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.

Table 1

<table>
<thead>
<tr>
<th>Category A</th>
<th>Category B</th>
<th>Category C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrared Spectroscopy</td>
<td>Capillary Electrophoresis</td>
<td>Color Tests</td>
</tr>
<tr>
<td>Mass Spectrometry</td>
<td>Gas Chromatography</td>
<td>Fluorescence Spectroscopy</td>
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<tr>
<td>Nuclear Magnetic Resonance Spectroscopy</td>
<td>Ion Mobility Spectrometry</td>
<td>Immunoassay</td>
</tr>
<tr>
<td>Raman Spectroscopy</td>
<td>Liquid Chromatography</td>
<td>Melting Point</td>
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<tr>
<td>X-ray Diffraclometry</td>
<td>Microcrystalline Tests</td>
<td>Ultraviolet Spectroscopy</td>
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<tr>
<td>Pharmaceutical Identifiers</td>
<td></td>
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<tr>
<td>Thin Layer Chromatography</td>
<td></td>
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<tr>
<td>Cannabis only:</td>
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<tr>
<td>Macroscopic Examination</td>
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<tr>
<td>Microscopic Examination</td>
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</tbody>
</table>

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

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 ...

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.

§ 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

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.

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.

Reporting

- Limitations
  - If you cannot determine the position of the Fluorine (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

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...

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 the website.

DISCLAIMER: Although SWGDRUG makes an effort to ensure the accuracy of spectra prior to entry, the library should only be used as an analytical tool. SWGDRUG recommends the use of traceable reference materials to support identifications of drugs. (Part IV - Quality Assurance Section 5.3)

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 8, 2013):
Drug Monographs

Scientific Working Group for the Analysis of Seized Drugs

Monographs:
The following monographs contain detailed information and analytical data for reference materials which have been analyzed, certified, 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.

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

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 Rodriguez-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?

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.

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](http://www.swgdrug.org/pending.htm)
- Comment Period open until May 3, 2013

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.
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.

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.

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
For "Classical" Drugs of Abuse

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

Further decom products:
For "Emerging" Drugs of Abuse

- Chemical structures and data analysis for compounds with molecular formulas C₂₅H₂₃O₃ and C₂₆H₂₃O₃.

- Naphthyl side and Indole side indicated in the diagrams.

- Detailed analysis of chemical spectra and mass spectrometry data.
A secondary technique is used to verify
- Depending on the vendor, other analytical information may be given

JWH-018 has a UV $\lambda_{max}$:
219, 246 nm

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

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 recommend minimum scientific standards for the evaluation of non-controlled substances being considered as analogs of controlled substances.
- Science is the key
- Legal decisions/legislation may be discussed but final considerations are strictly based on science

ACECSA Objectives
- To establish a working definition of "Analog" and related terms within the scope of Forensic Drug Analysis.
- To develop a rigorous scientific method for evaluation of non-controlled substances for analog consideration that is scientifically valid and peer-reviewed.
- To provide minimum scientific standards for 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

  3 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

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

Demo of Online Database Resources for the Identification of Novel and Emerging Drugs

Peter R. Stout, PhD

www.forensicCOE.org
CAUTION:
THIS PRESENTATION MENTIONS COMMERCIAL NAMES

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 FTIR 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

SWCDRUG 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

Commercial Disclaimer
**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 Cannabinimetics

**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**

**Database Search Capabilities**

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

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 information

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

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

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.

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.

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.

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.

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

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 Benzocyclidine 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
- Pentadone

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.

Utah

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

- 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 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 statute.
- 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.”
COLOR TESTS AND ANALYTICAL DIFFICULTIES WITH EMERGING DRUGS OF ABUSE

Jeremiah Morris
Johnson County Sheriff’s Office
Criminalistics Laboratory

Presumptive tests - failures

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

Presumptive test - success!

- Most cannabinoids react with Liebermann’s

<table>
<thead>
<tr>
<th>Reference</th>
<th>Cannabinoid Chemical Class</th>
<th>Source</th>
<th>Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>CB-007</td>
<td>Naphthalene derivatives</td>
<td>Reference Collection</td>
<td>Dark Yellow</td>
</tr>
</tbody>
</table>
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.

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

Substituted cathinones

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

Grand total of 672 possible combinations

Presumptive tests

- Note - all produce either no color or just blue specks with acidified CrSCN
**Arylcyclohexylamines**

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

![Arylcyclohexylamines](image)

**Presumptive tests**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Sample</th>
<th>Color (dry)</th>
<th>Color (wet)</th>
<th>Odor</th>
<th>Taste</th>
<th>Solubility</th>
<th>Test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-MeO-PCP</td>
<td>Brown</td>
<td>Yellow</td>
<td>Blue</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Methoxymethyl</td>
<td>Light yellow</td>
<td>Yellow</td>
<td>Blue</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>D, L-pseudoephedrine</td>
<td>Yellow-green</td>
<td>Blue</td>
<td>Blue</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3-10-Hydroxy-EC</td>
<td>Brown</td>
<td>Red</td>
<td>Red</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

**Tryptamines**

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

![Tryptamines](image)

**Variations on a tryptamine theme**

- Methyl or ethyl with mono-N alkyl substitution
- Hydroxyl, methoxy, acetoxo, halo
- Alkyl or dialkyl substitution (methyl, ethyl, propyl, isopropyl, allyl)

**Presumptive tests**

![Presumptive tests](image)

**Issues with acetoxo compounds**

- Vendors beginning to sell acetoxo tryptamines
  - 4-AcO-DMF (acetoxylated 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.
Acid/base extract (acetic acid)

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-analyses 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**

![Graph showing MS and retention times for acetylated compounds.]

**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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Marquis</th>
<th>Liebermann</th>
<th>Mecke's</th>
<th>Poulter's</th>
<th>Pinnick</th>
<th>Cinamyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>aMT</td>
<td>Yellow-brown</td>
<td>Black</td>
<td>Brown</td>
<td>Yellow</td>
<td>Purple</td>
<td>Red and purple</td>
</tr>
<tr>
<td>5-IT</td>
<td>Dark red</td>
<td>Dark brown</td>
<td>Brown</td>
<td>Red brown</td>
<td>Red</td>
<td>Red</td>
</tr>
</tbody>
</table>

**p-Dimethylaminocinnamaldehyde reagent**

![Images of TLC plates showing reactions.]

**What does this mean?**

- NMT easily excluded with acetylation
- 5-IT verses aMT? Your call
  - If pure enough for IR, you're golden
  - Are acetylated 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)**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Marquis</th>
<th>Liebermann</th>
<th>Mecke's</th>
<th>Poulter's</th>
<th>Pinnick</th>
<th>Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-AFB</td>
<td>Black</td>
<td>Black</td>
<td>Black</td>
<td>Dark purple</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>6-AFB</td>
<td>Purple</td>
<td>Dark purple</td>
<td>Purple</td>
<td>Purple</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Cordarboxine</td>
<td>Orange</td>
<td>Red</td>
<td>Dark red</td>
<td>Yellow</td>
<td>Red</td>
<td>--</td>
</tr>
<tr>
<td>Methoxypropionate</td>
<td>Orange</td>
<td>Red</td>
<td>Dark brown</td>
<td>Black</td>
<td>Light brown</td>
<td>--</td>
</tr>
<tr>
<td>MDAI</td>
<td>Orange</td>
<td>Green</td>
<td>Green</td>
<td>Green</td>
<td>--</td>
<td>Blue</td>
</tr>
<tr>
<td>8-AI</td>
<td>Brown</td>
<td>Dark brown</td>
<td>Brown</td>
<td>Orange</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Alkylation</td>
<td>Dark red</td>
<td>Brown</td>
<td>Brown</td>
<td>Yellow</td>
<td>Black</td>
<td>Green</td>
</tr>
<tr>
<td>2C-T-2</td>
<td>Red</td>
<td>Orange</td>
<td>Orange</td>
<td>Orange</td>
<td>--</td>
<td>Green</td>
</tr>
<tr>
<td>2C-P</td>
<td>Yellow</td>
<td>Green</td>
<td>Green</td>
<td>Green</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>5-methoxy 2C-D</td>
<td>Purple</td>
<td>Brown</td>
<td>Green</td>
<td>Red</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>
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

Sampling Plans

Statistical
- Inferences can be made about the entire population
  - Hypergeometric
  - Bayesian

Non-Statistical
- No inferences are made about the population
  - All/One
  - 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 N₁ positives...”

Example 1

<table>
<thead>
<tr>
<th>Population</th>
<th>95% confidence</th>
<th>99% confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>K=0.5</td>
<td>K=0.7</td>
</tr>
<tr>
<td>800</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>900</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>1000</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Population</th>
<th>95% confidence</th>
<th>99% confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>K=0.5</td>
<td>K=0.7</td>
</tr>
<tr>
<td>1-9</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>20</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>100</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>200</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>

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 plan

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.

When choosing a plan...

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

DOCUMENTATION

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

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

Thank you!

Jill.M.Head@usdoj.gov
Drug Enforcement Administration
Special Testing and Research Laboratory
GCMS Analytical Information

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

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

Goals

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

JWH-018 Fragmentation

2 vs. 1-Naphthyl Isomer of JWH-018

Indole vs. Indazole
Indole vs. Indazole

Cyclopropyl Rearrangement

JWH-250, -302, -201

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>JWH-250</td>
<td>0.4</td>
</tr>
<tr>
<td>JWH-302</td>
<td>1.3</td>
</tr>
<tr>
<td>JWH-201</td>
<td>7.2</td>
</tr>
</tbody>
</table>


Chloro-UR144

Smoking Experiment

AM2201 Isomers
AM1220 (azapane isomer)
1-(N-Methylazepan-3-yl)-3-(1-naphthoyl)indole

**Designated drug**

**MW:** 382.50532  
**MM:** 382.20451  
**C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>0**

**RI:** 348 (SE-30)

**GC/MS**
**EI:** 70 eV  
**TSQ 7000**
**Q1:** 996  
**Q2:** 382 
**Q3:** 7090  
**Q4:** 986

**DFA Special Testing and Research Laboratory**
**Emerging Trends Program**

---

**Fluoro Isomers**

**Unknown UR144 Related Compound**

**DFA Special Testing and Research Laboratory**
**Emerging Trends Program**

---

**Unknown UR144 Related Compound**

**DFA Special Testing and Research Laboratory**
**Emerging Trends Program**

---

**Unknown UR144 Related Compound**

**DFA Special Testing and Research Laboratory**
**Emerging Trends Program**
Unknown UR144 Related Compound


What we can learn: PB-22
What we can learn: PB-22

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

Investigation of JWH-018
Concentration in Spice Packages

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

Thank You

Questions???

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

CONE AND SAMPLING

CONV 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

<table>
<thead>
<tr>
<th>Package</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average JWH-018%</td>
<td>7.21</td>
<td>7.25</td>
<td>7.40</td>
<td>7.51</td>
<td>7.20</td>
</tr>
<tr>
<td>SD</td>
<td>0.33</td>
<td>0.43</td>
<td>0.19</td>
<td>0.61</td>
<td>0.03</td>
</tr>
<tr>
<td>CV (RSD)</td>
<td>4.51</td>
<td>5.87</td>
<td>2.59</td>
<td>8.26</td>
<td>0.43</td>
</tr>
<tr>
<td>Within Package Similarity</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

VARIABILITY IN IDENTICAL PACKAGES

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
### Within Brand Similarity

<table>
<thead>
<tr>
<th>Brand</th>
<th>K2 820 Summit</th>
<th>K2 Cloud 9</th>
<th>K2 Cloud 9 Blue Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average JWH-01%</td>
<td>0.73</td>
<td>0.86</td>
<td>1.46</td>
</tr>
<tr>
<td>STDEV</td>
<td>0.14</td>
<td>0.18</td>
<td>0.22</td>
</tr>
<tr>
<td>CV (RSD)</td>
<td>19.47</td>
<td>20.18</td>
<td>11.80</td>
</tr>
<tr>
<td>Within Brand Similarity</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Similar Package Variability

<table>
<thead>
<tr>
<th>Brand</th>
<th>Purple Flake - Teal Label</th>
<th>Purple Flake - Blue Label</th>
<th>Florida Spice</th>
<th>Florida Spice Melon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average JWH-01%</td>
<td>1.61</td>
<td>1.84</td>
<td>2.33</td>
<td>2.39</td>
</tr>
<tr>
<td>STDEV</td>
<td>0.049</td>
<td>0.022</td>
<td>0.066</td>
<td>0.01</td>
</tr>
<tr>
<td>CV (RSD)</td>
<td>3.84</td>
<td>11.80</td>
<td>2.80</td>
<td>4.75</td>
</tr>
<tr>
<td>Mean Statistically Similar to</td>
<td>Purple Flake - Teal Label</td>
<td>Purple Flake - Blue Label</td>
<td>Florida Spice Melon</td>
<td>Florida Spice</td>
</tr>
</tbody>
</table>

### Between Brand Similarity

<table>
<thead>
<tr>
<th>Brand</th>
<th>K2 820 Summit</th>
<th>K2 Cloud 9</th>
<th>K2 Cloud 9 Blue Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average JWH-01%</td>
<td>0.71</td>
<td>0.66</td>
<td>1.64</td>
</tr>
<tr>
<td>STDEV</td>
<td>0.14</td>
<td>0.18</td>
<td>0.049</td>
</tr>
<tr>
<td>CV (RSD)</td>
<td>19.47</td>
<td>20.18</td>
<td>2.04</td>
</tr>
<tr>
<td>Mean Statistically Similar to</td>
<td>Purple Flake - Blue Label</td>
<td>Purple Flake - Teal Label</td>
<td>Florida Spice Melon</td>
</tr>
</tbody>
</table>

### Variability Between Similar Packages

<table>
<thead>
<tr>
<th>Brand</th>
<th>Kush Green Label</th>
<th>Mango Platinum</th>
<th>Kush Blue Label</th>
<th>Kush Red Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average JWH-01%</td>
<td>3.94</td>
<td>3.45</td>
<td>3.60</td>
<td>3.54</td>
</tr>
<tr>
<td>STDEV</td>
<td>0.030</td>
<td>0.11</td>
<td>0.21</td>
<td>0.10</td>
</tr>
<tr>
<td>CV (RSD)</td>
<td>3.013</td>
<td>3.099</td>
<td>5.971</td>
<td>2.918</td>
</tr>
<tr>
<td>Mean Statistically Similar to</td>
<td>Mango Platinum</td>
<td>Kush Blue Label</td>
<td>Kush Green Label</td>
<td>Kush Red Label</td>
</tr>
</tbody>
</table>
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 SIMILARITIES

- 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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