Synthetic Drug Threats in the United States

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Overview of Synthetic Drugs

Synthetic drugs are man-made substances such as:

- Methamphetamine
- MDMA
- PCP
Overview of Emerging Synthetic Drug Threats

- Synthetic Cannabinoids
- Synthetic Cathinones
- Phenethylamine Hallucinogens
- Synthetic Opioids
SYNTHETIC CANNABINOIDS
What are Spice and K2?

“Spice” and “K2” were the earliest brand names of an herbal smoking blend that contained a synthetic cannabinoid.

Other terms used: herbal smoking blends, synthetic smoking blends, herbal incense

Synthetic Cannabinoids ≠ Synthetic Marijuana
Packaging

- Not for human consumption
- “Lab Tested”
- Keep out of reach of children
- Retailers take no responsibility...
- For aromatherapy only...
- DEA Compliant
- Legal in all 50 states
Synthetic Cannabinoid Processing
Synthetic Cannabinoid Processing
Dosing the Plant Material

The process can result in “hot spots” and inconsistent dosing.
A little history...

- 1980s-1990s: Developed as part of medicinal research
- 2006: First smoking blend seen in 2006*
- 2008: TC Pharma reports JWH-018 in a blend
- 2009: CP-47,497 reported in a blend
- 2009: European countries begin controlling
- 2009: K2 enters the market
- 2011: DEA emergency scheduling of 5 cannabinoids
- 2012: Synthetic Drug Abuse Prevention Act takes effect
- 2013: DEA emergency scheduling of 3 additional cannabinoids
- 2014: DEA emergency scheduling of 4 more cannabinoids
- 2015: DEA emergency scheduling of 3 other cannabinoids

*EMCDDA 2009 Thematic paper – Understanding the ‘Spice’ phenomenon, doi: 10.2810/27063
# Cannabinoids by Year

|------|-----------|------|------|------|------|------|
| 2009/2010 | JWH-018  
 JWH-073  
 JWH-250  
 CP-47,497 | JWH-019  
 JWH-081  
 JWH-122  
 JWH-200  
 AM2201  
 AM694  
 RCS-4  
 RCS-8 | JWH-203  
 UR-144  
 A 796,260  
 5F-UR-144  
 2NE1  
 STS-135  
 AKB48  
 AB-001 | MN-24 (NNE1)  
 AB-FUBINACA  
 ADB-FUBINACA  
 AB-PINACA  
 5F-AB-PINACA  
 PB-22  
 FUB-PB-22  
 THJ-018 | AB-CHMINACA  
 FDU-PB-22  
 NM2201  
 SDB-005  
 5F-AMB  
 5F-NPB-22  
 UR-144 Indazole  
 EG-018 | PX-2  
 MAB-CHMINACA  
 MDMB-CHMICA  
 APP-CHMINACA  
 5F-MDMB-PINACA  
 MDMB-FUBINACA |

*Note: The table lists cannabinoid compounds by year, with each year's entries categorized under the respective year's designation.*
Evolution of Cannabinoids

- JWH-018
- UR-144
- AKB48
- PB-22
- PX-2
- 5F-AMB
- FUB-PB-22
- AB-FUBINACA
What are all these letters and numbers?!?

- Developer/institution
  - JWH = John W. Huffman
  - AM = Alexandros Makriyannis

- Website
  - RCS-4 (SR-19, BTM-4)
  - RCS-8 (SR-18, BTM-8)

- Pharmaceutical companies
  - A = Abbott Laboratories
  - WIN = Sterling Winthrop

- Pop culture references
  - 2NE1
  - AKB48
  - STS135
  - XLR-11
  - BB-22

- Chemical names
  - QUPIC (PB-22)
  - AB-FUBINACA
  - AB-PINACA
    \[\text{N-(1-Amino-3-methyl-1-oxoButan-2-yl)-1-}(\text{Pentyl-1H-INdazole-3-CarboxAmide})\]
## Forensic Analysis of Scooby Snax

<table>
<thead>
<tr>
<th>Date Seized</th>
<th>Substance Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/18/2013</td>
<td>5F-UR-144</td>
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<tr>
<td>6/18/2013</td>
<td>5F-PB-22</td>
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<tr>
<td>6/20/2013</td>
<td>PB-22</td>
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<tr>
<td></td>
<td>5F-UR-144</td>
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<tr>
<td></td>
<td>5F-PB-22</td>
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<tr>
<td>2/21/2014</td>
<td>5F-UR-144</td>
</tr>
<tr>
<td></td>
<td>PB-22</td>
</tr>
<tr>
<td>3/27/2014</td>
<td>5F-UR-144</td>
</tr>
<tr>
<td></td>
<td>AB-FUBINACAC</td>
</tr>
</tbody>
</table>
E-Cigarettes

AB-PINACA and nicotine

AB-FUBINACA

AB-FUBINACA
## Cannabinoid Adulteration

<table>
<thead>
<tr>
<th>Date Seized</th>
<th>Location of Seizure</th>
<th>Substances Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/2015</td>
<td>South Central</td>
<td>THJ-2201, dimethyl sulfone</td>
</tr>
<tr>
<td>01/2015</td>
<td>Southeast</td>
<td>5F-AMB, nicotine</td>
</tr>
<tr>
<td>01/2015</td>
<td>South Central</td>
<td>AB-FUBINACA, 5F-AB-PINACA, dimethyl sulfone</td>
</tr>
<tr>
<td>02/2015</td>
<td>North Central</td>
<td>FDU-PB-22, PB-22, lidocaine</td>
</tr>
<tr>
<td>02/2015</td>
<td>Mid-Atlantic</td>
<td>5F-UR-144, 5Cl-UR-144, dimethyl sulfone</td>
</tr>
<tr>
<td>02/2015</td>
<td>Southeast</td>
<td>5F-UR-144, AB-CHMINACA, nicotine</td>
</tr>
<tr>
<td>03/2015</td>
<td>Southeast</td>
<td>UR-144, AB-PINACA, dimethyl sulfone</td>
</tr>
<tr>
<td>03/2015</td>
<td>Western</td>
<td>AB-CHMINACA, caffeine</td>
</tr>
<tr>
<td>04/2015</td>
<td>Southeast</td>
<td>AB-FUBINACA, dimethyl sulfone</td>
</tr>
<tr>
<td>05/2015</td>
<td>South Central</td>
<td>AB-FUBINACA, caffeine</td>
</tr>
</tbody>
</table>

This data was compiled from analytical results entered in the DEA LIMS. It encompasses exhibits seized 01/01/2015 through 06/30/2015 that were analyzed by 06/30/2015. This data is subject to change as the laboratory system obtains reference materials and analyzes exhibits in the backlog.
2015 National Trends – Cannabinoids Identified

Synthetic Cannabinoids
> 10 identifications
N = 1212

Notes:
1) This data was compiled from analytical results from the DEA laboratory system. It encompasses exhibits seized 01/01/2015 through 12/31/2015 that were analyzed by 12/31/2015. This data is subject to change as the laboratory system obtains reference materials and analyzes exhibits in the backlog.
2015 National Trends – Cannabinoids Identified

Synthetic Cannabinoids
< 10 identifications
N = 74

Notes:
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SYNTHETIC CATHINONES
What are “bath salts”? 

“Bath salts” are a designer drug typically containing synthetic cathinones or phenethylamines.

Like smoking blends, “bath salts” are often marketed as “legal highs” and are labeled with “Not for Human Consumption” and “Does Not Contain” statements.

Also called: plant food, glass cleaner, bug repellant, and research chemicals
Synthetic Cathinones

- “Bath salt” phenomenon has diminished
- Compounds are still found, but no longer in commercial packaging
Bulk Packaging

The synthetic cathinone is imported into the US

Packages are often mislabeled to get through Customs
Bulk Powder

• Currently no known domestic synthesis
• Typically powders enter the country pure and are cut here
A little history...

- 1920s: Cathinones, such as mephedrone, were first synthesized
- 2007: Mephedrone (followed soon by others) first appeared in Israel, then later in the UK and Australia
- 2009: Use becomes popular in Europe (from drug dealers or websites)
- 2010: Use becomes prevalent in the US (from convenience stores, head shops, or websites)
- 2010: European countries begin controlling
- 2011: DEA emergency scheduling of 3 cathinones
- 2012: Synthetic Drug Abuse Prevention Act takes effect
- 2013: Methylone permanently scheduled
- 2014: DEA emergency scheduling of 10 additional cathinones
Common Components

<table>
<thead>
<tr>
<th>Mephedrone</th>
<th>Butylone</th>
<th>Dimethylone</th>
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</thead>
<tbody>
<tr>
<td>Methylone</td>
<td>Naphyrone</td>
<td>Dibutylone</td>
</tr>
<tr>
<td>MDPV</td>
<td>Pentedrone</td>
<td>5-APB</td>
</tr>
<tr>
<td>Ethcathinones</td>
<td>Pentyline</td>
<td>6-APDB</td>
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<tr>
<td>Methcathinones</td>
<td>Buphedrone</td>
<td>Alpha-PVT</td>
</tr>
<tr>
<td>Fluoroamphetamines</td>
<td>Alpha-PVP</td>
<td>PV8</td>
</tr>
<tr>
<td>Fluorocathinones</td>
<td>Alpha-PBP</td>
<td>5-IAI</td>
</tr>
<tr>
<td>MXE</td>
<td>MPPP</td>
<td>MDAI</td>
</tr>
</tbody>
</table>

The use of adulterants/diluents such as inositol, benzocaine, lidocaine, caffeine, etc. is common.
The Story of “Molly”

- Ecstasy tablets in the 1980s-early 2000s typically contained MDMA
- In ~2006, ecstasy tablets featured mostly BZP/TFMPP combinations
- Rise in crystal or powder MDMA
  - Called “Molly”
- Many current “Molly” investigations have been found to be methylone or other substituted cathinones
  - Low cost and easy to obtain
Flakka/Gravel

- White, brown, purple, pink, or blue crystals
- Off-white, brown, or beige powder
- Typically alpha-PVP
- May be cut using a variety of chemicals
2015 National Trends – Stimulants Identified

Stimulants
N = 401

- Ethylene (219)
- α-PVP (119)
- Methylone (13)
- Dimethylone (8)
- α-PHP (8)
- MXE (6)
- 4-BMC (4)
- Butylone (4)
- 5-MAPB (3)
- MDPV (3)
- N-Ethylbuphedrone (3)
- < 3 identifications each

4-MEC (2) 4-FA (1)
Dibutylone (2) N,N-Dimethylpentylone (1)
PV8 (2) Pentedrone (1)
2-MAPB (1) α-PVT (1)

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Cathinone Adulteration

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</thead>
<tbody>
<tr>
<td>01/2015</td>
<td>Southeast</td>
<td>MDMA, ketamine, 4-MeO-MA, ethylone, caffeine</td>
</tr>
<tr>
<td>03/2015</td>
<td>Southwest</td>
<td>MDMA, 2C-B, DMT, caffeine, dimethyl sulfone</td>
</tr>
<tr>
<td>03/2015</td>
<td>Southwest</td>
<td>MDMA, methylone, cocaine</td>
</tr>
<tr>
<td>03/2015</td>
<td>Southwest</td>
<td>MDMA, ethylone</td>
</tr>
<tr>
<td>03/2015</td>
<td>Southwest</td>
<td>MDMA, butylone, dimethyl sulfone</td>
</tr>
<tr>
<td>04/2015</td>
<td>Southwest</td>
<td>MDMA, ethylone, caffeine, dimethyl sulfone</td>
</tr>
<tr>
<td>04/2015</td>
<td>Southeast</td>
<td>MDMA, ethylone, dimethyl sulfone</td>
</tr>
<tr>
<td>04/2015</td>
<td>Southeast</td>
<td>cocaine, ethylone, caffeine, lidocaine, PTHIT</td>
</tr>
<tr>
<td>04/2015</td>
<td>Southeast</td>
<td>heroin, fentanyl, acetylfentanyl, ethylone, quinine, diphenhydramine, caffeine, ibuprofen</td>
</tr>
<tr>
<td>04/2015</td>
<td>Southeast</td>
<td>MDMA, ethylone</td>
</tr>
<tr>
<td>05/2015</td>
<td>South Central</td>
<td>ethylone, dimethyl sulfone</td>
</tr>
</tbody>
</table>

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## Cannabinoids and Cathinones

<table>
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<tr>
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<th>Location of Seizure</th>
<th>Substances Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>02/2014</td>
<td>Northeast</td>
<td>alpha-PVP, AB-PINACA</td>
</tr>
<tr>
<td>02/2014</td>
<td>Northeast</td>
<td>5F-UR-144, alpha-PVP</td>
</tr>
<tr>
<td>12/2014</td>
<td>South Central</td>
<td>alpha-PVT, FDU-PB-22</td>
</tr>
<tr>
<td>12/2014</td>
<td>South Central</td>
<td>4F-alpha-PVP, lidocaine, MN-24</td>
</tr>
</tbody>
</table>

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Phenethylamine Hallucinogens

- Found as powder, tablets, liquids, blotter paper, sugar cubes, window panes, etc.
- Several groups fall in this class
  - 2C-X (such as 2C-I, 2C-B, 2C-C)
  - DOX (such as DOI, DOB, DOC)
  - 25X-NBOMe (25I-NBOMe, 25B-NBOMe, 25C-NBOMe)
    - Placed in Schedule I in November 2013
NBOMe

- 4,868 drug reports from January 2011 through August 2015 from 43 states
- Combinations of 25I-NBOMe, 25C-NBOMe, and 25B-NBOMe responsible at least 19 deaths between March 2012 and August 2013.
- Overdoses continuing through 2014-2015
- Also called N-bomb, Smiles, 25I, 25C, 25B

![Chemical Structure of NBOMe](image)

25I-NBOMe, 25C, NBOMe, 25-B-NBOMe DEA Fact Sheet, DEA/OD/ODE, November 2013
2015 National Drug Threat Assessment Summary, October 2015, DEA-DCT-DIR-008-16
2015 National Trends – Hallucinogens

- 25I-NBOMe (10)
- 25C-NBOMe (6)
- 2C-B (3)
- DOC (1)

Notes:
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2) To serve as a frame of reference, DEA reported 30 identifications of LSD during the same time period.
Fentanyl

- Potent synthetic opioid used in medical practice since the 1960’s
- Pharmaceutical preparations diverted or stolen for illicit abuse
- Clandestine manufacture of fentanyl from 2005-2007
  - Originated from a single laboratory in Toluca, Mexico
  - 1,013 confirmed non-pharmaceutical fentanyl-related deaths
- 20-25% purity at the wholesale level
Heroin Origin Determination

- The DEA’s Special Testing and Research Laboratory provides in-depth chemical analysis to determine the source area origin and purity of heroin found in the United States
- Analysis of seized heroin at wholesale and retail levels
- Provides a snapshot of the US heroin market
Fentanyl and Heroin

• High purity fentanyl exhibits have not been detected at either the wholesale or retail level (0-6%)
• Street level fentanyl can be found with or without heroin.

When heroin is present:
• Heroin can be found from trace to high purity (@85%) levels.
• South American (SA) heroin and SA-like heroin are the types typically laced with fentanyl.
• Typical powder heroin adulterants for the east coast markets such as caffeine, quinine, acetaminophen, diphenhydramine, etc. are found in fentanyl-laced heroin exhibits.
• Dipyrone is also identified in many exhibits
There have been over 700 deaths in the United States related to fentanyl and its analogs between late 2013 and late 2014. The deaths have continued in 2015.”

States Affected by Fentanyl Overdose Incidents and Deaths, 2013 - 2014
Profiling of Fentanyl

• As the majority of fentanyl submissions displayed only 10% or less fentanyl, the profiling attempts to determine synthetic routes were hindered.

• In addition, only minimal manufacturing impurities were found in the current fentanyl samples indicating skillful production batch after batch.
Acetyl fentanyl

- Schedule I substance (effective 7/17/2015)
- Not approved for medical use in the United States
- 1st identified in Maine in 2013
- More than 50 confirmed fatalities involving acetyl fentanyl in 2013-2015

According to DEA’s STARLiMS and National Forensic Laboratory Information System (NFLIS), federal, state and local forensic laboratories reported 10 exhibits identified as acetyl fentanyl in 2013 and 40 exhibits identified as acetyl fentanyl in 2014.

Acetyl fentanyl DEA Fact Sheet, DEA/OD/ODE, July 2015
Federal Register Volume 80, Number 137 (Friday, July 17, 2015)
2015 National Trends – Other Substances Identified

Opioids

• Fentanyl (239)
• Acetylfentanyl (62)
• Butyryl fentanyl (6)
• W-18 (2)
• β-Hydroxythiofentanyl (2)
• 4-ANPP (1)

Other

• Substance Unconfirmed (83)

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# Fentanyl Derivatives and Other Synthetic Opioids

## Fentanyl Derivatives
- Acetyl fentanyl
- Butyryl fentanyl
- β-Hydroxythiofentanyl
- p-Fluoro fentanyl
- Acryl fentanyl
- Furanyl fentanyl
- Valeryl fentanyl

## Synthetic Opioids
- MT-45
- AH-7921
- U-47700
- W-15
- W-18
Top 5 “Trending” Drug Identifications by Laboratory and NDEWS Sentinel Community Sites

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2) 2 = Northeast Laboratory; 3 = Mid-Atlantic Laboratory; 4 = Southeast Laboratory; 5 = North Central Laboratory; 6 = South Central Laboratory; 7 = Western Laboratory; 8 = Southwest Laboratory
Closing thoughts

• Over 300 new drugs in 10 years in the U.S.
• Availability of reference materials has increased
• China banned 116 NPS in 2015
• Continual evaluation of new drugs and drug classes
• Early and frequent communication regarding drug threats
Thank You!

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Fentanyl Analogs:
- Acetyl fentanyl (42 exhibits): 15 X less potent than fentanyl
- Butyryl fentanyl (6 exhibits): 1/4\textsuperscript{th} potency of fentanyl
- β-Hydroxythiofentanyl (2 exhibits)
- p-Fluoro fentanyl: 150 to 200 X more potent than morphine
- Acryl fentanyl
- Furanyl fentanyl: Slightly less potent than butyryl fentanyl
- Valeryl fentanyl: Highly less potent than butyryl?

Synthetic Opioids:
- MT-45 (IC-6 exhibits): Almost as potent as morphine
- AH-7921: Almost as potent as morphine
- U-47700: 7 to 8 X more potent than morphine
- W-15: 4 to 5 X more potent than morphine
- W-18 (2 exhibits): 10,000 times more potent than morphine?