

Toxicological Aspects of Synthetic Drugs

Barry K. Logan, PhD, DABFT



THE CENTER FOR
FORENSIC SCIENCE
RESEARCH & EDUCATION



WHEN YOU NEED TO KNOW

2008-2012

Benzylpiperazines (6+)

BZP, TFMPP, m-CPP

β-Keto amphetamines (30+)

Ephedrone, mephedrone, methylone, methedrone...

Phenethylamines (2C suite) (20+)

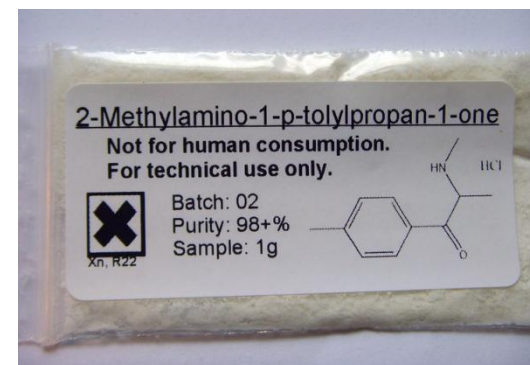
2C-B, 2C-E, 2C-I, 2C-B, 2C-T-7, NBOMe Series...

Pyrrolidophenones (pyrovalerones) (20+)

α-PVP, MDPV, PPP,...

Synthetic Cannabinoids (200+)

JWH series, AM Series, Adamantyls, Cyclopropyls...



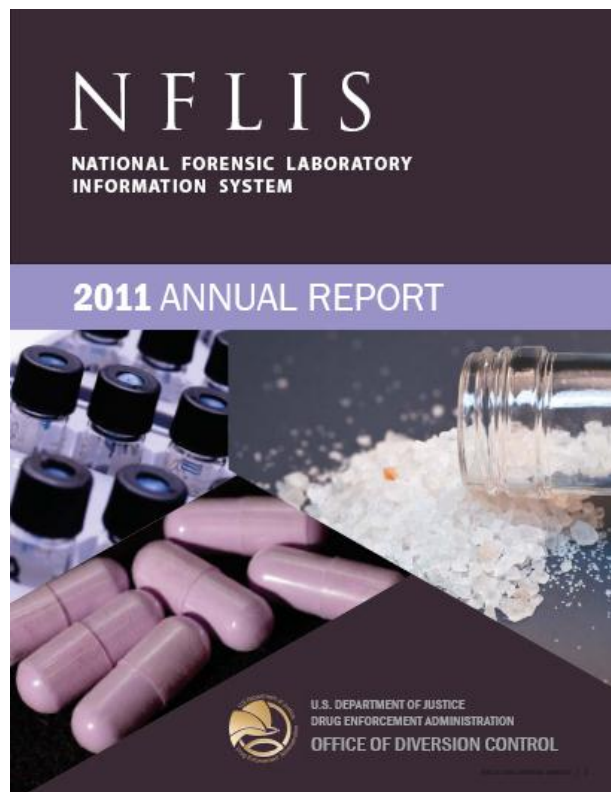


Table 2.3

HALLUCINOGENS

*Number and percentage of hallucinogen reports in the United States, 2011**

Hallucinogen Reports	Number	Percent
MDMA	9,305	20.50%
AM-2201	6,130	13.51%
Psilocin/psilocibin	3,896	8.58%
JWH-018 (AM-678)	2,954	6.51%
MDPV *	2,991	6.59%
5-MeO-DIPT	2,582	5.69%
JWH-250	2,481	5.47%
JWH-122	2,371	5.22%
JWH-210	1,695	3.73%
TFMPP (noncontrolled) *	1,499	3.30%
Methylone (MDMC) *	1,597	3.52%
LSD	1,064	2.34%
JWH-081	1,022	2.25%
RCS-4	560	1.23%
JWH-203	515	1.13%
JWH-073	505	1.11%
Other hallucinogens *	4,215	9.29%

<https://www.nflis.deadiversion.usdoj.gov/>

Drug	Count
DMAA	66
alpha-PVP	62
MDPV	39
Methylone	32
4-MEC	11
Buphedrone	10
Pentylone	8
MBZP	7
DMA	7
Ethylone	7
Butylone	6
3,4 DMMC	5
2C-I	4
1,4 DBZP	3
25I-NBOMe	3

Screen:

Basic Extraction
EI/GCMS

Confirmation:

GCMS
LCTOF
LCMSMS



Scope: Synthetic Cannabinoids

2010	2011	2012
JWH-018	AM-2201	AM-2201
JWH-073	AM-694	AM-694
JWH-019	JWH-018	JWH-018
JWH-250	JWH-019	JWH-019
	JWH-073	JWH-073
	JWH-081	JWH-081
	JWH-122	JWH-122
	JWH-200	JWH-200
	JWH-210	JWH-210
	JWH-250	JWH-250
	RCS-4	RCS-4
	RCS-8	RCS-8
		JWH-203
		JWH-022
		JWH-018 Cl-analog
		UR-144
		XLR-11
		AM-2233
		AM-1248
		A-796260

NMS Labs Synthetic Cannabinoids Screen, Blood (Forensic) Test



Tucker Cipriano smoked Spice, took mushrooms and drank alcohol in hours before a fatal baseball bat attack on his father

Published: Friday, December 21, 2012



Bath Salts Mystery: Ex-Universal Pictures Co-Chair Breaks Silence on LAPD Beatdown

8:00 AM PST 12/20/2012 by Daniel Miller

SHARE     Tweet 110  Like 102  +1 1 Comments (13) 

Page 1

1 2 3 NEXT >



| *The Times-Picayune* Greater New Orleans

22

comments

25-I banned after Voodoo Fest death, Legislature to move forward on anti-drug laws

The Louisiana Department of Health and Hospitals (DHH) **announced Friday it was banning** the possession, manufacture and distribution of 25-I, the synthetic drug that resulted in **the death of an Alabama student at last month's Voodoo Festival** in New Orleans. DHH Secretary Bruce Greenstein said he, along with the Legislature and police, would continue to target the class of drugs writ large.

Los Angeles Times

 | LOCAL

LOCAL U.S. WORLD BUSINESS SPORTS ENTERTAINMENT HEALTH

'Bath salts' suspect due in court in Glendale shovel attack

June 26, 2012 | 9:42 am

AA

Comments 0



+1 0

Tweet





Bath salts overdose killed teen, sickened 4 others, medical examiner says

 Recommend  Be the first of your friends to recommend this.

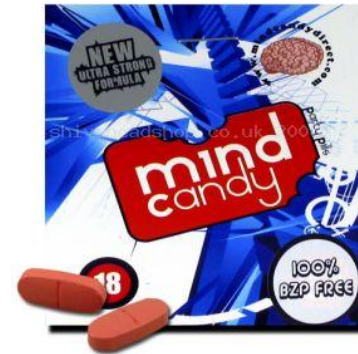
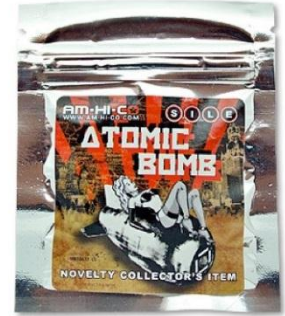


Posted: Apr 05, 2013 3:33 PM EDT
Updated: Apr 12, 2013 3:33 PM EDT



• Adverse Events

- Intoxication/Impairment
- Psychosis
- Medical Crises
- Death

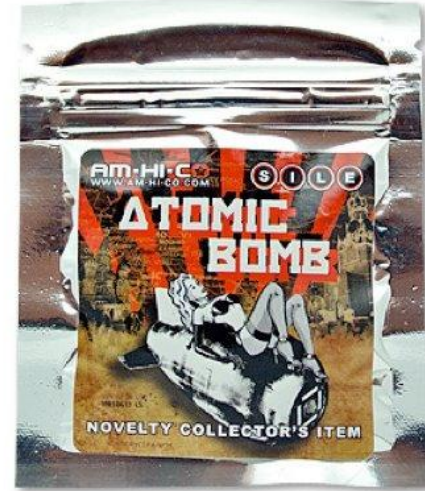


Designer Stimulants and Hallucinogens

“Bath Salts”

AKA:

- ☠ Bath Bubbles
- ☠ Bath Salts
- ☠ Pond Cleaner
- ☠ Soft Drink Additive
- ☠ Burial Powder
- ☠ Glass Cleaner
- ☠ Plant Food
- ☠ Plant Vitamin
- ☠ Insecticide

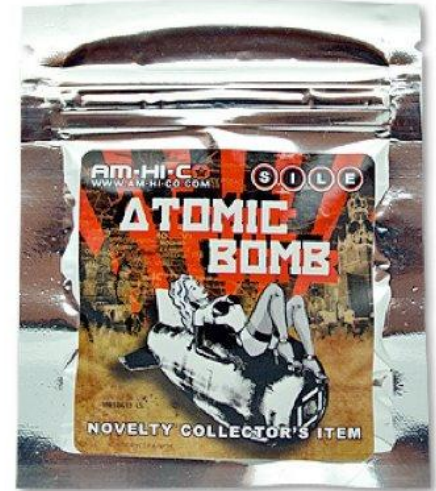


Effects	Agonists	Antagonists
Anxiety	25I-NBOMe	Clozapine
Appetite	2C-B	Olanzapine
Cognition	5-MEO-DMT	Quetipaine
Imagination	BZP	Risperidone
Learning	DMT	Ziprasidone
Memory		Haloperidol
Mood		Droperidol
Perception		
Sexual Drive		
Sleep		
Thermoregulation		

- Agitation
- Insomnia
- Mydriasis
- Myoclonus
- Tachycardia
- Hypertension
- Chest pain
- Paranoia
- Delusions/hallucinations
- Excited Delirium
 - *Combative behavior*
 - *Hyperthermia*
 - *Rhabdomyolysis*
 - *Kidney Failure*
 - *Seizures*
 - *Death*

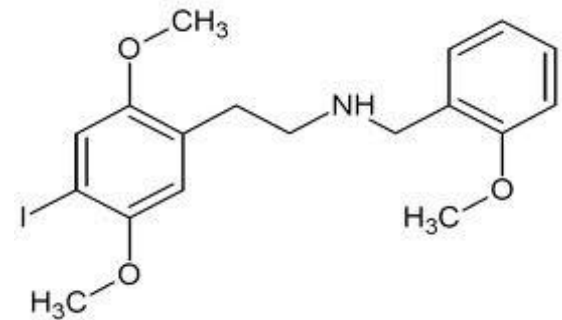


- ☠ Cathinones
- ☠ Phenethylamines (Shulgin/Nichols)
 - ☠ 2C-X
 - ☠ NBOMe's
- ☠ Pyrovalerones
- ☠ Pyrrolidophenones



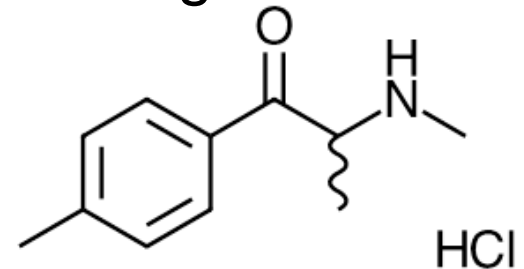
Rose SR, Poklis JL, Poklis A. A case of 25I-NBOMe (25-I) intoxication: a new potent 5-HT_{2A} agonist designer drug. Clin Toxicol (Phila). 2013 Mar;51(3):174-7.

- 18-year-old male presented to the emergency department (ED) with severe agitation and hallucinations after jumping out of a moving car. Tachycardiac (150 – 160 bpm) and hypertensive (150 – 170 mm Hg systolic and 110 mm Hg diastolic), required physical restraints and treatment with intravenous lorazepam administration.
- 0.76 ng/ml of 25-INBOMe



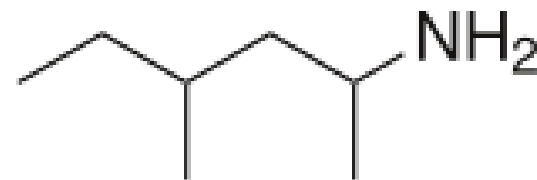
Cosbey SH, Peters KL, Quinn A, Bentley A. Mephedrone (methylnmethcathinone) in toxicology casework: a Northern Ireland perspective. J Anal Toxicol. 2013 Mar;37(2):74-82.

- 32 Impaired Driving arrest cases, including nine with mephedrone as the only drug present.
- Generally impaired driving, weaving, erratic, dilated pupils, poor performance, slurred speech.
- Blood concentrations ranged up to 0.74 mg/L (n=9; mean 0.21, median 0.10) although the most common value encountered is likely to lie between 0.2 and 0.3 mg/L.



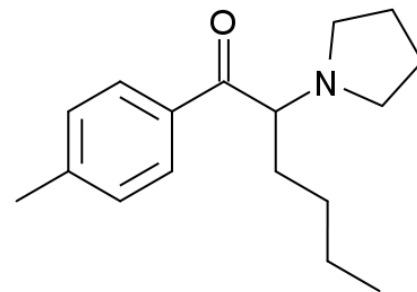
Gee P, Jackson S, Easton J. Another bitter pill: a case of toxicity from DMAA party pills. N Z Med J. 2010 Dec 17;123(1327):124-7.

- Consumed two capsules of 99.9% DMAA. Became confused, incontinent, drowsy, slurred speech, facial droop, asymmetric weakness, memory impairment, seizure. Pills were analyzed and contained only DMAA.



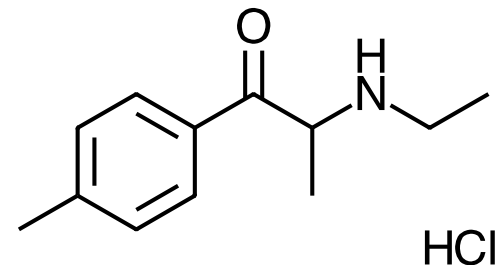
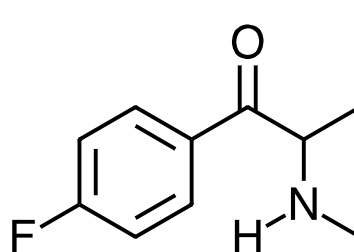
Sauer C, Hoffmann K, Schimmel U, Peters FT. Acute poisoning involving the pyrrolidinophenone-type designer drug 4'-methyl-alpha-pyrrolidinohexanophenone (MPHP). Forensic Sci Int. 2011 May 20;208(1-3):e20-5.

- A 27 year old man was admitted to hospital in an agitated state and with fractures of both feet after jumping from a window. Pronounced rhabdomyolysis and had to be treated by repeated hemodialysis. Elevated liver parameters indicated toxic liver damage.
- MPHP was found at 100 ng/ml



Thornton SL, Gerona RR, Tomaszewski CA. Psychosis from a bath salt product containing flephedrone and MDPV with serum, urine, and product quantification. J Med Toxicol. 2012 Sep;8(3):310-3..

- 23-year-old male with a prior psychiatric history, with bizarre behavior, suicidality, and hallucinations. MDPV levels of 186ng/mL and flephedrone of 346ng/mL in the serum. Agitated and complained of visual, tactile, and auditory hallucinations. He stated snakes were crawling on him and in his bed. Treated and stabilized with Lorazepam, and Droperidol.



HCl

- **Penders TM, Gestring RE, Vilensky DA. Excited delirium following use of synthetic cathinones (bath salts). Gen Hosp Psychiatry. 2012 Nov-Dec;34(6):647-50.**
- e.g. 31 year old male, found wandering in his neighborhood, fearful, confused, “Overheated”, sweating. Became combative. Reported seeing snakes who were threatening his life.
- Hallucinations, paranoia and agitation resolved after administration of haloperidol.
- No Toxicology confirmation.



Young C, Oladipo O, Frasier S, Putko R, Chronister S, Marovich M. Hemorrhagic stroke in young healthy male following use of sports supplement Jack3d. Mil Med. 2012 Dec;177(12):1450-4.

- 26 year old soldier in Afghanistan, takes 3 scoops of Jack3d, before exercising. Awakes with worsening headache, assymetrical dysesthesia, weakness and lack of coordination. Diagnosed with Dejerine-Roussy Thalamic stroke. 1 scoop contains 4g of DMAA.

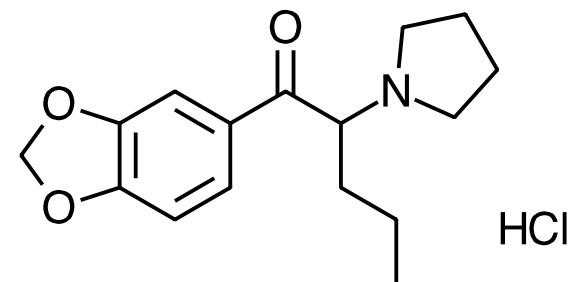


Regunath H, Ariyamuthu VK, Dalal P, Misra M. Bath salt intoxication causing acute kidney injury requiring hemodialysis. Hemodial Int. 2012 Oct;16 Suppl 1:S47-9.

- 39 y/o male brought to the emergency room by police. Combative and confused. Sedated for CAT scan. Elevated CK indicating renal problems. Diagnosed with acute tubular necrosis, and spent 13 days in dialysis. Admitted to recent increasing use of Bath Salt pills, and confirmed that the precipitating event had occurred immediately after such an administration.

Murray BL, Murphy CM, Beuhler MC. Death following recreational use of designer drug "bath salts" containing 3,4 Methylenedioxypropylamphetamine (MDPV). J Med Toxicol. 2012 Mar;8(1):69-75.

- 40-year-old male who injected and snorted "bath salts" containing MDPV and subsequently became agitated, aggressive, and experienced a cardiac arrest. He was resuscitated after his initial arrest; however, he developed hyperthermia, rhabdomyolysis, coagulopathy, acidosis, anoxic brain injury, and subsequently died.
- MDPV was quantified in his serum at 82 ng/mL.



Wyman JF, Lavins ES, Engelhart D, Armstrong EJ, Snell KD, Boggs PD, Taylor SM, Norris RN, Miller FP.

Postmortem tissue distribution of MDPV following lethal intoxication by "bath salts". J Anal Toxicol. 2013

Apr;37(3):182-5.

- 40-year-old male who injected and snorted "bath salts" containing MDPV and subsequently became agitated, aggressive, and experienced a cardiac arrest. He was resuscitated after his initial arrest; however, he developed hyperthermia, rhabdomyolysis, coagulopathy, acidosis, anoxic brain injury, and subsequently died.
- MDPV was quantified in his serum at 82 ng/mL.

Table I

Toxicology Results for MDPV Overdose

Source	Drugs detected ($\mu\text{g/mL}$ or $\mu\text{g/g}$)	
	MDPV	Methylone
Femoral blood	0.44	
Heart blood	0.50	
Urine	>5.0	Positive
Gastric	>2.0 = 50 mL	
Bile	0.88	
Cerebrospinal fluid	0.41	
Lung	0.60	
Kidney	0.84	
Liver	0.98	
Muscle	0.56	
Spleen	0.64	
Brain		
Parietal	0.36	
Cerebellum	0.42	
Lentiform nucleus	0.30	
Frontal	0.30	
Occipital	0.42	
Medulla	0.42	
Heart	0.12	
Hair	11,660 pg/mg	1,332 pg/mg

Wyman et al, 2013

Marinetti LJ, Antonides HM. Analysis of synthetic cathinones commonly found in bath salts in human performance and postmortem toxicology: method development, drug distribution and interpretation of results. J Anal Toxicol. 2013 Apr;37(3):135-46.

- Commonly poly drug cases with multiple synthetic or therapeutic drugs present.
- In five cases both peripheral and heart blood were tested with an average heart to peripheral blood ratio was 1.48, with a range of 1.3 to 1.7.
- Concentrations were not correlated with outcome.
- e.g. In PM Case 1, the death was caused by injuries sustained in an auto accident; however, this decedent had a blood methylone concentration of 729 ng/mL.

Synthetic Cannabinoids

Synthetic Cannabinoid Agonists

AKA:

- ☠ Legal high
- ☠ 50 state legal
- ☠ Incense
- ☠ Fake Weed
- ☠ Fake Pot
- ☠ K2
- ☠ Spice



Scope: Synthetic Cannabinoids



When you need to know™

2010	2011	2012
JWH-018	AM-2201	AM-2201
JWH-073	AM-694	AM-694
JWH-019	JWH-018	JWH-018
JWH-250	JWH-019	JWH-019
	JWH-073	JWH-073
	JWH-081	JWH-081
	JWH-122	JWH-122
	JWH-200	JWH-200
	JWH-210	JWH-210
	JWH-250	JWH-250
	RCS-4	RCS-4
	RCS-8	RCS-8
		JWH-203
		JWH-022
		JWH-018 Cl-analog
		UR-144
		XLR-11
		AM-2233
		AM-1248
		A-796260

NMS Labs Synthetic Cannabinoids Screen, Blood (Forensic) Test

- **Major Effects**

- **Cardiovascular**

- Hypertension
- Tachycardia

- **Gastrointestinal**

- Vomiting

- **Neurological**

- Agitation
- Confusion
- Hallucinations
- Seizures

- **Other Effects**

- Headache
- Muscle
- Numbness
- Slurred speech
- Syncope
- Vomiting
- Tremors
- Drowsiness

Texas Poison Center Networks

Marijuana/K2 Effects



<i>Red eyes / bloodshot</i>
<i>Burning of the eyes</i>
<i>Xerostomia (dry mouth)</i>
<i>Tachycardia</i>
<i>Changes in perception/mood</i>
<i>Balance and Coordination</i>
<i>Hallucinations</i>
<i>Sedation</i>
<i>Subjective thought disruption/loss of concentration</i>
<i>Impaired sense of time</i>
<i>Self assessed impairment</i>
<i>Arrhythmias</i>
<i>Seizures/Convulsions</i>
<i>Panic Attacks</i>
<i>Paranoia and Anxiety</i>
<i>Sickness</i>



Yeakel JK, Logan BK. Blood Synthetic Cannabinoid Concentrations in Cases of Suspected Impaired Driving. J Anal Tox (In Review, 2013).

- 12 cases of Suspected impaired driving involving synthetic cannabinoids. Other drugs and alcohol were ruled out. Attitude of the drivers was described as cooperative and relaxed, speech was noted to be slow and slurred, and coordination was noted to be poor. Pulse and blood pressure were generally elevated. The most consistent sign noted was a marked lack of convergence in all cases where it was assessed.
- JWH-018 (n=4), 0.1-1.1ng/mL; JWH-081 (n=2) qualitative only; JWH-122 (n=3) 2.5ng/mL; JWH-210 (n=4) 0.1ng/mL; JWH-250 (n=1) 0.38ng/mL; AM-2201 (n=6) 0.43 – 4.0ng/mL.

Synthetic Cannabinoid JWH-018 and Psychosis : An Explorative Study. Every-Palmer S. Drug Alcohol Depend. (2011).

- Semi-structured interviews regarding the use and effects of JWH-018 in 15 patients with serious mental illness in a New Zealand forensic and rehabilitative service.
- Anxiety and psychotic symptoms were common after use, with 69% of users experiencing or exhibiting symptoms consistent with psychotic relapse after smoking JWH-018. Although psychological side effects were common, no one reported becoming physically unwell after using JWH-018. Three subjects described developing some tolerance to the product, but no one reported withdrawal symptoms.


Centers for Disease Control and Prevention (CDC). Acute kidney injury associated with synthetic cannabinoid use--multiple states, 2012. MMWR Morb Mortal Wkly Rep. 2013 Feb 15;62(6):93-8.

- Three sentinel cases of AKI in patients in Wyoming.
- A case search defined as nausea, vomiting, abdominal or back pain, and AKI led to a cohort of 16 patients in 5 states.
- All had smoked products containing synthetic cannabinoids, confirmed in product samples and serum to be XLR-11.
- Five of the 16 patients required hemodialysis, and four patients received corticosteroids; none died.
- Other infectious, autoimmune, pharmacologic, or other toxic causes of AKI were not found.

Coroner: Lamar Jack ingested chemical found in fake marijuana before he died

By Nikie Mayo

Posted October 15, 2011 at 7:59 p.m.

 Discuss

 Print

A A A









Anderson University basketball player Lamar Jack died after ingesting a chemical that is a key ingredient in synthetic marijuana, the county coroner said Saturday.

Anderson County Coroner Greg Shore said specialists from an accredited laboratory in Pennsylvania ran toxicology tests and analyzed blood samples that were taken when Jack was admitted to AnMed Health Medical Center in Anderson. The lab testing and analysis revealed that Jack had the chemical JWH-018 in his body when he collapsed during a preseason warm-up with his team on Sept. 30. Just days later, on Oct. 4, Jack died. He was 19.



On the basis of an autopsy and the toxicology test results, Shore is ruling Jack's death accidental — caused by "acute drug toxicity with excited delirium that led to multiple organ failure."

- Adverse effects from both classes of drugs have been documented.
- They include intoxication, and the risks associated with cognitive and psychomotor impairment.
- Synthetic Stimulants and Hallucinogens
 - Cause suicidal and homicidal ideation
 - Induce psychosis
 - Cause excited delirium
 - Can result in serotonin syndrome
- Synthetic Cannabinoids
 - Induce psychosis
 - May be associated with Acute Kidney Injury

Questions?



www.nmslabs.com www.forensicscienceeducation.org