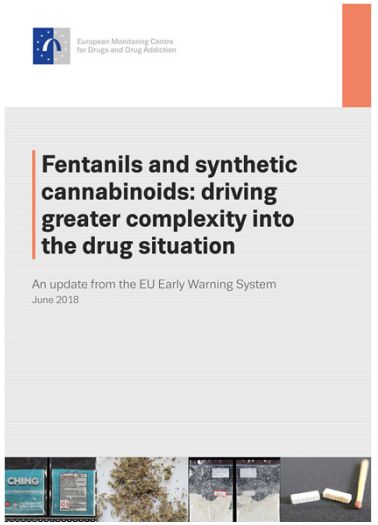
European Monitoring Centre
for Drugs and Drug Addiction

Roumen Sedefov, EMCDDA
Reduse 2018 - International Drug Checking Forum, 14 September 2018, Vienna

Highly potent drugs, high strength products
A problem for Europe?

- Decrease in new substances detected for the first time, 2016–17
- Availability of many new substances remains relatively high
- Stronger links with the established illicit drug market
- Increase in highly potent substances: high risk of poisoning & explosive outbreaks
- Global markets, glocal threats
- Expect the unexpected



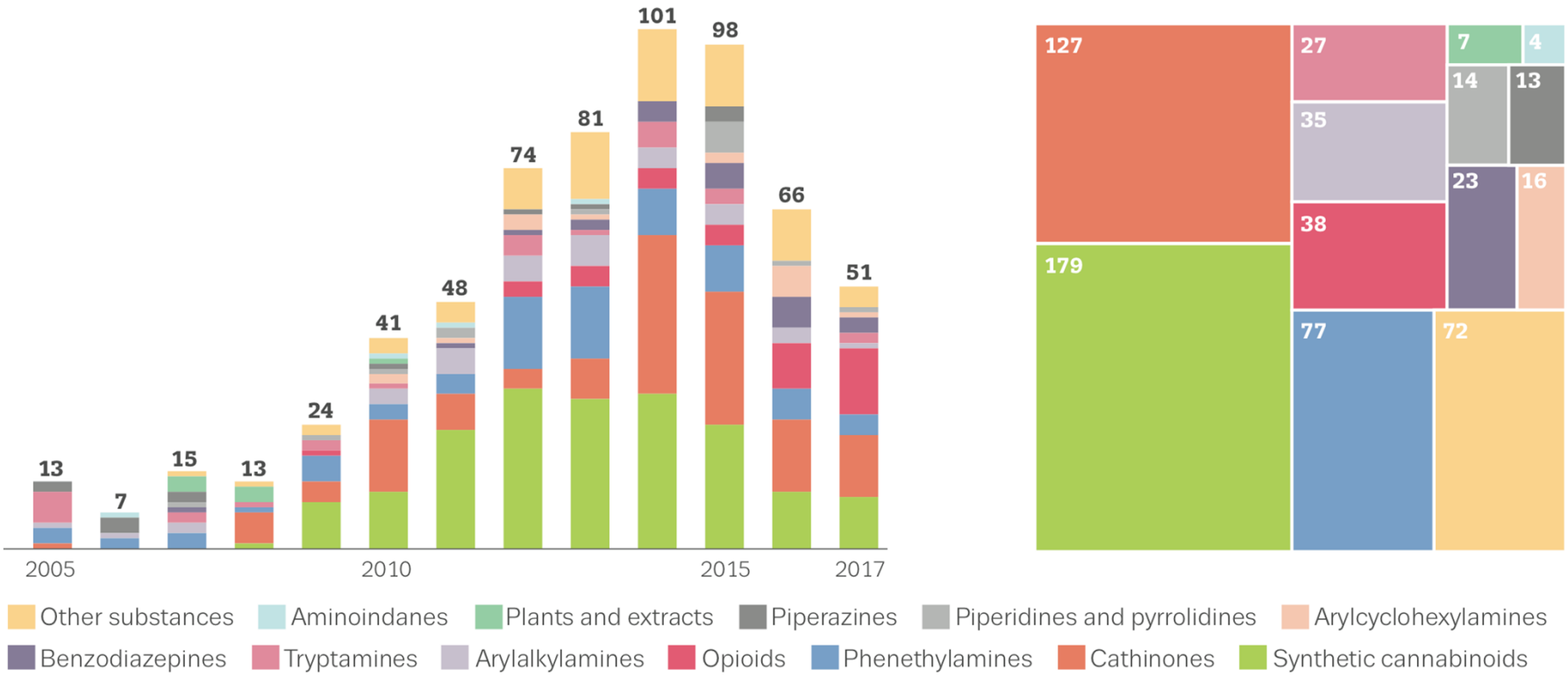
Overview

- Stronger, faster, higher, happier, harmful?

Case studies

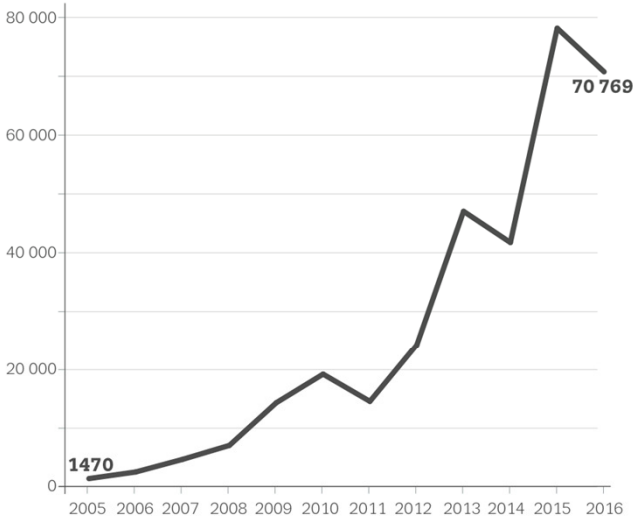
- Global markets, glocal threats: the case for better preparedness
- Changes in the market
- Synthetic cannabinoids
- Fentanils
- MDMA and cathinones
- Concluding thoughts

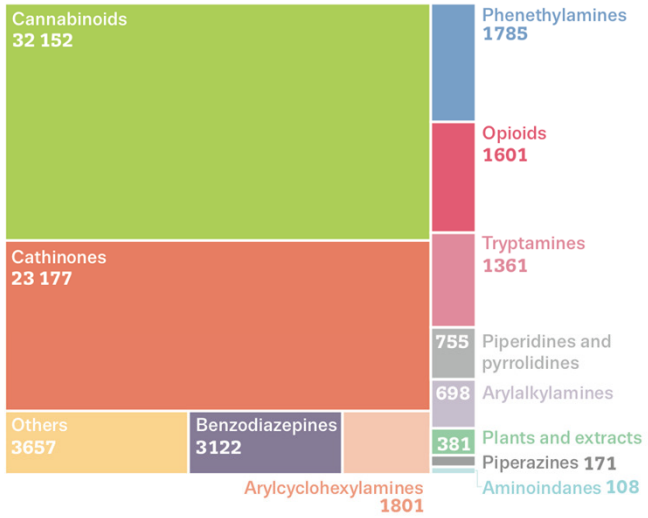
Number of new substances notified for the first time, 2005–17

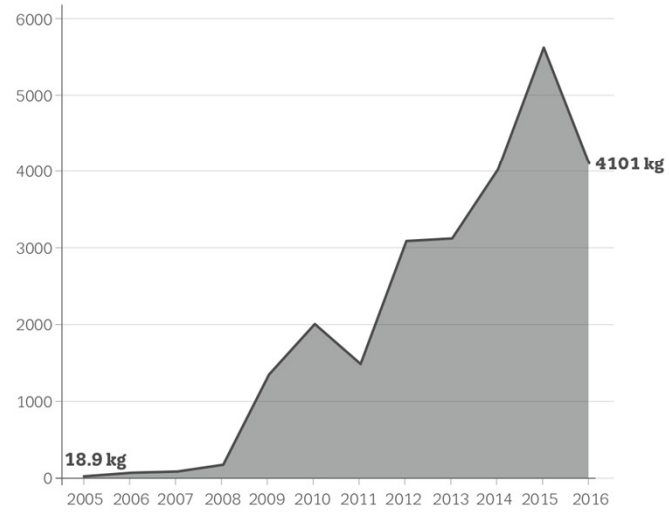


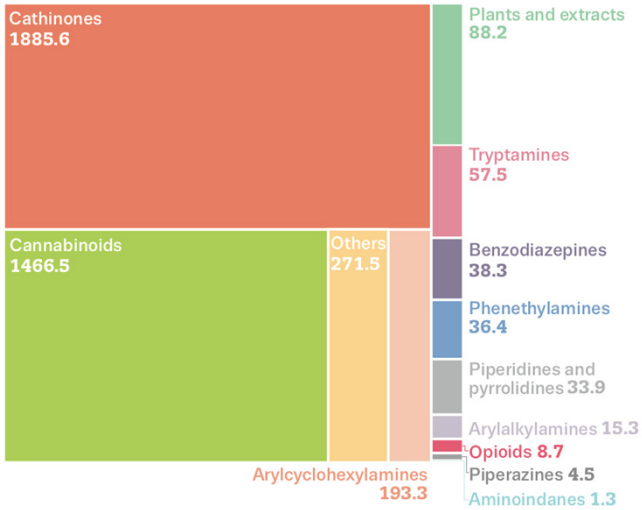
New psychoactive substances notified to the EU Early Warning System for the first time 2005–17. Number per year (left) and total number per category (right).

Number and quantity of seizures









Source: EU Early Warning System

Number of seizures of new psychoactive substance reported to the EU Early Warning System: trends and distribution by category in 2016

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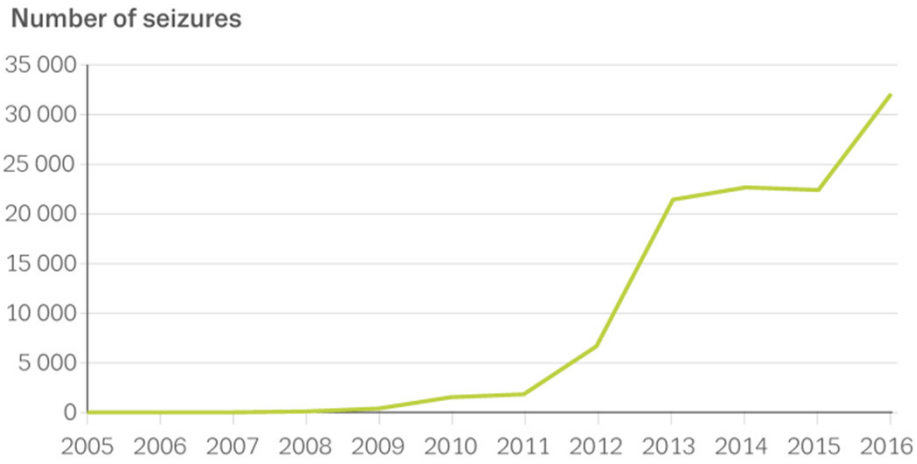
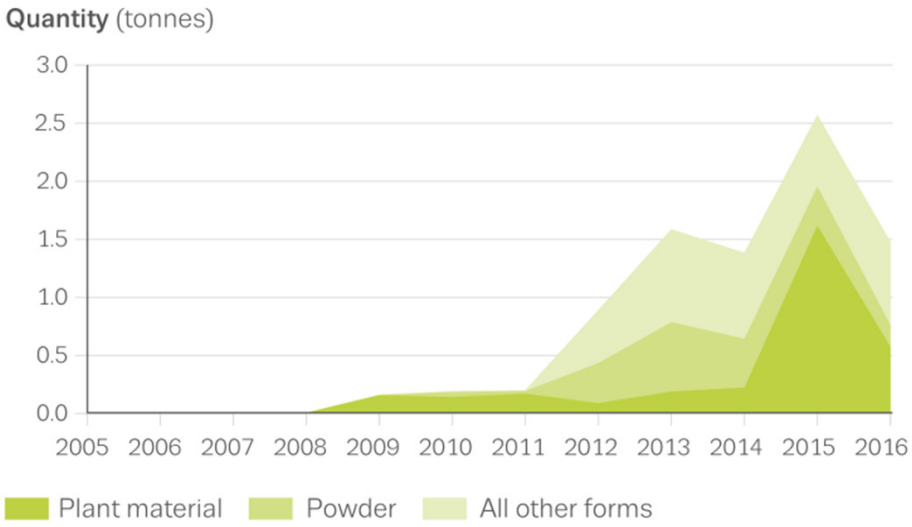
Number and quantity of seizures of cannabinoids



Most commonly seized, 2016

MDMB-CHMICA
AB-CHMINACA
UR-144
5F-AKB48
AMB-FUBINACA



Top 5 seized as powders, 2016

5F-NAPICA: 54 kg
CUMYL-4CN-BINACA: 50 kg
AMB-FUBINACA: 27 kg
5F-MDMB-PINACA: 15 kg
AB-FUBINACA: 7 kg

Top 5 seized as plant material, 2016

AB-FUBINACA: 361 kg
5F-AMB-PINACA: 116 kg
AMB-FUBINACA: 20 kg
5F-MDMB-PINACA: 15 kg
AB-CHMINACA: 13 kg

Seizures by law enforcement of cannabinoids reported to the EU Early Warning System. Trends in number and quantity seized, 2005–16.


ROX-CLAV 625
Amoxicillin and Clavulanic Potassium Tablets USP
Comprimés d'Amoxicilline et Potassium de Clavulanate USP
PDM
© Luxembourg Customs

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© Dr Jan Schäper, Bayerisches Landeskriminalamt

New Haven Overdoses Tied to Laced K2

Emergency personnel responded to at least 49 overdoses in New Haven, many on New Haven Green. Arnold Gold/Hearst Connecticut Media

By Ali Winston

Aug. 15, 2018

A park in the shadow of Yale's Old Campus became the scene of a mass overdose on Wednesday as ambulance crews rushed from person to person, desperately treating dozens of semiconscious and disoriented drug users in New Haven.

More than 70 people overdosed in the city during a 24-hour span, beginning Tuesday evening, and the authorities said they suspect a virulent batch of synthetic marijuana, possibly laced with an opioid, was the cause.

The sheer number of overdoses caused a strain on the city, said Dr. Sandy Bogucki, the city's director of emergency medical services. Emergency

New York Times

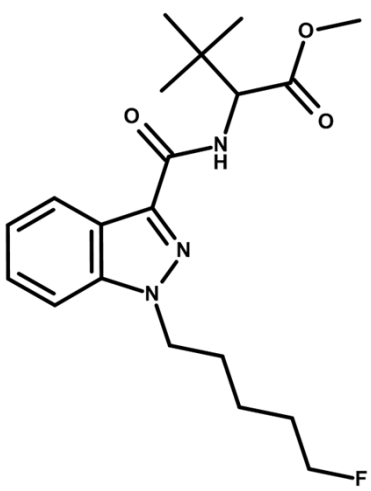
111. 5F-MDMB-PINACA on the streets: case series of 17 poisonings

Csaba Pap

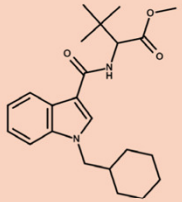
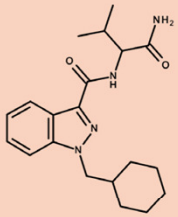
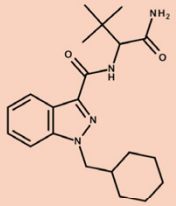
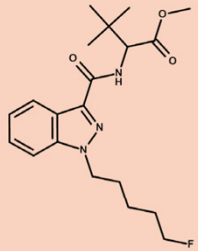
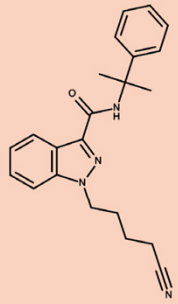
Department of Emergency Medicine and Clinical Toxicology, Péterfy Hospital, Budapest, Hungary

Objective: 5F-ADB (also known as 5F-MDMB-PINACA) is a synthetic cannabinoid from the indazole-3-carboxamide family. This substance was first identified in 2014 from post-mortem samples taken from a total of 10 people who had died from unexplained drug overdoses in Japan. In Hungary, it was first reported at the beginning of 2015 and has been scheduled since April 2015. We report a cluster of 17 cases of 5F-ADB abuse and describe the characteristics of their clinical picture, treatment, and evolution.

Case series: In the middle of August 2017 during a 36-hour period, 17 patients were found unconscious lying on the platform at tram stops or on the pavement in small segregated area in Budapest. One man was dead, and the others were admitted to our department. On site, they were assessed with the Richmond Agitation and Sedation Scale [RASS]; 2 patients were found with severely (RASS-5), 8 with moderately (RASS-4 or -3) and 6 with mildly (RASS-1 or -2) reduced level of consciousness. Two had vomited and 3 showed transient extrapyramidal symptoms. Based on the history, all patients had inhaled the smoke of a herbal mixture called "magic smoke". Ethanol was co-ingested in 2 patients (12.5% of cases) and there were no other co-ingestants. There were 13 men and 3 women. The average age was 25.12 (range 15–37) years. On admission, examination revealed mild central nervous system (CNS) depression in 11 patients and moderate CNS depression in 2 patients. Other findings were confusion (12.5%), agitation (18.75%), mild tachycardia (18.75%) with a heart rate between 100 and 120 bpm, mild systolic hypertension (18.75%) with a blood pressure between 140 and 160 mmHg, and mydriasis (25%). We took blood and urine samples for toxicological analysis at the time of admission. During the hospitalization, there were no episodes of bradycardia, arrhythmia, seizures, elevated temperature, or other complications. As for therapy, 11 patients were administered IV fluids and 3 patients were given IV midazolam. The length of stay averaged 4.1 hours (range 17 minutes to 11.3 hours). All of the patients were discharged. According to the Poison Severity Score, 12.5% of the patients had severe, 37.5% moderate, and 50% mild intoxication. Toxicological analysis revealed 5F-MDMB-PINACA in all samples.



https://doi.org/10.1080/15563650.2018.1457818

Common name	MDMB-CHMICA	AB-CHMINACA	ADB-CHMINACA	5F-MDMB-PINACA	CUMYL-4CN-BINACA
Chemical name	Methyl 2-[[1-(cyclohexylmethyl)-1H-indole-3-carbonyl]amino]-3,3-dimethyl-butanoate	N-(1-Amino-3-methyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide	N-(1-Amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide	Methyl 2-{[1-(5-fluoropentyl)-1H-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate	1-(4-Cyanobutyl)-N-(2-phenylpropan-2-yl)-1H-indazole-3-carboxamide
Chemical structure					
Category	Synthetic cannabinoid	Synthetic cannabinoid	Synthetic cannabinoid	Synthetic cannabinoid	Synthetic cannabinoid
Pharmacology	Full agonist at the CB_1 receptor; agonist at the CB_2 receptor	Full agonist at the CB_1 receptor; partial agonist at the CB_2 receptor	Full agonist at the CB_1 receptor; agonist at the CB_2 receptor	Full agonist at the CB_1 and CB_2 receptors	Full agonist at the CB_1 and CB_2 receptors
Formal notification to the EU Early Warning System	12 September 2014	10 April 2014	24 September 2014	8 January 2015	4 March 2016
Number of deaths	29	31	13	28	11
Number of countries where associated deaths occurred	6	6	3	2	2
Number of detections by law enforcement	>3 600	6 422	3 794	1 986	2 461
Number of countries where it has been detected (EU, Turkey and Norway)	25	26	19	27	12
Total quantity detected	67 kg herbal material; 46 kg powder	190 kg herbal material; 44 kg powder; 293 ml liquid; 194 g blotters	139 kg herbal material; 10 kg powder; 25.5 g blotters	100 kg herbal material; 13 kg powder; 309 g and 94 ml liquid; blotters	261 kg herbal material; 52 kg powder; blotters

Severe intoxication after uptake of alleged ecstasy tablets adulterated with the synthetic cannabinoid ADB-PINACA - a case report

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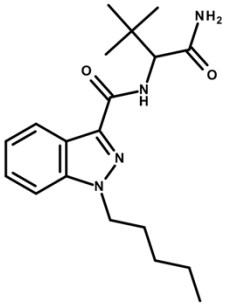


Case History

112 Police and paramedics were informed by an emergency call by patient S. that he and his girlfriend are in bad condition after the intake of ecstasy tablets.

Patient S. (♂, 24 years old) was found somnolent but responsive on the couch in his flat and was admitted to ER due to a suspected drug intoxication. He suffered from nausea and vomiting during transport.

Patient L. (♀, 22 years old) was found comatose on the floor after vomiting. She was cyanotic, spastic, tachycardic (up to 170 bpm) with no response to stimuli, requiring immediate intubation.

Due to the ecstasy-unlike symptoms, police searched the flat for additional drugs. One and a half tablets with a butterfly motive were the only findings.

Conditions on Admittance

Both patients were still under poor general conditions. S. was somnolent but responsive. L. was still comatose, intubated and not responsive to stimuli and admitted to the intensive care unit.

	Patient S.	Patient L.
BP [mmHG]:	130/81	160/80
heart rate [bpm]:	97	102
SpO_2 [%]:	95	99
Urine Screen:	Amph. positive	Amph. positive

Immunochemical drug testing

S. had a grand mal seizure on day one but was released after two days at good health.

L. also had multiples seizures on day one and no response to direct approach. Hypoxic brain damage was suspected at this time. She could be extubated the day after, and was released after three days without physical impairments.

Both patients were interrogated by the police after being discharged from the hospital and S. provided details about the purchase of six "Tomorrowland" tablets on the day of the incident from a dealer known to him.

Findings at the house search in the dealers appartment

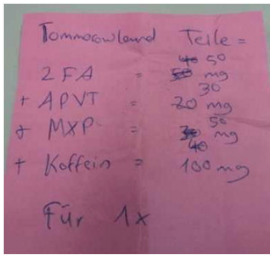
Police found large amounts of powders and tablets, including 2 brown tablets with a butterfly logo, 2.1 kg of caffeine powder, tobacco, a tablet press with different logos, a scale, and multiple handwritten notes containing information on NPS and different recipes including so-called "Tomorrowland Teile".

More than 50 labeled zip bags containing 3 to 10 g of white, white/brown, grey and brown powder, tobacco samples, and blood and urine samples of the two patients were sent in for analysis to the Forensic Science Institute at the State Office of Criminal Investigation.

The dealer was arrested and accused of drug trafficking, possession of narcotics and attempted homicide.

He admitted production of about 300 ecstasy tablets - named "Tomorrowland Teile" - containing 50 mg 2-FA, 50 mg PV-8, and 100 mg caffeine or taurine, each.

To confirm/exclude the initial charge of attempted homicide, the biological specimens of the two patients and aliquots of the questionable ecstasy tablets were sent to the Institute of Forensic Medicine Freiburg to assess their potential health risk.



- Tomorrowland tablets
- Severe poisoning, inc. CNS depression (coma)
- 20–28 mg ADB-PINACA (2-FA, α-PVT, MXP, caffeine, PV-8, diphenidine)
- Accident from mixing up different powders?

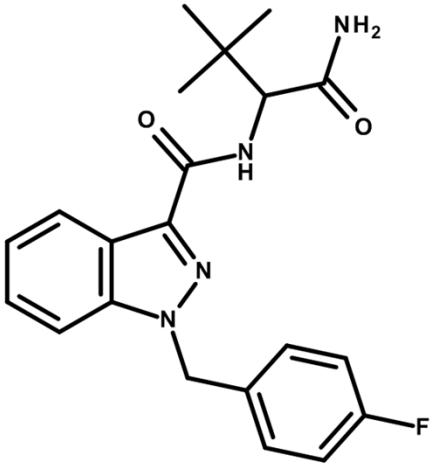
31. ADB-Fubinaca in the real world: a case series of 15 poisonings

Csaba Pap

Department of Toxicology, Péterfy Hospital, Budapest, Hungary

Objective: ADB-Fubinaca is a synthetic cannabinoid that has recently been identified in herbal blends. The aim of the present study was to describe toxicity following ADB-Fubinaca poisoning in Hungary. **Case series**: At the beginning of May 2015 during a two-day period 15 patients were admitted to our department after consuming a new recreational drug. There were 8 males and 7 females. Based on the history, all patients had taken one blue-coloured tablet never used before. Each tablet was marked with the sign of a very popular Internet social networking site. The only co-ingestant was ethanol in 2 patients (13.3%). The average age was 30.3 years, only two patients were younger than 21 (range 18–48 years). The mean time to admission was 2.1 hours. We took blood and urine samples for toxicological analysis at the time of admission. Symptoms that developed were central nervous system (CNS) depression (73.3%), confusion (60%) mild tachycardia (53.3%), hypertension (33.3%), mild acidosis (26.7%), hallucinations (26.7%), anxiety (20%), agitation (20%), aggression (20%), mydriasis (13.3%) vomiting (6.7%), hypotension (6.7%) and blurred vision (6.7%). There were no cases of bradycardia, seizure, elevated temperature or extrapyramidal symptoms. There were no fatalities; one patient was intubated and ventilated mechanically because of deep coma and respiratory insufficiency. Using the Poison Severity Score, 20% of patients had mild, 73.3% moderate and 6.7% severe intoxication. All patients required hospitalization; the length of stay averaged 45.78 hours (range 11–187 hours). Therapy included IV fluids, low molecular weight heparins for thrombosis prophylaxis and pantoprazole for stress ulcer prophylaxis. Naloxone proved to be ineffective in improving the level of consciousness in the first 4 patients, so was not used in the other cases. Administration of IV benzodiazepine (midazolam) was required in 6 patients because of confusion, agitation, aggressive behaviour or hallucinations. All but 3 patients were given oxygen intranasally. As a consequence of transient agitation, 3 patients developed moderate rhabdomyolysis. The patient that required mechanical ventilation developed pneumonia. There was no other complication. One patient was moved to psychiatry because of prolonged hallucinations and psychosis. Toxicological analysis performed within 2 days revealed ADB-Fubinaca in all samples. We reported the cases to the Hungarian National Focal Point. **Conclusion**: Toxicity following use of novel cannabinoid-typed designer drugs is unpredictable. ADB-Fubinaca can cause a short period of confusion and agitation followed by long-lasting CNS depression, hypoxaemia and fluctuating changing in level of consciousness.

https://doi.org/10.3109/15563650.2016.1165952

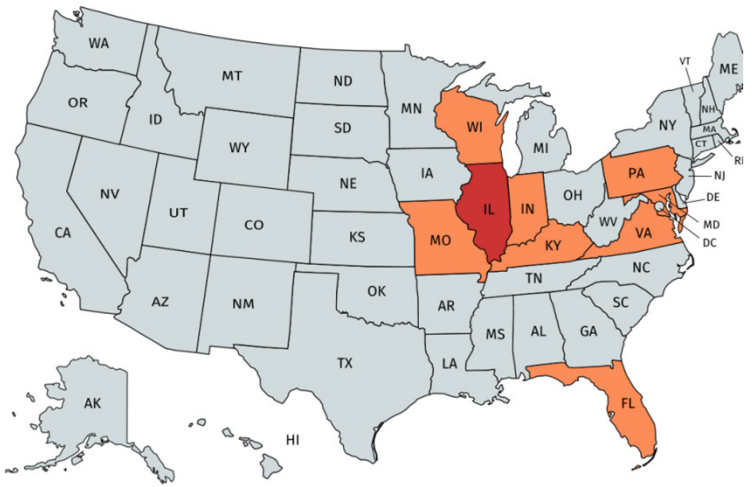


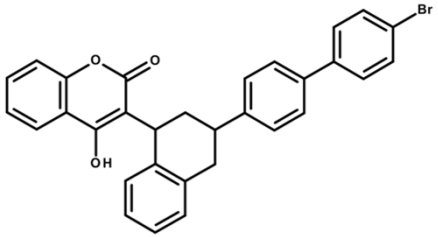
- Patients took 1 ‘Facebook’ tablet
- 70% long lasting CNS depression
- 60% confusion
- 27% hallucinations
- All required hospitalisation **(~46 hours; range 11–187h**)
- ADB-FUBINACA in biological samples

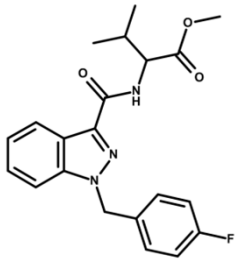
Outbreak of Severe Illness Linked to the Vitamin K Antagonist Brodifacoum and Use of Synthetic Cannabinoids — Illinois, March–April 2018

Case count: 202
States: 9
Deaths: 5

Synthetic cannabinoids, also known as K2 and spice, are heterogeneous psychoactive compounds identified as substances of abuse (*1*,*2*). On March 22, 2018, the Illinois Department of Public Health was notified by the Illinois Poison Center of four patients seen in emergency departments (EDs) during the preceding 2 weeks with unexplained bleeding and high international normalized ratios (INRs; range from 5 to >20 [normal <1.1]), indicating a clotting disorder, and reported synthetic cannabinoid use during the previous 3 days. None reported taking prescription anticoagulants or exposure to anticoagulant rodenticides. An investigation by the Illinois Department of Public Health, the Illinois Poison Center, CDC, local health departments, and law enforcement agencies was initiated to identify additional cases, ascertain epidemiologic links among patients, and implement control measures.





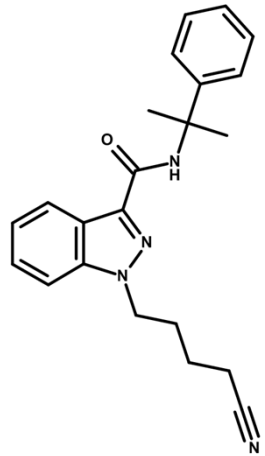


"Matrix and Blue Giant products from a convenience store in Chicago tested positive for brodifacoum and AMB-FUBINACA."

https://doi.org/10.15585/mmwr.mm6721a4

Acute Poisonings from a Synthetic Cannabinoid Sold as Cannabidiol — Utah, 2017–2018

By the end of January 2018, suspected cases were identified in 52 persons. Nine product samples (including one unopened product purchased by investigators from a store and brand reported by a patient) were found to contain a synthetic cannabinoid, 4-cyano CUMYL-BUTINACA (4-CCB), but no CBD.¶ Eight of the tested products were branded as "Yolo CBD oil" and indicated no information about the manufacturer or ingredients. Blood samples from four of five persons were positive for 4-CCB. Press releases were distributed to media outlets December 19–21, 2017, with a warning regarding the dangers of using the counterfeit product; information with a description of the product and associated symptoms was disseminated to health care providers and law enforcement. The number of reported cases peaked during this outreach and dropped shortly thereafter. Thirty-four suspected cases were reclassified as confirmed if the person reported use of a Yolo product or laboratory testing found 4-CCB. Approximately one quarter of persons were aged <18 years, nearly three fourths had vaped the CBD product, and approximately 60% were seen at an emergency department (Table).



https://doi.org/10.15585/mmwr.mm6720a5

Toxicologie Analytique et Clinique
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Case report

‘Spice-like’ herbal incense laced with the synthetic opioid U-47700

Vera Coopman, Jan Cordonnier

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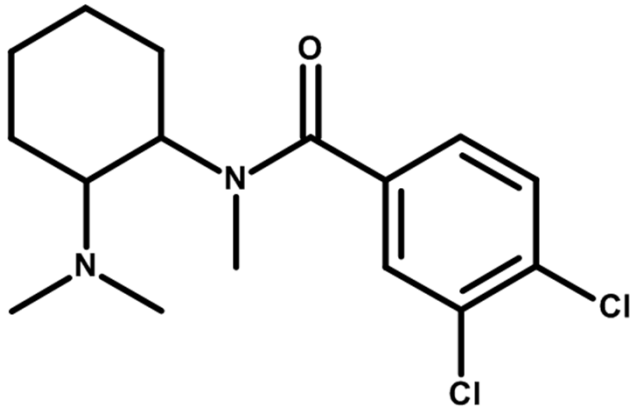
https://doi.org/10.1016/j.toxac.2017.07.004 Get rights and content

Summary

In the rapidly evolving ‘legal highs’ market, synthetic cannabinoids play a predominant role. These potent synthetic cannabinoid receptor agonists produce effects similiar to those of delta-9-tetrahydrocannabinol and are usually added to herbal smoking mixtures by soaking or spraying. Typical marketed as so-called herbal incense (potpourri), they are widely and openly sold on the web with the synthetic cannabinoids used in the mixtures continuously being substituted by ‘legal’ alternatives, in pace with new control measures. A seizure of ‘spice-like’ herbal incense was submitted to the laboratory for toxicological analysis. A methanolic sample solution was analyzed using liquid chromatography with diode array detector and gas chromatography-mass spectrometry. The μ-opioid receptor agonist U-47700 was found to be the only psychoactive substance present in the herbal mixture. Although considerable inter-batch differences in the concentration can be expected, a quantitative determination was performed in order to obtain an indication regarding the potency of the seized herbal mixture. In light of the emerging threat of synthetic opioids fatalities, the presence of U-47700 in ‘spice-like’ herbal incense raises great concerns, since the abuse may pose serious risk, as users will likely not be aware that they are using a potent synthetic opioid. This case illustrates once again that new psychoactive active substances openly sold on the Internet as ‘legal highs’ pose a risk for public health.

https://doi.org/10.1016/j.toxac.2017.07.004



- 5g herbal material bought online, May 2017
- ‘Contains no illegal substances’
- 112.5 mg/g of U-47700
- U-47700 detected in 18 countries and in 30+ deaths

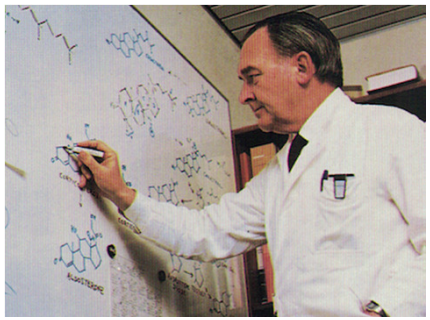

2
5

Acta anaesth. scand. 1982, 26, 262-268

Potent, New Analgesics, Tailor-Made for Different Purposes

P. A. J. JANSSEN

Janssen Pharmaceutica, Beerse, Belgium



There is a variety of conditions linked to intense pain and stress. Some may last for a relatively short period of time, such as certain surgical interventions; others may have a very extended duration. All of these conditions share a common need for potent analgesics that provide sufficient pain relief and alleviation of the stress response. Extensive research in the field of narcotic analgesics for more than 25 years has led to the development of a series of potent analgesics tailor-made for different purposes.

ON ANALGESIA

Although opium, the first known analgesic, was used to relieve pain during operations more than 2000 years ago, administration on a scientific basis was only possible after Sertürner in 1806 isolated an active principle of opium which he called "morphicum", and after Pravaz in 1853 invented the syringe and Wood the hollow needle. Claude Bernard in 1869 was probably the first to investigate the use of morphine for premedication and morphine was used by subcutaneous injection for minor surgery by 1872. In 1900, anaesthesia with morphine (70 mg) and scopolamine was described by Schneiderlein. Patients were oblivious to pain and only 70% required restraint during surgery! This technique, however, caused several deaths and was abandoned after a few years.

At the beginning of the 20th century, various *morphine derivatives* were introduced: hydrocodone bitartrate in 1923 and Pantopon (papaveretum), a stable solution of opium alkaloids, in 1901. The first entirely synthetic opiate, pethidine, was introduced in 1933 and the first opiate antagonist, nalorphine hydrochloride in 1951, thus giving the anaesthetist the opportunity to reverse the respiratory depression associated with the use of opiate analgesics. Our interest in narcotic analgesics started as early as 1953 and was highly stimulated by the discovery of dextromoramide in 1956. Dextromoramide (Fig. 1), a 3,3-diphenylpropylamine-like isomethadone, was found to be several times more potent than the available analgesics of that time (JANSSEN et al. 1963).

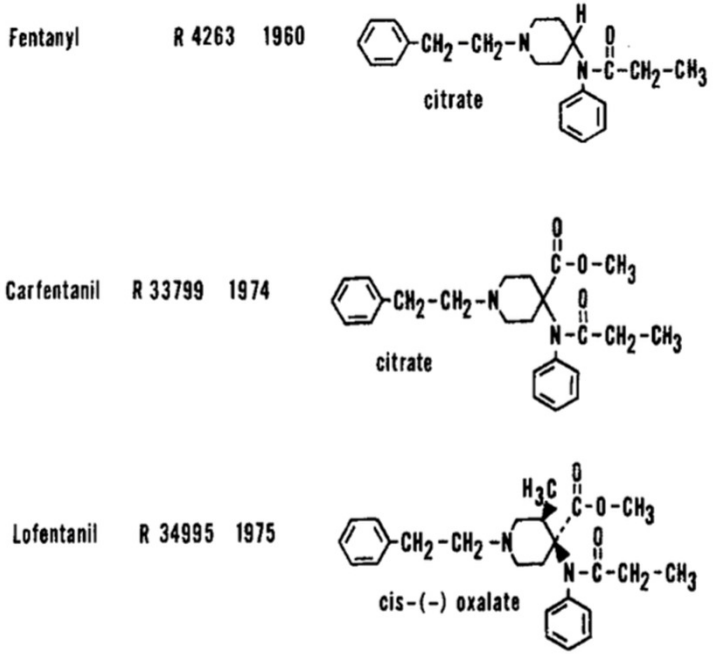
In pharmacology, the analgesic activity of a compound can be assessed by different test procedures in which a painful stimulus is used and the subsequent reaction of the exposed animal is measured. A reaction that can be very easily measured and quantified in rats is the withdrawal reaction after immersion of the rat tail in hot water. Normal control rats will immediately, within 3-6 s, withdraw their tails. In rats treated with morphine-like compounds, the tail withdrawal reaction may be delayed or completely blocked. The method allows measurement of the degree of analgesia obtained. Moreover, by measuring the tail withdrawal reaction at different time intervals after treatment, it is also possible to evaluate the onset, the time of peak effect, and the duration of the analgesic effect.

After injecting dextromoramide subcutaneously in rats, and measuring the tail withdrawal reaction time at different time intervals after the injection (Fig. 2), we found that analgesia of low intensity, defined as a reaction time ranging between 6 and 10 s, was obtained with a dose of 0.20 mg/kg and surgical analgesia, defined as the absence of tail withdrawal within 10 s, with a dose of 0.37 mg/kg.

Dextromoramide has a fast onset of reaction, reaches its peak effect ½ h after administration, and has a duration of action comparable to methadone and pethidine. The lowest ED_{50} of methadone is 1.91 mg/kg, that of morphine is 4.70 mg/kg and that of pethidine is 11.6 mg/kg. Thus dextromoramide subcutaneously is approximately 10 times more potent than methadone, 25 times more potent than morphine, and 50 times more potent than pethidine.

The history of the Janssen analgesics is the history of a continuous search for a better "morphine".

We have always tried to make more potent compounds, not for the sake of potency itself, but because we are convinced that the more potent the compounds, the more specific and the less toxic they are.



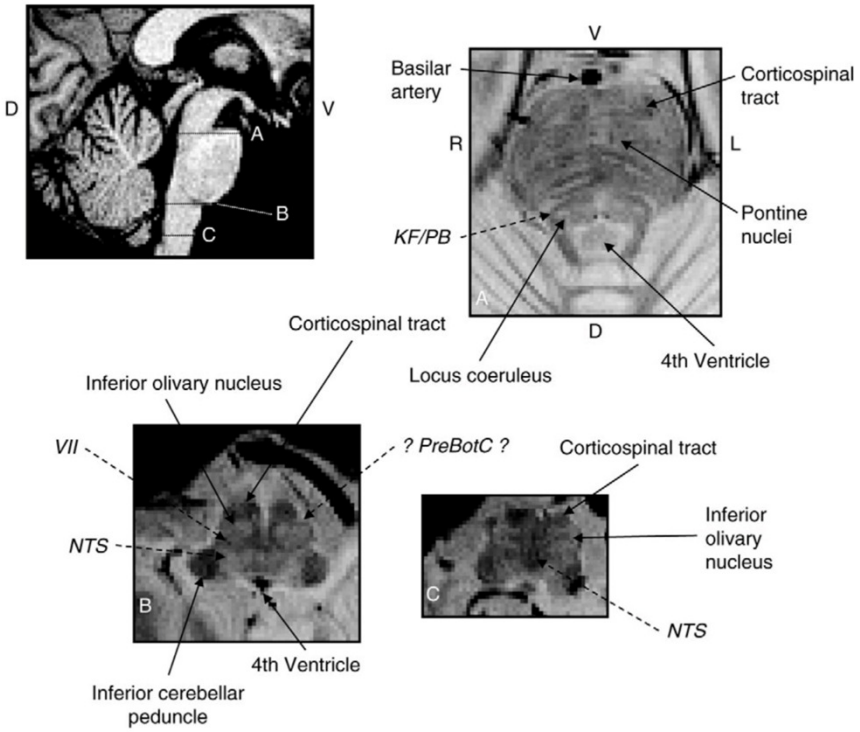
Paper presented at the International Symposium "Milestones in Anaesthesia 1940 - 1980", June 6, 1981, Lund, Sweden in honour of Eric Nilsson, M.D., Ph.D. on his retirement as Professor and Chairman of the Department of Anaesthesia, University of Lund

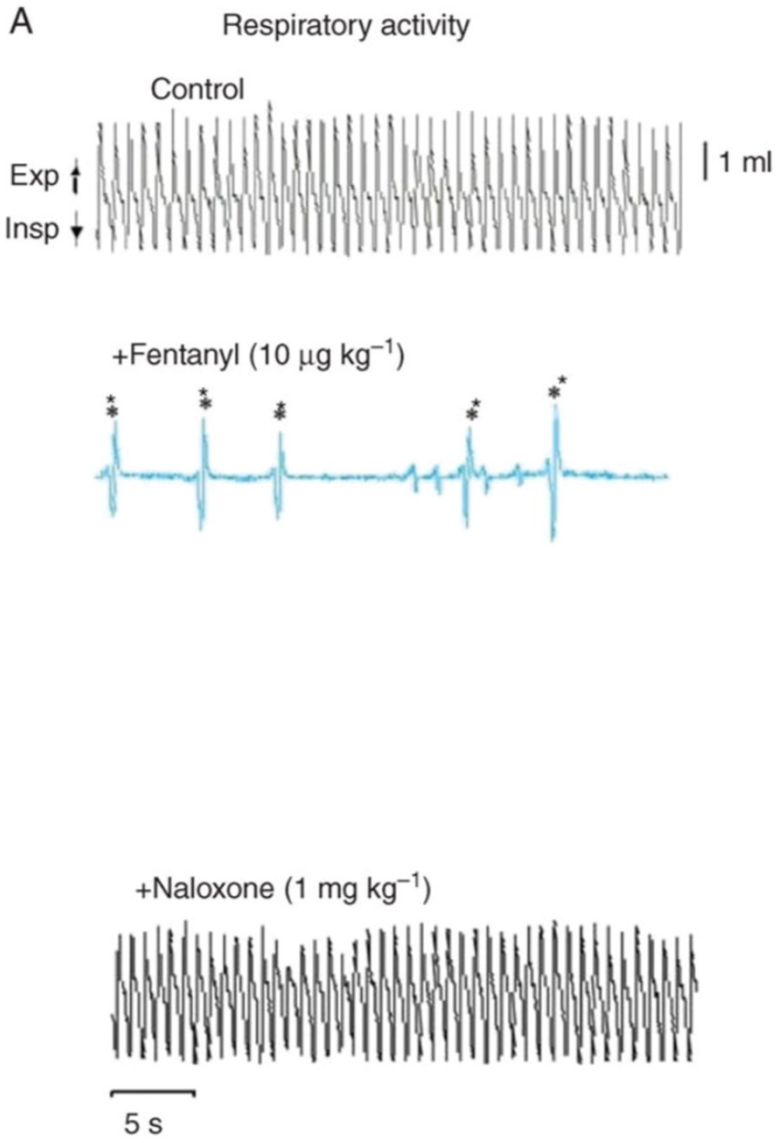
Opioids and the control of respiration

K. T. S. Pattinson*

Respiratory depression limits the use of opioid analgesia. Although well described clinically, the specific mechanisms of opioid action on respiratory control centres in the brain have, until recently, been less well understood. This article reviews the mechanisms of opioid-induced respiratory depression, from the cellular to the systems level, to highlight gaps in our current understanding, and to suggest avenues for further research. The ultimate aim of combating opioid-induced respiratory depression would benefit patients in pain and potentially reduce deaths from opioid overdose. By integrating recent findings from animal studies with those from human volunteer and clinical studies, further avenues for investigation are proposed, which may eventually lead to safer opioid analgesia.

Br J Anaesth 2008; **100**: 747–58





Fentanils, 1979–1995

2 deaths in California

December 1979

Analysis found no drugs present. Decedents used 'China White' or 'synthetic heroin'.

Subsequently α-MF was detected

Andrew Allen, in lab at Drug Enforcement Administration, examines drug called China White

112 deaths, 94% in California

1980–1988

40% of deaths occurred in 1984. Fentanyl, α-MF, 3-MF and 8 other fentanils detected in seizures and biological samples

DuPont chemist jailed for 3-MF manufacture/distribution

1986

Drugs worth $112 million. 4-FF also seized

16 deaths linked to 3-MF in Pennsylvania

1988

Sold as 'China White'

3-MF detected in Russia

1990

9 deaths linked to fentanyl in Sweden

May 1994—August 1995

Trace amounts of fentanyl detected in seizures containing up to 7% amphetamine; sold either as amphetamine or heroin

Precursors for 2-FF, 3-FF & 4-FF seized in Germany

1995

But… 2-FF and 3-FF not detected until 2016

Large seizure of 4-FF in Netherlands

June 1995

Thousands of tablets and capsules seized. Made by PhD organic chemist. Similar capsules seized in France

1980 1985 1990 1995 2000

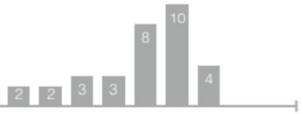
Fentanils, 2000–2018

3-MF detected in Finland

October 2002

Russian body packer carrying heroin and 10g of 3-MF (0.6%)

32 fentanils detected in EU



2012–2018

3-MF Detected in Estonia

1000+ deaths linked to fentanyl in United States

2005–2007

5 risk assessments

2017

Acrylfentanyl, 47 deaths
Furanylfentanyl, 23 deaths
THF-F, 20 deaths
4F-iBF, 14 deaths
Carfentanil, 61 deaths

85 deaths linked to 3-MF in Estonia

2004

3-MF & 3-MF-fentanyl account for most seizures in Estonia

2005

117 deaths linked to 3-MF in Estonia

2005–2006

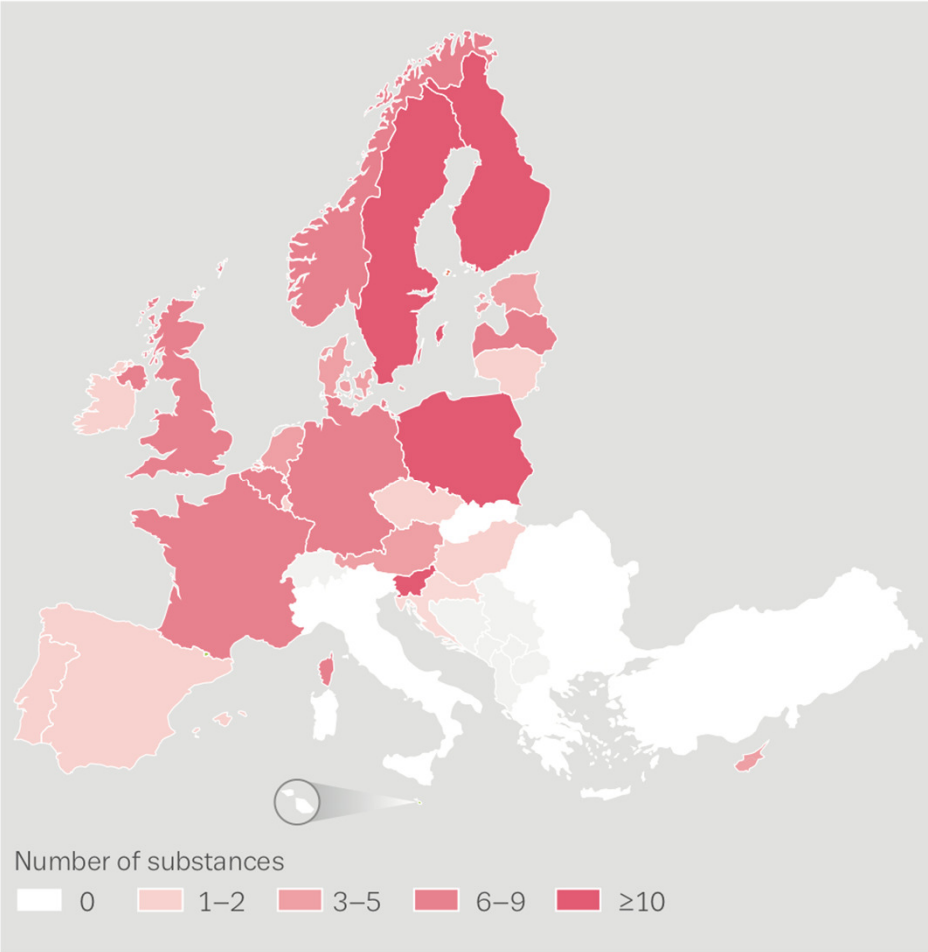
2 risk assessments

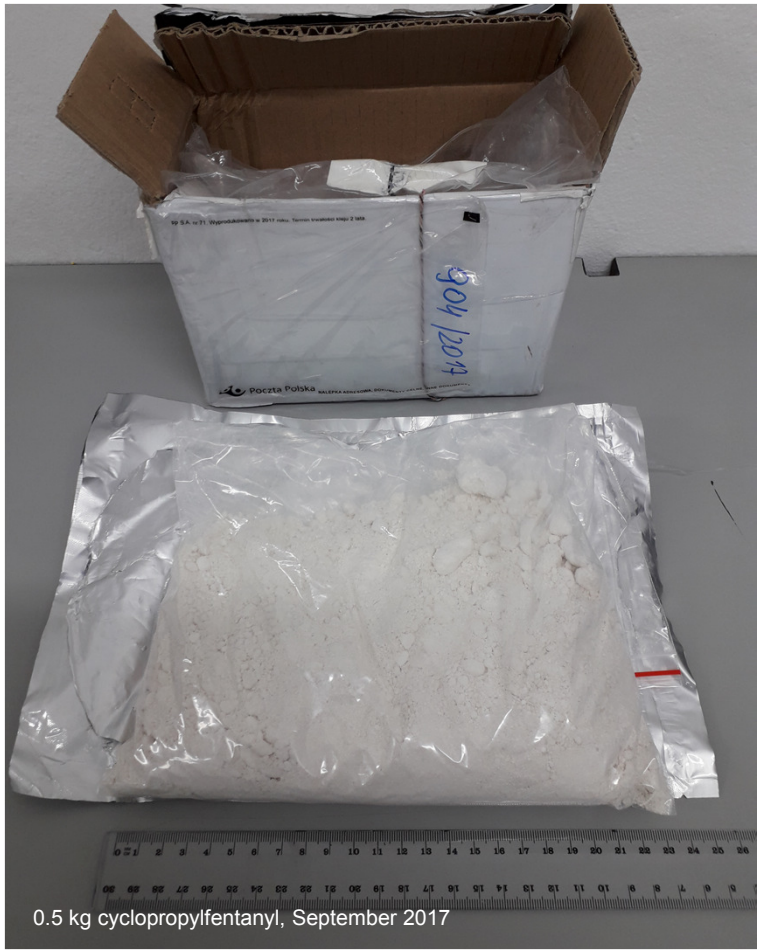
2018

CPF, 78 deaths
MAF, 13 deaths

2000 2005 2010 2015 2020

Detections of fentanils

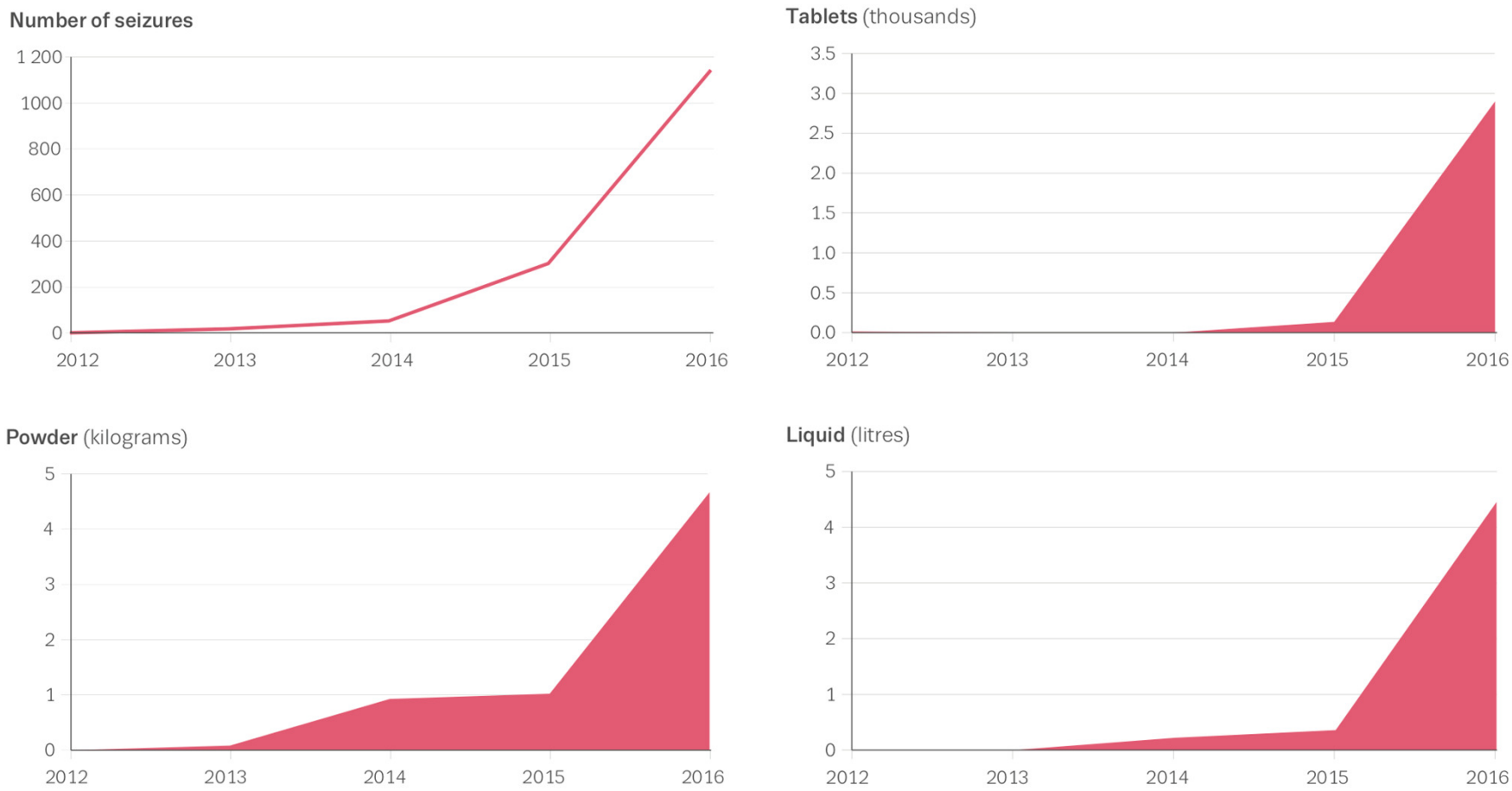




0.5 kg cyclopropylfentanyl, September 2017

Number of different fentanils detected by country reported to the EU Early Warning System, 2012–17.

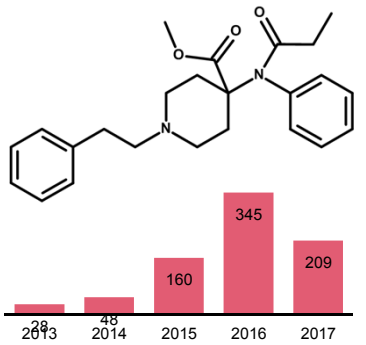
Number and quantity of seizures of fentanils

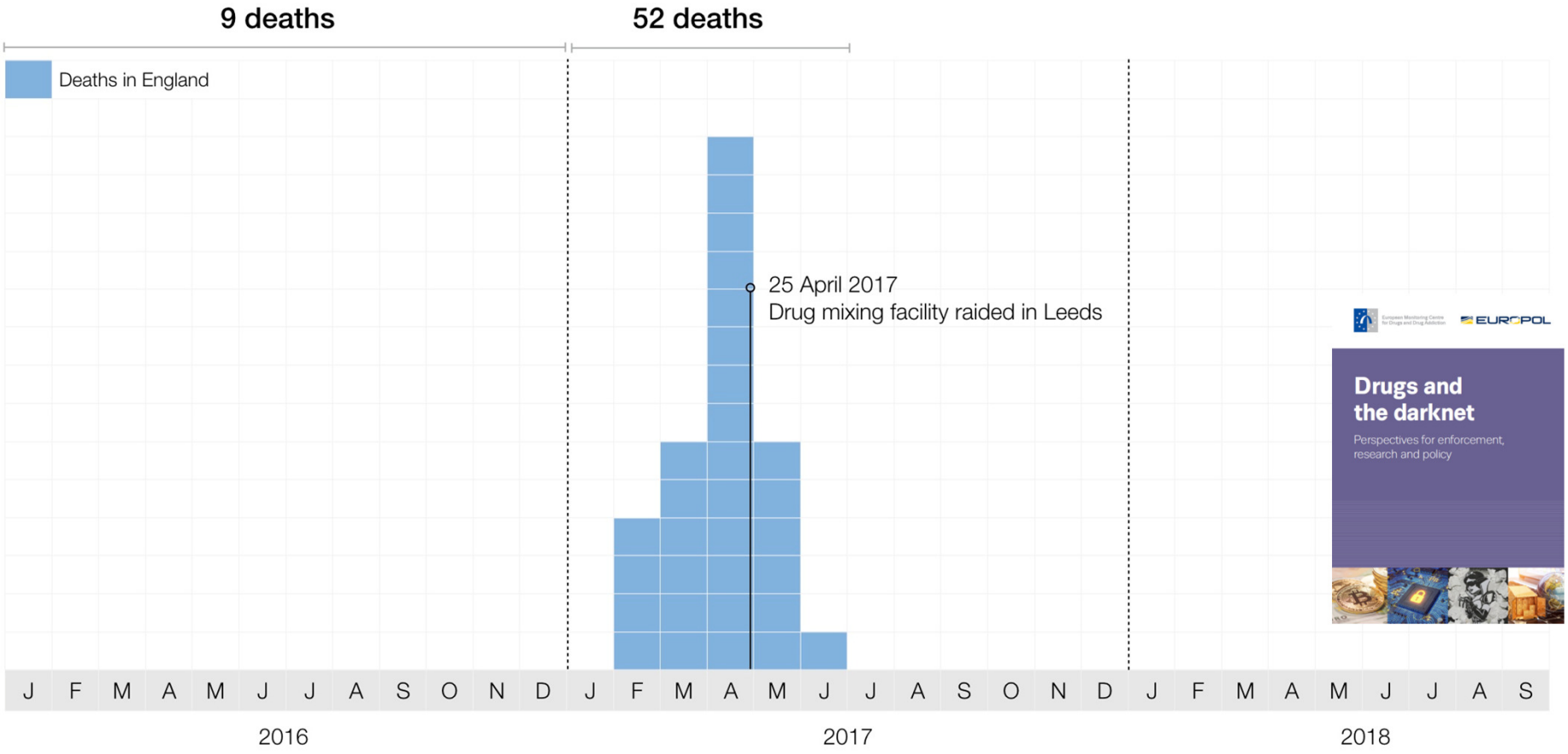


Seizures of fentanils reported to the EU Early Warning System: trends in number of seizures and quantity detected, 2012–16

Carfentanil

- Available since at least December 2012
- Detected by law enforcement in 7 countries
- 800+ detections, 25% in 2017
- 50% of cases detected in mixtures with heroin/fentanils
- 61 deaths in 8 countries






XANAX
© WR Brede, H-M Krabseth and co-workers

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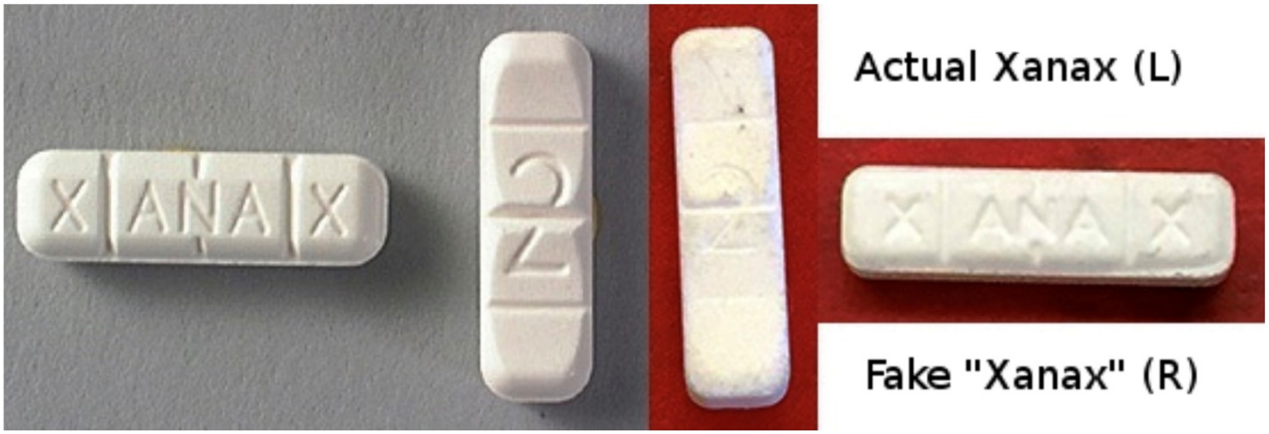
HEALTH ADVISORY

OCTOBER 22, 2015

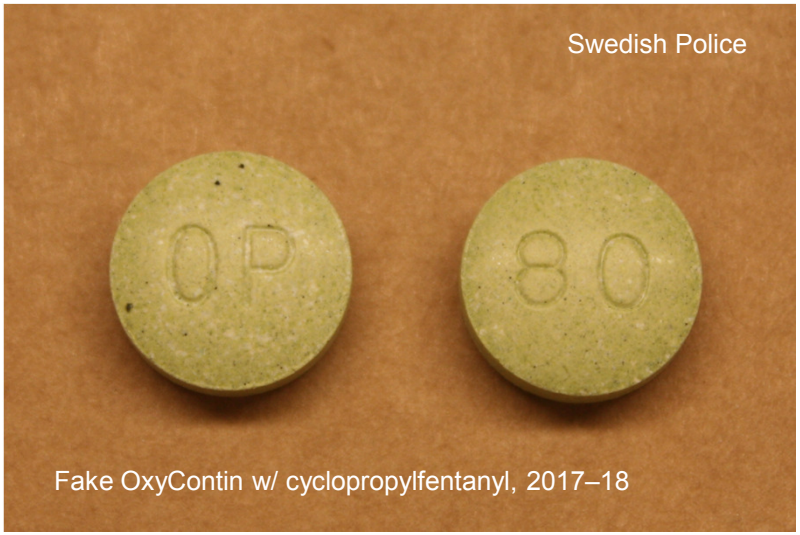
Severe Opioid Overdoses in San Francisco Caused by Fentanyl-Containing "Xanax" Pill

From October 15 to 17, 2015, three individuals between the ages 20-40 years were seen at the San Francisco General Hospital after ingesting a pill inscribed and sold as "XANAX" purchased off the street. All three patients suffered complications of opioid overdose, including peripheral neuropathy, rhabdomyolysis, and pulmonary edema, with one requiring intubation and intensive care. A fourth individual was found deceased with the same pill on his person; there may be additional deaths. Analysis of pills demonstrated fentanyl; one also had etizolam. The source of the pills is unknown.



https://www.sfcdcp.org/wp-content/uploads/2017/12/Overdose_publichealthadvisory_102215_final.pdf

Fake medicines containing fentanils



Fake OxyContin w/ cyclopropylfentanyl, 2017–18

Fake OxyCodone w/ methoxyacetylfentanyl, 2018

Fake OxyCodone w/ methoxyacetylfentanyl, 2018

Fentanils sold as cocaine…

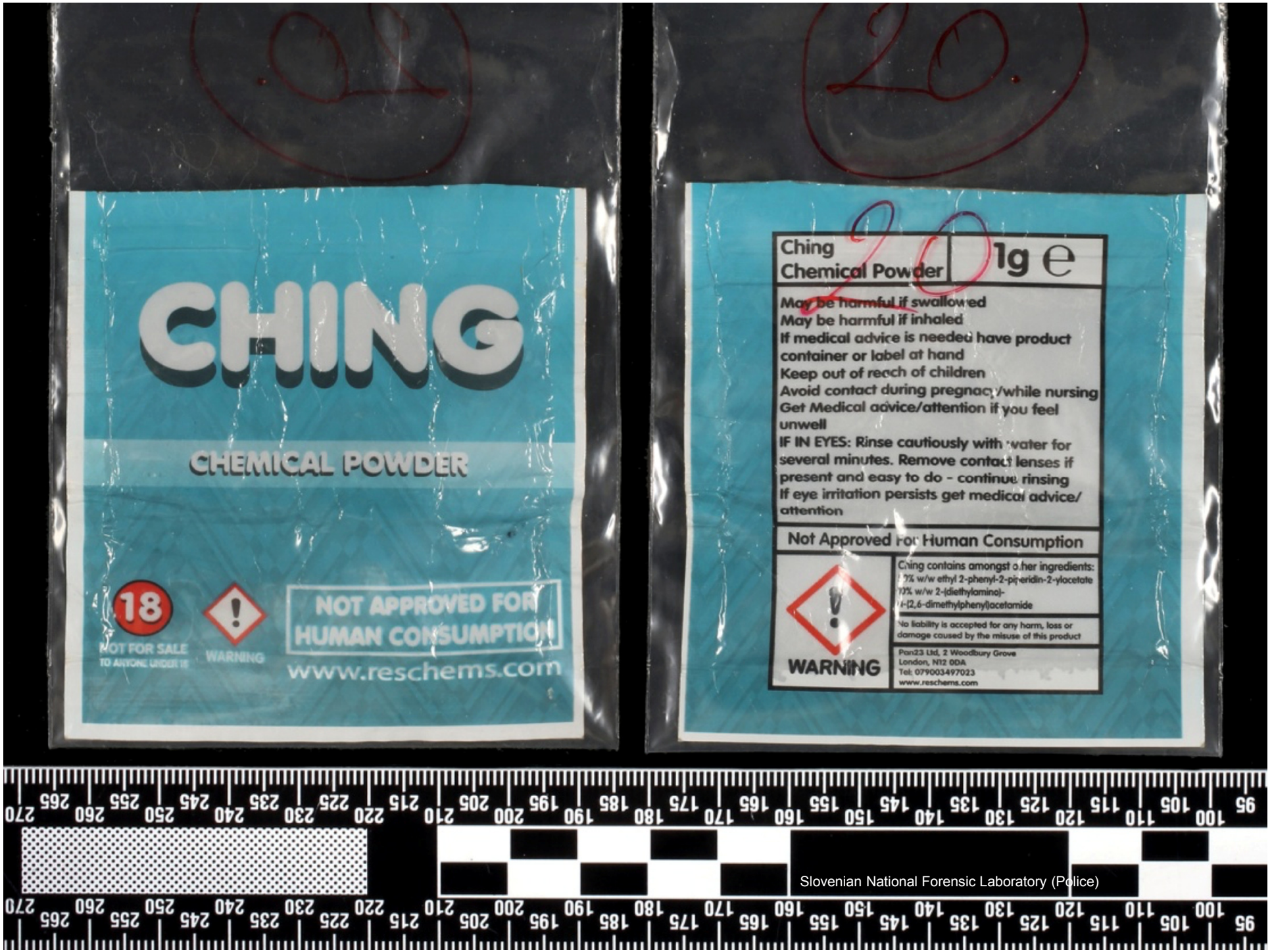
Multiple Fentanyl Overdoses — New Haven, Connecticut, June 23, 2016

Anthony J. Tomassoni, MD[1]; Kathryn F. Hawk, MD[1]; Karen Jubanyik, MD[1]; Daniel P. Nogee, MD[1]; Thomas Durant, MD[2]; Kara L. Lynch, PhD[3]; Rushaben Patel, PharmD[2]; David Dinh, PharmD[2]; Andrew Ulrich, MD[1]; Gail D'Onofrio, MD[1]

On the evening of June 23, 2016, a white powder advertised as cocaine was purchased off the streets from multiple sources and used by an unknown number of persons in New Haven, Connecticut. During a period of less than 8 hours, 12 patients were brought to the emergency department (ED) at Yale New Haven Hospital, experiencing signs and symptoms consistent with opioid overdose. The route of intoxication was not known, but presumed to be insufflation ("snorting") in most cases. Some patients required doses of the opioid antidote naloxone exceeding 4 mg (usual initial dose = 0.1–0.2 mg intravenously), and several patients who were alert after receiving naloxone subsequently developed respiratory failure. Nine patients were admitted to the hospital, including four to the intensive care unit (ICU); three required endotracheal intubation, and one required continuous naloxone infusion. Three patients died. The white powder was determined to be fentanyl, a drug 50 times more potent than heroin, and it included trace amounts of cocaine. The episode triggered rapid notification of public health and law enforcement agencies, interviews of patients and their family members to trace and limit further use or distribution of the fentanyl, immediate naloxone resupply and augmentation for emergency medical services (EMS) crews,

Twelve patients met the case definition for suspected fentanyl exposure (i.e., clinical signs of opioid toxicity and response to naloxone, with laboratory confirmation of fentanyl or fentanyl metabolites in blood, or history of direct association with a laboratory-confirmed fentanyl exposure) (Table 1). Among the four patients admitted to the ICU, three required endotracheal intubation and mechanical ventilation for respiratory failure that was relatively refractory to large doses of naloxone, and one required a continuous naloxone infusion for 12 hours. Two of the three intubated patients suffered acute kidney injury and pulmonary or gastrointestinal hemorrhage, one of whom (patient K) died 3 days later from multisystem organ failure. The third patient survived with permanent cardiac injury. Other intoxicated patients who arrived at the ED with signs or symptoms of the opioid toxidrome were excluded from this analysis because of inconsistent history (e.g., patient reported using a nonfentanyl opioid) or toxicology test results that did not identify fentanyl.

Shortly after arrival in the ED, serum toxicology screens, designed to detect a panel of nonopioid toxins, were performed for all patients, and qualitative urine immunoassay toxicology screens for drugs of abuse were performed for nine



Slovenian National Forensic Laboratory (Police)

MDMA

Seizures

Number

24 000 EU — **31 000** EU + 2

Quantity

5.3 EU — MILLION TABLETS — **9.1** EU + 2

295 EU — KG — **306** EU + 2

Price

(EUR/tablet)

16 €

6–11 €

4 €

Purity

(MDMA mg/tablet)

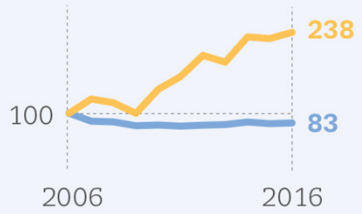
168

86–152

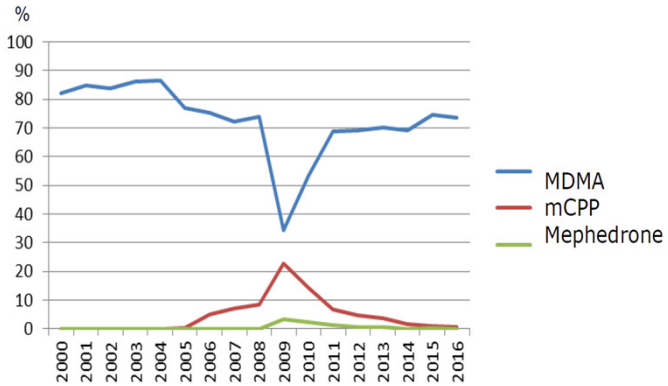
41

Indexed trends

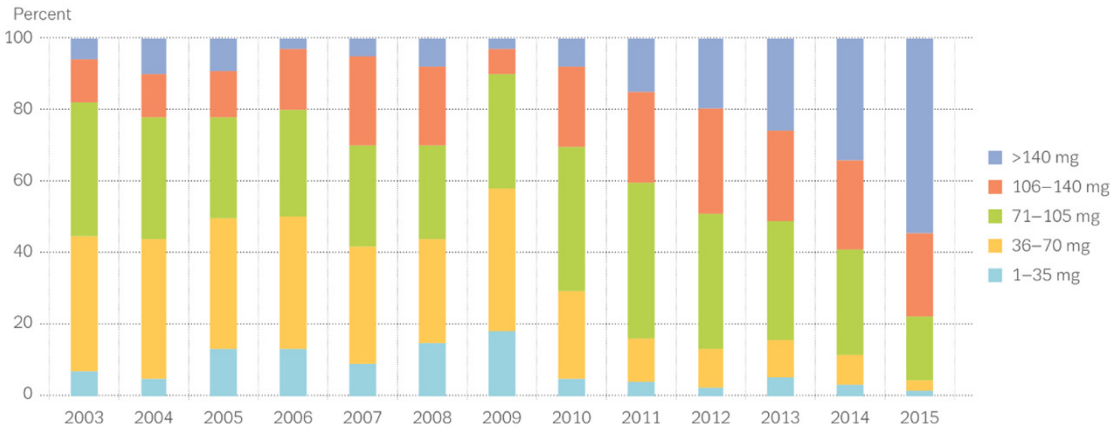
Price and purity



NB: EU + 2 refers to EU Member States, Turkey and Norway. Price and purity of MDMA: national mean values — minimum, maximum and interquartile range. Countries covered vary by indicator.



Netherlands Forensic Institute, 2016

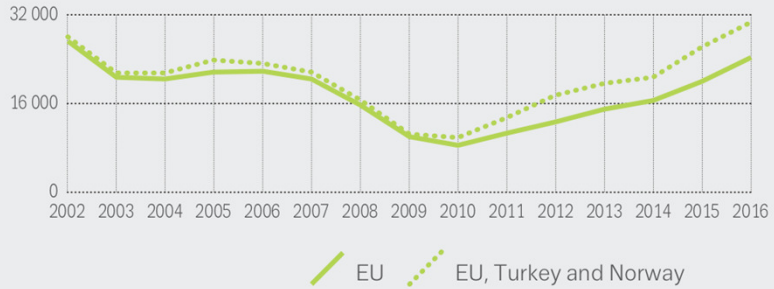


DIMS, 2015

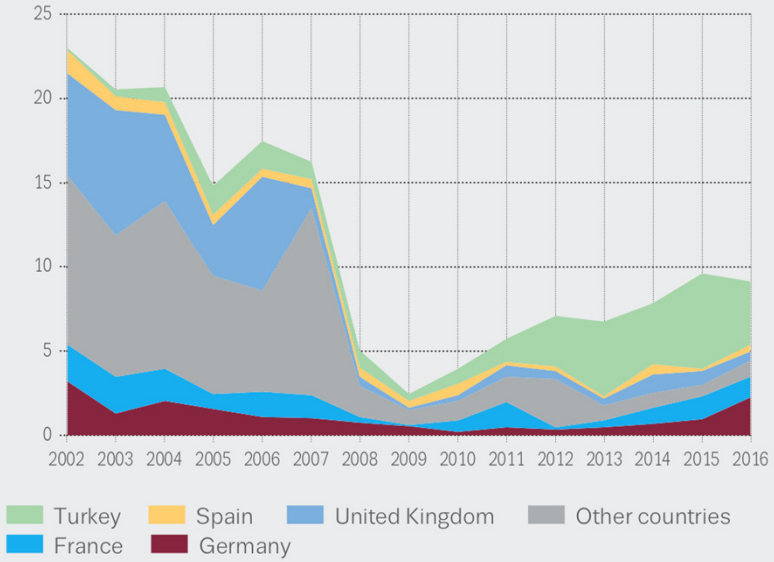
Number and quantity of seizures of MDMA

Number of MDMA seizures and quantity seized: trends and 2016 or most recent year

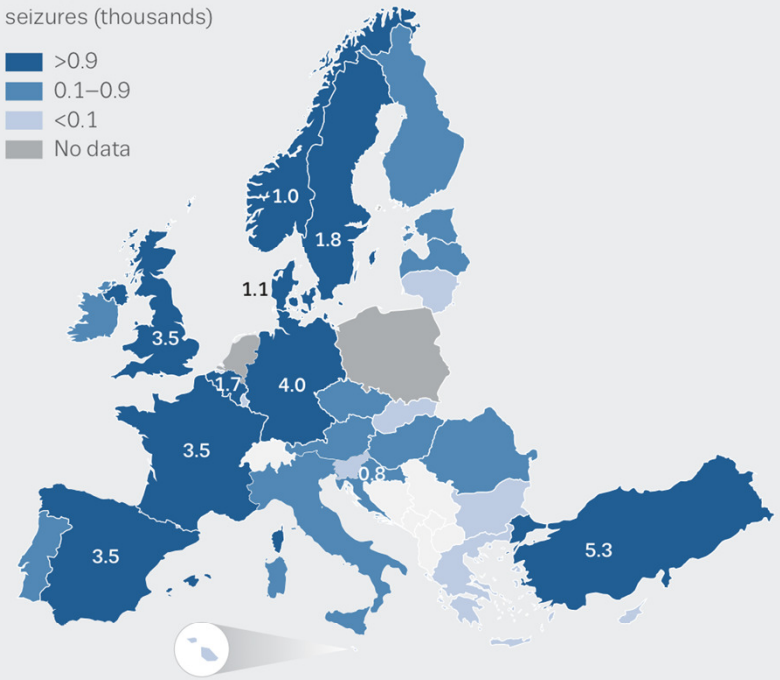
Number of seizures



Tablets (millions)

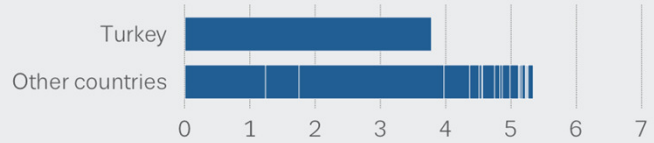


Number of MDMA seizures (thousands)



NB: Number of seizures (thousands) for the 10 countries with highest values.

MDMA tablets seized (millions)



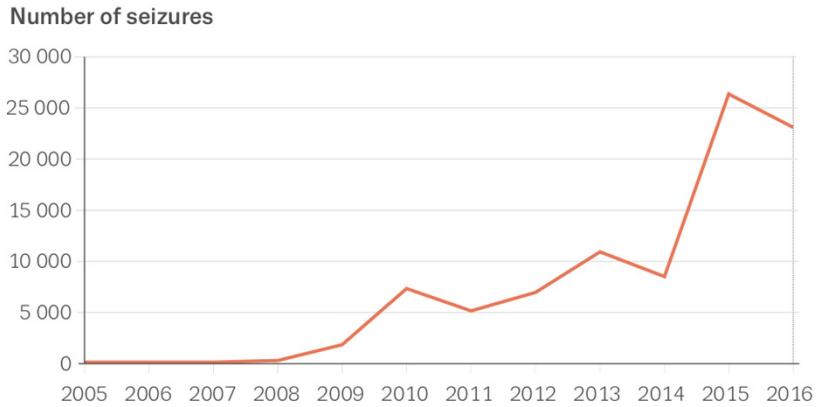
Identification and characterization of *N-tert*-butoxycarbonyl-MDMA: a new MDMA precursor

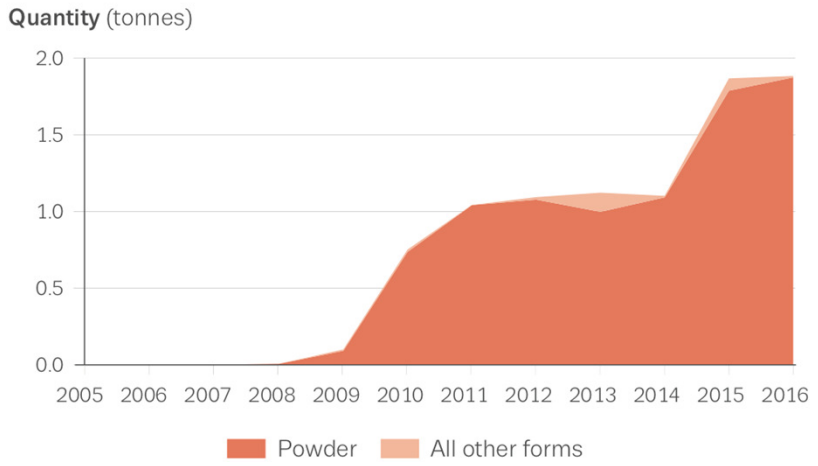
Michael Collins,[a]* Christopher Donnelly,[a] Shane Cameron,[b] Mark Tahtouh[b] and Helen Salouros[a]*

In September 2015, 80 litres of a viscous, light-red liquid, described as hair product, was seized by the Australian Border Force (ABF). Initial testing by ABF indicated that the liquid was the 3,4-methylenedioxymethamphetamine (MDMA) precursor chemical safrole and custody of the material was transferred to the Australian Federal Police (AFP) who coordinated all subsequent investigations. Initial gas chromatography–mass spectrometry (GC-MS) analysis by the AFP indicated that the material was not safrole and samples of the liquid were transferred to the National Measurement Institute Australia (NMIA) for identification. Using a combination of nuclear magnetic resonance spectroscopy (NMR), GC-MS, infrared spectroscopy, and synthesis, the unknown substance was identified as *N-tert*.-butoxycarbonyl-MDMA (*t*-BOC-MDMA). The substance was also converted in high yield to MDMA (aqueous HCl, 80 °C, 30 min). The possibility that the *t*-BOC-MDMA may act as a pro-drug following ingestion was explored by exposure to simulated gastric juice (pH 1.5) and monitored by NMR (37 °C) at various intervals. The majority of *t*-BOC-MDMA was converted to MDMA after 305 min, which suggested that this derivatized form might serve as a pro-drug *in vivo*. An investigation into the chemistry of potential pro-drugs showed that *t*-BOC derivatives of methamphetamine, pseudoephedrine and 4-methylmethcahtinone (mephedrone) could also be prepared using di-*tert*.-butyl dicarbonate. The appearance of *t*-BOC-derivatives on the drug market requires further monitoring. **© 2016 Commonwealth of Australia.** ***Drug Testing and Analysis*** **© 2016 John Wiley & Sons, Ltd.**

	Seizures		Stopped shipments		TOTALS	
Scheduled/*non-scheduled*	Number	Quantity	Number	Quantity	Number	Quantity
MDMA or related substances						
PMK (litres)	8	1 077	0	0	**8**	**1 077**
Safrole (litres)	5	63	0	0	**5**	**63**
Piperonal (kg)	2	1	4	7 700	**6**	**7 701**
Glycidic derivatives of PMK (kg)	16	5 905	1	1 000	**17**	**6 905**
N-t-BOC-MDMA (kg)	1	123	0	0	**1**	**123**

Number and quantity of seizures of cathinones





Most commonly seized, 2016

- alpha-PVP
- 4-chloromethcathinone
- 3-chloromethcathinone
- 4-methyl-*N*,*N*-dimethylcathinone
- 3-methylmethcathinone

Top 5 seized as powders, 2016

- 4-chloromethcathinone: 890 kg
- 4-chloroethcathinone: 247 kg
- *N*-ethylhexedrone: 186 kg
- 3-methylmethcathinone: 126 kg
- mexedrone: 50 kg

Seizures by law enforcement of cathinones reported to the EU Early Warning System. Trends in number and quantity seized, 2005–16.

13 hospitalised in Christchurch after taking drugs they thought were MDMA

14/03/2018 | **Newshub staff**

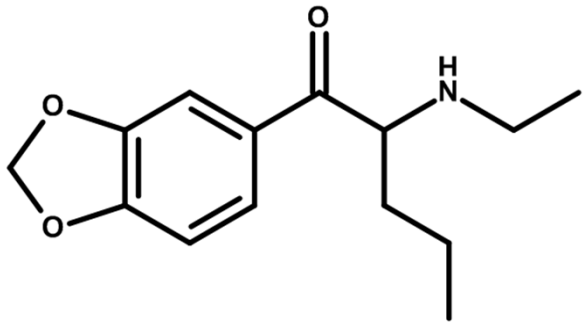
Tweet Share 0 Like 0

A medical examination has shown the substance that hospitalised 13 people in Christchurch was not MDMA, as they thought, but another drug three times as potent.

Police issued a warning about N-Ethylpentylone on Tuesday, advising people of the potential dangers of the drug.

This comes after 13 people, including a 15-year-old, were admitted to the Christchurch Hospital Emergency Department at the end of February with symptoms and side effects associated with having taken an MDMA-containing substance.

It was then assumed the people had taken a dodgy batch of ecstasy.



- *N*-Ethylpentylone detected in 26 countries
- Increase in seizures 2016–17
- Sold as crystal MDMA and ecstasy (ES, UK, NL)
- Severe stimulant-type poisoning, inc. hallucinations and prolonged insomnia

2018, so far

- 37 formal notifications (inc. 8 new opioids)
- Cyclopropylfentanyl risk assessment
  → seizures in 5 countries (detected in 6)
  → 78 deaths (Sweden, United Kingdom, Norway)
- Methoxyacetylfentanyl risk assessment
  → seizures in 9 countries (detected in 11)
  → 13 deaths (Belgium, Czech Republic, Sweden, and United Kingdom)
- Risk communications
  → Reducing the risk of occupational exposure to fentanils
  → Fake medicines containing fentanils
  → *Salmonella* linked to kratom (US)
  → Rat poison in synthetic cannabinoid products (US)
  → Synthetic cannabinoids sold as cannabidiol

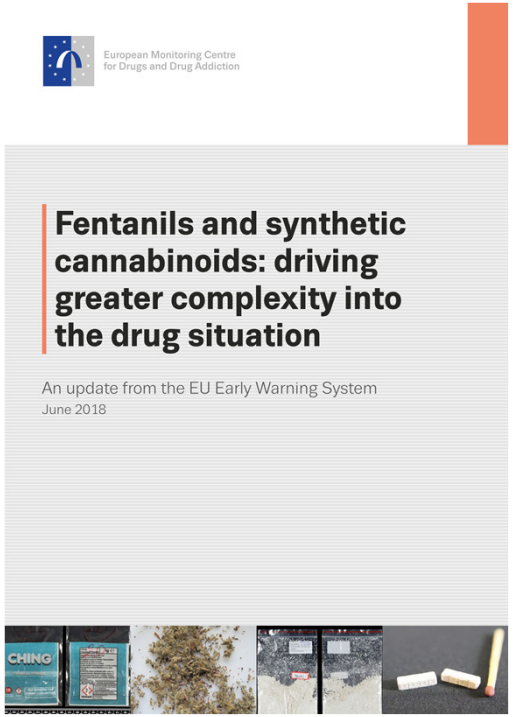
Concluding thoughts

- Some positive developments recently (↓in number of new substances appearing each year)
- But…Global markets, Glocal threats
- Increase in the number of highly potent substances appearing on the market
    - High risk of poisoning & explosive outbreaks
- What is next?
- More of the same?
- Increasing demand for enhancement drugs (nootropics)?
- Will increasing regulation of psychoactive medicines drive people to NPS?
- Early warning systems are critical to protect health

↑ awareness
↑ preparedness
↑ responses
↓ harm

Acknowledgments

- Early Warning System correspondents of the Reitox national focal points and experts from their national early warning system networks
- Europol national units and Europol Project Synergy
- Luxembourg Customs, Hungarian National Focal Point, Norwegian National Criminal Investigation Service, Central Customs and Tax Laboratory (Poland), Slovenian Police, Slovenian National Forensic Laboratory (Police), Swedish Police
- Dr Jan Schäper, Bayerisches Landeskriminalamt, Munich, Germany
- WR Brede, H-M Krabseth and co-workers, St. Olavs Hospital, Trondheim University Hospital, Norway
- Prof. Anders Helander, Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden



European Monitoring Centre
for Drugs and Drug Addiction

Email: Roumen.Sedefov@emcdda.europa.eu

http://www.emcdda.europa.eu/activities/action-on-new-drugs

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