



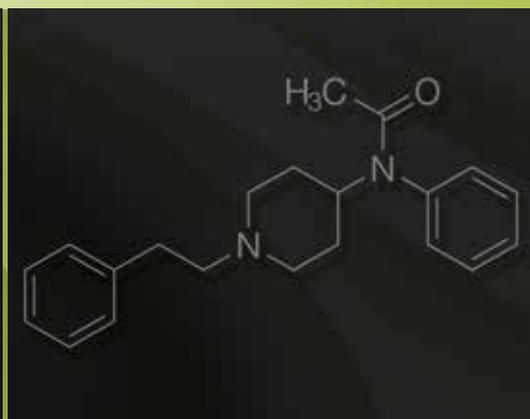
UNODC

United Nations Office on Drugs and Crime

GLOBAL SMART UPDATE

VOLUME 17
March

Fentanyl and its analogues - 50 years on



About the SMART Update

Synthetic drugs constitute one of the most significant drug problems worldwide. After cannabis, amphetamine-type stimulants (ATS) are the second 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. By July 2016, the emergence of NPS had been reported from 102 countries and territories. Trends on the synthetic drug 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 drug 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 Near and Middle East, Africa and Latin America; and regularly reviews the global amphetamine-type stimulants and *new psychoactive substances* situation. Its main products include online drug data collection, situation reports, regional assessments and the UNODC Early Warning Advisory (EWA) on *new psychoactive substances*. The EWA is a webportal that offers regular updates on *new psychoactive substances*, including trend data on emergence and persistence, chemical data, supporting documentation on laboratory analysis and national legislative responses (available at: www.unodc.org/NPS).

The Global SMART Update (GSU) series is published twice a year in English, Spanish and Russian and provides information on emerging patterns and trends of the global synthetic drug situation in a concise format. Each issue of the Global SMART Update contains a special segment and short segments on the topic of interest.* Electronic copies of the Global SMART Updates and other publications are available at: www.unodc.org/unodc/en/scientists/publications-smart.html. Past issues have covered topics such as UNGASS 2016 recommendations, injecting use of synthetic drugs, legal responses to NPS, key facts about synthetic cannabinoids and regional patterns of methamphetamine manufacture.

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* The information and data contained within this report are from official Government reports, press releases, scientific journals or incidents confirmed by UNODC Field Offices. An asterisk (*) indicates that information is preliminary as it stems from 'open sources' where UNODC is waiting for official confirmation. 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: UNODC, Global SMART Update Volume 17, March 2017.

Fentanyl and its analogues - 50 years on

ABSTRACT

Fentanyl and its analogues are potent synthetic opioids, which are liable to abuse. They are often sold under the guise of heroin or prescription medicines, such as oxycodone, and this exacerbates the risk of overdose and associated fatalities. An increasing number of deaths have been associated with the use of fentanyl and its analogues, particularly in North America. The facile synthesis of a number of these substances, coupled with the ease in obtaining the required precursor chemicals and equipment, has led to an increase in clandestine manufacture.

Introduction

Recent years have seen a sharp rise in opioid-related overdose deaths mainly in North America, and to a certain extent, in Europe. While the challenge posed by these fatalities is complex, more evidence is emerging about the role fentanyl and its analogues play in the current crisis. Fentanyl itself is a powerful opioid analgesic, with an established place in medicine. Yet, there has always been concern about its potential for abuse and dependence, and it was therefore placed under international control as far back as 1964. In the 1970s and 1980s, products containing fentanyl and its analogues appeared on the illicit drug market, and became notorious for accidental overdoses.¹ The problem seems to have resurfaced and the clandestine manufacturing of fentanyl has risen to unprecedented levels. The required materials and equipment for manufacture are readily available online, at low cost. This situation is aggravated by the rapid emergence of novel fentanyl analogues which have not been approved for medical use.

North America is particularly affected by an opioid overdose crisis. While originally, the sharp rise in overdoses was attributed to heroin, the current crisis is mainly attributed to clandestinely manufactured fentanyl

and fentanyl analogues. Evidence on fatalities associated with emerging fentanyl analogues is accumulating, also, in other regions of the world. The pills and powders containing such substances sold on the illicit market pose a threat to public health because of the variable quantity and potency of the active components, which in extreme cases, such as with carfentanil, may be 10,000 times more potent than morphine. Such products can prove particularly dangerous when sold as street heroin, together with heroin or as counterfeit prescription drugs, without the user's knowledge.

This publication aims to inform about the growing complexity of the opioid market, in particular the fentanyl group, international controls, evolving patterns of use and associated risks, global developments in manufacture and trafficking of fentanyl analogues and their precursors.

Good medicines, bad drugs?

Fentanyl belongs to a class of potent opioid analgesics, the 4-anilidopiperidines. These synthetic opioids have a high affinity for the μ -opioid receptor, which presents both benefits and drawbacks. On the one hand, strong μ -opioid receptor agonists from the fentanyl family have excellent pain-relieving properties. On the other hand, such drugs are liable to abuse and have high dependence-producing properties.

Fentanyl is the strongest opioid available for medical use in humans, with about 100 times the potency of morphine². It is highly valued for its analgesic and sedative effects and widely used in the management of severe pain and in anaesthesia. The three fentanyl analogues approved for pharmaceutical use, **sufentanil**, **alfentanil** and **remifentanil**, have very short onset and duration of action, and their medical use is limited to intravenous anaesthesia³. **Carfentanil**, estimated to be about 10,000 times more potent than morphine⁴, is intended only for veterinary use on large animals, and not approved for medical use in humans.

The liability of fentanyl and its analogues to abuse and the dependence-potential are reflected in the international legislative responses. Fentanyl was first synthesized in 1959, and was placed under international control as a Schedule 1 substance in 1964 under the Single Convention on Narcotic Drugs of 1961. During the ensuing decades, the list of scheduled substances has grown to include all fentanyl analogues approved for human medical use (sufentanil in 1980, alfentanil in 1984, and remifentanil in 1999), and several analogues which have not been developed into pharmaceutical products (acetyl- α -methylfentanyl, α -methylfentanyl and 3-methylfentanyl were placed under international control in 1988, and α -methylthiofentanyl, β -hydroxyfentanyl, β -hydroxy-3-methylfentanyl, 3-methylthiofentanyl, \textit{para} -fluorofentanyl and thiofentanyl in 1990).

1 Henderson GL. Fentanyl-related deaths: demographics, circumstances, and toxicology of 112 cases. *Journal of Forensic Science*. 1991 Mar 1;36(2):422-33.

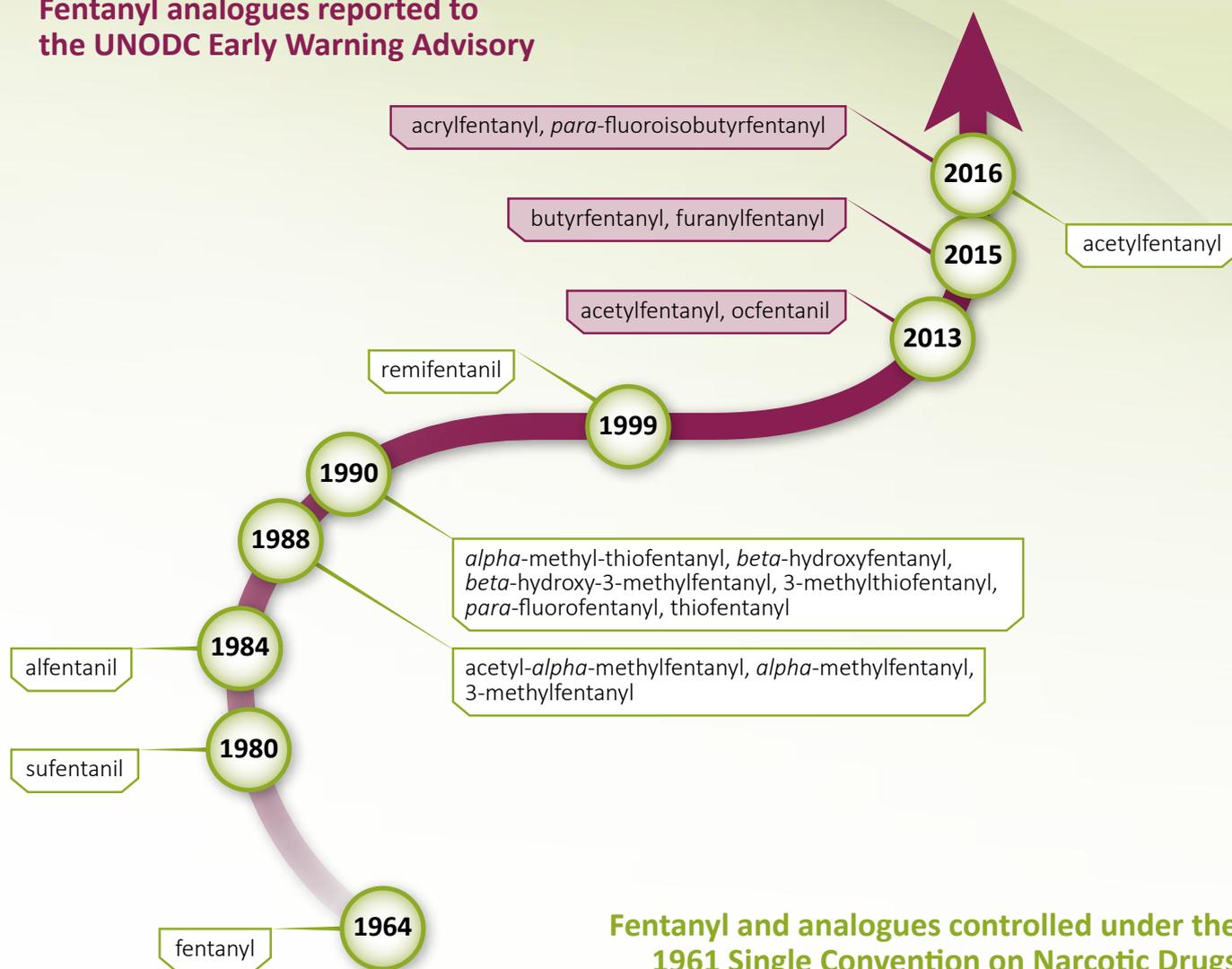
2 Chodoff P, Domino EF. Comparative pharmacology of drugs used in neuroleptanalgesia. *Anesthesia and Analgesia*, 44 (5) (1965), pp. 558-563

3 Lemmens H. Pharmacokinetic-pharmacodynamic relationships for opioids in balanced anaesthesia. *Clin Pharmacokinet*. 1995;29:231-242.

4 Janssen PA. Potent, new analgesics, tailor-made for different purposes. *Acta Anaesthesiol Scand*. 1982 Jun;26(3):262-8.

Figure 1: International control of fentanyl and its analogues, 1964-2016

Fentanyl analogues reported to the UNODC Early Warning Advisory



Fentanyl and analogues controlled under the 1961 Single Convention on Narcotic Drugs

Acetylfentanyl was placed under international control in 2016, while butyrfentanyl has been recommended for control by the WHO⁵. Carfentanyl, which was first synthesized in 1974 and remains the most potent commercially available opioid in the world, is not under international control.

Within the last five years, more than a dozen additional fentanyl analogues have entered the illicit opioid market. Some of these analogues have been re-discovered by traffickers from research work carried out between the 1960s and 1990s.

These substances were described in scientific literature but never developed into pharmaceutical products. Examples include **acetylfentanyl**, **butyrfentanyl**, **furanylfentanyl**, and **ocfentanil**. Other substances currently present in the illicit opioid market are newly designed fentanyl analogues, such as **acrylfentanyl** and **para-fluoroisobutyrfentanyl**. The countless possibilities to create new compounds by small changes in chemical structures pose a growing challenge to international control of the opioid trade. Between 2012 and 2016, seventeen fentanyl analogues were reported to the UNODC EWA from countries in East Asia, Europe and North America (see Table 1). So far, only one of them, acetylfentanyl, has been placed under international control.

Nonmedical use of fentanyl and its analogues can have severe health consequences. Tolerance and dependence develop very fast, and may reach extreme levels. Above all, each episode of nonmedical use carries a high risk of overdose and death as a result of respiratory depression – a common side-effect of opioids. A report from a drug consumption room in Sydney found that under medical surveillance, the risk of overdose upon injecting fentanyl was two times higher than upon injecting heroin, and eight times higher than upon injecting other prescription opioids⁶.

Overdoses can be effectively reversed by naloxone, a μ -opioid

⁵ Commission on Narcotic Drugs, Reconvened fifty-ninth session. Extract from the Report of the 38th Expert Committee on Drug Dependence, convened from 14 to 18 November 2016, at WHO headquarters in Geneva. 30 November 2016. https://www.unodc.org/documents/commissions/CND/CND_Sessions/CND_59Reconvened/ECN72016_CRP13_V1610192.pdf

⁶ Latimer J, Ling S, Flaherty I, Jauncey M, Salmon AM. Risk of fentanyl overdose among clients of the Sydney Medically Supervised Injecting Centre. *Int J Drug Policy*. 2016 Oct 14;37:111-114

Figure 2: Development of new fentanyl analogues by small changes in chemical structures.
(A) fentanyl, (B) acetylfentanyl, (C) butyrfentanyl

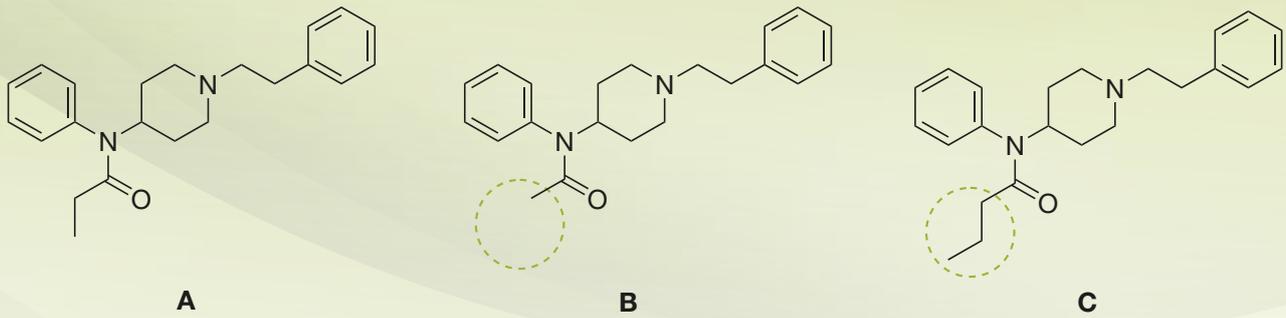


Table 1: NPS fentanyl analogues reported to the UNODC EWA, 2012-2016

COMMON NAME	REPORTED IN
3-fluorofentanyl	Europe
4-fluorobutyrfentanyl	Europe
4-methoxybutyrfentanyl	Europe
acetylfentanyl	Asia, Europe, North America
acrylfentanyl	Asia, Europe
<i>beta</i> -hydroxy-thiofentanyl	North America
butyrfentanyl	Asia, Europe, North America
despropionylfentanyl	Latin America, North America
despropionyl-2-fluorofentanyl	Europe
furanylfentanyl	Asia, Europe, North America
isobutyrfentanyl	Africa, Europe
(iso)butyr-F-fentanyl N-benzyl analogue	Europe
methoxyacetylfentanyl	Europe
ocfentanil	Europe
<i>para</i> -fluoroisobutyrfentanyl	North America
tetrahydrofuranylfentanyl	Europe
valerylfentanyl	Asia, Europe, North America

receptor antagonist medication. 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 introduced or expanded naloxone distribution programs. Canada authorised sale of naloxone without prescription, including the nasal spray version, in 2016⁷.

Risky practices

Although fentanyl is safe under clinical supervision, e.g. in a hospital

setting, the recreational use of products containing fentanyl may easily prove fatal with increase in the administered dose, or a change in the route of administration (e.g. extracting the drug from a transdermal patch into liquid to prepare an injection or nasal spray, inhaling volatilized fentanyl, or placing a transdermal patch on oral mucous membranes). A study conducted in rural Australia concluded that users typically did not revert to less potent opioids after becoming dependent on fentanyl, practiced unsafe preparation and administration methods, and their risk of overdose was exacerbated by misinformation circulating amongst peers⁸.

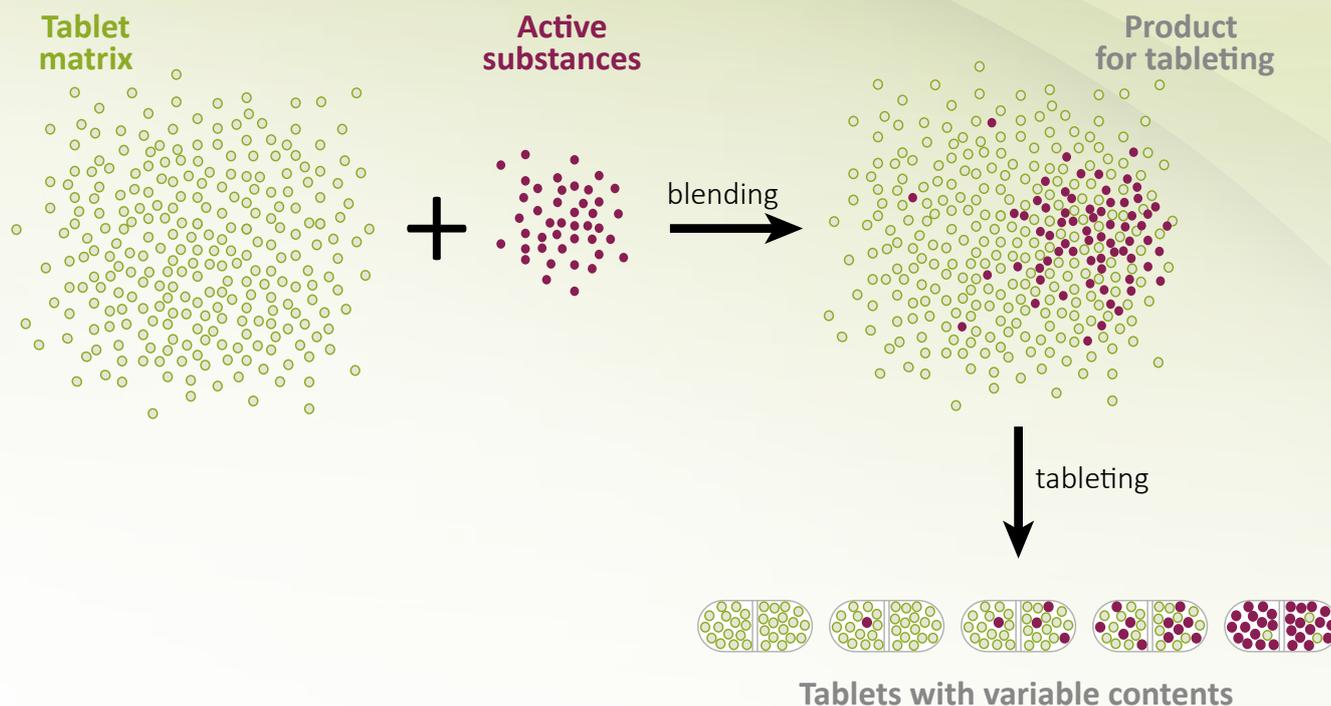
Use of illicitly manufactured fentanyl and its analogues amplifies the hazards because such products lack quality control, are typically not portioned in precise doses, and can be deadly in minuscule amounts due to the extreme potencies. Attempts to prepare a single dose by weighing without precision equipment are highly risky. Another approach is to bring a larger amount of the drug into solution, which is then apportioned into single doses; however, errors in calculations can be lethal. Users experimenting with new fentanyl analogues, whose potency is not well-defined, increase the odds of making a fatal mistake.

⁷ Health Canada. Notice - Availability of Naloxone Hydrochloride Nasal Spray (NARCAN®) in Canada. July 6, 2016. (<http://www.hc-sc.gc.ca/dhp-mps/prodp-harma/activit/announce-annonce/notice-avis-nasal-eng.php>)

⁸ Allan J, Herridge N, Griffiths P, Fisher A,

Clarke I, and Campbell, M. Illicit Fentanyl use in Rural Australia – An Exploratory Study. 2015 J Alcohol Drug Depend 3:196.

Figure 3: Variable dose of active substance in clandestinely manufactured pills



Risk of exposure to fentanyl and its analogues

Overdose may also result from 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 USA recorded incidents of hospitalization of law enforcement officers that carried out seizures of such chemicals. The USA Drug Enforcement Administration (DEA) has recently released safety alerts on fentanyl and carfentanil, advising on steps to follow in situations where such drugs might be present, including immediate application of naloxone in case of exposure^{9,10}.

Overdose deaths

The nonmedical use of fentanyl and its analogues has resulted in thousands of fatalities worldwide. In North America, illicitly manufactured fentanyl or fentanyl analogues have caused several epidemics of overdose deaths since the 1970s, and are to a large extent responsible

for the current overdose epidemic in the region. In the USA, fentanyl and its analogues have contributed to more than 5000 overdose deaths since fall 2013¹¹. In Canada, fentanyl was determined to be the cause, or a contributing factor, in at least 655 death cases that occurred between 2009 and 2014¹². In the European Union, death cases involving substances from the fentanyl group were first documented in the 1990s in Italy and Sweden, resurged in the early 2000s in Estonia (where most recorded overdose deaths are related to fentanyl and 3-methylfentanyl use¹³), and have also been reported more recently in several other EU Member States, including Finland, Germany, Greece, and the United Kingdom¹⁴. Australia has been experiencing a growing

trend in deaths resulting from use of diverted pharmaceutical fentanyl, with at least 123 fentanyl-associated deaths reported between 2000 and 2012¹⁵. Death cases resulting from self-administration of multiple fentanyl patches were also reported in Algeria¹⁶ and Morocco¹⁷.

In recent years, several emerging synthetic opioids have been documented to cause serious adverse events and deaths¹⁸. In 2016, a record spike in drug overdoses in Midwest USA was attributed to carfentanil, and at least two carfentanil fatalities in Canada were reported by the press.

Markets for specific products

Products sold on the illicit synthetic opioid market are highly diversified, and often region-specific. Injecting

9 <https://ndews.umd.edu/sites/ndews.umd.edu/files/DEA%20Fentanyl.pdf>

10 <https://www.dea.gov/divisions/hq/2016/hq092216.shtml>

11 Green TC1, Gilbert M2. Counterfeit Medications and Fentanyl. *JAMA Intern Med.* 2016 Oct 1;176(10):1555-1557.

12 Canadian Centre on Substance Abuse. Deaths involving fentanyl in Canada, 2009–2014. *CCENDU Bulletin*, Ottawa, ON (2015)

13 Uusküla A, Raag M, Vorobjov S, Rüütel K, Lyubimova A, Levina OS, Heimer R. Non-fatal overdoses and related risk factors among people who inject drugs in St. Petersburg, Russia and Kohla-Järve, Estonia. *BMC Public Health.* 2015 Dec 18;15:1255.

14 Mounteney J, Giraudon I, Denissov G, Griffiths P. Fentanyls: Are we missing the signs? Highly potent and on the rise in Europe. *Int J Drug Policy.* 2015 Jul;26(7):626-31.

15 NCIS. Deaths related to fentanyl misuse - An update: Fact Sheet. Retrieved 10 November 2016.

16 Salmi A. Fentanyl Patch... The Bad Use. *Journal of Clinical Toxicology.* 2015 Nov 9;2015.

17 Serghini I. Fentanyl intoxication: case report. *Reactions.* 2015 Feb;1539:148-21.

18 UNODC EWA. Deaths associated with use of emerging synthetic opioids. [news announcement]. 2016 Nov. https://www.unodc.org/LSS/Announcement/Details/466aa396-492d-4129-a1bc-f519ecb5d443#_ftn10

fentanyl diverted from pharmaceutical products (mostly extracted from transdermal patches), seems to be the major form of nonmedical fentanyl use in Australia¹⁹ and Germany²⁰, and was also reported in New Zealand²¹. Clandestinely manufactured fentanyl or its analogues may be sold in solid or liquid form as the consumer's drug of choice, such as is the case in Estonia, where fentanyl and 3-methylfentanyl are the most widely used opioids, and the primary injected drugs²².

In North America, heroin containing, or substituted with, drugs from the fentanyl group appeared already in the 1970s on the illicit drug market under names like "China White", "Tango and Cash" or "Synthetic Heroin". This trend is now making a comeback. Illicitly manufactured fentanyl is most commonly mixed with or sold as white powder heroin, but also as cocaine products²³ or black tar heroin. The most recent development is the emergence of counterfeit pharmaceutical preparations containing illicitly manufactured fentanyl and its analogues. The sale of counterfeit products to unwitting customers increases the danger of overdose, as they do not know which substance they are consuming, and cannot determine the safe amount. Importantly, clandestine manufacturers often lack the ability to ensure uniform distribution of such highly potent substances in marketed preparations, such as pills or powders. As a result, some pills or powders may contain a lethal dose. In a Californian study on an outbreak of poisonings caused by fentanyl-adulterated tablets purchased on the street

as hydrocodone/acetaminophen, the content of fentanyl in analysed pills varied between 600-6,900 µg/pill²⁴. New types of counterfeit prescription pills containing synthetic opioids continue to appear²⁵. Cases of fentanyl and analogues sold under the guise of heroin have also been observed in Europe. For example, ocfentanil has been sold on the hidden web as heroin, as revealed by analysis of samples collected in Spain and France²⁶.

Manufacturing and trafficking

According to the DEA²⁷, the current fentanyl crisis in the USA is largely fuelled by illicitly manufactured fentanyl and its analogues, 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. This facilitates the entry into small-scale manufacturing for minor drug-trafficking organizations. Most fentanyl recently seized in the USA was of non-pharmaceutical origin and synthesized via the so-called Siegfried method, which was first described in the 1980s, and is relatively easy to perform.²⁸ 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 the UNODC EWA in recent years, including acetylfentanyl, butyrfentanyl and

furanylfentanyl, can be synthesized from NPP or ANPP via the Siegfried route. However, the majority of fentanyl analogues that were put under international control between the sixties and the nineties and which do not appear to be linked to the current opioid crisis in the USA, cannot readily be produced from NPP or ANPP.

Data reported to the UNODC on dismantled laboratories 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 Slovakia (2011), three kitchen laboratories in the USA (one in 2013 and two in 2015), one kitchen laboratory in Germany (2015), and one case of manufacturing 3-methylfentanyl in Russia (2014).²⁹

Due to their extreme potencies, fentanyl and its analogues are often present in trace amounts in the products available, be it has 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 under-reporting of the extent to which these products appear on the illicitly-used drug market.

- ...
- 19 Roxburgh A, Burns L, Drummer OH, Pilgrim J, Farrell M, Degenhardt L. Trends in fentanyl prescriptions and fentanyl-related mortality in Australia. *Drug Alcohol Rev.* 2013 May;32(3):269-75.
 - 20 Erbas B, Arnold M. [Death from fentanyl: Causative and preventive approaches in Bavaria]. *German. MMW Fortschr Med.* 2016 Feb 18;158(3):54-6.
 - 21 Schauer CK, Shand JA, Reynolds TM. The Fentanyl Patch Boil-Up - A Novel Method of Opioid Abuse. *Basic Clin Pharmacol Toxicol.* 2015 Nov;117(5):358-9.
 - 22 Abel-Ollo K, Salekešin M, Vorobjov S, Vals K, Rüütel K. 2014 national report (2013 data) to the EMCDDA by the Reitox National Focal Point.
 - 23 Lucyk SN, Nelson LS. Novel Synthetic Opioids: An Opioid Epidemic Within an Opioid Epidemic. *Annals of emergency medicine.* 2017 Jan 1;69(1):91-3.

- ...
- 24 Sutter ME, Gerona RR, Davis MT, Roche BM, Colby DK, Chenoweth JA, Adams AJ, Owen KP, Ford JB, Black HB, Albertson TE. Fatal Fentanyl: One Pill Can Kill. *Acad Emerg Med.* 2016 Jun 20.
 - 25 Canadian Centre on Substance Abuse. Novel Synthetic Opioids in Counterfeit Pharmaceuticals and Other Illicit Street Drugs. *CCENDU Bulletin*, Ottawa, ON, June 2016
 - 26 Quintana P, Ventura M, Grifell M, Palma A, Galindo L, Fornís I, Gil C, Carbón X, Caudevilla F, Farré M, Torrens M. The hidden web and the fentanyl problem: Detection of ocfentanil as an adulterant in heroin. *International Journal of Drug Policy.* 2016 Nov 23.
 - 27 DEA. Counterfeit prescription pills containing fentanyls: A global threat. *DEA Intelligence Brief.* 2016 DEA-DCT-DIB-021-16.
 - 28 DEA. Counterfeit prescription pills containing fentanyls: A global threat. *DEA Intelligence Brief.* 2016 DEA-DCT-DIB-021-16.
- ...
- 29 UNODC Annual Reports Questionnaires, 2011-2015.



China: Six fentanyl analogues are placed under national control

BEIJING, China – September 2015. On 29 September, 2015 the Chinese Drug and Food Administration announced “Administrative Measures on Narcotics and Psychotropic Substances without Medical Use” by which 116 psychoactive substances, including six fentanyl analogues, were placed under national control. This decision came into effect on 1st October, 2015. The six fentanyl analogues that have been placed under national control are acetylfentanyl, butyrfentanyl, β -hydroxythiofentanyl, 4-fluorobutyrfentanyl, isobutyrfentanyl and ocfentanil. Various other NPS, have also been included to the list of controlled substances.

UNODC Early Warning Advisory on New Psychoactive Substances. “Drug Laws/Individual Listing for CHINA.”

China: Chinese Customs seizes fentanyl and acetylfentanyl destined for Mexico

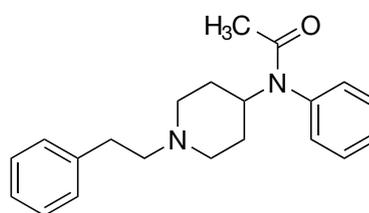
BEIJING, China – May 2015. In May 2015, Chinese Customs officials seized 46 kg of fentanyl and 26 kg of acetylfentanyl that had been concealed in a cargo container destined for Mexico. The substances had been transferred via five freight forwarders before arriving at customs where six customs officials became ill and one fell into a coma as a result of handling the drugs. Later, in March 2016, the Drug Enforcement Administration (DEA) and Homeland Security Investigations offices in the south-eastern United States also reported to have seized multiple shipments that had come from China containing mislabeled pill presses, as well as fentanyl, acetylfentanyl, and butyrfentanyl.

Drug Enforcement Administration (DEA). *DEA Intelligence Brief: Counterfeit Prescription Pills Containing Fentanyls: A Global Threat.* July 2016.

Japan: “Bath salt” containing acetylfentanyl and 4-methoxy PV8 linked to a case of acute poisoning

TOKYO, Japan – August 2016. In Japan, a forensic autopsy report on a man in his 30s has attributed this case of acute poisoning to a “bath salt” product containing acetylfentanyl and 4-methoxy PV8 (4-methoxy PHPP). It is suspected that the substances had been self-administered by an intravenous injection. The deceased had been a habitual user of “bath salts” and, for many years, had a history of methamphetamine use. A small plastic bag containing a pale brown white powder and a filled syringe were also found at the scene.

Yonemitsu, K. et al. (2016) “A fatal poisoning case by intravenous injection of “bath salts” containing acetylfentanyl and 4-methoxy PV8.” *Forensic Science International* 267: e6–e9.



Source: UNODC

Finland: International cooperation disrupts acetylfentanyl trafficking

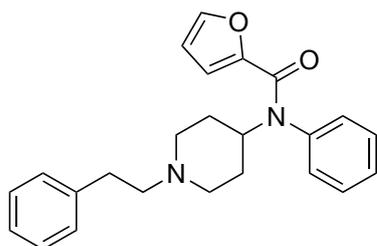
HELSINKI, Finland – June 2015. After being notified by Belgium Customs, 2.36 grams of acetylfentanyl that had been sourced in China were seized in Finland. The substance was in powder form and had been declared as acrylic paint phenolic resin for an individual in Finland. Previously, in 2014, Finland also reported three acetylfentanyl seizures in small quantities that had been discovered in the post and had originated from China and Belgium.

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA); Europol. *Acetylfentanyl.* Luxembourg: Publications Office of the European Union, 2016.

Sweden: Fentanyl analogues linked to several deaths and intoxications

STOCKHOLM, Sweden – August 2016. According to the National Board of Forensic Medicine, acrylfentanyl has been linked to 20 deaths that occurred in Sweden between April and August 2016. Results from the Swedish early warning system called the STRIDA project also showed that among patients with suspected NPS exposure at emergency departments in Sweden between April and November 2015, nine had analytically confirmed intoxications involving acetylfentanyl, three involving 4-methoxybutyrfentanyl, one involving furanylfentanyl, and another involving a combination of 4-methoxybutyrfentanyl and furanylfentanyl. All of these patients were aged 20-40 and mostly male. In 12 of the cases, patients were admitted to intensive care, where two required intubation and mechanical ventilation.

Helander A., Bäckberg M., and Beck O. (February 2016) "Intoxications involving the fentanyl analogs acetylfentanyl, 4-methoxybutyrfentanyl and furanylfentanyl: results from the Swedish STRIDA project." *Clinical Toxicology* 54 (4): 324-332.



Source: UNODC

Estonia: Furanylfentanyl is placed under national control

TALLINN, Estonia – July 2016. In July 2016, furanylfentanyl was added to Schedule I of the narcotic and psychotropic substances regulation. According to the Chemical Department of the Estonian Forensic Science Institute, furanylfentanyl had been submitted for analysis five times by June 2016 totaling a quantity of 14.185 grams. Although it has not yet been officially confirmed, the Estonian Forensic Science Institute also suspects that the deaths of three people in Estonia might have been linked to the use of furanylfentanyl.

Europäische Kommission. "Notifizierungsangaben: Entwurf zur Änderung der Verordnung Nr. 73 des Sozialministers." Available at: <http://ec.europa.eu/growth/tools-databases/tris/de/index.cfm/search/?trisaaction=search.detail&year=2016&num=331&mLang=EN>



Source: UNODC

UNODC: International control of acetylfentanyl and MT-45 enters into force

VIENNA, Austria – May 2016. On 17 May 2016, the decision adopted by the Commission on Narcotic Drugs (CND) during its 59th Session in March 2016 to add the synthetic opioids acetylfentanyl to Schedule I and IV and MT-45 to Schedule I of the Single Convention on Narcotic Drugs of 1961 entered into force.

UNODC Early Warning Advisory on New Psychoactive Substances. "June 2016 – UNODC: Commission on Narcotic Drugs decision on international control of acetylfentanyl and MT-45 enters into force." June 2016. Available at: <https://www.unodc.org/LSS/Announcement/Details/3ec66e50-249f-438e-8a79-470d5e269b8d>

Source: UNODC

UNODC: Increasing number of non-controlled fentanyl analogues reported to the Early Warning Advisory

VIENNA, Austria – November 2016. Of the 13 non-controlled fentanyl analogues that have been reported by Member States to the UNODC Early Warning Advisory (EWA) by November 2016, eight have been reported within the last year. These substances include 4-methoxybutyrfentanyl, butyrfentanyl, despropionylfentanyl, despropionyl-2-fluorofentanyl, furanylfentanyl, acrylfentanyl, *para*-fluoroisobutyrfentanyl, and valerylfentanyl. Additionally, (iso)butyrfentanyl, (iso)butyr-F-fentanyl N-benzyl analogue, acetylfentanyl (controlled under Schedule I of the Single Convention on Narcotic Drugs of 1961), ocfentanil, and *beta*-hydroxy-thiofentanyl have also been reported to the EWA.

UNODC Early Warning Advisory on New Psychoactive Substances. "Search NPS Data" November 2016.



**World Health
Organization**

World Health Organization: WHO Expert Committee on Drug Dependence reviews twelve psychoactive substances

GENEVA, Switzerland – November 2016. At the 38th meeting of the WHO Expert Committee on Drug Dependence (ECDD) from 14 to 18 November 2016, twelve psychoactive substances have been considered for review, among them two synthetic opioids: U-47700 and butyrfentanyl. The other substances reviewed are: 4-MEC; 3-MMC; ethylone; pentedrone; ethylphenidate; methiopropamine; MDMB-CHMICA; 5F-APINACA; JWH-073; and XLR-11. Recommendations from the WHO on whether or not to place specific substances under international control are addressed to the Secretary-General of the United Nations, and are subject to a vote by the United Nations Commission on Narcotic Drugs (CND).

UNODC Early Warning Advisory on New Psychoactive Substances. "August 2016- World Health Organization: NPS to be reviewed for potential scheduling under the International Drug Control Conventions." August 2016.

Belgium: Belgian Customs Service reports seizures of acetylfentanyl en route to France and Germany

Brussels, Belgium – 2015. Since June 2015, the Belgian Customs Service has reported of three seizure cases of acetylfentanyl that were perceived to have been sourced in China. In the first case, 103.57 g of packaged acetylfentanyl that was seized in the post and intended for onward trafficking to an individual in France, while the second seizure case involved 11.30 g of packaged acetylfentanyl that was also discovered in the post and intended for onward trafficking to an individual in Germany. In the third seizure case, three plastic sachets were discovered in the postal stream in a plastic package containing 2.42 grams of propylfentanyl, 2.41 grams of acetylfentanyl and 2.40 grams of flubromazepam. According to the Belgian Customs Service, the substances were sourced in China and intended for onward trafficking to an individual in Germany.

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA); Europol. *Acetylfentanyl*. Luxembourg: Publications Office of the European Union, 2016.



**Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive**

Ireland: Authorities in Dublin and Cork investigate deaths involving fentanyl analogues

DUBLIN, Ireland – 2016. Between April and July 2016, five deaths have been linked to the use of fluorofentanyl (isomer not specified) and ofentanil in Dublin and Cork. As a result of these fentanyl-related deaths, the Health Service Executive (HSE) of Ireland issued an alert in July 2016 highlighting the dangers of fentanyl and its analogues. According to the HSE, fentanyl analogues might be sold to drug users as heroin in powder form possibly mixed with heroin or mixed with caffeine and paracetamol to mimic the effect of heroin.

Health Service Executive. "Fentanyl Implicated in Overdose Deaths." 28 July, 2016. Available at: <http://www.hse.ie/eng/services/news/media/pressrel/Fentanyldeaths.html>



Source: UNODC

Brazil: Fentanyl and butylone implicated in acute poisonings

SÃO PAULO, Brazil – September 2016. In September 2016, the Laboratory of the Toxicology Faculty of Medicine (FCM) of Unicamp reported that fentanyl and butylone were suspected to have been linked to six cases of acute poisoning in August 2016 in Campinas, Sumaré, and Indaiatuba, in Brazil. According to toxicologists at the Center of Intoxication of Unicamp (JRC), drug users might not have been aware that they were using fentanyl and butylone because of the similarities in appearance to LSD and other drugs. The JRC has issued alerts to all emergency rooms in São Paulo to notify them of the symptoms and effects that these substances can have on drug users.

ProMED-mail International Society for Infectious Diseases. "Fentanil e butilona- Brasil (SP), uso recreacional, intoxicação, alerta." 10 September, 2016. Available at: <http://www.promedmail.org/direct.php?id=20160910.4479040>

Canada: Health Canada proposes national control of fentanyl precursor chemicals

OTTAWA, Canada – September 2016. On 3 September 2016, Health Canada issued a notice proposing to add six precursor chemicals used in the production of fentanyl to Part 1 of Schedule VI of the Controlled Drugs and Substances Act and to the schedule of the Precursor Control Regulations as Class A precursor chemicals: propionyl chloride; 1-phenethyl-4-piperidone (NPP) and its salts; 4-piperidone and its salts; norfentanyl (N-phenyl-N-piperidin-4-ylpropanamide) and its salts; 1-phenethylpiperidin-4-ylidenephethylamine and its salts; and N-phenyl-4-piperidinamine and its salts. These regulatory amendments came into force on 30 November 2016.

Government of Canada. "Canada Gazette." Vol. 150, No. 36, September 3, 2016. Available at: <http://www.gazette.gc.ca/rp-pr/p1/2016/2016-09-03/html/notice-avis-eng.php>



Source: RCMP

Canada: Promoting safe handling of fentanyl by first responders

BRITISH COLUMBIA, Canada – June 2016. Sponsored by the Justice Institute of British Columbia and the British Columbia Association of Chiefs of Police, the Royal Canadian Mounted Police (RCMP) has provided two-day workshops to train police, paramedics, firefighters, correctional officers, Canada Border Services agents and Transport Canada staff in safe handling of fentanyl in British Columbia. The RCMP also raised awareness of the dangers of fentanyl to first responders and the general public by releasing a video in September 2016 that featured two British Columbia RCMP officers who became sick immediately after inhaling or touching fentanyl that belonged to people they had come across during a car inspection.

British Columbia Government News. "Workshops safeguard first responders from deadly fentanyl." 14 June 2016. Available at: <https://news.gov.bc.ca/releases/2016PSSG0118-001025>

Royal Canadian Mounted Police (RCMP). "Video on the dangers of fentanyl." Available at: <http://www.rcmp.gc.ca/en/fentanyl-video?nr>



Source: DEA

United States: Counterfeit oxycodone and Xanax tablets contain fentanyl and analogues

LOS ANGELES, California – March 2016. In Los Angeles, the Drug Enforcement Administration (DEA) seized a counterfeit prescription pill manufacturing site in March 2016 that had employed the use of fentanyl and other synthetic opiates. Previously, in January 2016, the DEA of New Jersey arrested a counterfeit prescription pill producer who had manufactured tablets in New York to look like 30 milligram oxycodone tablets, but in fact contained either fentanyl citrate or acetylfentanyl. According to the DEA, nine people died of the use of counterfeit Xanax® tablets containing fentanyl in Pinellas County, in Florida between January and March 2016. In March and April 2016, another 52 overdoses and 10 deaths occurred in Sacramento, California, through the use of counterfeit Norco® pills containing fentanyl.

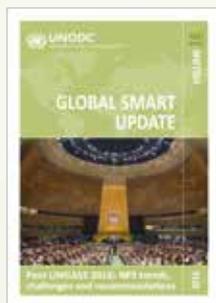
Drug Enforcement Administration (DEA). *DEA Intelligence Brief: Counterfeit Prescription Pills Containing Fentanyl: A Global Threat.* July 2016.

United States: Fentanyl analogues are placed under national control

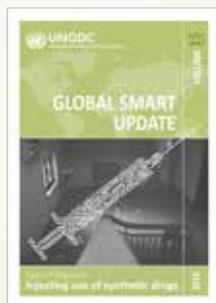
WASHINGTON D.C., United States – 2016. Based on the recent surge of fentanyl-related deaths, the DEA issued a nationwide alert on fentanyl and its analogues in March 2015. Since 17 July 2015, acetylfentanyl is a controlled substance in the United States under Schedule I of the Controlled Substances Act. In September 2016, the DEA issued a notice of intent to temporarily schedule the synthetic opioid furanylfentanyl.

UNODC Early Warning Advisory on New Psychoactive Substances. "July 2015 – United States of America: Acetylfentanyl placed under temporary control." July 2015. Available at: <https://www.unodc.org/LSS/Announcement/Details/a9a23075-6d57-4cc2-9a49-0bcce189e776>

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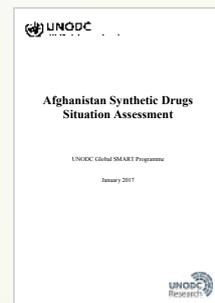
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Afghanistan Synthetic Drugs Situation Assessment 2017



World Drug Report 2016



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Early Warning Advisory Newsletter Volume 9, 10 and 11



Updated New Psychoactive Substance leaflet and poster (English and Spanish)

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