Classes and Structures of Emerging Cannabimimetics and Cathinones

Arthur Berrier
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Special Testing and Research Laboratory
Drug Enforcement Administration

Herbal Smoking Blends - SPICE

- SPICE and other herbal blends have been sold in head shops and on the Internet since 2006 for their cannabis-like intoxication
- The herbal blends sometimes have a fragrance which could include vanilla, potpourri, spice, blueberry, caramel, and strawberry
- The plant materials for the different blends have a wide variation in appearance

Herbal Smoking Blends - SPICE

- In late 2008, THC Pharma reported the presence of JWH 018, a synthetic cannabimimetic indole in some blends
- In early 2009, analogues of CP 47,497 (another synthetic cannabinoid) were also found in some blends by the U. of Freiburg
- In early 2009, several European Countries control Herbal Blends/JWH 018/CP 47,497

Herbal Smoking Blends - SPICE

- K2 enters market in April, 2009
- Interest booms in herbal smoking blends in 2009
- Many new products appeared, typically with JWH 018 and JWH 073
- States begin to control the blends/synthetic cannabinoids

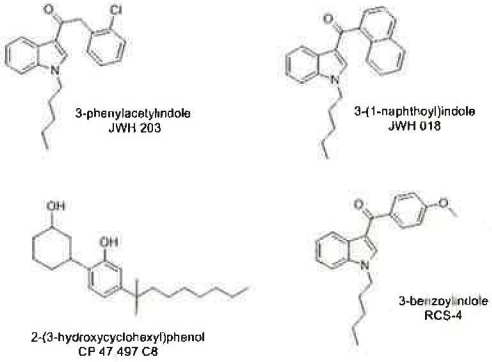
Herbal Smoking Blends - SPICE

- Products quickly reformulated with new, non-controlled synthetic cannabimimetics
- Five of the synthetic cannabimimetics controlled at the Federal level in 2011
- Synthetic Drug Abuse Prevention Act of 2012

Classes of Synthetic Cannabinoids Observed on Smoking Blends

i) 2-(3-hydroxycyclohexyl)phenol (CP 47,497)
ii) 3-(1-naphthoyl)indole (JWH 018)
iii) 3-(1-naphthoyl)pyrrole
iv) 1-(1-naphthylmethylene)indene
v) 3-phenylacetylindole or 3-benzoylindole

Structures of the Major Cannabimimetic Classes Detected



Cannabimimetics Observed in 2009 and 2010 – First Appearance of JWH Compounds

2009/2010

JWH 018
JWH 073
JWH 250
CP 47,497

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Cannabimimetics Observed Starting in 2011 – More JWH's, Introduction of Fluoroalkyls and the Beginning of Novel Materials

2009/2010 2011

2009/2010	2011
JWH 018 JWH 073 JWH 250 CP 47,497	JWH 019 JWH 081 JWH 122 JWH 200 AM 2201 AM 694 *RCS-4* *RCS-8*

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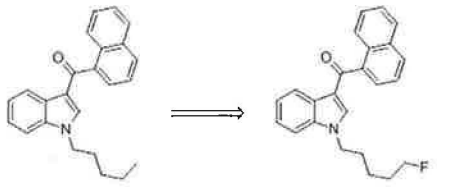
2011 – Introduction of Fluoroalkyl Derivatives



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2011 – Introduction of Novel Materials

- Materials identified never reported in scientific or patent literature
- Initially named after the website selling it
  - RCS-4
  - RCS-8
- Made by changing/modifying known material

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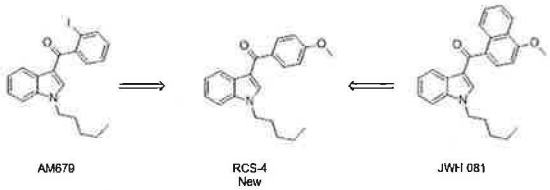
2011 – Introduction of Novel Materials RCS-4



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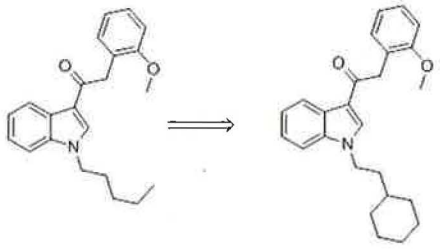
2011 – Introduction of Novel Materials
RCS-8

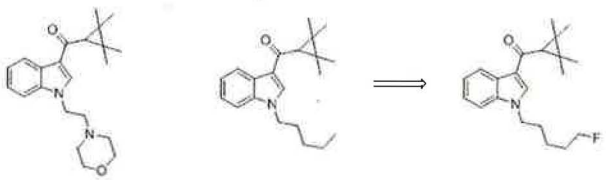


JWH 250 → RCS-8 (New)

Cannabimimetics Observed Starting in 2012 – Continuation of New Materials and New Classes

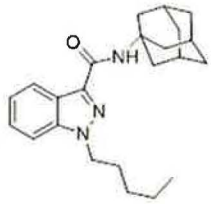
2009/2010	2011	2012
JWH 018 JWH 073 JWH 250 CP 47,497	JWH 019 JWH 081 JWH 122 JWH 200 AM 2201 AM 694 *RCS-4* *RCS-8*	JWH 203 UR 144 A 796,260 *5FUR144* *2NE1* *STS-135* *AKB48* *AB001*

2012 – Introduction of Tetramethylcyclopropyl Materials



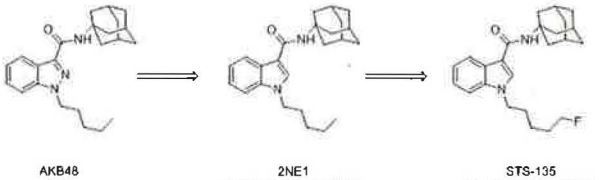
A-796,260 (Abbott Labs) → UR-144 (Abbott Labs) → 5FUR144 (New)

AKB48 – New Material in 2012



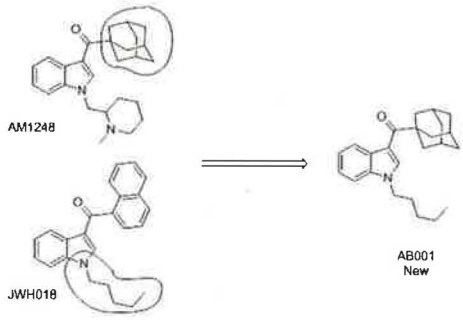
AKB48
Falls within claims of 2003 World Patent but not given as example

2012 – Continued Introduction of New Materials



AKB48 (New) → 2NE1 (Indole version of AKB48, New) → STS-135 (Fluoro version of 2NE1, New)

2012 – AB001, A New Material Derived from a Combination of Known Compounds

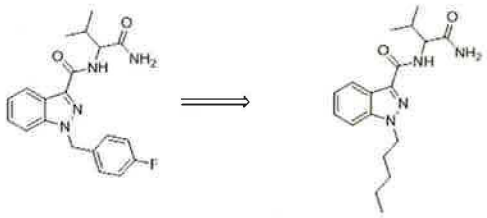


AM1248 + JWH018 → AB001 (New)

Cannabimimetics Observed Starting in 2013 – Continuation of New Materials and New Classes

2009/2010	2011	2012	2013
JWH 018 JWH 073 JWH 250 CP 47,497	JWH 019 JWH 081 JWH 122 JWH 200 AM 2201 AM 694 *RCS-4* *RCS-8*	JWH 203 UR 144 A 796,260 *5FUR144* *2NE1* *STS-135* *AKB48* *AB001*	MN-25 AB-FUBINACA ADB-FUBINACA *PB22* *5FPB22* *BB22* *ABPINACA* *ADBICA*

2013 – Introduction of Indazole Carboxamides and Derivatives



AB-FUBINACA
2009 Pfizer Patent

AB-PINACA
New

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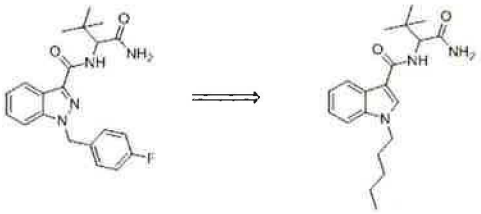
2013 – Introduction of Indazole Carboxamides and Derivatives



ADB-FUBINACA
2009 Pfizer Patent

ADBICA
New

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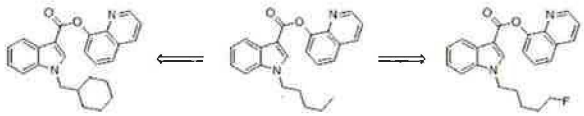
2013 – New Materials Derived From 8-Hydroxyquinoline



BB-22
New

PB-22
New
Ester, Quinoline

5FPB-22
New

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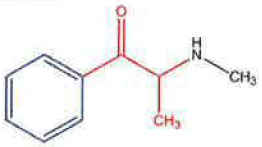
Designer Cathinones

Three parts of methcathinone can be modified:

- Aromatic ring
- Alkyl group
- Amine group



Aromatic Alkyl Amine

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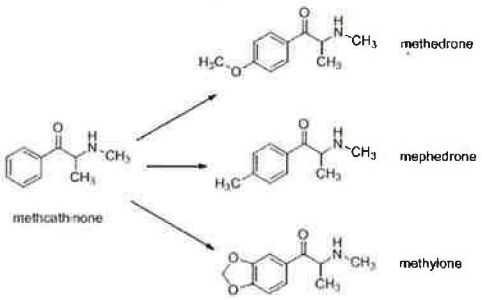
Designer Cathinones – Changes in the Aromatic Ring



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Designer Cathinones – Changes in the Alkyl Group

methcathinone → buphedrone

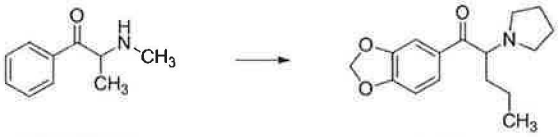
methcathinone → pentedrone

Designer Cathinones – Changes in the Amine Group

methcathinone → ethcathinone

methcathinone → α-PPP

Designer Cathinones – Changes in All Groups



methcathinone → MDPV

Just the changes discussed in the last three slides can produce 12 different Cathinone derivatives

Questions?

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Novel Hallucinogens and Plant-Derived Highs

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Special Testing and Research Laboratory
Drug Enforcement Administration

Outline

- Hallucinogens
  - 2C Compounds
  - NBOMe Compounds
  - DOX Compounds
- Empathogens
  - Aminoindanes
  - APDB
  - APB
- Plant-Derived Highs
  - Kratom
  - Fly Agaric Mushrooms
  - Kava Kava
  - Kanna

2C Compounds

- Psychedelic phenethylamines
- Synthesized by Alexander Shulgin
  - Published in PiHKAL
- 27 known compounds
  - Most common: 2C-C, 2C-B, and 2C-I

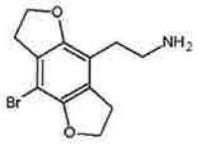
2C Compounds

Name	R^1	R^2
2C-B	H	Br
2C-C*	H	Cl
2C-D*	H	CH_3
2C-E*	H	CH_2CH_3
2C-F	H	F
2C-G	CH_3	CH_3
2C-G-3	$(CH_2)_3$	
2C-G-4	$(CH_2)_4$	
2C-G-N	(CH)$_4$	
2C-H*	H	H
2C-I*	H	I
2C-N*	H	NO_2
2C-O	H	OCH_3
2C-O-4	H	$OCH(CH_3)_2$
2C-P*	H	$CH_2CH_2CH_3$

Name	R^1	R^2
2C-Se	H	$SeCH_3$
2C-T	H	SCH_3
2C-T-2*	H	SCH_2CH_3
2C-T-4*	H	$SCH(CH_3)_2$
2C-T-7	H	$S(CH_2)_2CH_3$
2C-T-8	H	$SCH_2CH(CH_2)_2$
2C-T-9	H	$SC(CH_3)_3$
2C-T-13	H	$S(CH_2)_2OCH_3$
2C-T-15	H	$SCH(CH_3)_2$
2C-T-17	H	$SCH(CH_3)CH_2CH_3$
2C-T-21	H	$S(CH_2)_2F$
2C-TFM	H	CF_3

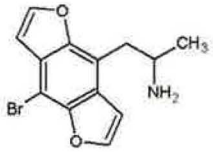
2C-B-FLY

- Psychedelic phenethylamine
- Synthesized by Aaron Monte



Bromo-DragonFLY

- Psychedelic phenethylamine

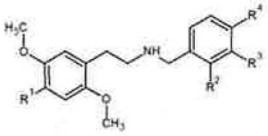


- Synthesized in the lab of David Nichols
- Deaths associated with misrepresentation as 2C-B-FLY

www.erowid.org

NBOMe Compounds

- Hallucinogenic phenethylamines
- Synthesized by Heim, *et al.*



- Isomers can be distinguished via RT and MS

Name	R^1	R^2	R^3	R^4
25B-NB2OMe	Br	OCH_3	H	H
25B-NB3OMe	Br	H	OCH_3	H
25B-NB4OMe	Br	H	H	OCH_3
25C-NB2OMe	Cl	OCH_3	H	H
25C-NB3OMe	Cl	H	OCH_3	H
25C-NB4OMe	Cl	H	H	OCH_3
25D-NB2OMe	CH_3	OCH_3	H	H
25D-NB3OMe	CH_3	H	OCH_3	H
25D-NB4OMe	CH_3	H	H	OCH_3
25E-NB2OMe	C_2H_5	OCH_3	H	H
25E-NB3OMe	C_2H_5	H	OCH_3	H
25E-NB4OMe	C_2H_5	H	H	OCH_3
25H-NB2OMe	H	OCH_3	H	H
25H-NB3OMe	H	H	OCH_3	H
25H-NB4OMe	H	H	H	OCH_3
25I-NB2OMe	I	OCH_3	H	H
25I-NB3OMe	I	H	OCH_3	H
25I-NB4OMe	I	H	H	OCH_3

Name	R^1	R^2	R^3	R^4
25N-NB2OMe	NO_2	OCH_3	H	H
25N-NB3OMe	NO_2	H	OCH_3	H
25N-NB4OMe	NO_2	H	H	OCH_3
25P-NB2OMe	$CH_2CH_2CH_3$	OCH_3	H	H
25P-NB3OMe	$CH_2CH_2CH_3$	H	OCH_3	H
25P-NB4OMe	$CH_2CH_2CH_3$	H	H	OCH_3
25T2-NB2OMe	CH_3CH_2S	OCH_3	H	H
25T2-NB3OMe	CH_3CH_2S	H	OCH_3	H
25T2-NB4OMe	CH_3CH_2S	H	H	OCH_3
25T4-NB2OMe	$(CH_3)_2CHS$	OCH_3	H	H
25T4-NB3OMe	$(CH_3)_2CHS$	H	OCH_3	H
25T4-NB4OMe	$(CH_3)_2CHS$	H	H	OCH_3
25T7-NB2OMe	$CH_3(CH_2)_2S$	OCH_3	H	H
25T7-NB3OMe	$CH_3(CH_2)_2S$	H	OCH_3	H
25T7-NB4OMe	$CH_3(CH_2)_2S$	H	H	OCH_3

NBOMe Compounds

NBOMe Dangers

- Compounds are highly hallucinogenic at very low dosages
  - As low as 50 µg
  - Has been seen in kilogram quantities
- Due to their potency, misjudging the dose of NBOMe series chemicals carries very real risks. A substantial dosage error could lead to undesirable or dangerous effects. *If one of these compounds is in pure powder form, small breezes, accidental inhalation, or touching the eyes or mouth after handling could result in full-blown effects or dangerous overdoses.* Because of these dangers, NBOMe series chemicals should be labeled clearly and handled with laboratory methods (goggles, gloves, mask) to minimize risks. www.erowid.org/chemicals/nbome/nbome_dose.shtml

DOX

- Psychedelic phenethylamine
- Synthesized by Alexander Shulgin
  - Published in PiHKAL
- Most common: DOB, DOC, DOI, DOM

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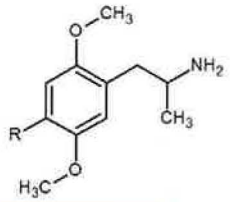
DOX Compounds

Name	R
DOAM	C_5H_{11}
DOB	Br
DOBU	C_4H_9
DOC	Cl
MEM	OCH_2CH_3
DOET	CH_2CH_3
Aleph-2	SCH_2CH_3
DOF	F
DOEF	C_2H_4F
DOI	I
Aleph-4	SC_3H_7
TMA-2	OCH_3



Name	R
DOM	CH_3
Aleph-1	SCH_3
DON	NO_2
Aleph-6	SC_6H_5
DOPR	C_3H_7
Aleph-7	SC_3H_7
DOTFM	CF_3

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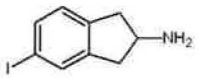
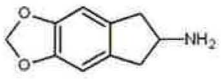
Aminoindanes

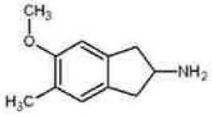
- Psychoactive empathogen
- Synthesized in the lab of David Nichols



5-IAI



MDAI



MMAI

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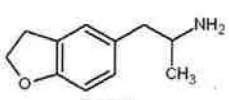
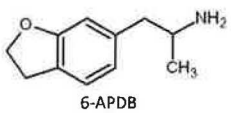
5-APDB and 6-APDB

- Phenethylamine empathogen
- Synthesized in the lab of David Nichols
- Different color test results
- Difficult to differentiate via RT or MS, but IR is different



5-APDB



6-APDB

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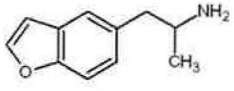
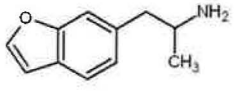
5-APB and 6-APB

- Phenethylamine empathogen
- Different color test results
- Difficult to differentiate via RT or MS, but IR is different



5-APB



6-APB

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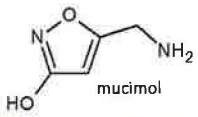
Kratom (*Mitragyna speciosa*)

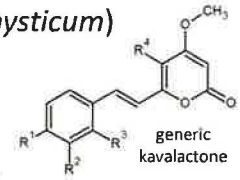
- Can be found as:
  - Whole or powdered leaf
  - Resin
- Legal status:
  - No federal regulation
  - Some states have controls in place

Fly Agaric Mushrooms (*Amanita muscaria*)

- Can be found as:
  - Dried mushroom material
  - Extract
- Legal status:
  - No federal regulation
  - LA and TN have controls in place



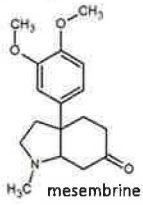
Kava Kava (*Piper methysticum*)



- Can be found as:
  - Ground or whole leaf
  - Ground root
  - Extract
- Legal status:
  - No federal regulation
  - FDA and CDC have issued warnings

Kanna aka Channa (*Sceletium tortuosum*)

- Can be found as:
  - Ground or whole leaf
  - Extract
- Legal status:
  - No federal regulation



Thank you

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References

- Reed, EC and Kiddon, GS. "The Characterization of Three FLY Compounds (2C-B-FLY, 3C-B-FLY, and Bromo-DragonFLY)." *Microgram Journal* (2007) Vol. 5, No. 1 – 4, pg 26.
- Maurer, HH. "Chemistry, Pharmacology, and Metabolism of Emerging Drugs of Abuse." *Therapeutic Drug Monitoring* (2010). Vol. 32, pg 544-549.
- Chan, KB, Pakiam, C, and Rahim, RA. "Psychoactive Plant Abuse: The Identification of Mitragynine in Ketum and in Ketum Preparations." *Bulletin on Narcotics* (2005) Vol. 57, No. 1 – 2, pg 249-256.
- Collins M. "Some New Psychoactive Substances: Precursor chemicals and synthesis-driven end-products." *Drug Testing and Analysis* (2011) Vol. 3, pg 404-416.
- Zuba, D, and Sekula, K. "Analytical characterization of three hallucinogenic N-(2-methoxy)benzyl derivatives of the 2C-series of phenethylamine drugs." *Drug Testing and Analysis* (2012) epub 31Aug2012.
- Zuba, D, Sekula, K, and Buczek, A. "25C-NBOMe – New potent hallucinogenic substance identified on the drug market." *Forensic Science International* (2013) Vol 227, No. 1 – 3, pg 7-14.
- Ratsch, C. *The Encyclopedia of Psychoactive Plants: Ethnopharmacology and Its Applications*. Inner Traditions International: 1998 (2005 English Translation).
- Casale, J and Hays, P. "The Characterization of 6-(2-Aminopropyl)benzofuran and Differentiation from its 4-,5-,and 7-Positional Analogues." *Microgram Journal* (2012) Vol. 9, No. 2, pg 61.
- Casale, J and Hays, P. "Characterization of Eleven 2,5-Dimethoxy-N-(2-methoxybenzyl) phenethylamine (NBOMe) Derivatives and Differentiation from their 3- and 4-Methoxybenzyl Analogues Part – 1." *Microgram Journal* (2012) Vol. 9, No. 2, pg 84.

European Monitoring Centre for Drugs and Drug Addiction

Emerging Trends in New Drugs in the European Union

Andrew Cunningham, Scientific Analyst
NIST/DEA Emerging Trends in Synthetic Drugs Workshop,
30 April 2013

Overview

EU Early warning system
Fundamental shift in the drugs market
Diversity of new drugs - monitoring in action
Concerns - getting new drugs in perspective
What next?

EWS institutional partners

European Monitoring Centre for Drugs and Drug Addiction
Reitox Focal Points

EWS

EUROPOL
Europol National Units

EUROPEAN MEDICINES AGENCY
Pharmacovigilance system

Council Decision 2005/387/JHA

I. Information exchange
Early warning system (EWS)
→ II. Risk assessment
→ III. Decision-making

EWS guidelines
Risk assessment guidelines
Council Decisions on control

European Database on New Drugs (EDND)
http://www.emcdda.europa.eu/drug-situation/new-drugs

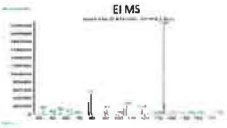
Risk assessment new psychoactive substances

- Formalized guidelines
- Health risks, Social risks, Organized crime
- Diffusion potential

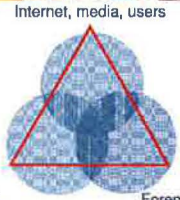
- **MBDB** (1998) — not controlled EU
- **4-MTA** (1999) — controlled EU
- **GHB** (2000) — controlled UN
- **Ketamine** (2000) —
- **PMMA** (2002) — controlled EU
- **2C-I, 2C-T-2, 2C-T-7, TMA-2** (2003) — controlled EU
- **BZP** (2007) — controlled EU
- **Mephedrone** (2010) — controlled EU
- **4-MA** (2012) — proposal for control EU
- **5-IT** (2013) — risk assessment held April 2013

EWS: Triangulation of information from different sources

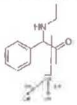
Internet, media, users



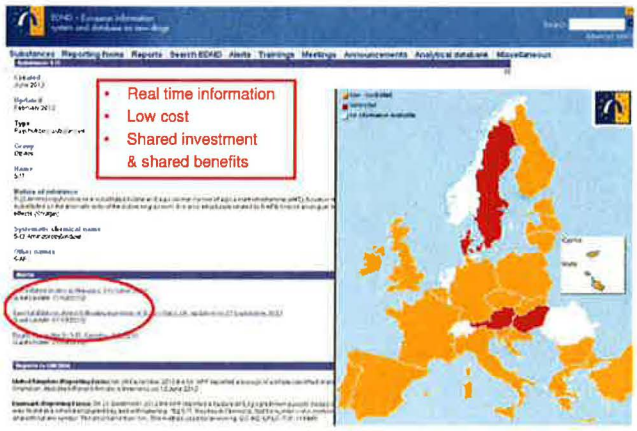
Research, test purchase, wastewater analysis, QSAR modelling



Forensic data/toxicology, law enforcement, surveys, health & care



European Database on New Drugs



Fundamental shift

Gary L. Henderson,[1] *Ph.D.*

Designer Drugs: Past History and Future Prospects

REFERENCE: Henderson, G. L., "Designer Drugs: Past History and Future Prospects," *Journal of Forensic Sciences*, JFSCA, Vol. 33, No. 2, March 1988, pp. 569-575.

Future Trends

In the view of this author, it is likely that the future drugs of abuse will be synthetics rather than plant products. They will be synthesized from readily available chemicals, may be derivatives of pharmaceuticals, will be very potent, and often very selective in their action. In addition, they will be marketed very cleverly.

The challenge we face today — has it changed?

U.S. Drug Sleuths Finally Solve Mystery of the Deadly China White

New Narcotic Identified After Monthlong Quest

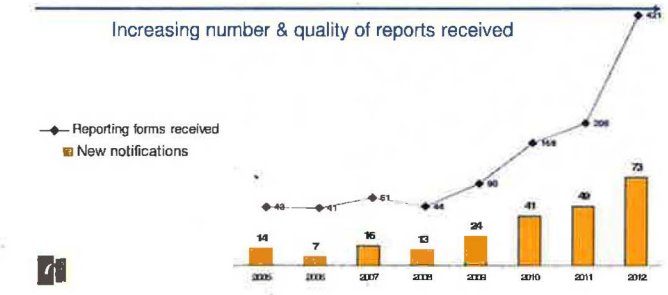
As Federal drug agents and California police stepped up their search for the sources of the China White, the forensic chemists turned their detection scales to a backlog of other, more routine cases. The challenge of identifying a new drug from the street comes no more than once or twice a year.

Substances reported via the EWS

Joint action 97/396/JHA
(June 1997 – May 2005)
~ 30 notifications

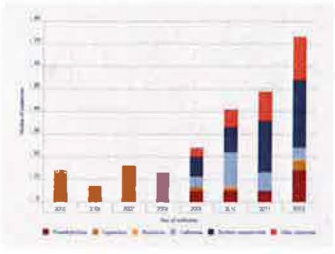
Council Decision 2005/387/JHA
(May 2005 – 2012)
~ 230 notifications

Increasing number & quality of reports received



236 new drugs notified since 2005

More than 280 monitored since the EWS started



Synthetic cannabinoids, phenethylamines and cathinones most common

More diverse and obscure substances being reported

Many more substances offered for sale that have not yet been identified by chemical analysis

What is driving this?

A complex web...

Globalisation and advances in information technology, internet as:
- Communication tool
- Access to information (medicinal chemistry, patents, etc., etc)
- Global market place

Available and cheaper organic synthesis capacity
- 'legally' sourced often outside Europe
- limited regulation/enforcement: availability on the open market
- differences in national laws

What is driving this?

A complex web...

Innovative marketing of products within a 'grey' regulatory zone

Changes in illicit drug market and interaction between markets
- Gaps in availability (such as poor quality of illicit stimulants or heroin drought?)
- Interaction between the markets in illicit drugs, 'legal highs' and medicines
- Creation of new drug markets

Users willing experiment... and substitute

Responding to new marketplace

'Specialist' shops
- Responses have been quite successful (IE, PO)

Internet
- A challenge!

The illicit market place
- Controlled and non controlled NPS increasingly present
- Some evidence manufacture in illicit labs
- Interaction with other synthetic drugs and stimulants
- Internet and darkweb

A new market place: monitoring the Internet

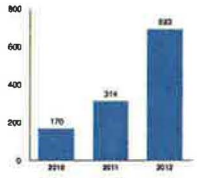
693 online shops identified selling to the EU in 2012
Up from 314 in 2011 and 170 in 2010

Other features of the online market include:

Legal highs may not be legal

Open market
- dietary supplements, lifestyle and self-medication products (e.g. phenibut, DMAA)

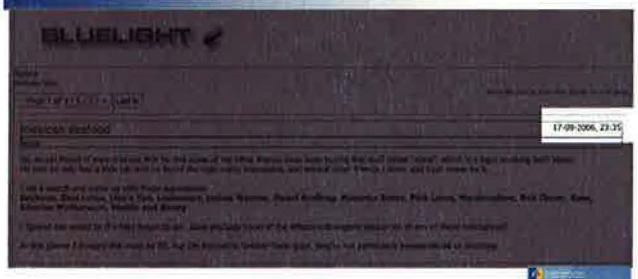
Developments:
- Spamdexing,
- diversification, &
- more covert strategies



The internet and drug diffusion - Spice

- Monitoring internet may also be important for understanding trends
- 'Mexican seafood' was asking about spice back in 2006 and 'mad scientist' told him that we did not know.
- It took another 2 years to confirm the nature of the ingredients.

The emergence of synthetic cannabinoids



First CRA in a smoking mixture sold as 'Spice' was JWH-018
First detected (analytically confirmed) in Europe, Dec. 2008
Now, EWS monitors more than 70 CRA´s

THEMATIC PAPERS

Risk Assessment 5-IT (5-(2-aminopropyl)indole)

Notified to EMCDDA in June 2012

Stimulant type drug (little known)

Sometimes sold as 'Benzofury' which has contained different drugs in the past (e.g. 5/6-APB).

Users may think they are taking a different drug

Analytical difficulties (cf. AMT)

24 deaths in 4 MS linked to the drug

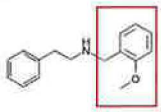
-NBOMe compounds (1)

N-2-methoxybenzyl derivatives of the '*2C*-series' of phenethylamines

Extremely potent, active at µg level

Binding affinities at 5-HT2A receptors Ki 0.16–1.49nM

Typically detected in 'blotters'/tabs, sugar cubes



Phenethylamine	-NBOMe derivative	Date	Country
2C-B	25B-NBOMe	Dec-12	Sweden
2C-C	25C-NBOMe	Jun-11	Finland
2C-D	25D-NBOMe	Apr-12	UK
2C-E	25E-NBOMe	Dec-12	Poland
2C-G	25G-NBOMe	Dec-12	Poland
2C-I	25I-NBOMe	Jun-12	Sweden
2C-N	25N-NBOMe	Dec-12	Poland

Information sources – The challenges

Speed of developments
- Increase in the number, type and availability
- More diverse, obscure compounds
- Products, mixtures and mislabelling (licit & illicit)

Forensic capacity limited, analytic challenges
- Lack of reference standards
- Increasing numbers of mixtures
- Difficulties in identification (don't know what your looking for)

Epidemiological challenges
- Self-reported data becoming increasingly less useful
- Mislabelling of products, change of composition over time and region
- Lack of standardised questions, common definitions and agreed terminology

Integrate more innovative & proactive monitoring approaches
- Waste water
- Test purchasing
- Internet monitoring
- Computational studies

Information sources – The challenges

Better conceptual models to understand diffusion potential

Need to develop hospital emergency data

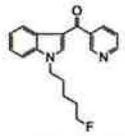
Increase capacity to respond rapidly to particularly toxic products – rapid and sound assessment of properties & risks
- identification of DID associated with NPS
- Evaluation of potential acute and chronic toxicity in humans
- Receptor binding and mode of action studies
- Assessment of psychoactivity

Follow – up over time important
- Re-emergence of controlled drugs and establishment on the licit market

What next?

Synthetic cannabinoids, not yet detected in Europe, e.g.

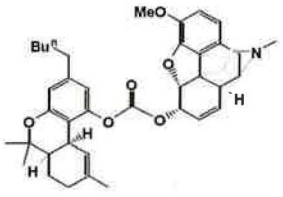
N. Uchiyama et al. / Forensic Science International xxx (2012) xxx–xxx



5-Fluoropentyl-3-pyridinoylindole (III)
$C_{19}H_{19}FN_2O$: 310

What next?

Dhooper, H. K., (2010), *Opioid-cannabinoid co-drugs with enhanced analgesic and pharmacokinetic profile*, University of Kentucky, KY



Codeine-Δ^9-Tetrahydrocannabinol Carbonate.

What next?

Synthetic 'co-drugs'

N. Uchiyama et al. / Forensic Science International xxx (2012) xxx–xxx

Reaction product of URB-754 with 4-Methylbuphedrone (II)
$C_{28}H_{31}N_3O_3$: 457

What next?

Let's see!

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Emerging Trends in Syntheti Drugs: Mid-Atlantic Region

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Objectives

- State Legislation
- Compound Trends
- Analytical Approaches
- Reporting Results

Mid-Atlantic Region

State Legislation

Legislation

- Virginia
  - Amendments to VA Code in March 2011, July 2012 and March 2013
  - Synthetic Cannabinoids - § 18.2-248.1:1
    - 26 Specifically Listed Compounds
    - Eleven Structural Classes
  - Schedule I - § 4.1-3446
    - 41 Specifically Listed Compounds added through legislation since July 2012

Legislation

- Synthetic Cannabinoid Definition:
  - Virginia:
    - Any substance that contains one or more cannabimimetic agents or that contains their salts, isomers, and salts of isomers
    - 'Cannabimimetic agent' is any substance within any of eleven defined structural classes or is specifically listed under § 18.2-248.1:1(A)(2)

Structural Classes

2012

a. Cyclohexylphenols
b. Napthoylindoles
   Napthylmethylindoles
c. Napthoylpyrroles
d. Napthylmethylindenes
e. Phenylacetylindoles
   3-Benzoylindoles

2013

f. 3-cyclopropoylindoles
g. 3-adamantoylindoles
h. N-(adamantyl)-indole-3-carboxamides
i. N-(adamantyl)-indazole-3-carboxamides

Legislation

- Virginia Code § 18.2-248.1:1(F)
  - "Designer Drug" (analog) clause
    - Privately compounded with intent to circumvent criminal penalties
    - Chemical changes
  - "emulate or simulate effects"

Legislation

- Maryland
  - 2008 Provision in Maryland law allowed for the use of Federal Controlled Dangerous Substances (CDS) Regulations
  - July 2012: Adoption of Synthetic and Drug Abuse Prevention Act of 2012
  - House Bill 1 – Effective October 1, 2013
    - Cannabimimetic Agents under Schedule I

Legislation

- Pennsylvania
  - Senate Bill No. 1006 (Enacted 2011)
    - Resembles legislation passed on Federal level
    - Synthetic cannabinoids and psychedelic phenethylamines ('2C-' compounds) added to Schedule I

Mid-Atlantic Region

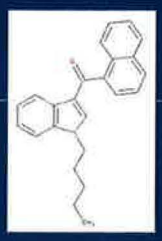
Compound Trends

Compound Trends

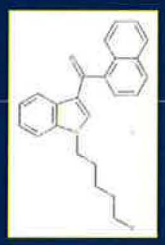
- Direct correlation to enacted legislation
- Many distributors are acutely aware of legislation and adapt quickly

Compound Trends

Virginia Synthetic Cannabinoids Trends



SB745/HB1434
Enacted-Effective
23Mar2011

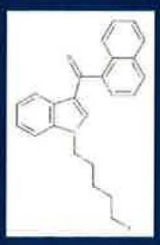


JWH-018
2010-2011

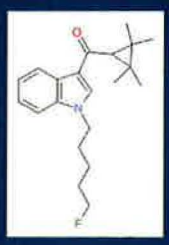
AM-2201
2011-2012

Compound Trends

Virginia Synthetic Cannabinoid Trends



HB508/SB273
Enacted – Effective
01Jul2012



HB1941
Enacted-
Effective
13Mar2013

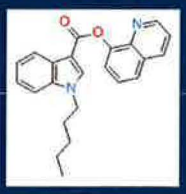
?

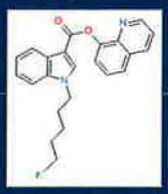
AM-2201
2011-2012

XLR-11
2012-2013

Compound Trends

- The wave of the (near) future:



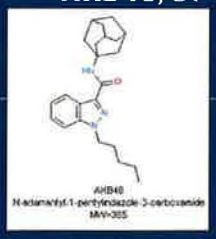


PB-22

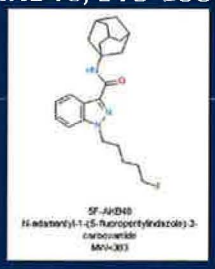
5F-PB-22

Compound Trends

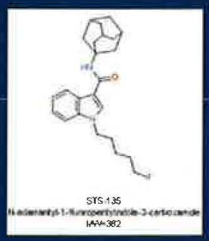
- AKB48, 5F-AKB48, STS-135



AKB48
N-adamantyl-1-pentylindazole-3-carboxamide
MW=365



5F-AKB48
N-adamantyl-1-(5-fluoropentyl)indazole-3-carboxamide
MW=383



STS-135
N-adamantyl-1-fluoropentylindole-3-carboxamide
MW=382

Trends

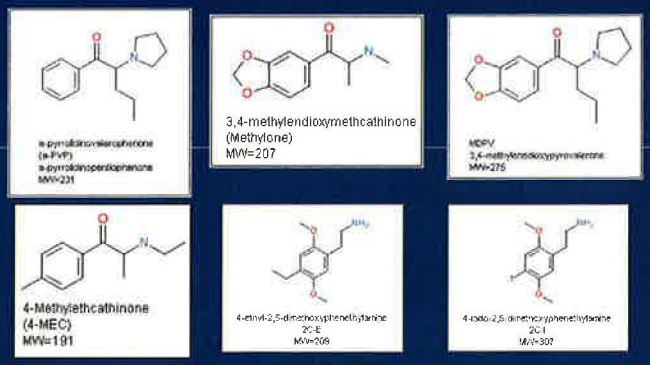
Brand	Compound
AK-47	XLR-11
AMPED	A-PVP, LIDOCAINE, BENZOCAINE, CAFFEINE
BAYOU BLASTER	XLR-11
BLAZE-IT	STS-135
CALIFORNIA DREAMS	UR-144 and XLR-11
CARE-FREE POTPOURRI	5-MEO-DALT
CLEAR	A-PVP, CAFFEINE
D.O.A.	UR-144 and MXE
DEMON FREE	XLR-11
GET SOME SUPER KUSH	AM-2201, AM-2233, JWH-210, AND AM-1248
GREEN COBRA	AM-2201 and JWH-210
HAMPSTER PURP	XLR-11
INCREDIBLE HULK PURPLE	UR-144 and XLR-11
CRONIC	
JUDGEMENT DAY	UR-144 and XLR-11
KUSH STRAWBERRY	UR-144
LEGAL RX	MITRAGYNINE(KRATOM)
MAKES SCENTS	UR-144
MR. HAPPY	UR-144 and XLR-11
MR. NICE GUY - DMG	UR-144 and XLR-11
OBLIVION	JWH-018
ORGAZMO	XLR-11
PURP	UR-144 and XLR-11
SATIVAH	NO CONTROLLED SUBSTANCES
SCOOBY SNAX	UR-144 and XLR-11
SKUNK 101	UR-144 and XLR-11
SONIC ZERO - BLUEBERRY	XLR-11
STRAWBERRY BASH	NO CONTROLLED SUBSTANCES
SUPER KUSH	XLR-11
YELLA	AM-2201

Compound Trends

- Mushrooms and Monkeys and Turtles, Oh My!

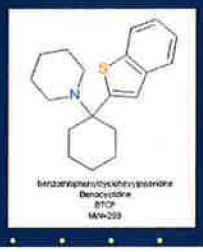
Compound Trends

Compound Trends



Compound Trends

- Illicit Tablets and Capsules
  - Caffeine and more Caffeine!
  - Recent Trend
    - BenzoThiophenylCyclohexylPiperidine
      - AKA: Benocyclidine, BTCP
    - 3,4-MDMA Returns



Compound Trends

- Blotter paper?
  - 25I-NBOMe

  - 25C-NBOMe
    - Five confirmed cases in Virginia

Compound Trends

- Lysergic Acid Diethylamide

- Food Items
  - Marijuana preparations
  - 4-Acetoxy-dimethyltryptamine
- Undosed plant material

Mid-Atlantic Region

Analytical Approaches

Analytical Approaches

- Traditional Approach
  - Color Tests
    - Marquis
      - 25I-NBOMe – Avocado green
      - BTCP – Indigo blue
  - GC/MS
    - R_t Comparison
      - Traditional: HP-5, HP-1 (15m x 0.25mm i.d.)
      - HP-35 (15m x 0.25mm i.d.)

Analytical Approaches

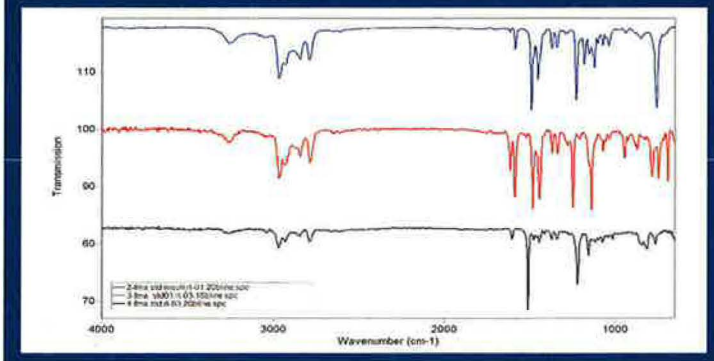
Compound	HP-1 R_t (min)	HP-5 R_t (min)	HP-35 R_t (min)
Cannabidiol	1.71	1.76	2.22
Δ 9-THC	1.89	1.95	2.47
Cannibinol	2.02	2.09	2.65
CP 47,497	2.06	2.14	2.67
CP 47,497 C8 homolog	2.26	2.34	2.89
CP 55, 940	2.87	3.03	4.12
JWH-203	2.73	2.91	4.24
HU-211	2.93	3.12	4.34
HU-210	2.94	3.14	4.35
JWH-250	2.75	2.95	4.39
RCS-4	2.87	3.09	4.72
JWH-201	2.95	3.2	4.91
JWH-015	3.04	3.33	5.55
JWH-073	3.11	3.42	5.79
JWH-018	3.37	3.73	6.41
JWH-019	3.68	4.12	7.21
JWH-122	3.83	4.33	8.04
AM-2201	3.71	4.22	8.18
JWH-210	4.07	4.64	8.66
AM-2233	4.04	4.60	9.11
JWH-081	4.41	5.10	10.53
AM-1220	4.93	5.76	12.54
JWH-200	5.09	6.09	14.57
Salvinorin A	3.42	3.80	5.61, 6.54
XLR-11	2.06	2.18	2.72
XLR-11 2FP isomer	1.86	1.94	2.39
XLR-11 3FP isomer	1.9	1.98	2.46
XLR-11 4FP isomer	1.95	2.04	2.55

Method parameters: 225-300C° @ 30C°/min

Analytical Approaches

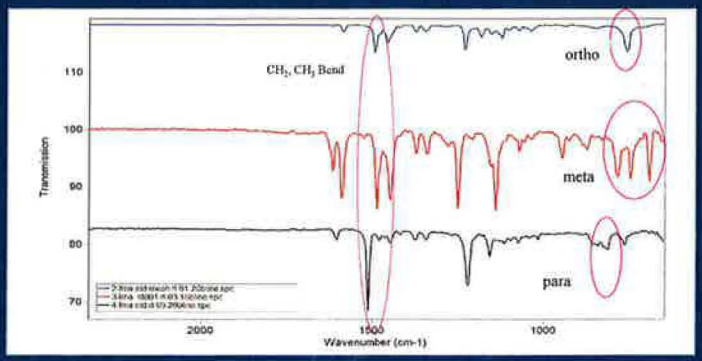
- 'Novel' Approach
  - DART-TOF
    - Efficient screening
    - Exact Mass
  - DiscovIR
    - GC/FTIR (solid state)

Analytical Approaches



Fluoromethamphetamine positional isomers

Analytical Approaches



Fluoromethamphetamine positional isomers

Mid-Atlantic Region

Reporting

Reporting

- Virginia
  - Synthetic Cannabinoids
    - When a Listed Synthetic Cannabinoid is present: "0.254 gram of powder, found to contain 1-pentyl-3-(1-naphthoyl)indole (JWH-018) (a synthetic cannabinoid listed in § 18.2-248.1:1)."
    - When a compound within a defined structural class is present (but not specifically listed): "0.254 gram of plant material, found to contain 1-propyl-2-methyl-3-(1-naphthoyl)indole (JWH-015). This compound is a synthetic cannabinoid as defined in § 18.2-248.1:1(A)(1)(b) and is within the structural class 3-(1-naphthoyl)indole."

Reporting

- Virginia
  - Synthetic Cannabinoids (cont)
    - When a Non-Listed/Non-Structural Class Synthetic Cannabinoid may be present, but is not identified:
      - "No controlled substances or synthetic cannabinoids defined in § 18.2-248.1:1(A) were identified."

Reporting

- Maryland
  - [Name of compound]
  - [Schedule]
    - "Not a Controlled Dangerous Substance"
    - "No Controlled Dangerous Substance Detected"
- Pennsylvania
  - Analog language:
    - Identified and scheduled substance to which it is structurally similar is indicated in results

Acknowledgements

- Maryland
  - Eileen M. Briley, Maryland State Police
  - Jessica Taylor, Maryland State Police
- Pennsylvania
  - Kristen Clemens, Cumberland County Office of the District Attorney

Questions

Emerging Trends in Synthetic Drugs: Legislation, Brands, Structures, and Approaches to Analysis in Florida

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FDLE Crime Lab - Overview

The FDLE crime lab provides timely, expert and professional examination of evidence to aid in the investigation, prosecution, and/or exclusion of criminal offenses by using scientific equipment and proven techniques.

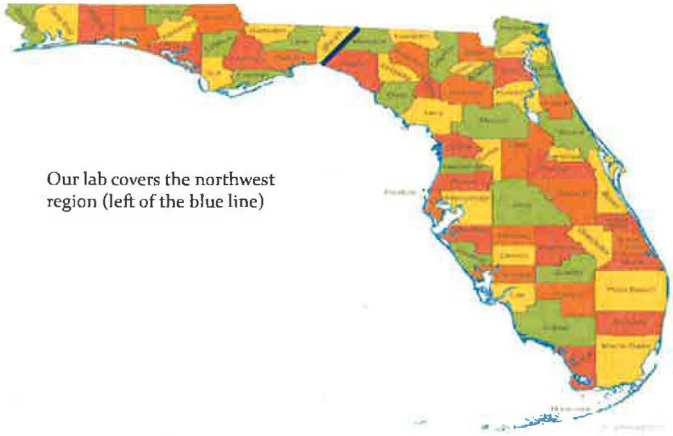
FDLE has 7 regional laboratories offering services in the following disciplines: Chemistry, Biology, Latent Prints, Firearms, Toolmarks, Crime Scene Services, Computer Evidence Recovery, Questioned Documents, Footwear/Tire Impression, Toxicology, Trace Analysis

FDLE has over 400 forensic personnel and works on average 76,000 service requests per year

FDLE - Pensacola

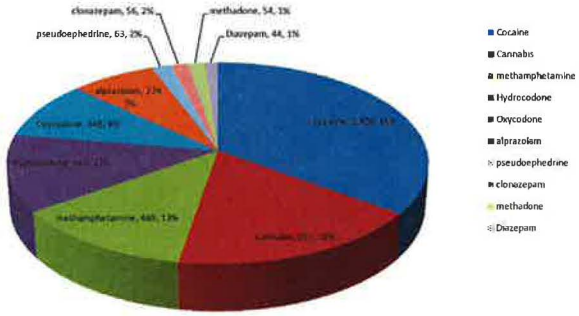
- The Chemistry lab in Pensacola provides controlled substance analysis for the 1st, 2nd, and 14th judicial circuits in Florida, covering 16 counties and a population of about 1.25 million.
- The lab averages about 400 cases per month.
- The lab has 3 full time analysts, 2 part time lab assistants, and a supervisor

FDLE - Pensacola

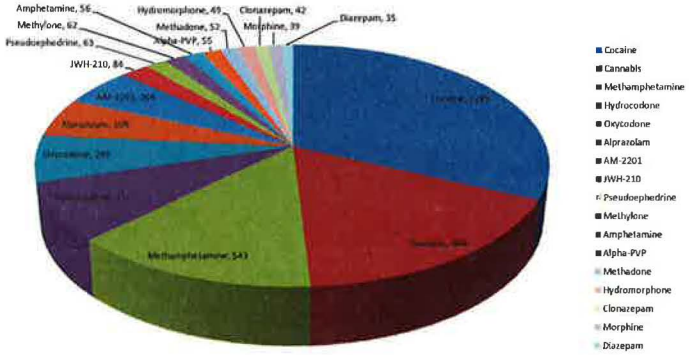


Our lab covers the northwest region (left of the blue line)

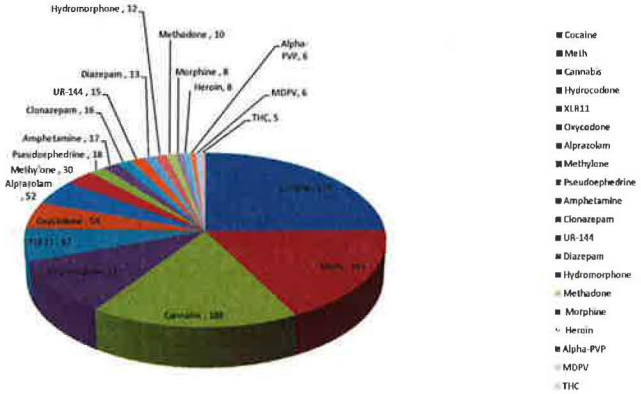
Top Drugs in our Region, 2011



Top Drugs in our Region, 2012



Top Drugs in our Region, 2013 to date



Designer Drugs, 2012 NW FL

- AM-2201 – 204 cases
- Methylone – 62 cases
- JWH-210 – 84 cases
- Alpha-PVP – 55 cases
- JWH-122 – 27 cases
- Pentedrone – 24 cases
- Pyrovalerone – 8 cases

Trends

- XLR11 & UR-144, both emergency controlled in December 2012, have moved to #4 and #12, respectively.
- AM-2201 & JWH-210, #7 and #8 last year, respectively, have dropped out of the top twenty. Both were controlled in March 2012. AM-2201 and JWH-210 were "replaced" by XLR11 and UR-144 after legislation.
- Methylone continues to climb. It was #10 last year, with 62 cases. It sits at #8 currently. 62 total last year, 30 already thru March.
- Heroin use on the rise – 0 cases in 2010, 11 in 2011, 21 in 2012, 8 through 3 months.
- PB-22 – 16 cases in 2013.

Florida Legislation - Timeline

- January 26, 2011 – The Florida Attorney General's Office emergency scheduled six drugs that were commonly seen in "Bath Salt" samples in Florida. They were added to schedule I.
  - 3,4-Methylenedioxymethcathinone (Methylone)
  - 3,4-Methylenedioxypyrovalerone (MDPV)
  - 4-Methylmethcathinone (Mephedrone)
  - 3-Methoxymethcathinone (3-MMC)
  - 3-Fluoromethcathinone (3-FMC)
  - 4-Fluoromethcathinone (Flephedrone, 4-FMC)

Florida Legislation - Timeline

- July 1, 2011 – HB1039 made the following designer cathinones permanently controlled, schedule I, FS893:
  - 3,4-Methylenedioxymethcathinone
  - Methylmethcathinone
  - Methylethcathinone
  - Methoxymethcathinone
  - Fluoromethcathinone
  - 3,4-Methylenedioxypyrovalerone (MDPV)
- Differences from emergency control legislation: Addition of Methylethcathinone (MEC); Removal of isomer designations on some; Removal of common names, with the exception of MDPV

Florida Legislation - Timeline

- July 1, 2011 – SB204/HB 39 Made the following synthetic cannabinoid compounds illegal, schedule I, FS893:
  - CP47,497
  - C8 homologue of CP47,497
  - HU-210
  - JWH-018
  - JWH-073
  - JWH-200
- Plant material coated with synthetic cannabinoids have reduced penalties if under 3 grams (misdemeanor). Automatic felony at any weight if in powder form.

Florida Legislation - Timeline

- March 23, 2012 – HB1175 added approx. 90 new drugs to FS893, schedule I. These include many synthetic cannabinoids, designer cathinones, and novel hallucinogens.
- Included: BZP, FPP, MPP, CPP, 12 Tryptamines, DOI, DOC, 2C-E, 2C-C, 2C-I, Butylone, Ethylone, Naphyrone, Buphedrone, 3,4-Dimethylmethcathinone, Pentylone, MDPBP, BTCP, alpha-PVP, PPP, and PBP, MPPP, 16 JWH compounds, CB-13, 25, and 52, AM-2201, AM-694, RCS-4 and 8

Florida Legislation - Timeline

- December 11, 2012 - The Florida Attorney General's Office emergency scheduled 22 new chemicals:
  - Pentedrone, Fluoroamphetamine, Fluoromethamphetamine, Methoxetamine, Methiopropamine, 4-Methylbuphedrone, APB, APDB, UR-144, XLR11, 5-Chloro-UR-144, AKB48, AM-2233, STS-135, URB-597, URB-602, URB-754, 2C-D, 2C-H, 2C-N, 2C-P, and 25I-NBOMe

Florida Legislation - Timeline

- Pending bills: S294 and H619 – Controlled Substances. They include the permanent addition of the emergency scheduled drugs from 12/11/12 to schedule I of FS893.
- Also adds PB-22, 5-Fluoro PB-22, BB-22, and 5-Fluoro AKB48
- Unanimously passed House and Senate; awaiting Governor's signature

Drug Generations - Florida

- 1st generation bath salts began in mid to late 2010 and ended shortly after the emergency rule.
  - 1st generation bath salts: Mephedrone, Methylone, MDPV. Methylone, however, has not disappeared. It is our 8th most popular drug in our region, even after being added to schedule I. "Molly" is the slang term. Generally seen in capsule form.
- 1st generation synthetic cannabinoids: JWH-018, JWH-073, JWH-200. These are long gone.

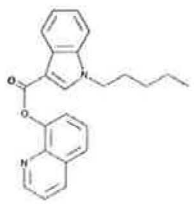
Drug Generations - Florida

- 2nd generation bath salts emerged after the July 1, 2011 legislation, and ended in March 2012 (with the next legislation). They include Naphyrone, Buphedrone, alpha-PVP, Pentylone, Pentedrone, MPPP
- 2nd generation synthetic cannabinoids, same time frame: JWH-250, AM-2201, JWH-210, JWH-122, JWH-081, JWH-203

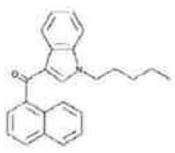
Drug Generations - Florida

- 3rd generation synthetic cannabinoids (after March 23, 2012, ending with emergency schedule 12/11/12): UR-144, XLR-11; to a lesser extent, AKB48 and STS-135
- 3rd generation bath salts: Pentedrone, Fluoroamphetamine
- 4th generation (current) synthetic cannabinoids: PB-22 and 5-Fluoro AKB48
- No 4th generation bath salts. Major dip in siezures/submissions after mid-2012. However, Methylone has moved in to the illicit drug market as "Molly"

PB-22



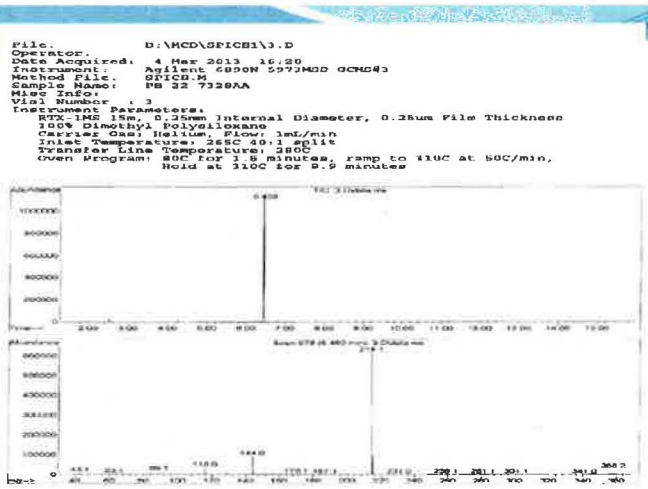
$C_{23}H_{22}N_2O_2$, MW 358
PB-22 is a potential analog of JWH-018 (8-hydroxyquinoline replacing naphthalene group)



JWH-018

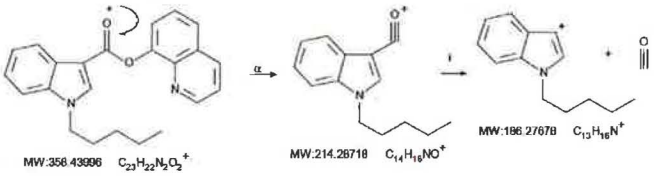
PB-22 Storage

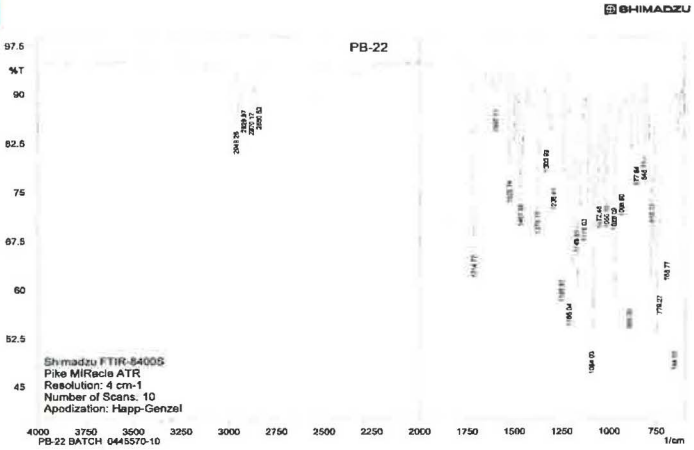
- Store cold (at least -20C)
- PB-22 is an ester and not stable in alcohols
- Transesterification will cause major degradation peaks on GC/MS if you store in alcohol
- Try acetonitrile as the solvent

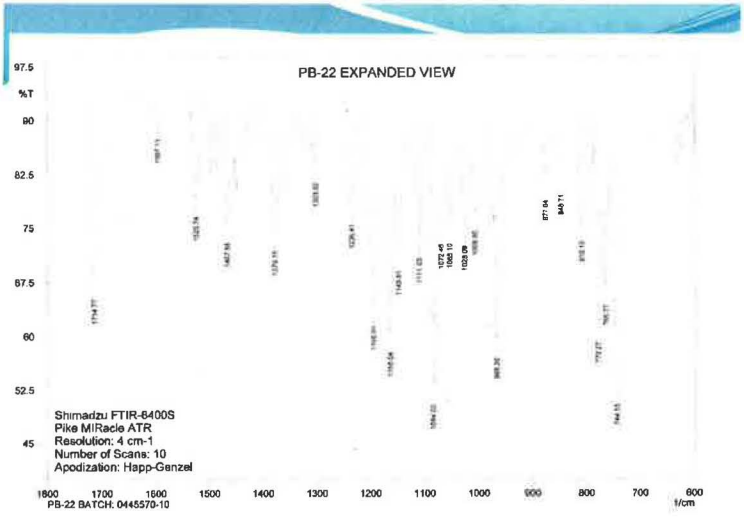


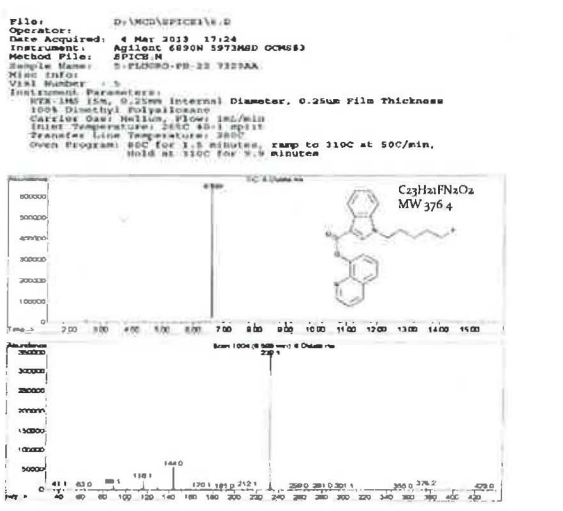
PB-22

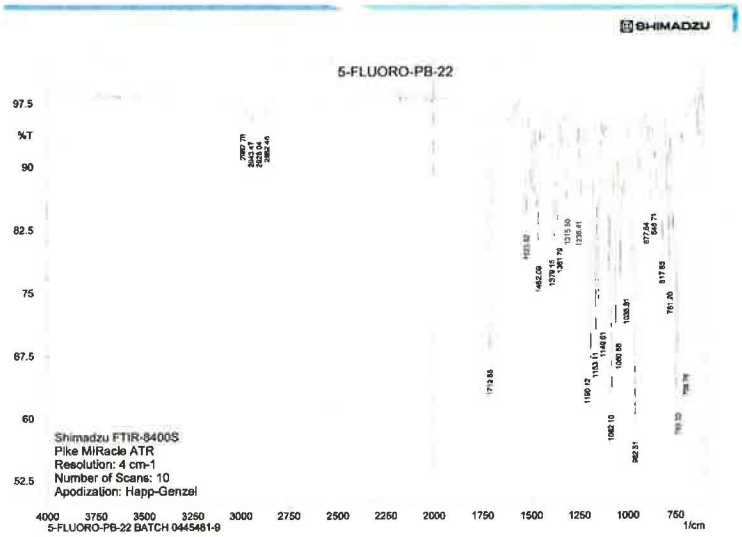
- Mass Spectrum is dominated by the product of an alpha-cleavage at the right of the oxo-group at nominal m/z 214

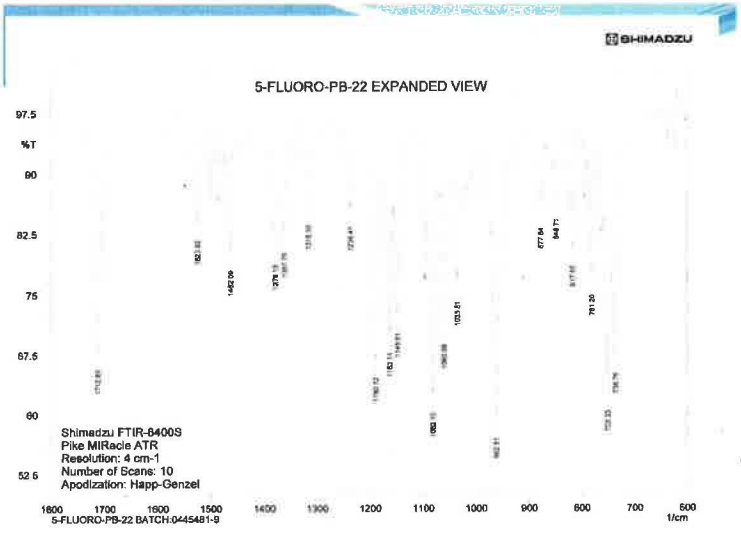




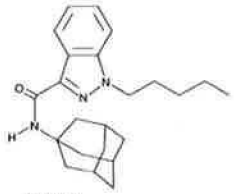




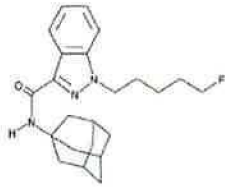




AKB-48 / 5-Fluoro AKB-48

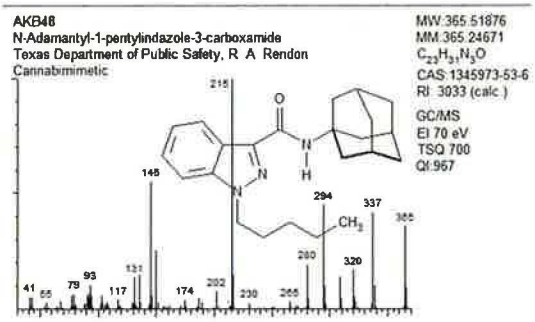


AKB48
$C_{23}H_{31}N_3O$
MW 365
Emergency controlled in FL, 12/11/12



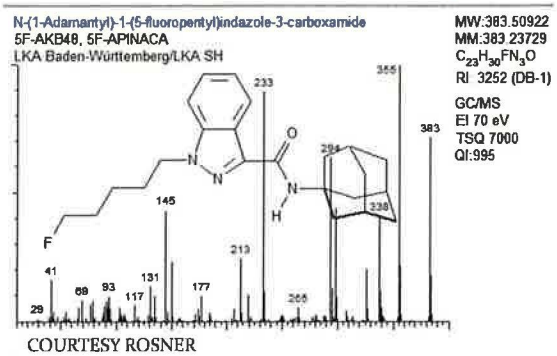
5-Fluoro AKB48
$C_{23}H_{30}FN_3O$
MW 383
LEGAL

AKB48 Mass Spectrum



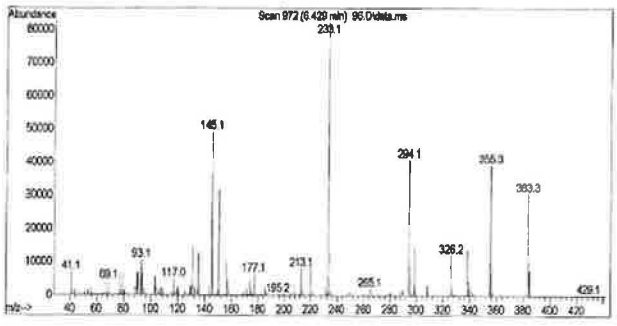
COURTESY ROSNER / TDPS

5-Fluoro AKB48 Mass Spectrum



COURTESY ROSNER

5-Fluoro AKB48 Mass Spectrum (standard purchased from Cayman Chemicals)

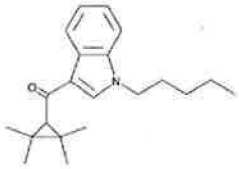


Where Do These Names Originate?

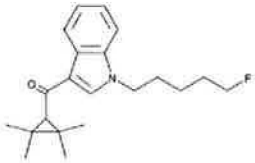
AKB48 – Japanese girl band

STS-135 – Final mission of the American Space Shuttle Program

UR-144 / XLR11

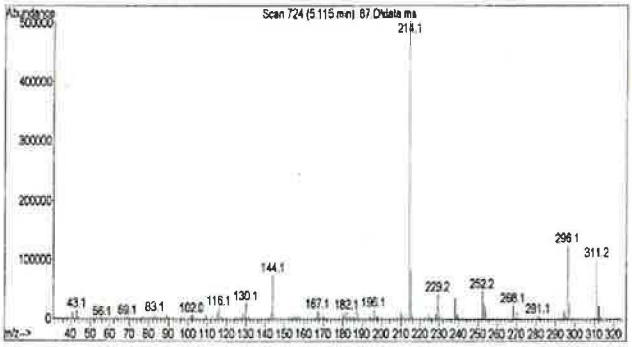


UR-144
$C_{21}H_{29}NO$
MW 311
Emergency Controlled in FL, 12/11/12

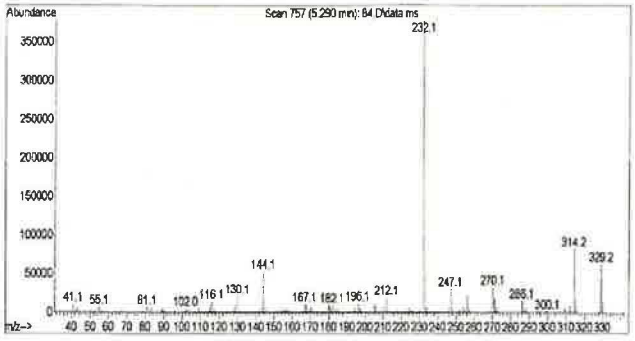


XLR11
AKA 5-Fluoro UR-144
$C_{21}H_{28}FNO$
MW 329
Emergency Controlled in FL, 12/11/12

UR-144 Mass Spectrum (Purchased from Cayman Chemicals)



XLR11 Mass Spectrum (Purchased from Cayman Chemicals)



Samples in the lab

Positive for Butylone

Samples in the lab

Positive for JWH-210

Samples in the lab

Positive for AM-2201

Samples in the Lab

Both Positive for AM-2201 and JWH-210

Samples in the lab

Positive for XLR11

Samples in the lab

T20 High Quality damiana not for human consumption. Legal under New FL Law HB/1175 (eff. 3/23/12) Potpourri

Popular Brands

- Most popular brands seen in the lab:
  - WTF: Next Generation
  - Dead Man Walking
  - Super POW
  - Scooby Snax
  - OMG
  - Master Kush
  - Forget-Me-Not
  - Bird of Paradise
  - Mad Hatter
  - Lick Me All Over
  - Down2Earth ClimaXXX and Reggie

Popular Brands

Popular Brands

Popular Brands

N-Ethylbuphedrone (NEB)

4-Fluoroamphetamine

Preparation tips

- Build libraries – buy standards and add them to your internal GC/MS libraries. Use free libraries like Cayman and SWGDRUG. Buy Mass Spectra of Designer Drugs by Rosner.
- Stay active – become a member of CLIC (they have an active Yahoo! Group). Use Forendex and Forendex Forums.
- Build an internal drug repository to store articles and data for easy search and retrieval.
- Read as many articles as you can get your hands on.

Websites for Spectra Searching

Designer Drugs (Rosner website):
https://db12.designer-drugs.de/db/main.pl

Forendex Forum:
http://forendexforum.southernforensic.org/

Forendex:
http://forendex.southernforensic.org/index.php/home/index

Drug Standards

https://www.caymanchem.com
http://www.cerilliant.com
http://www.lipomed.com
http://www.sigmaaldrich.com
http://www.steraloids.com
http://www.trc-canada.com
http://www.discoverysciences.com
http://www.usp.org/products

Analytical issues

- To reduce analytical issues, we try to name compounds in the statutes without isomer designations, and specify that all isomers are controlled. For instance, "Fluoroamphetamine" is controlled, all isomers. So instead of having to differentiate between the 2, 3, and 4, we just obtain a MS, and compare retention time against any of the 3 isomers. If it matches, we report out Fluoroamphetamine. This cuts down on standards needing purchasing; analytical procedures to differentiate; and reporting clearly and unambiguously.

Analytical issues

- Those that get added in statute with isomer designation (like TFMPP) are compared with the 3-TFMPP and a remark is placed on the report that "Specific isomer not determined"

How we report drugs

- If a controlled substance: *Name of substance.*
- If it is emergency scheduled, we add a comment under the remarks section that: **** was emergency controlled in the state of Florida December 11, 2012.*
- If it's a potential analog: ****, which is substantially similar to ***.*
- If we do not identify the specific isomer in statute, we add a remark that: *Specific isomer not determined.*

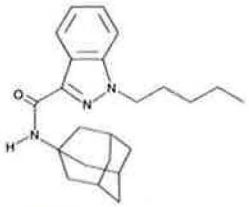
Analogs

- (2)(a) As used in this section, "controlled substance analog" means a substance which, due to its chemical structure and potential for abuse, meets the following criteria:
  1. Is substantially similar to that of a controlled substance listed in Schedule I or Schedule II of s. 893.03; and
  2. Has a stimulant, depressant, or hallucinogenic effect on the central nervous system or is represented or intended to have a stimulant, depressant, or hallucinogenic effect on the central nervous system substantially similar to or greater than that of a controlled substance listed in Schedule I or Schedule II of s. 893.03.

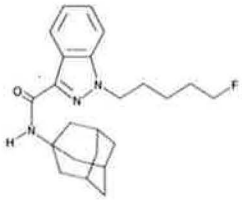
Analogs

- We only deal with prong 1 – whether it is substantially similar in chemical structure. We have a generally accepted practice in Pensacola for how to approach and determine potentially "substantially similar" compounds.

AKB48 vs 5-Fluoro AKB48



AKB48
$C_{23}H_{31}N_3O$
MW 365
Emergency controlled in FL, 12/11/12



5-Fluoro AKB48
$C_{23}H_{30}FN_3O$
MW 383
LEGAL

5-Fluoro AKB48, which is substantially similar to AKB48.

Thank you!!!

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Florida Department of Law Enforcement
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Toxicological Aspects of Synthetic Drugs

Barry K. Logan, PhD, DABFT

NMS LABS CENTER FOR INNOVATION

THE CENTER FOR FORENSIC SCIENCE RESEARCH & EDUCATION

WHEN YOU NEED TO KNOW

Synthetic Drugs

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…

WHEN YOU NEED TO KNOW

NFLIS 2011

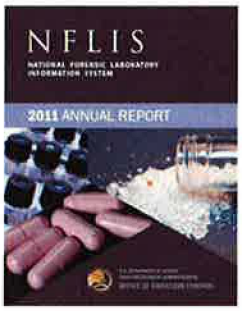


Table 2.3 *Hallucinogens*
*Number and percentage of hallucinogen reports in the United States, 2011**

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/

WHEN YOU NEED TO KNOW

Scope: Hallucinogens & Stimulants

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

WHEN YOU NEED TO KNOW

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

WHEN YOU NEED TO KNOW

December 12, 2012

PRESS & GUIDE

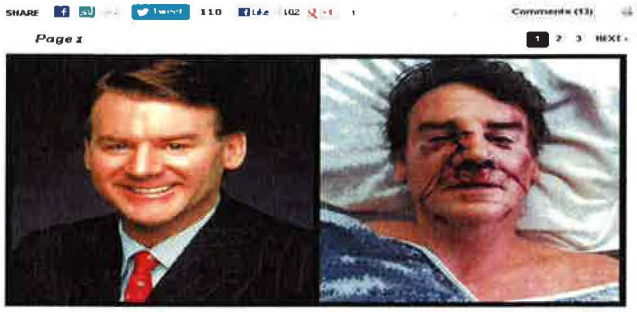
Tucker Cipriano smoked Spice, took mushrooms and drank alcohol in hours before a fatal baseball bat attack on his father

WHEN YOU NEED TO KNOW

December 23, 2012

NMS

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



WHEN YOU NEED TO KNOW

November 9, 2012

NMS

The Times-Picayune
Greater New Orleans

22 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.

WHEN YOU NEED TO KNOW

April, 2013

NMS

Los Angeles Times LOCAL

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

WHEN YOU NEED TO KNOW

April 2013

NMS

FOX 51 WOGX

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

WHEN YOU NEED TO KNOW

Toxicology of Synthetic Drugs

NMS

- Adverse Events
  - Intoxication/Impairment
  - Psychosis
  - Medical Crises
  - Death

WHEN YOU NEED TO KNOW

NMS

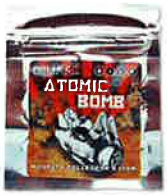
Designer Stimulants and Hallucinogens

WHEN YOU NEED TO KNOW

"Bath Salts"

AKA:

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



5-HT_{2A} Effects

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		

Synthetic Stimulants Adverse Effects

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

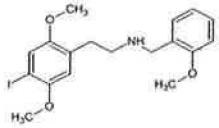
Containing

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

Intoxication - 25I-NBOMe

Rose SR, Poklis JL, Poklis A. A case of 25I-NBOMe (25-I) intoxication: a new potent 5-HT2A agonist designer drug. Clin Toxicol (Phila). 2013 Mar;51(3):174-7.

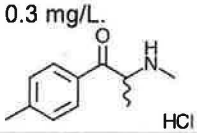
- 18-year-old male presented to the emergency department (ED) with severe agitation and hallucinations after jumping out of a moving car. Tachycardiac (150 – 160 bpm) and hypertensive (150 – 170 mm Hg systolic and 110 mg Hg diastolic), required physical restraints and treatment with intravenous lorazepam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



Intoxication - Mephedrone

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

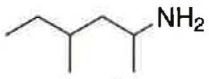
- 32 Impaired Driving arrest cases, including nine with mephedrone as the only drug present.
- Generally impaired driving, weaving, erratic, dilated pupils, poor performance, slurred speech.
- Blood concentrations ranged up to 0.74 mg/L (n=9; mean 0.21, median 0.10) although the most common value encountered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



Intoxication - DMAA

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.

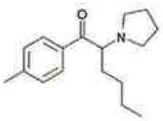
- Consumed two capsules of 99.9% DMAA. Became confused, incontinent, drowsy, slurred speech, facial droop, asymmetric weakness, memory impairment, seizure. Pills were analyzed and contained only DMAA.



Intoxication - MPHP

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.

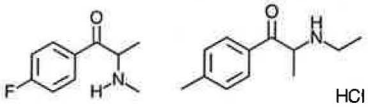
- A 27 year old man was admitted to hospital in an agitated state and with fractures of both feet after jumping from a window. Pronounced rhabdomyolysis and had to be treated by repeated hemodialysis. Elevated liver parameters indicated toxic liver damage.
- MPHP was found at 100 ng/ml



Psychosis – MDPV, 4-FMC

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.



Psychosis – "Bath Salts"

- **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.

Medical Crises - DMAA

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.

Medical Crises – Bath Salts?

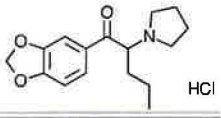
Regunath H, Ariyamuthu VK, Dalal P, Misra M. Bath salt intoxication causing acute kidney injury requiring hemodialysis. Hemodial Int. 2012 Oct;16 Suppl 1:S47-9.

- 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.

Death – MDPV

Murray BL, Murphy CM, Beuhler MC. Death following recreational use of designer drug "bath salts" containing 3,4 Methylenedioxypyrovalerone (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.



Death – Mephedrone

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.

MDPV PMD

Table 1
Toxicology Results for MDPV Overdose

Source	Drugs detected (μg/mL or μg/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

Death – MDPV, others

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 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

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

Cannabinoids Adverse Effects

- 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

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

Intoxication – Syn Canns

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.

Psychosis – Syn Canns

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

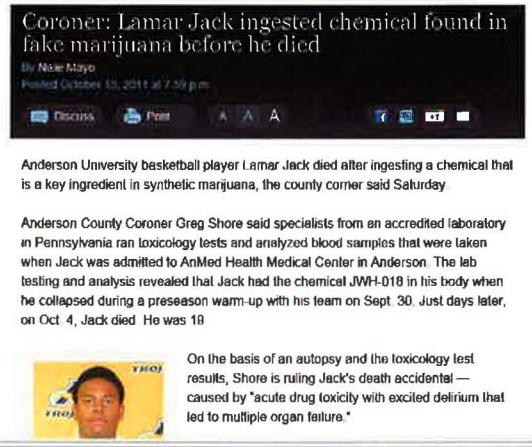
- Semi-structured interviews regarding the use and effects of JWH-018 in 15 patients with serious mental illness in a New Zealand forensic and rehabilitative service.
- Anxiety and psychotic symptoms were common after use, with 69% of users experiencing or exhibiting symptoms consistent with psychotic 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.

Medical Crises – Syn Canns

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.

Death? – Syn Canns



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

By Nikki Mayo

Posted October 13, 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 corner 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."

Conclusions

- 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?

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