SWGDRUG

Criteria for Identification of Synthetic Drugs

Scott R. Oulton, SWGDRUG Chair

Methods of Analysis/Synthetic Drug Identification

- SWGDRUG Recommendations PART IIIB Applies
- Validation to Ensure Specificity
- Use Appropriate Analytical Scheme(s)
- Account for any Limitations
- Accurately Report Results
- Reference Materials
- Tools and Resources

PART IIIB - Drug Identification

§ 1 Introduction

- ... It is recognized that the correct identification of a drug or chemical depends on the use of an analytical scheme based on validated methods (see PART IV B - Validation) and the competence of the analyst.
- An appropriately constructed analytical scheme will result in, effectively, no uncertainty in reported identifications (see PART IV C - Uncertainty).
- SWGDRUG requires the use of multiple uncorrelated techniques (e.g., GC-Partition, TLC-Adsorption).
- It does not discourage the use of any particular method within an analytical scheme and it is accepted that unique requirements in different jurisdictions may dictate the practices followed by a particular laboratory.

Drug Identification

§ 2 Categorizing analytical techniques

Techniques for the analysis of drug samples are classified into three categories (see Table 1) based on their maximum potential discriminating power. However, the classification ...

Table 1

Category A	Category B	Category C
Infrared Spectroscopy	Capillary Electrophoresis	Color Tests
Mass Spectrometry	Gas Chromatography	Fluorescence Spectroscopy
Nuclear Magnetic Resonance Spectroscopy	Ion Mobility Spectrometry	Immunoassay
Raman Spectroscopy	Liquid Chromatography	Melting Point
X-ray Diffractometry	Microcrystalline Tests	Ultraviolet Spectroscopy
	Pharmaceutical Identifiers	
	Thin Layer Chromatography	
	Cannabis only: Macroscopic Examination Microscopic Examination	

Drug Identification

§ 3 Identification criteria

- 3.1 When a validated Category A technique is incorporated into an analytical scheme, at least one other technique (from either Category A, B or C) shall be used.
- 3.2 When a Category A technique is not used, at least three different validated techniques shall be employed. Two of the three techniques shall be based on uncorrelated techniques from Category B.
  - Due to the variation of synthetic drugs and that they are not well known to the community, this analytical scheme is not recommended

Drug Identification

§ 3 Identification criteria

- 3.5 For the use of any method to be considered of value, test results shall be considered "positive." This addition is proposed: (i.e., it must meet the acceptance criteria defined in the method validation and operating protocol.) When possible, data from a test result should be compared to data generated from a reference material which has been analyzed under the same analytical conditions (see PART IV A Section 6.2). While "negative" test results provide useful information for ruling out the presence of a particular drug or drug class, these results have no value toward establishing the forensic identification of a drug.

Drug Identification

§ 3 Identification criteria

- 3.8 The chosen analytical scheme shall demonstrate the identity of the specific drug present and shall preclude a false positive identification and minimize false negatives. Where a scheme has limitations, this shall be reflected in the final interpretation (see PART IVC - Uncertainty).

Drug Identification

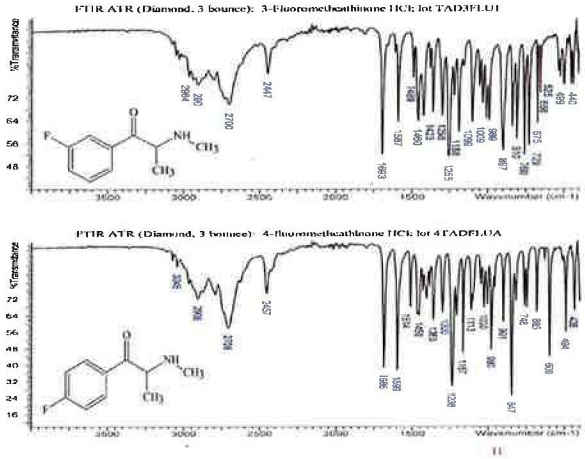
§ 4 Comment

These recommendations are minimum standards for the forensic identification of commonly seized drugs. However, it should be recognized that they may not be sufficient for the identification of all drugs in all circumstances. Within these recommendations, it is up to the individual laboratory's management to determine which combination of analytical techniques best satisfies the requirements of its jurisdiction.

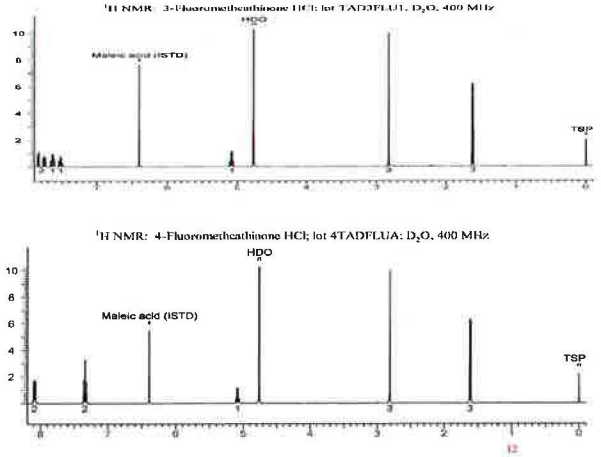
Validation of Analytical Scheme

- Must choose analytical scheme wisely
- PART IVB 1.2 An analytical scheme shall be comprised of validated methods that are appropriate for the analyte.
  - IVB.1.2.1 The combinations of methods chosen for a particular analytical scheme shall identify the specific drug of interest, preclude a false positive and minimize false negatives.

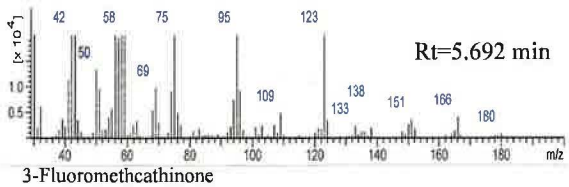
Analytical Scheme - FTIR

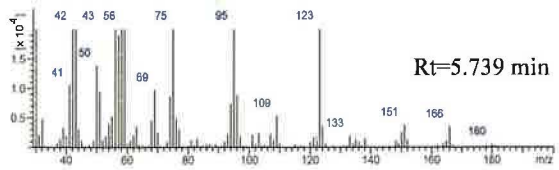


Analytical Scheme - NMR



Analytical Scheme - GCMS





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Reporting

- **Limitations**
  - If you cannot determine the position of the Flurorine (3, 4 or 5), can you report Fluromethcathinone?
    - Depends on your laboratory policy and jurisdictional requirements
    - When doing so, include verbiage that indicates position is not known

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Reference Materials - Current

§ 6.2 Verification of drug reference materials

6.2.1 The identity of certified reference materials shall be verified prior to their first use.

6.2.2 The identity of uncertified reference materials shall be authenticated prior to use by methods such as mixed melting point determination, Mass Spectrometry, Infrared Spectroscopy, or Nuclear Magnetic Resonance Spectroscopy.

6.2.3 Verification shall be performed on each new lot of drug reference material.

6.2.4 All verification testing shall be documented. The documentation shall include the name of the individual who performed the verification, date of verification, verification test data and reference used in verification.

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Reference Materials - Proposed

- Reference materials and reference data are critical to demonstrating the validity of quantitative and qualitative test results.
- Acceptance criteria order of preference
  - 1. Comparison to data obtained from a suitable drug reference material analyzed under the same analytical conditions as the test/case sample...
  - 2. Comparisons to external reference data may be used where a reference material is unavailable...
    - ✓ Veracity of data shall be assessed...
  - 3. When neither reference materials nor external reference data are available structural elucidation techniques may be employed...
    - ✓ Interpretations by competent analysts...

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Reference Materials - Proposed

- Assessment of reference materials
  - ISO/IEC 17025 specifies that reference materials shall, where possible, be traceable to SI units of measurement, or to certified reference materials (CRM). For seized drugs this requirement is difficult to fulfill because the concept of traceability for drug standards is not internationally established and CRM's for drug analysis are not readily available or affordable.
    - Note: A certificate does not necessarily define a material as a CRM.
  - Fit for purpose for qualitative work requires an assessment of chemical identity (structure), stability, matrix, and homogeneity.
  - For quantitative work, it is necessary to assess the purity and its associated uncertainty of measurement in addition to the parameters in Section 6.2.3.

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SWGDRUG MS Library

SWGDRUG Mass Spectral Library:
SWGDRUG has compiled a mass spectral library from a variety of sources, containing drugs and drug-related compounds. All spectra were collected using electron impact mass spectrometry systems. This library is available for download from this website.

DISCLAIMER: Although SWGDRUG makes an effort to review the accuracy of spectra prior to entry, this library should only be used as an analytical tool. SWGDRUG recommends the use of traceable reference materials to support identifications of drugs (Part IV B – Quality Assurance Section 2.3)

The SWGDRUG library is supported by the NIST MSSEARCH program, which is available on-line at no charge (see below). Additionally, the library was converted to Agilent Technologies format. Lastly, two raw data formats are included below depending upon your desired application. Click on the appropriate link below to download the compressed file and follow the instructions below.

SWGDRUG MS Library Version 1.8 (April 9, 2013):

NIST Format NIST

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Drug Monographs

Monographs:

The following monographs contain detailed information and analytical data for reference materials which have been analyzed, verified, and authenticated by the Drug Enforcement Administration Special Testing and Research Laboratory. These monographs may be used for the verification of acquired reference materials and for the identification of drug materials (subject to laboratory policy). Monographs are being uploaded as they are peer reviewed and approved for publication.

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Common Name	Other Names	Date
AB8.200	(1-[2-(morpholin-4-yl)ethyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone	12-28-12
4AcODMT	4-AcO-DMT; psilacetin; O-acetylpsilocin	03-15-13
AKB-48	APINACA: N1-adamantyl-1-pentylindazole-3-carboxamide; N-adamantyl-1-pentyl-1H-indazole-3-carboxamide	12-07-12
5-Fluoro-AKB-48	5F-APINACA; APINACA 5-Fluoropentyl analog; 5F-AKB-48	02-06-13

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Drug Monographs

- **Purpose:**
  - Reference material verification
  - Limited methodology
  - Limitations
- **Peer reviewed** (structural elucidation)
- **Availability:**
  - www.swgdrug.org
  - November 2012
  - monographs uploaded weekly
- **Prioritized based on community needs**

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Current SWGDRUG Projects

- **Reference Materials Sub-committee**
- **SWGDRUG Recommendations 6.1 (DRAFT)**
  - Assessment of reference materials
  - **Issues:** availability, companies, structural elucidation, etc.
  - Public comments: were due March 29, 2013
- **Analogues Sub-committee**
- **DRAFT** document
  - Addressing current issues regarding conclusions and opinions on analogues and structural class identifications
  - Public comments: Due May 3, 2013

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THANK YOU!

www.swgdrug.org

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SWGDRUG Draft Recommendations on Analogues and Structural Class Determinations

Linda C. Jackson
Virginia Department of Forensic Science
SWGDRUG Vice Chair

Problem

- Chemists are asked to determine whether chemicals encountered in evidence are analogues
- Chemists requested SWGDRUG to help with these determinations

Initial Discussions – July 2012

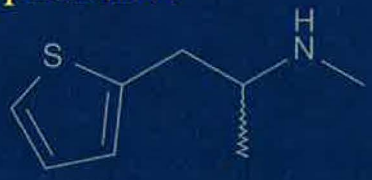
- Should SWGDRUG have a formal statement on analogues?
- Should SWGDRUG define what an analogue is or should the document only provide guidance on approach?
- Considerations:
  - Varied jurisdictional requirements
  - Ultimately the court decides as to whether a compound meets the legal definition

Initial Discussions

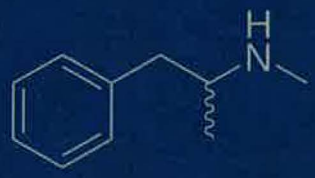
- Agreed that generally drug analysts can only discuss structural similarities
  - Physiological/pharmacological effects are significant but cannot be addressed by SWGDRUG
- Can we provide guidance to the community as to how to define structural similarity?
  - Subjective in nature
- Concentrate on emphasizing what a drug analyst can report and testify to during these cases

Your Opinion???

Methiopropamine



Methamphetamine



Analogue Sub-Committee

- Formed Analogue Sub-Committee to continue discussions and draft recommendations
- Members: Christian Matchett (chair), Linda Jackson, Scott Oulton, Robert Powers, Catherine Quinn, Sandra Rodriquez-Cruz and Udo Zerell

Discussions - January 2013

- Subjective nature of analogue determination
- Structural similarity is not indicative of pharmacological activity (or vice versa)
- What constitutes structural similarity?

Goals for the Recommendation

- To provide general guidance on:
  - Differentiation of structural class determinations vs. analogue determinations
  - Documentation of evaluations of structural similarity
  - Reporting conclusions and opinions
  - Reporting qualifications and limitations

Introduction

- SWGDRUG considers it fundamental for analysts to fully understand how analogues and structural classes are legally defined in a particular jurisdiction prior to developing or reporting opinions.
- Such opinions should only be rendered by those with proper training and experience.

Analogues

- Legal requirements are defined
- Generally involve a similarity evaluation of structural and/or pharmacological properties to a known controlled substance
- Similarity is assessed in a variety of ways
- The evaluation should be documented:
  - Compared to what compound?
  - How similar?
  - How different?

Analogues

2.5.1 Evaluation of similarity is a subjective matter and opinions may differ.

2.5.2 Structural comparisons in a forensic laboratory are likely to be limited to the structural class and functional group, ring or chain substitutions. As examples, isomers, homologues, salt forms, esters and ethers may be considered. The scope of the comparison conducted should be made clear in the report.

Analogue Pharmacology

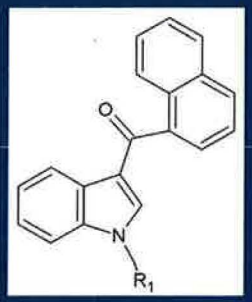
Structural Similarity ≠ Pharmacological Activity

- Drug analysts should limit pharmacological activity testimony to the citation of peer-reviewed literature, or relevant sworn statements

Structural Class Determinations

- Chemical compounds are controlled based upon structural class definitions

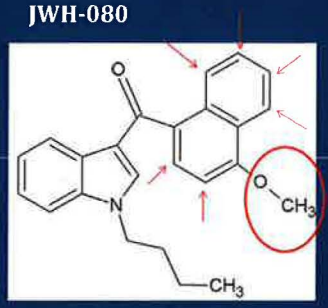
Example: "any substitution of 3-(1-naphthoyl)indole at the indole ring or naphthoyl ring to any extent"



Structural Class Determinations

1. Identify a specific compound and assign the compound as a member of a legal structural class
2. Identify sufficient features of a compound to assign it as a member of a legal structural class without making a conclusive identification of that compound.

JWH-080



Any relevant limitations of the analytical scheme and resulting classification shall be clear in reporting.

Reporting

- All conclusions and opinions expressed in written or oral form shall be based on sufficient supporting evidence, data, or information.
- The basis of any conclusion should be completely documented in the case notes and summarized in the written report and subject to the laboratory's review policy.

Reporting

- Conclusions and opinions reported shall be accurate, clear, objective, and meet the jurisdictional requirements. The report must also include any assumptions or limitations (e.g. potentially exculpatory information), to allow the court to make the final decision.

Reporting

- The report should clearly indicate what elements of the legal requirements were evaluated and what elements were not evaluated.
- The scope of opinions and conclusions reported shall not go beyond the knowledge, training and experience of the analyst.

Please Comment!

- www.swgdrug.org/pending.htm
- Comment Period open until May 3, 2013

Validation/Authentication of Physical Standards

Nicole Astor

Chemistry Technical Leader
Georgia Bureau of Investigation
Atlanta, Georgia

Accreditation Requirements

- ISO/IEC 17025:2005(E) Section 5.6.3.2 Reference Materials
  - Reference materials shall, where possible, be traceable to SI units of measurement, or to certified reference materials. Internal reference materials shall be checked as far as is technically and economically practicable.

ISO/IEC 17025 Second Edition 2005-05-15 General Requirements for the competence of testing and calibration laboratories

Accreditation Requirements

- ASCLD/LAB-*International* Supplemental Requirements, 2011 Edition, Section 5.6.3.2.1
  - Reference collections of data or items/materials encountered in casework which are maintained for identification, comparison or interpretation purposes (for example, **mass spectra**, motor vehicle paints or headlamp lenses, **drug samples**, typewriter print styles, wood fragments, bullets, cartridges, DNA profiles, frequency databases) shall be fully documented, uniquely identified and properly controlled.

ASCLD/LAB-International Supplemental Requirements for the Accreditation of Forensic Science Testing Laboratories

Typical State/Local Lab SOP for Verifying Physical Standards

- Verify by at least one structural elucidation technique (GC/MS, FTIR, NMR, etc) and compare to published reference spectra.

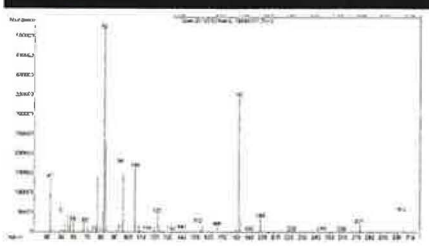
Typical State/Local Lab SOP for Verifying Physical Standards

- Verify by at least one structural elucidation technique (GC/MS, FTIR, NMR, etc) and compare to published reference spectra.
  - GBI: For newly encountered substances that have no previously published data, the Technical Leader approves the verification. Verification data utilizes different techniques and/or different extraction procedures.

For "Classical" Drugs of Abuse

- Obtain a standard from any established reference company
  - Certificate of Analysis shows a practical level of traceability
- Compare data any number of references
  - Instrumental Data for Drug Analysis (IDDA)
  - Peer reviewed scientific journals
  - Clarke's Analysis of Drugs and Poisons
  - Previously validated standards

For "Classical" Drugs of Abuse



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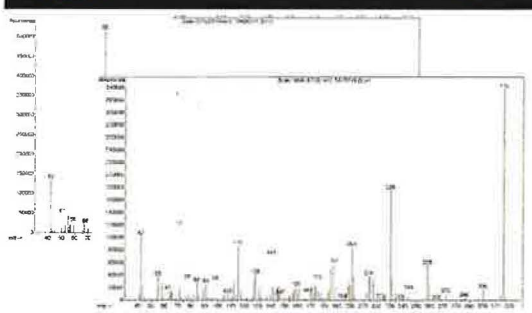

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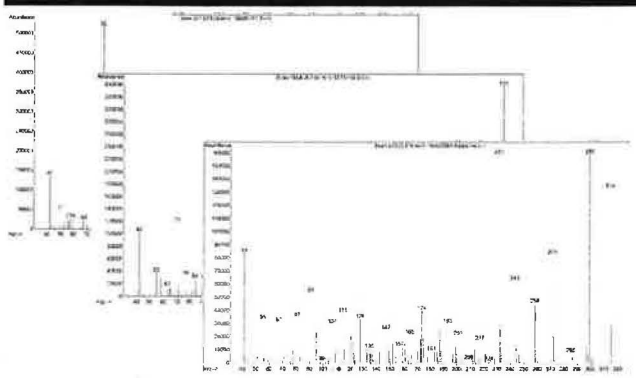


For "Emerging" Drugs of Abuse

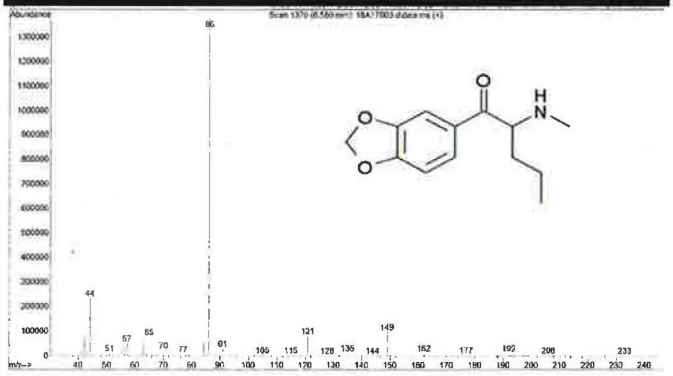
- Obtain a standard from any established reference company
  - Certificate of Analysis not always provided
- What do you compare your data to?
  - Company databases
  - Previously published data
    - Using the same manufacturer's standard?
    - Using the same lot of standard?
  - Data from other laboratories

How Do You Actually Verify?

- How can you ensure the standard is in fact what you ordered?
- How can you ensure the verification data is reliable and reproducible?

- Without historical validations, these questions can be very difficult for the state/local chemists to answer.

For "Emerging" Drugs of Abuse



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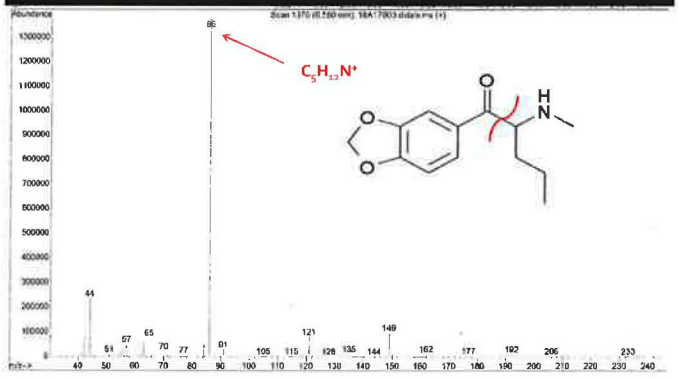

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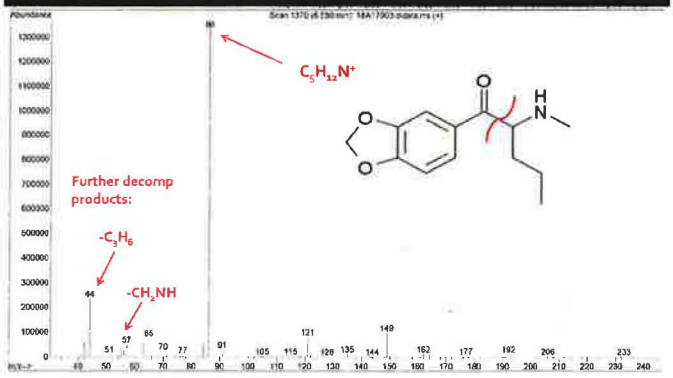

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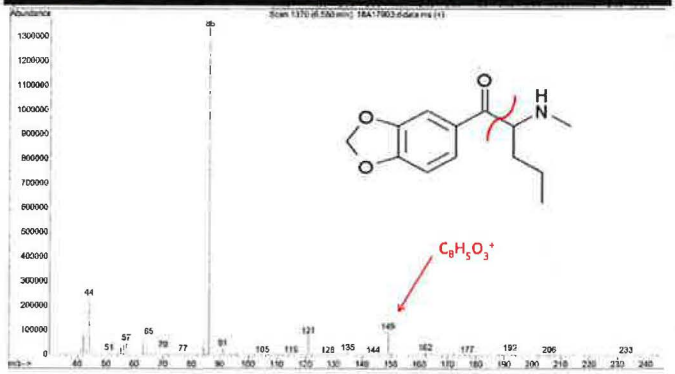

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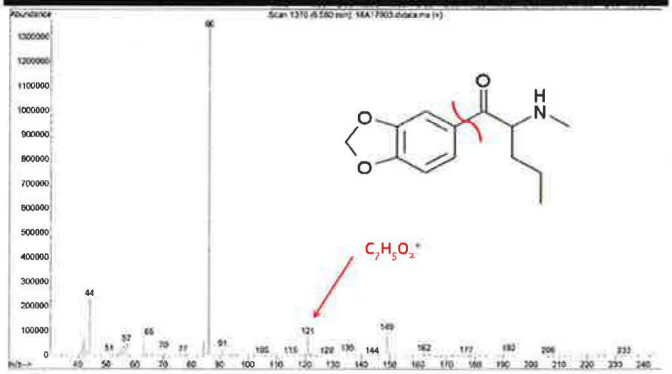

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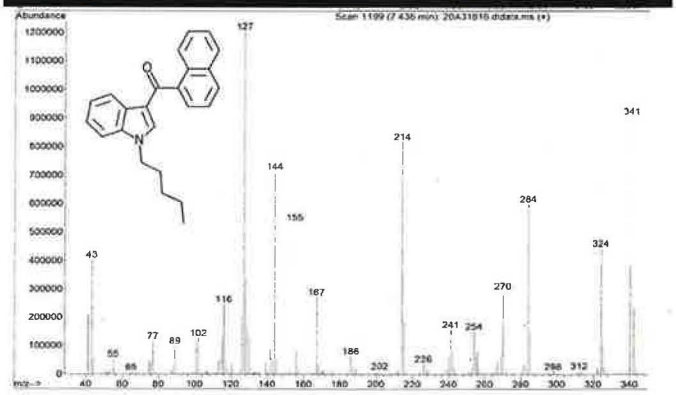

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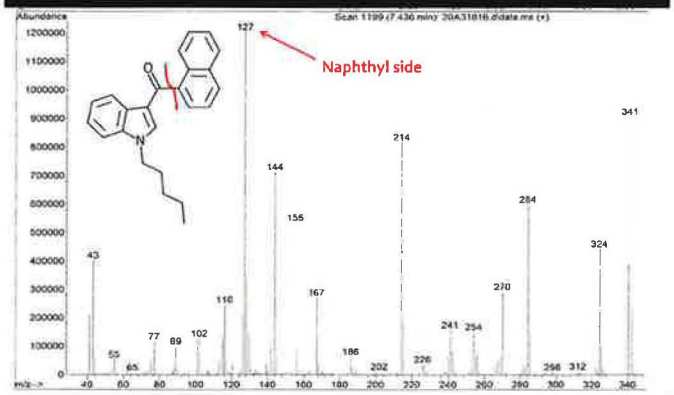

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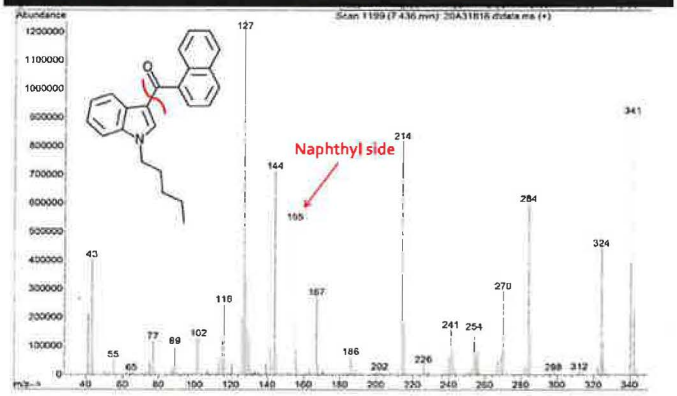

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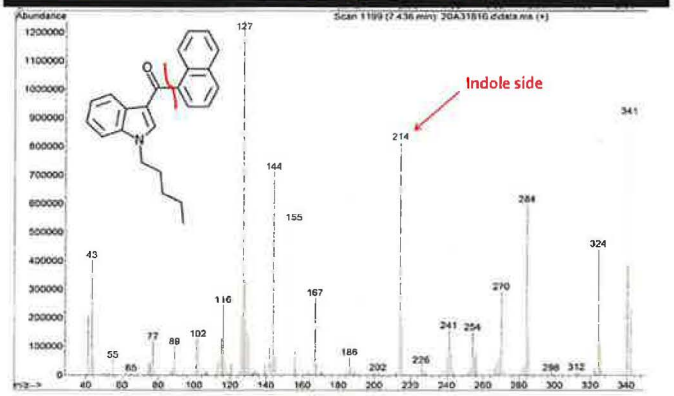

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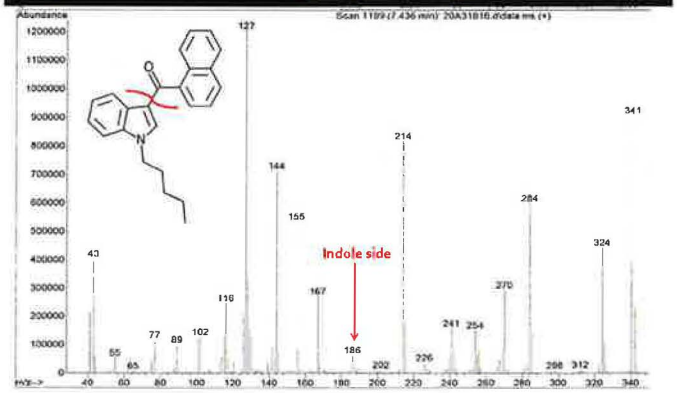

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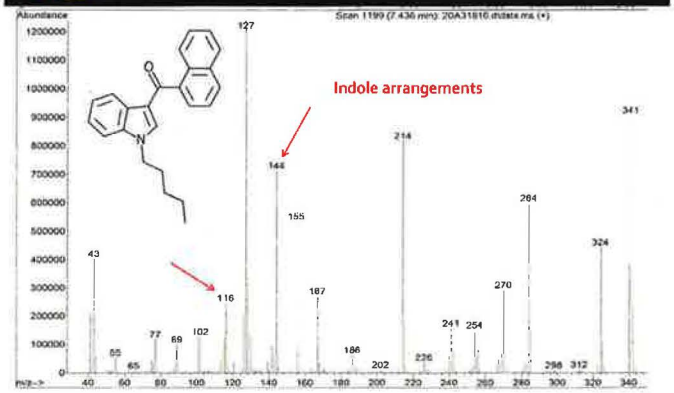

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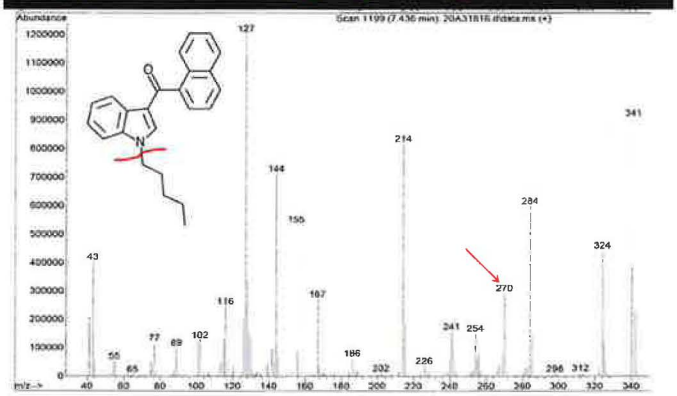

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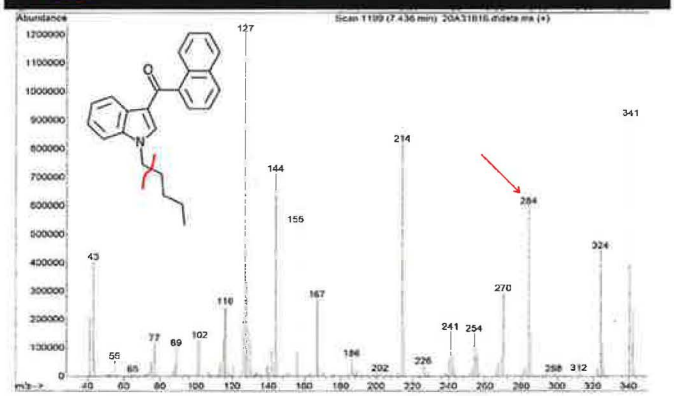
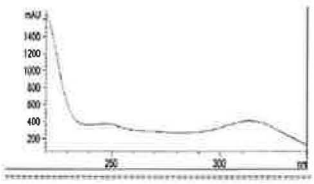


For "Emerging" Drugs of Abuse

- A secondary technique is used to verify
  - Depending on the vendor, other analytical information may be given



JWH-018 has a UV λ_{max}: 219, 246 nm

Wavelength reference: www.caymanchem.com Item Number 10900

Know Your References

- Vendors
  - Are they accredited?
  - What kinds of Quality Control measures do they use?
  - How often do they validate their products?

Know Your References

- Vendors
  - Are they accredited?
  - What kinds of Quality Control measures do they use?
  - How often do they validate their products?
- Databases
  - What kinds of source information are offered?
  - How were the spectra verified/authenticated?

Questions?

Analog Determination - a Scientific Method

NIST/DEA Emerging Trends in Synthetic Drugs Workshop
May 2013
Lindsay E. Reinhold, M.F.S., F-ABC

ACECSA

- Advisory Committee for the Evaluation of Controlled Substance Analogs
- www.druganalogs.org
- Core members
- Subject-Matter experts

ACECSA Mission

- The mission of the ACECSA is to recommen minimum scientific standards for the evalua of non-controlled substances being consider as analogs of controlled substances.
- Science is the key
- Legal decisions/legislation may be discussed but final considerations are strictly based or science

ACECSA Objectives

- To establish a working definition of "Analog and related terms within the scope of Foren Drug Analysis.
- To develop a rigorous scientific method for t evaluation of non-controlled substances for analog consideration that is scientifically va and peer-reviewed.
- To provide minimum scientific standards fo classifying compounds as analogs.

ACECSA Objectives

- To provide a means of information exchange within the forensic science community, law enforcement, legal counsel and government agencies regarding the scientific evaluation and classification of suspected analogs.
- To seek acceptance of ACECSA recommendations.
- To provide training and consultation to the forensic science, criminal justice and other interested stakeholders.
- To create a catalog of evaluated compounds and their scientific analog designations.

ACECSA Sub-Committees

- Structure
- Physicochemical Properties
- Computational Chemistry and Cheminformatics
- Synthetic Pathway
- Pharmacology/Toxicology
- Literature Support
  - *published, unpublished, dissertations, research, meeting abstracts*
  - *Catalog of evaluated compounds*

Structure

- "...the chemical structure of which is substantially similar to the chemical structure..."
- 3 Structural indicators for comparison
  - Core structure class
    - Acyclic, Single Ring, Multi-ring
    - Must be in the same class – no changes
  - Functional groups
  - Presence and location of double bonds
    - Important for 3-D structure

Physicochemical Properties

- Chemical reactivity cannot be separated from structure
- Aspects for comparison
  - Bioavailability
  - Molecular Weight
  - Polar Surface Area
  - Log P
  - Rings
  - Rotatable bonds
- Property estimation software

Synthetic Pathway

- Distinct routes separately patented?
- Distinct routes separately published?
- Must infer the pathway of construction
- Synthetic byproducts/contaminants may indicate pathway
- Commonly available building blocks

Pharmacology/Toxicology

- 3 Discussion Areas:
  - Human *in vivo* data
    - Best and only conclusive data
    - Not determined quantitative value "similar data"
  - Animal *in vivo* and/or *in vitro* data
    - Used after Human data has been evaluated
    - If no human data and animal data is incomplete, QSAR must be considered
  - QSAR
    - Use when no other data (or incomplete data) exists
  - Anecdotal Reports
    - Use as informational only – no scientific controls

Computational Chemistry

- Essential to define a core structure
- Define the Maximum Common Substructures
  - Markush-type representation
- Cheminformatics alert IT platforms
- Molecular Shape
- Med Chem "transformation" rules

- Molecular Similarity
- QSAR

Literature

- Creating a bibliography for anything related
- Organized and searchable
- Citations available
- Catalog of evaluated compounds

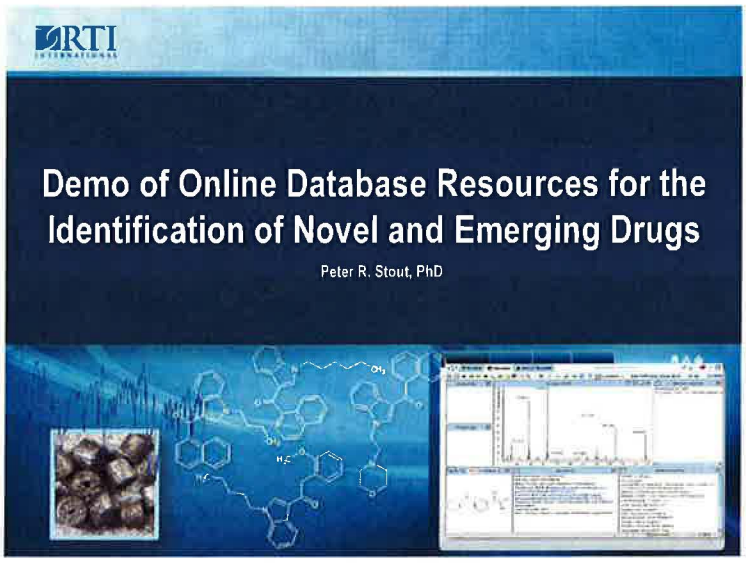
Future of the ACECSA

- First pass at a method
  - Still have criteria to develop
- Presentation of a scientific method
- Public comment / Peer review
- General acceptance (perhaps ASTM)

Questions?

Thank You!

Laura Ciolino
Randall Clark
Terry Dal Cason
Fran Diamond
Dale Forrester
George Jackson
Joey Graves
Heather Harris
Michael Hitchcock
Ling Huang
Justin McShane
John Meyers
Kevin Minbiole
Ashraf Mozayani
Ron Porche
Graham Rankin
Lindsay Reinhold
Warren Samms
Kevin Shanks
Pam Smith
Terry Stouch



Commercial Disclaimer

Overview

Outline

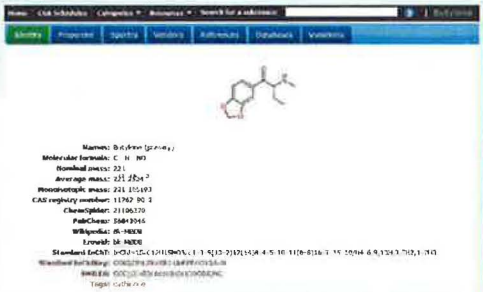
- Overview of existing databases and resources

Cayman Chemical Library

- EI-MS spectra of their forensic related compounds
  - Over 280 synthetic cannabinoids including parent compounds, isomers and metabolites
  - Over 200 emerging drug compounds of different classes
- Free download in NIST and Agilent ChemStation formats
- Frequently updated
- Each version includes a change log

Forendex

- Reference site of emerging compounds
- Over 300 compounds with FITR and EI-MS spectra as PDF files from various contributors
- Links to other databases, references, and vendors
- Name search
- Structure properties
- Active forum



Forensic Drug Review

- Collaboration between Cayman Chemical and SAFS
- PDF of verified compounds from various contributors
- Includes NMR, EI-MS, and FTIR
- Review and Editorial Committee
- Submission Process

SWGDRUG Mass Spectral Library and Drug Monographs

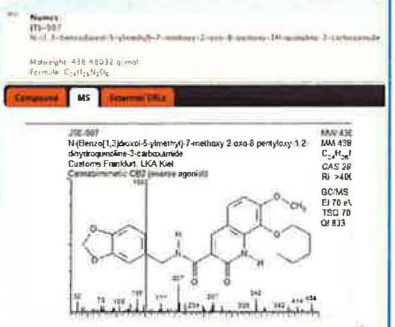
- Freely downloadable in several formats
- Approximately 1,835 spectra of parent compounds, metabolites, and derivatized compounds from various contributors
- No replicate spectra
- Drug monographs
  - peer reviewed data
  - NMR
  - FTIR
  - EI-MS

AAFS Mass Spectral Library

- EI-MS data freely downloadable in Agilent ChemStation or other platform as requested
- Over 2,800 spectra of pure compounds, metabolites and breakdown products
- Includes replicate spectra
- Spectra verified against independent library

Designer Drugs Online 2012

- Freely available EI-MS data
- Not downloadable
- Merged with commercial Mass Spectra of Designer Drugs database yearly
- Searchable by name, fragment and relative intensity
- E-mail sent to registered users with newly emerged drugs
- Reviewed and given a computerized Quality Index
- Molecular Index of Cannabimimetics



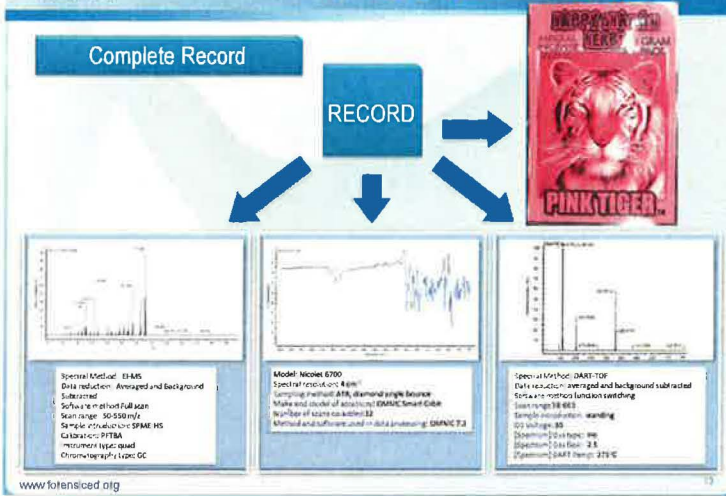
Designer Drug Trends

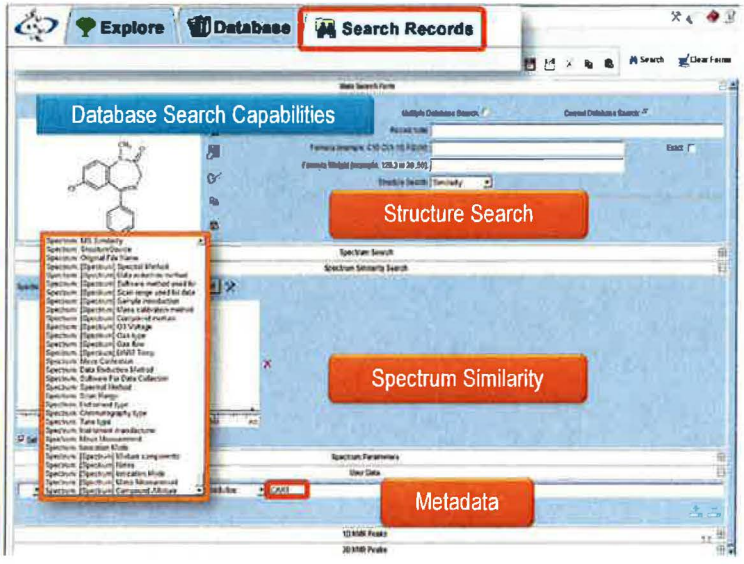
- Provided by NMS Labs
- Online resource for a variety of sectors including scientists, police officers, and policy makers
- Links to research, state-by-state policy and webinars

ForensicDB

- Free, Web-accessible and searchable database
- Over 3,200 records that include one or more instrumental techniques
  - FTIR, EI-MS, DART-TOF, and ESI-QTOF spectra from various contributors
- Replicate spectra
- Peer review process
- Frequent updates
- Download single records as JACAMP files

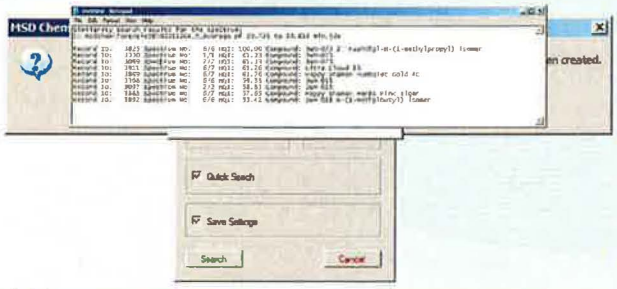
ForensicDB: Database Structure





ForensicDB: Agilent ChemStation

- Developed macros and applications for Agilent Chemstation
- Downloadable from database homepage
- Allows creation of a JACAMP
- Search ForensicDB directly from Agilent Chemstation



ForensicDB: Web-portal

- Developed a Web-portal
- Allows the community to submit spectral data
- Includes submission for EI-MS, DART-TOF, FTIR and other spectral methods
- Users fill out record information
- Users fill out ins

Other Database Resources

- NIST Chemistry WebBook
- Wiley Registry of Mass Spectral Data
- Mass Spectra of Designer Drugs
- MS and GC data of Drugs Poisons, Pesticides, Pollutants, and Their Metabolites
- Wiley Registry of Tandem MS Data
- NIST/EPA/NIH Mass Spectral Library
- Instrumental Data for Drug Analysis

THANK YOU AND CONTACT INFO

forensicDB@rti.org

pstout@rti.org

RTI INTERNATIONAL | **Cheminformatics Database**
www.forensicdb.org

Emerging Trends in Synthetic Drugs

Anthony J. Tambasco
Mansfield Division of Police
Forensic Science Laboratory

Midwestern Association of Forensic Scientists (MAFS)

- 900 Members throughout the U.S.
- Midwest Region includes Ohio, Indiana, Illinois, Iowa, North Dakota, South Dakota, Minnesota, Michigan, Wisconsin.
- Chemistry Section Coordinator – Jillian Baker, DuPage County Laboratory, Illinois
- 2013 Annual Meeting – Dayton, Ohio (September 30- October 4)

February 2010 – AAFS

- "Get Ready for the Cathinones and Synthetic Cannabinoids"
- Laboratory Director, U.S. Customs – Chicago

Michigan

- Substances became controlled in October 2010, August 2011 and July 2012.
- Core Cannabinoid Chemical Group included in the 2012 legislation.
- Any other synthetic compound that is a cannabinoid receptor agonist…not listed in Schedules II – V and is not approved by the federal food and drug administration as a drug.

Michigan

- Non-controlled substances are being reported as such with a follow up call to the agency advising what the substance may be.
- Current emergency ruling covering the substituted phenethylamines are in place until July 2013.

Illinois

- A limited number of synthetic compounds are listed by name with five classes of synthetic cannabinoids.
- State's Attorney's Office is not pursuing analog charges.
- Laboratory will use literature references from two reliable sources in the absence of an available standard.

Illinois

- Rush cases on approval of State's Attorney's Office.
- State law prohibits the use of sampling plans, so each packet is analyzed individually.
- 200 gram maximum.

Illinois

- Traditional GC/MS methods – run times up to 45 minutes.
- Recent drop-off in "Bath Salt" cases.
- Suspected LSD cases negative for LSD have been found to contain NBOMe compounds.

Indiana

- Utilizes CLIC and Cayman for searching by base peak or molecular weight.
- Standards are ordered after preliminary ID.
- Established a "Current Trend" list and forwards the list to the State Board of Pharmacy.

Indiana

- Board of Pharmacy will place the substance under emergency control in approximately 30 days.
- Substance is then considered for permanent control.
- HB 1196 signed by the Governor in 2012 lists Mitragynine (Kratom) as a synthetic drug.

Kentucky

- Structure related legislation.
- Legislation groups "Synthetic Cannabinoids with Piperazines".
- Synthetic Cannabinoids, Piperazines and Synthetic Cathinones use the language "not approved by the United States Food and Drug Administration".

Kentucky

- Pending legislation HB8 – July 2013
- Adding Tetramethylcyclopropanoylindoles, Adamatoylindoles and NBOMe compounds.
- Analysis is two tests and positive ID with at least two reference sources.
- Reports document chemical name (street name) and schedule of control.

Ohio

- House Bill 64 (Spice/K2/Bath Salts – Analogs) - October 2011
- Analog Committee
- House Bill 334 December 2012 – Established Cannabinoid Categories (7) and Substituted Cathinone definition.

Ohio – Court Issues

- State vs. Silmi – December 2012 – Cuyahoga County
- "There is no definition of substantially similar"
- Retired DEA Laboratory Director
- Motion granted to exclude laboratory report.

Ohio – Court Issues

- State vs. Salash – March 2013– Dayton, Ohio
- Defense expert does not request a sample for analysis, only the data files via court order.
- Defense expert uses Automated Mass Spectral Deconvolution & Identification System (NIST)

Ohio – Court Issues

- "…matches declared by the analyst are like beauty, in the eye of the beholder"
- "I reserve the right to amend or change these opinions"
- Motion filed to exclude expert testimony
- Laboratory analysts allowed to testify to structural similarity.
- Convicted to be sentenced in May.

Case Sampling Issues

- New ASCLD/LAB accreditation requirement - How many do we do?
- "We are wrapping up a case that required 1104 GC/MS runs and have two others that are even bigger".
- What about a validated Hypergeometric sampling procedure?

Case Sampling Issues

- "We do straight Hypergeometric - 90% at 95% confidence."
- "I refuse to do hypergeometric sampling. The heck if I or anyone else in the lab is going to explain statistics in court".

Case Sampling

- If you have 49 vials of MDPV a Schedule I, how many will you do?
- GC/MS on all 49 vials.
- 90% at 95% confidence = 19 vials
- Bulk = 10 (20%) = 2 vials

Management Issues

- Time is $$
- Consumable $$
- Instrument backup
- Increases Backlog
- Turn-around time

Local Perspective

- A shirtless man was swimming in a snow bank on Park Avenue West….trying to get away from snipers.
- "This is not your mother's bath salt"

January 2011

- METRICH Enforcement Unit begins undercover purchases.
- What are these things?
- Are they controlled?
- They cost how much?

What Do We Do?

- Call DEA?
- Charge harmful intoxicants?
- "How can you charge me with something I can buy at J and J Foodmart?
- Get these products off the shelves.

June 2011

- Mansfield City Council Prohibits the Use, Possession, and Sale of Synthetic Cannabinoids and Other Synthetic Drugs.
- Other local communities follow utilizing the same legislative format.

June 2011

- METRICH Enforcement Unit advises all businesses involved in the sale of these substances that they have 10 days to remove these products.
- 11 Days later METRICH cleans out 4 businesses that have not complied with the local ordinance.

July 2011

- Law Director review of new cases
- Be careful what you wish for
- Standards are located and purchased
- Laboratory Reports are prepared

MANSFIELD POLICE FORENSIC SCIENCE LABORATORY
DRUG ANALYSIS REPORT

DATE SUBMITTED: October 5, 2011 — REPORT NO: 29740-11
SUBMITTED BY: Ptl. Butler — LAB NO: LAB-111011
DATE ANALYZED: October 16, 2011
CHARGE: Drugs
SUSPECT: [redacted]
OCCURRENCE: 437 Park Avenue West

This report states the results of examinations and tests conducted by this laboratory as part of an official criminal investigation.

ITEMS SUBMITTED:

#1: A sealed plastic bag containing vegetable matter in cellophane. Note: The analysis of the sample revealed the presence of AM2201. AM2201 is currently a banned substance (Synthetic Cannabinoid) in the City of Mansfield

RESULTS OF EXAMINATION:

#1 Vegetable matter, weighing 0.69 grams, failed to reveal the presence of a controlled substance

ANTHONY J. TAMBASCO
FORENSIC SCIENTIST

November 2011 – First Trial

- Trafficking in Harmful Intoxicants
- Testimony of Police Officer making the purchase "Just like Marihuana".
- Testimony of the drug....6 minutes, no cross examination.
- Testimony of Ph.D Forensic Toxicologist.
- Guilty – 2 years suspended - $$

What's Next?

- MDPV begins to vanish – "Bath Salts" are gone
- Window Cleaner?
- $19.00 a package…
- Pyrovalerone appears – Schedule V Controlled Substance

Next Wave

- Pyrovalerone goes away
- Pipe Cleaner
- Stain Remover
- Hookah Cleaner
- Alpha-Pyrrolindinopentiphenone appears

June 2012

- Bath Salt sample, packaging begins to disappear, samples are in vials.
- Possible 4-Methyl-a-pyrrolindohexiophenone (MPHP), 4-Methyl-a-PVP (MPPP) and Benzocylidine appear in separate cases .

June 2012

- 5-Methoxy-diisopropyltryptamine (5-MeO-DiPT) appears in suspected ecstasy tablets.
- No standards, save for a rainy day.

June 2012 – White Rabbit

- 5-fluoro UR-144 (XLR11)
- UR-144
- URB-602
- URB-754
- AKB48
- Next generation of synthetic cannabinoids - no standards, another rainy day.

August 2012 – 1 Case

- Ethylone
- Ethylphenidate
- 4-MeMABP
- Methiopropamine
- Pentradone

September 2012 – Guilty Plea

- 5300 units of MDPV
- Four year sentence
- Included a bribery case involving an MPD officer.
- Conspiracy to commit felonious assault.

Current Trend

- Local "smoke shops" are sending samples to us.
- They continue to receive "Certificates of Analysis" indicating the absence of synthetic cannabinoids and even refer to Ohio House and Senate Bill numbers.
- They all have been found to contain the new URB compounds or AM2201.

What's Next?

- March 2013 PB-22 & 5-fluoro PB-22 indicated in samples.
- Notified local agencies of new synthetic cannabinoids.
- Cities of Shelby and Ontario ban PB-22, 5-fluoro PB-22 and BB-22 in April 2013.
- I'm waiting for a rainy day.

Emerging Trends in Synthetic Drugs Workshop

Southwestern US

May 1, 2013

Roger Schneider
Phoenix Police Department
Laboratory Services Bureau
Controlled Substances Section

Nevada

Sources:

Diane Machen, Washoe County Sheriff's Office, Forensic Science Division

David Gouldthorpe, Las Vegas Metropolitan Police Department, Forensic Laboratory

Nevada

- Nevada generally follows the Federal CS Schedules with other emerging controlled substances added by definition via the Nevada State Board of Pharmacy from input provided by crime labs and others.
- Defined in the Nevada Revised Statutes, Chapter 453 and the Nevada Administrative Code, Chapter 453.

Nevada

- Nevada Analogue Statute
- 'chemical structure substantially similar to…' **AND** 'stimulant, depressant, hallucinogenic effect… substantially similar'

Nevada

- Nevada Analogue Statute Use
  - Not being used
- Lack of prosecutorial resources. Large number of non-analogue cases vs. a small number of analogue cases
- Lack of reliable effect data

Nevada

- Nevada Emerging Controlled Substances
- Washoe County: 6-8 items per quarter in 2012. Items varied between synthetic cannabinoids, substituted cathinones, and 2C related compounds.
- LVMPD: Emerging controlled substances are a small part of day-to-day business. Synthetic cannabinoids>substituted cathinones>>2C related compounds.

Nevada

- Nevada Analytical Changes
- Washoe County and LVMPD are considering adding GC-IR to enhance controlled substance identification.

Utah

Source:

Jennifer McNair, Utah Department of Public Safety, Forensic Services Division

Utah

- Utah generally follows the Federal CS Schedules with other emerging controlled substances added by legislative action (Listed Controlled Substances; substituted cathinones and synthetic cannabinoids)
- Defined in the Utah Code, Title 58, Chapter 37.

Utah

- Utah Analogue Statute

  a. 'chemical structure substantially similar to…' ;

  b. 'stimulant, depressant, hallucinogenic effect… substantially similar'
- The word **AND** is not used between a. and b.

Utah

- Utah Analogue Statute Use
  - Routinely being used
- Synthetic cannabinoids (e.g. AM-694, AM-2201)
- Mixed trial outcomes

Utah

- Utah Emerging Controlled Substances
- Large number of synthetic cannabinoids, substituted cathinones, and 2C compounds received in evidence.
- ~30% of the evidence submitted to the lab is emerging drugs.

Utah

- Utah Analytical Changes
- Utah DPS does not test marijuana. The lab trains local law enforcement agencies to identify marijuana.
- GC/MS Pilot Program – grant funds were used to purchase a portable GC/MS unit. FIDOs will screen suspected controlled substances by GC/MS and library search prior to submitting them to the lab.

Colorado

Source:

Barry Shearer, Colorado Bureau of Investigation, Forensic Services Section

Colorado

- Colorado generally follows the Federal CS Schedules with other emerging controlled substances added by legislative action (e.g. cathinones, synthetic cannabinoid)
- Defined in the Colorado Revised Statutes, Chapter 18, Article 18.

Colorado

- Colorado Analogue Statute
- 'chemical structure substantially similar to…' **AND** 'stimulant, depressant, hallucinogenic effect… substantially similar'

Colorado

- Colorado Analogue Statute Use
  - Routinely being used
- Synthetic cannabinoids

Colorado

- Colorado Emerging Controlled Substances
- Large number of synthetic cannabinoids and substituted cathinones received in evidence
- Limited number of 2C compounds received in evidence

New Mexico

Source:

New Mexico Department of Public Safety, Forensic Laboratory Bureau, Controlled Substances Unit

- Laura Hernandez
- Adam Wolff

New Mexico

- New Mexico generally follows the Federal CS Schedules with other emerging controlled substances added by definition via the New Mexico Board of Pharmacy from input provided by crime labs and others at public hearings.
- Defined in the New Mexico Administrative Code, Title 16, Chapter 19, Part 20.

New Mexico

- New Mexico Analogue Statue
- 'chemical structure substantially similar to…' **OR** 'stimulant, depressant, hallucinogenic effect… substantially similar'
  - synthetic cannabinoids defined by name (or analogues or homologues) e.g. AM-2201
  - synthetic cannabinoids defined by structural class e.g. naphthoylindoles with specific substitutions e.g. indole N substituted by haloalkyl

New Mexico

- New Mexico Analogue Statue
- Synthetic cannabinoids continued:
  - requires cannabinoid receptor binding activity. Which receptor is not specified.
- Substituted cathinones defined by name e.g. alpha-PVP

New Mexico

- New Mexico Analogue Statue Use
  - Not being used

New Mexico

- New Mexico Emerging Controlled Substances
- Synthetic cannabinoids>substituted cathinones>>2C related compounds.

Arizona

- Arizona does not follow the Federal CS Schedules.
- Three main drug categories:
  - Marijuana
  - Dangerous Drugs
  - Narcotic Drugs

Arizona

- Historically, no analogue statue.
- Defined in the Arizona Revised Statutes, Title 13, Chapter 34. Emerging controlled substances added by legislative action.
- April 3, 2013 HB2327 signed into law
- Adds synthetic cannabinoids, substituted cathinones and 2C compounds by name.

Arizona

- HB2327 continued:
- Adds 'mimetic' substances
  - Cannabimimetic
  - Cathinomimetic
  - Methoxyphenethylamine mimetic
- ACMD-like language, but specific substitutions are not defined.

Arizona

- HB2327 continued:
- Not tied to effects
- Not tied to receptor activity
- No exclusions listed

Arizona

- HB2327 continued:
- Cannabimimetic example:

3-(NAPHTHOYL)INDOLE OR 3-(NAPHTHYLMETHANE)INDOLE BY SUBSTITUTION AT THE NITROGEN ATOM OF THE INDOLE RING, WHETHER OR NOT FURTHER SUBSTITUTED ON THE INDOLE RING TO ANY EXTENT, WHETHER OR NOT SUBSTITUTED ON THE NAPHTHOYL OR NAPHTHYL RING TO ANY EXTENT.

Arizona

- HB2327 continued:
- Cathinomimetic:

...DERIVED FROM CATHINONE, (2-AMINO-1-PHENYL-1-PROPANONE) BY ANY SUBSTITUTION AT THE PHENYL RING, ANY SUBSTITUTION AT THE 3 POSITION, ANY SUBSTITUTION AT THE NITROGEN ATOM OR ANY COMBINATION OF THE ABOVE SUBSTITUTIONS.

Arizona

- HB2327 link:
- www.azleg.gov
- Bills, Bill Info, HB2301 through 2350
- HB2327, Bill Versions: Show Versions, House Engrossed

Arizona

- Emerging controlled substances seen in evidence since early April 2013:
- PB-22 (QUPIC)
- Fluoro PB-22

Arizona

- Phoenix PD Analytical Changes
- Raman Pilot Program – grant funds were used to purchase a portable Raman spectrometer. FIDOs will screen suspected controlled substances by Raman.
- Maricopa County Attorney's Office will charge individuals based on FIDO's field identification.

Arizona

- Another approach to emerging controlled substances…
- Yavapai County
- Public Nuisance Lawsuit
- Filed against individuals and businesses selling 'Spice' and 'Bath Salts'
- Cites Federal analogue statute
- Cites burden imposed on law enforcement, public health system and public safety

Arizona

- Yavapai County: Public Nuisance Lawsuit
- "The acquisition, possession, sale and transfer of any and all synthetic cannabinoids, synthetic cathinones, and their analogues, as defined by the federal Controlled Substances Act, 21 U.S.C. § 801 et seq., (collectively referred to as "dangerous synthetic drugs"), is a Public Nuisance pursuant to A.R.S. § 13-2917."

Arizona

- Yavapai County: Public Nuisance Lawsuit link http://www.yavapai.us/coatty/press-releases/court-pleadings-bath-salt-ban/

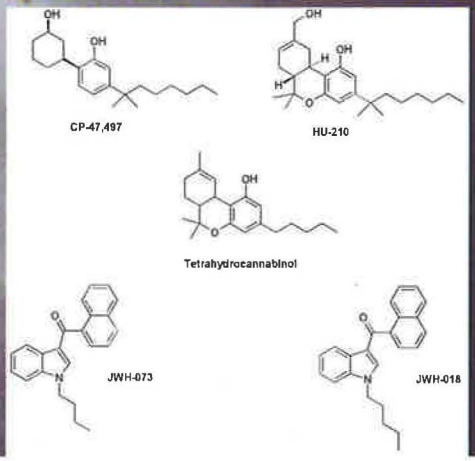
Thank You

- NIST and DEA
- WCSO, LVMPD, Utah DPS, CBI, New Mexico DPS, Arizona DPS, Mesa PD
- Phoenix PD, Laboartory Services Bureau, Controlled Substances Section

COLOR TESTS AND ANALYTICAL DIFFICULTIES WITH EMERGING DRUGS OF ABUSE

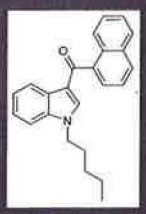
Jeremiah Morris
Johnson County Sheriff's Office
Criminalistics Laboratory

Synthetic cannabinoids



Presumptive tests - failures

- Nothing suitable published so far
- No color with Duquenois-Levine
- Structural interferences
  - para-Dimethylaminobenzaldehyde reagent (Ehrlich's)
  - Test with glutaconic aldehyde
- Vegetation interferences
  - Fast Blue B and 2B reagents
  - Sulfuric based color tests
  - UV fluorescence of indole nucleus
  - Color test for aromatic carbonyls



Presumptive test – success!

- Most cannabinoids react with Liebermann's

Reference	Cannabinoid Chemical Class	Source	Color
JWH-307	Naphthoylpyrrole	Reference Collection	Dark Yellow
AB-001	Adamantoyl indole	Reference Collection	Dark Yellow
CB-13	Dinaphthylene methanone	Reference Collection	Dark Green
JTE-907	1,2-Dihydroquinoline-3-carboxamide	Reference Collection	Black (Bubbling)
UR-144	Tetramethylcyclopropanoylindole	Reference Collection	Dark Red
URB597	FAAH inhibitor	Reference Collection	Yellow-Brown
URB602	FAAH inhibitor	Reference Collection	Dark Brown
URB754	FAAH inhibitor	Reference Collection	Light Brown
AM-1248	Adamantoyl Indole	Reference Collection	Dark Yellow
AB-034	Tetramethylcyclopropanoylindole	Reference Collection	Red-Orange>Dark Red
A-796, 260	Tetramethylcyclopropanoylindole	Reference Collection	Red-Orange>Dark Red
A-834-735	Tetramethylcyclopropanoylindole	Reference Collection	Red-Orange>Dark Red
FUR-144	Tetramethylcyclopropanoylindole	Reference Collection	Dark Red
AKB48	Adamantyl amidoindazole	Reference Collection	No color change
JWH-073	Naphthoylindole	Cayman Chemical	Yellow-Brown
JWH-018	Naphthoylindole	Cayman Chemical	Yellow-Brown
JWH-200	Naphthoylindole	Cayman Chemical	Dark Yellow-Brown
AM-2201	Naphthoylindole	Cayman Chemical	Yellow-Brown
JWH-203	Phenylacetylindole	Cayman Chemical	Yellow-Orange
RCS-4-C4 homolog	Benzoylindole	Cayman Chemical	Brown
AM694	Benzoylindole	Cayman Chemical	Dark-Yellow
MAM2201	Naphthoylindole	Cayman Chemical	Green-Brown
AM2233	Benzoylindole	Cayman Chemical	Yellow
STS-135	Adamanty lamidpindole	Reference Collection	Brown

Extraction procedure

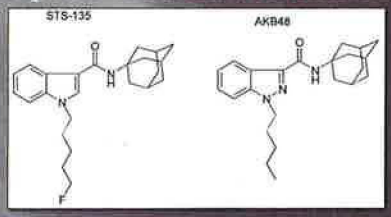
- A small amount of vegetative sample was added to a clear test tube followed by enough methylene chloride-acetonitrile solution to fully immerse the sample. The tube was then shaken quickly and the liquid was immediately pipetted off of the sample and into another clear test tube. Several drops of Liebermann's reagent were then added to the liquid and mixed thoroughly. Samples containing synthetic cannabinoids formed a yellow, yellow-orange, orange, to orange-red color. A negative result was indicated by no color change or a white color. A blank was also prepared for side-by-side comparisons of the blank and the samples.

Results of commercial products

Product Name	Cannabinoids Present	Color
Green Buddha	AM-2201, JWH-122, AM-2233	Yellow-Orange
Zombie Matter	Fluoro UR-144	Yellow-Orange
Space Monkey	AM-2201, JWH-122	Yellow
K8	Fluoro UR-144	Orange
Juicy Chong	AM-2201	Light Yellow
Cherry Cheech	AM-2201	Light Yellow
Hindu Magic	AM-2201	Light Yellow
Ultra Cloud 10	Fluoro-amphetamine, AM-2201	Yellow-Green
Happy Hour	None	White
Wicked X	None	Clear
Canna Boost	No Cannabinoids, Yohimbine	Light Orange
Bang!	JWH-250, JWH-081	Yellow-Orange
Devilz Lettuce	None	White-Yellow
Mary Jane Private	UR-144, JWH-122	Orange
Mary Jane Watermelon	UR-144	Orange
Impact Cotton Candy	AM-2201	Yellow
Impact Blueberry	UR-144	Orange
Mind Wave Blueberry	UR-144	Orange
Marijuana	None	Dark Brown
Salvia	None	Light Brown
Mary Jane Kratom	None	Brown (Bubbling)
White Rabbit KratumMaeng Da	None	Blue>Brown (Bubbling)

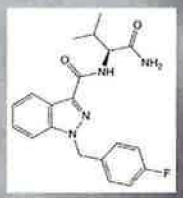
Other comments about presumptive testing

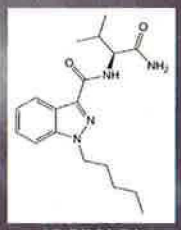
- AKB48 (an adamantyl indazole carboxy amide) does not produce a color with Liebermann's

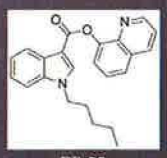


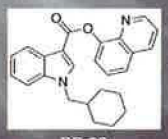
- Other positive reactions reported with Meyer's and other general alkaloid reagents

What about these cannabinoids?


AB-FUBINACA


AB-PINACA


PB-22


BB-22

Substituted cathinones

Unsubstituted
3- or 4-methyl
3- or 4-halo (F, Cl, Br, or I)
3- or 4-ethyl
3- or 4-hydroxy
3- or 4-methoxy
3,4-methylenedioxy
3,4-dimethyl
3,4-dihalo (F, Cl, Br, or I)
Replace phenyl with naphthyl

Propyl
Butyl
Pentyl
Hexyl

Unsubstituted
N-methyl
N-ethyl
N,N-dimethyl
Pyrrolidine
Phthalamido
N-benzyl

Grand total of 672 possible combinations

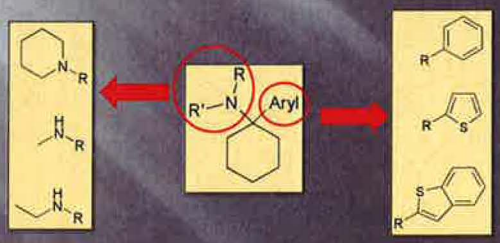
Presumptive tests

Compound	Marquis	Liebermann's	Mecke	Froehde	CoSCN (a)	Nitrite	Modified CoSCN
4-Me-PPP	—	Orange	—	—	Blue	Slow blue	—
Brephedrone	—	Yellow	—	—	—	Blue	Purple
4-MEC	—	Orange	—	—	Blue	Blue	Purple
Pentedrone	—	Yellow	—	—	Blue	Blue	Light purple/blue
4-methyl buphedrone	—	Yellow	—	—	Blue	Blue	Blue
Buphedrone	—	Yellow	—	—	—	Blue	—
Butylone	Yellow	Yellow→ brown	Yellow→ orange	Yellow→ green	Blue	Blue	Purple
3, 4-DMMC	Green particles (?)	Orange	—	Light brown	Blue	Blue	—
Naphyrone	Green	Brown	Brown-orange	Orange	—	—	—
Benzedrone	—	Orange	—	—	—	—	—

Note – all produce either no color or just blue specks with *acidified* CoSCN

Arylcyclohexylamines

- Comprise the most common class of dissociatives
  - Complex pharmacology
  - CNS appears dose dependent and spans entire range



11

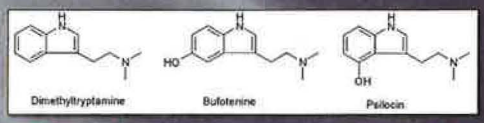
Presumptive tests

Compound	Marquis	Liebermann's	Mecke	Froehde	Co(SCN)4 (a)	Na nitro	Modified Co(SCN)
4-MeO-PCP	Slow red	Brown	Yellow→ green→ red	Light yellow	Blue	—	—
Methoxetamine	Slow pink	Orange-brown	Yellow→ green→ red	Yellow-green	Blue	—	—
Fluorolintane	—	Pale yellow	—	—	Blue	—	Lavender ppt
3-HO-PCE	Brown	Dark brown	Brown	Black	Weak blue	—	—

12

Tryptamines

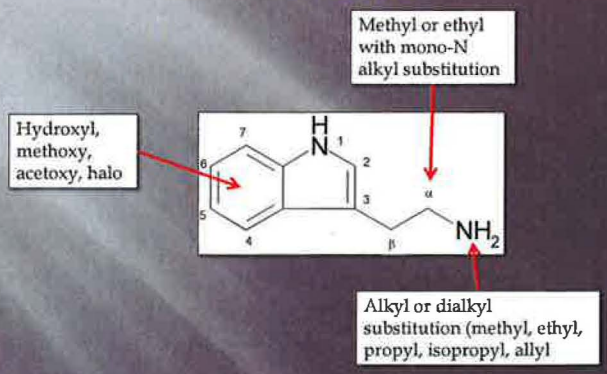
- Class of highly potent hallucinogens
  - Present in a diverse group of botanical materials
  - All contain substituted indole compound





13

Variations on a tryptamine theme



14

Presumptive tests

Compound	Marquis	Liebermann's	Mecke	Froehde	Co(SCN)4 (a)	Na nitro	PDMB
5-MeO-DALT	Olive→ black	Dark brown/black	Olive→ brown	Yellow	—	—	Purple
4-methyl-aET	Light brown	Brown	Brown	—	—	—	Purple
4-AcO-DALT	Yellow→ brown	Black	Black	Yellow→ green	Blue	—	Purple
4-HO-MET	Yellow→ brown	Black	Black	Yellow→ green	Blue	—	Purple
4-HO-MIPT	Yellow→ brown	Black	Black	Yellow→ green	Blue	—	Purple
4-AcO-DET	Yellow→ brown	Black	Black	Yellow→ green	Blue	—	Purple

15

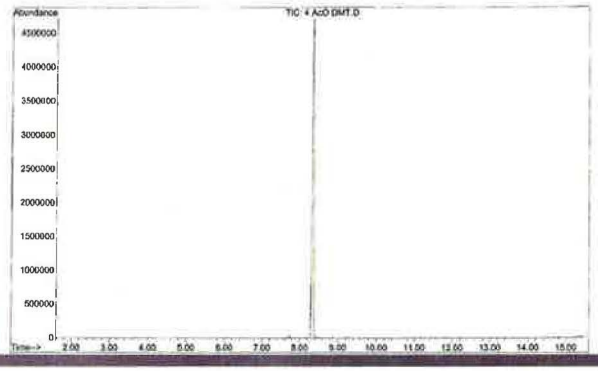
Issues with acetoxy compounds

- Vendors beginning to sell acetoxy tryptamines
  - 4-AcO-DMT (acetylated psilocin)
  - 5-AcO-DALT
- A number of reports about 4-AcO-DMT being unstable and converting into psilocin
  - As solid (slightly over a few months)
  - In solution (within a day)
  - During acid-base extractions
- This is a concern because psilocin is controlled while 4-AcO-DMT is not.

16

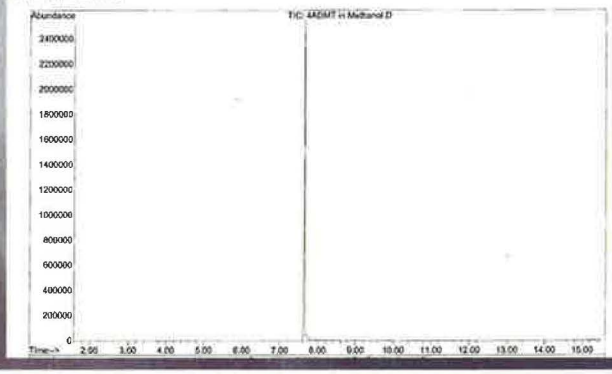
Initial analysis

```
File       :C:\MSDChem\1\DATA\MFRC screen data\4 AcO DMT.D
Operator   :
Acquired   : 21 May 2012  14:21      using AcqMethod TEMPRO.M
Instrument :    HP1
Sample Name: 4-acetoxy-dimethyltryptamine
Misc Info  : 4-AcO-DMT, lot# MFRC-2012-A44
Vial Number: 13
```



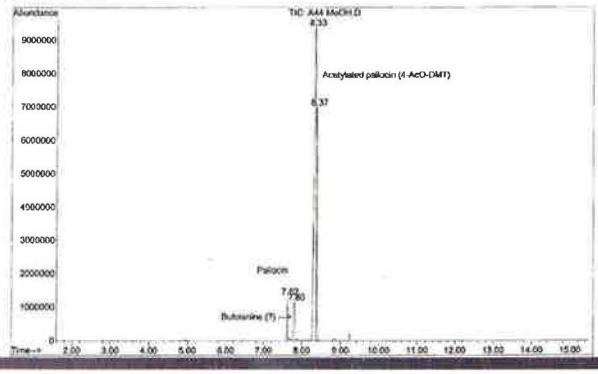
One month later

```
File       :C:\MSDChem\1\DATA\MFRC OFFICIAL DATA\4AOMT in Methanol.D
Operator   :
Acquired   : 16 Jun 2012  00:21      using AcqMethod TEMPRO.M
Instrument :    HP1
Sample Name: 4-Aco-DMT A44
Misc Info  : Lot# MFRC-2012-A44, in basic Methanol
Vial Number: 43
```



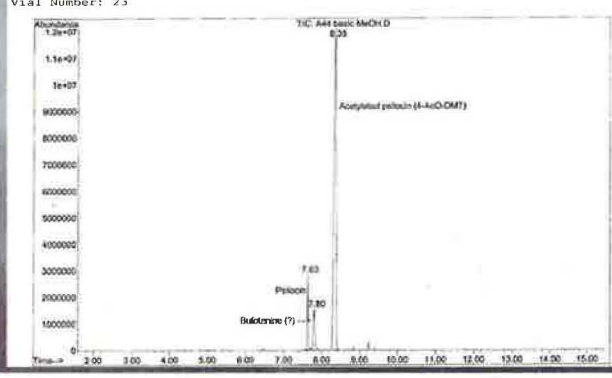
Two months later

```
File       :C:\MSDChem\1\DATA\080712\A44 MeOH.D
Operator   :
Acquired   :  7 Aug 2012  16:21      using AcqMethod TEMPRO.M
Instrument :    HP1
Sample Name: A44
Misc Info  :
Vial Number: 22
```



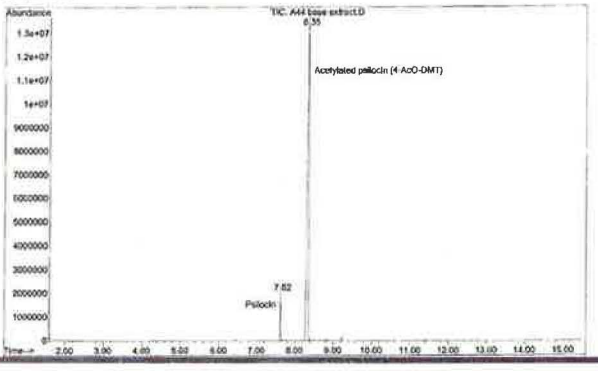
Basic methanol

```
File       :C:\MSDChem\1\DATA\080712\A44 basic MeOH.D
Operator   :
Acquired   :  7 Aug 2012  16:41      using AcqMethod TEMPRO.M
Instrument :    HP1
Sample Name: A44
Misc Info  :
Vial Number: 23
```



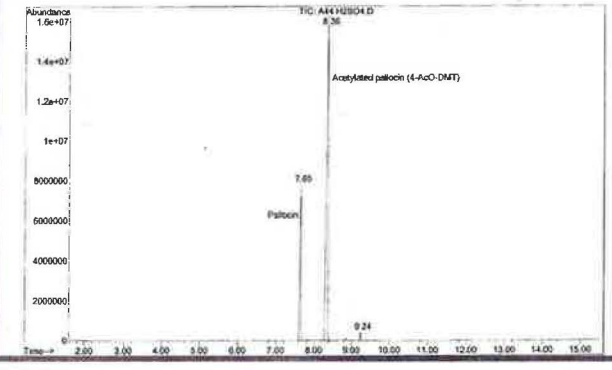
Basic extract

```
File       :C:\MSDChem\1\DATA\080712\A44 base extract.D
Operator   :
Acquired   :  7 Aug 2012  17:00      using AcqMethod TEMPRO.M
Instrument :    HP1
Sample Name: A44
Misc Info  :
Vial Number: 24
```



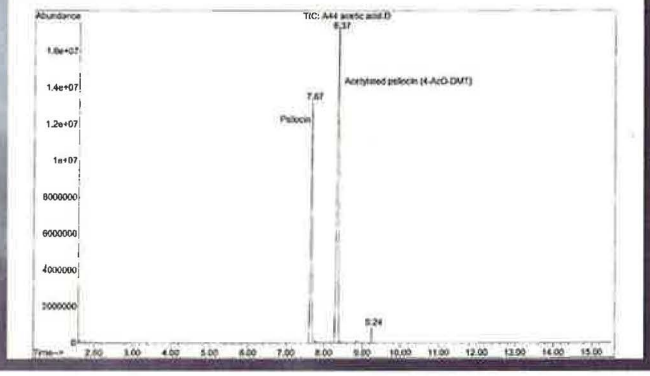
Acid/base extract (H_2SO_4)

```
File       :C:\MSDChem\1\DATA\080712\A44 H2SO4.D
Operator   :
Acquired   :  7 Aug 2012  17:20      using AcqMethod TEMPRO.M
Instrument :    HP1
Sample Name: A44
Misc Info  : 0.1 N H2SO4 then base extract
Vial Number: 25
```



Acid/base extract (acetic acid)

```
File          :G:\MSDChem\1\DATA\080712\A44 acetic acid.D
Operator      :
Acquired      :  7 Aug 2012  17:40      using AcqMethod TEMPRO.M
Instrument    :    HP1
Sample Name: A44
Misc Info     : 10% acetic Acid then base extract
Vial Number: 26
```

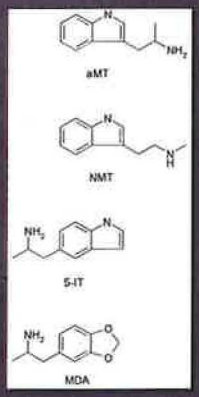


Recommendations

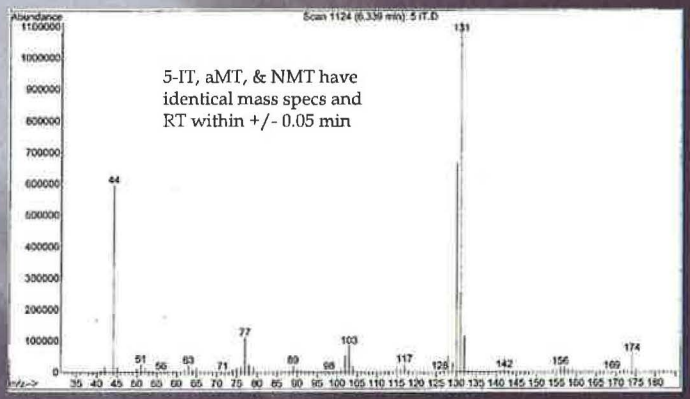
- Remember, these are just my thoughts!
- If your 4-AcO-DMT sample has low levels of psilocin you don't know if it was there originally (degradation over time)
- All psilocin/4-AcO-DMT mixtures should be re-analyzes using either methanol extract or basic methanol extract to exclude extraction degradation
- Be *extremely* cautious about reporting out psilocin in these cases

5-IT

- 5-(2-Aminopropyl)indole
  - 5-IT
  - Only recently hit markets in Europe
  - Positional isomer of *alpha*-methyltryptamine (aMT) and N-methyltryptamine (NMT)
  - 5-IT and aMT often sold by same vendors
- This is a problem

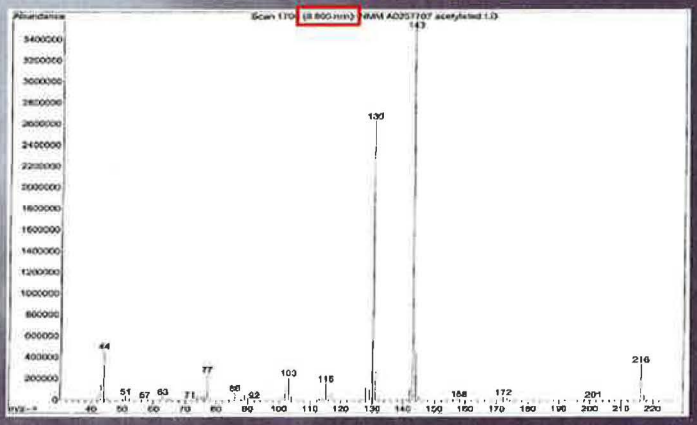


GC/MS results

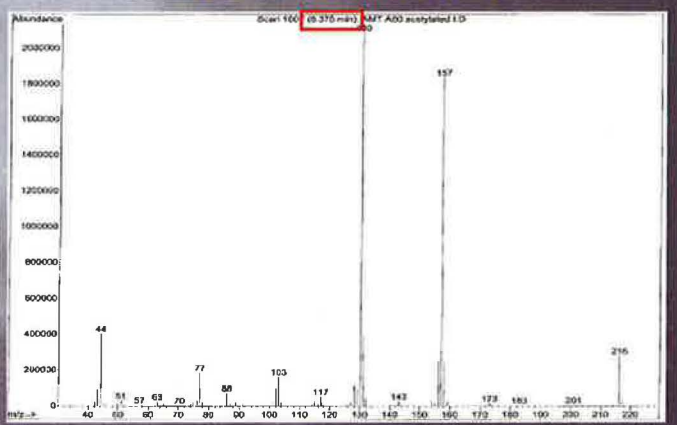


5-IT, aMT, & NMT have identical mass specs and RT within +/- 0.05 min

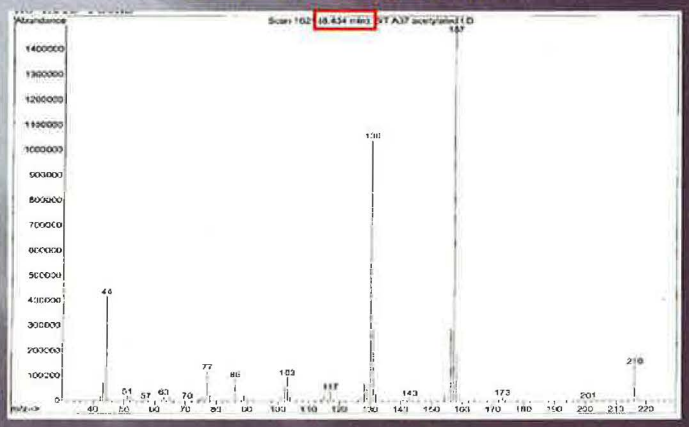
Acetylated NMT



Acetylated aMT



Acetylated 5-IT



Where we stand

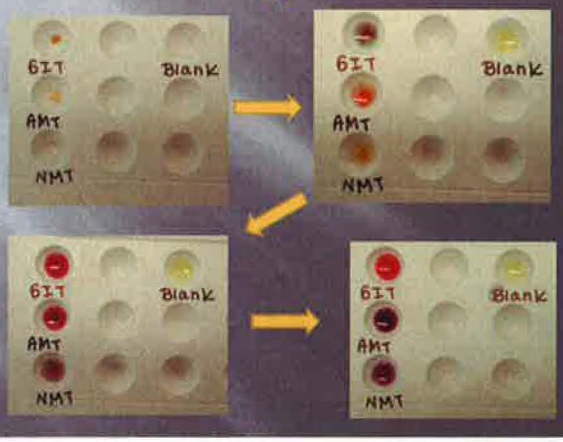
- All three have identical MS and indistinguishable retention times as parent compounds
- NMT separates out from aMT and 5-IT when acetylated
- aMT and 5-IT have indistinguishable RTs but slightly different mass specs
- Is this enough?

Other options

- FTIR
  - All three easily differentiated
  - Sample purity is critical
- TLC
  - Some Rf differences with *Clarke's* TA solvent (10 cm plate)
  - What about 20 cm plate?
- Color tests

Compound	Marquis	Liebermann	Mecke's	Froehde's	PDMB	Cinnamoyl
aMT	Yellow-brown	Black	Brown	Yellow	Purple	Red → purple
5-IT	Dark red	Dark brown	Brown	Red brown	Red	Red

p-Dimethylaminocinnamaldehyde reagent



What does this mean?

- NMT easily excluded with aceytlation
- 5-IT verses aMT? → Your call
  - If pure enough for IR, you're golden
  - Are aceytlated derivatives different enough?
  - Are color test differences enough?
- You must carefully consider what you can actually report out with possible aMT sample

Presumptive color tests (misc)

Compound	Marquis	Liebermann	Mecke's	Froehde's	CoSCN	Na Nitro
5-APB	Black	Black	Black	Dark purple	—	—
6-APB	Purple	Dark purple	Purple	Purple	—	—
Camfelamine	Orange → red	Dark red	Yellow	Tan→ dark yellow	Blue	Blue
Methiopropamine	Dark brown	Dark brown	Black	Light brown	—	Blue
MDAI	Orange	Green→ black	Green	Green→ black	—	—
5-IAI	Brown	Dark brown	Brown	Orange	—	—
Allylescaline	Dark red	Brown-black	Yellow→ brown (fast)	Green→ black (fast)	—	Green particles
2C-T-2	—	Red	Orange→ red→ purple	Orange → purple	—	Green specks
2C-P	Yellow	Green	Green	Green	—	—
β-methoxy-2C-D	Purple	Green	Brown→ green	Red	—	—

Acknowledgements

- Special thanks to:
  - Malinda Spangler
  - Bethany Poyner
  - Jason Stenzel
  - Elizabeth Kiely
- This work was funded by subcontract SC-12-370 through Ames Laboratory and the Midwest Forensic Resource Center

Questions?

Sampling Approaches to Synthetic Drug Seizures

Jill M. Head
Supervisory Chemist
Special Testing and Research Laboratory
Drug Enforcement Administration

Why are sampling plans used?

- To determine the net weight of a population
- To determine the presence of a drug in a population
- Limited resources (efficiency, cost, etc.)

To "...minimize the total number of required analytical determinations, while assuring that all relevant legal and scientific requirements are met."

SWGDRUG Recommendations Part III A

When are sampling plans used?

Processing Facility

Forensic Laboratory

Processing Facilities

What may be present?

- Powder
- Solvents
  - Acetone, alcohol
- Plant Material
  - Dosed and Undosed
- Packages
- Equipment
  - Sprayers, mixers, etc.

Laboratory Sampling

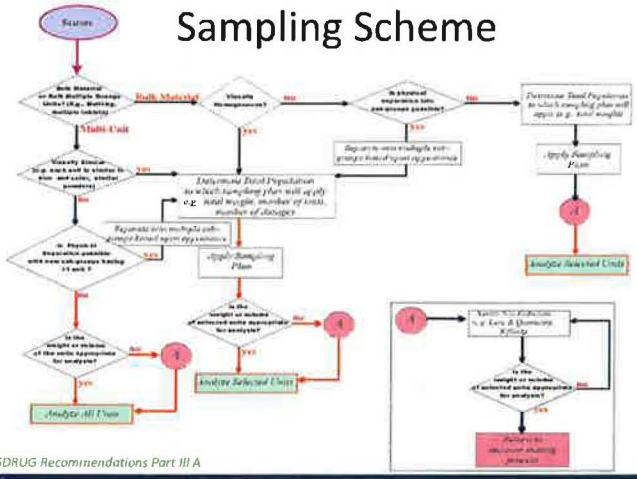
One submission may be hundreds or thousands of packets

Sampling Approach Design

Consider:

- ✓Laws
- ✓Jurisdictional requirements
- ✓Purpose of the investigation
- ✓Customer requests
- ✓Current laboratory policies
- ✓Accreditation requirements

Sampling Scheme



SWGDRUG Recommendations Part III A

Sampling Plans

Statistical	Non-Statistical
Inferences can be made about the entire population	No inferences are made about the population
▪ Hypergeometric	▪ All/One
▪ Bayesian	▪ Square root
	▪ Judicial Requirements

Example 1

You open a box containing multiple packets of the same brand of suspected cannabimimetics

Example 1

Are there multiple units?

Yes

Are they visually similar?

Yes

Determine total population

1000

Apply Sampling Plan

Hypergeometric

- Commonly used in controlled substance analysis cases
- "The probability that a sample of size n contains X positives (units containing illegal drugs), given that the population of size N contains N_1 positives..."

Guidelines on Representative Drug Sampling, ENFSI

Example 1

Population	95% confidence			99% confidence		
	K=0.5	K=0.7	K=0.9	K=0.5	K=0.7	K=0.9
800	5	9	28	7	13	42
900	5	9	28	7	13	43
1000	5	9	28	7	13	43
5000	5	9	29	7	13	44

Where k=ratio of positives guaranteed in the population

Consider laws, jurisdictional requirements, lab policy, and the purpose of the investigation

Analyzing 28 items will guarantee with 95% confidence that at least 90% of the packages contain that drug.

Example 2

You open a box containing multiple packets of many different brands of suspected cannabimimetics

Example 2

Are there multiple units?
Yes
Are they visually similar?
No
Is physical separation possible?
Yes
Separate and determine total population
31 brands, 125 units
Is the weight of the units appropriate for analysis
Yes
Apply Sampling Plan

Example 2

Population	95% confidence			99% confidence		
	K=0.5	K=0.7	K=0.9	K=0.5	K=0.7	K=0.9
1-9	All	All	All	All	All	All
10	3	5	8	4	6	9
20	4	6	12	5	9	15
↓	↓	↓	↓	↓	↓	↓
100	5	8	23	7	12	33
200	5	9	26	7	13	38

If the same approach is taken as in Example 1, all 125 units would be analyzed

Threshold

- Non-statistical sampling plan
- Analyze samples to meet an established threshold

Example:
3000 vials of suspected cocaine base
Threshold is 50g
*Analyze up to 50g of the sample

What are the threshold limits for cannabimimetics and cathinones?

Laboratory Sampling

There is known variability between packets of different brands and even within the same brand

BUT

we can use the knowledge of the dosing process to assist in developing a sampling span

Other Non-Statistical Approaches

Variable results may be due to:

- Small sampled portions which can give hot spots or false negatives
- Multiple components present from contamination in sprayers, cement mixers, etc.

DEA Special Testing and Research Laboratory
Emerging Trends Program

When choosing a plan...

- ✓Evaluate statistical and non-statistical plans
- ✓Evaluate the legislative need
- ✓Address SWGDRUG recommendations
- ✓Address accreditation requirements

Document "...the sampling plan and procedures used by the laboratory or other bodies where these are relevant to the validity or application of the results"

ASCLD-Lab ISO/IEC 17025:2005(E)

DEA Special Testing and Research Laboratory
Emerging Trends Program

Best plan...

DOCUMENTATION

Reports should be clear regarding what has been tested and NEVER state more than you actually know.

DEA Special Testing and Research Laboratory
Emerging Trends Program

Resources

SWGDRUG
www.swgdrug.org

European Network of Forensic Science Institutes, Guidelines on Representative Drug Sampling
www.enfsi.eu

American Society for Testing Materials
www.astm.org

DEA Special Testing and Research Laboratory
Emerging Trends Program

Thank you!

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Drug Enforcement Administration
Special Testing and Research Laboratory

GCMS Analytical Information

Joshua C. Yohannan
Forensic Chemist
Special Testing and Research Laboratory
Drug Enforcement Administration

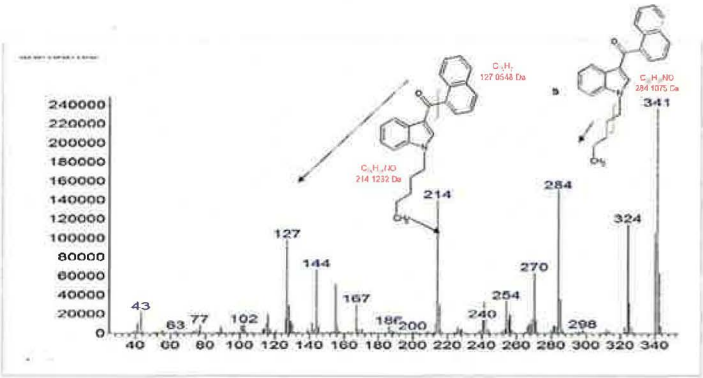
Goals

- GCMS Fragmentation
  - Nitrogen Rule
  - Isotope ratios
  - Synthetic cannabinoid fragmentation patterns
- Cyclopropyls
  - Ring-opened products
- URB597
- Isomers
  - JWH Methoxy isomers
  - AM2201 isomers
  - Azepene/Azepane
- Derivitization
  - Fluoromethamphetamine isomers
  - UR144 – ring opened – alcohol
- PB-22

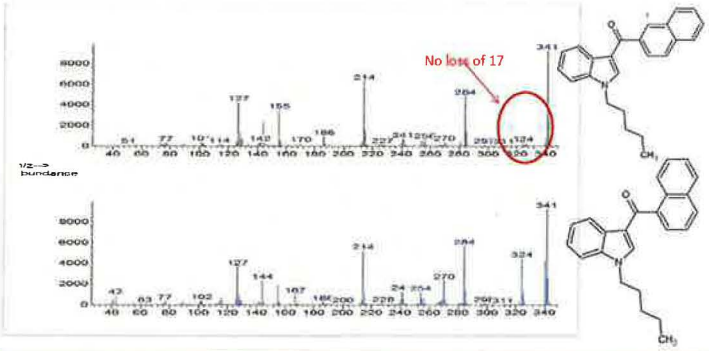
GCMS Fragmentation

- Fragmentation can be predicted to occur at the site with the lowest ionization energy
- Nitrogen Rule
  - A compound with an even molecular weight will have zero or an even number of nitrogens
  - A compound with an odd molecular weight will have an odd number of nitrogens
- Isotope ratios (M:M+2)
  - Chlorine – 3:1
  - Bromine – 1:1

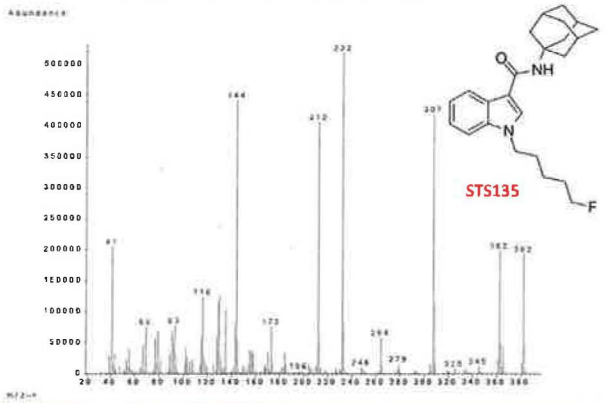
JWH-018 Fragmentation



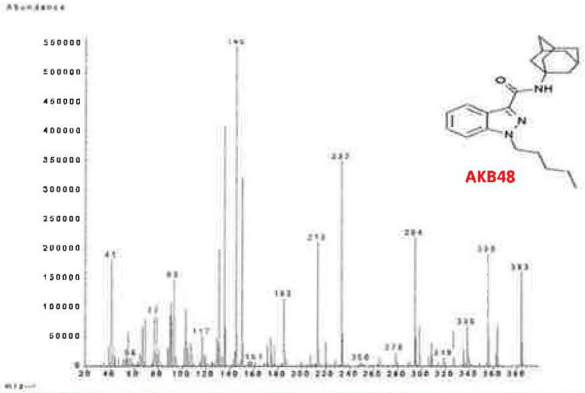
2 vs. 1-Naphthyl Isomer of JWH-018



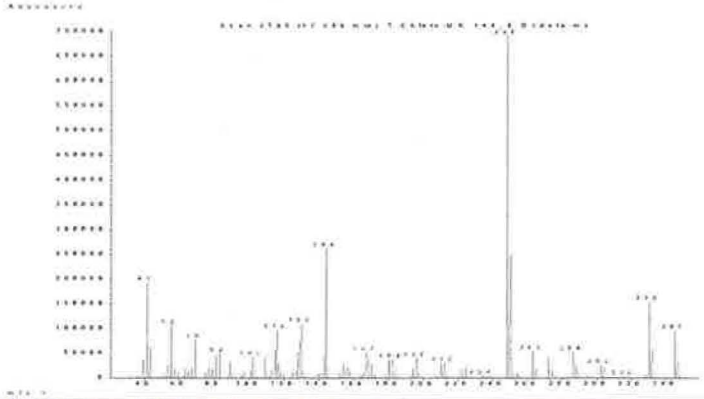
Indole vs. Indazole



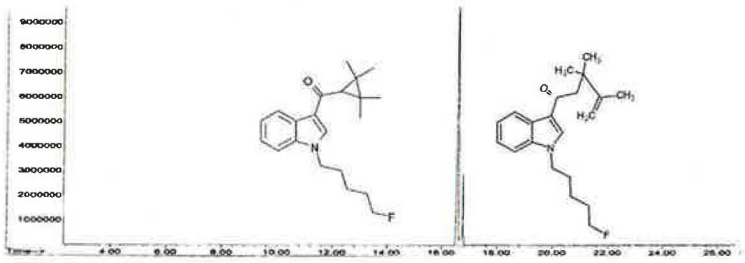
Indole vs. Indazole



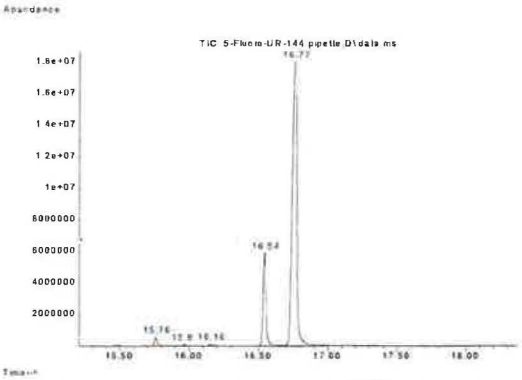
Chloro-UR144



Cyclopropyl Rearrangement



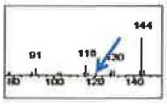
Smoking Experiment



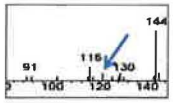
JWH-250, -302, -201

Focus on the 121:91 ion ratio (use tabulate in Chemstation).

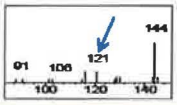
JWH-250



JWH-302



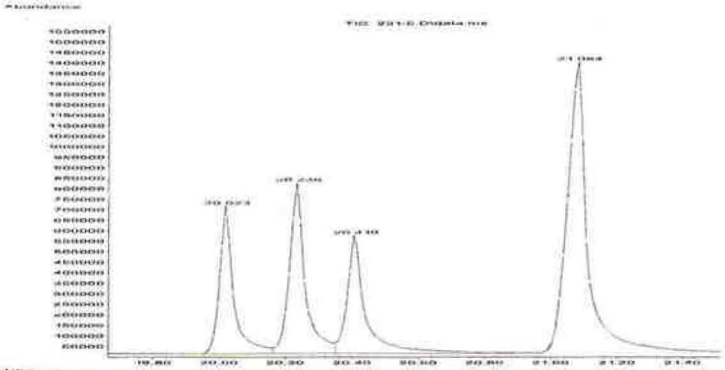
JWH-201



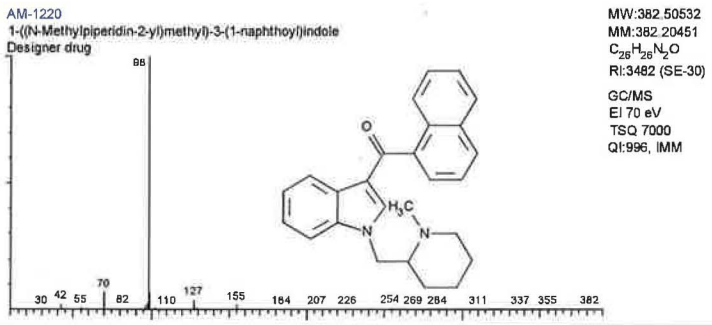
Compound	Ratio
JWH-250	0.4
JWH-302	1.3
JWH-201	7.2

Harris, D.; Hokanson, S.; Miller, V. *"GC–MS Differentiation of Three Synthetic Cannabinoid Positional Isomers: JWH–250, JWH–302, and JWH–201."* CLIC Journal, October 2011, 21(4), 23-32.

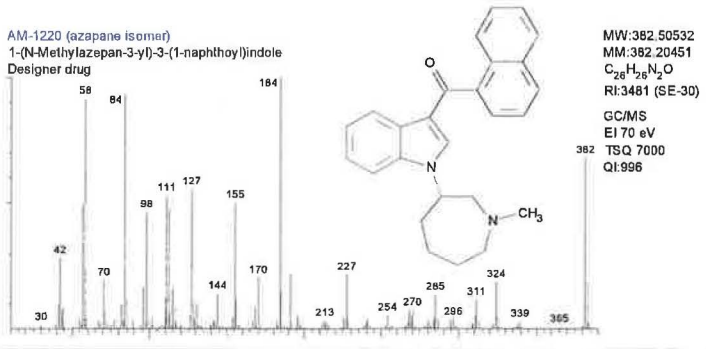
AM2201 Isomers



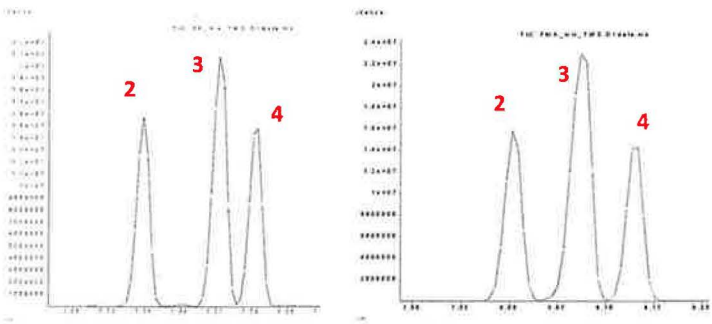
AM1220



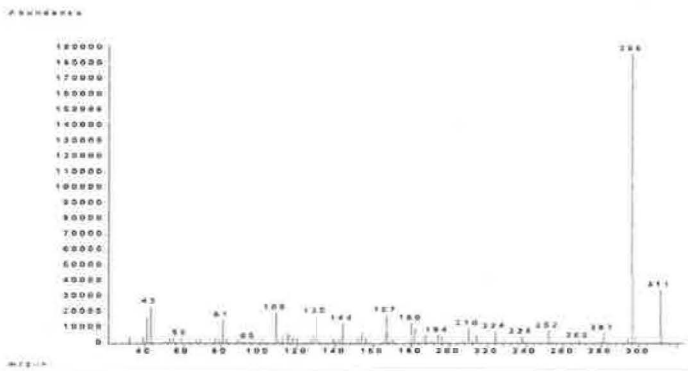
AM1220 Azepane Isomer



Fluoro Isomers



Unknown UR144 Related Compound



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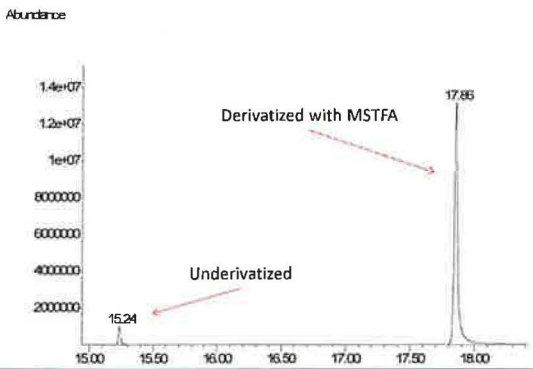

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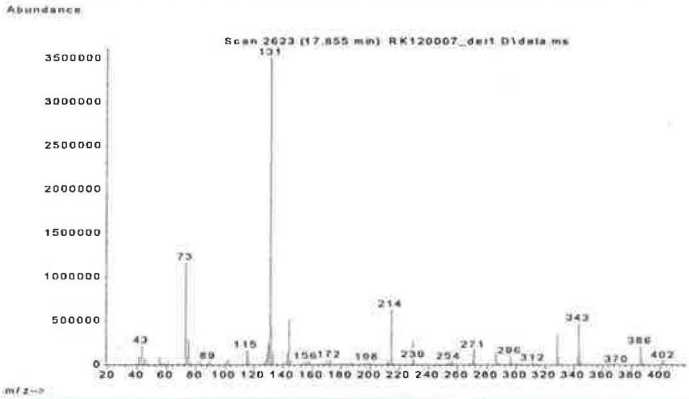
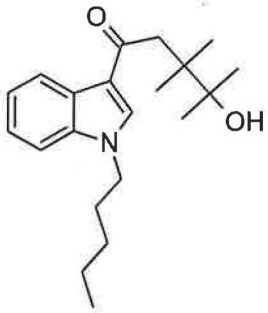
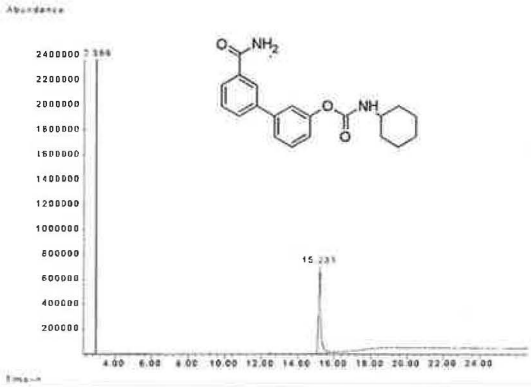


Unknown UR144 Related Compound

- "UR-144 in products sold via the Internet: Identification of related compounds and characterization of pyrolysis products", Andrej Grigoryev, Et al. **Drug Testing and Analysis**, January 2013
- "Identification and analytical properties of new synthetic cannabimimetics bearing 2,2,3,3-tetramethylcyclopropanecarbonyl moiety", Yuri Shafran, Et al. **Forensic Science International**, 2012



URB597



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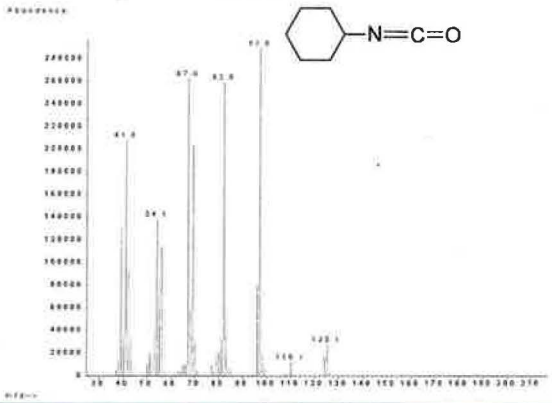

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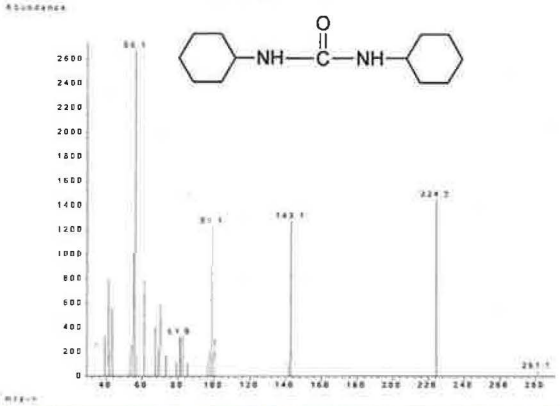
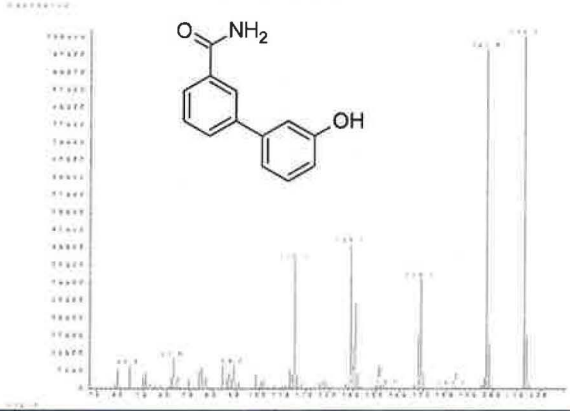
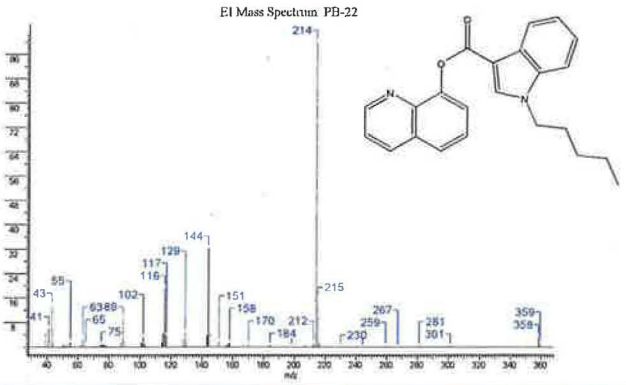


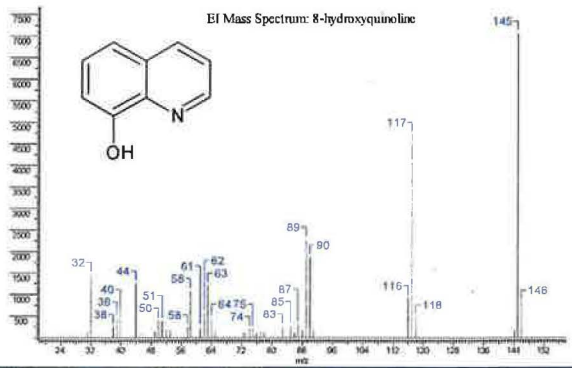
URB597



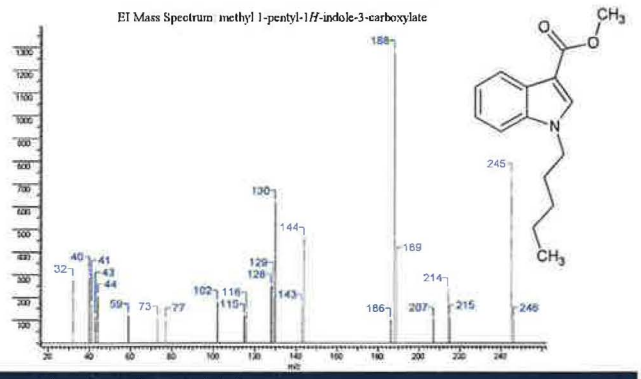
What we can learn: PB-22



What we can learn: PB-22



What we can learn: PB-22



Thank You

Questions????

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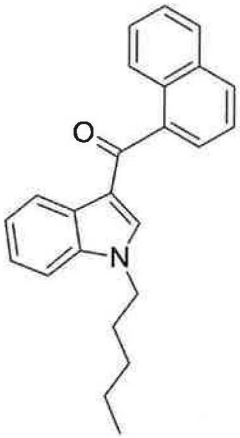
Investigation of JWH-018 Concentration in Spice Packages

Elizabeth Guest
Forensic Chemist
Special Testing and Research Laboratory
Drug Enforcement Administration

JWH-018

- Synthesized by John W. Huffman in 1995
- Sold as a research chemical "bonsai fertilizer" and in smoking blends
- Users take orally or through inhalation



MANUFACTURING

- Cannabinoid is dissolved in solvent
  - Acetone or alcohol are usually used
- Solution is added to the plant material
  - Either sprayed on or mixed in
  - 1kg powder for 10 – 60kg plant material
- Plant material is spread out to dry and then packaged

Investigate the JWH-018 Concentration Variability

- Cone and sample technique
- Grinding
- Variability within a package
  - Same brand name
  - Same flavor
  - Same artwork on the package
- Variability between different brands or packaging
  - Same brand name but different flavor or packaging
  - Different artwork on the package

PROCEDURES

- Samples were screened with GC/MS to identify packets that contained JWH-018
- GC/FID was used to quantitate JWH-018
  - Internal standard - 0.3mg/mL papaverine HCl in dimethyl sulfoxide
  - Standard solution - 0.5mg/mL JWH-018 in internal standard solution
  - Plant material - final concentration is approximately 0.5mg/mL
    - Dilute the sample with the internal standard solution
    - Let the sample sit 24 hours
    - Filter an aliquot through a cotton plugged pipette into a GC vial
  - 12 minute GC/FID run

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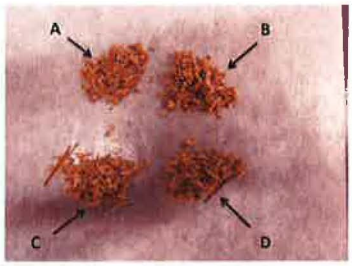
CONE AND SAMPLING



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CONE AND SAMPLING RESULTS

- Three separate portions (A, B, and C) each from five individual packets
  - ➢Cone and sampling is not a good representation of sample concentration in plant material

Package	1	2	3	4	5
Average JWH-018%	7.21	7.25	7.40	7.51	7.20
STDEV	0.33	0.43	0.19	0.62	0.03
CV (RSD)	4.51	5.87	2.59	8.26	0.48
Within Package Similarity	Yes	Yes	Yes	No	No

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VARIABILITY IN IDENTICAL PACKAGES

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ANALYSIS OF IDENTICAL PACKAGES

- The JWH-018 concentration was compared in different brands using one-way analysis of variance (ANOVA)
  - ANOVA compares the means of different samples
- Looked at seven different brands
  - Five packets were examined for each brand
  - Three replicate measurements were done for each packet

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WITHIN BRAND SIMILARITY

Brand	K2 420 SUMMIT	K2 CLOUD 9	[illegible]
Average JWH-018%	0.71	0.86	1.86
STDEV	0.14	0.18	0.22
CV (RSD)	19.47	20.98	11.80
Within Brand Similarity	No	No	Yes

Brand	FLORIDA SPICE MELON	KUSH - green label	[illegible]	[illegible]
Average JWH-018%	2.39	3.43	3.50	3.54
STDEV	0.11	0.11	0.21	0.10
CV (RSD)	4.75	3.10	5.97	2.91
Within Brand Similarity	No	No	Yes	Yes

VARIABILITY BETWEEN SIMILAR PACKAGES

SIMILAR PACKAGE VARIABILITY

Brand	*PURPLE FLAKE TEAL LABEL*	*PURPLE FLAKE BLUE LABEL*	*FLORIDA SPICE*	*FLORIDA SPICE MELON*
Average JWH-018%	1.61	1.86	2.35	2.39
STDEV	0.049	0.22	0.066	0.11
CV (RSD)	3.04	11.80	2.80	4.75
Mean Statistically Similar to:	*PURPLE FLAKE BLUE LABEL*	*PURPLE FLAKE TEAL LABEL*	*FLORIDA SPICE MELON*	*FLORIDA SPICE*

Variability between brands

BETWEEN BRAND SIMILARITY

Brand	*K2 420 SUMMIT*	*K2 CLOUD 9*	*PURPLE FLAKE TEAL LABEL*	*PURPLE FLAKE BLUE LABEL*	*FLORIDA SPICE*	*FLORIDA SPICE MELON*
Average JWH-018%	0.71	0.86	1.61	1.86	2.35	2.39
STDEV	0.14	0.18	0.049	0.22	0.066	0.11
CV (RSD)	19.47	20.98	3.04	11.80	2.80	4.75
Mean Statistically Similar to:			*PURPLE FLAKE BLUE LABEL*	*PURPLE FLAKE TEAL LABEL*	*FLORIDA SPICE MELON*	*FLORIDA SPICE*

BETWEEN BRAND SIMILARITY

Brand	[illegible]	*KUSH - green label*	*Matrix Platinum*	*KUSH - blue label*	*KUSH - red label*
Average JWH-018%	2.94	3.43	3.50	3.54	4.48
STDEV	0.090	0.11	0.21	0.10	0.065
CV (RSD)	3.063	3.099	5.971	2.908	1.447
Mean Statistically Similar to:		*Matrix Platinum*	*KUSH - blue label*	*Matrix Platinum*	
			KUSH - green label		

CONCLUSIONS – CONE AND QUARTERING

- Grinding the plant material provides a more homogenous sample with repeatable quantitation results
- A cone and quartering technique can be used to identify the compounds added to the plant material but the quantitation results may not be repeatable.

CONCLUSIONS - WITHIN BRAND SIMILIARITIES

- The manufacturing process may use a more uniform procedure for dosing the plant material
  - Using a cement mixer to mix the plant material and chemicals versus spraying the plant material

CONCLUSIONS – DIFFERENT BRAND SIMILARITIES

- Florida Spice and Florida Spice Melon are similar
  - The addition of melon flavoring did not change the dosing amount of JWH-018
  - Possibly manufactured at the same facility at about the same time
- The two Purple Flake brands are similar
  - Manufacturer may have switched to another label during the manufacturing process
- Kush—green label, Kush—red label, and Matrix Platinum all are statistically similar in JWH-018 concentration

CONCLUSIONS

- K2 was one of the first cannabinomimetic brands in the U.S. market
- Due to its popularity, it was manufactured by numerous individuals throughout the country
- Packages analyzed may not have been manufactured at the same facility
  - Supported by the vast difference in JWH-018 concentrations between K2 Melon, K2 420 Summit, K2 Cloud 9

Acknowledgements

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Questions?

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