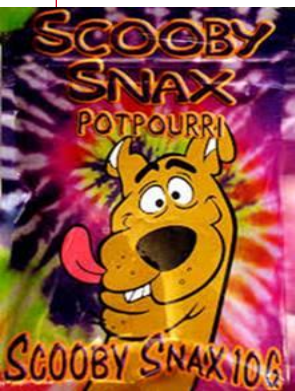


Pink, Iso, Brororphine, Tranq, Smiles, Krokodil, Dragonfly, Tia & Trash Can: The New Language of Drugs



pink
U4
pinky
u-47700

Christopher Welsh M.D.
Associate Professor
Division of Addiction Research & Treatment
Department of Psychiatry
University of Maryland School of Medicine

LEARNING OBJECTIVES

1. Participants will be able to name 3 new illicit drugs which are being used in the United States.
2. Participants will be able to name 3 adulterants that are being used as an adulterant /substitute for heroin.
3. Participants will be able to list 3 possible medical complications of adulterants.

CONFLICT OF INTEREST

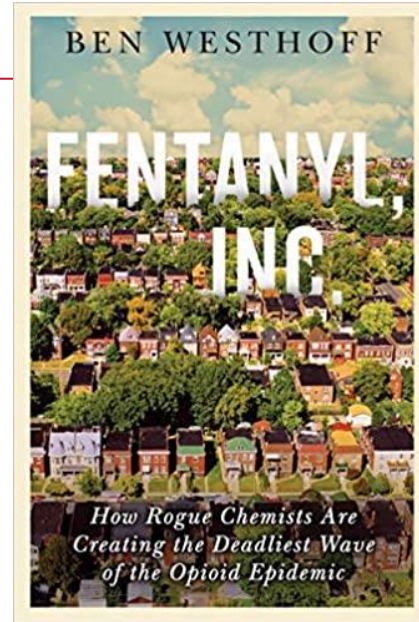
- I have received no money from the manufacturers or distributors of any of the drugs I will discuss.

“DESIGNER DRUGS”

- “Novel/New Psychoactive Substances”, “NPS”, “Synthetics”, “Club Drugs”
- The term “Designer Drug” coined in 1988 by Henderson
 - to describe attempts to produce fentanyl analogues
- Used to describe any drug produced by making a slight change in the chemical structure of a controlled substance (CSA of 1970)
- These newer substances were “legal” until 1986
 - Controlled Substances Analogues Enforcement Act
 - makes any drug “substantially similar to” a schedule I or II drug illegal

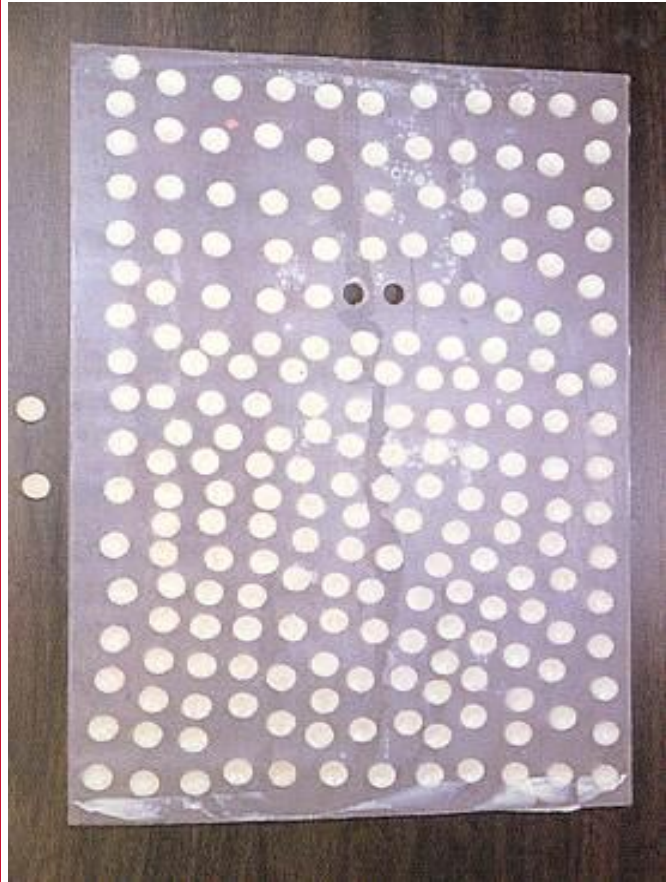
“NPS”

- Many are not truly new
- Many based on chemicals synthesized by chemists for legitimate reasons
- Some are marketed for legitimate medical reasons but are diverted for illicit use
- Others have never been used medically but synthesizing methods have been published and are easily obtained
- 100s of designer drugs have been made
 - only a handful have become popular
- In the past, was a relatively small problem compared to heroin, etc.





MACS



MACS



Welcome! Silk Road		
silkroad:--onion/index.php		Startpage
Silk Road anonymous market	messages 0 orders 0 account \$0.0000	the Dread Pir
Shop by Category		
Drugs 12,072		
Cannabis 2,821		
Dissociatives 200		
Ecstasy 1,290		
Intoxicants 63		
Opioids 362		
Other 31		
Precursors 86		
Prescription 3,674		
Psychedelics 1,303		
Stimulants 1,425		
Tobacco 316		
Apparel 530		
Art 14		
Biotic materials 2		

Vallium (Aparime) 10mg x 100 \$1.6865	Oxycontin 30 mg "Roxys" Pharmacy Fresh Free Ship! \$0.4260	10 Grams Pure Crystal Meth Methamphetamine \$6.1324

Keith Richards: 'I Snorted My Father'

By Associated Press

TUE APR 3, 11:52 PM



Keith Richards appears in the press room of the ...

LONDON - Keith Richards has acknowledged consuming a raft of illegal substances in his time, but this may top them all. In comments published Tuesday, the 63-year-old Rolling Stones guitarist said he had snorted his father's ashes mixed with cocaine.

"The strangest thing I've tried to snort? My father. I

snorted my father," Richards was quoted as saying by British music magazine NME.

"He was cremated and I couldn't resist grinding him up with a little bit of blow. My dad wouldn't have cared," he said.

"... It went down pretty well, and I'm still alive."

“DESIGNER” OPIOIDS

➤ AKA:

- NPFs (Non-Pharmaceutical Fentanyls)
- IMFs (Illicitly-Manufactured Fentanyls)
- FASH (Fentanyl Adulterated/Substituted Heroin)
- HPSO (High Potency Synthetic Opioids)
- NPOs (Novel Potent Opioids)

➤ >30 different fentanyl analogues

- alpha-methylfentanyl (**AMF**)
- 3-methylfentanyl (**TMF**)
- carfentanil

➤ Originally (1970s-80s) referred to as “China White” (the term reserved for very pure heroin), “Tango & Cash”, “Persian White”, “Goodfella”

- “Gunpowder heroin”- newer term

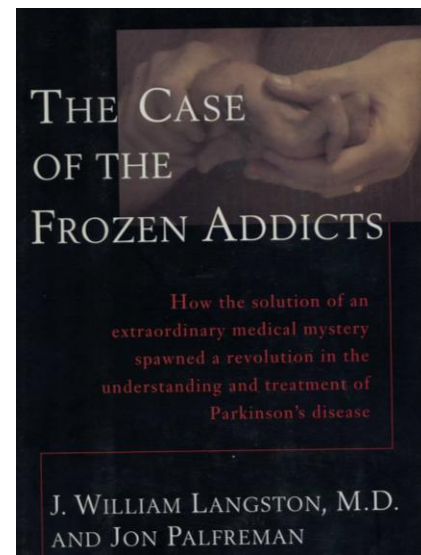
➤ TMF & carfentanil 1000s of times more potent than morphine

- 3-Methylbutyrfentanyl, 3-MBF
- 3-Methylfentanyl, 3-MF
- 4-Chloroisobutyrfentanyl, 4-ClIBF, p-ClIBF
- 4-Fluorobutyrfentanyl, 4-FBF, p-FBF
- 4-Fluoroisobutyrfentanyl, 4-FIBF, p-FIBF
- 4-Methoxybutyrfentanyl, 4-MeO-BF, p-MeO-BF
- 4-Fluorofentanyl, 4-FF, p-FF
- Acetyl fentanyl, AF
- Acrylfentanyl
- AH-7921
- α -Methylfentanyl, "China White"
- Butyrfentanyl, BF
- Cyclopentylfentanyl, CP-F
- Desmethylprodine, MPPP
- Furanylfentanyl, Fu-F
- MT-45
- O-Desmethyltramadol
- Tetrahydrofuranlylfentanyl, THF-F
- U-47700
- U-51754^[82]
- Valeryl fentanyl, VF



MACS “DESIGNER” OPIOIDS: HISTORY

- AMF appeared in late 1970s
 - 15 deaths in California in 1979-1980
 - made Schedule I of CSA in 1981
- TMF appeared in 1983
 - >100 deaths attributed to it through 1980s
 - spread to East Coast in late 1980s
 - 30 deaths in Baltimore in 1992
- MPPP tested as an analgesic in 1970s
 - 1-methyl-4-phenyl-propionoxy-piperidine
 - Meperedine analog
 - appeared on the streets in mid 1970s
 - 1st MPTP induced Parkinson’s syndrome reported in 1979



CESAR *FAX* →

April 6, 1992
Vol. 1 Issue 8

A Weekly FAX From the Center for Substance Abuse Research

University of Maryland At College Park *

Demographic Characteristics of 23 Fentanyl Related Deaths in Maryland in 1992

Two-thirds of Fentanyl related deaths in Maryland involved a black male or female and were over 30 years of age. Almost all of the incidents occurred in Baltimore City or Baltimore County in February or March. 550 envelopes containing Fentanyl have been seized by the state police. State police indicate the Fentanyl to be licitly manufactured rather than produced in clandestine labs. Heroin addicts should be alerted that drugs sold as heroin may contain Fentanyl ("China White").

Demographics of Maryland Fentanyl Incidents

RACE:	f	%	AGE:	f	%
-------	---	---	------	---	---



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Need alcohol or drug help for
yourself or someone else?[CLICK HERE >](#)

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East Coast Hit by Rash of Heroin Deaths, Overdoses

May 8, 2006

News Summary

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Heroin users from Chicago to Maryland have been killed or sent to the hospital by a powerful drug mix that includes the painkiller fentanyl, [USA Today](#) reported May 5.

More than two dozen deaths and 300 hospitalizations have been tied to use of the mixture during the past three weeks, according to state and federal officials. The heroin-fentanyl mix first appeared in Chicago on April 13, and has killed 11 people there and caused overdoses in 144 other users. Since then, the drug has surfaced in Camden, N.J.; Wilmington, Del.; [Salisbury, Md.](#); Harrisburg, Pa.; and a handful of other communities.

Experts say the heroin-fentanyl mix is unusual because the painkiller is expensive, whereas heroin is usually cut with cheap substances like sugar or flour to boost dealer profits. Typically, it is midlevel dealers in the U.S. who cut the drugs.

(Fentanyl Adulterated/Substituted Heroin)

“HERONYL”/“FENTOIN”

Vancouver Coastal Health
 VCH HIV/AIDS & Harm Reduction
 May 29, 2013

Toxic Fentanyl sold as Heroin

Powder fentanyl can cause overdoses

Fentanyl overdoses can be harder to reverse

Try not to use alone
 Inject slowly
 Use Insite
 Carry Naloxone
 Call 911 right away if someone ODs

This is an official
CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
 June 20, 2013, 15:15 ET (3:15 PM ET)
 CDCHAN-00350

Recommendations for Laboratory Testing for Acetyl Fentanyl and Patient Evaluation and Treatment for Overdose with Synthetic Opioids

Summary: Recently, a number of intravenous drug users have overdosed on a new, non-prescription injected synthetic opioid, acetyl fentanyl. Acetyl fentanyl is a fentanyl analog previously undocumented in illicit drug use that is up to five times more potent than heroin. CDC recommends increased vigilance by public health agencies, emergency departments, state laboratories, medical examiners, and coroners for patients with symptoms consistent with opioid overdose and laboratory results showing an enzyme-linked immunosorbent assay (ELISA) positive for fentanyl.

CDC also recommends that public health officials work with laboratories to carry out ELISA screens for fentanyl, and if the results of these screens are positive for fentanyl, conduct gas chromatography-mass spectrometry (GC/MS) confirmatory testing on specimens to confirm or rule out fentanyl and its analogs, including acetyl fentanyl.

Background:

Since March 6, 2013, 14 overdose deaths related to a novel, injected non-prescription synthetic opioid have occurred among intravenous drug users in Rhode Island. Ten of those deaths occurred in March. On May 30, 2013, Rhode Island Department of Health confirmed that the implicated synthetic opioid is acetyl fentanyl, a fentanyl analog previously undocumented in illicit drug use. Acetyl fentanyl is not available as a prescription drug in the U.S.

The age of the persons who died from an acetyl fentanyl overdose ranged from 19 – 57 years, and 10 of the decedents were male. The toxicology testing results for most of the decedents showed, in addition to acetyl fentanyl, varying mixtures of drugs, including cocaine, heroin (morphine), ethanol, and benzodiazepines. However, none of these additional substances were present in all decedents and none of these persons tested positive for fentanyl by GC/MS after testing positive for fentanyl by ELISA. Toxicology results for one decedent showed only acetyl fentanyl (by GC/MS) and no other substances. These deaths represent a significant increase in the number of illicit drug overdose deaths compared with the number of cases typically reported in one month in Rhode Island.

There have been unconfirmed reports from other states of increases in illicit opioid-related overdose events seen in emergency departments. Media stories have associated these events with “fentanyl-contaminated heroin” or, in some cases, to fentanyl alone. It is possible that these events are related to acetyl fentanyl, but confirmatory testing is needed. States other than Rhode Island have not informed CDC that they are testing for acetyl fentanyl.

Montreal police warn: Dangerous new street drug 40 times stronger than heroin
 Pills and sophisticated drug-making equipment were seized in seven raids last month
 Katherine Wilson, THE GAZETTE May 15, 2013



The Quebec Health Department and Montreal police are sounding the alarm about a dangerous new street drug that can be 40 times stronger than heroin.

Photograph by: . . . Montreal police

MONTREAL — Almost three weeks ago, two men walked into a UPS store in Lachine and told the clerk they wanted to use a microwave oven and a toaster at an address in Colorado.

The men had been regular customers over the last few months and always shipped the same items to various addresses in the United States.

On their last visit on April 25, Montreal police raided the store as the men were filling out an address coupon.

CARFENTANIL

- Fentanyl analog
- Synthesized by Jansen Pharmaceuticals in 1974
- One of the most potent opioids known
- Used commercially as a large animal tranquilizer (*Wildnil*)
- On illicit opioid scene in N. America since 2015



Journal of Analytical Toxicology

ABOUT THIS JOURNAL CONTACT THIS JOURNAL SUBSCRIPTIONS

Oxford Journals > Science & Mathematics > Journal of Analytical Toxicology > Volume 36, Issue 1



Analysis of Clothing and Urine from Moscow Theatre Siege Casualties Reveals Carfentanil and Remifentanyl Use

James R. Riches, Robert W. Read, Robin M. Black, Nicholas J. Cooper and Christopher M. Timperley*

* Author Affiliations

* Author to whom correspondence should be addressed. E-mail: cmtimperley@dstl.gov.uk

Abstract

On October 26, 2002, Russian Special Forces deployed a chemical aerosol against Chechen terrorists to rescue hostages in the Dubrovka theatre. Its use confirmed Russian military interest in chemicals with effects on personnel and caused 125 deaths through a combination of the aerosol and inadequate medical care. This study provides evidence from liquid chromatography–tandem mass spectrometry analysis of extracts of

To put this in perspective, wild African elephants—an animal that Carfentanil is used on—weigh between 5,000 and 14,000 lbs as reported by National Geographic, which is roughly 26 to 72 times the weight of your average adult male of 195.5 lbs.



F/HPSO

(Fentanyl & Other High Potency Synthetic Opioids)

“Iso” (isotonitazene)*

U-47700 (“Pink”)

Brorphine (Purple Heroin)



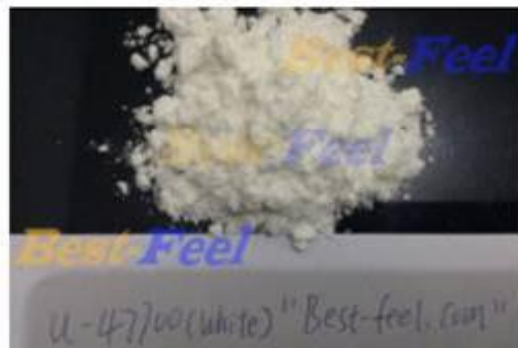
Isotonitazene
A New and Potentially
Deadly Synthetic Opioid



* also Metonitazene, Butonitazene, Etonitazene, Metodesnitazene

“PINK”

- U-47700
- Synthesized by Upjohn in 1976
- “Pink”, “Pinky”; “U4”
- 7-10 Xs more potent than Morphine
- Never tested in humans. Relegated to research.
- Also U-48800



U-4770*

★★★★★ 4.50 out of 5, (34) reviews

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NITAZENES

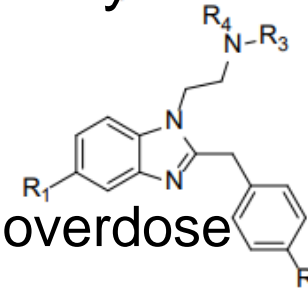
(1-benzyl-benzimidazoles or benzimidazoles)



➤ Class of opioids first developed in the late 1950s by CIBA (Switzerland)

➤ Slightly more potent than fentanyl

➤ Unclear if higher naloxone dose needed to reverse overdose



	R ₁	R ₂	R ₃	R ₄
metonitazene	NO ₂	OCH ₃	CH ₂ CH ₃	CH ₂ CH ₃
metodesnitazene	H	OCH ₃	CH ₂ CH ₃	CH ₂ CH ₃
etonitazene	NO ₂	OCH ₂ CH ₃	CH ₂ CH ₃	CH ₂ CH ₃
etodesnitazene	H	OCH ₂ CH ₃	CH ₂ CH ₃	CH ₂ CH ₃
protonitazene	NO ₂	OCH ₂ CH ₂ CH ₃	CH ₂ CH ₃	CH ₂ CH ₃
butonitazene	NO ₂	OCH ₂ CH ₂ CH ₂ CH ₃	CH ₂ CH ₃	CH ₂ CH ₃
isotonitazene	NO ₂	OCH(CH ₃) ₂	CH ₂ CH ₃	CH ₂ CH ₃
clonitazene	NO ₂	Cl	CH ₂ CH ₃	CH ₂ CH ₃
flunitazene	NO ₂	F	CH ₂ CH ₃	CH ₂ CH ₃
etonitazpyne	NO ₂	OCH ₂ CH ₃	-CH ₂ CH ₂ CH ₂ CH ₂ -	CH ₂ CH ₃
etonitazepipne	NO ₂	OCH ₂ CH ₃	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -	CH ₂ CH ₃

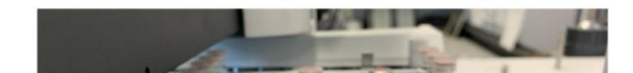
➤ 10 were already Schedule I in U.S.; others emergently scheduled in 2020

➤ Etonitazene and clonitazene seen in illicit drug supply late 1990s-mid 2000s

➤ Isotonitazene appeared in U.S. summer, 2019

➤ Started in Midwest but spreading to south, east, west coasts

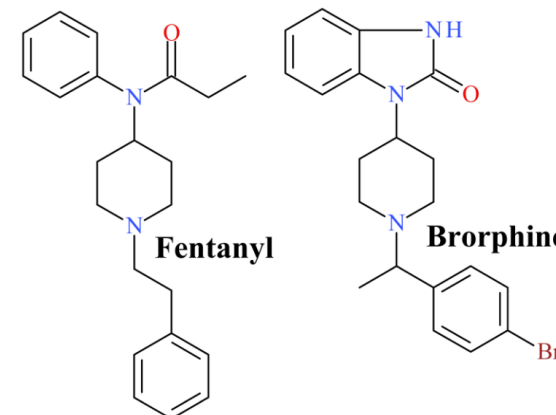
➤ Most manufactured in China



BRORPHINE

(1-(1-(1-(4-bromophenyl)ethyl)piperidin-4-yl)-1,3-dihydro-2 H-benzo[d]imidazol-2-one)

- Synthesis first reported 2018
 - Analogues synthesized in the 1960s
- “Purple Heroin”
 - Often purple, grey or white
 - Typically mixed with other synthetic opioids
- Piperidine-based
 - Similar to fentanyl but not an “analogue”
 - Also similar to nitazenes
- @ 100 X more potent than morphine; similar potency to fentanyl
- Reported in U.S., Canada, Sweden, Belgium
 - First reported in U.S. Summer, 2019 (> 30 fatalities in: Illinois, Minnesota, Arizona, Louisiana)
- DEA emergent Schedule I on 12/3/2020
- Potent [hERG](#) potassium ion channel inhibitor
 - May increase risk of Torsades



July 2020

The Rise of Brorphine — A Potent New Synthetic Opioid Identified in the Midwestern United States

Purpose: The objective of this announcement is to notify public health and safety, law enforcement, first responders, clinicians, medical examiners and coroners, forensic and clinical laboratory personnel, and all other related communities about new information surrounding the emergent synthetic opioid **brorphine**.

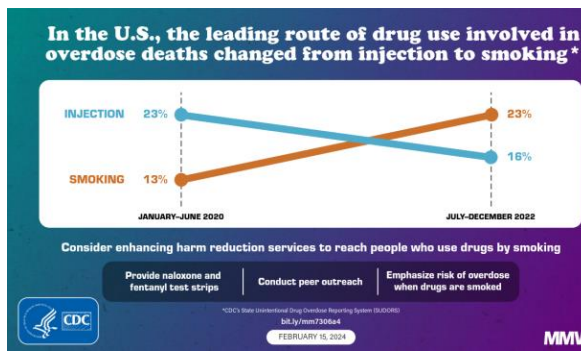
Background: Synthetic opioids are chemically manufactured drugs, often accompanied with unknown potency and adverse effects or health risks. New synthetic opioids may be mixed with more traditional opioids, creating additional

“SMOKING”

- Historically done with “Mexican black tar heroin”
- Initially seen in U.S. west of the Mississippi
- Moved across Midwest & Appalachia in the 2000s
 - In Virginia, West Virginia and western Pennsylvania
 - Increasing in western and southern Maryland
- “Chasing the Dragon”; “Foiling”
 - More like vaping
 - leukoencephalopathy
 - botulism, etc. if injected



➤ “Smoking” powdered Fentanyl



KROKODIL

- Contains desomorphine
 - Synthesized in the U.S. in 1932
- Synthesized from codeine (OTC in some places)
- Increase in popularity in Siberia @ 2002
 - spreading to rest of Russia since 2010
- More reports in rest of Europe
- Few, but increasing, reports in U.S. since early 2000-teens
- More potent than heroin
- Shorter acting than heroin
- Associated with significant abscesses, etc
 - Likely due to impurities from manufacture (solvents, phosphorous, etc)



The INDEPENDENT

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Krokodil: The drug that eats junkies

A home-made heroin substitute is having a horrific effect on thousands of Russia's drug addicts

SHAUN WALKER | WEDNESDAY 22 JUNE 2011

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Cyprus tries to stem tide of cash leaving the country after €10bn bailout

Bits left fery queasy after 30-hour trip that left them just SIX

Oleg glances furtively around him and, confident that nobody is watching, slips inside the entrance to a decaying Soviet-era block of flats, where Sasha is waiting for him. Encooned in the dingy kitchen of one of the apartments, they empty the contents of a blue carrier bag that Oleg has brought with him - painkillers, iodine, lighter fluid, industrial cleaning oil, and an array

Related articles

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The Sketch: I Can't Believe It's Not Heroin!

Heroin found in The National Archives



KRATOM



- *Mitragyna speciosa*
 - a tropical tree in same family as the coffee tree
- AKA: “Thang”, “Biak Biak”, “Ketum”, “Kakuam”, “Thom”
 - “4x100”: M. speciosa leaves, coca cola, cough syrup (often w/codeine), ice
- Native to Southeast Asia
 - primarily used in Thailand, Malaysia, Indonesia
- Used by field workers for energy and relief from muscle strain
- Also used as opium substitute
 - Assist with symptoms of opioid withdrawal since 1800’s
- Fresh leaves chewed, dried leaves smoked or steeped in tea
- Increase in U.S., especially Pacific Northwest; S.F.
 - Widely available online and in “head”/smoke shops



KRATOM



- Contains **mitragynine, mitraphylline, 7- α -hydroxymitragynine**
- Structurally similar to hallucinogens like psilocybin
- Psychostimulant effects at low doses
 - Increased alertness, physical energy, talkativeness
- Opioid receptor agonist at higher doses
 - High affinity for κ -opioid receptor
 - Pain relieving properties by partial agonist activity at μ - and δ -opioid receptors
- Effects occur within 20-30 minutes after ingestion
- Effects last 2-5 hours
- Acute side effects: nausea, itching, dry mouth, constipation, loss of appetite
- Psychosis and respiratory depression reported
- Withdrawal syndrome possible with chronic use
 - Irritability, muscle aches, rhinorrhea

KRATOM



- Thailand: Narcotics Act B.E. 2522 classifies kratom with marijuana as Class V (1979)
- Malaysia: Poison Act 1951 (2003)
- United States: DEA “drug of concern”
 - DEA announced emergency scheduling of Kratom on August 11, 2016
 - Retracted under pressure from lobbyists and federal lawmakers
 - Open for public commenting through December 1, 2016; over 60,000 comments posted
- > 10 states and many cities have banned Kratom



KRATOM & PREGNANCY

- Limited data
 - primarily case reports
 - Most with use of multiple other substances
- No evidence of teratogenicity
- Reports of withdrawal in mothers similar to opioid withdrawal
 - Most treated with buprenorphine or other opioid agonist
- Reports of withdrawal in newborns similar to NOWS
 - Most developed NOWS
 - > half received pharmacologic treatment
 - Successful management with morphine
- X

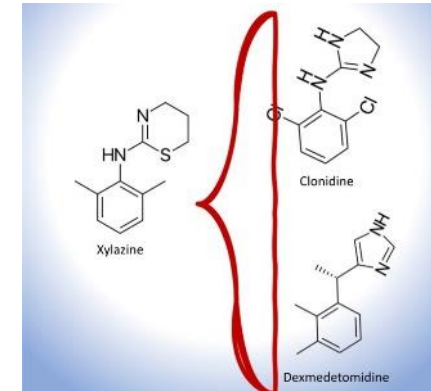
XYLAZINE: BASICS



➤ Synthesized in 1962 in Germany

➤ Partial α -2 agonist

- Important in sympathetic nervous system
- Works on pre-synaptic central adrenergic receptors & postsynaptic peripheral receptors
- Causes decreased release of dopamine and norepinephrine
- Similar to Clonidine and Dexmedetomidine (Precedex)
- Structural similarity to phenothiazines and tricyclic antidepressants



➤ FDA approved in U.S. in 1972 as a sedative, analgesic, & muscle relaxant

- **Only for animals** (dogs, cats, horses, elk, fallow deer, mule deer, sika deer, and white-tailed deer)
 - Rompun, Anased, Sedazine, Xylamed, Chanazine
 - A parenteral liquid (20, 100, 300 mg/ml)

➤ Administered subcutaneously, intramuscularly, intravenously

➤ Reports of accidental overdose during administration to animals

➤ Not currently scheduled by DEA



XYLAZINE: “MISUSE”

- Illicit use dating back to late 1970s
- Often by veterinarians or individuals in the equestrian industry
- Often from diverted veterinary supply
- Popular in Puerto Rico (“Anestesia de Caballo”) since early 2000s
- Appeared in continental U.S. in Philadelphia late 2000s
- Increasing adulterant in illicit drug supply
 - Primarily heroin/fentanyl
 - Also in cocaine, methamphetamine, benzodiazepines
- Possibly added to:
 - prolong effects of fentanyl
 - delay withdrawal from fentanyl
 - decrease proportionate amount of opioid w less resp. depression
- Liquid dried to a powder
- Increasingly coming from China as a powder

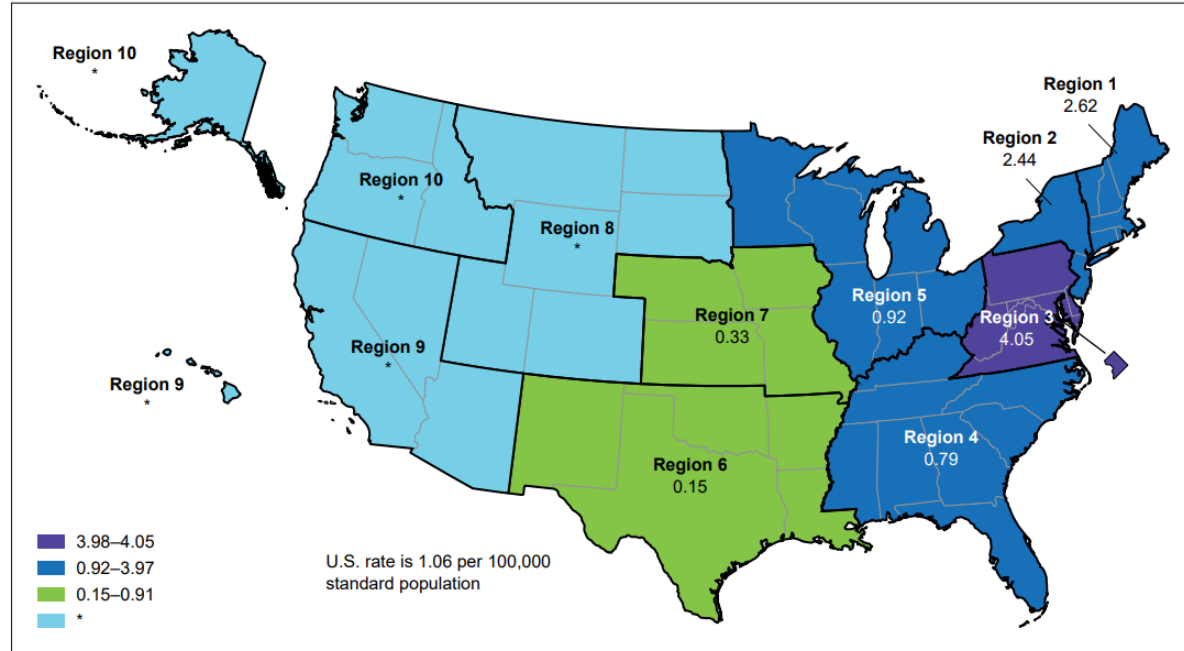


XYLAZINE: “MISUSE”

- “Tranq”, “Tranq-Dope”, “Sleep Cut”, “Philly-Dope”, “Zombie Drug”
- “Wipeout”- fentanyl + cocaine+ xylazine
- Vast majority of individuals not seeking it out
- Reported use IV, IN, IM, SC, “smoking”*
 - no reports of actual vaping
- Rapid onset- minutes
- Effects typically last 8 hours but can last for up to 72 hours

XYLAZINE: FATAL OD

Figure 4. Age-adjusted rate of drug overdose deaths involving xylazine, by region: United States, 2021



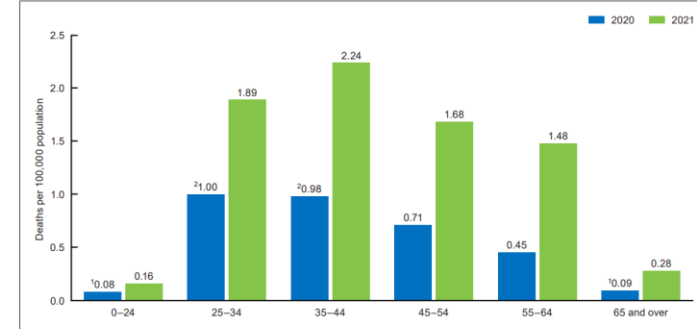
* Rate does not meet the National Center for Health Statistics reliability criteria of 20 deaths or more and as a result is not reported.
 NOTES: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent (listed) drug. Age-adjusted death rates were calculated using the direct method and adjusted to the 2000 U.S. standard population. Regions are the U.S. Department of Health and Human Services public health regions: Region 1 (CT, MA, ME, NH, RI, and VT), Region 2 (NJ and NY), Region 3 (DC, DE, MD, PA, VA, and WV), Region 4 (AL, FL, GA, KY, MS, NC, SC, and TN), Region 5 (IL, IN, MI, MN, OH, and WI), Region 6 (AR, LA, NM, OK, and TX), Region 7 (IA, KS, MO, and NE), Region 8 (CO, MT, ND, SD, UT, and WY), Region 9 (AZ, CA, HI, and NV), and Region 10 (AK, ID, OR, and WA). Except for Regions 1 and 2, differences in rates between all regions were significant ($p < 0.05$).
 SOURCE: National Center for Health Statistics, death certificate literal text from the National Vital Statistics System as of May 24, 2023.

Table. Most frequent concomitant drugs for drug overdose deaths involving xylazine: United States, 2018–2021

Year	Referent drug	Number of drug overdose deaths involving referent drug	Most frequent concomitant drug		Second most frequent concomitant drug		Third most frequent concomitant drug	
			Concomitant drug	Number and percent of deaths involving both drugs	Concomitant drug	Number and percent of deaths involving both drugs	Concomitant drug	Number and percent of deaths involving both drugs
2021	Xylazine	3,468	Fentanyl	3,437 (99.1)	Cocaine	1,216 (35.1)	Methamphetamine	652 (18.8)
2020	Xylazine	1,499	Fentanyl	1,490 (99.4)	Cocaine	489 (32.6)	Methamphetamine	232 (15.5)
2019	Xylazine	627	Fentanyl	621 (99.0)	Cocaine	194 (30.9)	Heroin	151 (24.1)
2018	Xylazine	102	Fentanyl	99 (97.1)	Cocaine	41 (40.2)	Heroin	30 (29.4)

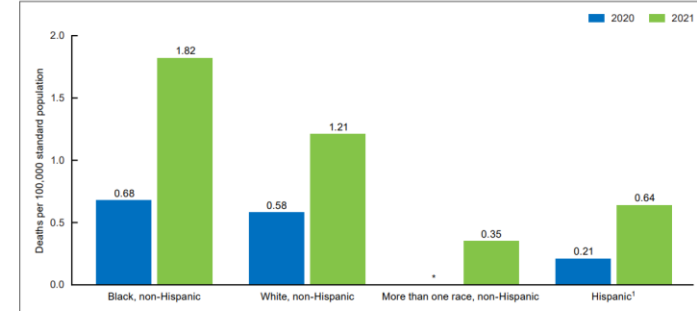
NOTES: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to xylazine. Age-adjusted death rates were calculated using the direct method and adjusted to the 2000 U.S. standard population. When comparing rates across years, note that trends may be influenced by improvements in drug reporting. The reporting of at least one specific drug or drug class in the literal text, as identified by multiple cause-of-death codes T36–T50.8, improved from 92.0% of drug overdose deaths in 2018 to 95.2% in 2021.

Figure 2. Rate of drug overdose deaths involving xylazine, by age group: United States, 2020–2021



*Significantly lower than all other age groups ($p < 0.05$) for 2020.
 *Significantly higher than all other age groups ($p < 0.05$) for 2021.
 NOTES: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent (listed) drug. When comparing rates across years, note that trends may be influenced by improvements in drug reporting. The reporting of at least one specific drug or drug class in the literal text, as identified by multiple cause-of-death codes T36–T50.8, improved from 94.4% of drug overdose deaths in 2020 to 95.2% in 2021. Differences in rates between 2020 and 2021 were significant for all groups ($p < 0.05$). In 2021, differences in rates were significant between all groups ($p < 0.05$).
 SOURCE: National Center for Health Statistics, death certificate literal text from the National Vital Statistics System as of May 24, 2023.

Figure 3. Age-adjusted rate of drug overdose deaths involving xylazine, by race and Hispanic origin: United States, 2020–2021



*Rate does not meet the National Center for Health Statistics reliability criteria of 20 deaths or more and as a result is not reported.
 *People of Hispanic origin may be of any race.
 NOTES: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent (listed) drug. Age-adjusted death rates were calculated using the direct method and adjusted to the 2000 U.S. standard population. When comparing rates across years, note that trends may be influenced by improvements in drug reporting. The reporting of at least one specific drug or drug class in the literal text, as identified by multiple cause-of-death codes T36–T50.8, improved from 94.4% of drug overdose deaths in 2020 to 95.2% in 2021. Difference in rates between 2020 and 2021 and within a given year for all groups was significant ($p < 0.05$). Asian, non-Hispanic, Native Hawaiian or Other Pacific Islander non-Hispanic, and American Indian or Alaska Native non-Hispanic people are not reported because the 2020 and 2021 rates do not meet the reliability criteria of 20 deaths or more (see <https://www.cdc.gov/nchs/data/verner/2019a-08-08.pdf>).
 SOURCE: National Center for Health Statistics, death certificate literal text from the National Vital Statistics System as of May 24, 2023.

JAMA Network Open

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Original Investigation | Substance Use and Addiction

January 5, 2024

Xylazine in Overdose Deaths and Forensic Drug Reports in US States, 2019-2022

Manuel Cano, PhD¹, Raminta Daniulaityte, PhD², Flavio Marsaglia, PhD^{1,3}

JAMA Netw Open. 2024;7(1):e2350630. doi:10.1001/jamanetworkopen.2023.50630

- 43 states reported at least 1 xylazine-related overdose death from 2019 to 2022
- In 2019, 16 states had zero xylazine reports (NFLIS reports)
- In 2022, only 2 states had zero xylazine reports
- In 2022, all but 3 states had recorded an increase in xylazine's representation in NFLIS reports.
- In 2022, of states with data available (21), xylazine-involved overdose death rates were highest in Vermont (10.5/ 100 000 residents) & Connecticut (9.8/ 100 000 residents)

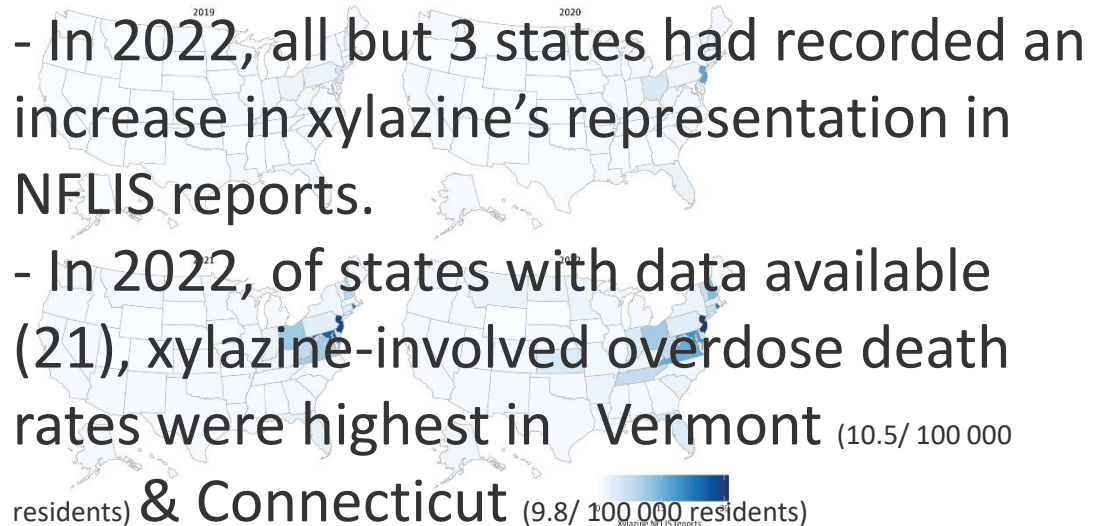


Table. Reported Xylazine-Related Overdose Deaths, 2019-2022

State	2019	2020	2021	2022	Additional information	Source
AK	NR	NR	NR	NR	NA	NA
AL	NR	NR	14 (0.3)	55 (1.1)	NA	Gulf Coast HIDTA, ³⁰ 2023
AR	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
AZ	NR	NR	NR	NR	Jan 2021-June 2022: between 10-99 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
CA	NR	NR	NR	NR	2021: 0.5% of sampled deaths xylazine-positive, 0.3% xylazine-involved	CA Department of Public Health, ²⁴ 2023
CO	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
CT	71 (2.0)	141 (4.0)	298 (8.3)	354 (9.8)	Xylazine-involved deaths	CT Department of Public Health, ^{24,25} 2023
DC	NR	3 (0.4)	6 (0.9)	11 (1.6)	Xylazine-involved deaths	DC Office of the Chief Medical Examiner, ²⁶ 2023
DE	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
FL	NR	NR	NR	(1.1) ^{b,c}	Xylazine-involved; based on first half of year	FL Department of Law Enforcement, ²⁸ 2023
GA	NR	15 (0.1)	116 (1.1)	222 (2.1)	Xylazine-involved	GA Department of Public Health, ²⁴ 2023
HI	NR	NR	NR	NR	NA	NA
IA	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
ID	NR	NR	NR	NR	NA	NA
IL	53 (0.4)	64 (0.5)	188 (1.5)	NA (2.3) ^{b,c}	Xylazine-involved; 2022 rate based on first half of year	Feinberg School of Medicine, ²⁷ 2023
IN	NR	NR	NR	NR	Jan 2021-June 2022: 82 IMF deaths xylazine-involved	Karisa et al, ⁷ 2023
KS	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
KY	NR	NR	NR	NR	In 2022: 1-5 xylazine-positive deaths	KY Office of Drug Control Policy, ³¹ 2023
LA	3 (0.1)	21 (0.5)	39 (0.8)	25 (0.5) ^d	Xylazine-involved	LA State Board of Medical Examiners, ⁴² 2023
MA	NR	NR	NR	NR	In 2022: of opioid deaths with toxicology, 5% xylazine-positive	MA Department of Public Health, ²⁴ 2023
MD	103 (1.7)	344 (5.7)	495 (8.0)	NR	Xylazine-positive	Friedman et al, ⁹ 2022
ME	NR	NR	53 (3.9)	46 (3.4)	Xylazine-involved	Sorg et al, ⁴⁴ 2022; Sorg et al, ⁴⁶ 2023
MI	NR	NR	60 (0.6)	92 (0.9)	Xylazine-positive	MI Department of Health and Human Services, ⁴⁴ 2023
MN	4 (0.1)	8 (0.1)	24 (0.4)	34 (0.4) ^d	Xylazine-involved	MN Department of Health, ⁴⁵ 2023
MO	4 (0.1)	2 (0.0)	39 (0.6)	109 (1.8) ^d	Xylazine-involved	Nickelson, ⁴⁶ 2023
MS	NR	NR	NR	NR	Jan 2020-Jun 2022: 19 Xylazine-involved deaths	MS State Department of Health, ¹⁶ 2023
MT	NR	NR	NR	NR	NA	NA
NC	NR	NR	NR	NR	NA	NA
ND	NR	NR	NR	NR	Jan 2019-July 2023: 9 Xylazine-positive deaths	ND Department of Health and Human Services, ⁴¹ 2023
NE	NR	NR	NR	NR	2021-2022: 4 Xylazine-involved deaths	NE Department of Health and Human Services, ³⁷ 2023
NH	NR	NR	NR	3 (0.2) ^d	Xylazine-involved	NH Office of Chief Medical Examiner, ³⁸ 2023
NJ	13 (0.1)	34 (0.4)	226 (2.4) ^d	210 (2.3) ^d	Bureau of Justice Assistance, ²⁷ 2023	
NM	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
NV	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
NY	NR	NR	NR	NR	2021: 429 xylazine-involved opioid deaths in NYC; 135 in New York State outside NYC	NY State Department of Health, ³⁹ 2023
OH	15 (0.1)	45 (0.4)	75 (0.6)	119 (1.0) ^d	Xylazine-involved	OH Department of Health, ⁴² 2023
OK	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
OR	NR	2 (0.0)	9 (0.2)	9 (0.2) ^d	Xylazine-positive	OR Health Authority, ⁴³ 2023
PA	259 (2.0)	377 (2.9)	576 (4.4)	760 (5.9)	Xylazine-involved	PA Department of Health, ⁴⁴ 2023
RI	NR	NR	NR	NR	Jan 2021-June 2022: between 10-99 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
SC	NR	NR	NR	NR	Jan 2021-June 2022: 178 IMF deaths involving xylazine	Karisa et al, ⁷ 2023
SD	NR	NR	NR	NR	NA	NA
TN	NR	56 (0.8)	94 (1.3)	NR	Xylazine-involved	TN Department of Health, ⁴⁷ 2022
TX	NR	NR	11 (0.0)	19 (0.1)	Xylazine-involved	TX Department of State Health Services, ⁴⁸ 2023
UT	NR	NR	NR	NR	NA	NA
VA	NR	NR	NR	NR	Jan 2021-June 2022: between 10-99 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
VT	6 (1.0)	5 (0.8)	29 (4.5)	68 (10.5)	Xylazine-involved	VT Department of Health, ⁴⁹ 2023
WA	NR	NR	NR	NR	Jan 2021-June 2022: between 1-9 IMF deaths xylazine-positive	Karisa et al, ⁷ 2023
WI	NR	NR	NR	NR	2019-2020: 6 xylazine-positive deaths reported in Milwaukee	Friedman et al, ⁹ 2022
WV	10 (0.6)	67 (3.8)	(4.5) ^{b,c}	NR	Xylazine-positive	Sibbesen et al, ⁵ 2023
WY	NR	NR	NR	NR	NA	NA

Abbreviations: IMF, illicitly manufactured fentanyl; NA, not available; NR, not reported.

^a Death counts were most recently accessed from each source October 27 to 30, 2023. Rates are per 100 000 population and calculated using population estimates from the National Center for Health Statistics.

^b Totals provided for a half-year period, and not included.

^c Data provided for half of year only.

^d Data source indicates this figure is based on provisional data.



UNKNOWN SUBSTANCE REPORTED IN FREDERICK, CECIL & HARFORD COUNTIES

On Thursday, July 23, our office received reports of an unknown substance in Frederick, Cecil, and Harford Counties that can cause very serious wounds at the site of injection.

In Frederick County, the substance is being sold under the name "No Shorts" and distributed in capsule form. Reports indicate that individuals purchasing the substance believe that they are purchasing heroin. After injecting the substance, individuals report injuries that begin as a small discoloration and progress into an open wound. An article citing a warning from Frederick County Health Department can be found here: <https://wtop.com/frederick-county/2020/07/frederick-county-warns-of-possibly-fake-heroin-causing-gangrene/>.

The High Intensity Drug Trafficking Area program is currently awaiting results from a forensic lab analysis from Frederick County. HIDTA's initial concern is related to a substance called "krokodil" (desomorphine), but lab results are required before any final determination is made. Read more about krokodil here: <https://www.drugs.com/illicit/krokodil.html>.

The Cecil County Health Department believes that a similar substance, branded as "Don't Make Me Mad," is present in Cecil County, where two confirmed cases have been reported. Both of the cases involved individuals engaged in wound-care services. CCHD will continue to monitor the situation and share information with the community as it becomes available.

Harford County has issued the following public health alert:

"The Harford County Health Department Harm Reduction Program has received reports of soft tissue injuries, including abscesses and development of gangrene, associated with injection drugs recently in circulation. Similar reports have also been made in Frederick and Cecil Counties, MD.

Development of abscesses and cellulitis after injecting heroin cut with xylazine (commonly used as a horse tranquilizer) has been seen. Bags containing this substance are stamped "Ohh yeah."

Reports also include development of gangrene after injecting contents of a gel capsule containing what was believed to be heroin, sold under the name "No Shorts." The powder turns pink/red when water is added. The injury starts as a small discoloration (purplish) at the injection site and progresses outward into an open wound, sometimes almost black in color.

If you have an injection-related wound that shares any of the similarities above it is recommended you seek immediate medical attention.

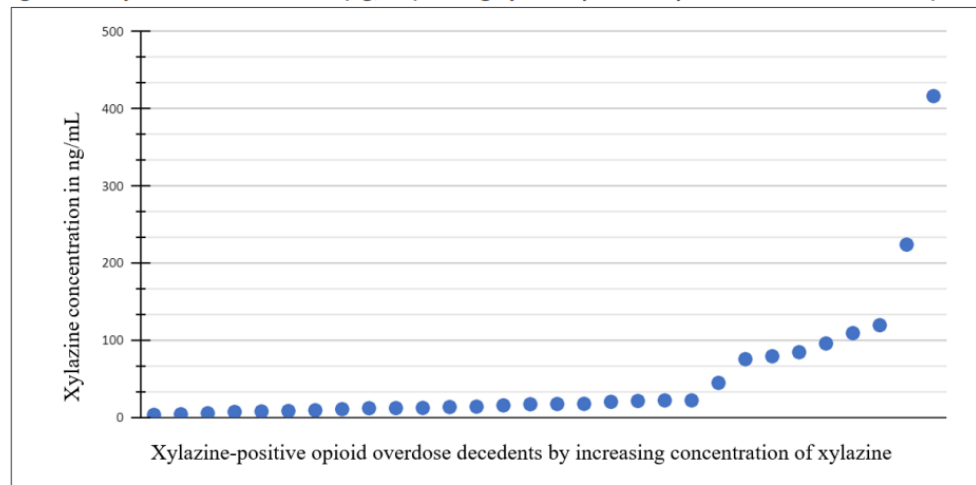
*Call the Harm Reduction Program at (410) 612-1779 for information on overdose prevention (including free Narcan®) and wound care. Contact Behavioral Health at (410) 877-2340 for information on substance use treatment and peer recovery services.**

Please report any further information related to the above to Help.OOCC@Maryland.gov.

XYLAZINE TOXICOLOGY PROJECT (MD OCME; 2022)



Figure 5.1. Xylazine concentrations (ng/mL) among xylazine-positive opioid overdose decedents (n=30)



We classified opioid overdose decedents into three groups based on concentration of xylazine, i.e., <10 ng/mL, 10-20 ng/mL, and >20 ng/mL. More than one-half (n=17) were in the bottom two categories. There were 7 decedents with concentrations <10 ng/mL, 10 cases with concentrations between 10-20 ng/mL, and 13 cases with xylazine concentrations >20 ng/mL (Table 5.1).

Table 5.1. Classification of decedents (n=30) by concentration of xylazine (ng/mL)

Concentration	n	Mean	(SD)
<10 ng/mL	7	6.5	(2.1)
10-20 ng/mL	10	14.2	(2.4)
>20 ng/mL	13	102.6	(105.5)

Table 5.2. Substances found in xylazine-positive opioid overdose decedents (n=30)

SUBSTANCES DETECTED	% of cases positive
Fentanyl and Fentanyl analogs	100%
Prescription Opioids¹	23%
Methadone	13%
Morphine	10%
Tramadol	7%
Stimulants	50%
Cocaine	37%
Amphetamine, methamphetamine	13%
Benzodiazepines	13%
Alcohol (Blood Alcohol Concentration >0.05%)	17%
Miscellaneous	
Antidepressants	23%
Antihistamines	17%
Quinine	50%

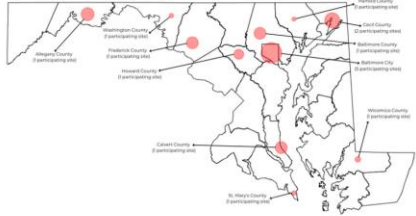
The **Rapid Analysis of Drugs (RAD)** is a statewide drug checking program that tests routinely returned paraphernalia voluntarily provided by **Maryland Syringe Services Program (SSP)** participants in partnership with the National Institute of Standards and Technology (NIST). RAD was piloted in 8 SSPs starting in October 2021. In September of 2022, RAD was expanded and became an ongoing service available to all MD SSPs, and the types of testable paraphernalia expanded to include syringes. It is important to note that all RAD data is deidentified, meaning there is no way to know the number of unique participants submitting samples, and all sampling is associated with a syringe service program which biases the sample to people who inject drugs.

As of October 31st, 2023, a total of 2,210 samples have been tested across the 16 SSPs currently participating in RAD. There have been 530 syringes tested since September of 2022.

Key Findings from the RAD Data

Before taking a deeper dive into the presence of xylazine within RAD samples, Figure 1 shows the jurisdictions that have SSPs submitting samples. The size of the circle represents the proportion of overall samples submitted by each site (a larger circle means more samples are submitted within that jurisdiction).

Figure 1: Proportional Sample Size by RAD Participant Jurisdiction in Maryland



RAPID ANALYSIS OF DRUGS REPORT

CENTER FOR HARM REDUCTION SERVICES
MARYLAND DEPARTMENT OF HEALTH

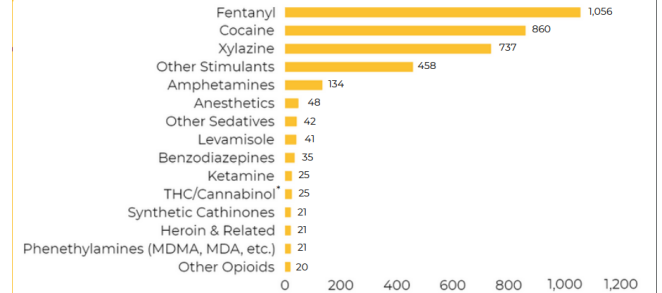
VOLUME 1: XYLAZINE

Contributors:

- Emily M. Martin, MHS
- Elizabeth Spradley, RN
- Kristin E. Schneider, PhD
- Jasmine Lopes, MPH
- Maggie Rybak, MPH
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Figure 2: Number of Samples Containing Each Substance



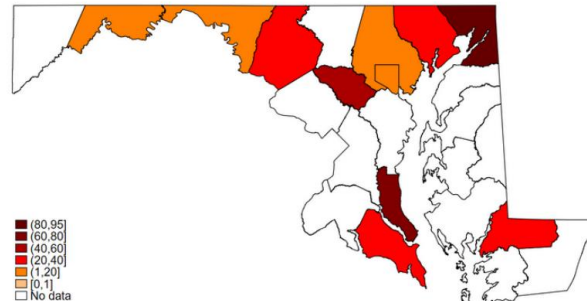
*Undetermined if from regulated supply as of July 2023

Of the 2,210 samples analyzed between October 2021 and October 2023, fentanyl has been present in 1,056 samples, xylazine has been present in 737 samples, and cocaine has been present in 860 samples (Figure 2). Notably, there is a very low level of heroin (21) present in RAD samples.

Xylazine in Maryland

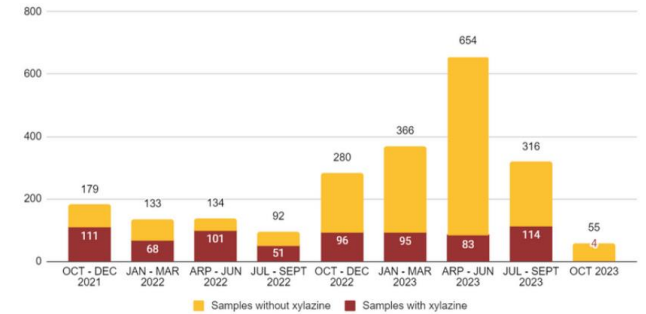
Xylazine is a veterinary sedative, commonly referred to as "tranq". It is often mixed and sold with fentanyl, as well as other opioids, and has been seen in cocaine, methamphetamine, and other illicitly manufactured depressants. Figure 3 shows the SSPs participating in RAD with a heat map of the proportion of samples containing xylazine since October 2021. Cecil County (84%) and Calvert County (76%) are seeing the highest level of xylazine present in their RAD samples, while Baltimore City (9%) and Baltimore County (10%) are seeing the lowest.

Figure 3: Percent of Samples Containing Xylazine by County



Data source: Maryland Center for Harm Reduction Services

Figure 5: Xylazine in RAD Samples, October 2021 - October 2023



In the past year, xylazine has decreased in prevalence throughout RAD results (Figure 5). This trend has been seen in Maryland law enforcement seizure data. However, RAD continues to see xylazine in greater than 20% of samples on average, and shows great variation by jurisdiction (with some consistently over 75%-80% prevalence). An increase in wounds in people who use drugs is also linked to xylazine's presence in the drug supply.

XYLAZINE: TESTING



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90mL Urine Specimen Collection



Xylazine and Fentanyl Combo Test

SKU AT-DOA-125

\$62.50

(25 Tests)

A rapid test for the detection of Xylazine and Fentanyl in human urine or powder.

For forensic use only. Not for in vitro diagnostic use.

The Multi-Drug Rapid Test Cassette (Urine & Powder) is a rapid chromatographic immunoassay for the qualitative detection of multiple drugs and drug in human urine or powder at the following cut-off concentrations

Xylazine (XYL) cut off 1000 ng/mL

Fentanyl (FYL) cut off 10 ng/mL

ALLTEST Xylazine Tests

SKU AT-DXYL-114

\$37.50

(25 Tests)

A rapid test for the qualitative detection of xylazine in human urine or powder.

For forensic use only. Not for in vitro diagnostic use.

The Xylazine (XYL) Rapid Test Panel (Urine & Powder) is a rapid chromatographic immunoassay for the detection of xylazine in human urine or powder at a cut-off concentration of 1,000 ng/mL.

This assay provides only a qualitative, preliminary test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography/Mass Spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

XYLAZINE: INTOXICATION

- Clinical effects:
 - Primarily- hypotension, bradycardia, sedation (with immobility)
 - Less effect on respiration
 - Some reports of hyperglycemia & anemia (primarily in animals)
- Does not respond to naloxone **but should always be given** as usually mixed w opioids
- Activated charcoal, IV fluids, atropine(?), intubation (if with respiratory distress)
- Atipamezole
 - Selective α -2 antagonist
 - FDA approved for animals anesthetized with α -2 agonists
 - Some proposal to use in humans
- Very few fatalities from Xylazine alone reported
 - 1 suicide used IV with serum level 2,900 ng/ml

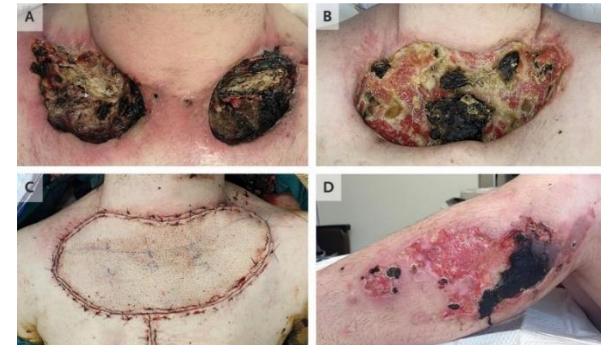


XYLAZINE: WITHDRAWAL

- Clinical effects
 - Primarily from rebound adrenergic effects
 - Increased blood pressure, heart rate, diaphoresis
 - May appear as worsened opioid withdrawal
 - Locus ceruleus
- IMPORTANT TO TREAT THE OPIOID WITHDRAWAL!!!
- No standardized management.
- Reports of use of:
 - Clonidine
 - Dexmedetomidine (Precedex)
 - Benzodiazepines
 - Tizanidine
 - Guanfacine

MACS XYLAZINE: WOUNDS

- The vast majority **not** confirmed by toxicology
- May develop rapidly and resolve slowly
- Reported in those who deny IV use
- Reported at sites other than where person injected
- Often large, granular, w/ a necrotic center
 - Common course of progression-several small “punch-hole” wounds appearing in a cluster, then coalesce into a single larger wound
 - Not typically purulent
- Unclear pathophysiology
 - Likely related to decreased oxygenation of tissues
- Management more like managing burns
 - Clean well w/ soap & water or saline
 - Keep moist
 - Cover w/ non-adherent dressing (Xeroform)
 - Antibiotics may not be needed



XYLAZINE & PREGNANCY

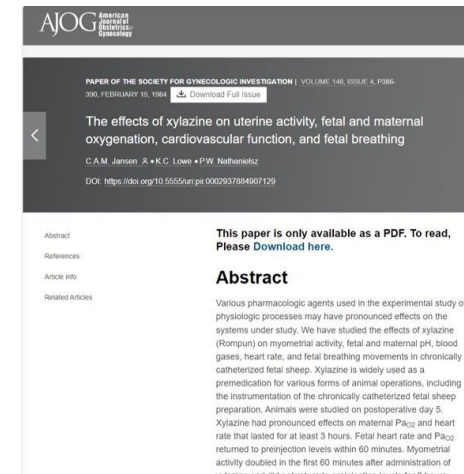
➤ Animal Studies

- Mostly in cows, sheep, mice
- Decreased uterine blood flow
- Decreased maternal (17%) and fetal (6%) heart rate
- Increased uterine vascular resistance (but not umbilical)
- Decreased fetal growth (though were also exposed to ketamine)

➤ Human Studies

- Practically no data
- Found in umbilical chord
 - Unclear if there is a minimal level needed
- Some evidence that chronic Clonidine exposure in pregnancy may increase risk for fetal growth restriction
 - Not uniformly seen

No information on lactation





House Committee advances AVMA-backed xylazine language

White House announces federal plan to fight illicit xylazine-fentanyl combination

By Malinda Larkin
July 21, 2023

The House Energy and Commerce Committee moved the SUPPORT Act out of committee on July 19. This legislative package was originally passed in 2018 to address the growing threat of the opioid crisis and the reauthorization contains key components from the Combating Illicit Xylazine Act—a bipartisan bill that the AVMA helped develop, introduce, and co-sponsor.



The xylazine language included in the SUPPORT Act would schedule xylazine as a Schedule III drug while exempting from scheduling the FDA-approved animal drug, which, if enacted, means veterinarians would be able to use it like they always have under federal law.

In the Senate, the Combating Illicit Xylazine Act has yet to be taken up by the Judiciary Committee; however, this proposed bill would make the manufacture, distribution, dispensing, or possession of xylazine with intent to traffic for human use subject to Schedule III penalties under the federal Controlled Substances Act. At the same time, the legitimate veterinary uses would remain under their current prescription status and would not be scheduled.



Notes from the Field: Xylazine, a Veterinary Tranquilizer, Identified as an Emerging Novel Substance in Drug Overdose Deaths — Connecticut, 2019-2020

Weekly / September 17, 2021 / 70(37):1303-1304
Shobha Thangapa, PhD¹; Heather A. Clinton¹; Sarah Al, MPH¹; Jacqueline Nunez, MD¹; James R. Gil, MD¹; Robert F. Lawlor¹; Susan B. Logan, MS, MPH¹ (ORCID iD)¹; Allison G. ...

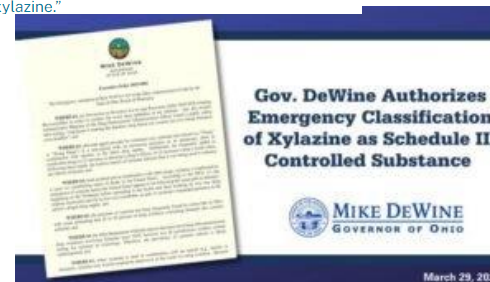


PUBLIC SAFETY ALERT

DEA Reports Widespread Threat of Fentanyl Mixed with Xylazine

WASHINGTON—The U.S. Drug Enforcement Administration is warning the American public of a sharp increase in the trafficking of fentanyl mixed with xylazine. Xylazine, also known as “Tram,” is a powerful sedative that the U.S. Food and Drug Administration has approved for veterinary use.

“Xylazine is making the deadliest drug threat our country has ever faced, fentanyl, even deadlier,” said Administrator Milgram. “DEA has seized xylazine and fentanyl mixtures in 48 of 50 States. The DEA Laboratory System is reporting that in 2022 approximately 23% of fentanyl powder and 7% of fentanyl pills seized by the DEA contained xylazine.”



FENTANYL ADULTERATED OR ASSOCIATED WITH XYLAZINE RESPONSE PLAN

JULY 2023

THE WHITE HOUSE
EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF NATIONAL DRUG CONTROL POLICY



FACT SHEET: In Continued Fight Against Overdose Epidemic, the White House Releases National Response Plan to Address the Emerging Threat of Fentanyl Combined with Xylazine

Earlier this year, Biden-Harris Administration used executive designation authority for the first time to declare xylazine combined with fentanyl as an emerging threat to the United States.

WASHINGTON, DC — Today, in the continued efforts to fight the dangerous and deadly combination of fentanyl mixed with fentanyl, the White House Executive Office of National Drug Control Policy (ONDCP) released a National Response Plan to coordinate a whole-of-government response against this threat. Earlier this spring, ONDCP exercised the design and an executive designation authority to designate fentanyl combined with xylazine as an emerging threat to the United States and proactively address this dangerous threat head-on.



Fentanyl & Xylazine:

Learn about how street drugs are changing in Maryland

Maryland's Office of Overdose Response

Maryland's Office of Overdose Response promotes collaboration across all state and local agencies working to address substance use and overdose in the state. Learn more here.

Learn more here: StopOverdose.maryland.gov/about.

Addressing Stigma

Tackle the stigma of addiction.

CALL OR TEXT 988



Community Town Halls

Community Overdose Action
Town Hall Series

Hosted by **Maryland's Office of Overdose Response**

Maryland's Office of Overdose Response is visiting each of Maryland's 24 local jurisdictions to hear directly from community members about how we can do more to address the overdose crisis. See a full list of upcoming town halls and summaries of previous events here: <https://www.maryland.gov/newsroom/2023/03/01/overdose-response-town-halls/>

Xylazine "tranq" is in Maryland

What you need to know to stay safe

About Xylazine

Xylazine, which some may refer to as "tranq," is being mixed with street drugs and a person may not even be aware.

Xylazine is not an opioid. It is a very strong sedative used in veterinary medicine. It is not approved for use in humans. (Opioids are a group of drugs that include heroin and prescription medications like oxycodone, hydrocodone, morphine, fentanyl, and methadone.)

Xylazine is being added to street drugs and is **often found in combination with fentanyl** (a powerful synthetic opioid). It has increasingly been detected in overdose deaths.

Xylazine may be added to street drugs, at least in part, to extend the effects of fentanyl. Not everyone who uses fentanyl is intentionally seeking out xylazine. In some cases, people are not aware that xylazine is in the drugs they are buying and using.

The main effect of xylazine is heavy sedation, so the person who has overdosed will likely be unresponsive. When xylazine is found in combination with fentanyl, the signs and symptoms can include blue/grayish skin and slowed breathing and heart rate.

Naloxone

Naloxone (also known as Narcan) will not reverse a xylazine overdose. However, because xylazine is almost always found in combination with opioids, including fentanyl, **naloxone should still be administered whenever an opioid-involved overdose is suspected.**

Learn more about how to find and administer naloxone in Maryland at <https://beforeitstoolate.maryland.gov/naloxone/>.

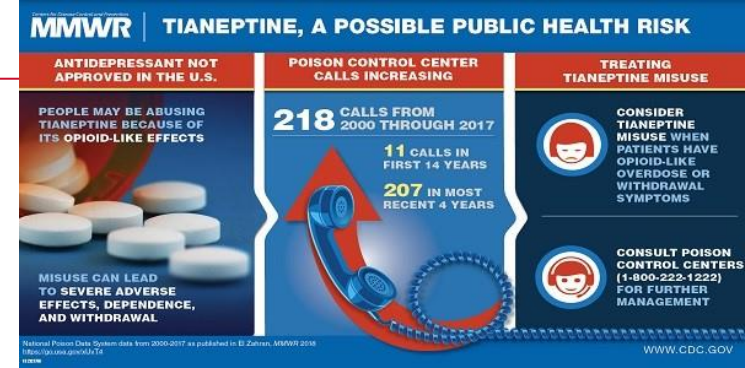


Wound Care

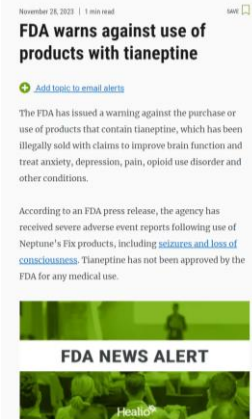


Xylazine is associated with severe wounds that spread and worsen quickly. The wounds occur regardless of how people use: smoking, snorting, or injecting. **People should seek urgent medical attention** if they exhibit extreme pain, fever or chills, if the wound turns black, if there is a foul odor, or if they experience bone and/or tissue tenderness or damage.

TIANEPTINE



- “Tiana”, “Tia”, “Zaza”, “Gas Station Heroin”
- Atypical antidepressant
 - Approved to treat depression & anxiety in > 60 countries- Europe & Asia (Stablon, Coaxil, etc)
 - Most similar to tricyclic antidepressants
- Available in U.S. through DarkWeb
- Misuse in U.S. reported since @ 2000; Increase @ 2015
- μ opioid receptor agonist & δ opioid receptor agonist
- Binds to serotonin transporter but appears to enhance reuptake
- Effects on NMDA Glutamate receptor
 - May increase synaptic plasticity (similar to Ketamine)
- Reports of deaths from respiratory suppression
 - + response to naloxone



TIANEPTINE & PREGNANCY

- Limited data- primarily case reports
- Reports from Europe of neonatal abstinence syndrome
 - Similar to NOWS
 - excessive sucking, poor feeding, sweating, regurgitation, high-pitched crying, frequent yawning & sneezing
 - Treated with morphine
- W

MACS “DESIGNER BENZOS”

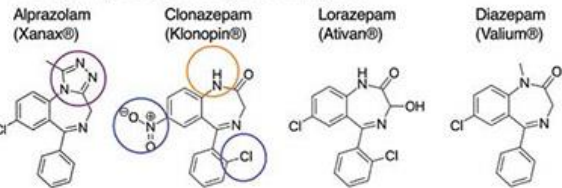


New benzodiazepines in Europe – a review

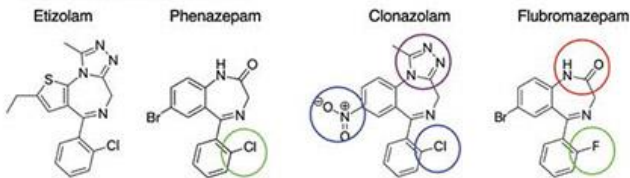
- Many not regulated
- Some available in other countries
 - Available in U.S. on-line
- Used in manufacture of “knock-off” benzos in U.S.

F1 Examples of benzodiazepines approved or not approved by FDA

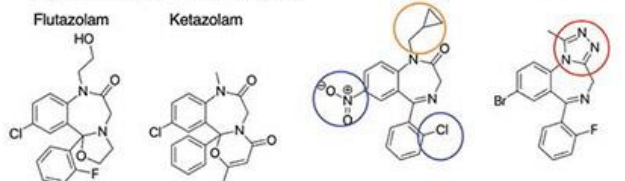
Prescription (FDA-approved) Benzodiazepines



Non (FDA-approved) Benzodiazepines Approved in Other Countries



Atypical Designer Benzodiazepines

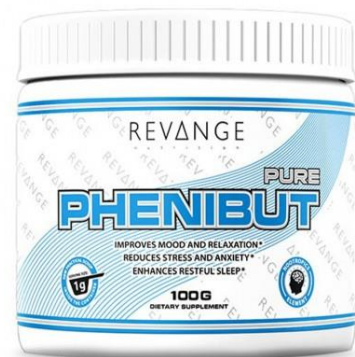


Timeline of benzodiazepines formally notified to the EU Early Warning System for the first time, 2007–2020



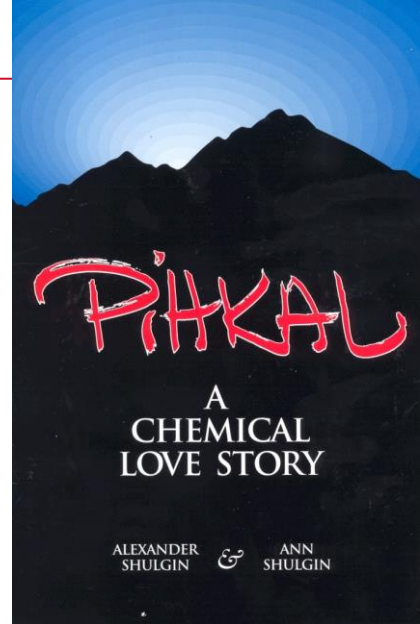
PHENIBUT

- Full agonist GABA-b
- Similar to baclofen
- Anvifen, Fenibut, Bifren, Noofen (Анвифен, Фенибут, Бифрен, Ноофен,)
- Medical use in Russia, Ukraine, Belarus, Latvia
- Unscheduled in U.S.



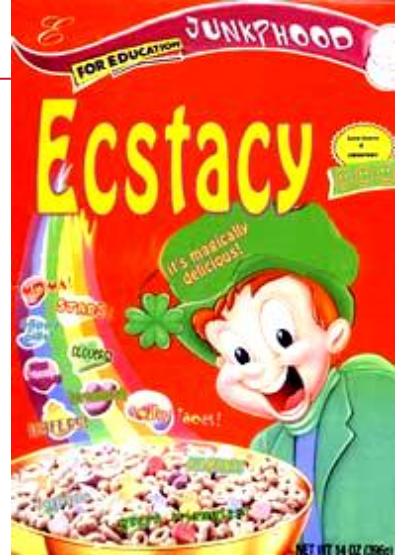
“PSYCHEDELIC/ STIMULANTS”

- “methylated amphetamines”
- over 1000 have been synthesized
- chemically similar to mescaline & amphetamine
- have physiologic and psychological effects of stimulants and hallucinogens
- MDMA
- MDEA, MDA, STP(DOM), 2C-B(Nexus), Aminorex

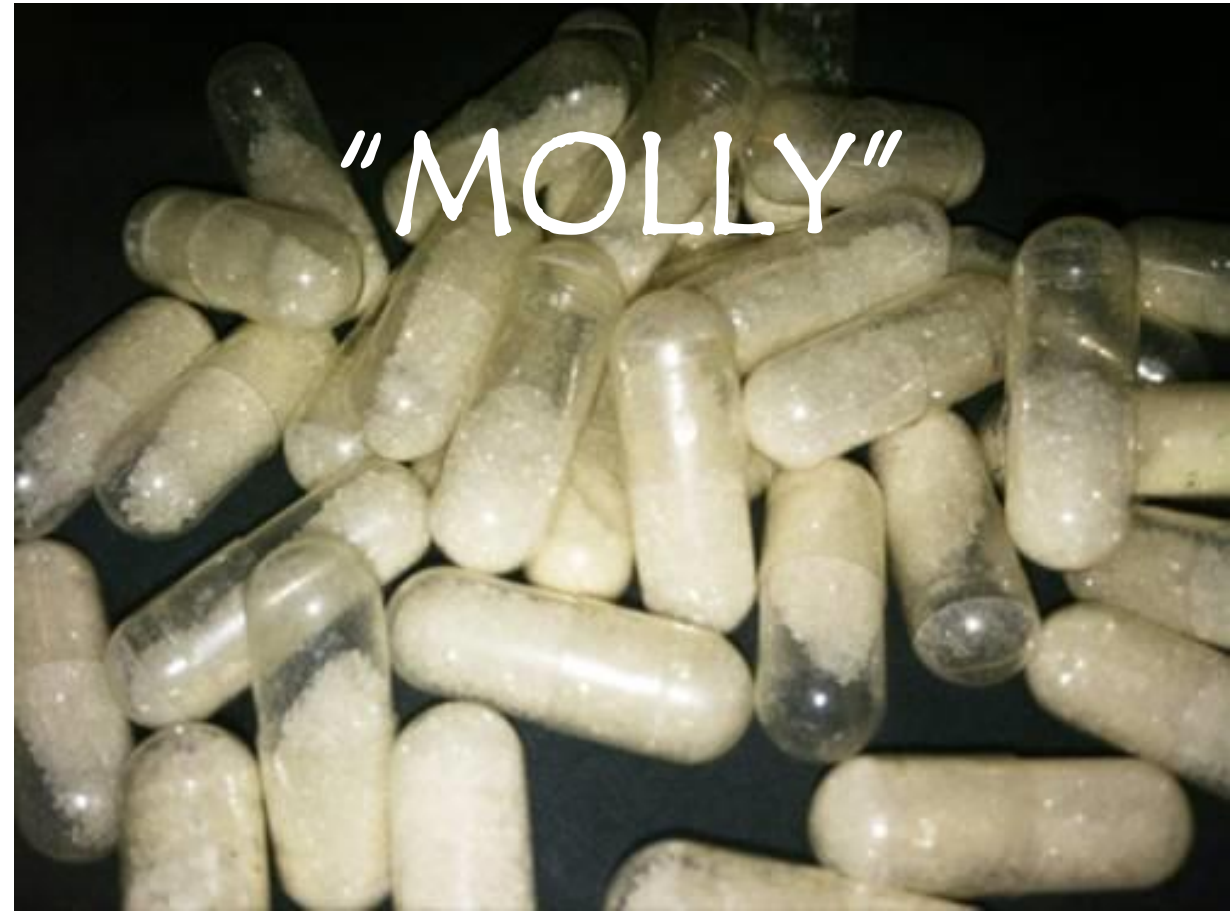


MDMA: HISTORY

- Synthesized by Merck in Germany in 1912
- ? as an appetite suppressant
- Some military research in the 1950s
- Not really used until the early 1970s
 - (after MDA was made schedule I)
- Used in the 1970s & 1980s by therapists to enhance psychotherapy
- Made Schedule I in 1985
- Use peaked in late 1990s-mid 2000s
- Resurgence @ 2012 as MOLLIE(Y)
- New research for PTSD, depression



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- Terrorism
- Economy
- Immigration
- Disasters
- Military
- Education
- Environment
- Pe

Investigators say deaths in Boston, New York, and DC may be linked to 'Molly'

Published September 08, 2013 / FoxNews.com



NBC NEWS INVESTIGATIONS

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Molly deaths may be caused by other drugs



Electric Zoo music festival canceled after 2 deaths blamed on drugs

By Morgan Winsor, CNN
Updated 8:17 AM ET, Tue September 3, 2013

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- Do You Know the Signs of Dementia? 9 Surprising Facts

'Molly' Is Taking A Party Toll in the United States

Reuters | Posted: 09/28/2013 2:59 am EDT | Updated: 09/28/2013 9:28 am EDT

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Wesleyan Students Hospitalized After Molly Overdose

By Jessie Sawyer and Ari Mason

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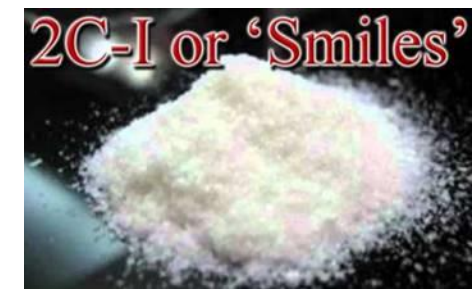


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“SMILES”

- 2C-I
- 2C class are phenethylamines
- Synthesized by Alexander Shulgin
- Used illicitly since the mid-1990s
- Available in Dutch shops in early 2000s.
- Usually in a powder; occasionally a tablet.
 - Some reports of mixing with chocolate.
- Typically snorted or swallowed.
- Effects last 4-12 hours
- DEA Schedule I



N-BOMB

- 25-NBOMe
- AKA: “25I”, “25C”, GNOME”
- Similar to 2-C series
- Action at 5-HT 2A
- DEA Schedule I

engage / buzz
 maskmatters.org

THE NEW DRUG N-BOMB

A new drug marketed as an alternative to LSD or mescaline has surfaced. Commonly known as the “N-bomb,” the drug has been mistaken for LSD, but is considered to be a powerful and potentially deadly synthetic drug. Other street names for the drug include Smiles, 25-I and 25INBOMe.

The N-bomb has raised concern among parents, law enforcement and federal officials because there is no way to determine what they are made of or how the body will react when taken. Vince Figarelli, superintendent of the Arizona Department of Public Safety’s crime lab, says that officials are having trouble dealing with synthetic drugs like the N-bomb because, “one of the problems with all these drugs is that we don’t know how they extract out of the blood and how to recover them.”

There have been several deaths related to the N-bomb in states including Arizona, North Dakota and Louisiana. In one incident,

2-(4-iodo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine (25I-NBOMe) Grams MG 51

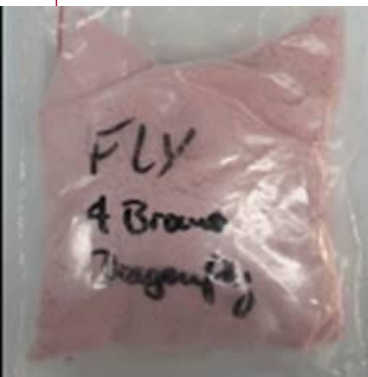
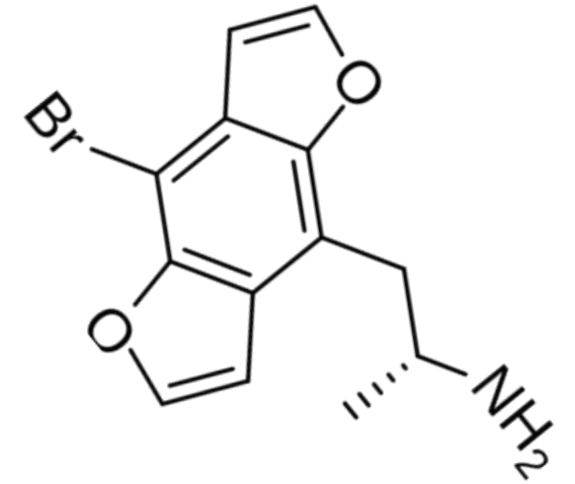
PROUDLY SPONSORED BY CBI COMMUNITY BRIDGES, INC. Thank You

a 19-year-old man spent four days in the hospital in an induced coma because doctors could not stop his seizures. A week later, the agitation and hallucinations resolved, but the man was still suffering from episodes of forgetfulness.

Because there have not been in-depth medical studies on the N-bomb, it’s been difficult for law enforcement to keep up with new developments in such street drugs on a day-to-day basis. The chemical makeup of the N-bomb is so simple, some suggest that a person with a basic knowledge of chemistry could reproduce it. This is the biggest problem that law enforcement faces: staying up to date on the constantly changing realm of synthetic drugs, identifying them, and spreading the word about the dangers they pose.

BROMO-DRAGONFLY

- 3C-Bromo-Dragonfly; “DOB-Dragonfly”; “Fly”
- Synthesized in 1998.
- Similar to phenethylamines.
- Acts at several serotonin receptor types.
- Very potent (1/5 that of LSD).
- Effects can last several days.
- May see vasoconstriction.
- Usually a powder or on blotter paper.
- Popular in Scandinavia but seen in U.S.
- Deaths reported from seizures & vomiting blood.
- Not DEA scheduled in the U.S.



A photograph of a blue product label for "Dragonfly". The label contains the following information:

PRODUCT NAME	Dragonfly
CHEM. NAME	1-(3-bromobenzyl)-2-(2,4,5-trimethoxyphenyl)propan-1-amine
CHEM. FORMULA	C ₁₃ H ₁₂ BrNO ₂
MOLECULAR MASS	294.15 g/mol
CONTENTS	solution

FOR INTERNAL USE ONLY (仅供内部使用) - 内部使用
FORMULA: 1-(3-bromobenzyl)-2-(2,4,5-trimethoxyphenyl)propan-1-amine

PIPERAZINES



- Original research in 1970s as antihelminthics
- Most popular benzylpiperazine (BZP)
 - Schedule I in 2002
- Trifluoromethylphenylpiperazine (TFMPP)
- 6-(2-aminopropyl)benzofuran (6-APB)
- Very popular in Australia and New Zealand
- “Cosmic Jet”, “Charge”, “Benzo Fury”, “Exotic Super Strong”, “XXX Strong as Hell”
- Stimulant effects at lower dose
- Hallucinogenic effects at higher dose
 - Effects serotonin reuptake, increases release & acts as agonist
- Typically snorted or taken orally
- Delayed onset of action (1-2 hours)
- Effects last 6-8 hours.
- Reports of seizures, QT prolongation, Serotonin Syndrome



5-MEO-DMT

- 5-methoxy-dimethyltryptamine
- Similar to DMT
- Found in several South American plants and in the venom of the *Bufo alvarius* toad
- Typically smoked, inhaled or injected
- Can be ingested orally with an MAO inhibitor
- Can be extracted from plants or synthesized
- About \$300 per gram through mail order

Venom of *Bufo alvarius*



KETAMINE

- Similar to phencyclidine (PCP)
- Dissociative anesthetic
- Modulated NMDA receptor; some effects on NE, DA, 5-HT
- *Special K, K, Jet, Super K, Vitamin K, Kit Kat, Cat Valiums*
- First manufactured in 1965
- Misuse probably began in the late 1960s
- Much of what is misused is diverted from manufacturers and suppliers of medical & veterinary drug
- Comes in a liquid form or a white powder
 - Liquid often “cooked” in microwave to get powder
- Typically snorted; can be smoked or injected
- Onset typically 30 seconds to 30 minutes



METHOXETAMINE

- Synthetic analog of ketamine
- 3-MeO-PCE (also 3-MeO-PCP, 4-MeO-PCP)
- Aka: “MXE”; “M-Ket”; “Kmax”; “Mexxy”; “Roflcopter”
- First reported in Europe in 2010
- Typically a white powder
- Usually snorted; occasionally ingested
- Primarily inhibits NMDA; effect on DA & 5-HT reuptake
- Reportedly more intense than ketamine; less than PCP
- Onset in 5-10 minutes
- Duration 1-2 hours with some reports of much longer
- Unscheduled in U.S.
- Also methoxyketamine 2-MeO-ketamine



STIMULANTS

- Cocaine
- Methamphetamine
- Prescription

- Methylphenidate- (Ritalin, Concerta, Contempla, Daytrana, Focalin)
- Amphetamine- (Adderall, Adzenys, Dyanavel)
- Lisdexamfetamine- (Vyvanse)

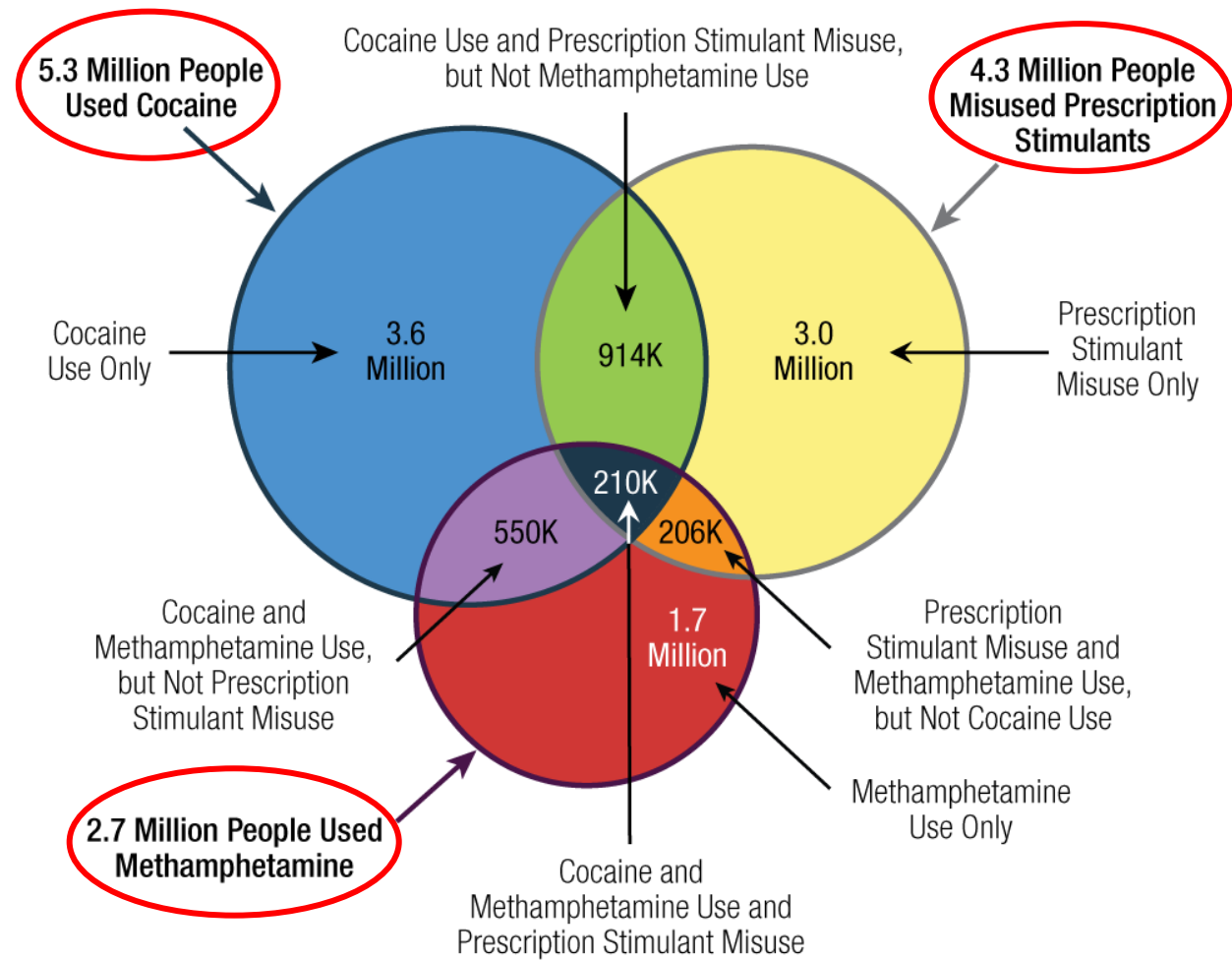
- Other Non- Amphetamine

- Cathinone (“Khat”) -MDPV (“Bath Salts”)
- Metcathinone -alpha PVP (“Flakka”)
- Eutylone -MDMA (“Mollie”) and others



STIMULANT MISUSE

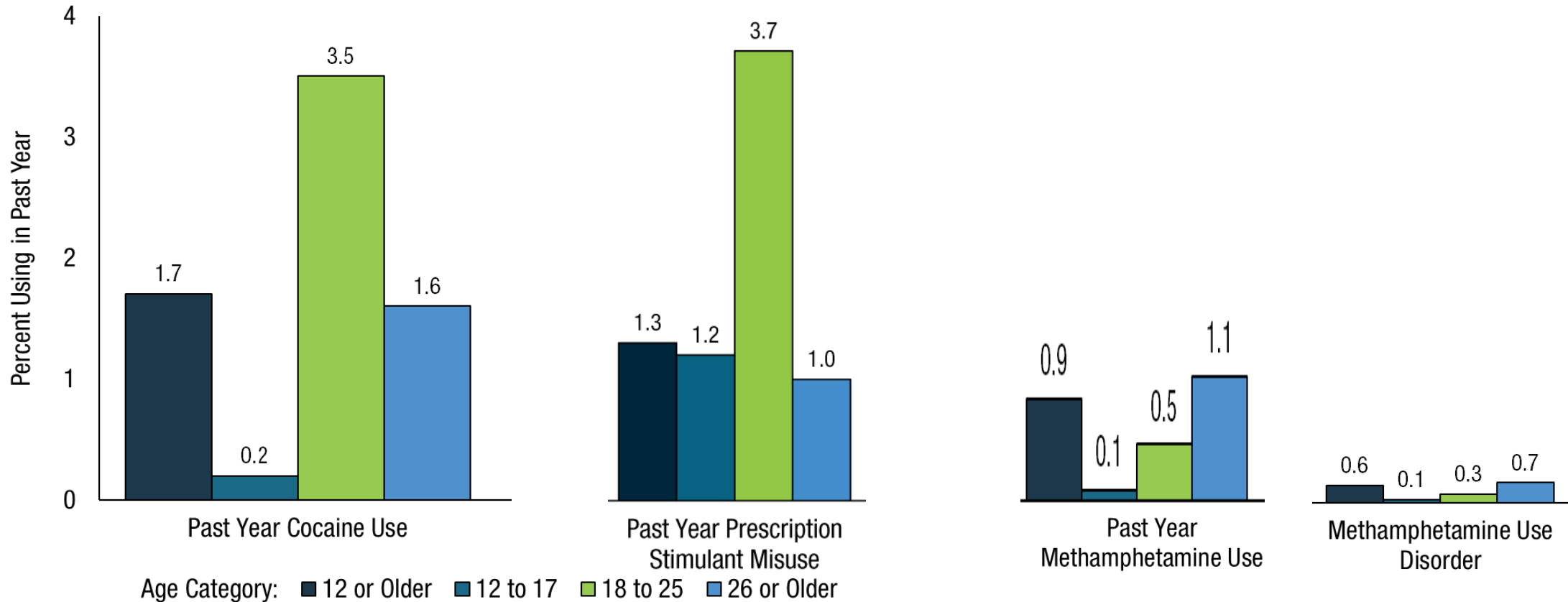
(PAST YEAR; AGED 12 OR OLDER; NSDUH; 2022)



10.2 Million People Aged 12 or Older with Past Year CNS Stimulant Misuse

STIMULANT MISUSE

(past year; aged 12 or older; NSDUH; 2021)



OVERDOSE DEATHS INCLUDING STIMULANTS:

Past 12 Months(CDC; 2022)

“P2P”?

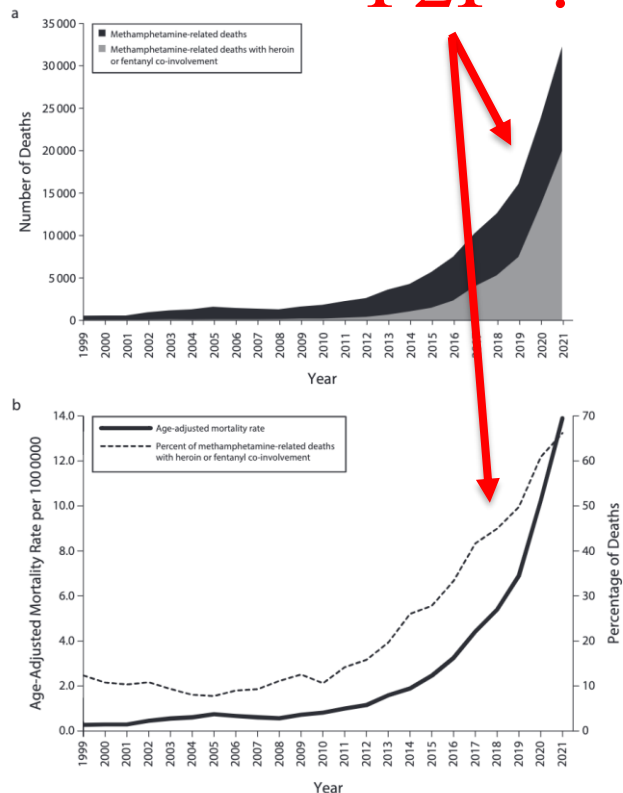
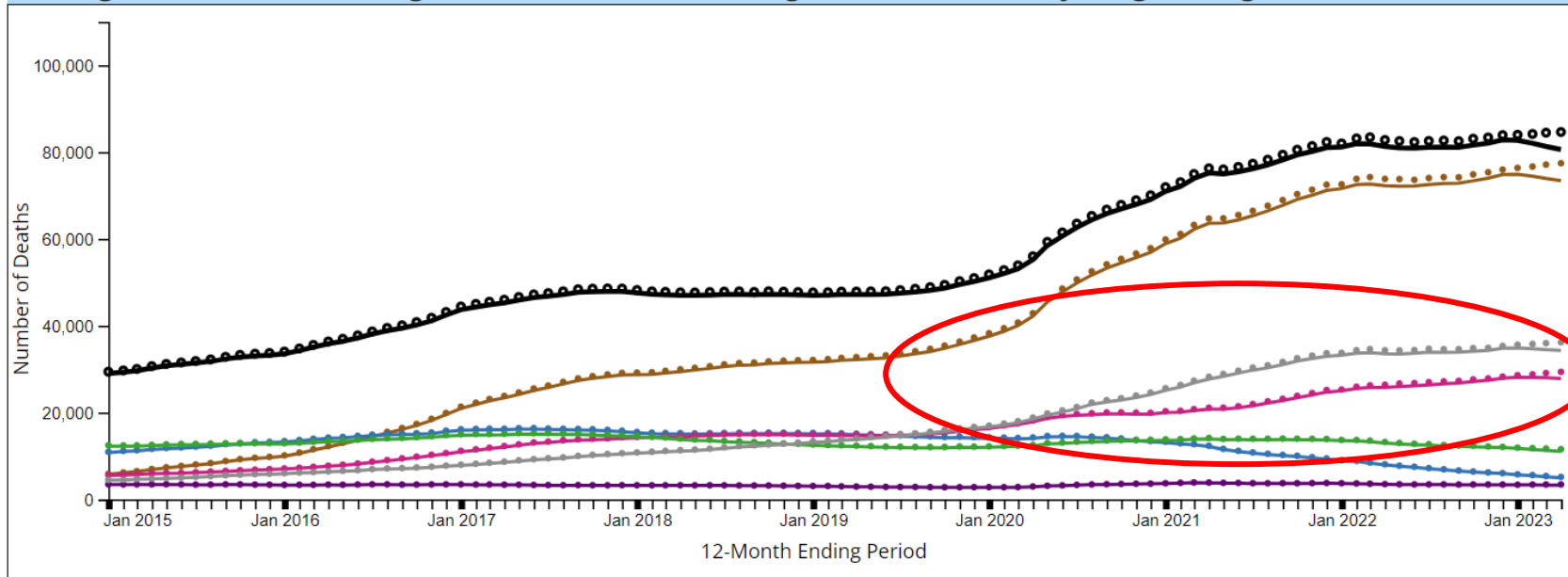


Figure 2. 12 Month-ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class: United States



Legend for Drug or Drug Class

Cocaine (T40.5)

Heroin (T40.1)

Methadone (T40.3)

Natural & semi-synthetic opioids (T40.2)

Opioids (T40.0-T40.4,T40.6)

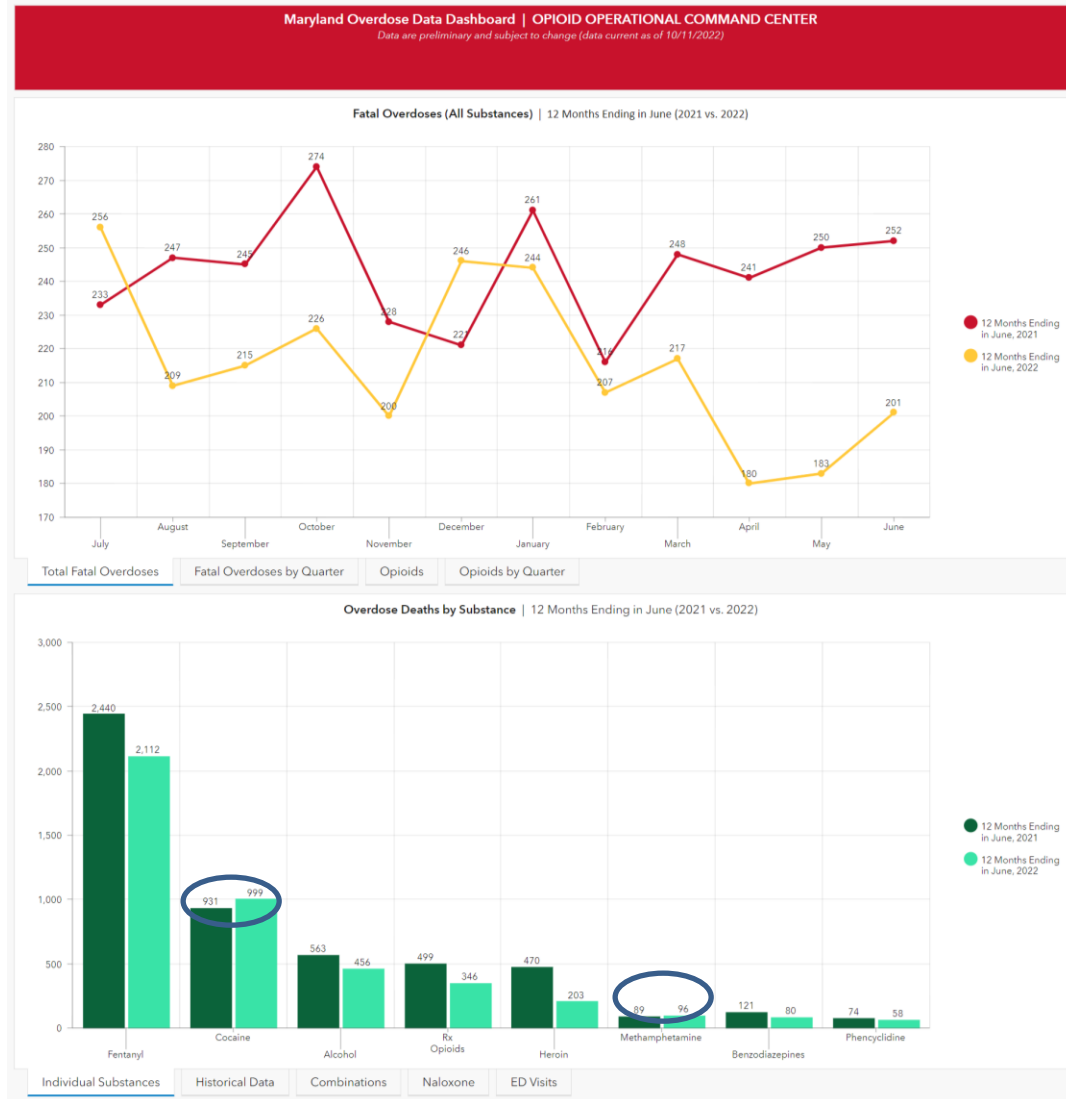
Psychostimulants with abuse potential (T43.6)

Synthetic opioids, excl. methadone (T40.4)

--- Reported Value

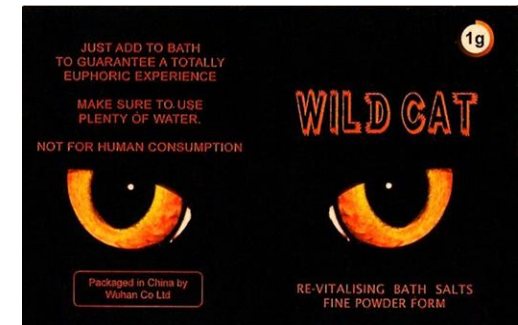
○ Predicted Value

FATAL OVERDOSES: MD (OCC; 2022)



SYNTHETIC STIMULANTS

- Many are Cathinones
- Often contain
 - methylenedioxypropylamphetamine (MDPV)
 - Mephedrone
- Similar to Methcathinone (Ephedrone)
- “Bath Salts”
 - Ivory Snow, Red Dove, Cloud Nine, Vanilla Sky, Ivory Wave, Lunar Wave, Bliss, White Lightning and Hurricane Charlie, Meow Meow, Bliss, Blast, Bloom, PeeVee, Meph
- First reported in U.S. around 2008
- \$20-\$80 per packet
- MDPV 10X more potent than cocaine w/ stimulant effects
- Typically snorted; occasionally injected
- Effects last 2-8 hours
- Reports of continued psychosis for weeks
- Blocks DA & NE reuptake similar to cocaine
- Not a transporter substrate



**EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF NATIONAL DRUG CONTROL POLICY**
Washington, DC 20503

FOR IMMEDIATE RELEASE:

Tuesday, February 1, 2011

CONTACT:

ONDCP Public Affairs: 202-395-
6618

MediaInquiry@ondcp.eop.gov

Statement from White House Drug Policy Director on Synthetic Stimulants, a.k.a “Bath Salts”

Washington, D.C. – Today, Gil Kerlikowske, Director of National Drug Control Policy, released the following statement following recent reports indicating the emerging threat of synthetic stimulants, including MDPV (3,4-methylenedioxypropylvalerone) and mephedrone. These stimulants are often sold and marketed in stores as “bath salts” under names such as “Ivory Wave” or “Purple Wave.”

EUTYLONE

- A Cathinone
- Synthesized in 1960s
- Illicit use beginning @ 2019
- “Replacing” methylone/ethylone
- Less potent than some others

“TRASH CAN”



Unidentified Dangerous Substance Distributed in “Trashcan” Containers Tied to ED Patients with Combative Behavior

Prepared By: Natalie Butler Report Date: 09/18/2020
 Information Type: Drug - General Report ID: 1487

Synopsis:
 Several patients in a Baltimore City hospital exhibited erratic and combative behavior after ingesting an unknown substance distributed in “trashcan” containers.

Details:
 The Behavioral Health Administration of the Maryland Department of Health (BHA MDH) shared information about incidents on August 19, 2020 at the Emergency Department at Union Memorial Hospital in Baltimore, MD involving irregular, at times combative, patient behavior after ingesting an unidentified dangerous substance referred to as “Trash Can.” Patients presented with “excited delirium,” hallucinations, erratic behavior and were combative. Five or six patients were reported to have taken “Trash Can,” described as a clear capsule with a hinge that was being distributed in the area as free samples. Users reported to have opened the capsule and ingested or snorted the contents. All of the patients had hallucinations and were combative requiring massive doses of sedatives. Some patients reported that they have used what they thought to be a synthetic drug.

- Patient 1: 39 years old, male; discharged after five hours, required Haldol and 6 mg Ativan.
- Patient 2: 52 years old, male; was admitted “out of it.” Required Benadryl, Haldol PO and IM, midazolam IV and IM x 2. No tachycardia (heart rhythm disorder) or hypertension (high blood pressure), was writhing at times.
- Patient 3: female, age unknown; was admitted for at least nine hours, combative, was given Naloxone by EMS due to shallow breathing, has history of substance abuse, was given Haldol 7.5 mg total + 2 mg Ativan, had to be restrained and woke up with no memory of the incident.
- Patient 4: 53 years old, female; admitted for 3 hours, vitals were stable, was given Haldol, Benadryl, Ativan, and IV fluids.

- Plastic containers with hinged lid
- Cylinder or cone
- 1st seen in Maryland in 2019
 - Found in northeast, eastern shore, southern, western Maryland & Baltimore City
- Found to contain:
 - Heroin
 - Fentanyl
 - Cocaine
 - Xylazine
 - Eutylone



Suspected drug was reported to be a synthetic cannabinoid or cathinone; however these drugs often cause tachycardia or high blood pressure.

Secondary suspected drug: PCP or similar drugs. Additional comments from the MDH point to an uptick in PCP-related visits at the UM Capital Region Medical Center in Prince George’s County, MD.

No specific treatment was recommended.

Analyst Note:
 The “trashcan” drug packaging type has made appearance in several counties in Maryland throughout 2019-2020 containing a variety of drugs. In 2019, the Heroin Coordinator Intelligence Sharing Network reported seizures of plastic “trashcan” containers with suspected heroin in southern Maryland and in the Eastern Shore region. During 2020, several locations reported seizures of green, fluorescent yellow, pink, blue, clear, and orange containers with a hinged lid. In the north-east part of Maryland, seized “trashcans” contained suspected heroin, crack cocaine, and possibly a mixture of fentanyl and tranquilizer Xylazine, often referred to as “Tranq.” Most recent seizures revealed “trashcans” with substance that tested positive for Eutylone, also known as “bath salts.” Several drug samples submitted to the Maryland State Police Forensic Sciences Division during 2020 in similar containers tested positive for Eutylone. The Carroll County Health Department reported a patient with a history of multiple overdose incidents, who exhibited behavior similar to the symptoms reported in the Union Memorial hospital. The substance has not been confirmed.

Image 1: “Trashcan” Drug Packaging Type Seized in Maryland in 2019 – 2020.



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METHAMPHETAMINE

- “Meth”, “Crystal”, “Speed”
- Seeing more in Maryland
 - especially west, eastern shore, southern and northeast
- “P2P Meth” (phenyl-2-propanone)
 - Not ephedrine/pseudoephedrine-based
 - Seems to produce more d-isomer
- May cause more psychiatric and medical problems



MACS SYNTHETIC CANNABINOIDS

- Cyclohexphenols (non-classical) developed in mid 1980s
- First “classical” synthesized in Israel (Hebrew University) in 1988 (HU-210)
- John W. Huffman created first ones in the mid 1990s (JWH-018; JWH-250)
- Methods for synthesizing were published in scientific literature, & thus available to all
- Appeared in Europe’s underground drug market in 2004, then in the U.S. around 2006
- Sprayed onto herbs (bay bean, blue lotus, etc)
- Marketed as incense or aromatic potpourri
- Most commonly smoked (joint, bowl or bong)



MACS SYNTHETIC CANNABINOIDS

- Variable similarity in function to THC
- Full Agonist at CB1 & CB2 receptors (THC is a partial agonist)
 - Aminoalkylindoles, Cyclohexylphenols, Dibenzopyrans
 - Bind CB1 50-30X greater than THC
- Metabolites are also active
- Faster onset
- Lack cannabidiol (CBD; may blunt some of the adverse actions of THC)
- Likely higher risk of causing psychosis
- Seizures and other medical complications not seen with marijuana



Schedules of Controlled Substances:

Temporary Placement of Five Synthetic Cannabinoids Into Schedule I Notice of Intent

by Drug Enforcement Administration, U.S. Department of Justice

v1.0 - Nov 24, 2010

from the Federal Register: November 24, 2010 (Volume 75, Number 226), pp 71635-71638

The following DEA notice is a notice of *intent* to emergency schedule five synthetic cannabinoid receptor agonists. It does not become final, and the substances are NOT placed in Schedule I, until a mandatory 30-day comment period has elapsed and a final notice has been published in the Federal Register.

[Federal Register: November 24, 2010 (Volume 75, Number 226)]

[Proposed Rules]

[Page 71635-71638]

From the Federal Register Online via GPO Access [wais.access.gpo.gov]

[DOCID:fr24no10-45]

JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol

Synthetic Drug Abuse Prevention Act of 2012

Posted: July 18th, 2012



From the July 10, 2012 ONDCP announcement...

Dear Friends:

Yesterday, President Obama signed the Synthetic Drug Abuse Prevention Act of 2012 into law as part of S. 3187, the Food and Drug Administration Safety and Innovation Act. This important piece of legislation provides a critical boost to our nation's efforts to address the threat of synthetic drugs. The legislation bans synthetic compounds commonly found in synthetic marijuana ("K2" or "Spice"), synthetic stimulants ("Bath Salts"), and hallucinogens, by placing them under Schedule I of the Controlled Substances Act.

Although this Federal ban provides a valuable tool in keeping these dangerous substances off the shelves, we would encourage states that have not already done so to incorporate these substances into their state drug schedules to ensure that state law enforcement agencies have full authority to act against these substances. The Drug Enforcement Administration will continue to work with state and local authorities to investigate major distribution networks, but retail and community-level enforcement will continue to occur largely on a state and local level.

We expect that this law will have an impact on illicit sales of these newly scheduled synthetic drugs, at least in the short term. However, Federal and state agencies will have to continue to update the list of banned substances as new synthetic compounds emerge. In addition, some states and localities have also experienced success in using additional health, safety, or agricultural authorities to remove these substances from retail shelves.

Research shows that preventing drug use before it begins is a cost-effective, common-sense approach to promoting safe and healthy communities. In the coming weeks, ONDCP will be unveiling a *Synthetic Drug Prevention Toolkit*, which we hope will serve as a resource for communities dealing with this issue.

ONDCP is committed to partnering with our state, local, and community partners in addressing this challenge. As always, we are eager to hear from you on what you are seeing in your community and what is working in your own efforts.

Sincerely,

R. Gil Kerlikowske

S. 605 Dangerous Synthetic Drug Control Act of 2011



Sponsor
Charles Grassley

CoSponsors

Bill Status Placed on Senate Legislative Calendar under General Orders. Calendar No. 122.

Summary

Full Text

Bill Activity

Analysis (1)

Comments (0)

7/29/2011--Reported to Senate without amendment. (There is 1 other summary)

(This measure has not been amended since it was introduced. The summary of that version is repeated here.)

Dangerous Synthetic Drug Control Act of 2011 or David Mitchell Rozga Act - Amends the Controlled Substances Act to add as a schedule I controlled substance any material, compound, mixture, or preparation which contains specified cannabimimetic agents (or the salts, isomers, or salts of isomers thereof).

Extends the period during which the Attorney General may temporarily schedule a substance in schedule I to avoid an imminent hazard to public safety to two years with a one-year extension (currently, one year with a six-month extension).

S. 3187 (112th): Food and Drug Administration Safety and Innovation Act

Subtitle D—Synthetic Drugs

SEC. 1151. SHORT TITLE.

This subtitle may be cited as the "Synthetic Drug Abuse Prevention Act of 2012".

SEC. 1152. ADDITION OF SYNTHETIC DRUGS TO SCHEDULE I OF THE CONTROLLED SUBSTANCES ACT.

(a) CANNABIMIMETIC AGENTS.—Schedule I, as set forth in section 202(c) of the Controlled Substances Act (21 U.S.C. 812(c)) is amended by adding at the end the following:

"(d)(1) Unless specifically exempted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of cannabimimetic agents, or which contains their salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation.

"(2) In paragraph (1):

"(A) The term 'cannabimimetic agents' means any substance that is a cannabinoid receptor type 1 (CB1 receptor) agonist as demonstrated by binding studies and functional assays within any of the following structural classes:

"(i) 2-(3-hydroxycyclohexyl)phenol with substitution at the 5-position of the phenolic ring by alkyl or alkenyl, whether or not substituted on the cyclohexyl ring to any extent.

"(ii) 3-(1-naphthoyl)indole or 3-(1-naphthylmethane)indole by substitution at the nitrogen atom of the indole ring, whether or not further substituted on the indole ring to any extent, whether or not substituted on the naphthoyl or naphthyl ring to any extent.

"(iii) 3-(1-naphthoyl)pyrrole by substitution at the nitrogen atom of the pyrrole ring, whether or not further substituted in the pyrrole ring to any extent, whether or not substituted on the naphthoyl ring to any extent.

"(iv) 1-(1-naphthylmethylene)indene by substitution of the 3-position of the indene ring, whether or not further substituted in the indene ring to any extent, whether or not substituted on the naphthyl ring to any extent.

"(v) 3-phenylacetylindole or 3-benzoylindole by substitution at the nitrogen atom of the indole ring, whether or not further substituted in the indole ring to any extent, whether or not substituted on the phenyl ring to any extent.

"(B) Such term includes—

"(i) 5-(1,1-dimethylheptyl)-2-[(1R,3S)-3-hydroxycyclohexyl]-phenol (CP-47,497);

"(ii) 5-(1,1-dimethylhexyl)-2-[(1R,3S)-3-hydroxycyclohexyl]-phenol (cannabicyclohexanol) or CP-47,497 C8-homolog;

"(iii) 1-pentyl-3-(1-naphthoyl)indole (JWH-018 and AM208);

"(iv) 1-butyl-3-(1-naphthoyl)indole (JWH-073);

"(v) 1-hexyl-3-(1-naphthoyl)indole (JWH-019);

"(vi) 1-[2-(4-morpholinyl)ethyl]-3-(1-naphthoyl)indole (JWH-200);

"(vii) 1-pentyl-3-(2-methoxyphenylacetyl)indole (JWH-250);

"(viii) 1-pentyl-3-[1-(4-methoxynaphthoyl)indole (JWH-081);

"(ix) 1-pentyl-3-(4-methyl-1-naphthoyl)indole (JWH-122);

"(x) 1-pentyl-3-(4-chloro-1-naphthoyl)indole (JWH-398);

"(xi) 1-(5-fluoropentyl)-3-(1-naphthoyl)indole (AM2201);

"(xii) 1-(5-fluoropentyl)-3-(2-iodobenzoyl)indole (AM694);

"(xiii) 1-pentyl-3-[(4-methoxy)benzoyl]indole (SR-19 and RCS-4);

"(xiv) 1-cyclohexylethyl-3-(2-methoxyphenylacetyl)indole (SR-18 and RCS-8); and

"(xv) 1-pentyl-3-(2-chlorophenylacetyl)indole (JWH-203)."

(b) OTHER DRUGS.—Schedule I of section 202(c) of the Controlled Substances Act (21 U.S.C. 812(c)) is amended in subsection (c) by adding at the end the following:

"(18) 4-methylmethcathinone (Mephedrone);

"(19) 3,4-methylenedioxypropylverone (MDPV);

"(20) 2-(2,5-Dimethoxy-4-ethylphenyl)ethanamine (2C-E);

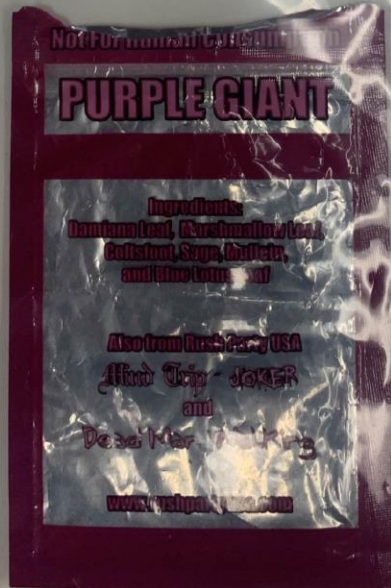
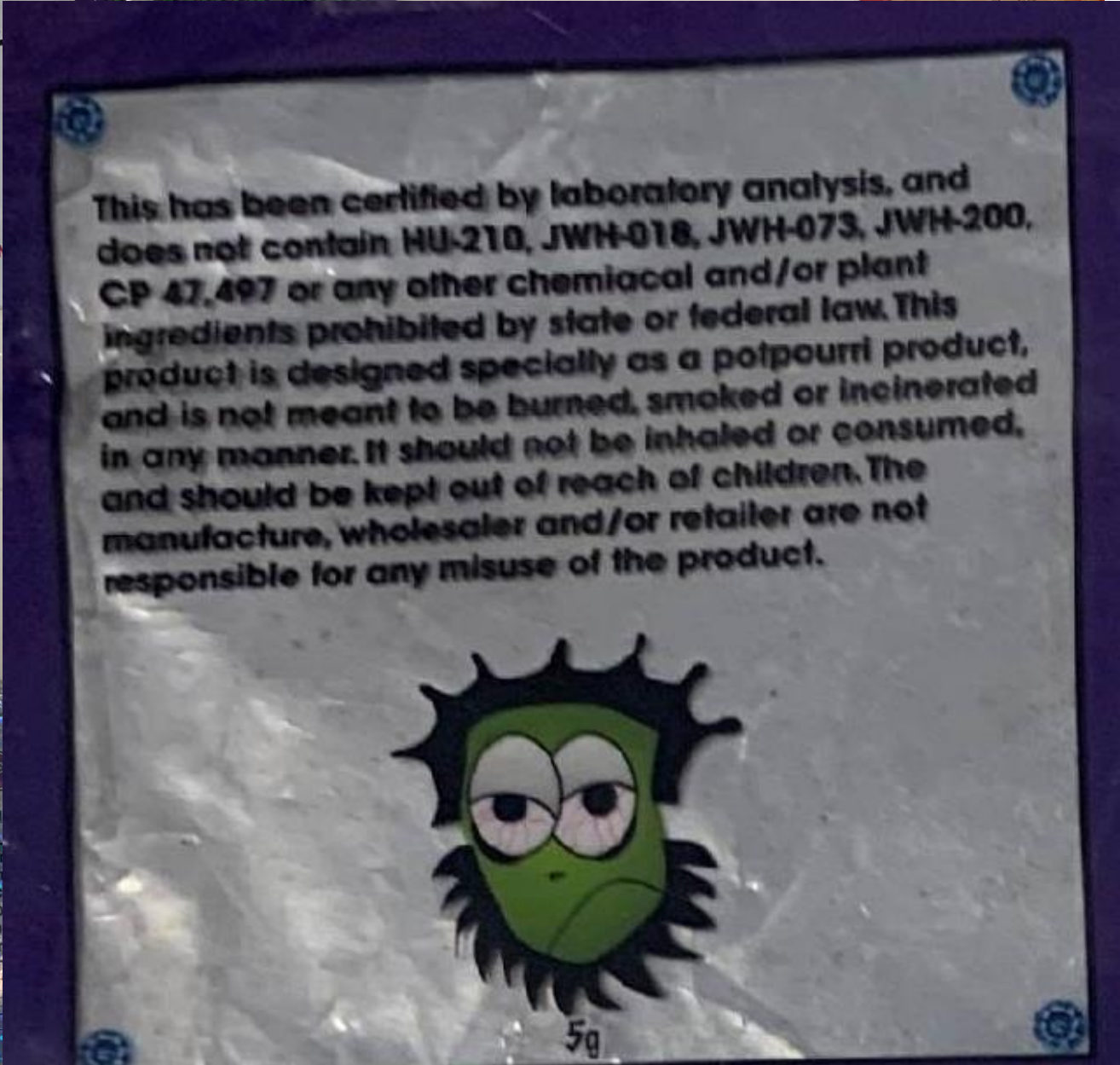
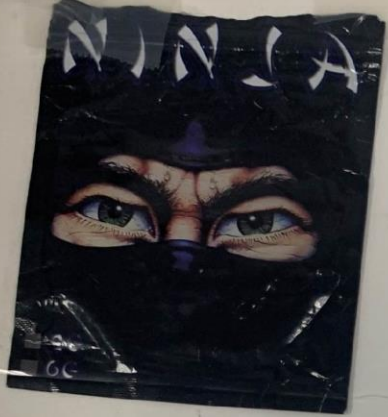
"(21) 2-(2,5-Dimethoxy-4-methylphenyl)ethanamine (2C-D);

"(22) 2-(4-Chloro-2,5-dimethoxyphenyl)ethanamine (2C-C);

"(23) 2-(4-Iodo-2,5-dimethoxyphenyl)ethanamine (2C-I);

"(24) 2-(4-Ethylthio-2,5-dimethoxyphenyl)ethanamine (2C-T-2)."

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SYNTHETIC CANNABINOIDS:

“THE NEXT GENERATION”

- Newer compound, URB-754: Does NOT bind to CB receptors itself, but inhibits enzyme that breaks down endocannabinoids
 - More endocannabinoid around → more binding to receptors
- AND, one “spice” sample was found to contain URB + a cathinone, which reacted with one another and together created a whole new psychoactive compound



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URB-754: A new class of designer drug and 12 synthetic cannabinoids detected in illegal products[☆]

Nahoko Uchiyama, Maiko Kawamura, Ruri Kikura-Hanajiri, Yukihiro Goda *

National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo 158-8501, Japan

To Your Health

Synthetic marijuana leaves two dead and dozens with severe bleeding



Synthetic cannabinoids, also known as K2, are man-made drugs often marketed as a safe, legal alternative to marijuana. (Elyse Samuels/The Washington Post)



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SEARCH

FIRST MARYLAND CASE OF BLEEDING REPORTED IN USER OF SYNTHETIC CANNABINOIDS

[Home](#) / [News Center](#) / [News \(2018\)](#) / [First Maryland Case of Bleeding Reported in User of Synthetic Cannabinoids](#)

[Back to Home](#)

[News Center](#)

[Archive](#)

Maryland Poison Center notified of a case in which a user of synthetic cannabinoids experienced bleeding and was hospitalized on April 3.

By: Maryland Department of Health
Thursday, April 5, 2018

Baltimore, Md. — The Maryland Poison Center and the Maryland Department of Health are warning the public of the danger of bleeding that can be linked to use of synthetic cannabinoids, also known as spice, K2, or fake weed.

The Maryland Poison Center at the University of Maryland School of Pharmacy was notified of a case in which a user of synthetic cannabinoids experienced bleeding and was hospitalized on April 3, 2018.

The symptoms in the Maryland case are similar to the description of dozens of cases in the Chicago region reported over the past two months to the Illinois Poison Center.



SALVIA DIVINORUM

- AKA: "Yerba Maria", "The Shepherdess", "la pastora", "Diviner's Mint", "Diviner's Sage"
- Indigenous to Southern Mexico
- Used in traditional healing and divination
- Smoked, chewed, or made into tea
- Currently not controlled in U.S.
- Available in stores in 5X, 6X, and 10X conc.
- \$50-\$100/ounce leaves; \$20-\$50/gram conc.
- Salvinorin A
 - K-opioid receptor agonist
 - No serotonin activity



Flowering *Salvia divinorum*
Photo by Knehnay



Salvia Divinorum Leaves
Photo by Knehnay, © 2001 Erowid.org

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THANK YOU

