Synthetic Cannabinoids: Information and Guidance for Clinicians

Clinician Outreach and Communication Activity (COCA) Call

March 31, 2016

Office of Public Health Preparedness and Response
Division of Emergency Operations

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Objectives

At the conclusion of this session, the participant will be able to:

- **Describe the epidemiology and clinical effects of synthetic cannabinoid use**
- **Discuss recent clusters of severe disease associated with synthetic cannabinoid use in the U.S.**
- **Identify opportunities for clinicians to support surveillance and response efforts**

TODAY'S PRESENTER

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Epidemic Intelligence Service Office
National Center for Environmental Health
Centers for Disease Control and Prevention

TODAY'S PRESENTER

Robert Galli, MD

Professor
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University of Mississippi School of Medicine
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The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention

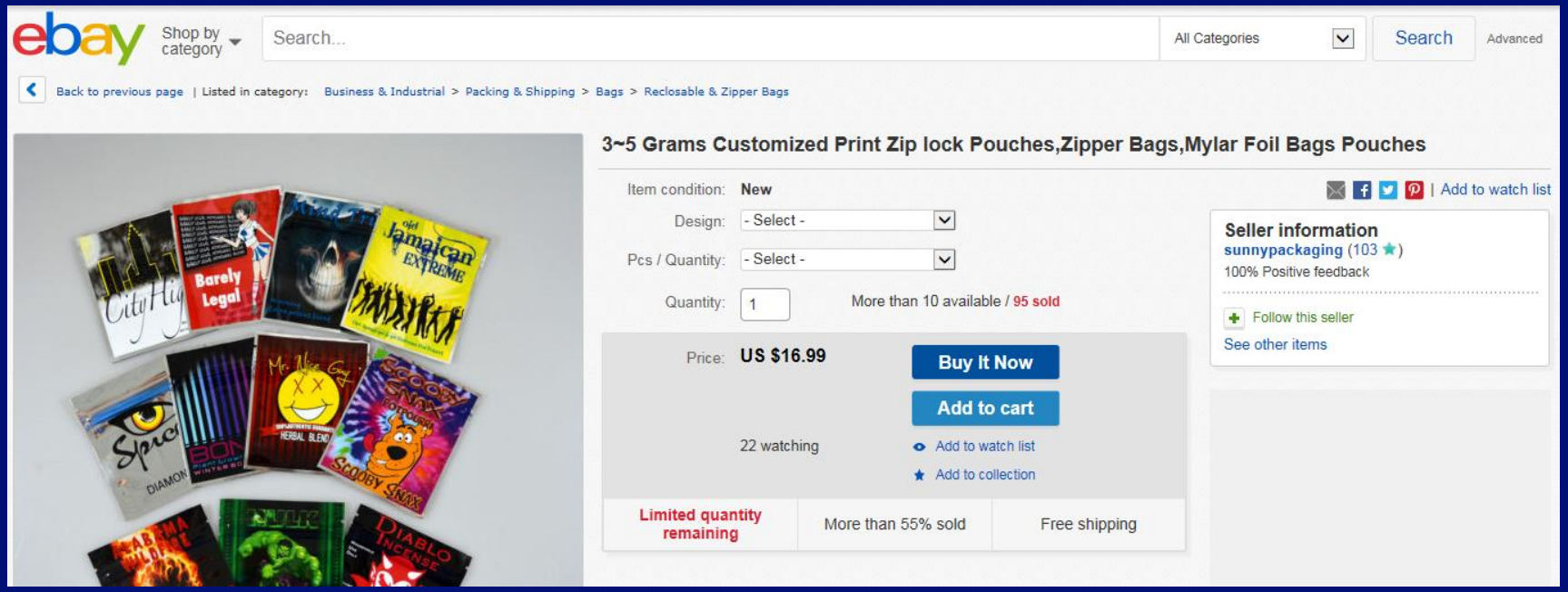
National Center for Environmental Health
Health Studies Branch

Overview

- What are synthetic cannabinoids?
- Are they a threat to public health?
- What do we know?
- What don’t we know?
- What are our next steps?

What are They?

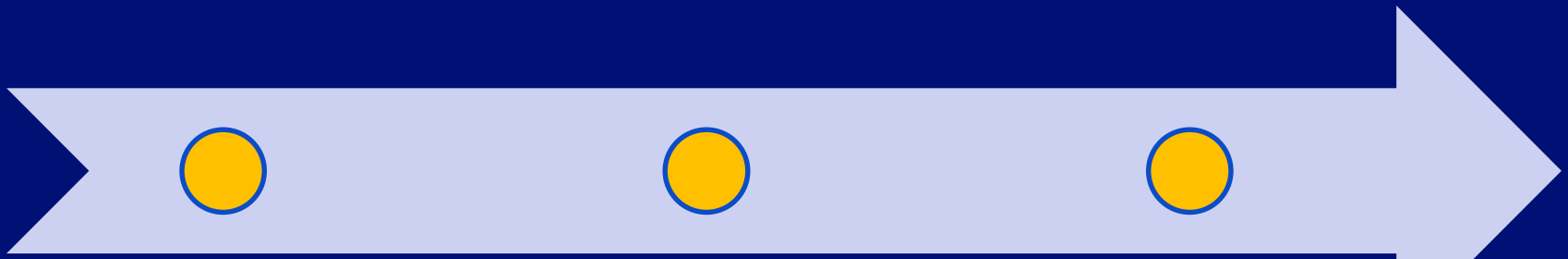
Source: http://wreg.com/2015/05/22/mississippi-spice-use-continues-to-skyrocket/



Source: http://www.ebay.com/itm/3-5-Grams-Customized-Print-Zip-lock-Pouches-Zipper-Bags-Mylar-Foil-Bags-Pouches-/161826761880. Retrieved January 25, 2016


MR.
FOR HUMAN CONSUMPTION
ww.buy-herbal-incense.com

Synthetic Cannabinoid Timeline



1960s

- SCs first synthesized

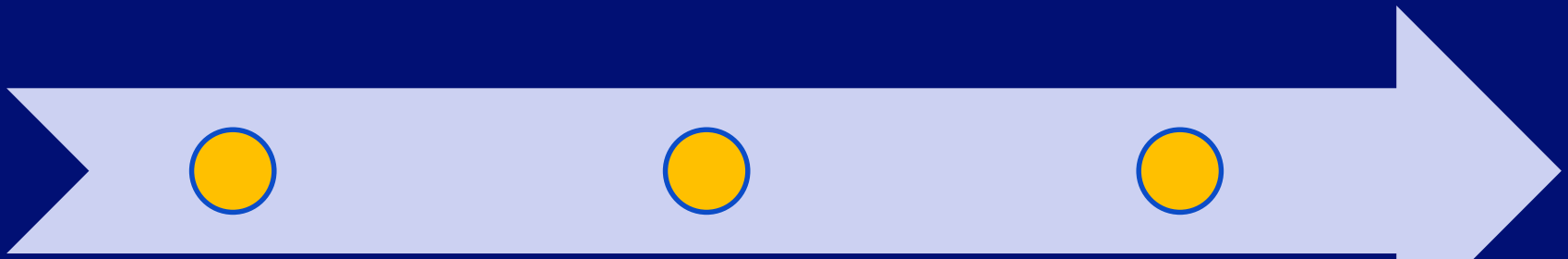
1980s

- SCs developed to study human endocannabin-oid system

1986

- Controlled Substance Analogue Enforcement Act signed

Synthetic Cannabinoid Timeline



2004

SCs appear on the internet, smoke shops in Western Europe

2008

First seizure of SC products in US

2009

Germany bans some SCs

Synthetic Cannabinoid Timeline

2011

Five SCs placed on emergency Schedule I

2012

- 51 new SCs identified

- Synthetic Drug Abuse Prevention Act signed

2015

Largest multistate outbreak of adverse events from SCs to date

An Emerging Public Health Threat

- **Increasing use**
- **Health effects unpredictable, can be severe**
  - More potent than cannabis
- **Increasing severity of illness**
- **Widespread misperception of safety, legality**
- **Unknown contents**
  - Not regulated
  - Blended with other substances

Recent Outbreaks

- **Multistate (WY, OR, NY, OK, RI, KS) – Feb 2012**
  - 16 patients with acute kidney injury after SC use
  - Flank pain, nausea, vomiting
  - 8 patients positive for XLR-11

Recent Outbreaks

- **Colorado – August 2013**
  - 263 people with agitated delirium linked to SC use
    - 10 admitted to ICU, no deaths
    - Patients positive for ADB-PINACA
- **Georgia – August-September 2013**
  - 22 patients seen in the ED for agitated delirium
    - 6 admitted to ICU, no deaths
    - Patients positive for ADB-PINACA

Recent Outbreaks

- **Multistate (MS, AL, NY, VA, MD, TX) – Apr 2015**
  - 721 suspected cases and 9 deaths in MS
  - Altered mental status
  - MAB-CHMINACA, blends of different SCs

What We Know: How?

- Usually smoked
- Can be vaped, ingested, insufflated (snorted)

What We Know: Why?

- Inexpensive
- Readily available
- Psychoactive effects
- Perceived safety
- Not detected by most routine drug screening

What We Know: Who?

- Residents of rural and urban areas
- Predominately young men aged 20–30 years
- Use of other substances (tobacco, alcohol, marijuana)
- Clusters of illness reported in adolescents, prison population, military, homeless

What Don't We Know

- Baseline number of users and patterns of use
- Health effects of emerging compounds
- How to rapidly diagnose intoxication
- Specific treatments (antidotes)
- Long-term effects, dependence
  - Treatment?

What Are Our Next Steps?

- **Continue collaboration to reduce harm**
- **Develop understanding of baseline SC use**
- **Characterize health effects in more depth**
- **Encourage reporting of suspected SC clusters**
- **Develop diagnosis and treatment guidelines**
- **Targeted messaging**
  - High-risk populations
  - Health care providers

References

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Centers for Disease Control and Prevention. Notes from the field: severe illness associated with reported use of synthetic marijuana — Colorado, August–September 2013. *Morb. Mortal. Wkly. Rep.* 2013;62:1016–7.

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Robert Galli, MD

UMMC
Department of
Emergency Medicine

University of Mississippi Medical Center

April 2, 2015

Call from ED Nurse Manager!

3 psychotic patients in ED

One more in triage

Screaming “Spice”

Two Weeks Later

>400 Patients reported statewide

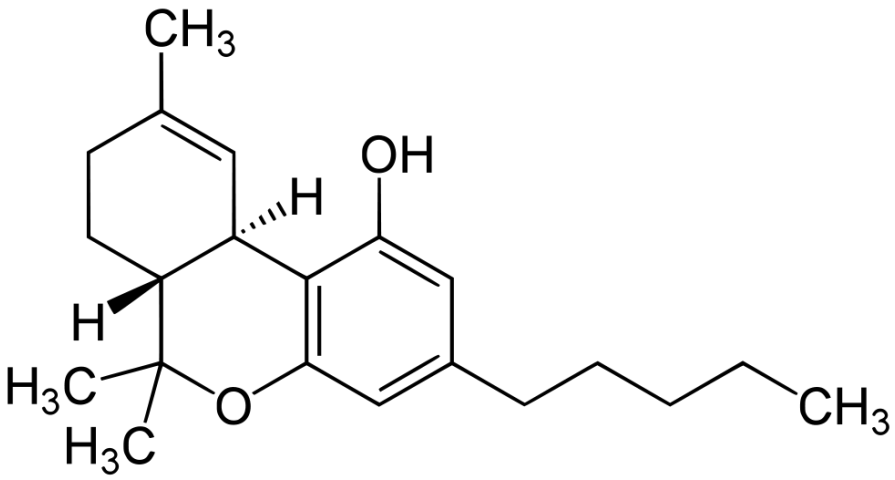
6 Potential Deaths

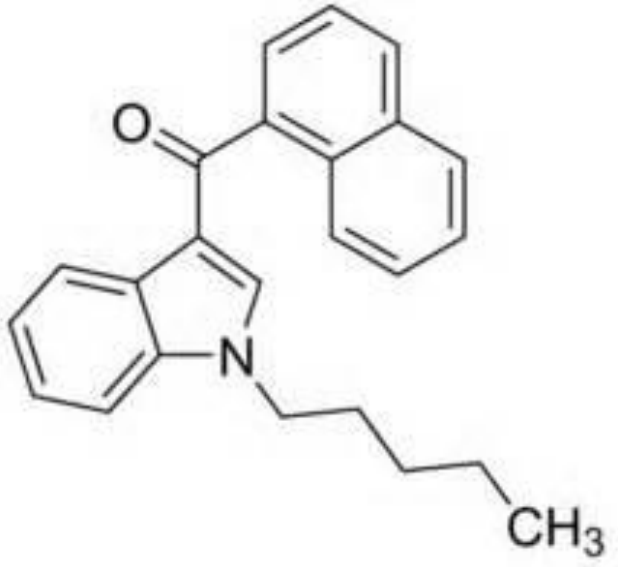
Also Heard

- Bath Salts
- MDMA Spice
- Take him down with a ketamine dart
- Synthetic marijuana

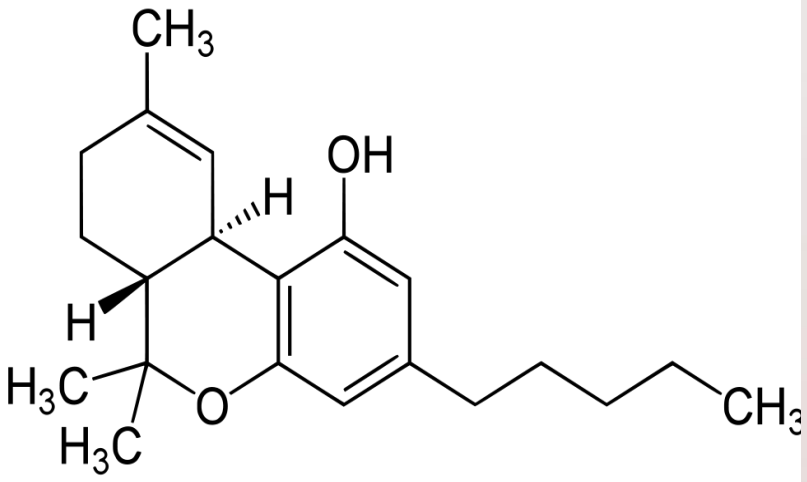

DANGEROUS
Spice or K2
is NOT
Marijuana
Spice
DIAMOND
Do Not Use!
Message by UBlueE2
Photo by Schorle

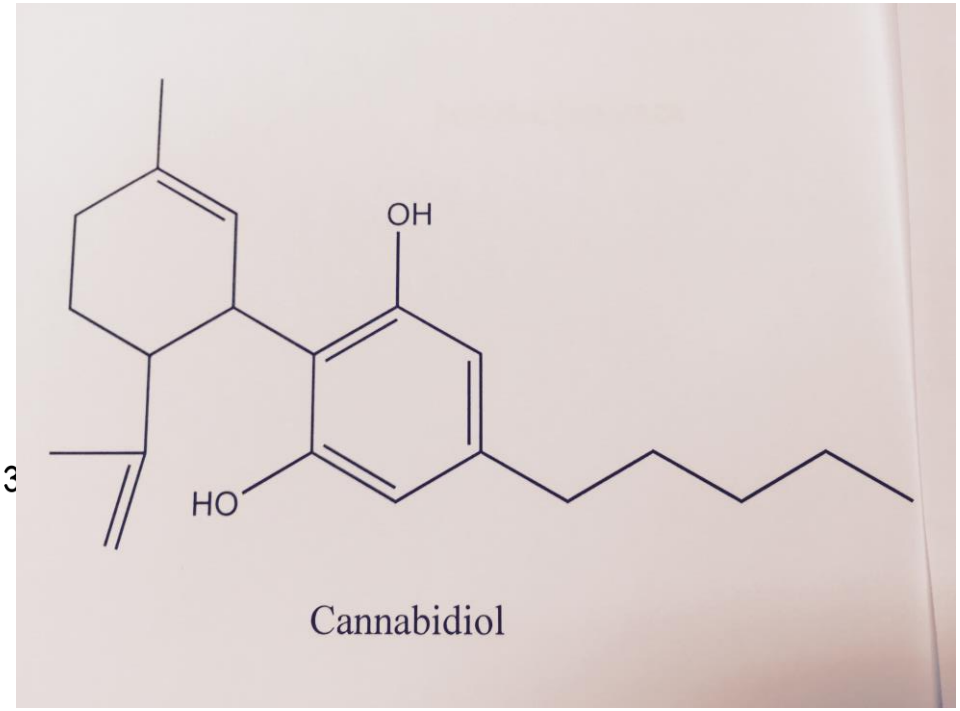
Marijuana Vs. Synthetic Cannabinoids



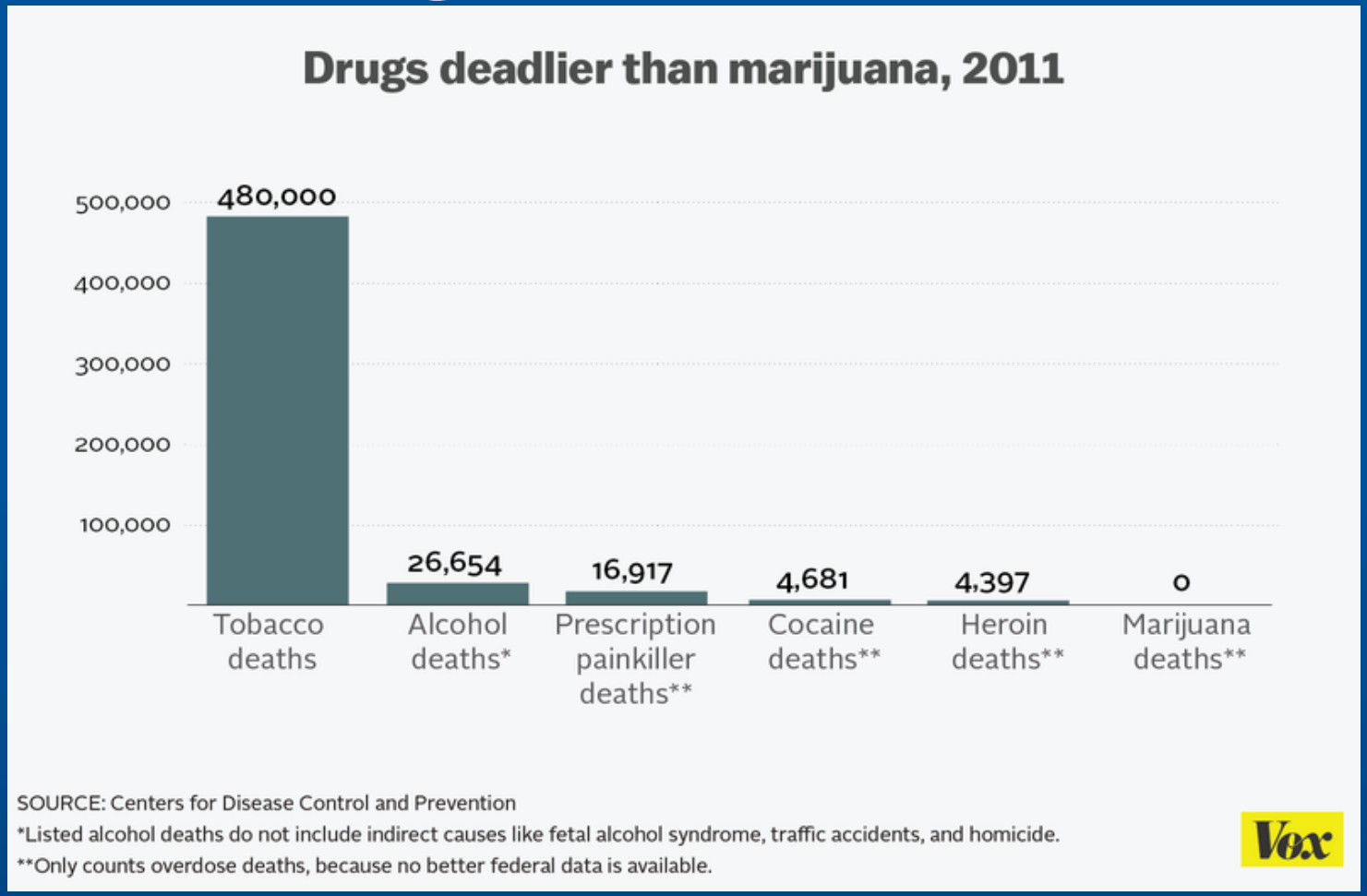


C & C





Now Larger Modifications



Officials: Man choked to death on a bag of weed

Posted: Sep 11, 2015 2:34 PM CDT
Updated: Sep 14, 2015 9:24 AM CDT

By Jeremy Turnage CONNECT

(Source: WIS)

COLUMBIA, SC (WIS) - A Richland County man died after Richland County sheriff's investigators, hospital officials, and a review of the Fifth Circuit Solicitor's Office say he choked to death on a bag of marijuana.

Zachary McDaniels was pronounced dead at Palmetto Health Baptist on Sept. 6, 2014 after he was pulled off life support by his family, according to the sheriff's department.

McDaniels, according to a review from the Fifth Circuit Solicitor's Office, died due to "subsequent cardiac arrest which resulted in diffuse anoxic brain injury" because the bag of marijuana became lodged in his throat, cutting off vital air supply to his brain.

Sheriff's investigators say McDaniels and a second man stole a car from the Widewater Square Shopping Center on Broad River Road before deputies attempted to pull the pair over on Metze Road.

McDaniels and his partner, however, jumped out of the car and fled on foot, officials said.

Deputies chased the pair and eventually caught up with McDaniels, who became "combative" and resisted arrest, authorities said. Once in custody, investigators said, McDaniels began having trouble breathing.

EMS workers were called and McDaniels became unresponsive, investigators said. Those EMS workers also attempted to intubate McDaniels, but his airway was blocked with the bag that he had apparently tried to ingest.

Hospital workers attempted to remove the bag from McDaniels' airway, but were ultimately unsuccessful. McDaniels' condition drastically deteriorated and he was pronounced brain dead before his family removed life support.

An autopsy at the hospital revealed McDaniels actually managed to ingest four other bags of marijuana before the fifth became stuck.

"The Sheriff's Department takes all necessary steps to ensure the safety and well being of anyone in our custody; in this instance Mr. McDaniels swallowed packages that unfortunately took his life," a statement from the sheriff's department said.

MORE

PHOTO GALLERY: Midlands Most Wanted

Do you know these people? Click here to view the photos of the most wanted people in the Midlands. If you have any information about any of these people, call Crimestoppers at 1-888-CRIME-SC. MORE

Cannabinoid Receptor Agonists

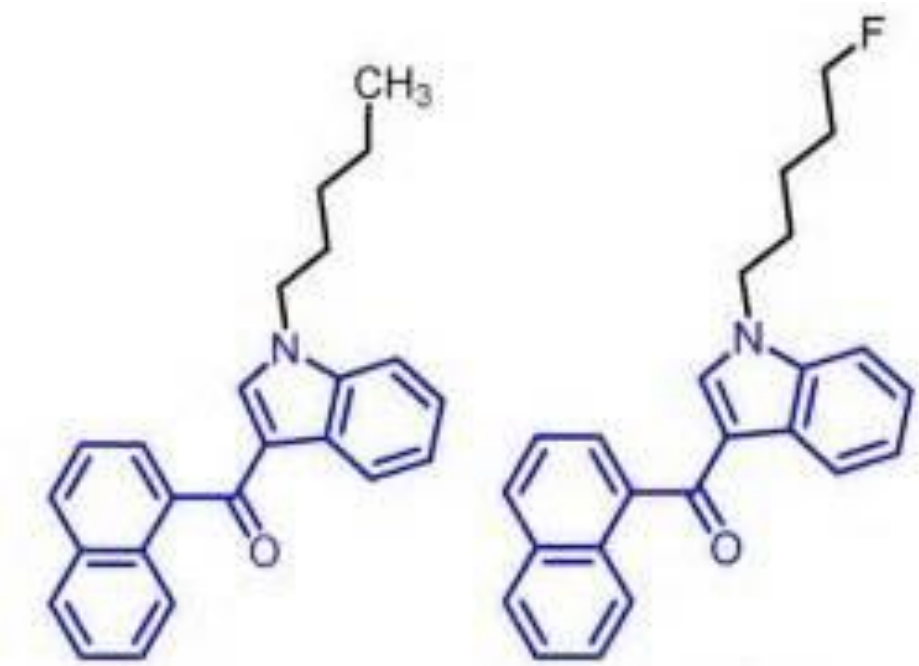
- Full agonist Vs Partial
- CB1-CNS
  - Applications-Analgesia, Anxiolytic
- CB2 – Peripheral neuro and immune syst
  - Applications-Suppress of neurodegerative disorders
    - EG-Alzheimer's

Synthetic Cannabinoids

- Developed beginning in 1980's
- Several Series
  - JWH- XXX — John William Huffman
  - AM-XXX — Alexandros Makriyannis
  - HU-XXX — Hebrew University
  - CP-XXX — Pfizer

Designed for Pharmaceutical use →
Analgesics, MS, HIV/AIDS, Chemo

Spice K2



JWH-018
341.1780

AM-2201
359.1685

Spice

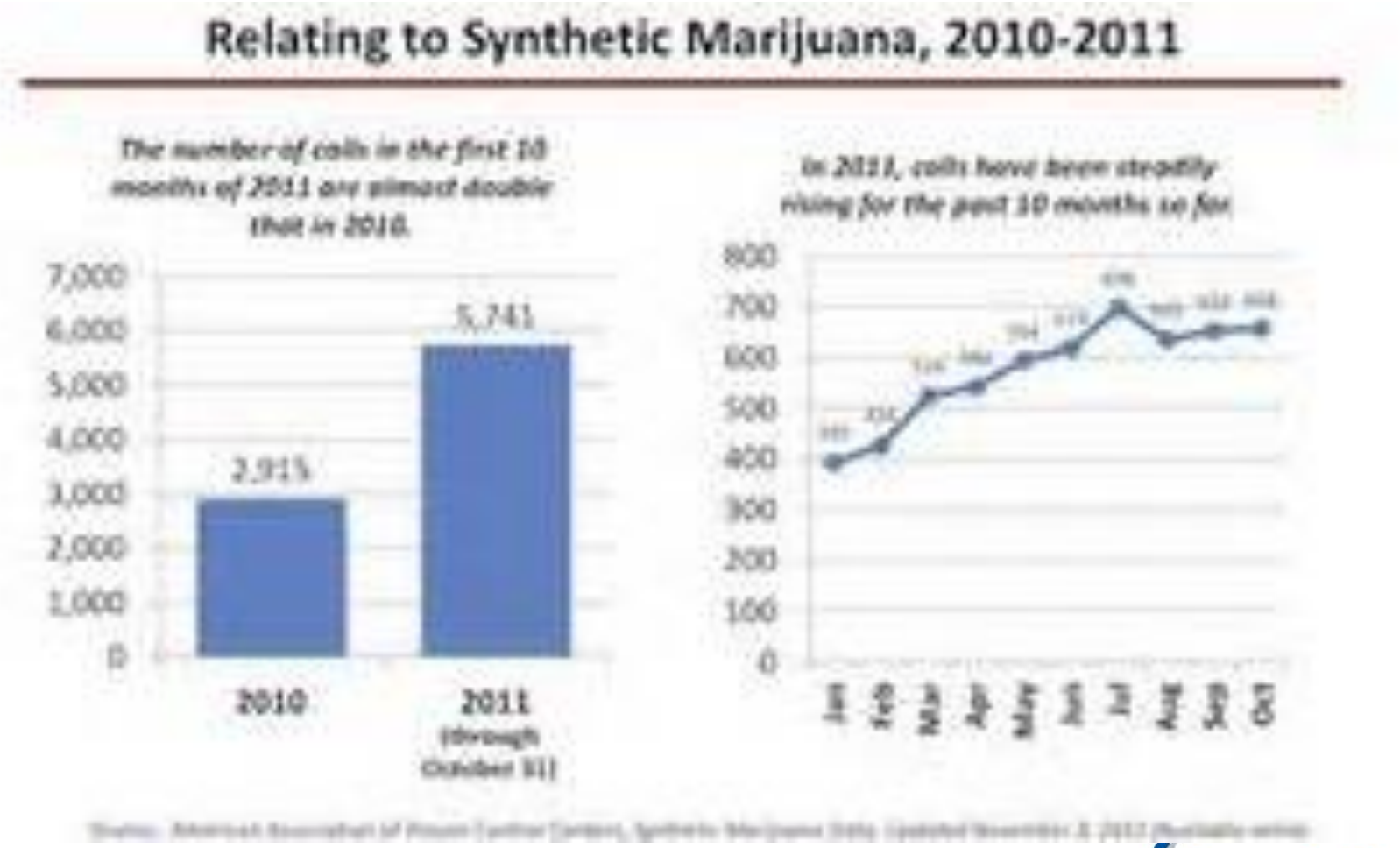
Nature of Herbals for Incense

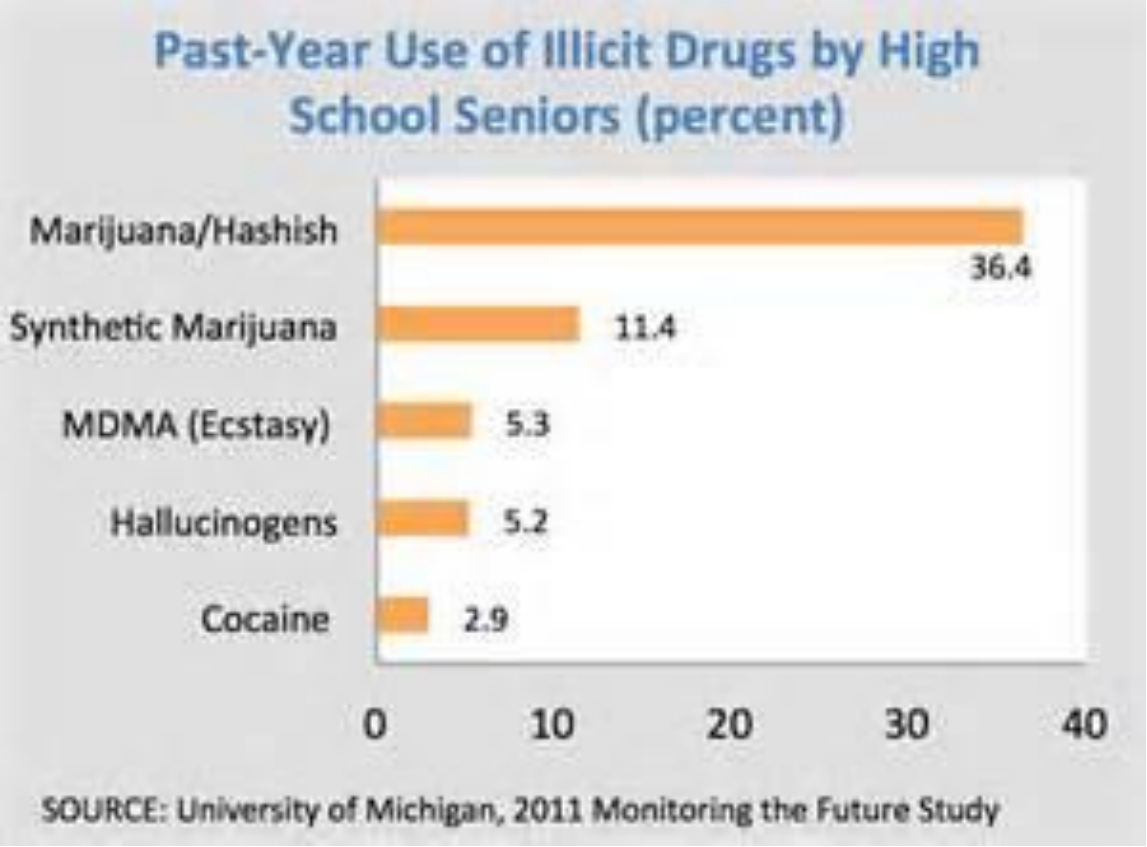
"Not for human consumption"

Lab Analysis 2008

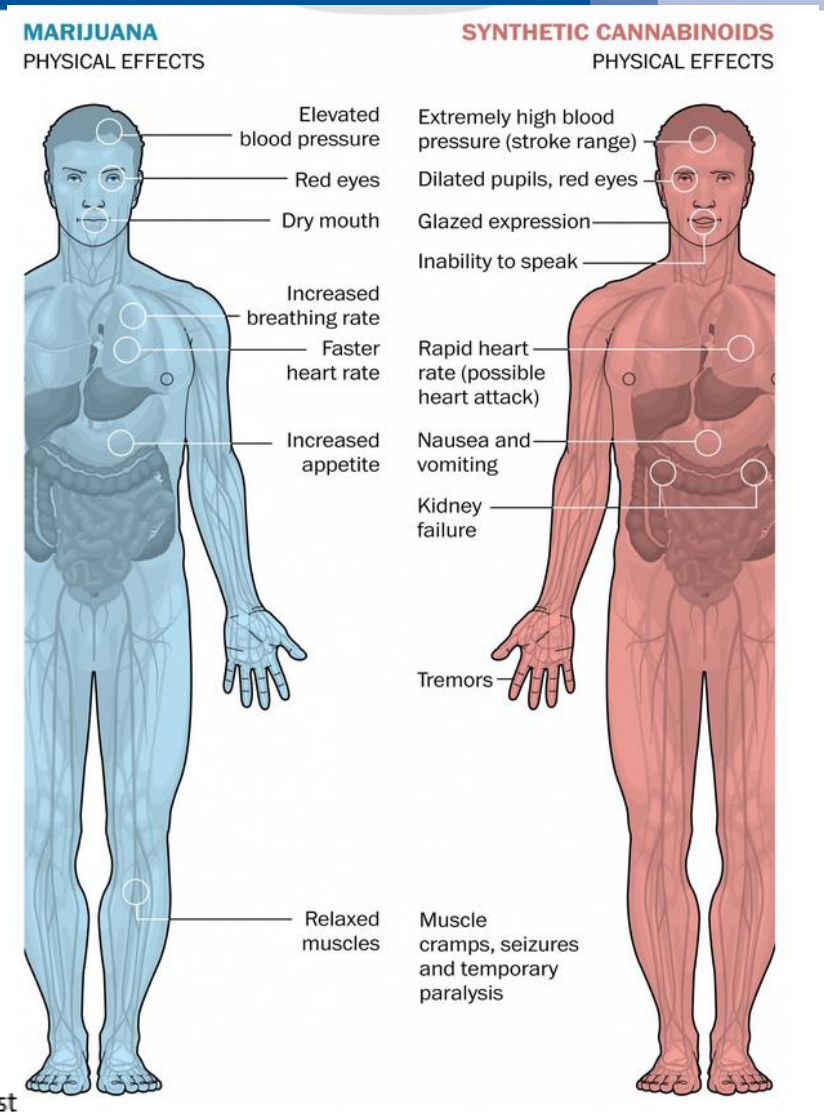
- Cannabicyclohexanol (CP 47,497)
- JWH-018
- JWH-073
- HU-210

Not Synthetic Marijuana!




Past-Year Use of Illicit Drugs by High School Seniors (percent)
Marijuana/Hashish
36.4
Synthetic Marijuana
11.4
MDMA (Ecstasy)
5.3
Hallucinogens
5.2
Cocaine
2.9
0
10
20
30
40
SOURCE: University of Michigan, 2011 Monitoring the Future Study

Physical Reactions



A.Hauslohner and P. Hermann- Washington Post

Psychological Reactions

MARIJUANA

EFFECTS ON THE BRAIN

Paranoia
Anxiety
Depression
Slow reaction time
Distorted sense of time
Short-term memory loss
Feeling of relaxation
Strange feelings
or "random" thinking

SYNTHETIC CANNABINOIDS

EFFECTS ON THE BRAIN

Paranoid delusions
Anxiety
Depression
Suicidal thoughts
Psychosis
Severe agitation
Inability to feel pain
Hallucinations
Total memory loss

A.Hauslohner and P. Hermann- Washington Post

SC Clinical Effects

Desired Effect is the same as THC

David Mitchell Rozga Act

- Teen from Indianola, Iowa
- June 6, 2010- self-inflicted GSW to head
- Friends admit he smoked K-2 one hour before

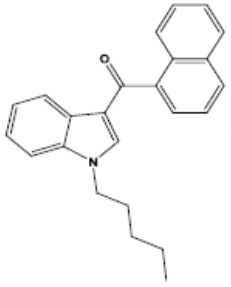
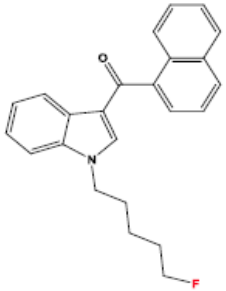
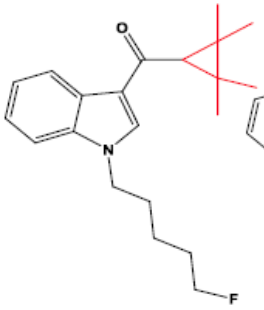
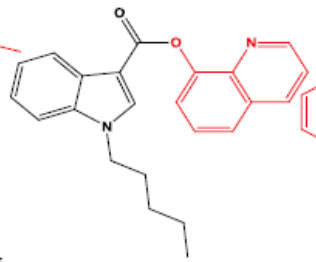
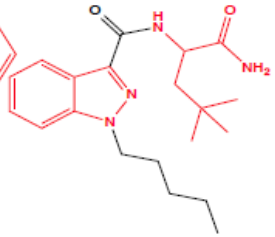
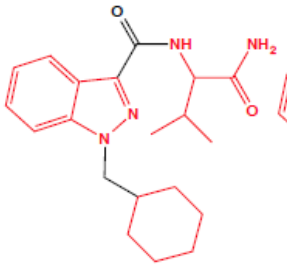
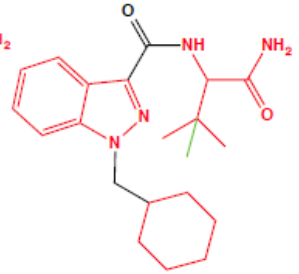
Legislation

- Introduced by Senator Chuck Grassley (R-IA)
- Passed June, 2011
- Synthetic Drug Abuse Prevention Act of 2012
  - Places SCs as Schedule 1, Controlled Substances Act
- Several States Also Enact Legislation

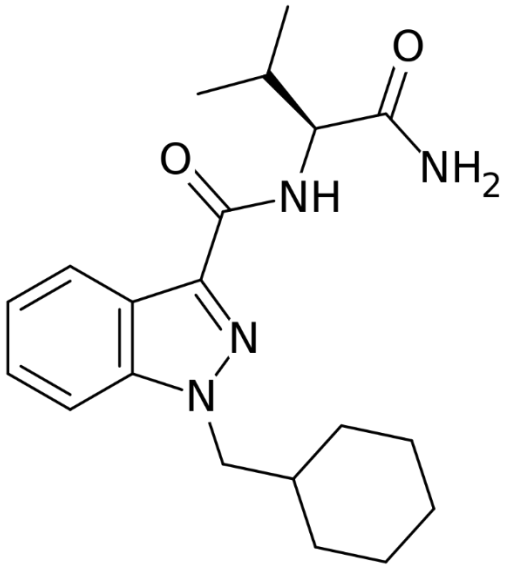
Next Generation

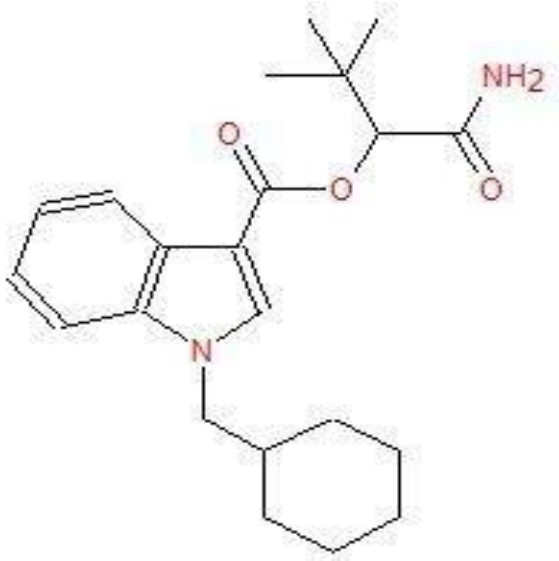
- New Drugs Developed
- Rogue Chemists
- Mild Modifications
- Law Changed to Cover Analogues

MOLECULAR EVOLUTION OF SYNTHETIC CANNABINOIDS

JWH-018	AM-2201	XLR-11	PB-22	ADB-PINACA	AB-CHMINACA	MAB-CHMINACA or ADB-CHMINACA
						
1st Generation 2010-Q2 2011	2nd Generation Q2 2011- Q3 2012	3rd Generation Q2 2012- Q2 2013	4th Generation Q2 2013-	5th Generation Q3 2013-	6th Generation Q2 2014-	7th Generation Q3 2014-

AB-CHMINACA & MAB-CHMINACA

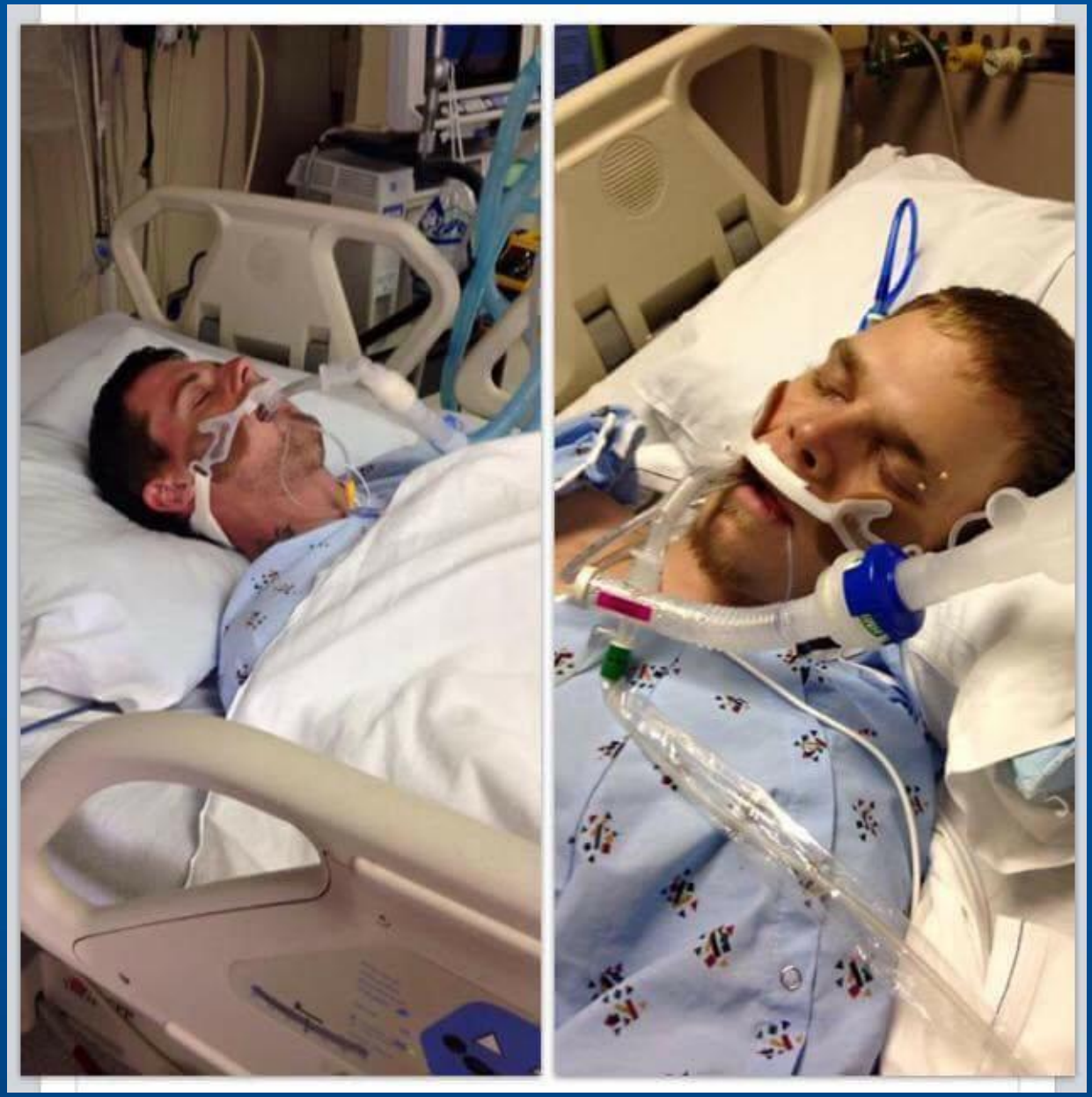




SC Clinical Effects

- Meant to be Same as Previous
- Instead Adverse Reactions More Severe

Hypertension	Agitation
Tachycardia	Vomiting
Dysrhythmias	Hallucinations
MI	Psychosis
Death	Seizures




16 WAPT NEWS
WOMAN AWAY IN HANDCUFFS EARILER


Fmeane acrd
5006


BOTANICALS
Item# 201380-31
DAMIANA LEAF C/S
TURNERA DIFFUSA
Origin: MEXICO
Kosher Certification Services


Damiana Leaf


2 PLY
PAPER
TOWELS


ScoobySnax
blueberry bliss
POTPOURRI
10g

Blood and Urine Analysis, UCSF

Of 273 cases

- 216 analyzed
- 101 confirmed MAB-CHMINACA
- 113 predicted metabolites
- 138 either MAB-CHMINACA or metabolite
- 73 both MAB-CHMINACA and metabolite

Other Synthetic Cannabinoids Detected

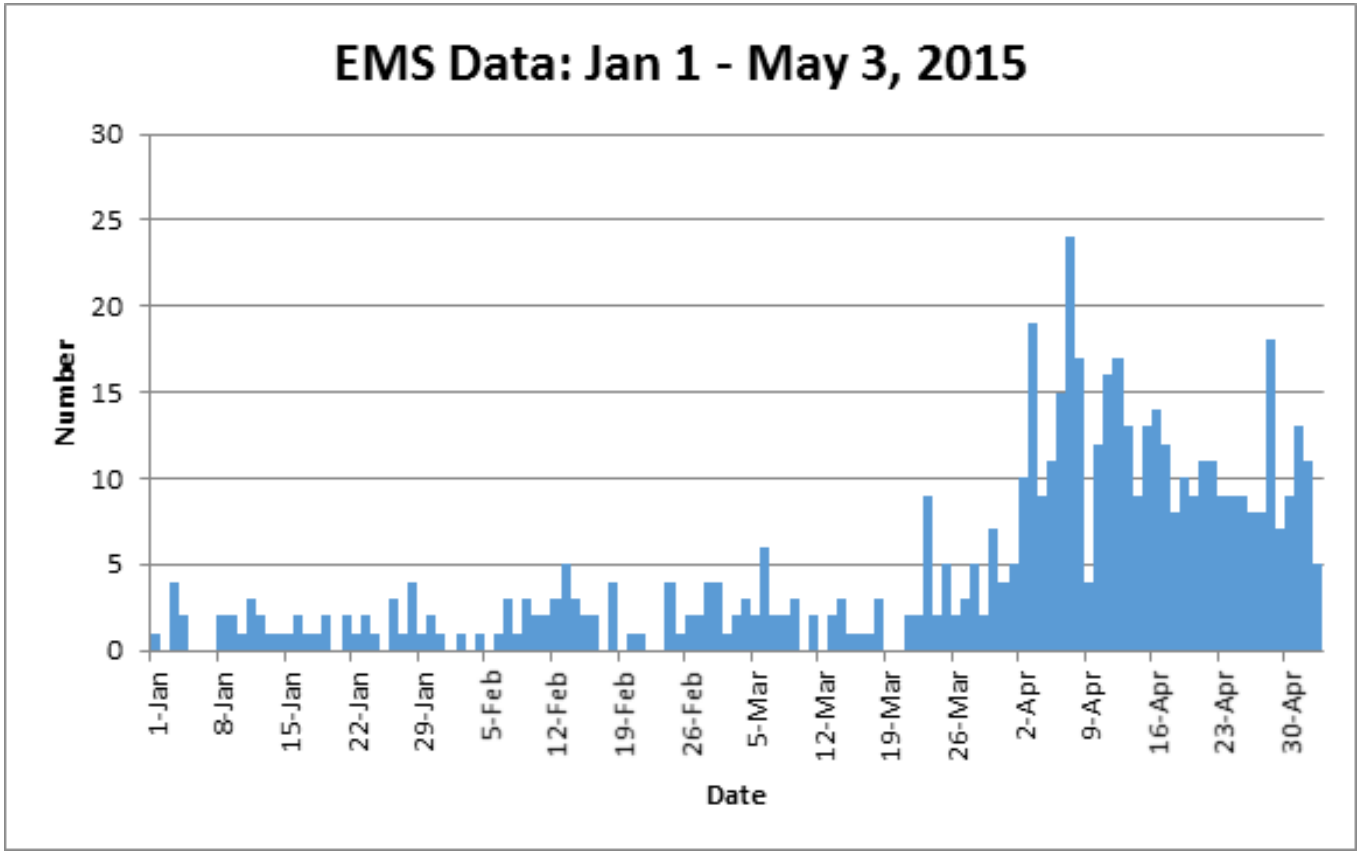
Drug	Confirmed	Possible Formula Match
AB-CHMINACA	36	
AB-FUBINACA	10	
AB-PINACA	6	
UR-144	5	
AKB-48	4	
AM-2201 N-(3-chloropentyl) isomer	3	(8)
5-Fluoro-AB-PINACA	2	
5-Fluoro-ADBICA, 5-Fluoro-AMB, XLR-11, JWH-018	1	
5-Fluoro-THJ	0	25
JWH-210	0	5
FUB-AMB	0	3
MAM 2201	0	3
AM-1248	0	2
MDMB-CHMINACA, 5-Cl-NNEI	0	1

Treatment

- Agitation
  - Ativan
  - Zyprexa
  - Geodon
- Elevated Creatinine
  - Fluids
- Rhabdo
  - fluids

Excited Delirium

- Various Presentations
  - Mild-Reassurance
  - Moderate-Zyprexa, Geodon
  - Severe- Paralysis, Intubation


EMS Data: Jan 1 - May 3, 2015
Number
30
25
20
15
10
5
0
1-Jan
8-Jan
15-Jan
22-Jan
29-Jan
5-Feb
12-Feb
19-Feb
26-Feb
5-Mar
12-Mar
19-Mar
26-Mar
2-Apr
9-Apr
16-Apr
23-Apr
30-Apr
Date

Current numbers in MS

- ED Visits- 1263
- Hospitalizations-
  - ED 14%
  - ED and 23 Hour Obs 59%
  - Admissions 22%
  - ICU Admissions 5%
- Suspicious Deaths- 17

What next?

DEA
MS Bureau of Narcotics
CDC/Public Health
- Epidemiology
- Education

Blasphemy: CO, OR, AK, DC

UAB MEDICINE

Knowledge that will change your world

Practitioners, Poison Centers & Public Health Collaborations

JUSTIN ARNOLD, DO, MPH

UNIVERSITY OF ALABAMA AT BIRMINGHAM

REGIONAL POISON CONTROL CENTER, CHILDREN'S OF ALABAMA

Poison Centers – History

U.S. Poison Centers originated in Chicago in 1953

- Within 10 years, expanded services to public
- 1970s saw number of centers expand to more than 600 centers
- 1978 American Association of Poison Control Centers (AAPCC) regionalized services
- 1980s and 1990s saw consolidation of centers and more consistent services
- 2003 saw amendment of Title XII of the Public Health Services Act to include Poison Centers
- 2006 saw the implementation of a web-based electronic reporting system for all Poison Centers

U.S. Based Poison Centers Today

55 Poison Centers (2014)

- 2,165,142 human exposures
- 56,265 animal exposures
- 663,305 information calls

- 2,617,346 calls originated from Poison Centers

1-800-222-1222

U.S. Based Poison Centers Today

Available 24-hours a day, every day of the year

Free of charge to users

Confidential

Manage user calls:

- Exposure calls
- Information calls

Provide follow-up calls to monitor progress and outcome

Poison Center Services

Lay public

- Accidental poisonings, intentional poisonings, & envenomations
- Pill identification
- Education, prevention, and outreach
- Pet calls*

Medical professionals

- Accidental poisonings, intentional poisonings, & envenomations
- Pill identification
- Consultation with Medical Toxicologists

Established Public Health Benefits of Poison Centers

Key roles:

- **1) Accessible & Affordable**
  - Free, 800-222-1222
  - No direct cost to the user
- **2) Reduction in Health-Care Costs**
  - Reduced ED Visits
  - Reduced Length of Stay
- **3) Toxico & Public Health Surveillance**
- **4) Public & Professional Education**
- **5) Research (Toxicity & Drug Monitoring)**
  - CDC, FDA, Consumer Product Safety Commission, EPA, State/L

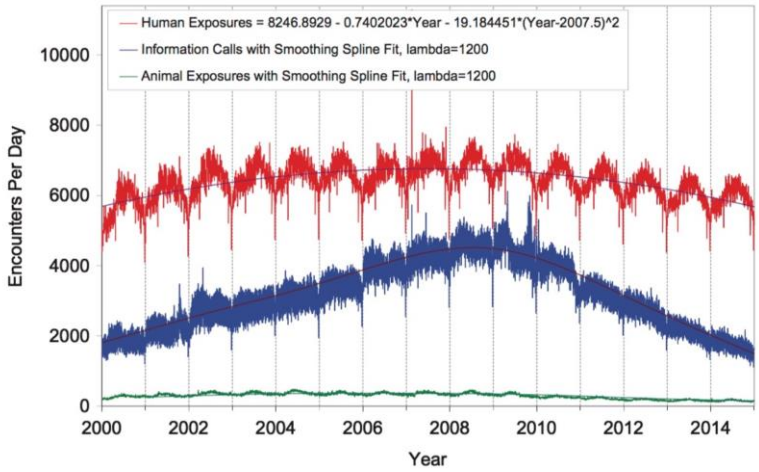
Poison Center Organization

Staffed by:

- **Managing Director** (Pharmacist or RN with ABAT certification)
- **Medical Director** (Physician board-certified in medical toxicology)

- **Specialists in Poison Information (SPIs)**
  - Often Pharmacists or RNs
  - Front-line
  - Have received specialized training in toxicology

- **Certified Specialists in Poison Information (CSPIs)**
  - Minimum 2,000 calls
  - Minimum 2,000 hours at Poison Center
  - Pass certification examination



Both linear and second order (quadratic) terms were statistically significant for least-squares second order regressions of Human Exposures (RSqr = 0.377). Smoothing spline fit with lambda=1200 was used for Information Calls (RSqr = 0.768) and Animal Exposures (RSqr = 0.882).

Figure 1. Human Exposure Cases, Information Calls and Animal Exposure Cases by Day since 1 January 2000.

Table 2. Site of Call and Site of Exposure, Human Exposure Cases.

	Site of caller		Site of exposure	
Site	**N**	**%**	**N**	**%**
Residence				
Own	1,506,125	69.56	1,976,666	91.29
Other	30,229	1.40	47,340	2.19
Workplace	22,688	1.05	36,544	1.69
Health care facility	458,938	21.20	6,229	0.29
School	9,878	0.46	27,271	1.26
Restaurant/food service	441	0.02	4,417	0.20
Public area	6,871	0.32	19,452	0.90
Other	124,255	5.74	25,178	1.16
Unknown	5,717	0.26	22,045	1.02

National Poison Data System (NPDS)

Introduced in April 12, 2006

- Serves as ***the only near real-time public health surveillance tool in the U.S.***
  - **Actively monitored by AAPCC & CDC for anomalies of public health significance**
  - **Utilized by some Poison Centers and Health Departments to monitor other locally relevant events***

- Repository for all data obtained by U.S. Poison Centers
  - Incorporated into research (public health, industry, individual health practitioners)
  - Incorporated into annual report published by AAPCC

All AAPCC member poison centers upload data to NPDS every

8 minutes

providing a near real-time snapshot of poison call conditions nationwide.

NPDS Data Flow

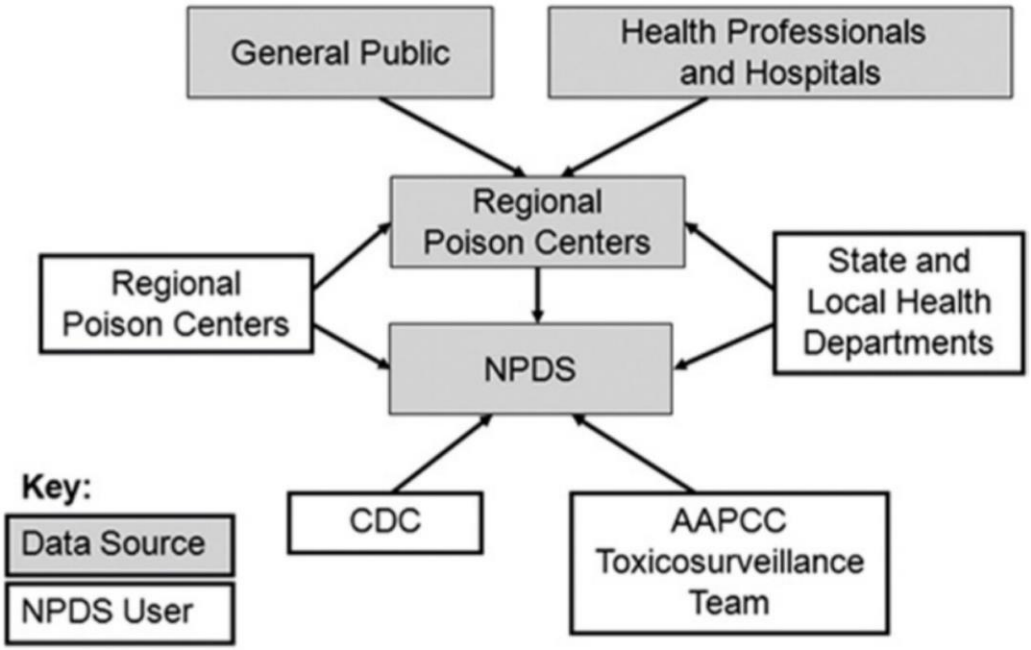


Figure 2. Illustration of data flow for NPDS users.

National Poison Data System Surveillance

Data is continuously monitored using surveillance algorithms

Surveillance algorithms monitor:

- Total and human call volume
- Clinical effects volume (signs, symptoms, lab abnormalities, etc)
- Case-based specific volume (substances, clinical effects, outcomes, etc)

- Utilizes historical averages for the same location and time period using previous NPDS data.
- Anomaly reports are generated automatically and alert:
  - AAPCC Surveillance Team
  - CDC's Health Studies Branch
  - Designated Poison Center Staff
  - Designated Public Health Agency Staff

Table. Description of 11 case-based definitions CDC uses to identify persons with potentially high-priority chemical and poison exposures in NPDS.

Definition Name	Definition Description
Acute radiation syndrome	Human exposure to nonradiopharmaceutical isotopes *or* caller reporting symptoms of cytopenia *and* vomiting or diarrhea *or* coma or confusion; excluding anyone reporting disseminated intravascular coagulation, suspected suicide, intentional misuse, or exposure to radon or radon gas
Arsenic	Human exposure to arsenic *or* caller reporting symptoms of hypotension *and* abdominal pain *and* diarrhea *and* nausea or vomiting; excluding any dermal or malicious exposures
Botulism	Human exposure to botulism *or* caller reporting symptoms of dysphagia or muscle weakness *and* blurred vision *or* photophobia or visual defect; excluding any callers with ocular irritation
Ciguatera	Human exposure to ciguatera
Cyanide	Human exposure with caller reporting symptoms of acidosis *and* agitation *or* coma *or* confusion *or* drowsiness *and* hypotension; excluding any suspected suicide or exposure to ethylene glycol, methanol, aspirin, lithium, acetaminophen
Nerve agents/organophosphates/carbamates	Human exposure with caller reporting symptoms of excess secretions *or* diaphoresis *or* lacrimation *and* diarrhea *or* fecal incontinence
Paralytic shellfish	Human exposure to paralytic shellfish
Puffer fish	Human exposure with caller reporting ingestion of tetrodotoxin; excluding any exposure to a bite/sting or exposure to salamanders
Radiation injury	Human exposure to nonradiopharmaceutical isotopes *or* radiopharmaceuticals *and* caller reporting symptoms of cytopenia *or* vomiting *or* coma *or* burns; excluding any exposure to radon or radon gas
Ricin	Human exposure with caller reporting vomiting *and* diarrhea *and* abdominal pain *or* elevated liver enzyme levels *and* hypotension *or* hematemesis *or* renal failure *or* oliguria/anuria *or* increased creatinine level *or* cytopenia *or* rhabdomyolysis; excluding any exposure involving mushrooms or known formulations
Smallpox	Human exposure to smallpox *or* other biological weapon

NPDS Data Flow

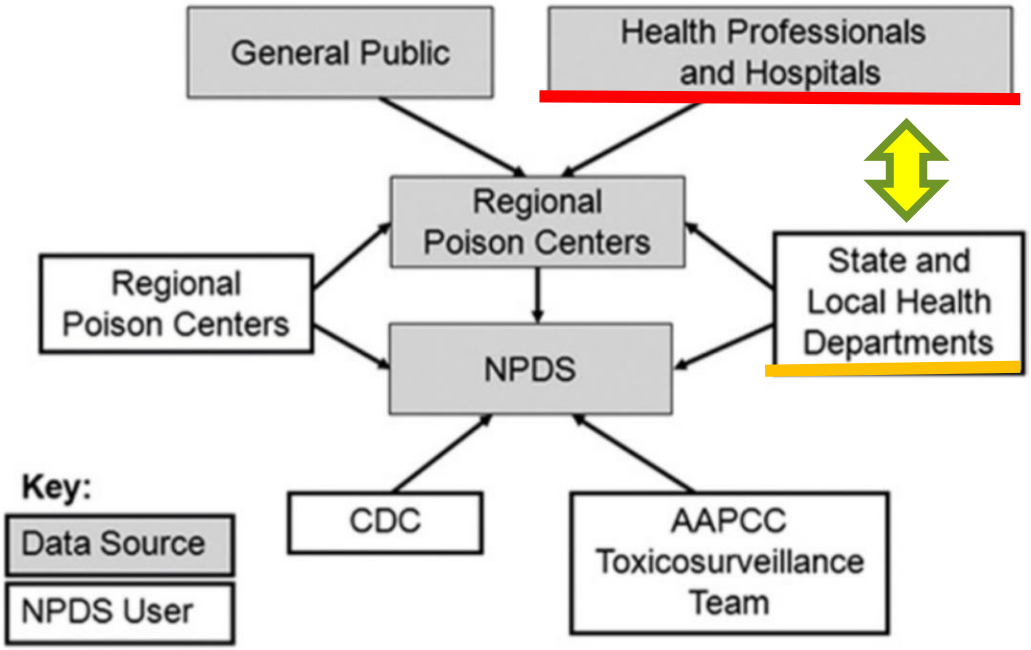


Figure 2. Illustration of data flow for NPDS users.

Poison Center's Expanded Role

Augmenting local public health response to emergencies

- Customize surveillance definitions
- Access & share their regional & national aggregate data
- Share NPDS real time surveillance with external organizations (e.g. public health & regulatory agencies)

Serving as an **"always staffed"** public health resource

- Assist with public-health after hours lines (Rabies)
- Assist with outbreak information and messaging and monitoring (Ebola, Flu)
- Assist as a centralized data repository (Synthetic Cannabinoids)

Key Collaborations

Rapid data collection, interpretation, and integration into a public health response can only occur with coordination and collaboration between various local, state, and federal agencies.

- **Local practitioners** play a key role in accurately reporting cases and symptoms to rapidly identify and describe public health emergencies.
- **State and local health departments** are poised to aid in both data collection and monitoring as well as in implementing public health interventions.
- **Poison Centers** and NPDS must maintain flexibility to be able to adapt and respond to public health emergencies.

Synthetic Cannabinoids Mississippi, 2015

Great example of collaboration of both contributors and end-users of poison center data

- Initially, MSDH reached out to practitioners using a data collection tool
- Data was collected by MDOH and Mississippi Poison Control Center
- Data was entered into NPDS
- Data was used during the event to monitor:
  - Identification of new cases
  - Demographics
  - Clinical features
  - Severity of cases

Additionally, cases from adjacent states and national trends were monitored by CDC and shared with MSDH on a daily basis.

MSDH was able to provide public health interventions, resources, and tools to front line practitioners.

MISSISSIPPI
STATE DEPARTMENT OF HEALTH

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Practitioners

Poison Centers

Health Departments

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