁶ Practical outcomes of this MOU include regular sharing of latest smuggling trends with frontline courier staff and timely exchange of information

on suspicious cargoes and legitimate goods.⁵⁷

Governments might also wish to consider working with private industries to develop and implement voluntary codes of practice, to effectively deter trafficking activities and diversion of precursor chemicals through additional self-regulation measures beyond what is legally prescribed. Such codes of practices may include voluntary implementation of policies and procedures such as due diligence on the legitimacy of end-users, reporting requirements to authorities, tamper-proofing of chemicals during delivery and training of staff to identify illicit activities.⁵⁸ These policies may also be extended to other associated private businesses to make the supply chain resistant to illicit diversion. An example is the *National Code of Conduct: Private Public Partnership to Prevent Division of Chemical Precursors and Equipment Used for the Illicit Production of Drugs*, jointly developed by France's Mission Nationale de Contrôle des Précurseurs Chimiques (MNCPC) and other chemical industry unions/associations for companies involved in the entire supply chain of substances and equipment that may be used in the illicit production of drugs.⁵⁹

International and Regional Cooperation

International and regional cooperation is also fundamental in bridging information, capacity and resource gaps in precursor control within the international community. Member states might wish to consider

53 Almond M. A. and Syfert S. D., "Beyond Compliance: Corruption, Corporate Responsibility and Ethical Standards in the New Global Economy," *North Carolina Journal of International Law and Commercial Regulation*, Vol. 22, No. 2 (1997), pp. 442-446.

54 Roger E. and Weber E. P., "Thinking Harder About Outcomes for Collaborative Governance Arrangements," *The American Review of Public Administration*, Vol. 40, No. 5 (2010), pp. 546-567.

55 Office of National Drug Control Policy, *21st Century Drug Trafficking Advisories on Fentanyl and Other Synthetics* (August 2019).

56 Hong Kong Customs and Excise Department, "Hong Kong Customs signs MOU with Express Courier Operators in Enforcement Cooperation," *Custom News*, Issue No. 54 (June 2015), pp. 7.

57 *Ibid.*

58 Governments can refer to INCB's resources on establishing voluntary public-private partnerships to develop and implement a voluntary code of practice.

59 Mission Nationale de Contrôle des Précurseurs Chimiques (MNCPC), *Code National De Conduite ; Partenariat Public/Privé Visant A Prévenir Le Détournement De Précurseurs Chimiques Et D'équipements Pouvant Servir A La Production Illicite De Drogues*.

actively contributing resources and information to international precursor projects and real-time data management tools provided by the International Narcotics Control Board (INCB) such as Project Cohesion, Project Prism and Precursors Incident Communication System (PICS) to assist in the identification of new precursor trends and address gaps in the international precursor control regime. Policy tools such as the United Nations Toolkit on Synthetic Drugs also provide Member States and other stakeholders a wide range of electronic resources provided by various entities within the UN on addressing the key challenges presented by synthetic drugs.⁶⁰ The Precursors and Forensics modules are particularly relevant in addressing gaps in understanding and implementation of an effective precursor control regime.

Participation and support for regional precursor programmes and meetings such as those administered by UNODC in South-East Asia, the Cooperation Programme between Latin America, the Caribbean and the European Union on Drugs Policies (COPOLAD) and the Inter-American Drug Abuse Control Commission (CICAD) are also crucial in coordinating information, intelligence sharing, technical assistance, and capacity building between international, regional organisations and member countries. Operationally, programmes such as the World Customs Organization (WCO) Regional Intelligence Liaison Offices (RILO) and the UNODC-WCO Container Control Programme (CCP) provide essential operational support and training to

build the capacities of law enforcement agencies and encourage cross-border intelligence sharing amongst national authorities through dedicated platforms and regional meetings. At the technical level, work done by regional forensic networks such as the Asian Forensic Sciences Network (AFSN) and the European Network of Forensic Science Institutes (ENFSI) are important in contributing to research and development, information sharing, and building the competencies of national forensic laboratories.

D. PRECURSOR CONTROL BEYOND 2020

In the 2009 Plan of Action, the international community recognized that the absence of a systematic global approach of monitoring and controlling the manufacturing, diversion and trafficking of precursor chemicals, hindered a full understanding of the global illicit synthetic drug market.⁶¹ More than a decade on, the international community has considerably more information on the synthetic drug market at their disposal. Yet, we are still far from developing effective comprehensive international and domestic control regimes to keep pace with developments in precursor trends. Trends in amphetamine, methamphetamine and fentanyl manufacture are poignant reminders that effective albeit short term market disruptions proffered by precursor regulations has less long-lasting effects than in the past. Developments such as the rapid emergence of “designer” precursors, increased sophistication, diversification and scale of

illicit drug manufacturing operations makes it easier to overcome these market disruptions and move on to alternate non-scheduled precursor chemicals.

Yet in the face of such immense challenges, there are options for Member States to adapt precursor control regimes by bridging the information, time and capacity gaps between the initial emergence of new precursor chemicals and the introduction of control measures. Measures to close these gaps include understanding clandestine manufacturing through drug profiling, undertaking new national legal approaches to precursor control building on the 1988 Convention, establishing public-private partnerships and enhancing international/regional cooperation amongst relevant organizations and Member States. The development of a comprehensive international/domestic precursor control regime is a substantial challenge, however it can potentially offer the benefit of eliminating the harms associated with drug trafficking and use at its source. With a renewed resolve to work towards the elimination of the diversion of and illicit trafficking in precursors as reiterated in the Ministerial Declaration made during the 62nd Commission on Narcotic Drugs, the international community has a challenging but rewarding task ahead.⁶²

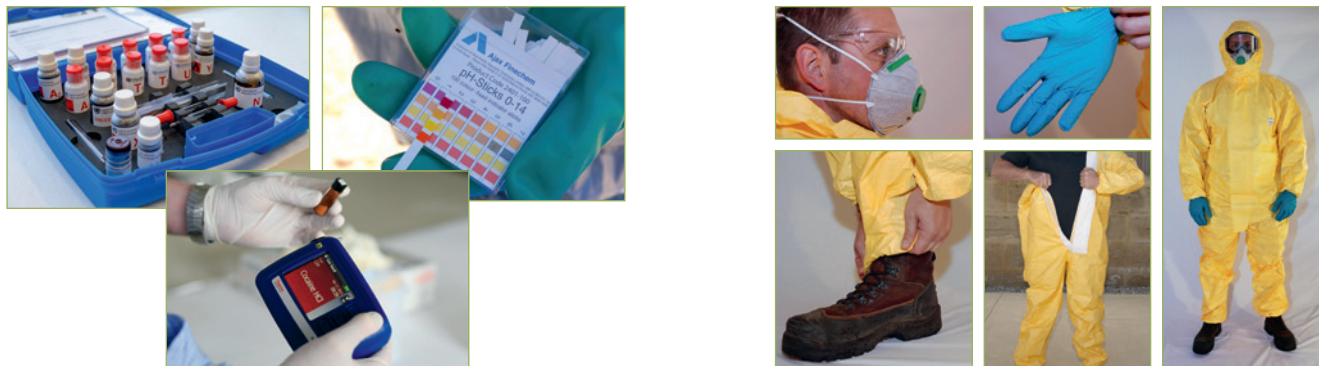
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⁶⁰ The UN Toolkit on Synthetic Drugs may be accessed at <https://www.unodc.org/unodc/en/opioid-crisis/un-toolkit-on-synthetic-drugs.html>.

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⁶¹ UNODC, *Political Declaration and Plan of Action on international cooperation towards an integrated and balanced strategy to counter the world drug problem*, High-level segment Commission on Narcotic Drugs, Vienna, 11-12 March 2009, pp. 34.

...
⁶² UNODC, *Ministerial declaration on strengthening our actions at the national, regional and international levels to accelerate the implementation of our joint commitments to address and counter the world drug problem*, Ministerial Segment Commission on Narcotic Drugs, Vienna, 14-15 March 2019, pp. 3.

Case Study Box 1: Identification and handling of precursor chemicals in the field and laboratory

FIG. 7: Various types of precursor test kits and Personal Protective Equipment (PPE) for handling of chemicals.



Source: UNODC⁶³

The growing diversity of precursor chemicals and increase in clandestine production of synthetic drugs in recent years have placed great pressures on law enforcement officers, technical and scientific staff of forensic laboratories in their operations. These new developments have inadvertently increased the complexity of identification, creating the need for additional or more advanced means. Also, large volumes of precursors, known and unknown, recovered during field operations can potentially pose a significant risk to frontline officers, laboratory personnel, communities and the environment if not managed properly.⁶⁴

In terms of identification, UNODC recommends that frontline officers be minimally equipped with rapid simple colour test kits to presumptively identify commonly known

chemicals.⁶⁵ Additionally, frontline officers can be equipped with more advanced field testing methods such as rapid precursor test kits and handheld devices such as those utilising Raman and Fourier-transform infrared spectroscopy technologies.⁶⁶ Officers should also be trained and equipped with field test kits such as pH test kits, cyanide test strips, peroxide test strips and water test strips to identify key hazard information for chemicals that cannot be identified on site with the available field testing methods.⁶⁷ Laboratories, on the other hand, should actively review scientific literature, and develop a combination of screening and specific analytical techniques such as chromatography and spectroscopy to identify unknown chemicals.⁶⁸ They may also consider participating regularly in proficiency

testing such as UNODC's International Collaborative Exercises (ICE) programme or participate in interlaboratory comparisons, to monitor their own performance and ensure a high level of proficiency.

In order to minimise danger, frontline officers and laboratory operators should be trained in the use of appropriate personal protective equipment (PPE), adoption of safety procedures, identification of hazard labels and chemical classes prior to managing any chemicals. The level of PPE and safety procedures to be adopted depends on the risks posed by the chemicals present and the type of illicit laboratory being dismantled. Without expert technical support, officers should use the highest level of PPE available to maximise the amount of protection. Also, in the presence of significant hazards such as highly reactive chemicals, strong vapour/gases and other immediate physical or chemical hazards, frontline officers should not enter these environments but rather obtain expert technical support.⁶⁹

⁶³ UNODC, *Precursor Related tools and Services; Rapid Testing Methods of Drugs of Abuse; Illustrated Guide for the Disposal of Chemicals used in the Illicit Manufacture of Drugs; Guidelines on Handheld Raman Field Identification Devices for Seized Material; Guidelines for the Safe Handling and Disposal of Chemicals used in the Illicit Manufacture of Drugs*.

⁶⁴ UNODC, *Illustrated Guide for the Disposal of Chemicals used in the Illicit Manufacture of Drugs*, pp. 3.

⁶⁵ UNODC, *Rapid Testing Methods of Drugs of Abuse; Precursor Related Tools and Services*.

⁶⁶ *Ibid*; UNODC, *Guidelines on Handheld Raman Field Identification Devices for Seized Material*.

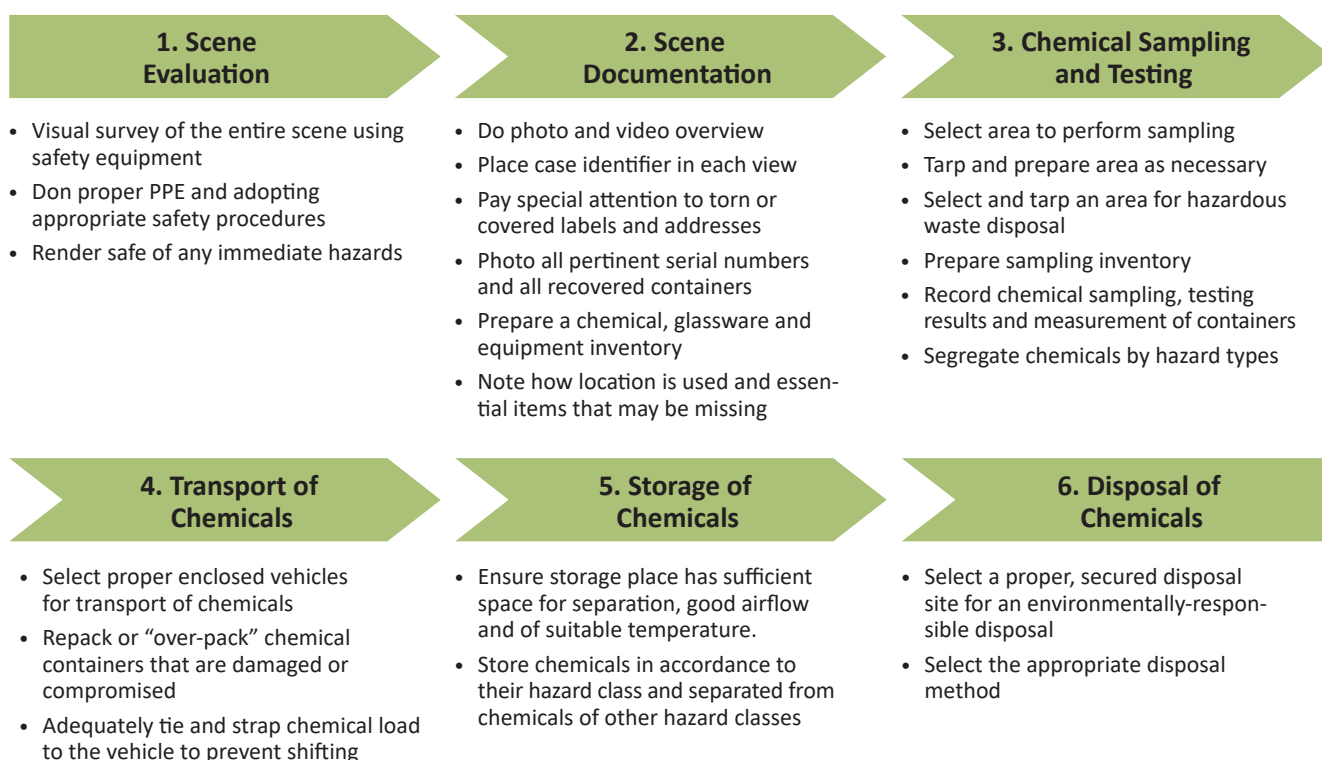
⁶⁷ UNODC, *Illustrated Guide for the Disposal of Chemicals used in the Illicit Manufacture of Drugs*, pp. 25; *Guidelines for the Safe Handling and Disposal of Chemicals used in the Illicit Manufacture of Drugs*, pp. 71-76.

⁶⁸ UNODC, *Rapid Testing Methods of Drugs of Abuse*, pp. 6.

⁶⁹ UNODC, *Illustrated Guide for the Disposal of Chemicals used in the Illicit Manufacture of Drugs*, pp. 7-26.

Case Study Box 2: Dismantling of crime scenes involving precursor chemicals

FIG. 8: Flowchart depicting the processing of a crime scene involving precursor chemicals.



Source: UNODC, *Guidelines for the Safe Handling and Disposal of Chemicals used in the Illicit Manufacture of Drugs and Illustrated Guide for the Disposal of Chemicals used in the Illicit Manufacture of Drugs*.

Frontline officers may encounter precursor chemicals at various sites including clandestine laboratories, storage and illicit dump sites situated in urban or remote locations. Illicit operators of such sites frequently ignore conventional manufacturing practices in order to avoid detection. As a result, there are often occurrences of leakages, spillages and improper disposal of hazardous chemicals at such sites, which pose serious immediate risks to human health, communities, the environment and natural resources.⁷⁰ Despite

these known risks, many frontline and technical officers tasked to dismantle these sites are often insufficiently trained or equipped to reduce or eliminate these risks. In some instances, officers may unintentionally exacerbate the harm caused by such hazardous chemicals through improper handling and disposal of chemicals at sensitive locations such as human dwellings, waterways and agricultural land.

Proper training and guidelines should therefore be instituted for frontline and other technical offi-

cers to safely document, process and dismantle such sites, and to eliminate/reduce the associated health and environmental risks. A flowchart underlying the basic considerations for the processing of such sites, and the subsequent storage and disposal of hazardous chemicals is depicted in Figure 8. Once the site is rendered safe and has been processed for evidentiary purposes, further assessments have to be conducted to determine if the site continues to pose risks to human and environmental health. Remediation activity should be carried out until it is sufficiently safe and suitable for its proposed use.⁷¹

⁷⁰ UNODC, *Illustrated Guide for the Disposal of Chemicals used in the Illicit Manufacture of Drugs*, pp. 1; Australian Government, *Clandestine Drug Laboratory Remediation Guidelines*.

⁷¹ Australian Government, *Clandestine Drug Laboratory Remediation Guidelines*.

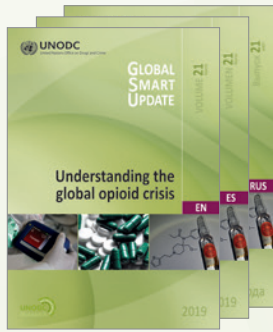
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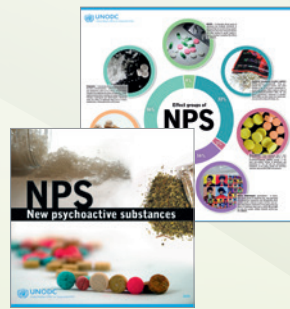
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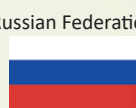
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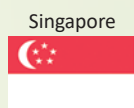
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