Xylazine Trends and Toxicology:
Role of an Overdose Fatality Review

May 2023

BJA Director Karhlton F. Moore

Appointed by President Biden in February 2022, Director Moore leads BJA's programmatic and policy efforts on providing a wide range of resources, including training and technical assistance, to law enforcement, courts, corrections, treatment, reentry, justice information sharing, and community-based partners to address chronic and emerging criminal justice challenges nationwide.

Policy Office	Programs Office	Operations Office	Public Safety Officer Benefits Office
provides national leadership to criminal justice organizations that partner with BJA to identify effective program models for replication and infuse data-driven, evidence-based strategies into operational models, practices, and programs.	administers state, local, tribal, and territorial grant programs. It acts as BJA's direct line of communication to states, local jurisdictions, territories, and tribal governments by providing customer-focused grants management support and careful stewardship over federal funds.	coordinates all communication, formulates and executes the budget, manages contracts, measures grantees' performance, and provides administrative support to BJA.	provides death and education benefits to survivors of fallen law enforcement officers, firefighters, and other public safety officers, and disability benefits to officers catastrophically injured in the line of duty.

Overdose Fatality Review Team

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Presentation Agenda

- Provide an overview of overdose fatality reviews.
- Describe xylazine and fentanyl drug trends.
- Review medical use and signs and symptoms of fentanyl and xylazine use and withdrawal.
- Explain xylazine toxicology, lab testing, and medical treatment.
- Summarize the roles of High Intensity Drug Trafficking Areas (HIDTA) and poison centers/toxicologists as OFR members.

Overdose Fatality Review Overview

- OFRs involve analysis and **review of aggregate data** to understand overdose trends, select cases to review, and provide context for case findings and recommendations
- OFRs involve a series of **confidential individual death reviews** by a multidisciplinary team to effectively **identify system gaps and innovative community-specific** overdose prevention and intervention strategies
- These recommendations are presented to a governing committee that supports and provides resources for implementation framework for accountability for action

The "SOS" Process

Shared understanding	OFRs increase members' understanding of area agencies' roles and services as well as the community's assets and needs, substance use and overdose trends, current prevention activities, and system gaps.
Optimized capacity	OFRs increase the community's overall capacity to prevent future overdose deaths by leveraging resources from multiple agencies and sectors to increase system-level response.
Shared accountability	OFRs continually monitor local substance use and overdose death data as well as recommendation implementation activities. Status updates on recommendations are shared at each OFR team meeting and with a governing committee, reinforcing accountability for action.

OFR
Overdose Fatality Review

Director of White House Office of National Drug Control Policy (ONDCP) Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States

Source: https://www.whitehouse.gov/ondcp/briefing-room/2023/04/12/biden-harris-administration-designates-fentanyl-combined-with-xylazine-as-an-emerging-threat-to-the-united-states/

Xylazine: Drug Enforcement Administration (DEA) Findings

- Between 2020 and 2021, forensic laboratory identifications of xylazine rose in all four U.S. census regions, most notably in the south (193%) and the west (112%).
- Xylazine-positive overdose deaths increased by 1,127% in the south, 750% in the west, more than 500% in the Midwest, and more than 100% in the northeast.

Source: https://www.dea.gov/sites/default/files/2022-12/The%20Growing%20Threat%20of%20Xylazine%20and%20its%20Mixture%20with%20Illicit%20Drugs.pdf

Adverse Effects and Overdoses

- When combined with fentanyl or other synthetic opioids, xylazine can increase the potential for fatal overdoses, as the similarity in pharmacological effects can further reduce the already decreased respiratory function.
- Overdoses associated with xylazine may be more difficult to identify in clinical settings, as they often appear similar to opioid overdoses and may not be included in routine drug screening tests.
- A comprehensive count of xylazine-positive a overdose deaths in the United States is not currently possible, as not all jurisdictions routinely conduct testing for xylazine in postmortem toxicology. Testing procedures can vary even within the same state

Source: https://www.dea.gov/sites/default/files/2022-12/The%20Growing%20Threat%20of%20Xylazine%20and%20its%20Mixture%20with%20Illicit%20Drugs.pdf

Xylazine

05/18/2023

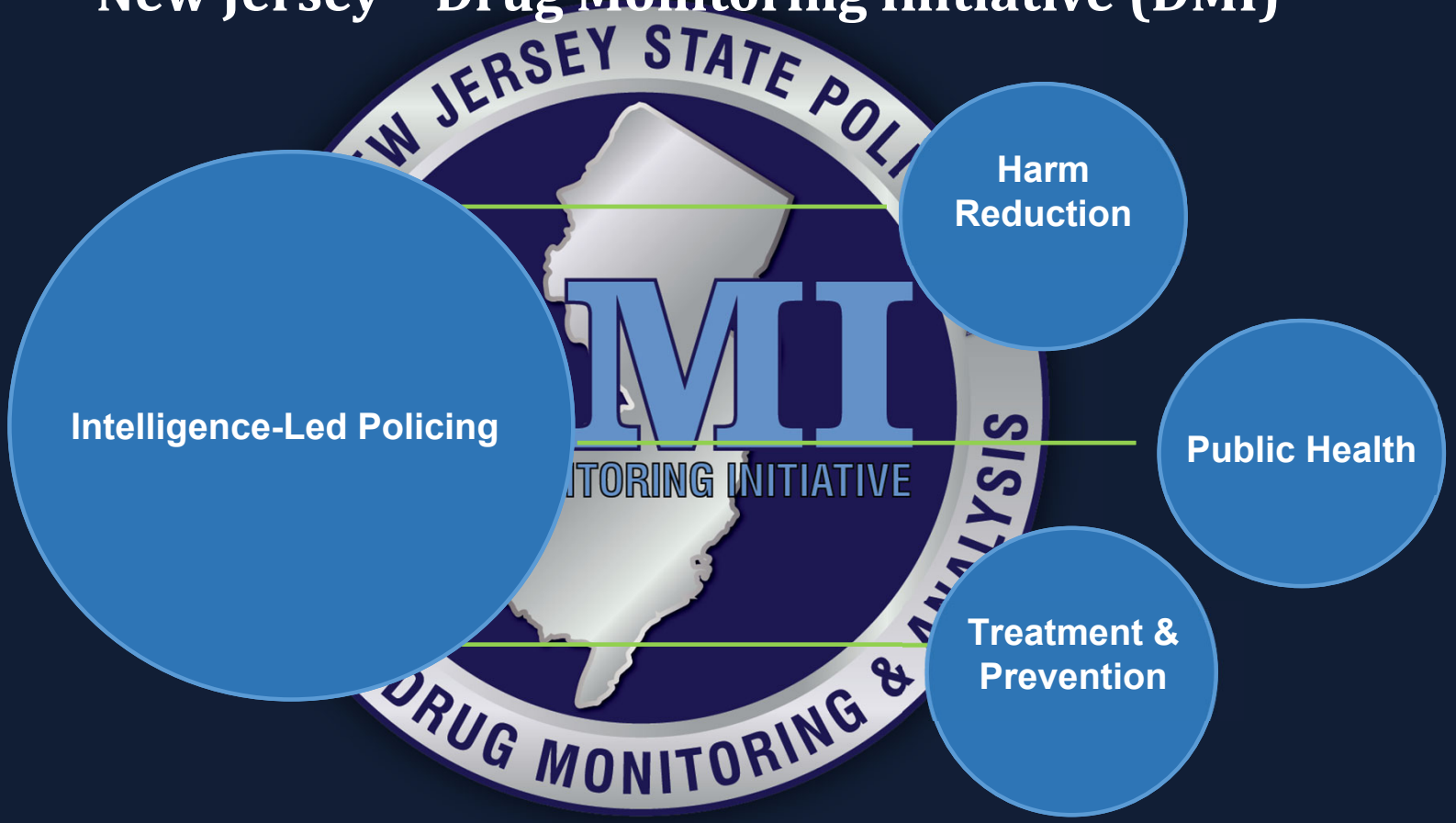
ROIC202210-26048D

Office of Drug Monitoring & Analysis (ODMA)
Drug Monitoring Initiative (DMI)

New Jersey State Police

Office of Drug Monitoring & Analysis (ODMA)

New Jersey – Drug Monitoring Initiative (DMI)



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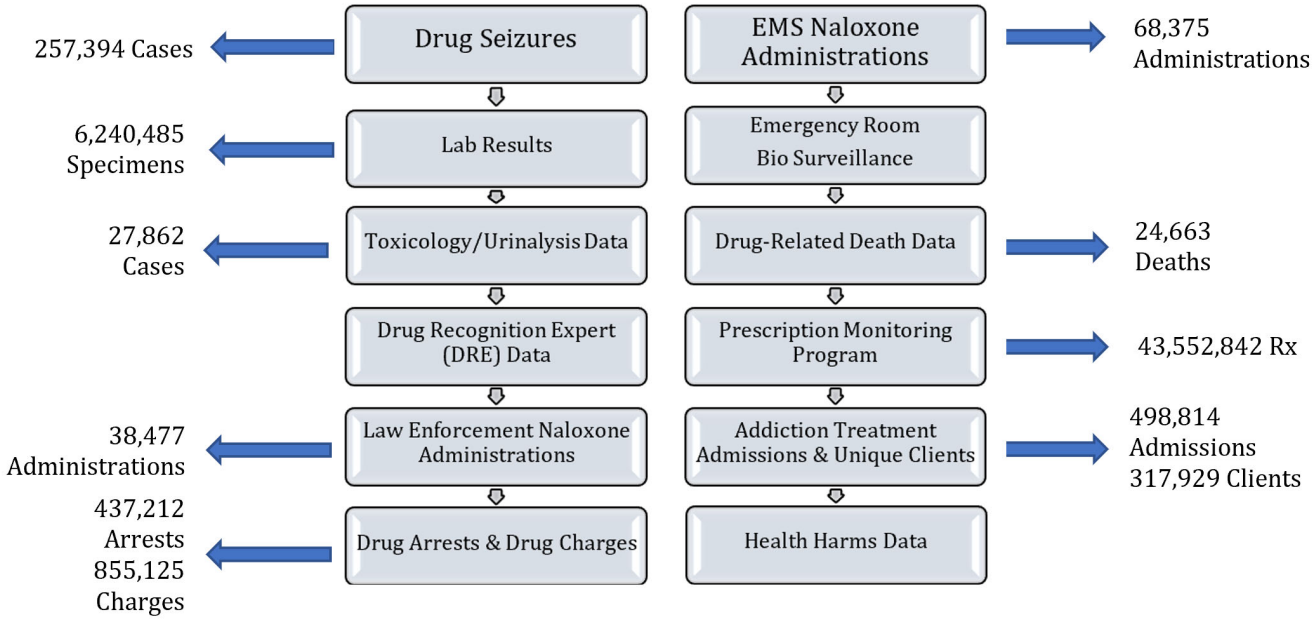
Office of Drug Monitoring & Analysis (ODMA)



Note: Data totals provided are from 01/01/2015 – 09/30/2022. Total: 49,688,442

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New Jersey State Police

Office of Drug Monitoring & Analysis (ODMA)

New Jersey – Drug Monitoring Initiative (DMI)

2016

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Drug Monitoring Initiative

Xylazine ~ Emerging Dangerous Drug

Overview

Incidents

Pictures of Xyzaline in New Jersey

Empire | Power | Drake

Outlook

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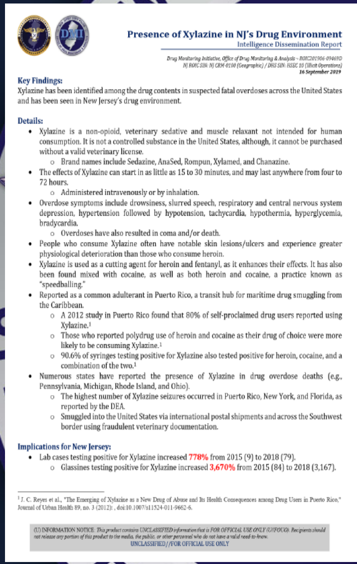
2019



Presence of Xylazine in NJ's Drug Environment

Intelligence Dissemination Report

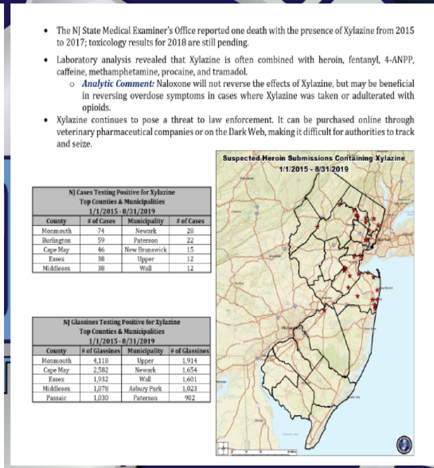
Key Findings:

Xylazine has been identified among the drug contents in suspected fatal overdoses across the United States and has been seen in New Jersey's drug environment.

Details:

Implications for New Jersey:

- Lab cases testing positive for Xylazine increased 778% from 2015 (9) to 2018 (79).
  - Glassines testing positive for Xylazine increased 3,670% from 2015 (84) to 2018 (3,167).



- The NJ State Medical Examiner's Office reported one death with the presence of Xylazine from 2015 to 2017; toxicology results for 2018 are still pending.
- Laboratory analysis revealed that Xylazine is often combined with heroin, fentanyl, 4-ANPP, caffeine, methamphetamine, procaine, and tramadol.
  - *Analytic Comment:* Naloxone will not reverse the effects of Xylazine, but may be beneficial in reversing overdose symptoms in cases where Xylazine was taken or adulterated with opioids.
- Xylazine continues to pose a threat to law enforcement. It can be purchased online through veterinary pharmaceutical companies or on the Dark Web, making it difficult for authorities to track and seize.

NJ Cases Testing Positive for Xylazine
Top Counties & Municipalities
1/1/2015 - 8/31/2019

County	# of Cases	Municipality	# of Cases
Monmouth	74	Newark	20
Burlington	59	Paterson	22
Cape May	46	New Brunswick	15
Essex	38	Upper	12
Middlesex	38	Wall	12

NJ Glassines Testing Positive for Xylazine
Top Counties & Municipalities
1/1/2015 - 8/31/2019

County	# of Glassines	Municipality	# of Glassines
Monmouth	4,110	Upper	1,914
Cape May	2,582	Newark	1,654
Essex	1,932	Wall	1,601
Middlesex	1,078	Asbury Park	1,023
Passaic	1,030	Paterson	902

Suspected Heroin Submissions Containing Xylazine 1/1/2015 - 8/31/2019

2020

UNCLASSIFIED//LAW ENFORCEMENT SENSITIVE

JOINT INTELLIGENCE BRIEF

(U//FOUO) Tramadol and Xylazine Identified in Street-level Heroin

DEA-NJX-DIB-007-20 | May 2020

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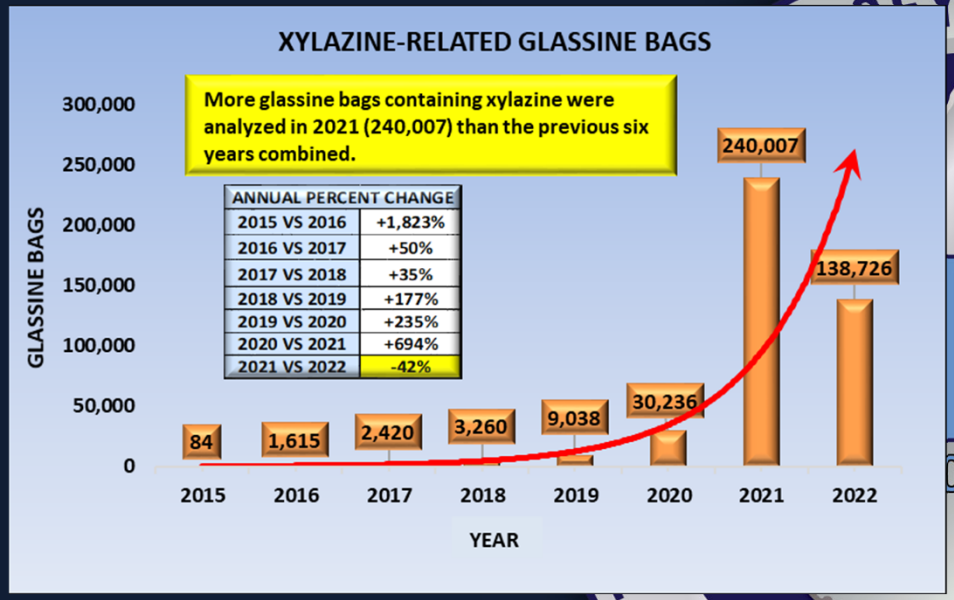
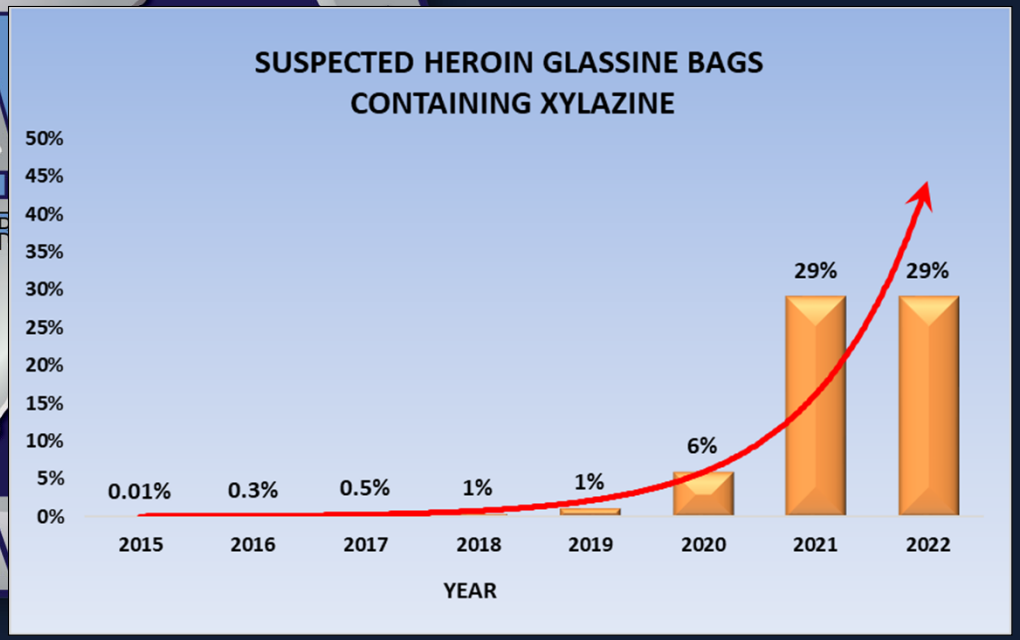
Office of Drug Monitoring & Analysis (ODMA)

Xylazine in New Jersey





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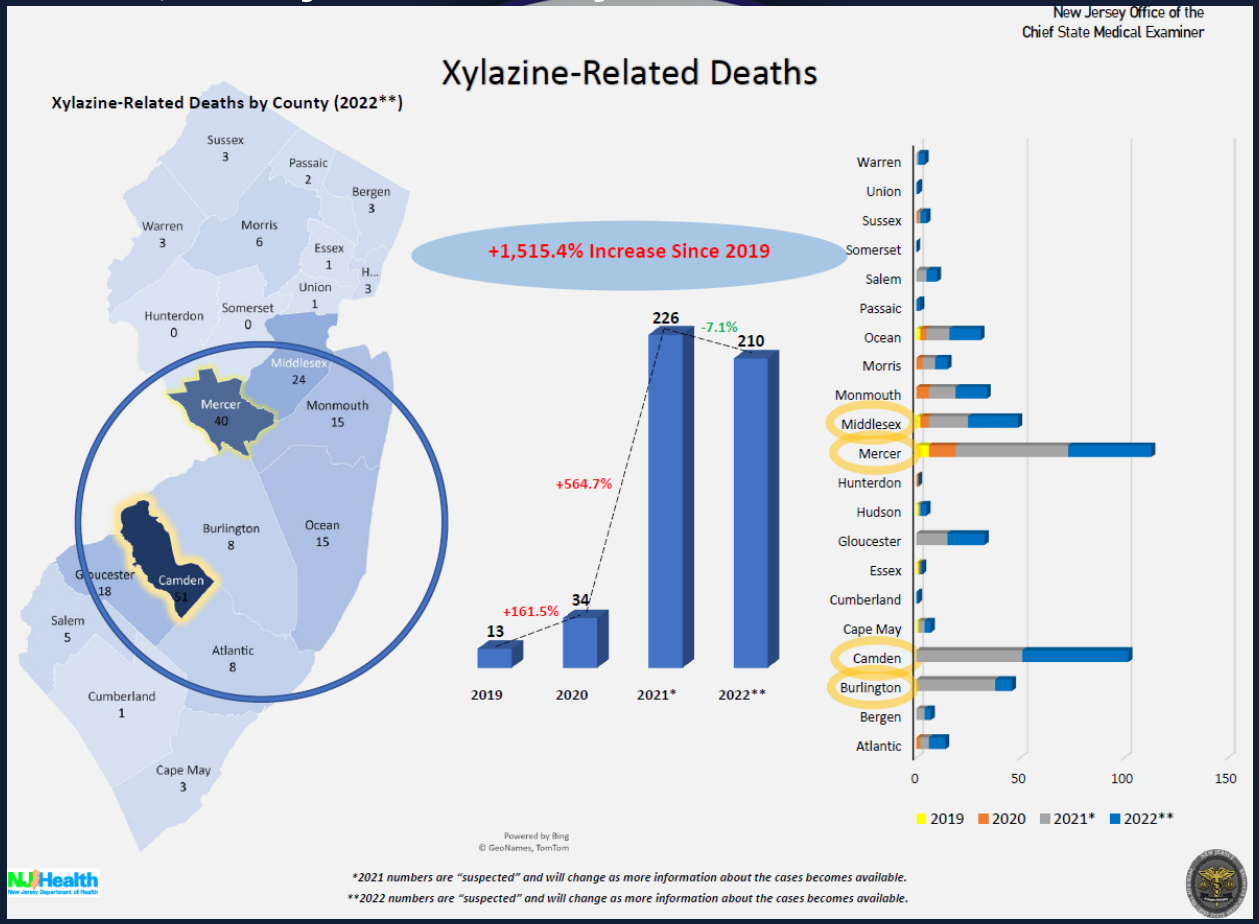
New Jersey OCSME Xylazine-Related Deaths



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New Jersey OFS Laboratory Analysis Submissions by County

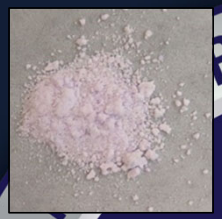
XYLAZINE-RELATED SUBMISSIONS												
COUNTY	2015 - 2018		2019		2020		2021		2022		TOTAL	
ATLANTIC	0	0%	10	3%	90	11%	399	13%	261	10%	760	11%
BERGEN	10	5%	15	4%	28	3%	75	2%	83	3%	211	3%
BURLINGTON	55	28%	73	20%	101	12%	324	11%	234	9%	787	11%
CAMDEN	1	1%	17	5%	93	11%	636	21%	432	17%	1,179	17%
CAPE MAY	38	19%	20	5%	90	11%	128	4%	115	4%	391	6%
CUMBERLAND	0	0%	4	1%	10	1%	28	1%	39	2%	81	1%
ESSEX	23	12%	49	13%	73	9%	202	7%	130	5%	477	7%
GLOUCESTER	1	1%	6	2%	30	4%	146	5%	69	3%	252	4%
HUDSON	0	0%	2	1%	2	0.2%	8	0.3%	39	2%	51	1%
HUNTERDON	0	0%	0	0%	11	1%	17	1%	28	1%	56	1%
MERCER	3	2%	6	2%	78	9%	388	13%	375	14%	850	12%
MIDDLESEX	16	8%	48	13%	39	5%	102	3%	134	5%	339	5%
MONMOUTH	29	15%	66	18%	84	10%	192	6%	199	8%	570	8%
MORRIS	7	4%	22	6%	18	2%	60	2%	40	2%	147	2%
OCEAN	1	1%	0	0%	3	0.4%	15	0.5%	11	0.4%	30	0.4%
PASSAIC	13	7%	25	7%	65	8%	242	8%	326	13%	671	9%
SALEM	0	0%	0	0%	7	1%	20	1%	32	1%	59	1%
SOMERSET	0	0%	0	0%	7	1%	24	1%	13	0.5%	44	1%
SUSSEX	1	1%	2	1%	14	2%	13	0.4%	16	1%	46	1%
UNION	1	1%	0	0%	4	0.5%	5	0.2%	1	0.04%	11	0.2%
WARREN	0	0%	3	1%	8	1%	31	1%	18	1%	60	1%
TOTAL	199		368		855		3,055		2,595		7,072	
	3%		5%		12%		43%		37%			

New Jersey State Police

Office of Drug Monitoring & Analysis (ODMA)

New Jersey Xylazine Seizures

Fentanyl/Xylazine*
Blue powder



Fentanyl/4-ANPP/Xylazine*
Purple powder in blue wax fold

Heroin/Fentanyl/4-ANPP/Tramadol/Xylazine*
Purple powder

Fentanyl/Cocaine/4-ANPP/Fluorofentanyl/Xylazine*
White powder in pink flip-top vial

Fluorofentanyl/Fentanyl/4-ANPP/Xylazine*
White powder in pink flip-top vial

Fluorofentanyl/Fentanyl/Cocaine/Tramadol/Xylazine*
Loose white substance, no container

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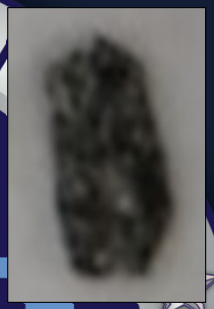
New Jersey Xylazine Seizures



Fluorofentanyl/Fentanyl/Cocaine/ Tramadol/Xylazine*

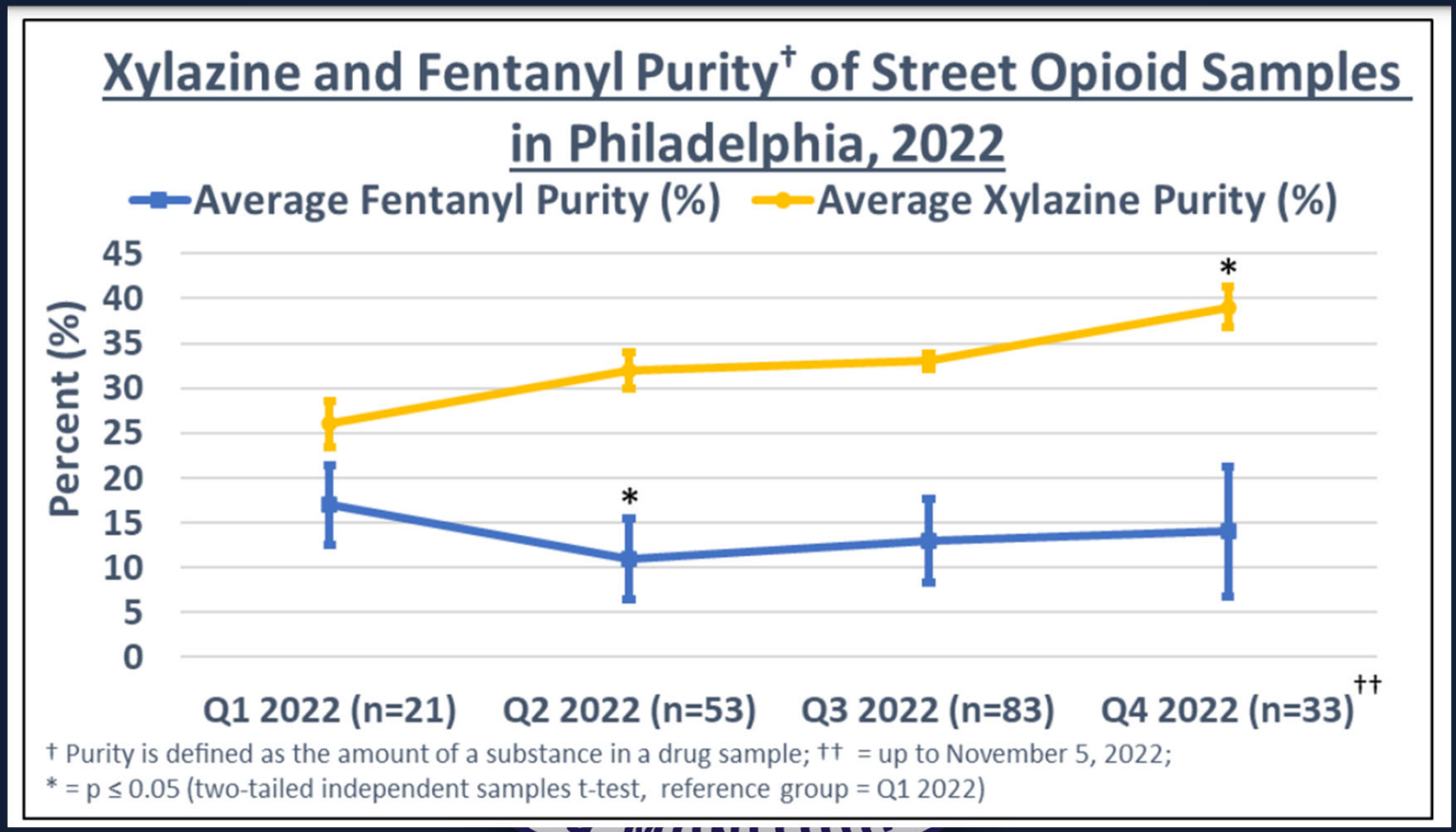
Dark brown substance

Heroin/Fentanyl/Xylazine* Nicotine

Hard dark substance in clear wax fold

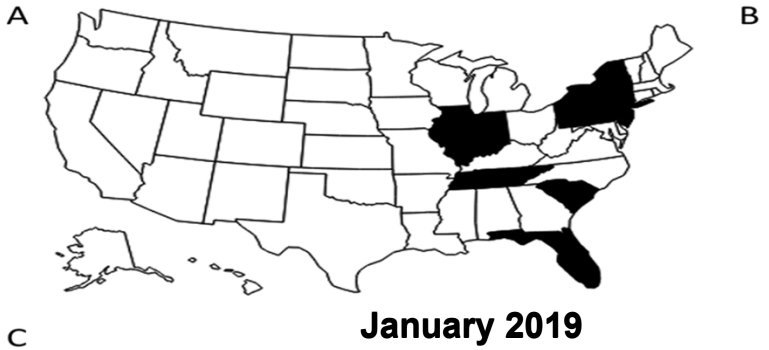
New Jersey State Police

Office of Drug Monitoring & Analysis (ODMA)



Philadelphia, Pennsylvania, Department of Public Health. Substance Use Prevention & Harm Reduction. Health Update. ***Xylazine (tranq) exposure among people who use substances in Philadelphia. 12/8/22***

Spread of Xylazine Across USA: January 2019 to June 2021



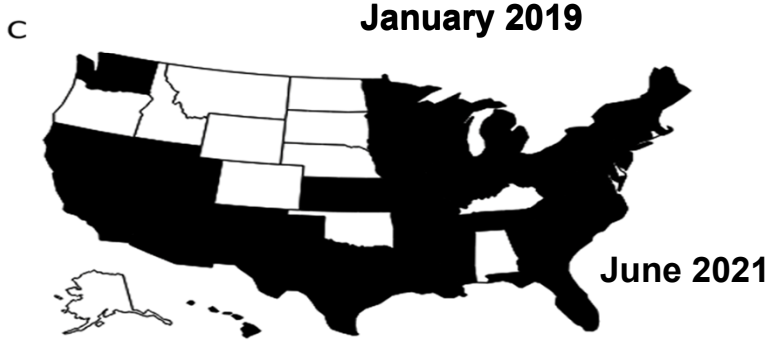


Figure 1. States with at least one positive xylazine detection in A) January 2019, B) January 2020 and C) June 2021. Note: in 2019 no testing had been performed in AL, DE, MD, MA, MT, ND, OK, RI or SD. By the end of the study period at least one case from every state, with the exception of SD, had been tested.

Sherri L. Kacinko, Amanda L. A. Mohr, Barry K. Logan, Edward J. Barbieri, 2022, "Xylazine: Pharmacology Review and Prevalence and Drug Combinations in Forensic Toxicology Casework," *Journal of Analytical Toxicology* 46(8): 911–917, https://doi.org/10.1093/jat/bkac049

Xylazine Presence – National Presence

- Between 2020 and 2021, DEA Laboratory identification of xylazine increased across all four regions (Northeast, South, Midwest, and West)

- The South had the largest reported increase (193%). The Northeast had the highest total number of identifications of xylazine of the four regions

(U) Figure 1. DEA Forensic Laboratory Identifications of Xylazine by Region

Region	2020	2021	Percent Increase
Northeast	346	556	61%
South	198	580	193%
Midwest	110	118	7%
West	77	163	112%

Source: DEA

(U) Figure 2. Number of Xylazine-Positive Overdose Deaths by Region

Region	2020	2021	Percent Increase
Northeast	631	1,281	103%
South	116	1,423	1,127%
Midwest	57	351	516%
West	4	34	750%

Source: DEA

New Jersey State Police
Office of Drug Monitoring & Analysis (ODMA)

Xylazine Presence – State Perspective

- **Alaska:** During 2022, xylazine was identified ten times. Half the time, it was in light blue tablets mixed with fentanyl; the remainder indicated a dark substance mixed with heroin

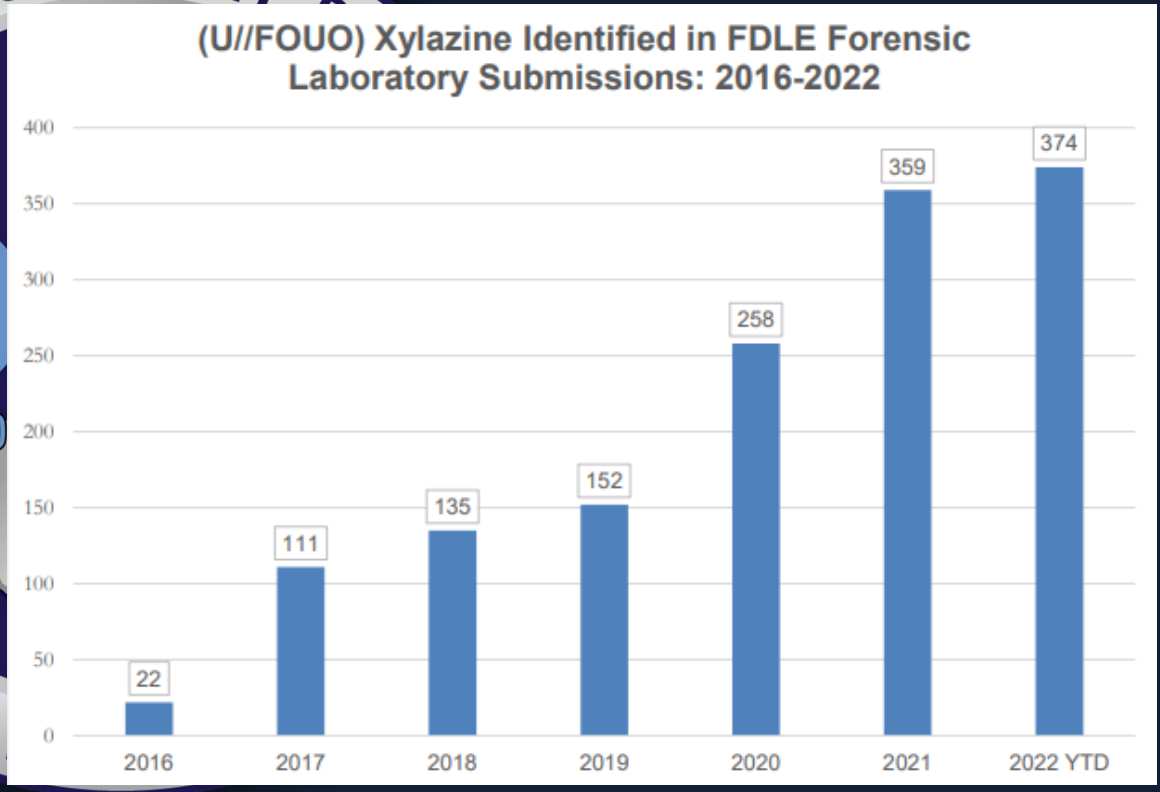
- **Arizona:** Xylazine has become common and widespread, appearing in field testing as well as in overdose deaths. It is important to note that xylazine is generally seen in the presence of other drugs, rather than being the only drug present

- **Delaware:** Xylazine began appearing in October 2021. There have been a total of 283 cases involving xylazine from October 2021 to January 31, 2023

- **Connecticut:** The Connecticut Intelligence Center (CTIC) has reported on the presence of xylazine in suspected heroin

Xylazine Presence – State Perspective

- **Florida:**
  - Positive identification of xylazine in submissions at the Florida Department of Law Enforcement (FDLE) Forensic Laboratories is up 1,600% between July 2016 and October 2022
  - The Florida Medical Examiners Commission (MEC) reported one occurrence of xylazine in deceased persons in 2018, 17 occurrences in 2019, 99 in 2020, and 236 in 2021
  - Fentanyl was found in 98% of xylazine-involved deaths



Xylazine Presence – State Perspective

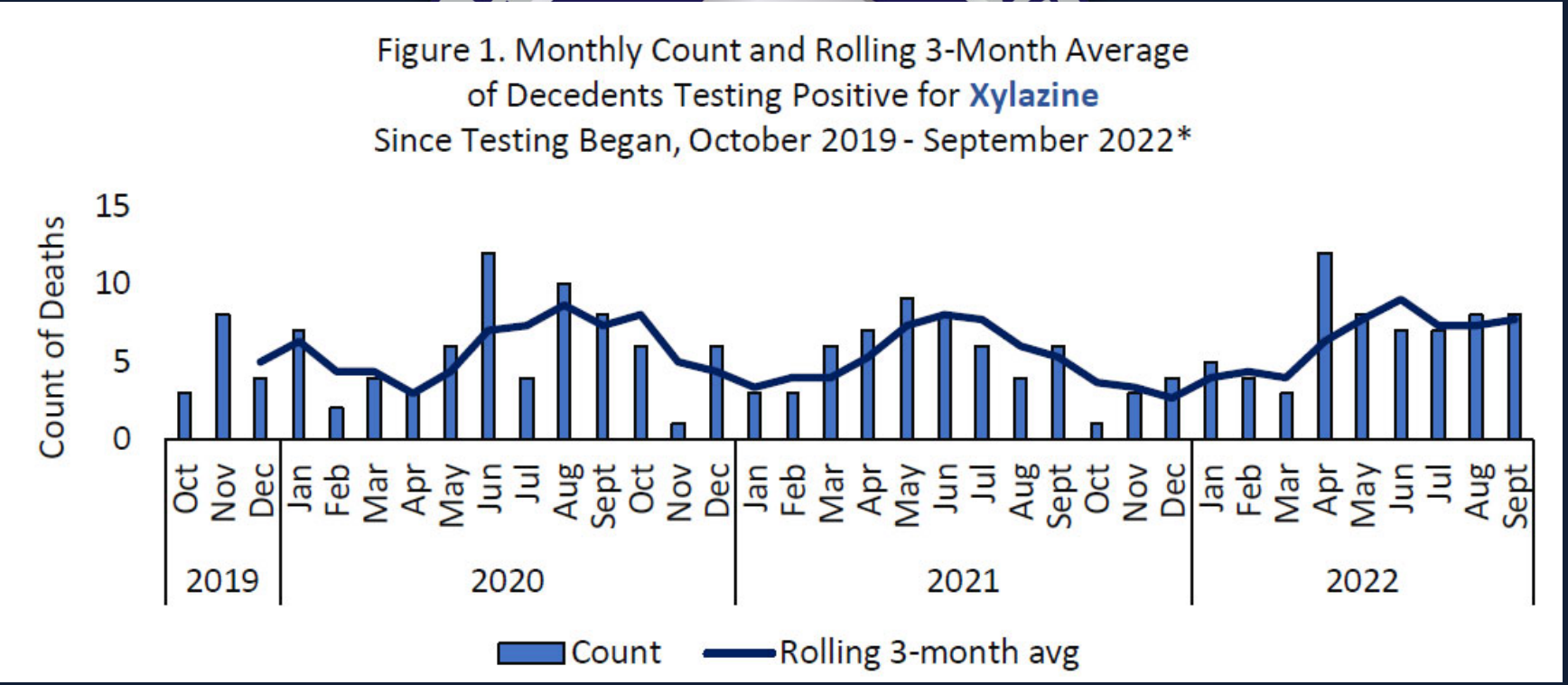
- **Hawaii:** As of August 2022, the Honolulu Police Department recovered several pills containing fentanyl and xylazine. As of January 2022, the Maui Police Department recovered a fine, light blue powder substance that included xylazine and fentanyl

- **Louisiana:** As of June 2022, xylazine was observed in fatal overdoses in 16 parishes in Louisiana

- **Maine:** Since 2017, the State Health and Environmental Testing laboratory has reported 204 confirmed cases of xylazine. The laboratory is working with a seven-month backlog; Maine will not know its true numbers until the laboratory is able to catch up

Xylazine Presence – State Perspective

- **Michigan:** As of September 2022, there were 206 xylazine-positive decedents; 100% also tested positive for fentanyl



Xylazine Presence – State Perspective

- **Utah:** Data from the Utah Department of Public Safety laboratories indicates xylazine in 23 items tested since December 2018

Total # of Items by Month Testing for Xylazine

Date	# of Items
Dec-18	1
Jan-20	2
Jun-20	1
Oct-20	3
Jun-21	1
Feb-22	4
Apr-22	3
Jul-22	1
Sep-22	2
Nov-22	2
Dec-22	3
TOTAL	23

Any agency with questions about this product or any other products may contact the Office of Drug Monitoring & Analysis (ODMA), Drug Monitoring Initiative (DMI), at:

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DMI@njsp.gov

Xylazine, Poison Control Centers, and Medical Toxicology Input for Overdose Fatality Review Committees

May 18, 2023

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Banner Poison & Drug Information Center
Clinical Professor of Medicine and Emergency Medicine
University of Arizona COM-Phoenix, Arizona

Outline

Overview of Xylazine

Introduction to U.S. Poison Centers

Medical Toxicology (Tox) Services

Tox Work With Overdose Fatality Review (OFR) Committees

Xylazine Overview

Xylazine: Background/Overview

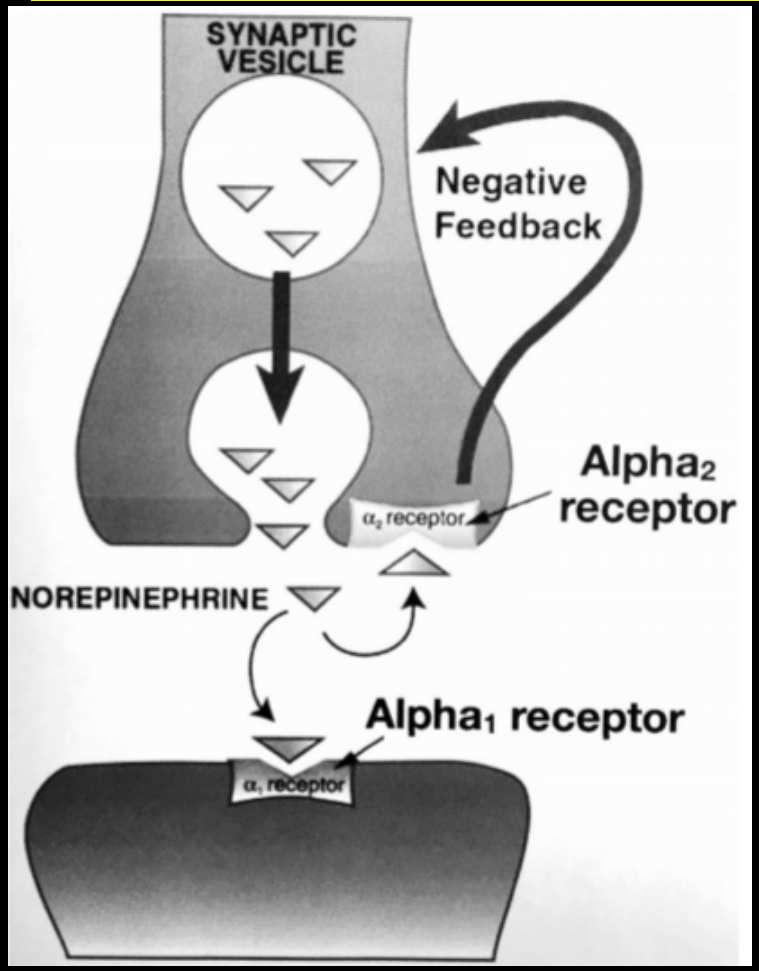
Veterinarian (large-animal) tranquilizer

Mechanism of action: central alpha$_2$-agonist
(same mechanism as clonidine and dexmedetomidine)

Prevents release of neurotransmitters
(norepinephrine, epinephrine=adrenaline)

Negative feedback = relaxes CNS/CV cells

Xylazine: Background/Overview



Giovannitti, J. A., et al., 2015, "Alpha2-adrenergic Receptor Agonists: A Review of Current Clinical Applications," *Anesth Prog* 62(1): 31

Xylazine: Clinical Effects/Treatment

Clinical Effects:

Bradycardia Hypotension Lethargy

Synergistic effects with opioids, alcohol, antipsychotics

Massive doses can cause shock and coma

Treatment:

Supportive care

No known effective antidote (naloxone does NOT work)

Okay to use naloxone if clinical picture fits

Xylazine: Autopsies/Necrosis

Xylazine identified but not always measured;

UNKNOWN if it played a causative role in death

2021 Arizona Overdose Data: ~ 2,000 OD deaths

6 autopsies found xylazine; 0 caused death

Xylazine-induced skin necrosis from IV injection?

Mechanism of injury = unknown

Wounds at sites where xylazine was not injected

Causation has NOT been confirmed

Xylazine Data

(U) Figure 1. DEA Forensic Laboratory Identifications of Xylazine by Region

Region	2020	2021	Percent Increase
Northeast	346	556	61%
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Midwest	110	118	7%
West	77	163	112%

Source: DEA

CTPER | Center for Toxicology and Pharmacology Education and Research

A CENTER OF THE UNIVERSITY OF ARIZONA COLLEGE OF MEDICINE - PHOENIX AND BANNER HEALTH

The Poison and Drug Information Centers of Arizona

FOR IMMEDIATE RELEASE:

Date: December 15, 2022

Arizona Poison & Drug Information System and Public Health Authorities warn of increase danger of illicit drugs due to xylazine contamination.

PHOENIX, AZ - The Arizona poison system, part of the Center for Toxicology & Pharmacology Education and Research (CTPER) at the University of Arizona College of Medicine Phoenix, and Arizona Public Health and Safety Agencies are warning all Arizona healthcare providers about the risks of illicit drugs, including fentanyl, being contaminated with xylazine. It is added in hopes of prolonging the euphoric effects of the illicit drug (e.g., fentanyl) but can result in life-threatening coma and respiratory failure.

Overview of U.S. Poison Control Centers

55 U.S. Poison Control Centers

Federal (HRSA) Accreditation

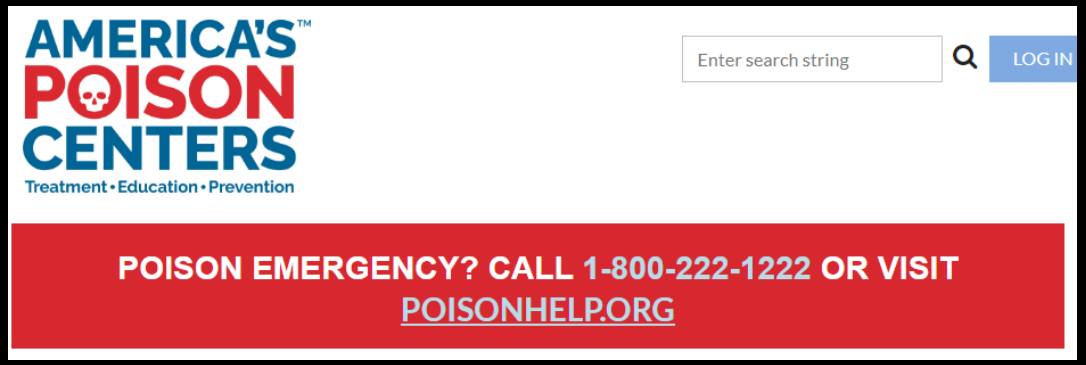
CDC Collaboratives

Require Medical Directors
(Physicians = Medical Toxicologists)

America's Poison Centers—Annual Report

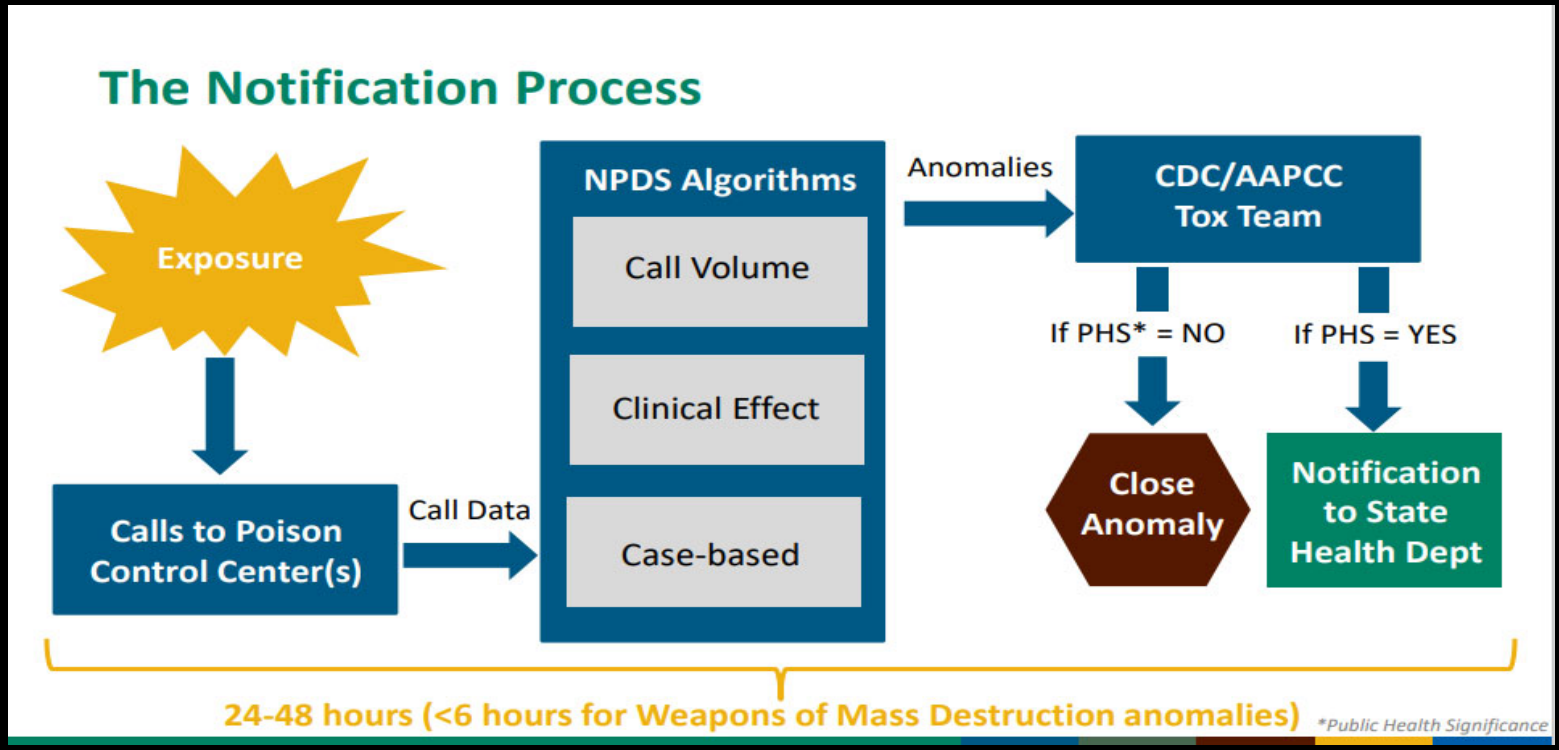
National Poisoning Data System

(all PCC data uploaded every ~ 8 minutes)

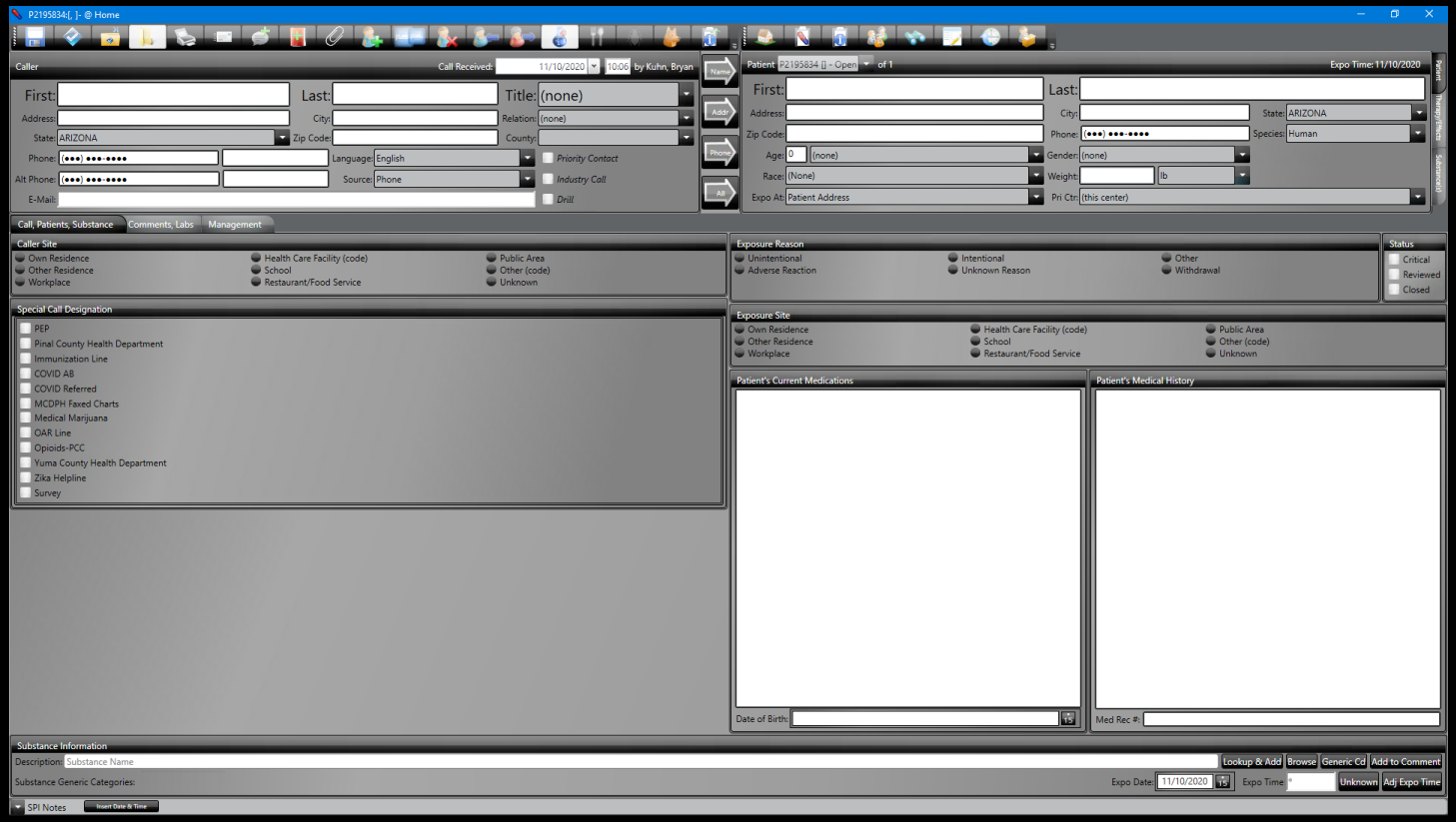


aapcc.org

NPDS Toxico-Surveillance



All 55 PCCs electronically upload all data every ~ 8 minutes


P2195834[,]- @ Home
Caller
Call Received: 11/10/2020 10:06 by Kuhn, Bryan
First:
Last:
Title: (none)
Address:
City:
Relation: (none)
State: ARIZONA
Zip Code:
County:
Phone: (•••) •••-••••
Language: English
Priority Contact
Alt Phone: (•••) •••-••••
Source: Phone
Industry Call
E-Mail:
Drill
Patient P2195834 [] - Open of 1
Expo Time:11/10/2020
First:
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City:
State: ARIZONA
Zip Code:
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Species: Human
Age: 0 (none)
Gender: (none)
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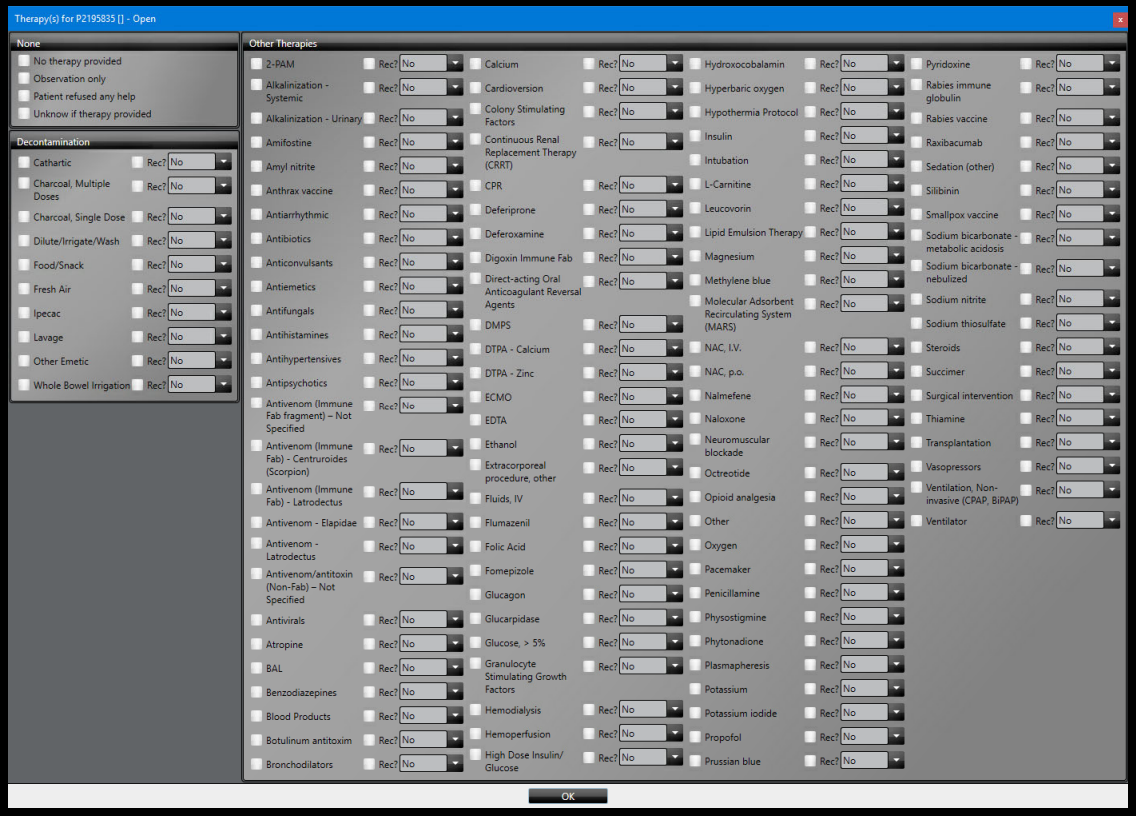
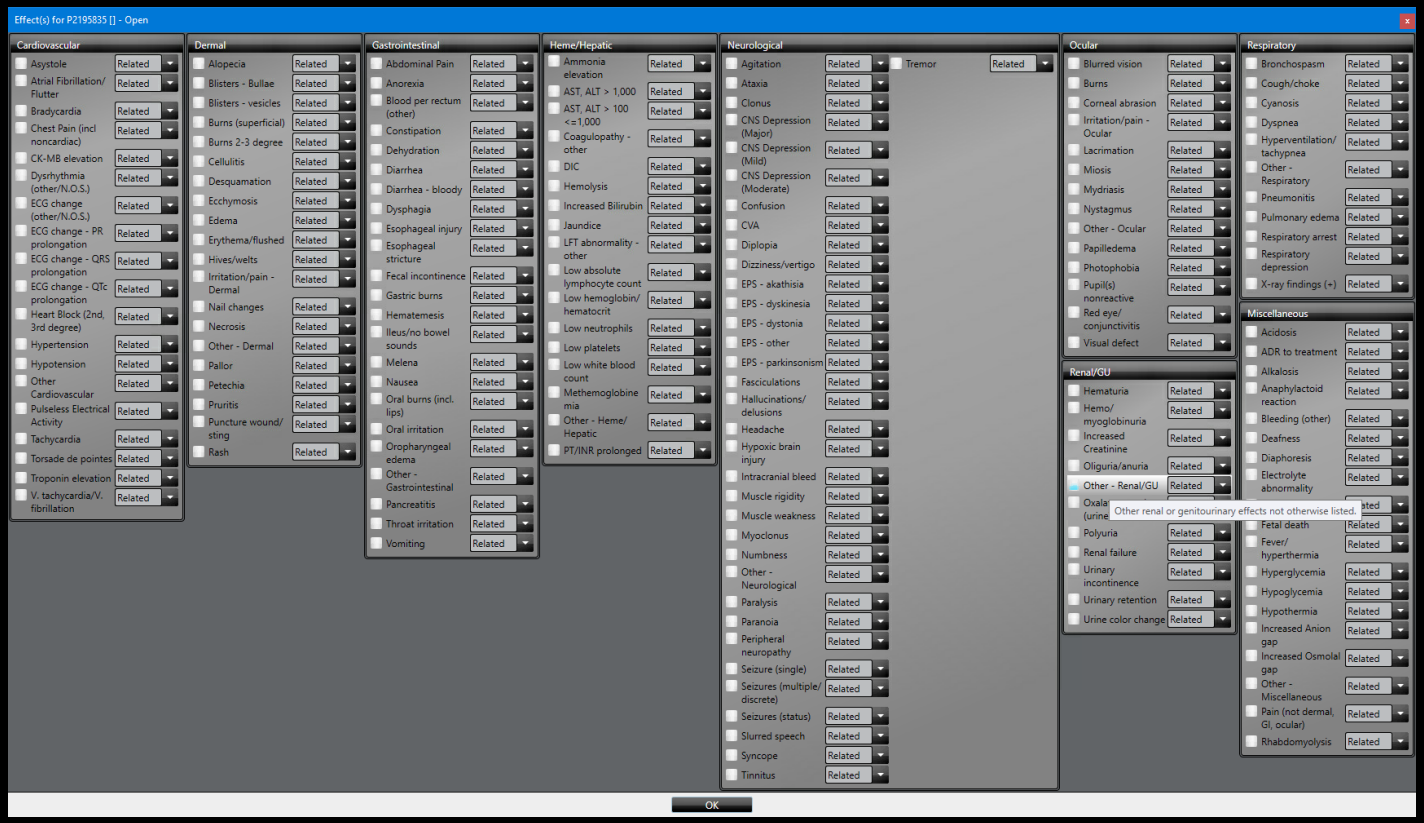
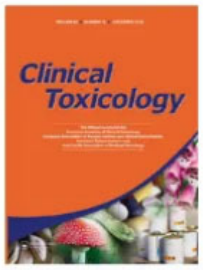
Expo At: Patient Address
Pri Ctr: (this center)
Call, Patients, Substance
Comments, Labs
Management
Caller Site
Own Residence
Other Residence
Workplace
Health Care Facility (code)
School
Restaurant/Food Service
Public Area
Other (code)
Unknown
Exposure Reason
Unintentional
Adverse Reaction
Intentional
Unknown Reason
Other
Withdrawal
Status
Critical
Reviewed
Closed
Special Call Designation
PEP
Pinal County Health Department
Immunization Line
COVID AB
COVID Referred
MCDPH Faxed Charts
Medical Marijuana
OAR Line
Opioids-PCC
Yuma County Health Department
Zika Helpline
Survey
Exposure Site
Own Residence
Other Residence
Workplace
Health Care Facility (code)
School
Restaurant/Food Service
Public Area
Other (code)
Unknown
Patient's Current Medications
Patient's Medical History
Date of Birth:
Med Rec #:
Substance Information
Description: Substance Name
Lookup & Add
Browse
Generic Cd
Add to Comment
Substance Generic Categories:
Expo Date: 11/10/2020
Expo Time:
Unknown
Adj Expo Time
SPI Notes
Insert Date & Time


Therapy(s) for P2195835 [] - Open
None
No therapy provided
Observation only
Patient refused any help
Unknow if therapy provided
Decontamination
Cathartic
Charcoal, Multiple Doses
Charcoal, Single Dose
Dilute/Irrigate/Wash
Food/Snack
Fresh Air
Ipecac
Lavage
Other Emetic
Whole Bowel Irrigation
Rec?
No
Other Therapies
2-PAM
Alkalinization - Systemic
Alkalinization - Urinary
Amifostine
Amyl nitrite
Anthrax vaccine
Antiarrhythmic
Antibiotics
Anticonvulsants
Antiemetics
Antifungals
Antihistamines
Antihypertensives
Antipsychotics
Antivenom (Immune Fab fragment) – Not Specified
Antivenom (Immune Fab) - Centruroides (Scorpion)
Antivenom (Immune Fab) - Latrodectus
Antivenom - Elapidae
Antivenom - Latrodectus
Antivenom/antitoxin (Non-Fab) – Not Specified
Antivirals
Atropine
BAL
Benzodiazepines
Blood Products
Botulinum antitoxim
Bronchodilators
Calcium
Cardioversion
Colony Stimulating Factors
Continuous Renal Replacement Therapy (CRRT)
CPR
Deferiprone
Deferoxamine
Digoxin Immune Fab
Direct-acting Oral Anticoagulant Reversal Agents
DMPS
DTPA - Calcium
DTPA - Zinc
ECMO
EDTA
Ethanol
Extracorporeal procedure, other
Fluids, IV
Flumazenil
Folic Acid
Fomepizole
Glucagon
Glucarpidase
Glucose, > 5%
Granulocyte Stimulating Growth Factors
Hemodialysis
Hemoperfusion
High Dose Insulin/ Glucose
Hydroxocobalamin
Hyperbaric oxygen
Hypothermia Protocol
Insulin
Intubation
L-Carnitine
Leucovorin
Lipid Emulsion Therapy
Magnesium
Methylene blue
Molecular Adsorbent Recirculating System (MARS)
NAC, I.V.
NAC, p.o.
Nalmefene
Naloxone
Neuromuscular blockade
Octreotide
Opioid analgesia
Other
Oxygen
Pacemaker
Penicillamine
Physostigmine
Phytonadione
Plasmapheresis
Potassium
Potassium iodide
Propofol
Prussian blue
Pyridoxine
Rabies immune globulin
Rabies vaccine
Raxibacumab
Sedation (other)
Silibinin
Smallpox vaccine
Sodium bicarbonate - metabolic acidosis
Sodium bicarbonate - nebulized
Sodium nitrite
Sodium thiosulfate
Steroids
Succimer
Surgical intervention
Thiamine
Transplantation
Vasopressors
Ventilation, Non-invasive (CPAP, BiPAP)
Ventilator
OK


Effect(s) for P2195835 [] - Open
Cardiovascular
Asystole
Atrial Fibrillation/ Flutter
Bradycardia
Chest Pain (incl noncardiac)
CK-MB elevation
Dysrhythmia (other/N.O.S.)
ECG change (other/N.O.S.)
ECG change - PR prolongation
ECG change - QRS prolongation
ECG change - QTc prolongation
Heart Block (2nd, 3rd degree)
Hypertension
Hypotension
Other Cardiovascular
Pulseless Electrical Activity
Tachycardia
Torsade de pointes
Troponin elevation
V. tachycardia/V. fibrillation
Dermal
Alopecia
Blisters - Bullae
Blisters - vesicles
Burns (superficial)
Burns 2-3 degree
Cellulitis
Desquamation
Ecchymosis
Edema
Erythema/flushed
Hives/welts
Irritation/pain - Dermal
Nail changes
Necrosis
Other - Dermal
Pallor
Petechia
Pruritis
Puncture wound/ sting
Rash
Gastrointestinal
Abdominal Pain
Anorexia
Blood per rectum (other)
Constipation
Dehydration
Diarrhea
Diarrhea - bloody
Dysphagia
Esophageal injury
Esophageal stricture
Fecal incontinence
Gastric burns
Hematemesis
Ileus/no bowel sounds
Melena
Nausea
Oral burns (incl. lips)
Oral irritation
Oropharyngeal edema
Other - Gastrointestinal
Pancreatitis
Throat irritation
Vomiting
Heme/Hepatic
Ammonia elevation
AST, ALT > 1,000
AST, ALT > 100 <=1,000
Coagulopathy - other
DIC
Hemolysis
Increased Bilirubin
Jaundice
LFT abnormality - other
Low absolute lymphocyte count
Low hemoglobin/ hematocrit
Low neutrophils
Low platelets
Low white blood count
Methemoglobinemia
Other - Heme/ Hepatic
PT/INR prolonged
Neurological
Agitation
Ataxia
Clonus
CNS Depression (Major)
CNS Depression (Mild)
CNS Depression (Moderate)
Confusion
CVA
Diplopia
Dizziness/vertigo
EPS - akathisia
EPS - dyskinesia
EPS - dystonia
EPS - other
EPS - parkinsonism
Fasciculations
Hallucinations/ delusions
Headache
Hypoxic brain injury
Intracranial bleed
Muscle rigidity
Muscle weakness
Myoclonus
Numbness
Other - Neurological
Paralysis
Paranoia
Peripheral neuropathy
Seizure (single)
Seizures (multiple/ discrete)
Seizures (status)
Slurred speech
Syncope
Tinnitus
Tremor
Ocular
Blurred vision
Burns
Corneal abrasion
Irritation/pain - Ocular
Lacrimation
Miosis
Mydriasis
Nystagmus
Other - Ocular
Papilledema
Photophobia
Pupil(s) nonreactive
Red eye/ conjunctivitis
Visual defect
Renal/GU
Hematuria
Hemo/ myoglobinuria
Increased Creatinine
Oliguria/anuria
Other - Renal/GU
Other renal or genitourinary effects not otherwise listed.
Polyuria
Renal failure
Urinary incontinence
Urinary retention
Urine color change
Respiratory
Bronchospasm
Cough/choke
Cyanosis
Dyspnea
Hyperventilation/ tachypnea
Other - Respiratory
Pneumonitis
Pulmonary edema
Respiratory arrest
Respiratory depression
X-ray findings (+)
Miscellaneous
Acidosis
ADR to treatment
Alkalosis
Anaphylactoid reaction
Bleeding (other)
Deafness
Diaphoresis
Electrolyte abnormality
Fetal death
Fever/ hyperthermia
Hyperglycemia
Hypoglycemia
Hypothermia
Increased Anion gap
Increased Osmolal gap
Other - Miscellaneous
Pain (not dermal, GI, ocular)
Rhabdomyolysis
Related
OK

NPDS Annual Report From U.S. PCCs



Taylor & Francis

Clinical Toxicology

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2021 Annual Report of the National Poison Data System© (NPDS) from America's Poison Centers: 39th Annual Report

David D. Gummin, James B. Mowry, Michael C. Beuhler, Daniel A. Spyker, Laura J. Rivers, Ryan Feldman, Kaitlyn Brown, P. T. Pham Nathaniel, Alvin C. Bronstein & Julie A. Weber

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Most Common Exposures

Table 17A. Substance Categories Most Frequently Involved in Human Exposures (Top 25)

Substance (Major Generic Category)	All substances	%[a]	Single substance exposures	%[b]
Analgesics	283,695	11.23	178,714	9.82
Cosmetics/Personal Care Products	148,558	5.88	141,004	7.75
Antidepressants	141,802	5.61	64,568	3.55
Sedative/Hypnotics/Antipsychotics	119,500	4.73	44,277	2.43
Cardiovascular Drugs	116,165	4.60	47,693	2.62
Antihistamines	114,595	4.53	75,493	4.15
Dietary Supplements/Herbals/Homeopathic	87,305	3.45	74,868	4.11
Foreign Bodies/Toys/Miscellaneous	82,772	3.28	79,769	4.38
Stimulants and Street Drugs	75,852	3.00	44,451	2.44
Pesticides	71,574	2.83	66,780	3.67
Alcohols	70,760	2.80	22,529	1.24
Vitamins	63,245	2.50	50,120	2.75
Anticonvulsants	62,137	2.46	24,578	1.35
Topical Preparations	60,512	2.39	58,706	3.23
Hormones and Hormone Antagonists	55,040	2.18	35,173	1.93
Plants	53,951	2.13	51,363	2.82
Chemicals	50,045	1.98	42,255	2.32
Gastrointestinal Preparations	48,192	1.91	33,480	1.84
Cold and Cough Preparations	43,667	1.73	28,518	1.57
Antimicrobials	43,346	1.72	32,780	1.80
Fumes/Gases/Vapors	39,698	1.57	36,772	2.02
Bites and Envenomations	35,786	1.42	35,136	1.93
Electrolytes and Minerals	32,678	1.29	25,697	1.41
Other/Unknown Nondrug Substances	32,018	1.27	29,476	1.62

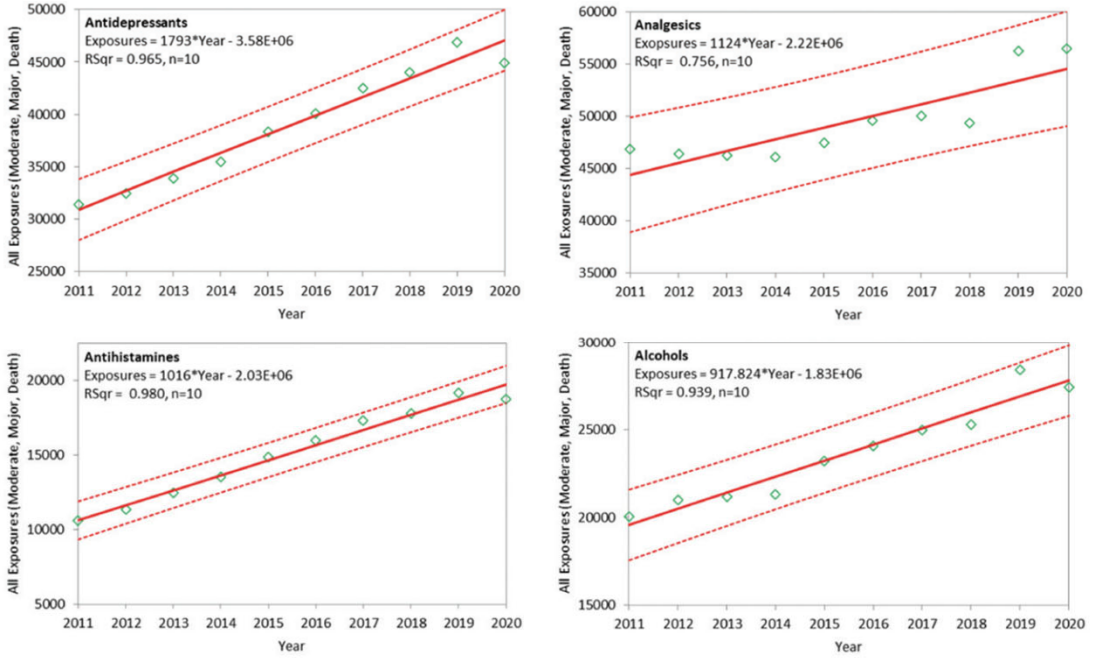


Figure 4. Substance Categories with the Greatest Rate of Exposure Increase since 1 January 2010 for More Severe Outcomes (Top 4). Solid lines show least-squares linear regressions for the human exposure cases per year for that category (◇). Broken lines show 95% confidence interval on the regression.

Publish Unique Deaths—Case Reports

Case 304. Acute buprenorphine ingestion: undoubtedly responsible.

Scenario/Substances: A 2 y/o male had an acute cardiorespiratory arrest at home. Parents reported that he went to bed normally but they heard him gasp and found him apneic later in the night. It was reported that there was buprenorphine/naloxone in the home.

Physical Exam: Child presented in cardiac arrest.

Laboratory Data: UDS was negative.

Clinical Course: The patient was intubated and resuscitated with epinephrine, vasopressin dopamine, norepinephrine, IVF, insulin and antibiotics. The patient's initial ''brain study'' was abnormal. His pupils were fixed and dilated. BP, 80s/60s, HR 124, RR 18, O2 sat 95–98%, T 36.8°C. He remained unresponsive with no purposeful movements. On Day 2 a brain flow study determined brain death. Based on the prognosis, the family opted for institution of comfort measures and he died on Day 3.

Autopsy findings: Cause of death was listed as complications of out of hospital cardiorespiratory arrest due to buprenorphine intoxication. A peripheral serum sample drawn on Day 2 found a buprenorphine concentration <0.2 ng/ml. A buprenorphine tablet that was submitted as evidence and the mother was charged with murder.

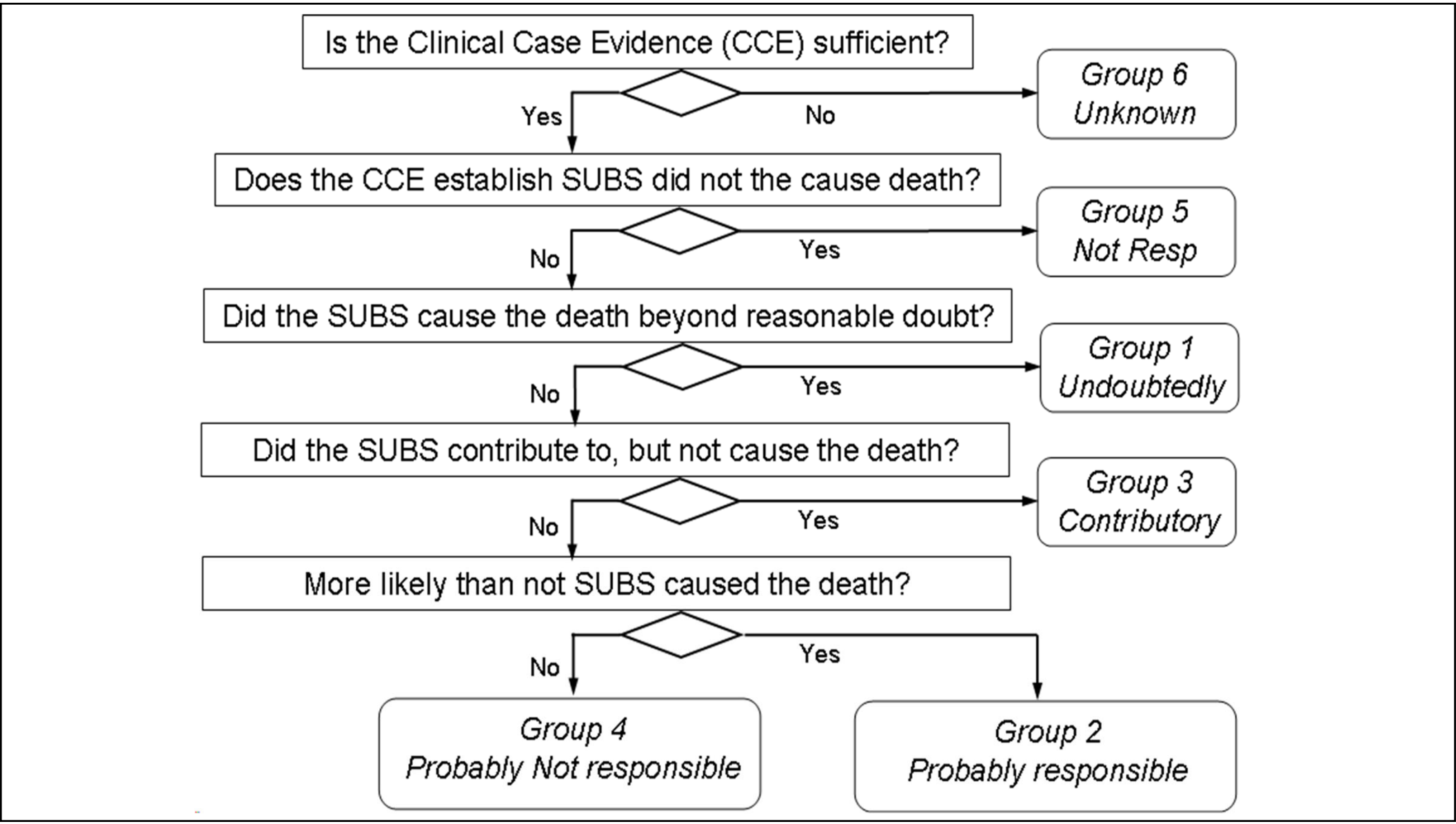
NPDS scoring system based on Relative Contribution to Fatality (RCF)

NPDS: Relative Contribution to Fatality

RCF	Title	Criteria
1	Undoubtedly Responsible	Exposure caused the death.
2	Probably Responsible	> 50% chance the exposure caused death.
3	Contributory	Exposure caused the death because the patient had other active medical issues.
4	Probably Not Responsible	< 50% chance the exposure caused death.
5	Clearly Not Responsible	Exposure did not cause the death.
6	Unknown	Unknown

RCF = 1–3 considered death caused by the exposure

More specific information available on the NPDS website


Is the Clinical Case Evidence (CCE) sufficient?
Yes
No
Group 6
Unknown
Does the CCE establish SUBS did not the cause death?
No
Yes
Group 5
Not Resp
Did the SUBS cause the death beyond reasonable doubt?
No
Yes
Group 1
Undoubtedly
Did the SUBS contribute to, but not cause the death?
No
Yes
Group 3
Contributory
More likely than not SUBS caused the death?
No
Yes
Group 4
Probably Not responsible
Group 2
Probably responsible

Medical Toxicology and OFRCs

Medical Toxicology

Banner University Medical Center-Phoenix

- **Only Level One Toxicology Center in the United States**
- **Phoenix Childrens Hospital**
- **Admit patients**
- **Consults/Outpatient services**

Medical Toxicology

Our department admits and cares for ~ 1,600 patients/year

Clinical care in the ED, ICU, inpatients, and clinic

Comprehensive laboratory testing

Access to antidotes

Collaborate with State Lab and Public Health/Safety

Medical Toxicology and OFRC Work

Use clinical experience/training to help interpret pre-fatal events

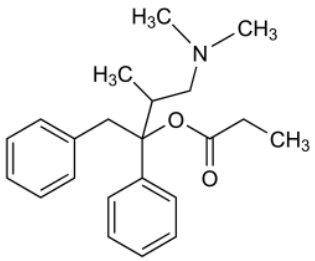
Use NPDS methodology to help determine cause(s) of death

Interpret data: tests used, cut-off values, post-mortem redistribution, and drug concentrations

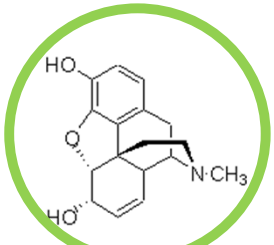
Basic Urine Drug Screens (drugs of abuse)

Barbiturates	Amphetamines/Methamphetamine
Benzodiazepines	Cocaine
Opiates	Oxycodone/Methadone/Propoxyphene
Tricyclics	Cannabinoid (THC)
	Fentanyl (and some derivatives)

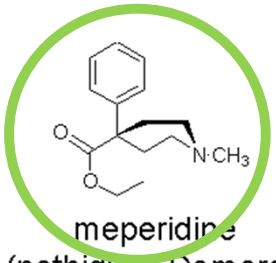
UDS—Backbone Structures



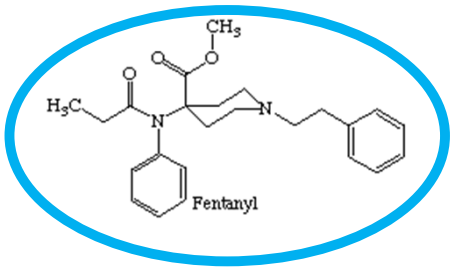
propoxyphene

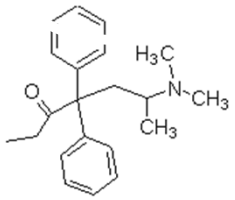


morphine

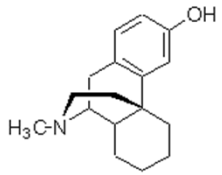


meperidine
(pethidine, Demerol)





methadone



dextromethorphan

Drug Analyzed	Cut-off Concentration (ng/mL)
Amphetamine Methamphetamine MDMA	500 2,100 34,300
Barbiturates	200
Benzodiazepines	100
Buprenorphine	10 ng/mL
Cannabinoid (THC)	50
Cocaine	300
Fentanyl (screen only)	1
Methadone	300
Opiate	300
Phencyclidine	25
Propoxyphene	1000
Tricyclics	1000

Urine Comprehensive Drug Test

Gas chromatography with mass spectroscopy

Provides a ‘fingerprint’ of the drugs in the patient

Requires hours to perform

Qualitative, NOT quantitative

Example of GC-MS Results

Result type: GC/MS Screen
Result date: 30 November 2012 16:00 MST
Result status: Auth (Verified)
Performed By: D, C on 30 November 2012 18:34 MST
Verified by: D, C on 30 November 2012 18:34 MST
Encounter info: XXXXXXXX, BGSMC, Inpatient, 11/30/2012 -

*** Final Report ***
Drugs/chemicals detected with analysis by gas chromatography/mass spectrometry:

- Acetaminophen
- Caffeine
- Dextromethorphan
- Diphenhydramine
- Doxylamine
- Polyethylene Glycol -n (pharmaceutical)

Comprehensive Drug Testing for Medical Purpose

(not forensic/criminal purposes)

*** Final Report ***

Compounds detected:

1. Acetaminophen
2. Caffeine'
3. Cocaine
4. Ecgonine methyl ester
5. Norcocaine*
6. Hydrocodone
7. Dihydrocodeine*
8. Norhydrocodone*
9. Levamisole
10. Norfentanyl*
11. O-desmethylvenlafaxine
12. Theobromine*

*This compound was identified using a commercial spectral library; it has not been validated using this GC/MS method. Interpret results with caution.

2.) (Medium Importance) Interpretive Data by SYSTEM on August 22, 2020 2:05 US/Arizona
Cutoff concentration for positive fentanyl drug screen result is 1.0 ng/mL

Positive results are unconfirmed unless reported with a confirmation and are for medical purposes only.

Tox Work on Arizona OFRCs

AZ OFR: Tox Work/Input

Presented, trained NPDS methodology for RCF

Assigning the Relative Contribution to Fatality: how to determine if death was caused by an opioid medication(s)

Instructions: use all available case records to determine the Relative Contribution to Fatality (RCF) for each overdose case. Final RCF codes correspond to the definitions in Table 1.

Only cases with RCF scores of 1, 2 or 3 will undergo further evaluation by the Arizona Overdose Fatality Review Committee.

Case ID#: _____

RCF reviewers: _____

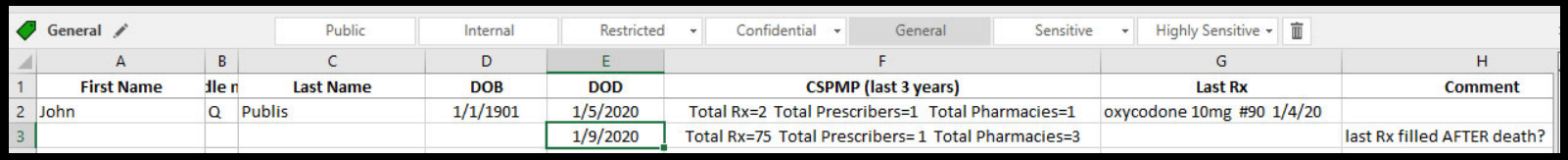
Assigned RCF Code: _____

TABLE 1. RCF Definitions.

RCF Number and Title		Criteria
1	Undoubtedly Responsible	Exposure caused the death.
2	Probable Responsible	> 50% chance the exposure caused death.
3	Contributory	Exposure caused the death because the patient had other active medical issues.
4	Probably Not Responsible	< 50% chance the exposure caused death.
5	Clearly Not Responsible	Exposure did not cause the death.
6	Unknown	Unknown.

AZ OFR: Tox Work/Input

Used PCC role to review, interpret, and report Controlled-Substance Prescription Monitoring Program (CS-PMP) data



General | Public | Internal | Restricted | Confidential | General | Sensitive | Highly Sensitive

	A	B	C	D	E	F	G	H
1	First Name	dle n	Last Name	DOB	DOD	CSPMP (last 3 years)	Last Rx	Comment
2	John	Q	Publis	1/1/1901	1/5/2020	Total Rx=2 Total Prescribers=1 Total Pharmacies=1	oxycodone 10mg #90 1/4/20	
3					1/9/2020	Total Rx=75 Total Prescribers= 1 Total Pharmacies=3		last Rx filled AFTER death?

Worked with OFRC on Reference Drug Concentrations associated with Death (RDCaD)

AZ OFR: Tox Data/Analysis Case #1

OVERDOSE FATALITY REVIEW TEAM DECISION FORM 1

REVIEW DATE

RECORD ID # 2020-01

ASSIGNED RCF CODE 1

FIRST NAME: [redacted]
LAST NAME:
DOB:

DOD: 07/24/2020

LOCATION OF DEATH: Residence [redacted] e

COUNTY OF DEATH: [redacted]

CAUSE OF DEATH: Mixed drug (Fentanyl and Diphenhydramine) intoxication

MANNER OF DEATH: Accident

PMP (3 YEARS)
Rxs:
Prescribers: Ø
Pharmacies:
LAST Rx:

DID MENTAL HEALTH CONDITIONS CONTRIBUTE TO THE DEATH?	[X] YES	[ ] PROBABLY	[ ] NO	[ ] UNKNOWN
DID SUBSTANCE USE DISORDER CONTRIBUTE TO THE DEATH?	[X] YES	[ ] PROBABLY	[ ] NO	[ ] UNKNOWN
WAS THIS DEATH LISTED AS ACCIDENTAL?	[X] YES	[ ] PROBABLY	[ ] NO	[ ] UNKNOWN
WAS THIS DEATH A SUICIDE?	[ ] YES	[ ] PROBABLY	[X] NO	[ ] UNKNOWN

Toxicology Data
(RCD= approximate Reference Concentration associated with Death):

Fentanyl 15 ng/mL
Diphenhydramine 350 ng/mL (~15,000)
Δ9 THC 3.5 ng/mL

BAC 0.155 (VAC 0.181)

DRUG RELATEDNES: SELECT ALL THAT APPLY

- [ ] PRESCRIPTION DRUG RELATED
  Antidepressant, Pain Medication (opiate), Pain Medication (non-opiate), Methadone, Other Rx-specify:
- [ ] OVER-THE-COUNTER DRUG RELATED
  Pain / Cold Medicine, Other OTC-specify:
- [X] ILLICIT DRUG RELATED
  Diverted Medications Cocaine, Heroin, Other illicit drug-specify:
- [ ] OTHER SUBSTANCES-RELATED
  Please specify:

- [ ] COMPLETE
  All records necessary for adequate review of the case were available
- [X] ADEQUATE
  Minor gaps (i.e. information that would have been beneficial but was not essential to the review of the case)
- [ ] LIMITED
  Major gaps (i.e. information that would have been crucial to the review of the case)
- [ ] INADEQUATE
  Minimal records available for review (i.e. death certificate and no additional records)
- [ ] NO RECORDS

CASE NOTES:
[redacted] YO found dyspneic in bed p̄ using a "street Percocet" and alcohol, [illegible] found dead [illegible].

Moved fr NY ⇒ AZ ([illegible] in AF)

? ACEs

AZ OFR: Tox Data/Analysis Case #2

OVERDOSE FATALITY REVIEW TEAM DECISION FORM 1

REVIEW DATE

RECORD ID # 2020-25

ASSIGNED RCF CODE 3

FIRST NAME: [redacted]

LAST NAME:

DOB:

DOD: 6/17/2020

LOCATION OF DEATH: Shelter - [redacted]

COUNTY OF DEATH: [redacted]

CAUSE OF DEATH: Methadone and Methamphetamine toxicity; pulmonary embolism

MANNER OF DEATH: Accident

PMP (3 YEARS)
Rxs:
Prescribers: Ø
Pharmacies:
LAST Rx:

	YES	PROBABLY	NO	UNKNOWN
DID MENTAL HEALTH CONDITIONS CONTRIBUTE TO THE DEATH?	☑	☐	☐	☐
DID SUBSTANCE USE DISORDER CONTRIBUTE TO THE DEATH?	☒	☐	☐	☐
WAS THIS DEATH LISTED AS ACCIDENTAL?	☑	☐	☐	☐
WAS THIS DEATH A SUICIDE?	☐	☐	☑	☐

Toxicology Data
(RCD= approximate Reference Concentration associated with Death):

Methadone 630 ng/mL (~1000) Meth 10 (~2000 ~~[illegible]~~)
Hydroxyzine 19 ng/mL (~? 4200) Amph 6.7
Risperidone 9.5 ng/mL (?~1000)

ESTIMATE THE DEGREE OF RELEVANT INFORMATION (RECORDS) AVAILABLE FOR THIS CASE:

☑ COMPLETE
All records necessary for adequate review of the case were available

☐ ADEQUATE
Minor gaps (i.e. information that would have been beneficial but was not essential to the review of the case)

☐ LIMITED
Major gaps (i.e. information that would have been crucial to the review of the case)

☐ INADEQUATE
Minimal records available for review (i.e. death certificate and no additional records)

☐ NO RECORDS

DRUG RELATEDNES: SELECT ALL THAT APPLY

PRESCRIPTION DRUG RELATED
☐ Antidepressant, Pain Medication (opiate), Pain Medication (non-opiate), Methadone, Other Rx-specify:

☐ OVER-THE-COUNTER DRUG RELATED
Pain / Cold Medicine, Other OTC-specify:

☒ ILLICIT DRUG RELATED
Diverted Medications Cocaine, Heroin, Other illicit drug-specify: Meth., Methadone

☒ OTHER SUBSTANCES-RELATED
Please specify: THC

CASE NOTES:
[redacted] YOM found dead in bed at a shelter, last seen ~ 2 hr prior.
Partial (R) pulm artery PE on autopsy
2 prior ODs
Found as pt
Had just told his counselor @ Narcan rescue

Take-Home Points

Xylazine = animal sedative; illicit drug contaminant; can cause human harm

Poison centers are great (free) resources for patient care and public safety work

Medical toxicologist can assist OFRC with case reviews

Questions/Slides

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CTPER: http://phoenixmed.arizona.edu/centers/toxicology