# “Flakka”: The Truth Behind the Latest Designer Drug Media Storm

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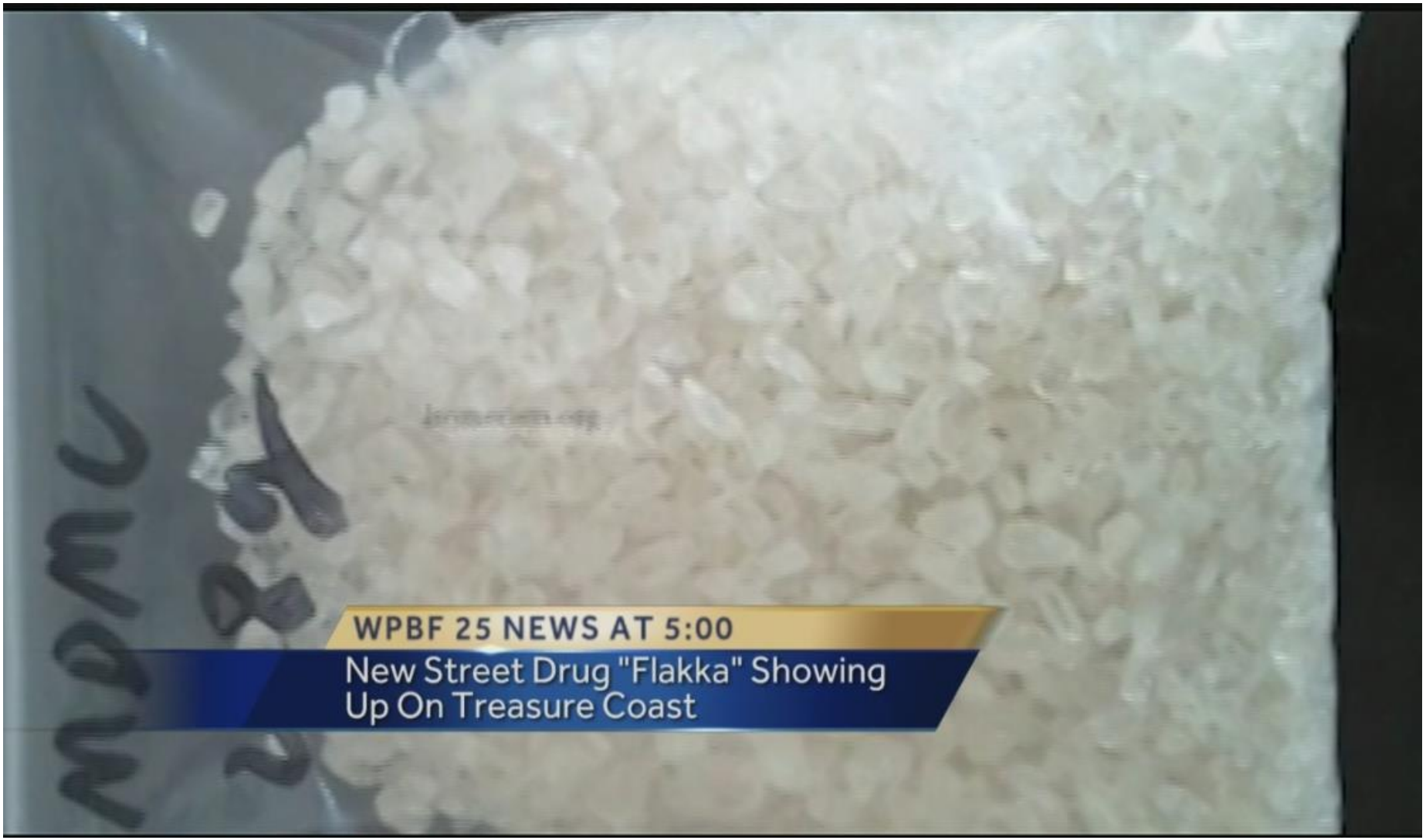
# “Flakka”

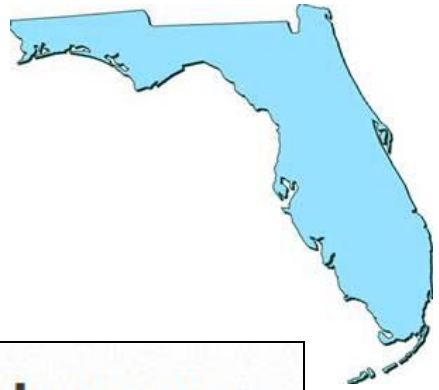

WPBF 25 NEWS AT 5:00
New Street Drug "Flakka" Showing
Up On Treasure Coast

# “Flakka” Headlines

**Florida teen on flakka claimed she was Satan, police say**

17-year-old arrested in Melbourne

Published On: May 14 2015 08:39:35 AM EDT | Updated On: May 14 2015 12:01:54 PM EDT



**Spokane PD seeing spike in "Flakka" drug use**

**New Street Drug Flakka Hits Florida, Ohio & Texas**

By Vittorio Hernandez @ibtimesau on April 14 2015 12:37 PM

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# What is “Flakka”?

- “Flakka” = Spanish slang for thin, pretty girl
- Active compound is alpha-pyrrolidinovalerophenone (Alpha PVP, α-PVP, α-pyrrolidinopentiophenone )
- Acts as a stimulant on the body
  - Comparable to cocaine and amphetamine
- Other street names
  - “Gravel” (alpha PVP & benzodiazepines)
  - “Bath Salts”


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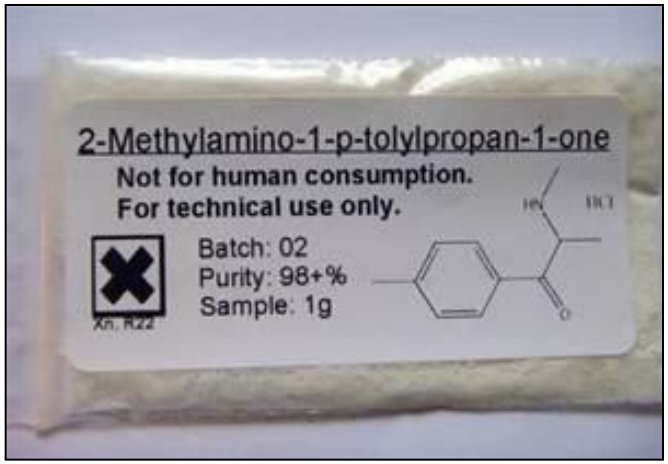
# NPS Movement

- NPS: Novel Psychoactive Substances

- Other names:
  - Research Chemicals
  - Legal Highs




- Appeal to recreational users
  - Easily accessible
  - “Grey” legal zone
  - Circumvent routine drug testing

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# Google Trends

# Google Trends


2005 2007 2009 2011

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# 2012 NFLIS Report – Alpha PVP

**Figure 3.3** Percentage of total drug reports identified as alpha-PVP, by State, 2011*

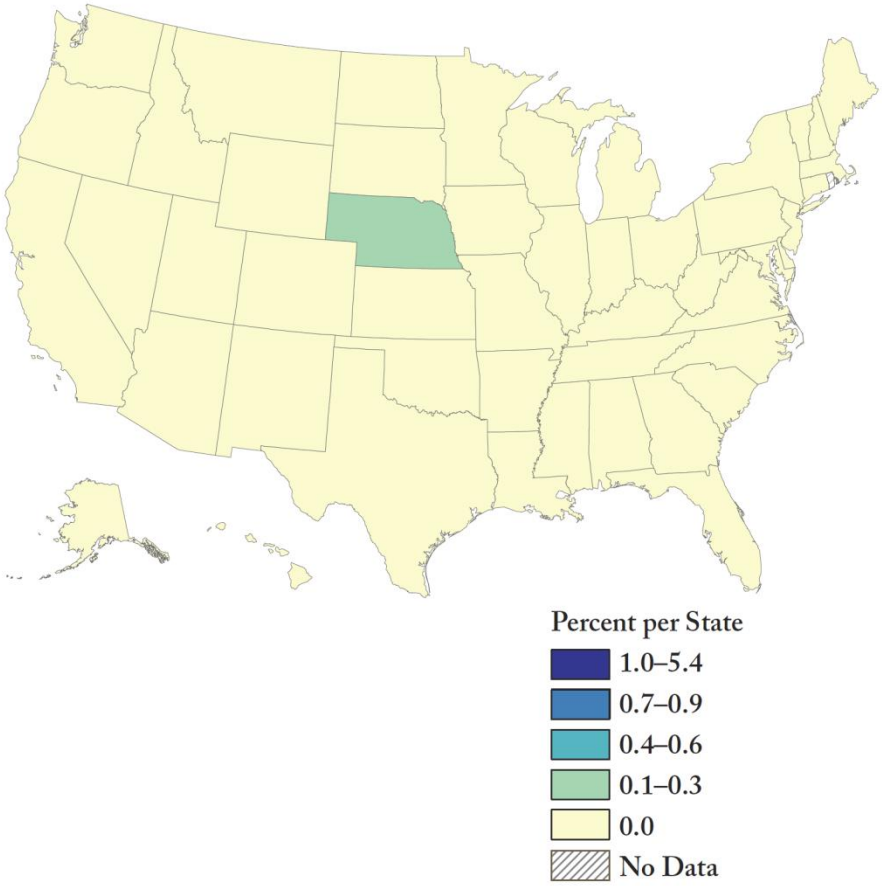
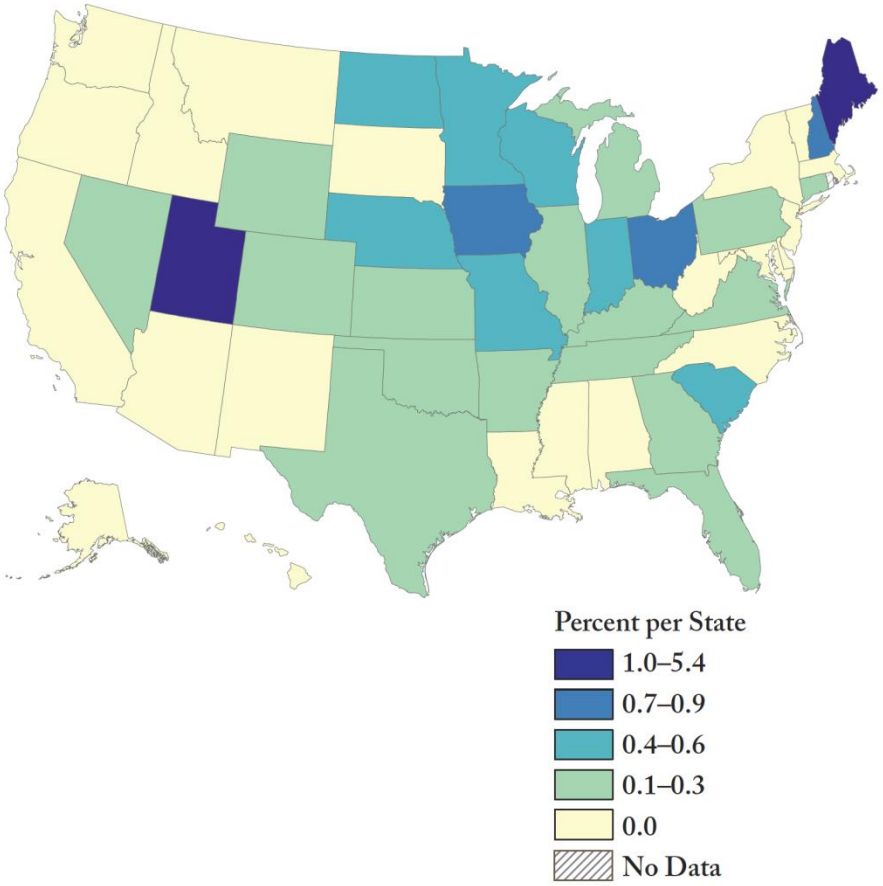



**Figure 3.4** Percentage of total drug reports identified as alpha-PVP, by State, 2012*




** Includes drug reports submitted to State and local laboratories during the calendar year that were analyzed within three months of the reporting period.*

# NFLIS Synthetic Cathinone Report, 2010-2013

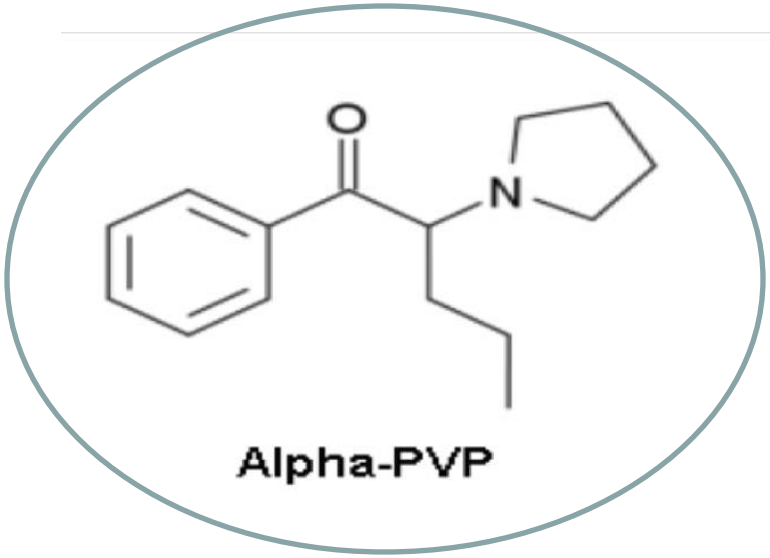
**Table 3** *National Semiannual Estimates of Synthetic Cathinone Reports in NFLIS, 2010–2013*

| Synthetic Cathinone Reports[1] | Total | | 2010 | | | | 2011 | | | | 2012 | | | | 2013 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Jan–June | | Jul–Dec | | Jan–June | | Jul–Dec | | Jan–June | | Jul–Dec | | Jan–June | |
| | Number | Percent | Number | Percent | Number | Percent | Number | Percent | Number | Percent | Number | Percent | Number | Percent | Number | Percent |
| Methylone (MDMC) | 11,795 | 39.78% | 7 | 4.92% | 48 | 10.43% | 516 | 29.00% | 1,306 | 27.42% | 1,843 | 26.52% | 2,859 | 37.84% | 5,215 | 65.22% |
| MDPV | 7,990 | 26.95% | 54 | 37.85% | 193 | 41.99% | 934 | 52.47% | 2,575 | 54.08% | 2,036 | 29.29% | 1,574 | 20.83% | 624 | 7.80% |
| alpha-PVP | 4,262 | 14.38% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 5 | 0.10% | 1,289 | 18.54% | 1,767 | 23.38% | 1,202 | 15.03% |
| 4-MEC | 1,934 | 6.52% | 0 | 0.00% | 3 | 0.65% | 32 | 1.78% | 125 | 2.63% | 497 | 7.16% | 697 | 9.22% | 580 | 7.25% |
| Pentedrone | 1,038 | 3.50% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 94 | 1.98% | 543 | 7.82% | 275 | 3.64% | 125 | 1.57% |
| Mephedrone (4-MMC) | 668 | 2.25% | 77 | 53.89% | 208 | 45.31% | 206 | 11.55% | 107 | 2.25% | 26 | 0.37% | 25 | 0.33% | 20 | 0.24% |
| Butylone | 504 | 1.70% | 0 | 0.00% | 2 | 0.53% | 47 | 2.65% | 161 | 3.37% | 172 | 2.48% | 78 | 1.03% | 43 | 0.54% |
| Fluoromethcathinone | 353 | 1.19% | 0 | 0.00% | 3 | 0.65% | 39 | 2.19% | 168 | 3.52% | 76 | 1.10% | 47 | 0.62% | 20 | 0.25% |
| Pentylone | 230 | 0.78% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 34 | 0.72% | 109 | 1.56% | 54 | 0.72% | 33 | 0.41% |
| 4-MePPP | 229 | 0.77% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 57 | 1.19% | 128 | 1.85% | 29 | 0.38% | 15 | 0.19% |
| alpha-PBP | 108 | 0.36% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 29 | 0.42% | 36 | 0.47% | 43 | 0.53% |
| Ethylone | 105 | 0.35% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 9 | 0.19% | 65 | 0.94% | 24 | 0.31% | 7 | 0.08% |
| Buphedrone | 41 | 0.14% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 16 | 0.23% | 11 | 0.14% | 15 | 0.18% |
| Methcathinone | 38 | 0.13% | 5 | 3.35% | 1 | 0.22% | 5 | 0.26% | 10 | 0.20% | 15 | 0.22% | 2 | 0.03% | 0 | 0.00% |
| Naphyrone | 25 | 0.08% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 9 | 0.18% | 8 | 0.12% | 7 | 0.09% | 1 | 0.01% |
| MDPBP | 24 | 0.08% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 6 | 0.13% | 17 | 0.24% | 0 | 0.00% | 1 | 0.01% |
| MPHP | 23 | 0.08% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 9 | 0.12% | 14 | 0.18% |
| Ethylcathinone | 23 | 0.08% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 1 | 0.02% | 14 | 0.20% | 5 | 0.06% | 3 | 0.04% |
| 3,4-DMMC | 22 | 0.08% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 4 | 0.09% | 15 | 0.22% | 2 | 0.03% | 1 | 0.01% |
| Methedrone | 21 | 0.07% | 0 | 0.00% | 0 | 0.00% | 2 | 0.09% | 5 | 0.11% | 11 | 0.16% | 2 | 0.03% | 1 | 0.01% |
| 4-Methylbuphedrone | 17 | 0.06% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 3 | 0.04% | 12 | 0.16% | 3 | 0.03% |
| MDPPP | 13 | 0.04% | 0 | 0.00% | 1 | 0.22% | 0 | 0.00% | 0 | 0.00% | 5 | 0.07% | 7 | 0.09% | 0 | 0.00% |
| 3-MEC | 10 | 0.03% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 8 | 0.11% | 2 | 0.03% | 0 | 0.00% |
| Other synthetic cathinones | 176 | 0.59% | 0 | 0.00% | 0 | 0.00% | 0 | 0.00% | 86 | 1.81% | 25 | 0.36% | 33 | 0.44% | 32 | 0.40% |
| **Total Synthetic Cathinones[2]** | **29,648** | **100.00%** | **142** | **100.00%** | **460** | **100.00%** | **1,780** | **100.00%** | **4,762** | **100.00%** | **6,950** | **100.00%** | **7,557** | **100.00%** | **7,997** | **100.00%** |

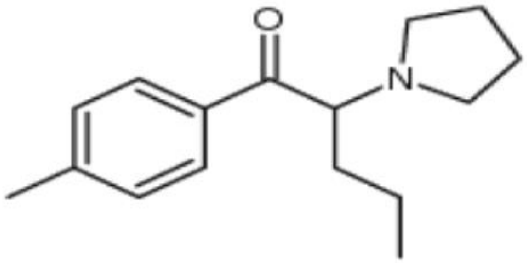
[1] For further information on these drugs, see the DEA's drug and chemical information at http://www.deadiversion.usdoj.gov/drug_chem_info/index.html and a forensic cheminformatic database at https://www.forensicdb.org/. See this report's Appendix A for the chemical names of these drugs.

[2] Numbers and percentages may not sum to totals because of rounding.

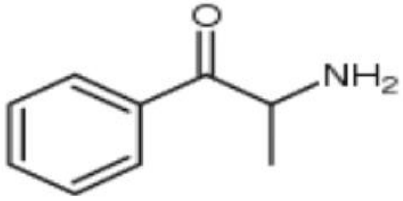
# Cathinone & Synthetic Cathinones



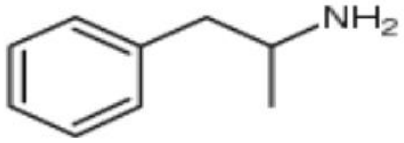

Alpha-PVP




Pyrovalerone




Cathinone




Amphetamine

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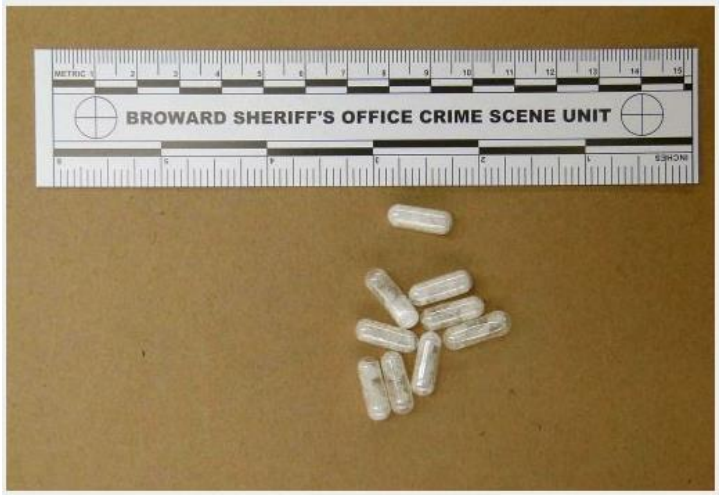
# Exposure

- Typically sold as powder or crystals
- Routes of administration
  - Snorting
  - Oral
  - Injection
  - Smoking
    - Use with electronic cigarettes increasing
- Desired effects last for a few hours
- Adverse side effects can last from hours to days

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# Mechanism of Effect

- Amphetamine-like effects on brain and peripheral nervous system
  - Stimulate release of norepinephrine and dopamine in brain
    - Inhibit re-uptake
  - “Fight or Flight” response
- Also stimulates release of serotonin, to a lesser extent
- Effects include those on mood, cognition, and reward system


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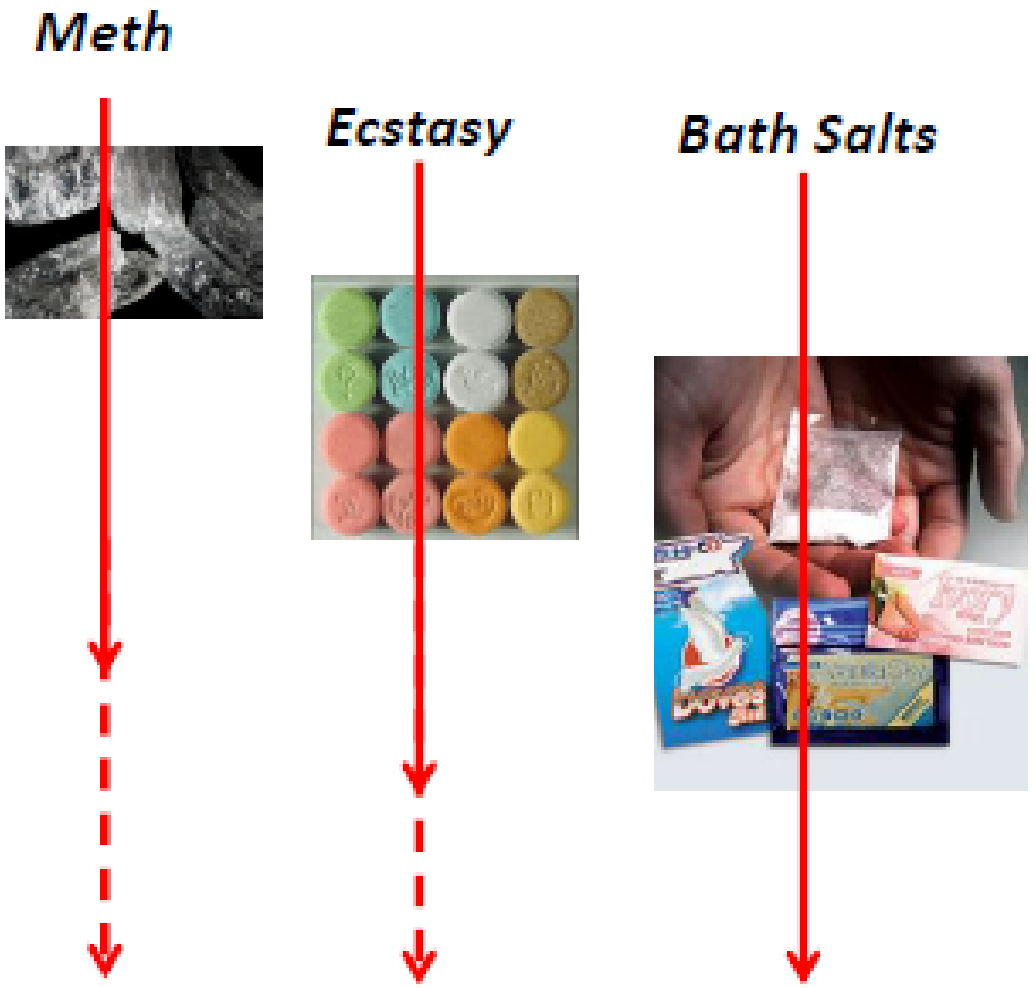
# “Bath Salts” Effects

| |
|---|
| Excitement |
| Euphoria |
| Tachycardia |
| Increased pupil size |
| Rapid Speech |
| Motor Restlessness |
| Anxiety |
| Paranoia |
| Mood Changes |
| Withdrawal/Depression |
| Delusions |
| Hallucinations |
| Seizures/Convulsions |
| Death |



# Synthetic Cathinones Effects Summary Sheet

- Aggression
- Agitation
- Breathing difficulty
- Bruxism (grinding teeth)
- Confusion
- Dizziness
- Extreme anxiety progressing to violent behavior
- Fits and delusions
- Hallucinations
- Headache
- Hypertension
- Increased alertness/awareness
- Increased body temp/chills/sweating
- Insomnia
- Kidney pain
- Lack of appetite
- Liver failure
- Loss of bowel control
- Muscle spasms
- Muscle tenseness
- Vasoconstriction
- Nausea, stomach cramps, digestive problems
- Psychotic delusions
- Pupil dilation
- Renal failure
- Rhabdomyolysis (breakdown of muscle)
- Severe paranoia
- Suicidal thoughts
- Tachycardia
- Tinnitus

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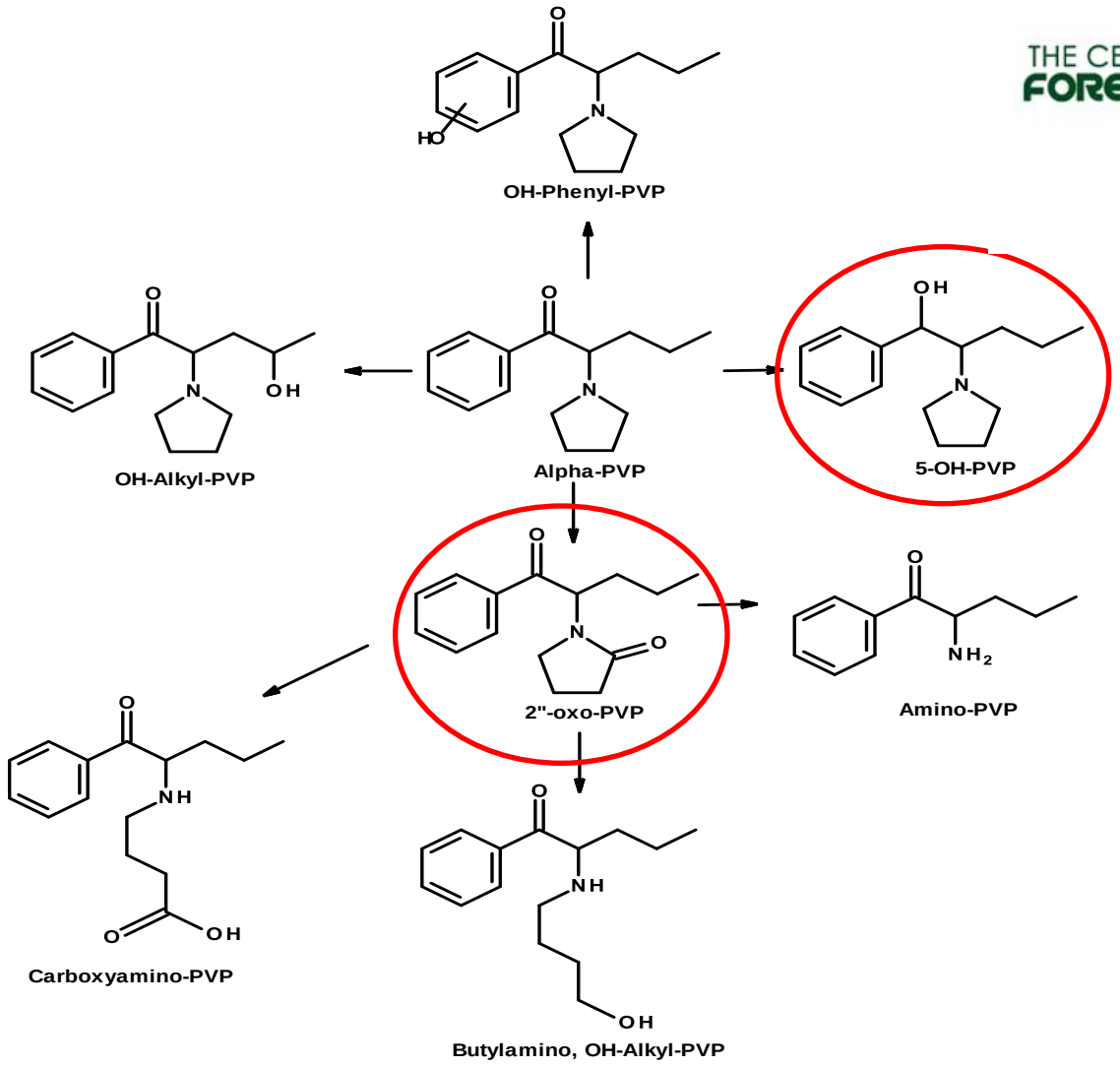
# Alpha PVP Metabolism

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- Ongoing research into metabolic profile
- 2 metabolites found in both human blood and urine samples

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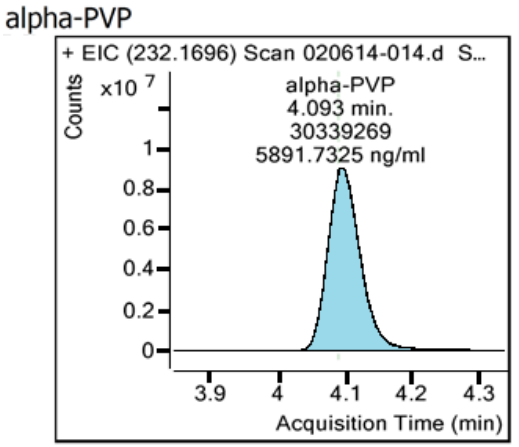
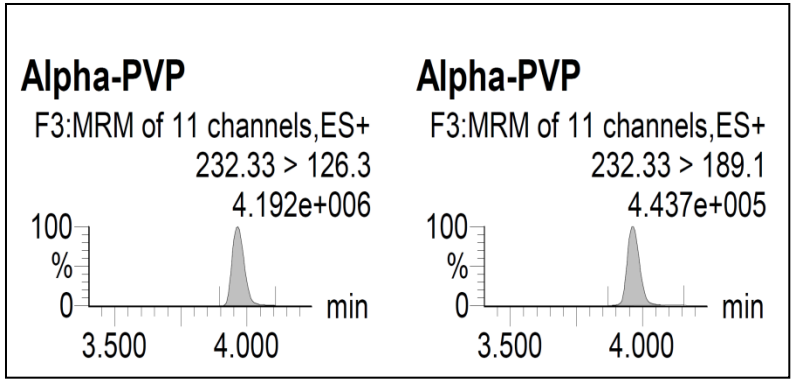
# Analytical Testing

- Screening
  - LC-TOF/MS
    - LC-TOF Agilent Jet Stream 6230
    - RL = 2 ng/mL
- Confirmation
  - LC-MS/MS
    - Waters TQD Tandem Mass Spectrometer with a Waters ACQUITY Ultra Performance LC
    - RL = 2 ng/mL

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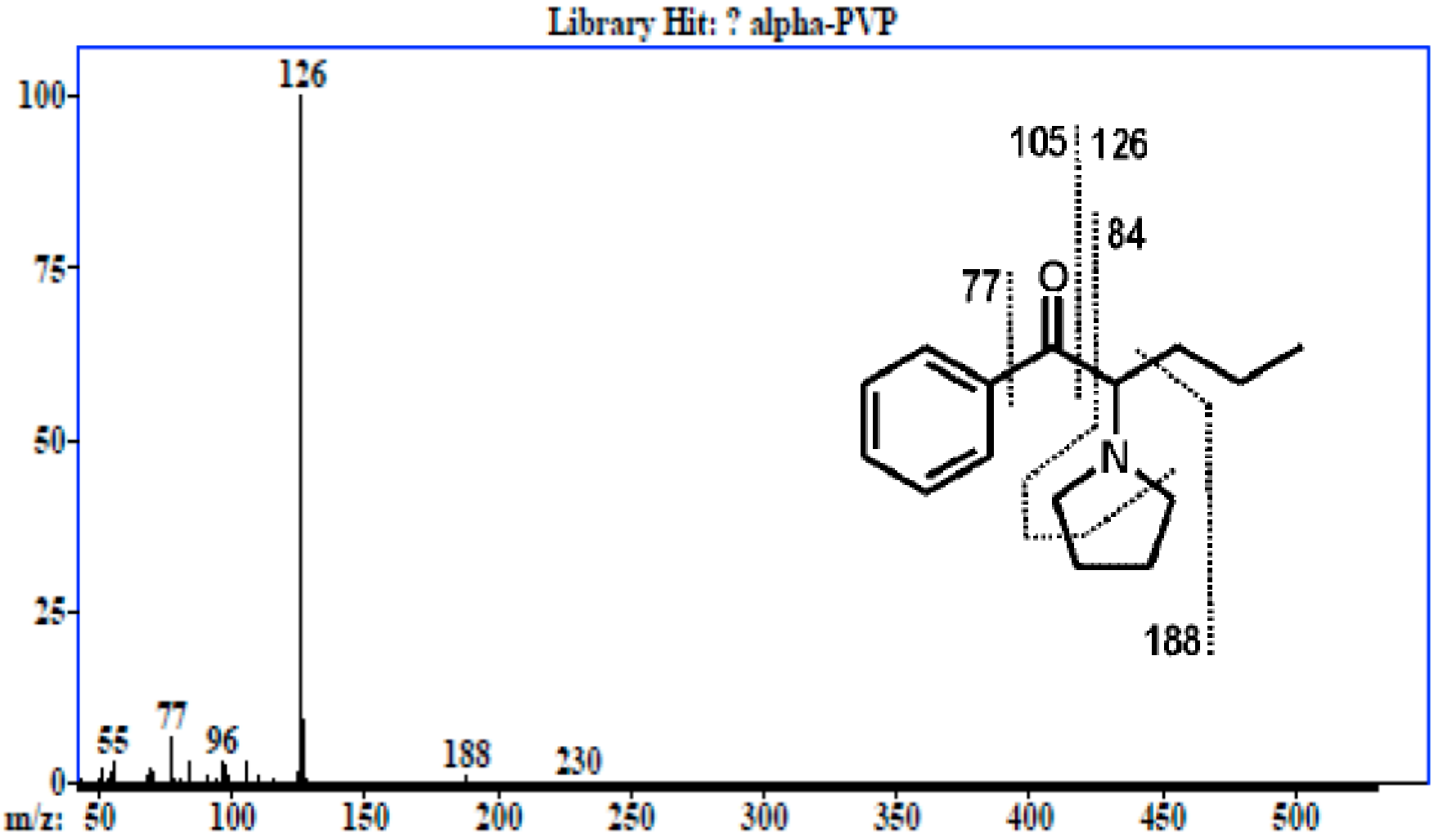
# GC/MS Screening



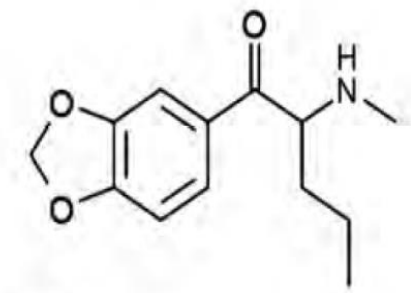
# Analysis of Synthetic Cathinones Commonly Found in Bath Salts in Human Performance and Postmortem Toxicology: Method Development, Drug Distribution and Interpretation of Results

*Published 2013*

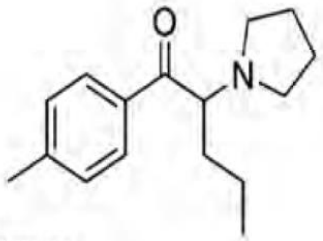
Laureen J Marinetti* and Heather M Antonides

Montgomery County Coroner's Office (MCCO)/Miami Valley Regional Crime Laboratory (MVRCL), Dayton, Ohio

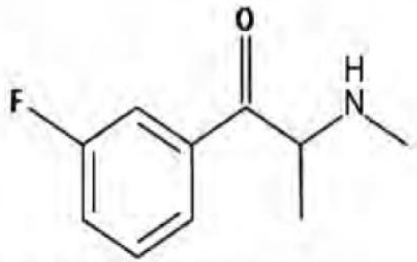
To date, the Toxicology Section of the Montgomery County Coroner's Office/Miami Valley Regional Crime Laboratory has identified six synthetic cathinones, commonly found in bath salt products, in 43 cases. Thirty-two cases will be reviewed here, including all of the postmortem cases, all of the human performance cases that had blood specimens submitted, and one urine-only human performance case. The following compounds have been confirmed: 3,4-methylenedioxypyrovalerone (MDPV), 3,4-methylenedioxymethcathinone (methylone), pyrovalerone, pentylone, alpha-pyrrolidinopentiophenone (alpha-PVP) and methedrone. The method also screens for mephedrone, butylone and 3-fluoromethcathinone. Case demographics show 42 white males and females ranging in age from 19 to 53 years. The remaining case was that of a 34-year-old Hispanic male. The 43 cases represent 17 driving under the influence, two domestic violence, four suicides, 12 overdoses, six accidents, one drug-facilitated assault and one homicide. Data will be presented on the distribution of some of these cathinones in various matrices. After review, blood concentration does not appear to predict outcome regarding fatalities or impairment. The highest MDPV concentration occurred in a suicide by hanging and the highest methylone concentration was in a driver. The confirmation method is a liquid–liquid extraction with detection by liquid chromatography triple quadrupole mass spectrometry using electrospray ionization in multiple reaction monitoring mode.



Pentylone



Pyrovalerone



3-Fluoromethcathinone

# Alpha PVP and Psychotic Behavior

- "Bath Salts" – Induced Psychosis in a Young Woman. Khan S, et al. Jan 2013.
  - 19 y/o female presented to ER with severe agitation, aggressive behavior, and psychosis
  - Reported auditory and visual hallucinations
  - Snorted "Ivory Wave" bath salt product
- A case of severe psychosis induced by novel recreational drugs. Dragogna F, et al. March 2015
  - 46 y/o male developed severe psychotic episodes after recreational use of alpha-PVP, MDPV, mephedrone, and butylone

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# Toxicity & Death following Alpha-PVP Use

- 2 men purchased legal high Energy-3 (NRG-3)
- 32 y/o male insufflated NRG-3 purchased on internet & consumed alcohol
  - Complained of feeling ill
  - Hands became purple
  - Developed difficulty breathing & lost consciousness
- Pronounced dead upon arrival at ER
- Post mortem tox analysis revealed presence of alpha PVP in blood and urine

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Eiden C et al. Toxicity and death following recreational use of 2-pyrrolidino valerophenone. *Clin Tox*. (2013). 51; 899-903.

# Toxicity & Death following Alpha-PVP Use

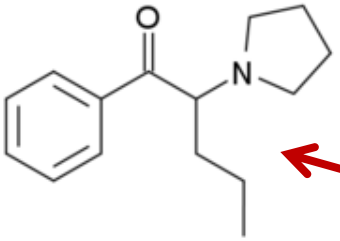
- 21 y/o male w/o history of psychiatric illness or past drug addiction insufflated “NRG-3”
- Presented to ER with tachycardia, mydriasis, rhabdomyolisis, visual hallucinations, and other behavioral disturbances
- Tox showed presence of alpha PVP

**Table 1.** Toxicological analysis.

| Patient | 1 | 2 |
|---|---|---|
| PVP plasma concentration | 1500 ng/ml | 235 ng/ml |
| Time between consumption and sampling (hours) | 20 (post-mortem sampling) | 5–7 |
| PVP urine concentration | > 5000 ng/ml | > 5000 ng/ml |
| Delay between consumption and sampling (hours) | 20 (post-mortem sampling) | 12 |
| Blood concentrations of associated substances | **THC: 3.3 ng/ml<br>THCCOOH: 14.2 ng/ml<br>11-OH-THC: 2 ng/ml<br>alcohol: 3.65 g/L | No* |
| Urinary substances associated | THC: positif*<br>alcohol: positif | THC: positif* |


Eiden C et al. Toxicity and death following recreational use of 2-pyrrolidino valerophenone. *Clin Tox*. (2013). 51; 899-903.

# “NRG-3” tested to be alpha PVP



Alpha PVP

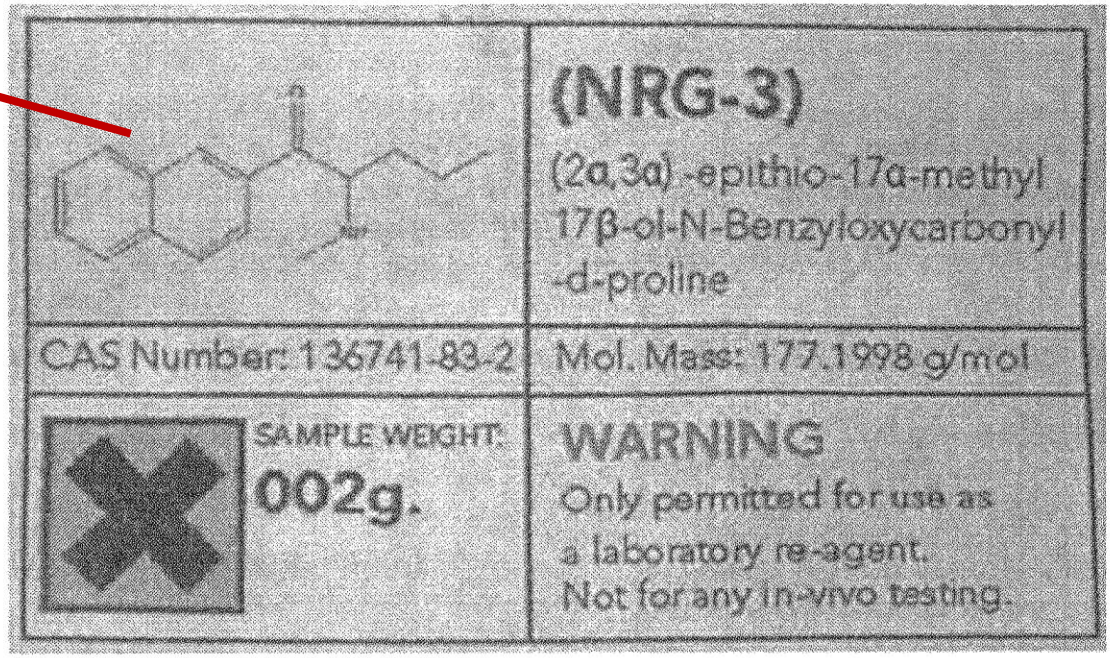



**Fig. 3.** NRG-3 package powder (powder residue was tested for PVP by the police laboratory) (colour version of this figure can be found in the online version at www.informahealthcare.com/ctx).

* Manufacturers misrepresent both composition and legal status of products*

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# Case reports

## Death due to intravenous use of α-pyrrolidinopentiophenone

Intoxication with synthetic cathinones (psychoactive designer drugs) can involve cardiovascular, autonomic, neuromuscular and neuropsychiatric features. We report a case of cardiac arrest and subsequent death in a 44-year-old man after intravenous use of one such drug — α-pyrrolidinopentiophenone. We believe this is the first death associated with this drug to be reported in Australia. Currently, no specific antidote exists for cathinone exposure.

Serum: 411 ng/mL Alpha PVP

## Sudden death after sustained restraint following self-administration of the designer drug α-pyrrolidinovalerophenone☆

Hisashi Nagai, Kanju Saka, Makoto Nakajima, Hidyuki Maeda, Ryohei Kuroda, Atsuko Igarashi, Takako Tsujimura-Ito, Akina Nara, Masatomo Komori, Ken-ichi Yoshida *

*Department of Forensic Medicine, Graduate School of Medicine, The University of Tokyo, Japan*

## Suspected Impaired Driving Case Involving α-Pyrrolidinovalerophenone, Methylone and Ethylone

Justin L. Knoy*, Brianna L. Peterson and Fiona J. Couper

Toxicology Laboratory Division, Washington State Patrol, 2203 Airport Way S., Suite 360, Seattle, WA 98134, USA

Blood: 63 ng/mL Alpha PVP

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# Combined “Bath Salt” Fatality

- A fatal case of Pentedrone and alpha-pyrrolidinovalerophenone poisoning. Sykutera M, et al. March 2015. Journal of Analytical Toxicology
  - 28 y/o male presented to ER in cardiac arrest
  - Blood Toxicology
    - Pentedrone: 8,794 ng/mL
    - Alpha PVP: 901 ng/mL
    - OH-alpha PVP: 185 ng/mL

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# Toxicology Concentrations

| Cases | N | Average /Median Concentrations (ng/mL) | Range (ng/mL) | Average Age | Age Range |
|---|---|---|---|---|---|
| Police Cases | 79 | 64.6 (35) | (3.4 - 440) | 35 | 19-63 |
| Postmortem Cases | 28 | 237 (100) | (3.5 - 1500) | 33 | 19-57 |

- Gender breakdown approximately the same for both types of cases
  - 67% Male
  - 33% Female

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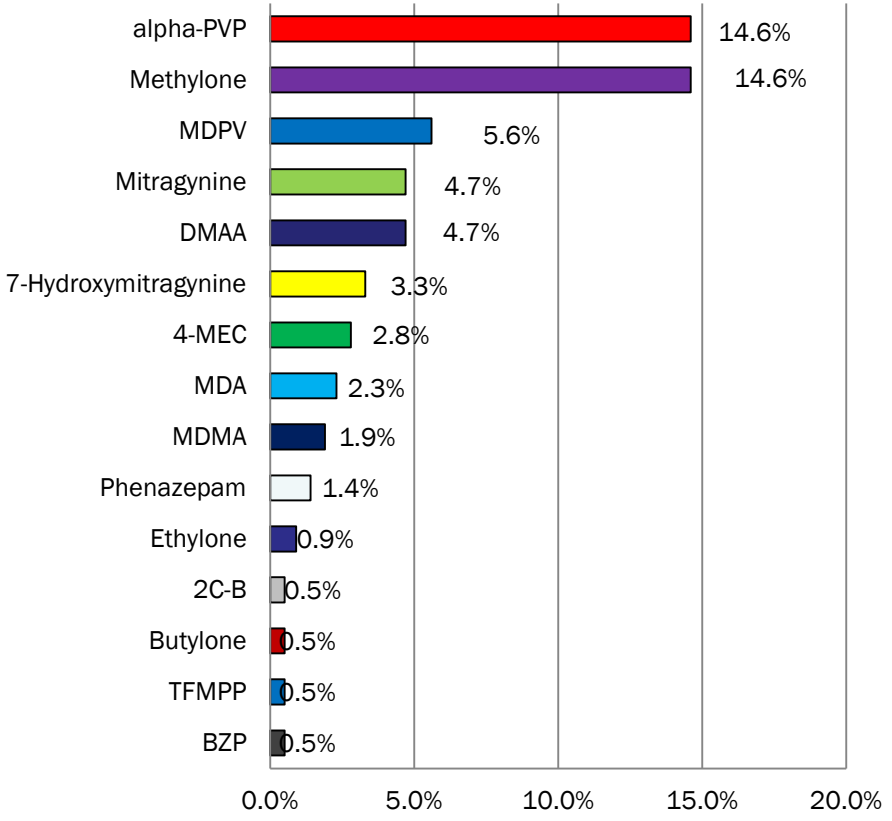
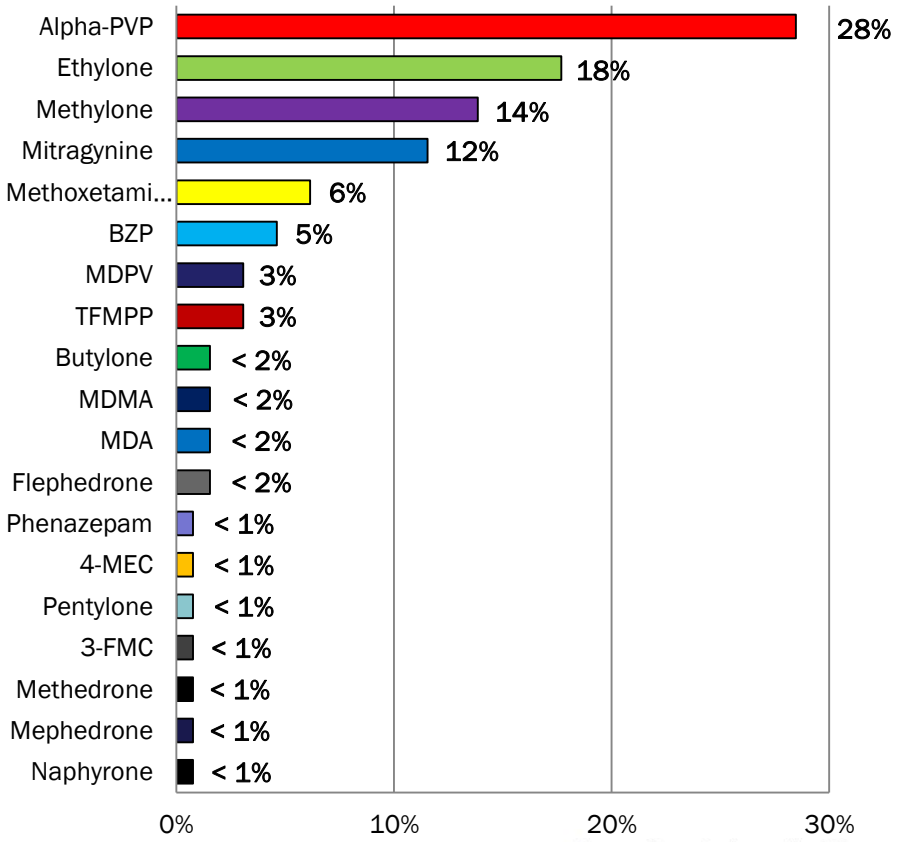
# 8756B Positivity

## 2013




Source: Of the 472 blood samples submitted to NMS Labs in 2013, 30% confirmed positive for 1 or more analytes in the Expanded Bath Salts & Stimulants Panel (8756B). Alpha PVP was outside the scope of the assay prior to 7/2013 updates; positive results were verified by secondary analysis. Since the updated scope with alpha PVP, there have been 31 positives in 362 blood cases for alpha PVP. Confirmed positive cases (n=145) included methamphetamine and amphetamine; of the 213 positive analytes, methamphetamine and amphetamine were 41.4% of the positives.

## 2014




Source: Of the 459 blood samples submitted to NMS Labs in 2014, 28.3% samples were positive for 1 or more analytes in the Expanded Bath Salts & Stimulants Panel

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# Challenges: Cathinone Stability

- Proper collection and storage is important to optimize the possibility for detection
- Mephedrone, methylone and other cathinone bath salts can degrade quickly in biological samples
- Citric acid preservative helps to prevent breakdown and extend stability
- Alpha PVP particularly unstable in serum/plasma, especially at RT
- Preserved blood and urine preferred specimens

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# Designer Stimulants – Legal Status

- Federal vs. state regulations
  - Synthetic Drug Abuse Prevention Act of 2012
    - Banned MDPV, Mephedrone, methylone, 15 specific “cannabimimetic agents”, and 9 synthetic “2C” compounds
  - 1/28/14 DEA filed notice of intent for 10 more synthetic cathinones
    - 4-MEC, MePPP, Alpha PVP, Alpha PBP, Butylone, Pentedrone, Pentylone, 4-FMC, 3-FMC, & Naphyrone
    - Final order on March 7, 2014

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# Summary – “Flakka”

- Alpha PVP is an NPS with stimulant properties; predominately cardiovascular and psychological adverse side effects
- Alpha PVP has been found in many forensic investigations, including DUIs and deaths
- If Alpha PVP is suspected, it is important to ensure the analyte is covered by scope of testing
- Blood concentrations have limited value for interpreting effects; research is still ongoing
- Toxicology usually compounded by other impairing drugs
- Alpha PVP is federally scheduled

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# NMS Tests

**Update Coming Soon!**

| Analysis Code | Test Name |
|---|---|
| 0245B | Alpha PVP, Blood |
| 0245SP | Alpha PVP, Serum/Plasma |
| 0245U | Alpha PVP, Urine |
| 8756B | Bath Salts and Stimulants Designer Drugs - Expanded, Blood |
| 8756SP | Bath Salts and Stimulants Designer Drugs - Expanded, Serum/Plasma |
| 8756U | Bath Salts and Stimulants Designer Drugs - Expanded, Urine |
| 2626B | Bath Salts Panel, Blood |
| 2626SP | Bath Salts Panel, Serum/Plasma |
| 2626U | Bath Salts Panel, Urine |

8756B: Novel Psychoactive Substances Screen

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# Questions?

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