DEA TOX

DRUG ENFORCEMENT ADMINISTRATION

TOXICOLOGY TESTING PROGRAM

2022 ANNUAL REPORT

U.S. Department of Justice
Drug Enforcement Administration
Diversion Control Division
Drug and Chemical Evaluation Section

Contents

Introduction

The Drug Enforcement Administration's Toxicology Testing Program (DEA TOX) began in May 2019 as a surveillance program aimed at detecting new psychoactive substances within the United States. In response to the ongoing synthetic drug epidemic, the Drug Enforcement Administration (DEA) awarded a contract with the University of California at San Francisco (UCSF) to analyze biological samples generated from overdose victims of synthetic drugs.

In many cases, it can be difficult to ascertain the specific substance responsible for the overdose. The goal of DEA TOX is to connect symptom causation to the abuse of newly emerging synthetic drugs (e.g. synthetic cannabinoids, synthetic cathinones, synthetic opioids, other hallucinogens, etc.).

DEA has reached out to local health departments, law enforcement partners, poison centers, drug court laboratories, hospitals, and other medical facilities to offer testing of leftover or previously collected samples for analysis of synthetic drugs. DEA TOX is interested in patients thought to have ingested a synthetic drug, where the traditional drug screen has produced little or no viable options to explain the symptoms exhibited by the patient (alcohol and delta-9 THC are exempted). DEA TOX may approve leftover unused biological samples (or biological samples) or occasionally non-biological samples for testing from a medical facility or law enforcement partner only.

Once DEA TOX is contacted (**DEATOX@DEA.GOV**) and upon approval by DEA of the request for testing of specific samples, the originating laboratory is invited to send their samples to the Clinical Toxicology and Environmental Biomonitoring (CTEB) Laboratory at UCSF. DEA covers the full cost of analysis for each sample approved for testing. Using liquid chromatography quadrupole time-of-flight mass spectrometry, synthetic drugs identified within the samples are confirmed and quantified. Levels denoted in the tables below with a defined range represent the low and high concentrations reported when the frequency of detection is greater than one. The CTEB laboratory currently maintains a comprehensive drug library consisting of the following:

912 new psychoactive substances (**NPS**);
161 traditional illicit drugs (**TID**);
93 prescription or over-the-counter (**OTC**) drugs;
15 dietary supplement stimulants (**DSS**); and
Multiple precursor chemicals, additives or impurities (**P/A/I**)

Each sample is analyzed by targeted and suspect screening through liquid chromatography- quadrupole time-of-flight mass spectrometry (LC-QTOF/MS) using non-targeted data acquisition. Confirmed drugs are quantified through targeted LC-QTOF/MS testing using the isotope dilution method (See Appendix 1 for method details).

This publication presents the results of cases analyzed and completed by the CTEB laboratory from January 1, 2022 through December 31, 2022.

Summary

Between January 1, 2022 through December 31, 2022, 356 biological samples, 19 drug products, and 1 drug paraphernalia from 370 cases originating in 24 states (Fig.1) were submitted to DEA TOX. These samples were analyzed for NPS, TID, prescription or OTC drugs, DSS, and P/A/I. The biological samples submitted consisted of 41 serum, 38 plasma, 151 whole blood, 1 liver tissue, 1 muscle tissue and 124 urine samples. The drug products are further described on page 19.

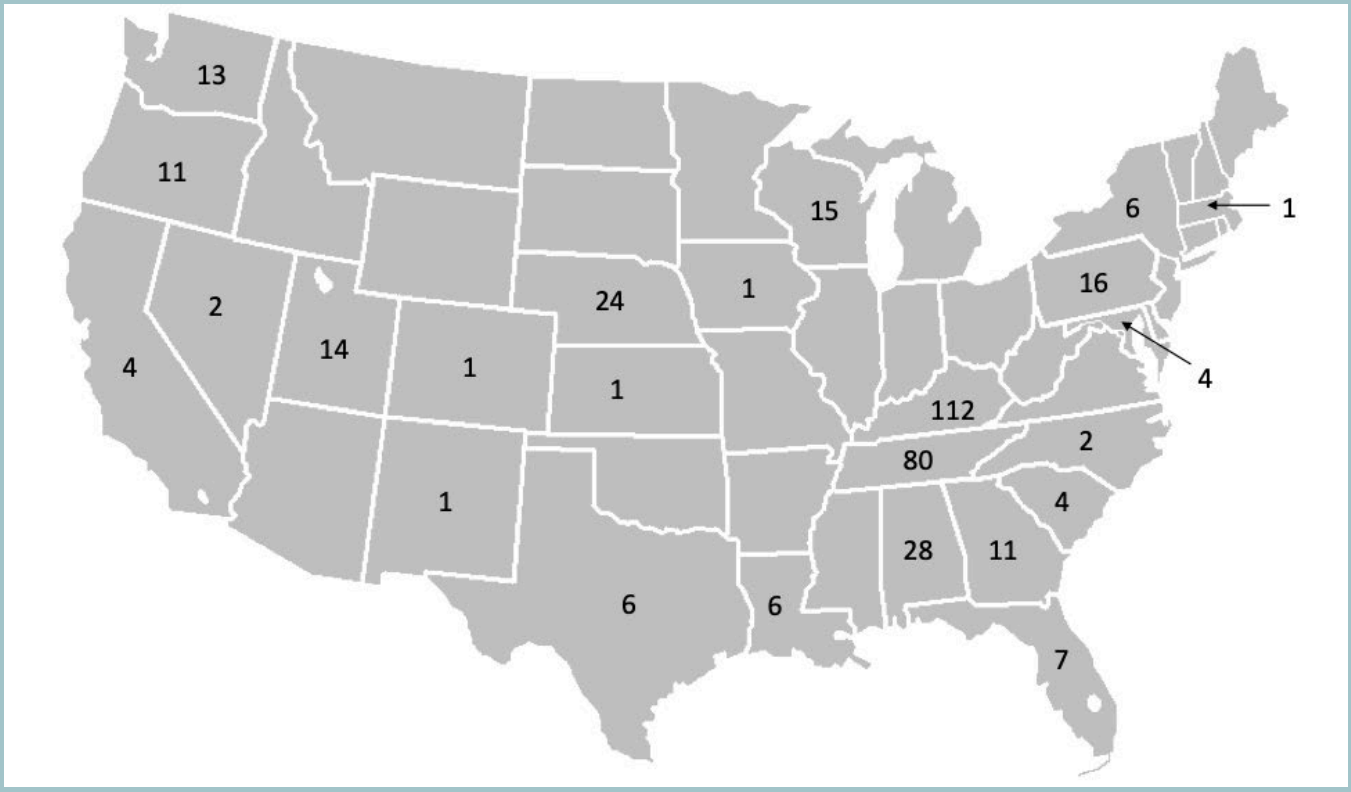

Figure 1. Geographic distribution of cases referred to DEA TOX in 2022.

DEA TOX identified and confirmed a total of 2,378 drugs and metabolites that consisted of 282 NPS detections, 951 TID detections, 996 prescription or OTC drug detections, 3 DSS, and 146 P/A/I detections during this reporting period (Fig. 2A). While some drugs identified could be placed in more than one category, for purposes of this report and for consistency, DEA TOX placed such substances in a single category only. Many prescription drugs that are commonly abused and encountered are listed as TID. Substances that are not approved by the Food and Drug Administration for medical use within the U.S. are considered NPS or adulterants.

A breakdown of the 2,378 total drug and metabolite confirmations demonstrated 140 different drugs, which consisted of 32 NPS, 17 TID, 83 prescription and OTC drugs, 2 DSS and 6 P/A/I (Fig. 2B).

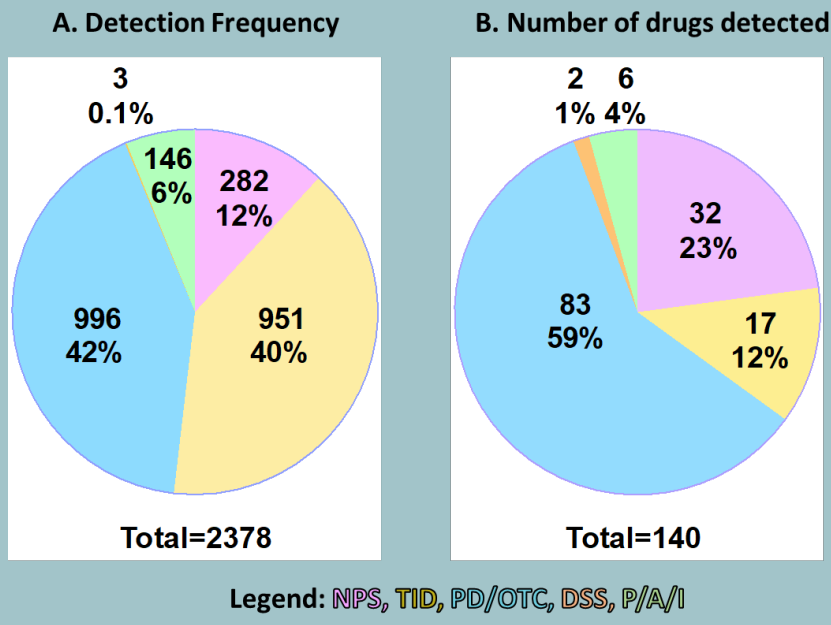

Figure 2. Detection frequency and number of drugs detected in each drug category

Case Types

The cases referred in 2022 can be classified into four categories: deaths (147), overdoses (186), urinalysis (19), and drug products (18). One case submitted only drug paraphernalia. The general drug classes found in overall, overdose, and death cases are presented in Figure 3. Overall, NPS accounted for 41% (153 of 370) of the cases. This increased to 67% (98 of 147) in death cases. In cases where only TID's were found, fentanyl was the predominant substance identified, especially in non-fatal submissions.

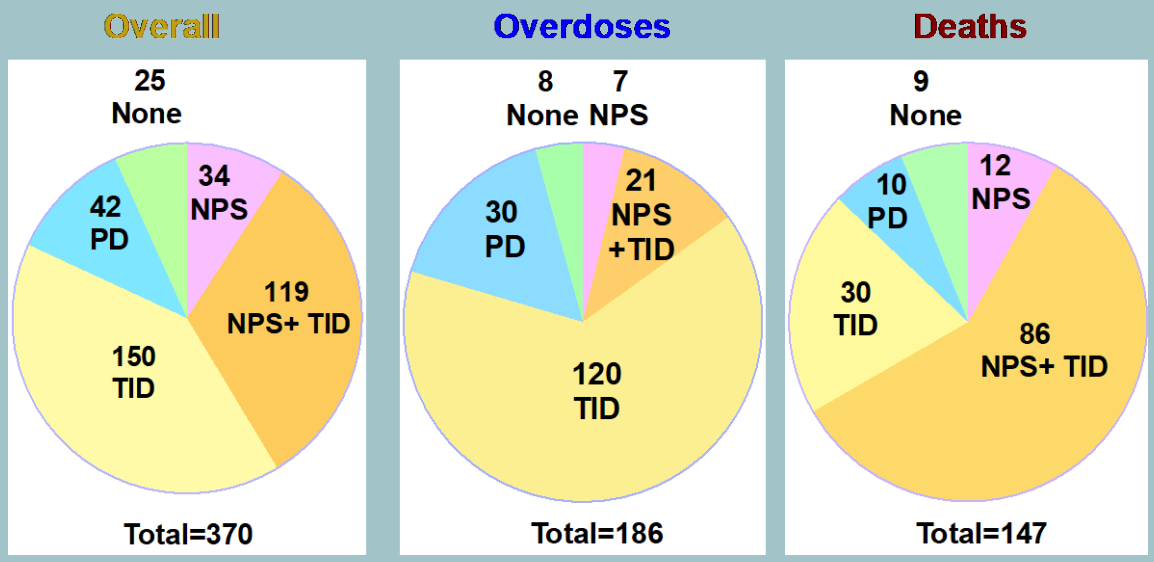

Figure 3. Drug class distribution in all, overdose and death cases

Gender and Age of Subjects

Information on gender and/or age was available for 352 cases, of which 236 are males and 115 females (one case was not identified) (Fig. 4). The average age for males is 37 (range: 1.3-67) while the average for females is 38 (range: 1.9-70). The overall average age is 37 (range: 1.3-70).

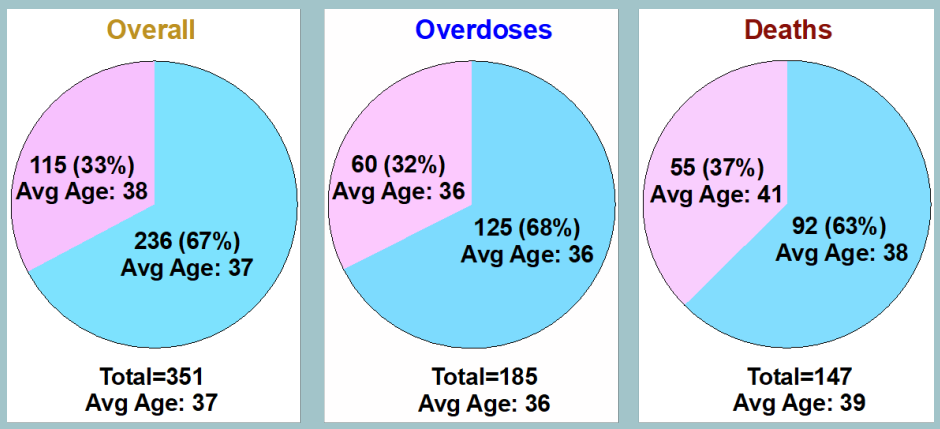

Figure 4. Gender distribution and average age of subjects

Polydrug use

The number of NPS and TID detected were tallied for each of the 352 cases with known gender and/or age. Two or more substances were confirmed in 219 (62%) cases. The highest number found in death cases was nine, while the highest number in overdose cases was seven. The distribution of number of drugs detected in the cases is summarized in Fig 5.

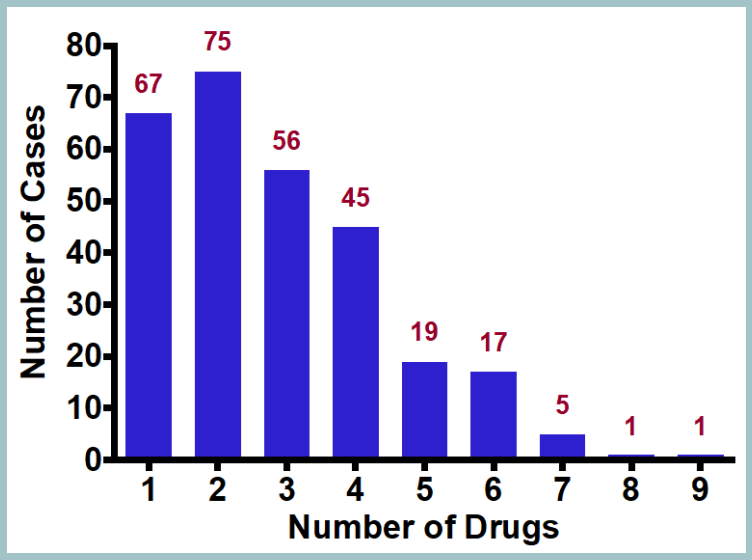

Figure 5. Distribution of the number of NPS and TID in cases

New Psychoactive Substances

DEA TOX confirmed 282 detections comprising of 32 NPS[§] from seven different classes of drugs (Fig. 6) in 2022. The total encounters for each NPS class are summarized in Figure 7. The quantitative levels found in the cases are presented for each NPS pharmacological class in Tables 1-4. Phenibut is outside these classes. There were 10 cases confirmed from Alabama and one each from Maryland and Washington. The levels quantified were 92,000 (serum) and 28.4 (plasma) ng/mL. No quantitation was requested in the 10 urine samples referred.

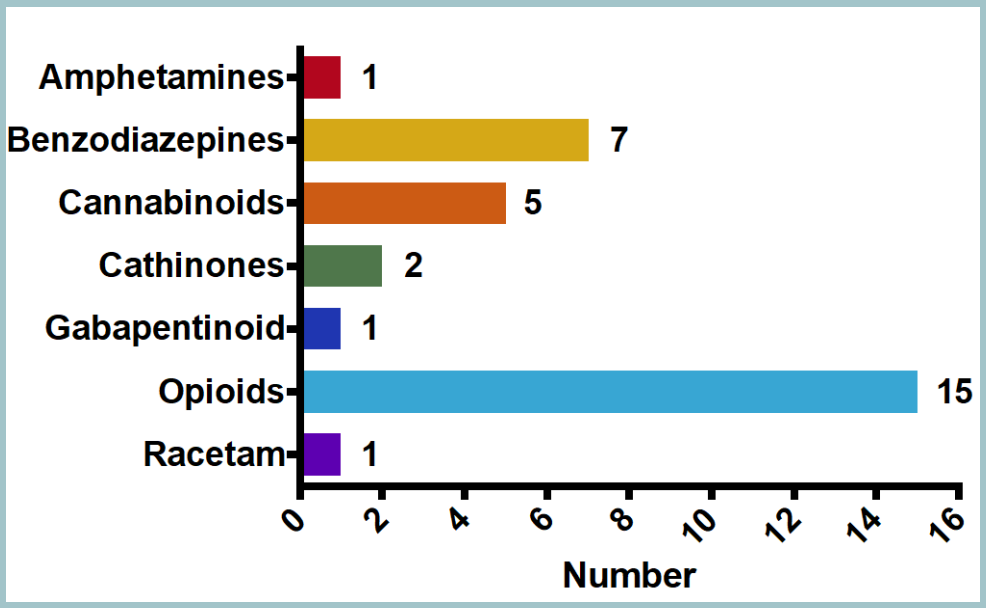

Figure 6. Number of drugs in each NPS class detected in cases

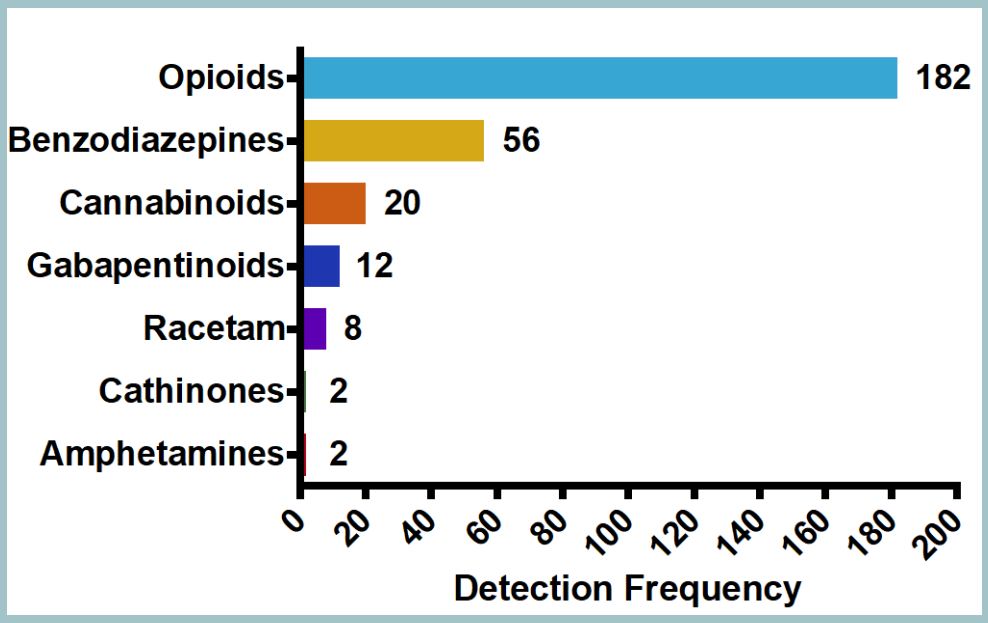

Figure 7. Detection frequency of each NPS class detected in cases

Table 1. NPS stimulants detected in 2022

Drug Class	Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
				S	P	WB	U
Amphetamine	MDEA	2	GA			0.8-1.2	
Cathinones	Eutylone	1	FL				
	Pentylone	1	TN			1.1	
Racetam	Phenylpiracetam	8	AL(6), TN, WA	36400			

Table 2. NPS cannabinoids detected in 2022

Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
			S	P	WB	U
4F-ABUTINACA	1	WA				
4F-MDMB-BUTICA	5	FL				
11-nor-9-carboxy-delta-8-THC	4	KY(3), TX	46.9	178		107-3230
ADB-BUTINACA	6	FL(5), UT(1)		6.1		
Delta-8-THC	3	KY(3)	5.7			128
Delta-10-THC	1	KY				

Table 3. NPS benzodiazepines detected in 2022

Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
			S	P	WB	U
8-Aminoclonazolam	20	GA(3), KS, KY, LA, MD, NE, TN(11), UT	0.4-7.4	0.4	0.4-47.2	471
Bromazolam	21	GA(2), KY(2), NM, TN(15), UT,	17.5-46.6	3	0.1-62.9	
Clonazolam	1	UT		1.2		
Deschloroetizolam	1	KY			6.8	
Etizolam	3	IA, TN, WA			0.7-18.5	
Flualprazolam	4	GA(2), TN, UT	1.8-3.3	2.9	5.1	
Flubromazepam	3	TN(3)			1.1-20.7	
Flubromazolam	3	IA, WA(2)			0.7	

Table 4. NPS opioids detected in 2022

Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
			S	P	WB	U
2-Methyl-AP-237	2	KS, WA			313-379	
5-Amino Isotonitazene	1	TN			1.2	
7-OH Mitragynine	5	GA, KY(2), LA, TN	15.1		2.9	1370-1960
Acetyl Fentanyl	10	KY, WA(9)				
Despropionyl *para*-Fluorofentanyl	36	AL, CA, GA(3), KY(3), NE(4), TN(20), WA(3), WI	0.6		0.1-3.3	62.5-276
Isotonitazene	1	TN			0.9	
Metonitazene	15	KY, TN(14)			1.1-13.8	
Mitragynine	16	GA(2), KS, KY(4), LA(2), PA, TN(4), UT, WA	15.3-139	4.4	0.7-113	12.1-1070
N-Methyl Norfentanyl	2	KY, WA				98
N-Piperidinyl Etonitazene	3	TN(3)			1.6-12	
N-Pyrrolidino Etonitazene	1	LA			1.1	
para-Bromofentanyl	1	WA				
para-Chlorofentanyl	1	WA				
para-Fluoro acetylfentanyl	3	CA, TN, WA			0.4-1.0	
para-Fluorofentanyl	74	AL, CA(3), GA(6), KY(7), NE(7), TN(44), WA(4), WI(2)	1.2-17.7		0.2-111	1.9-1120
Protonitazene	1	TN				4
Remifentanil Acid	3	KY, LA(2)			3.4-7.5	353
Tianeptine	7	AL, TN			9.9	135-7880

* AL – Alabama; CA – California; GA – Georgia; KS – Kansas; KY – Kentucky; LA – Louisiana; NE – Nebraska, PA – Pennsylvania; TN – Tennessee; UT – Utah; WA – Washington; WI – Wisconsin;
**S – Serum; P – Plasma; WB – Whole Blood; U – Urine
§ - Parent drugs or metabolites are only counted once for the number of drugs detected in Tables 1-4. If only a metabolite is encountered in the absence of a parent drug, it will still be counted as a unique drug. Both parent drugs and metabolites are counted as detections.

Traditional Illicit Drugs

DEA TOX confirmed 951 detections comprising of 17 TIDs[§] (Table 5) in 2022.

Table 5. TID detected in 2022

Drug Class	Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
				S	P	WB	U
Amphetamines (4)	4-Hydoxymeth-amphetamine	19	KY(16), NE, TN(2)			1.3-19.8	12.1-8075
	Amphetamine	46	GA(2), KY(16), NE(6), NM, OR, TN(16), TX, UT(2), WI	13.7-978	45.6	4.3-435	722-15400
	HMMA‡	3	KY				3.5-835
	MDA	1	KY			14.5	
	MDMA	2	KY, UT		88.6	660	
	Methamphetamine	122	AL(3), CA, GA(4), KY(45), NC, NE(9), NM, OR(3), PA(3), SC, TN(39), TX, UT(7), WA(2), WI(2)	2.5-5940	7.9-1430	1.1-7870	1.5-204000
Arylcyclohexyl-amines (1)	Ketamine	18	GA, KY(15), PA, WI	9.1-398			99.6-50700
Cannabinoids (2)	11-nor-9-carboxy-delta-9-THC	44	CO, FL, GA, IA, KS, KY(21), MA, NE, OR(3), PA(3), SC, TN(2), TX(2), UT(3), WI(2)	60.6-232	35.5-342	37.6-141	60.6-38800
	11-OH-delta-9-THC	1	KY				685
	Cannabidiol	1	KY				NQ

Drug Class	Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
				S	P	WB	U
	Delta-9-THC	4	KS, TN, UT(2)		23	34.0-56.8	99.5
Cocaine (1)	Benzoylecgonine	99	AL(2), FL(2), GA(8), KY(32), MA, NE(13), OR(3), PA(12), TN(17), UT(2), WI(7)	12.3-1700	0.9-998	1.5-1880	4.0-129000
	Cocaethylene	27	AL, FL(2), GA(4), KY(7), NE(8), TN(4), WI	NQ		NQ	NQ
	Cocaine	59	AL, FL(2), GA(5), KY(14), MD, NE(10), PA(6), TN(13), WA(2), WI(5)	0.4-94.2	1.0-30.8	0.2-996	2.4-257000
	Ecgonine methyl ester	62	AL(2), FL(2), GA(6), KY(19), MD, NE(6), OR(3), PA(12), TN(6), WI(5)	NQ	NQ	NQ	NQ
Opioids (9)	6-Acetyl Morphine	1	WI				261
	Beta-Hydroxyfentanyl	41	CO, FL, KY(11), MD, NE(4), NM, TN(19), WI(3)		0.3-1.4	0.5-2.9	4.3-410
	Codeine	6	TN(5), UT			0.2-2.3	
	Desmethyl-cis-Tramadol	7	KS, KY(4), TN(2)			0.5-49.9	5.2-58.3

Drug Class	Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
				S	P	WB	U
	Fentanyl	174	AL, CO, GA(8), FL(2), IA, KY(44), MA, MD, NC, NE(13), NM, NV(2), OR(3), PA(11), SC, TN(59), TX(4), UT(3), WA(11), WI(6)	0.8-104	0.8-71.0	0.5-106	4.9-6160
	Hydrocodone	10	KY(4), TN(6)			0.2-19.2	51.2-177
	Hydromorphone	13	KY(7), TN(6)	20.6		1.8-2270	19.2-247
	Morphine	31	IA, KY, NE(2), TN(24), UT(2), WI		7.3	0.5-113	1520 - 8160
	Norfentanyl	122	AL, CO, FL(2), GA, IA, KY(43), MA, MD, NE(13), NM, OR(3), PA(11), SC, TN(31), TX, UT, WA(3), WI(6)	0.1-9.6	0.3-10.5	0.3-20.6	1.7-42800
	Oxycodone	22	KY(6), LA, NE, OR, TN(9), UT ,WI(3)		3.4-20.2	0.3-281	14.7-157000
	Oxymorphone	1	KY				NQ
	Tramadol	15	KY(6), TN(6), UT, WA(2)		3.4	0.2-1020	7.0-80.8

*AL – Alabama; CA – California; CO – Colorado; FL – Florida; GA – Georgia; IA – Iowa; KS – Kansas; KY – Kentucky; LA – Louisiana; MA – Massachusetts; MD – Maryland; NC – North Carolina; NE – Nebraska; NM – New Mexico; NV – Nevada; OR – Oregon; PA – Pennsylvania; SC – South Carolina; TN – Tennessee; TX – Texas; UT – Utah; WA – Washington; WI – Wisconsin

**S – Serum; P – Plasma; WB – Whole Blood; U – Urine; NQ – Not Quantified

‡ HHMA (3,4-Dihyroxymethamphetamine is a metabolite of MDMA)

§ - Parent drugs or metabolites are only counted once for the number of drugs detected in Table 5. If only a metabolite is encountered in the absence of a parent drug, it will still be counted as a unique drug. Both parent drugs and metabolites are counted as detections**.**

Prescription and Over the Counter Drugs

DEA TOX confirmed 996 detections comprising of 83 prescription or OTC drugs[§] (Table 6) in 2022. Drugs for the prescription/OTC drugs panel are not typically quantitated unless specifically requested thus "Confirmed Levels" are not provided.

Table 6. Prescription or OTC drugs detected in 2022

Drug Class	Drug	Freq.	States Found*
Anesthetic	Lidocaine	35	AL, CA(2), GA, KY(14), MD, NC, NE(3), PA(2), SC, TN(7), UT, WA
Antibiotic	Linezolid	2	GA, TN
	Sulfomethoxazole	3	KY, TN(2)
Anticonvulsant	Carbamazepine	3	KY(2), TN
	Gabapentin	54	AL, GA, KY(15), LA, NE(5), OR, TN(29), WI
	Lamotrigine	9	GA, KY(6), TN, UT
	Levetiracetam	7	GA, KY(3), TN(3)
	Oxcarbazepine	5	KY(3), TN(2)
	Topiramate	1	NE
Antidepressant	Amitriptyline	7	KY(6), TN
	Citalopram	19	KY(6), NC, NE(3), OR, TN(4), TX, UT(2), WA
	Doxepin	1	TN
	Duloxetine	4	KY, OH, TN(2)
	Fluoxetine	16	AL, KY(10), LA, NE, TN(2), WA
	mCPP[‡]	18	KS, KY(8), LA, NE, TN(5), UT, WI
	Nordoxepin	1	KY
	Norfluoxetine	14	KS, KY(7), LA, NE, NY, TN(2), WA
	Nortriptyline	7	KY(6), TN
	Paroxetine	4	AL, TN(2), WI
	Pipradol	1	WI
	Protriptyline	2	KY(2)
	Sertraline	11	GA, KY(3), OR, NE, TN(4), WI
	Trazodone	23	KS, KY(8), LA, NE(2), TN(9), UT, WI
	Venlafaxine	4	KY(3), UT
Antidiabetic	Metformin	4	KY(2), OR, TN

Drug Class	Drug	Freq.	States Found*
Antidiarrheal	Loperamide	6	GA, KY, TN(2), WI(2)
Antihistamine	Chlorpheniramine	6	AL, KY(2), NE, TN(2)
	Cimetidine	2	KY, WA
	Diphenhydramine	75	GA, KS, KY(25), NC, NE(2), NY, OR(2), PA, TN(37), TX, UT(2), WI
	Doxylamine	5	AL, NE, TN(2), WI
	Hydroxyzine	21	CA, GA, IA, KY(7), NE(2), OR, TN(3), UT, WI(4)
	Promethazine	6	KY(2), NE, TN(2), WI
	Pseudoephedrine	2	CA, NE
Antipsychotic	Aripiprazole	5	GA(2), TN(3)
	Clozapine	1	KY
	Haloperidol	5	OR, TN(2), UT(2)
	Olanzapine	8	GA, KY(4), OR, UT(2)
	Ziprasidone	3	OR, TN(2), UT(2)
Antiretroviral	Emtricitabine	1	WI
	Tenofovir	1	WI
Anxiolytic	Buspirone	6	NE, TN(4), WI
Benzodiazepine	7-amino Clonazepam	17	GA(2), KS, KY(6), LA, NE, PA, TN(2), UT, WI(2)
	7-amino Nitrazepam	1	GA
	Alpha-hydroxy Alprazolam	11	IA(2), KY(3), NE, TN(2), UT, WI(2)
	Alprazolam	23	AL, GA, IA. KY(2), NE(3), NY, TN(11), UT, WI(2)
	Chlordiazepate	2	KY, WI
	Clobazam	3	KY (3)
	Clonazepam	5	KY(2), NE, LA, WI
	Diazepam	15	GA, KY(3), LA, NE(2), TN(6), TX, UT
	Lorazepam	28	CO, GA, KY(18), OR(2), TN(3), UT(2), WI
	Midazolam	49	AL, CO, FL, GA, KY(32), LA, NC, NE, OR(3), PA, TN(2), UT(2), WA, WI
	Mirtazapine	3	AL, KY, PA
	Nitrazepam	1	KY
	Nordiazepam	19	GA(2), KY(5), LA, NE(2), TN(6), TX, UT, WI

Drug Class	Drug	Freq.	States Found*
	Oxazepam	11	KY(7), NC, NE, TN, WI
	Temazepam	8	KY(2), NC, NE, TN(2), TX, WI
	Zolpidem	1	KY
Cardiovascular	Amiodarone	14	AL, GA, KY(3), LA, NE(2), TN(4), TX, WA
	Atenolol	4	CA, GA, KY(2)
	Atorvastatin	5	IA, KY, LA, TN(2)
	Atropine	12	AL, KY(6), NE, PA, TN(2), TX
	Carvedilol	4	KY(2), LA, NE
	Clonidine	7	KY(3), NE, TN(3)
	Diltiazem	3	AL, TN, WI
	Furosemide	2	KY(2)
	Labetalol	2	KY, SC
	Lisinopril	7	IA, KY(5), TN
	Metoprolol	10	IA,KY, TN(6), WI(2)
	Propanolol	2	KS, TN
	Verapamil	1	WI
	Warfarin	2	NE, WI
Cough Suppressant	Dextromethorphan	19	AL, GA, KY(8), OR, NE(3), PA(2), TN(3)
	Dextrorphan	15	AL, KY(8), NE(2), PA, TN(3)
Decongestant	Norpseudoephedrine	5	KY(3), TN(2)
	Phenylephrine	1	KY
	Pseudoephedrine	9	KY(8), TN
Diuretic	Furosemide	4	KY(3), WI
Muscle Relaxant	Baclofen	7	IA, KY(5), UT
	Cyclobenzaprine	9	KY(5), TN(3), WI
	Methocarbamol	1	TN
	Orphenadrine	1	NE
Opioid	Buprenorphine	16	KY(10), OR, TN(2), UT, WI(2)
	EDPP	9	GA(2), KY, NE(5), TN
	Methadone	12	GA(2), KY(3), NE(5), TN(2)
	Naloxone (Antagonist)	98	AL, FL(2), GA(3), KY(39), LA, MD, NE(12), PA(7), TN(23), TX(4), WI(5)
	Naltrexone (Antagonist)	1	KY
	Norbuprenorphine	10	KY(5), OR, TN, WI(3)

Drug Class	Drug	Freq.	States Found*
Pain Reliever	Acetaminophen	86	FL(2), GA(3), AL(2), CO, KY(46), LA, NE, NM, OR, PA(3), TN(14), TX, UT(3), WA(6), WI
	Naproxen	4	FL, KY, NE(2)
Respiratory	Albuterol	3	KY(3)
Stimulant	Methylphenidate	1	TN
Tuberculostatic	Levofloxacin	5	GA, KY, TN(3)

*AL – Alabama; CA – California; CO – Colorado; FL – Florida; GA – Georgia; IA – Iowa; KS – Kansas; KY – Kentucky; LA – Louisiana; MA – Massachusetts; MD – Maryland; NC – North Carolina; NE – Nebraska; NM – New Mexico; NV – Nevada; OR – Oregon; PA – Pennsylvania; SC – South Carolina; TN – Tennessee; TX – Texas; UT – Utah; WA – Washington; WI – Wisconsin

**S – Serum; P – Plasma; WB – Whole Blood; U – Urine; NQ – Not Quantified

‡- - The mcPP (meta-Chlorophenylpiperazine) detected in these cases is the metabolite of trazodone.

§ - Parent drugs or metabolites are only counted once for the number of drugs detected in Table 6. If only a metabolite is encountered in the absence of a parent drug, it will still be counted as a unique drug. Both parent drugs and metabolites are counted as detections.

Dietary Supplement Stimulants

DEA TOX confirmed three detections comprising of two DSS (Table 7) in 2022.

Table 7. DSS detected in 2022

Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
			S	P	WB	U
Hordenine	2	WI(2)				NQ
Yohimbine	1	LA			NQ	

*LA – Louisiana; WI – Wisconsin
**S – Serum; P – Plasma; WB – Whole Blood; U – Urine; NQ- Not Quantified

Precursors/Additives/Impurities

DEA TOX confirmed 146 detections comprising of six P/A/I§ (Table 8) in 2022.

Table 8. P/A/I detected in 2022

Drug Class	Drug	Freq.	States Found*	Confirmed Levels (ng/mL)**			
				S	P	WB	U
Adulterant (4)	Brodifacoum	4	FL				
	Phenacetin	3	KY, PA(2)		6.1-94.9		
	Quinine	16	GA(2), KY(6), NE(3), TN(3), TX, WI	7.5-13.5	1.5-2.1	0.6-25.4	111-846
	Xylazine	22	AL, KY(6), NE, TN(14)			0.1-35.4	15.4-139
Impurity	N,N-dimethyl-amphetamine	17	GA(2), KY(5), NE(5), NM, TN(4)	146-546		1.8-26.7	4.7-9570
Precursor	4-ANPP	84	GA(3), IA, KY(13), MD, NE(5), NM, OR, PA(2), TN(44), WA(11), WI(2)	1.1-8.9	0.9-2.7	0.2-164	3.9-104

*AL – Alabama; FL – Florida; GA – Georgia; IA – Iowa; KY – Kentucky; MD – Maryland; NE – Nebraska; NM – New Mexico; OR – Oregon; PA – Pennsylvania; TN – Tennessee; TX – Texas; WA – Washington; WI – Wisconsin

**S – Serum; P – Plasma; WB – Whole Blood; U – Urine; NQ – Not Quantified

§ - Parent drugs or metabolites are only counted once for the number of drugs detected in Table 8. If only a metabolite is encountered in the absence of a parent drug, it will still be counted as a unique drug. Both parent drugs and metabolites are counted as detections.

Drug Paraphernalia

DEA TOX received 20 exhibits and confirmed 91 detections in 19 drug products and one drug paraphernalia in 2022 (Table 9).

Table 9. Drug Paraphernalia exhibits analysis in 2022

Product (Weight)	Drug	Drug Class	State	Confirmed Level: mg drug/ g drug product	Actual Amount within Drug Product
Green herbal mixture	4F-MDMB-BUTICA	Synthetic cannabinoid	FL	7.9	Bulk material provided
	Brodifacoum	Additive		1.4	
	ADB-BUTINACA	Synthetic cannabinoid		0.38	
Green herbal mixture	4F-MDMB-BUTICA	Synthetic cannabinoid	FL	3.9	Bulk material provided
	Brodifacoum	Additive		1.7	
	ADB-BUTINACA	Synthetic cannabinoid		0.32	
	Eutylone	Synthetic cathinone		0.14	
Green herbal mixture	4F-MDMB-BUTICA	Synthetic cannabinoid	FL	6.1	Bulk material provided
	ADB-BUTINACA	Synthetic cannabinoid		0.21	
Green herbal mixture	Brodifacoum	Additive	FL	6.3	Bulk material provided
	4F-MDMB-BUTICA	Synthetic cannabinoid		0.58	
	ADB-BUTINACA	Synthetic cannabinoid		0.061	
Green herbal mixture	4F-MDMB-BUTICA	Synthetic cannabinoid	FL	3.1	Bulk material provided
	ADB-BUTINACA	Synthetic cannabinoid		1.1	
	Brodifacoum	Additive		0.19	
Gray crystal (188.2 mg)	Fentanyl	Opioid	KY	26.0	4.9 mg
	Cocaine	Stimulant		15.0	2.8 mg
	para-Fluorofentanyl	Opioid		11	2.1 mg
	4-ANPP	Precursor		5.2	0.98 mg
	Diphenhydramine	Antihistamine		2.1	0.40 mg
	Norfentanyl	Precursor		0.80	0.15 mg
	Methamphetamine	Stimulant		0.098	0.018 mg
	Phenacetin	Additive		0.075	0.014 mg
	Despropionyl-*para*-fluorofentanyl	Precursor		0.048	0.009 mg

	Lidocaine	Anesthetic		0.043	0.0081 mg
	Acetyl Fentanyl	Opioid		0.021	0.004 mg
	Tramadol	Opioid		0.021	0.004 mg
Blue "M30" Tablet (103.2 mg)	Acetaminophen	Pain Reliever	WA	533	55.0 mg
	Fentanyl	Opioid		18	1.9 mg
	4-ANPP	Precursor		11	2.1 mg
	Acetyl Fentanyl	Opioid		0.015	0.0015 mg
Blue "M30" Tablet (112.0 mg)	Acetaminophen	Pain Reliever	WA	966	108 mg
	Fentanyl	Opioid		35	3.9 mg
	4-ANPP	Precursor		3.2	0.36 mg
	N-Methyl Norfentanyl	Opioid		0.015	0.0017mg
	Acetyl Fentanyl	Opioid		0.014	0.0016 mg
Green "S 90 3" Tablet	Flubromazolam	Benzodiazepine	WA	40	0.89 mg
White Rock (230.0 mg)	4-ANPP	Precursor	WA	49	11 mg
	Fentanyl	Opioid		46	11 mg
	Acetyl Fentanyl	Opioid		0.28	0.064 mg
	Norfentanyl	Precursor		0.11	0.025 mg
White Powder (73.7 mg)	Fentanyl	Opioid	WA	51	3.8 mg
	4-ANPP	Precursor		8	0.6 mg
	Acetyl Fentanyl	Opioid		0.14	0.010 mg
	Cocaine	Cocaine		0.030	0.0022mg
	Norfentanyl	Precursor		0.029	0.0021 mg
Blue "M30" Tablet (107.6 mg)	Acetaminophen	Pain Reliever	WA	390	42 mg
	Fentanyl	Opioid		14	1.5 mg
	4-ANPP	Precursor		3.9	0.42 mg
	Acetyl Fentanyl	Opioid		0.013	0.0014 mg
Blue "M30" Tablet (114.1 mg)	Acetaminophen	Pain Reliever	WA	480	54 mg
	Fentanyl	Opioid		21	2.4 mg
	4-ANPP	Precursor		3.1	0.35 mg
	Acetyl Fentanyl	Opioid		0.015	0.0017 mg
White Powder (60.0 mg)	Fentanyl	Opioid	WA	99	5.9 mg
	4-ANPP	Precursor		13	0.78 mg
	Methamphetamine	Amphetamine		7.8	0.47 mg
	Acetyl Fentanyl	Opioid		0.26	0.016 mg
Blue Powder (303.1 mg)	Acetaminophen	Pain Reliever	WA	75	23 mg
	Fentanyl	Opioid		43	13 mg
	Methamphetamine	Amphetamine		19	5.8 mg
	4F-ABUTINACA	Synthetic Cannabinoid		3.7	1.1 mg
	Etizolam	Benzodiazepine		1.7	0.52 mg

	4-ANPP	Precursor		0.69	0.21 mg
	para-Fluorofentanyl	Opioid		0.66	0.20 mg
	Flubromazolam	Benzodiazepine		0.24	0.073 mg
	Lidocaine	Anesthetic		0.16	0.048 mg
	Tramadol	Opioid		0.076	0.023 mg
	Acetyl Fentanyl	Opioid		0.061	0.018 mg
	Cocaine	Cocaine		0.038	0.012 mg
	Despropionyl-*para*-Fluorofentanyl	Precursor		0.007	0.002 mg
Blue "M30" Tablet (106.7 mg)	Acetaminophen	Pain Reliever	WA	430	46 mg
	Fentanyl	Opioid		16	1.7 mg
	4-ANPP	Precursor		4.3	0.46 mg
	para-Fluorofentanyl	Opioid		0.053	0.0057 mg
White Powder (97.0 mg)	*para*-Fluorofentanyl	New Synthetic Opioid	WA	12	1.2 mg
	Fentanyl	Opioid		3.0	0.29 mg
	Despropionyl-*para*-Fluorofentanyl	Precursor		2.1	0.20 mg
	para-Fluoroacetylfentanyl	Opioid		0.11	0.011 mg
	4-ANPP	Precursor		0.078	0.0076 mg
	para-Chlorofentanyl	Opioid		0.038	0.0037 mg
White Rock (94.9 mg)	Fentanyl	Opioid	WA	151	14.3 mg
	4-ANPP	Precursor		18	1.7 mg
	para-Fluorofentanyl	Opioid		2.1	0.20 mg
	Tramadol	Opioid		0.97	0.092 mg
	Norfentanyl	Opioid		0.17	0.016 mg
	Despropionyl-*para*-Fluorofentanyl	Precursor		0.16	0.015 mg
	Acetyl Fentanyl	Opioid		0.10	0.0095 mg
	para-Bromofentanyl	Opioid		0.030	0.0028 mg
Vape Liquid (259.1 mg)	Delta-8 THC	Cannabinoid	KY	600	155 mg
	Delta-10 THC	Cannabinoid		212	55 mg

Selected Drug Trends in Death and Overdose Cases

Fentanyl

DEA TOX confirmed fentanyl in 184 samples from 174 cases (47%) of total cases) submitted by 20 states (Fig. 8). The samples consisted of 87 whole blood, 21 plasma, 20 serum, 44 urine and 12 drug products.

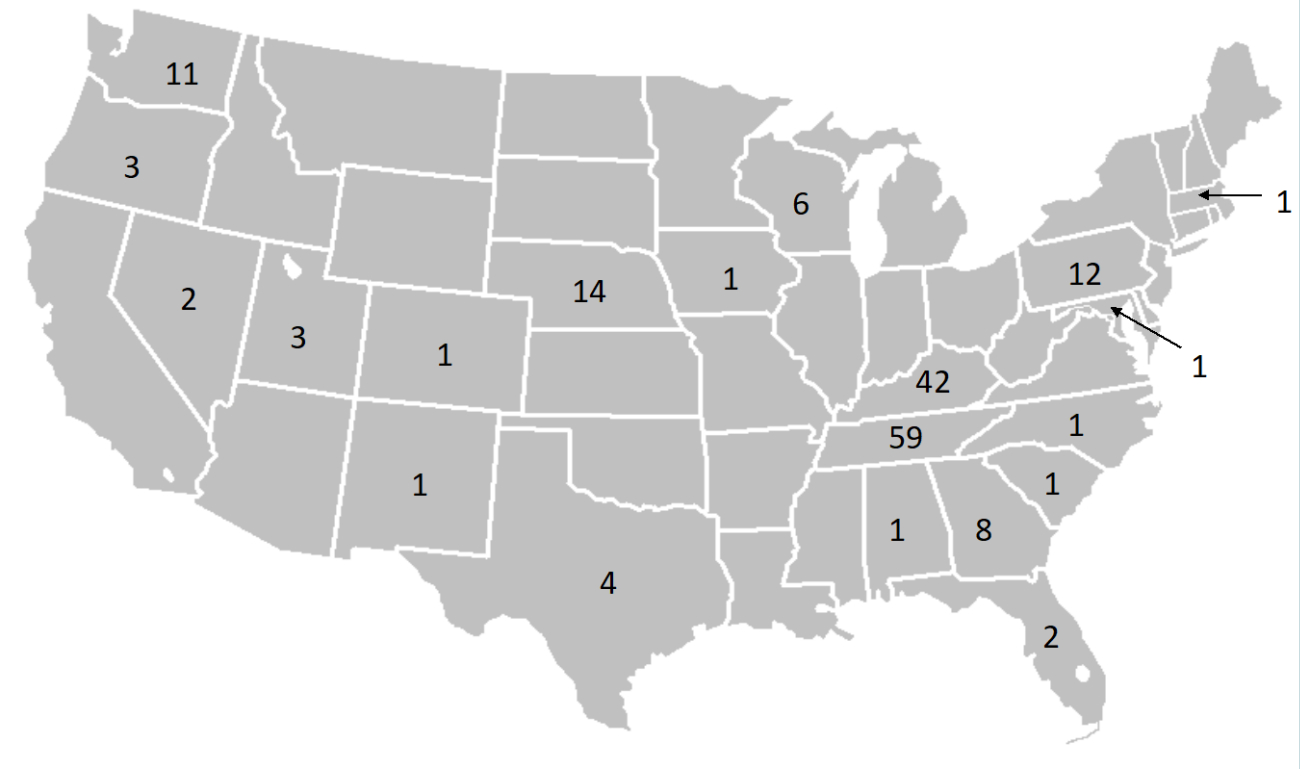

Figure 8. Geographic distribution of cases with confirmed fentanyl

There were 87 deaths and 76 overdoses. The gender distribution and average age in these cases are presented in Figure 9A. There were 87 and 37 blood samples in death and overdose cases, respectively. The mean fentanyl concentration in death cases (17.6 ng/mL) is 2.35x higher than in overdose cases (7.5 ng/mL) but significant overlap in concentrations was observed (Fig. 9B).

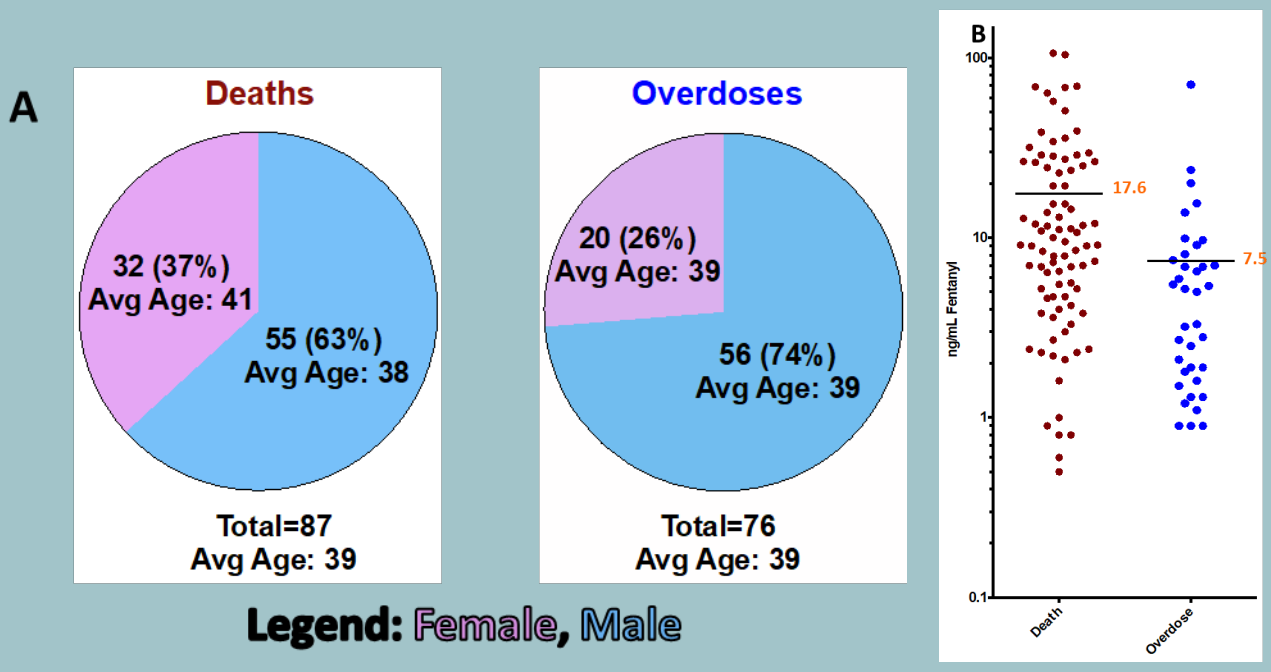

Figure 9. Gender and age (A) and blood fentanyl concentration (B) distribution in death and overdose cases

The concentration ranges for fentanyl found in blood samples from various states in death and overdose cases are presented in Table 10.

Table 10. Blood concentration ranges of fentanyl observed in cases from different states

State	Death Cases		Overdose Cases	
	Concentration (ng/mL)*	Frequency	Concentration (ng/mL)*	Frequency
Alabama	10	1		
Colorado			1.9	1
Florida	5.2- 69.5	2		
Georgia	0.8- 104 (**Avg = 16.6**)	8		
Iowa	6.5	1		
Kentucky	11.1	1	0.9-8.1 (**Avg = 3.8**)	11
Massachusetts			0.9	1
Maryland			20.1	1
Nebraska	0.9- 106 (**Avg = 21.5**)	13	5	1
Nevada			1.2-1.3	2
New Mexico	26.2	1		
North Carolina			7.5	1
Oregon			1.8-2.8 (**Avg = 2.2**)	3
Pennsylvania			0.5-71 (**Avg = 14.6**)	11
South Carolina			2.7	1
Tennessee	0.5- 69 (**Avg = 16.7**)	59		
Texas	0.8	1	1.1-5.9	2
Utah			1.6- 5.2	2

* Average is given in parenthesis for detection frequency ≥ 3

Polydrug use is prevalent in cases involving fentanyl (Fig. 10). Of the 174 cases, 163 were biological samples; 91% of these cases (149 of 163) have two or more drugs confirmed.

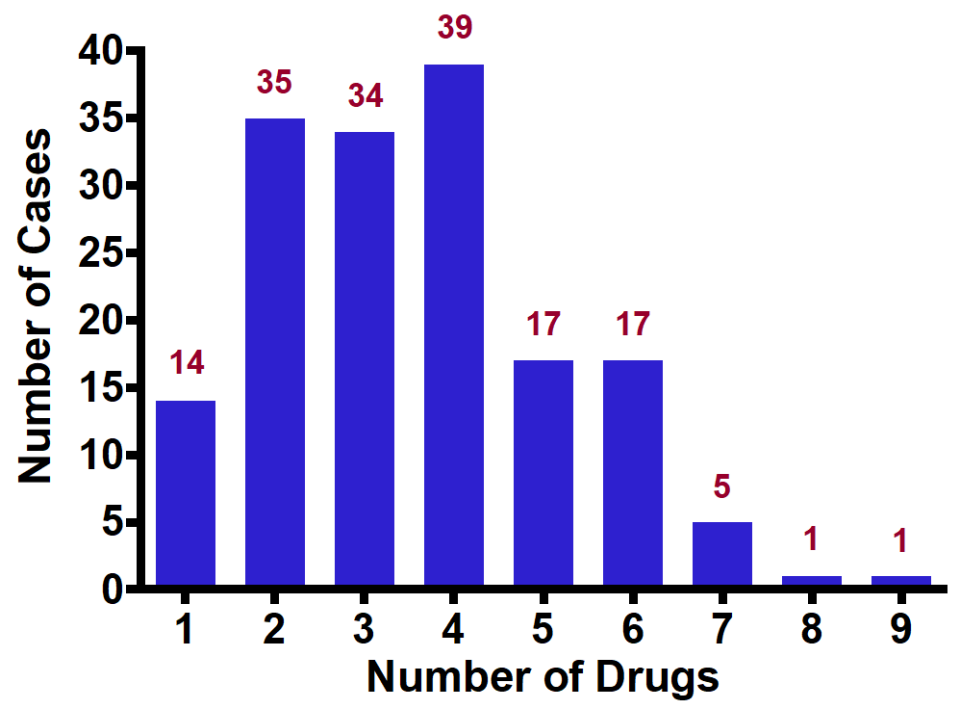

Figure 10. Distribution of the number of NPS and TID in fentanyl cases

In 163 cases, biological samples were analyzed. Fentanyl was detected along with other NPS and TID in these cases. Drugs that co-occurred with fentanyl in more than 10 cases are summarized in Table 11.

Table 11. Co-occurrence frequency of other drugs and adulterants in fentanyl cases

Drug	Co-occurrence Frequency		
	Overall	Deaths	Overdoses
Methamphetamine	76	39	37
Cocaine/ Benzoylecgonine	61	26	35
para-Fluorofentanyl	54	47	7
Metonitazene	12	11	1
Morphine	26	24	2
Oxycodone	11	9	2
Bromazolam	19	17	2
Clonazolam	16	14	2
Delta-9 THC	13	5	8
Xylazine	22	15	7
Quinine	11	5	6

The distribution between overdose and death cases in some of these co-occurrences and the average concentration of co-occurring drug and fentanyl in death cases are presented in Fig. 11.

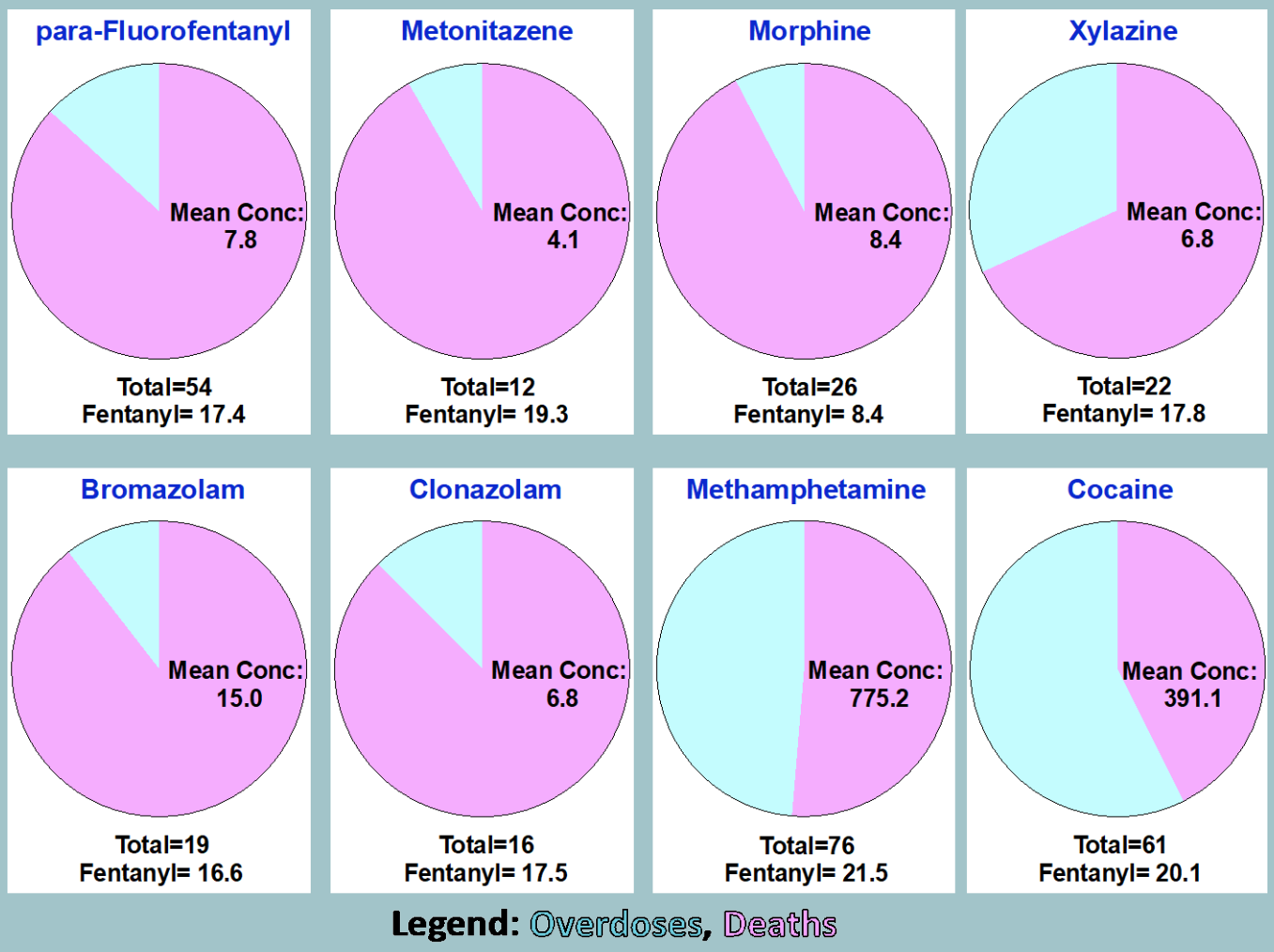

Figure 11. Distribution between deaths and overdoses in co-occurrence of fentanyl with selected drugs along with the average concentration in ng/mL of the co-occurring drug (in pie chart) and fentanyl in death cases

para-Fluorofentanyl

DEA TOX confirmed *para*-fluorofentanyl in 74 samples from 74 cases (20% of total cases) submitted by 8 states (Fig. 12). The samples consisted of 58 whole blood, 4 serum, 7 urine and 5 drug products.

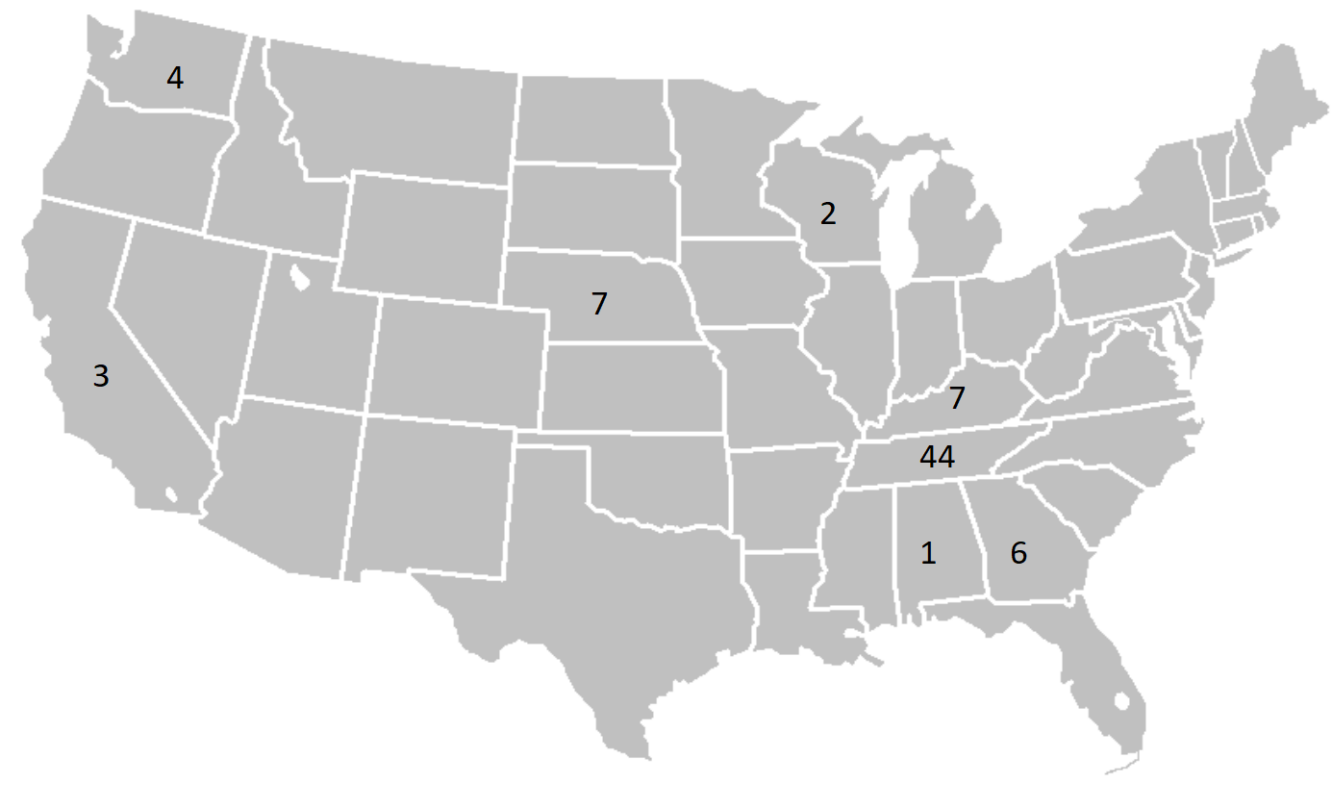

Figure 12. Geographic distribution of cases with confirmed para-fluorofentanyl

There were 60 deaths and 10 overdoses. The gender distribution and average age in these cases are presented in Figure 13A. 60 samples were submitted in death cases, while two samples were submitted in overdose cases. The distribution in blood *para*-fluorofentanyl concentrations observed in death cases is shown in Fig. 13B. The mean blood concentration in the death cases is 10.4 ng/mL.

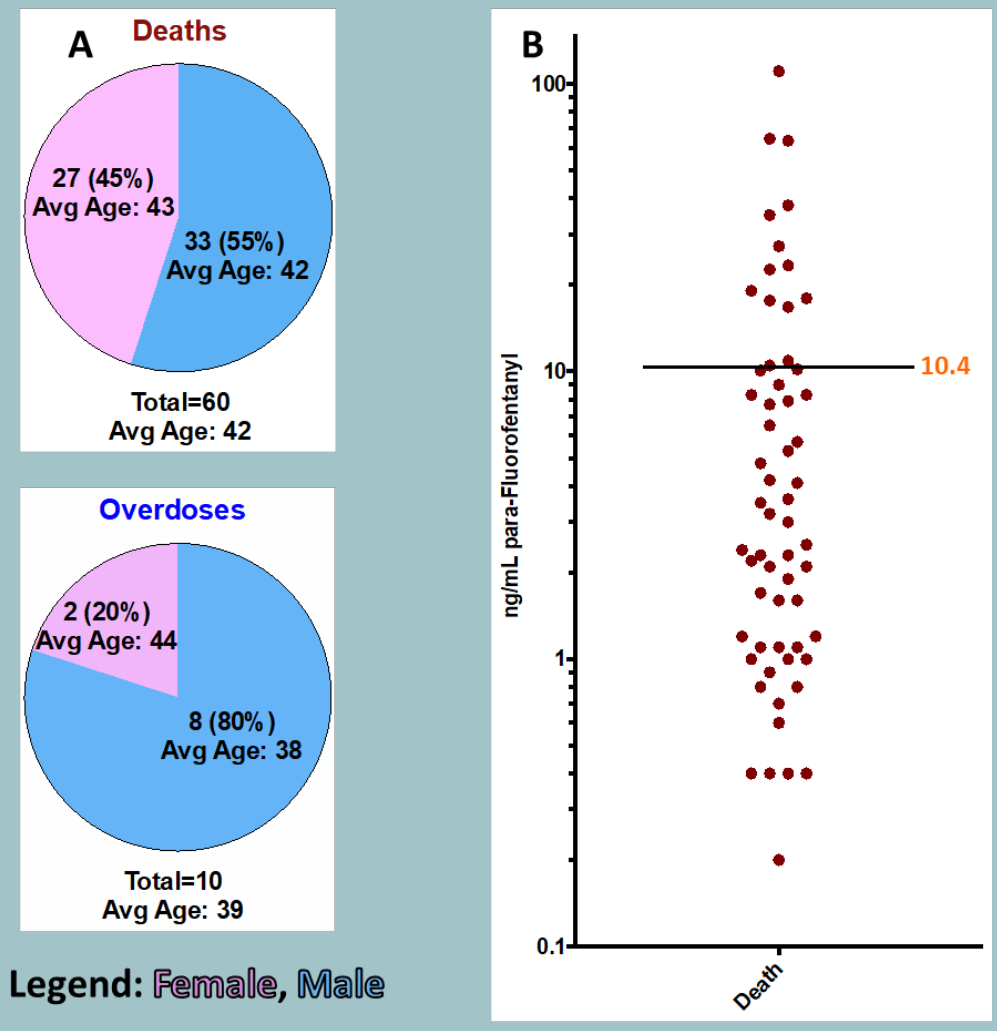

Figure 13. Gender and age (A) and blood para-fluorofentanyl concentration (B) distribution in deaths

The concentration ranges for *para*-fluorofentanyl found in blood samples from various states in death and overdose cases are presented in Table 12.

Table 12. Blood concentration ranges of *para*-fluorofentanyl observed in cases from different states

State	Death Cases		Overdose Cases	
	Concentration (ng/mL)	Frequency	Concentration (ng/mL)	Frequency
Alabama	6.5	1		
California	1.6-8.3 (**Avg = 6.8**)	3		
Georgia	0.7-22.7 (**Avg = 7.6**)	6		
Kentucky	3.2	1		
Nebraska	0.4-64.6 (**Avg = 21.4**)	5	14-14.2	2
Tennessee	0.2-111 (**Avg = 10**)	44		

Polydrug use is also prevalent in *para*-fluorofentanyl cases (Fig. 14). Of the 69 cases with biological samples two or more drugs were confirmed in 67 cases (97%).

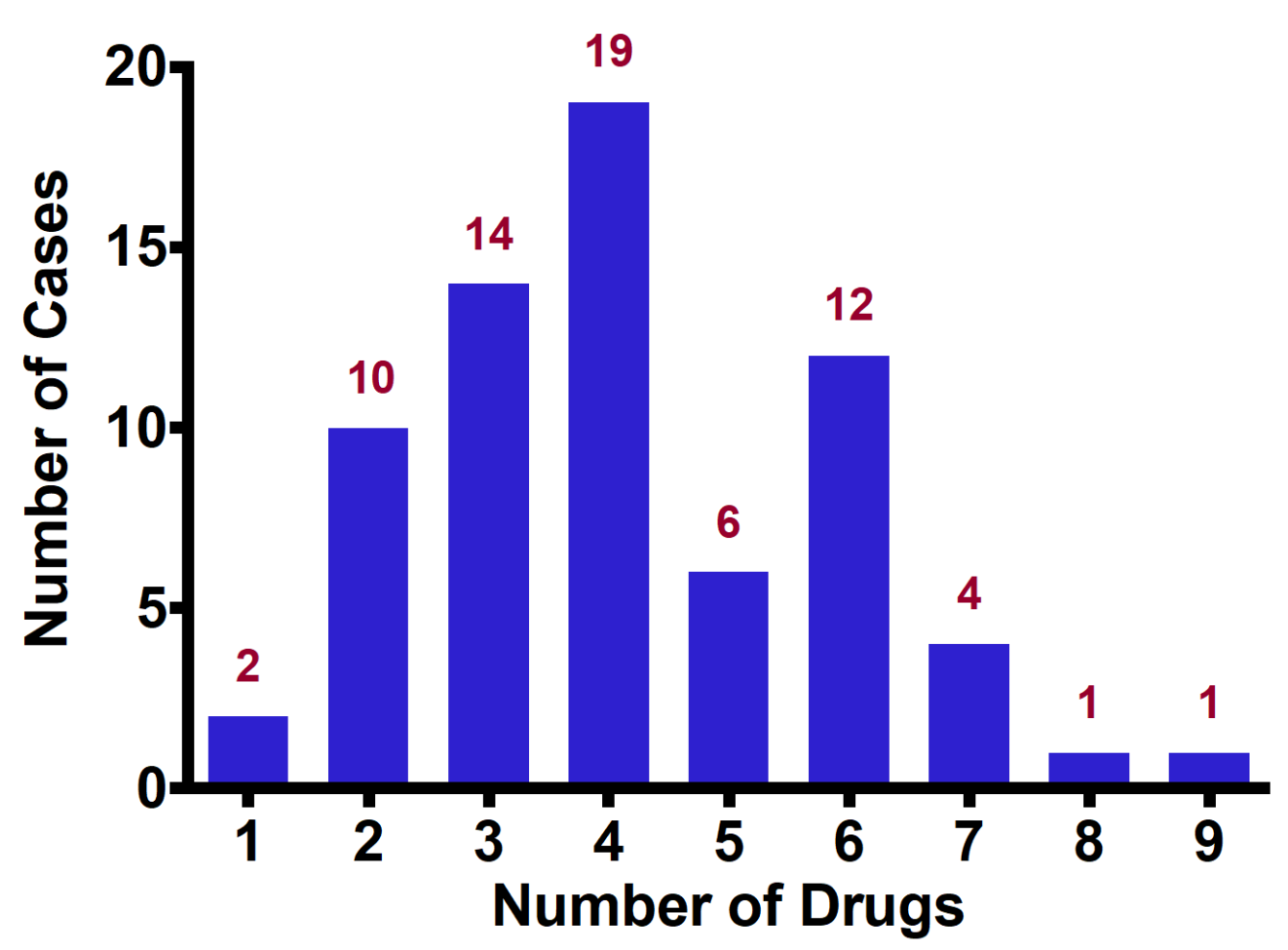

Figure 14. Distribution of the number of NPS and TID in para-fluorofentanyl cases

Like fentanyl, other drugs are confirmed with *para*-fluorofentanyl. Drugs with 7 or more co-occurrences are summarized in Table 13.

Table 13. Co-occurrence frequency of *para*-fluorofentanyl with other drugs and adulterants

Drug	Co-occurrence Frequency		
	Overall	Deaths	Overdoses
Methamphetamine	28	22	6
Cocaine/Benzoylecgonine	31	23	8
Fentanyl	54	47	7
Morphine	18	18	0
Bromazolam	12	12	0
Xylazine	10	10	0
Quinine	7	5	2

The distribution between overdose and death cases in these co-occurrences and the average concentration of co-occurring drug and *para*-fluorofentanyl in death cases are presented in Fig. 15.

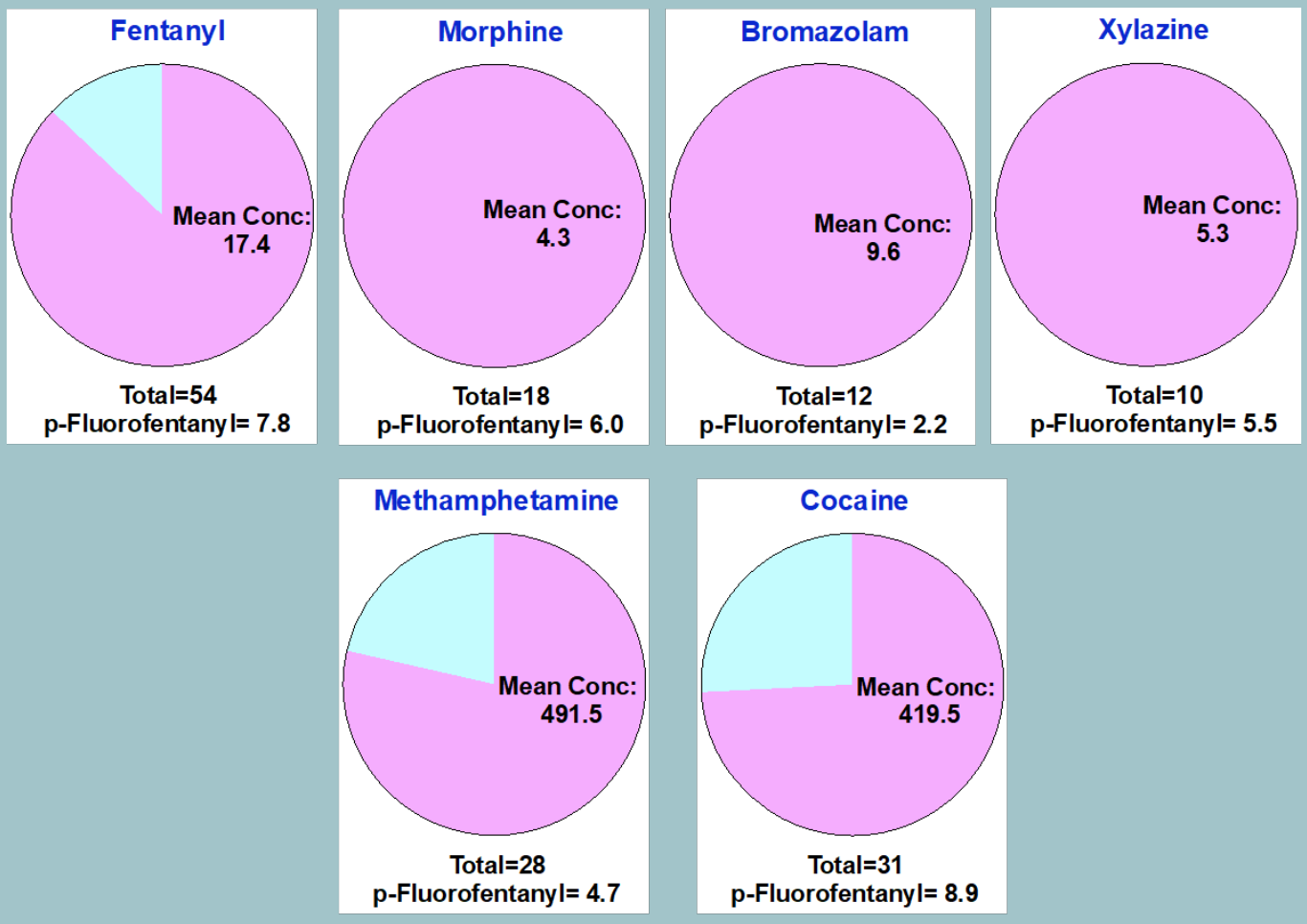

Figure 15. Distribution between deaths and overdoses in co-occurrence of *para*-fluorofentanyl with selected drugs along with the average concentration in ng/mL of the co-occurring drug (in pie chart) and *para*-fluorofentanyl in death cases

Metonitazene

DEA TOX confirmed metonitazene in 15 whole blood samples from 15 cases in 2022. All are death cases except for one overdose case. All death cases were referred from Tennessee while the overdose case was from Kentucky. The gender distribution and average age and the distribution of blood metonitazene concentrations are shown in Fig. 16A and 16B, respectively.

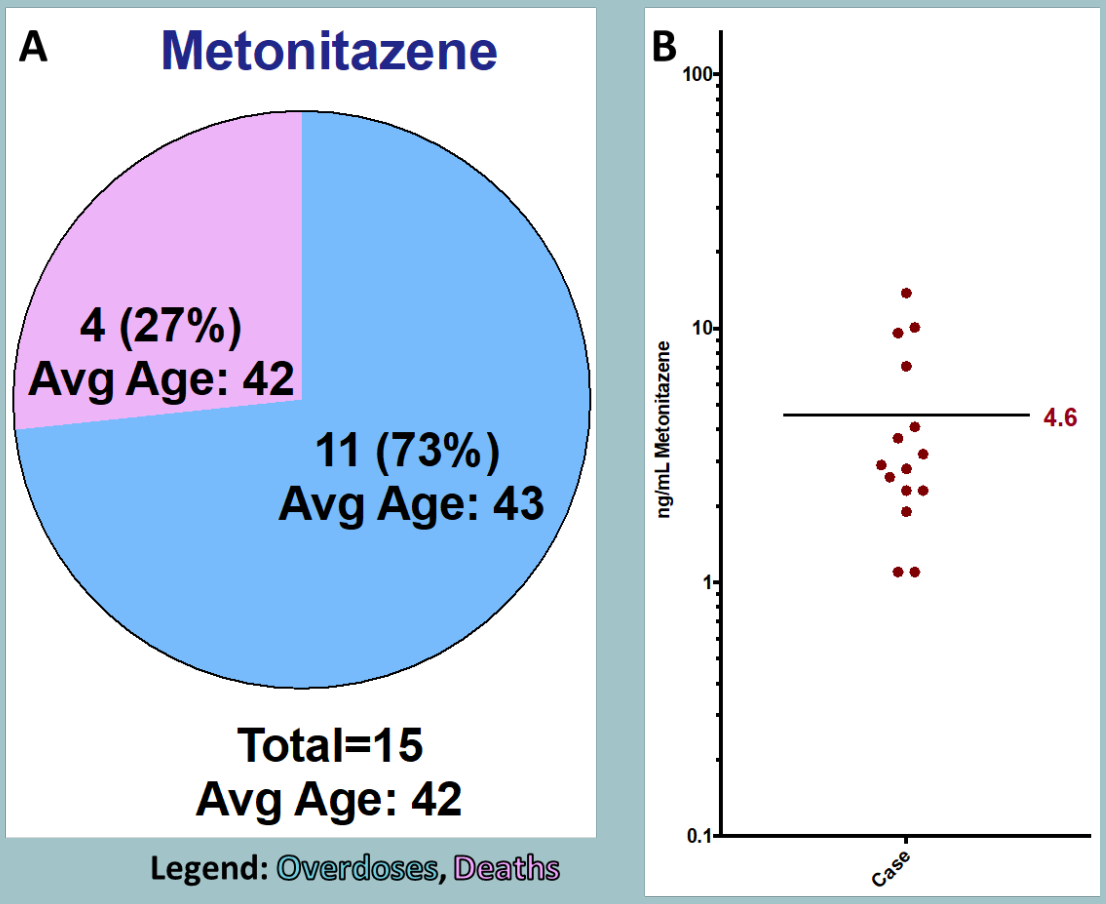

Figure 16. Gender and age (A) and blood concentration (B) distribution in metonitazene cases

Metonitazene was confirmed in these cases along with other drugs. The drugs that often co-occurred with metonitazene are summarized in Table 14. Fentanyl and methamphetamine are detected in 80% of metonitazene cases.

Table 14. Co-occurrence frequency and blood concentration ranges of other drugs with metonitazene

Drug	Detection Frequency	Blood Concentration Range, ng/mL
Fentanyl	12	1.6- 63.8 (Avg = 18.2)
Methamphetamine	12	1.1- 4510 (Avg = 604.1)
Morphine	5	0.6- 4.2 (Avg = 2.2)
Xylazine	5	1.7- 5.9 (Avg = 3.9)

Bromazolam and Clonazolam

Bromazolam and clonazolam (detected as the metabolite 8-aminoclonazolam) are the most detected designer benzodiazepines in DEA TOX in 2022. The sources of the cases along with the blood concentration ranges observed involving these drugs are shown in Table 15.

Table 15. Detection frequency (DF) and blood concentration ranges of bromazolam and 8-amino clonazolam observed in cases from different states

State	Bromazolam		8-Amino Clonazolam	
	Blood Concentration (ng/mL)	DF	Blood Concentration (ng/mL)	DF
Georgia	17.5-46.5	2	0.4-7.4	3
Kansas			4.6	1
Kentucky	5-22.1	2		1
Louisiana			0.4	1
Maryland			11.6	1
Nebraska			0.7	1
New Mexico	2.1	1		
Tennessee	0.9-62.9	15	1.6-47.2	11
Utah	3	1	0.4	1

The average age and gender distribution as well as the distribution between death and overdose cases involving these drugs are shown in Fig. 17.

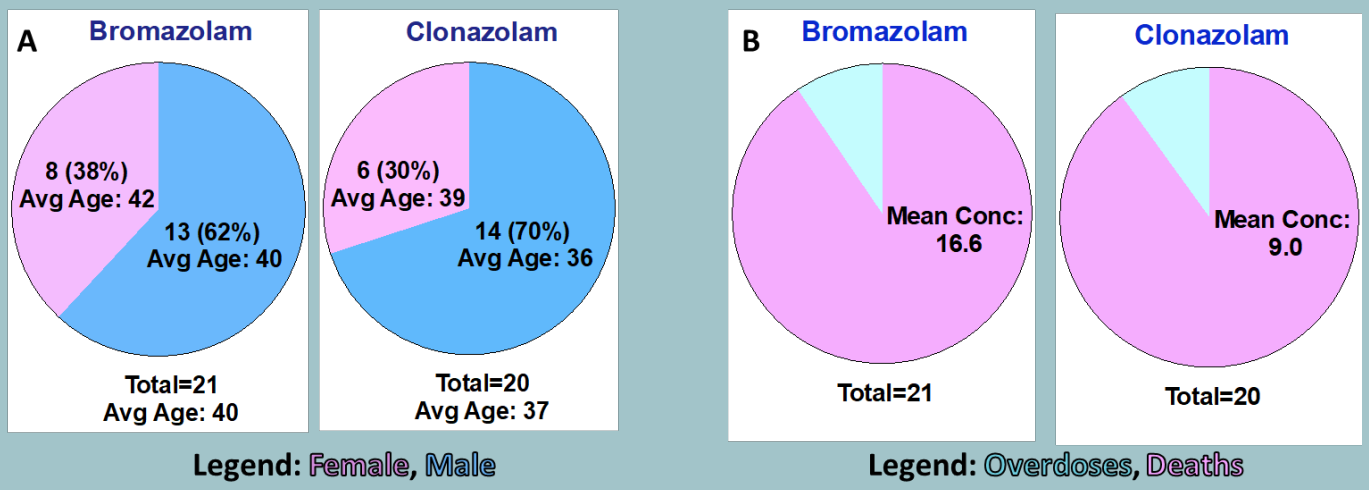

Figure 17. A. Gender distribution and average age in cases with bromazolam and clonazolam. B. Distribution between deaths and overdoses and average blood concentration (ng/mL) in death cases with bromazolam and clonazolam

Other drugs are confirmed in cases with clonazolam and bromazolam. The more frequently co-occurring drugs are summarized in Table 16. Bromazolam co-occurred more frequently with fentanyl (90%) than clonazolam (75%).

Table 16. Co-occurrence frequency and average blood concentration of other drugs with clonazolam and bromazolam

Drug	Co-occurrence Frequency (Ave Blood Concentration in Death Cases, ng/mL)	
	Bromazolam	**Clonazolam***
Bromazolam	21 (Avg = 16.6)	5 (Avg = 16.4)
Clonazolam	5 (Avg = 7.1)	20 (Avg = 9.0)
Fentanyl	19 (Avg = 16.6)	15 (Avg = 18.7)
para-Fluorofentanyl	12 (Avg = 2.3)	4 (Avg = 2.5)
Methamphetamine	12 (Avg = 763.7)	7 (Avg = 686.6)
Cocaine/Benzoylecgonine	5 (Avg = 213.1)	6 (Avg = 368)
Morphine	5 (Avg = 3.6)	5 (Avg = 26.4)
Oxycodone	2	4
Mitragynine	3	4
Delta-9 THC	2	4
Xylazine	3	4

* Measured as 8-Amino Clonazolam

Xylazine

DEA TOX confirmed xylazine in 22 cases, 20 of which also had confirmed fentanyl; the other two cases had confirmed *para*-fluorofentanyl. The 22 cases were referred from Alabama (1), Kentucky (5), Nebraska (1) and Tennessee (15). Xylazine was confirmed in 16 whole blood (15 deaths, 1 overdose) and 6 urine (overdoses) samples. The gender and age, case type, and blood concentration distribution in cases with confirmed xylazine are shown in Fig. 18.

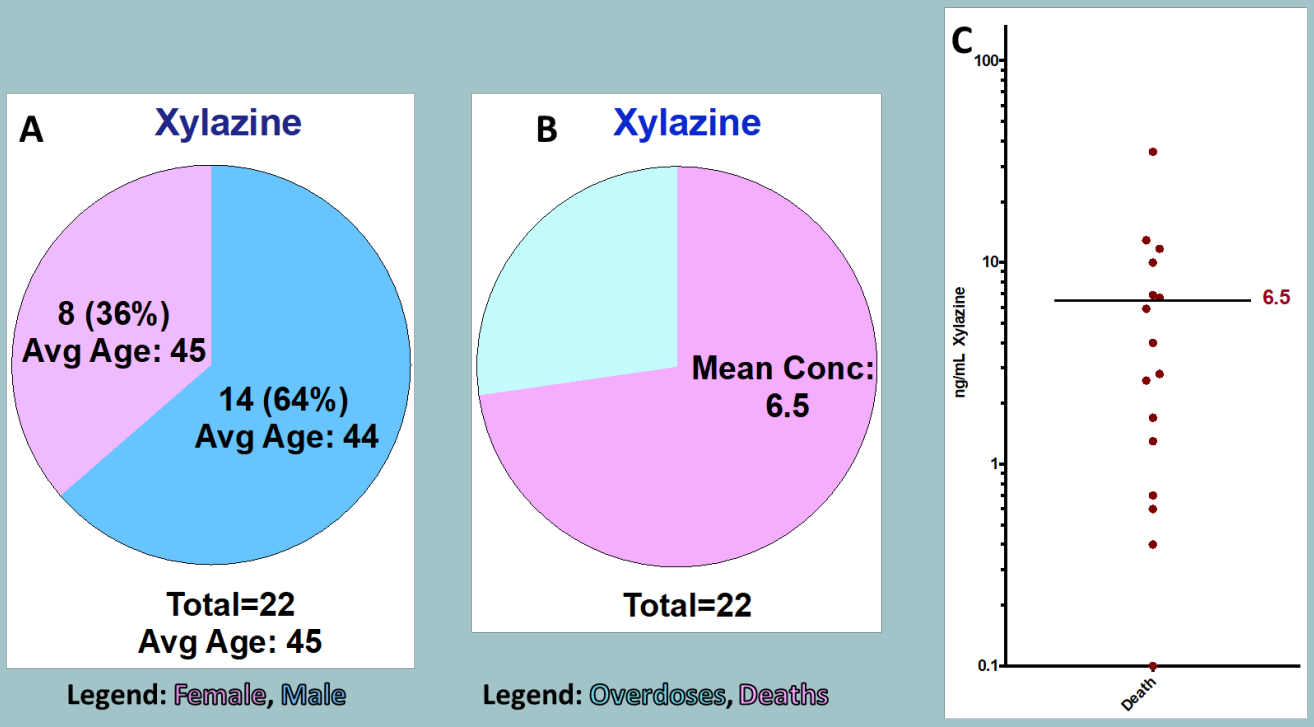

Figure 18. Gender and age (A), case type (B) and blood concentration (C) distribution in xylazine cases. The mean concentration given is in ng/mL.

Although xylazine was often detected as a fentanyl product adulterant, there are other drugs that were frequently confirmed along with it. Drugs that co-occurred five times or more with xylazine along with their blood concentration ranges in death cases are presented in Table 17.

Table 17. Co-occurrence frequency and blood concentration ranges of other drugs with xylazine

Drug	Detection Frequency	Blood Concentration Range in Death Cases, ng/mL
Fentanyl	20	2.1- 57.8 (Avg = 16.7)
para-Fluorofentanyl	11	0.8- 35.1 (Avg = 7.0)
Methamphetamine	11	1.1- 4510 (Avg = 705.5)
Cocaine	8	198- 1010 (Avg = 811.2)
Morphine	10	0.6-10.2 (Avg = 3.5)
Metonitazene	5	1.9- 3.7 (Avg = 2.7)
Quinine	5	4.3- 25.4 (Avg = 14.8)

Contact Information

We invite medical and law enforcement facilities to contact our program if you encounter an overdose of a suspected synthetic drug and desire to have any leftover biological samples (blood preferred) analyzed further for such synthetic substances.

- **Sample Qualification:**
    - Patients thought to have ingested a synthetic drug, where the traditional drug screen has produced little or no viable options to explain the symptoms exhibited by the patient (alcohol and THC are exempted).

- **How to Contact Us and Send Your Samples:**
    - Once the above qualification is satisfied:
        - Email **DEATOX@DEA.GOV** with a brief description of the case (including initial toxicology screen and history) and a request for testing.
        - DEA will respond to each inquiry, and if approved, will send the instructions for packing and shipping of sample(s) to UCSF.
            - The main reason for disapproval of a case would be the identification of substances including methamphetamine, heroin, fentanyl, cocaine, LSD, PCP etc. in a routine toxicology screening at your facility.
            - This program's goal is to connect symptom causation to abuse of newly emerging synthetic drugs (e.g. synthetic cannabinoids, synthetic cathinones, fentanyl-related substances, other hallucinogens etc.).
    - Ensure that you de-identify and label the sample with a numerical value, sex, date of birth or age, and the date and time the sample was collected in accordance with the labeling instructions (sent with shipping instructions).
    - Keep a master list of the patients and the numerical values you allocated to each sample at your institution.

- **Cost of Sample Analysis:**
    - DEA will cover the full cost of testing the patient samples.
        - The sender will only be responsible for paying for packing and shipping samples to UCSF.

- **Turn-around Time:**
    - Results are expected within three to four weeks of receipt of the sample at UCSF except in rare occurrences when a novel substance is identified.

Public Domain Notice

Suggested citation:
U.S. Drug Enforcement Administration, Diversion Control Division. (2023). *DEA TOX: 2022 Annual Report*. Springfield, VA.

OBTAINING COPIES OF THIS PUBLICATION
Electronic copies of this publication can be downloaded from the DEA TOX website at:
https://www.deadiversion.usdoj.gov/dea_tox/dea-tox.html

This report was produced in conjunction with the CTEB laboratory at UCSF.

Clinical Toxicology
and Environmental Biomonitoring Laboratory

DEA PRB 05-15-2023-11

Appendix

Laboratory Method

Sample Analysis

Each sample is analyzed by targeted and suspect screening through LC-QTOF/MS using non-targeted data acquisition. Confirmed drugs are quantified through targeted LC-QTOF/MS using the isotope dilution method.

Sample extracts or diluted samples are analyzed by LC-QTOF/MS (Agilent LC1260- QTOF/MS 6550, Sta. Cruz, CA) using our published comprehensive drug screening method. Chromatographic separation through an Agilent Poroshell 120 column (2.1X 100mm, 2.7 µm) is achieved by gradient elution. Eluates from the chromatographic column are ionized in the QTOF/MS using an electrospray ionization source in positive polarity on one run and negative polarity on a subsequent run. Using non-targeted data acquisition, TOF-MS (parent ion) and MS/MS (fragment ions) spectra are collected in automated MS/MS mode (information-dependent acquisition). Quantification of confirmed drugs is performed by isotope dilution method using a contemporary six to eight-point calibration curve and deuterated or carbon-13-labelled drug isotopologues as internal standards. In cases where a suspected drug is exceptionally potent or rapidly metabolized, the sample is also analyzed using a higher-sensitivity targeted method.

Data Analysis

To confirm the presence of specific drugs in each sample, the total ion chromatogram (TIC) obtained from the LC-QTOF/MS run is analyzed using Agilent MassHunter Qualitative Analysis software. Both targeted and suspect screening are performed in analyzing each sample using the “Find by Formula” algorithm. For targeted screening, a database of 1193 drugs, including 912 NPS, is used as reference for compound matching using the following criteria: mass error ≤ 10 ppm; retention time ≤ 0.15 min; target score ≥ 70 (indication of isotopic pattern match) for peaks that did not exhibit detector saturation; and, the presence of at least one major fragment ion peak in its MS/MS spectrum. For suspect screening, suspect NPS databases are used with the following criteria for a suspect compound match: mass error ≤ 10 ppm; target score ≥ 70 for peaks that did not exhibit detector saturation; and, retention time plausibility. Suspect compounds are confirmed by verifying that the retention time and mass spectral properties of the suspect compound match those of the relevant reference

standard, including fragmentation patterns observed in MS/MS data collected from the analyzed samples and standards.

Quantitative analysis of confirmed compounds is performed using the Agilent MassHunter Quantitative Analysis software. A linear regression fit between the peak area ratios of spiked reference standard and relevant internal standard, and the known concentrations of the spiked reference standards in a matrix blank is used to quantify the concentration of the confirmed compound. Because it is too expensive and impractical to buy an internal standard for each of the 1193 drugs in our comprehensive drug library, we use a mixture of 15 internal standards that cover the entire range of retention times of our target drugs. The internal standard with a retention time closest to a target drug is used for quantitation. This is a common approach used for comprehensive drug panels.