Drug-Control Laws

• The U.S. federal law known as the Controlled Substances Act (CSA) will serve to illustrate a legal drug-classification system created to prevent and control drug abuse.

• This federal law establishes five schedules of classification for controlled dangerous substances on the basis of a drug’s:
  – potential for abuse
  – potential for physical and psychological dependence
  – medical value
Controlled Substances Disclaimer

- Department of Justice (DOJ)/Drug Enforcement Administration (DEA)/Office of Diversion Control

- Definition: Title 21 Code of Federal Regulations

- List of substances and schedules: Section 1308 of the Controlled Substances Act (21 U.S.C. §801 et seq.) (CSA)

- List of Defined Abbreviations (e.g. THC: Tetrahydrocannabinols)

- http://www.deadiversion.usdoj.gov/schedules/#disclaimer
Schedules

• Schedule I drugs: have a high potential for abuse and have no currently accepted medical use (e.g., heroin, marijuana, methaqualone, and LSD, etc)

• Schedule II/IIN drugs: have a high potential for abuse and have medical use with severe restrictions (e.g., cocaine, morphine, opium, fentanyl, PCP, amphetamine, etc)

• Schedule III/IIN drugs: have less potential for abuse and a currently accepted medical use. (products that contain less amount of codeine (Tylenol with Codeine®), buprenorphine, (Suboxone®), anabolic steroids, etc)
Schedules-continued

- Schedule IV drugs: have a low potential for abuse relative to substances in Schedule III (alprazolam (Xanax®), carisoprodol (Soma®), clonazepam (Klonopin®), clorazepate (Tranxene®), diazepam (Valium®), etc)

- Schedule V drugs: have a low potential for abuse relative to substances listed in Schedule IV and consist primarily of preparations containing limited quantities of certain narcotics (cough preparations containing not more than 200 milligrams of codeine per 100 milliliters or per 100 grams (Robitussin AC®, Phenergan with Codeine®), and ezogabine)
Classification

- Narcotic drugs (pain killers): opiates (morphine, codein), heroin, methadone, oxycondone, fentanyl, etc

- Depressants: substances used to calm irritability and anxiety and may induce sleep, alcohol and tranquilizers, (barbiturates, methaqualone, meprobamate, diazepam, chlordiazepoxide, ethanol)

- Stimulants: substances taken to increase alertness or activity, followed by a decrease in fatigue and a loss of appetite (amphetamines, cocaine, caffeine, nicotine)

- Hallucinogens: cause marked changes in normal thought processes, perceptions, and moods (marijuana, LSD, phencyclidine)
The process involves the extraction of compounds from poppy plants, followed by chemical reactions to produce morphine, codeine, and heroine.
morphine  oxycondone  methadone

LD_{50} = 2 \text{ mg}  
\sim 29,000 \text{ deaths in 2017, USA}
Hallucinogens

• Hallucinogens cause marked changes in normal thought processes, perceptions, and moods.

• Marijuana is the most controversial drug in this class because its long-term effects on health are still largely unknown.

• The chemical substance largely responsible for the hallucinogenic properties of marijuana is known as tetrahydrocannabinol (THC).
Marijuana

THC
Other Hallucinogens

LSD

PCP

MDMA (Ecstasy)
Stimulants

• Stimulants are substances taken to increase alertness or activity, followed by a decrease in fatigue and a loss of appetite.

• Sometimes disguised as agents that help weight loss
Stimulants

- Amphetamine and methamphetamine (METH or ice or crystal), often injected intravenously, cause an initial “rush,” followed by an intense feeling of pleasure.
Pseudoephedrine HCl

Sudafed
Stimulants

• Cocaine, extracted from the leaves of *Erythroxylon coca*, causes increased alertness and vigor, accompanied by the suppression of hunger, fatigue, and boredom.

• **Crack** is a powder cocaine mixed with baking soda (NaHCO$_3$) and water, then heated.

• **Crack** is often smoked in glass pipes, and, like cocaine, stimulates the brain’s pleasure center.
Crack (mixture with sodium bicarbonate and powder cocaine)
Toluene in glue damages brain permanently

Brain images show marked atrophy (shrinkage) of brain tissue in a toluene abuser (B) compared to a nonabusing individual (A). Note the smaller size and the larger empty (dark) space within the toluene abuser's brain. (The white outer circle in each image is the skull.)

Courtesy of Neil Rosenberg, M.D.
Drug Identification (Seized Drugs)

• The challenge or difficulty of forensic drug identification comes in selecting analytical procedures that will ensure a specific identification of a drug.

• This plan, or scheme of analysis, is divided into two phases.

   – **Screening test** (preliminary test): nonspecific and preliminary in nature to reduce the possibilities to a manageable number

   – Confirmation test: a single test that specifically identifies a substance.
Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG)

• Recommend minimum standards for the forensic examination of seized drugs and to seek their international acceptance.
• Drug monographs (chemical and physical properties, FTIR, NMR, Mass data, etc)
• Developed questions as a resource and training tool
• Provided workshop, meeting, etc
• http://www.swgdrug.org/
<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>
</tr>
<tr>
<td>Nuclear Magnetic Resonance Spectroscopy</td>
<td>Ion Mobility Spectrometry</td>
<td>Immunooassay</td>
</tr>
<tr>
<td>Raman Spectroscopy</td>
<td>Liquid Chromatography</td>
<td>Melting Point</td>
</tr>
<tr>
<td>X-ray Diffractometry</td>
<td>Microcrystalline Tests</td>
<td>Ultraviolet Spectroscopy</td>
</tr>
<tr>
<td></td>
<td>Pharmaceutical Identifiers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thin Layer Chromatography</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cannabis only:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Macroscopic Examination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Microscopic Examination</td>
<td></td>
</tr>
</tbody>
</table>
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.

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.
Biological Samples

- Biological samples (drug test)
  - Urine (most common)
  - Blood (most accurate)
  - Oral Fluid/Saliva
  - Breath air (alcohol)
  - Sweat
  - Hair
Why You Need Drug Test

• Workplace requirement (urine)
  – Federal Workplace: Confirm by mandate: (YR 1986)
    • Executive Order 12564 >> Drug-free Federal workplace
    • Tested in certified labs by Substance Abuse and Mental Health Services Administration (SAMHSA)
  – Non-Federal Workplace: No guidelines

• Legal: Court requirement (urine)
  – Very strict by policy

• Forensic: Crime investigation (many samples)
  – Very strict by policy

• Medical/clinical (urine)
  – Verify drug dependency and monitor treatment progress

• Sports: Doping test (urine)
Window of Detection for Various Matrices

Very broad estimates that depend on substance, the amount and frequency, other factors.
THC Distribution in a Body

Δ-9-tetrahydrocannabinol (THC)
Types of Drug/Alcohol Test Required by the Organization

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>63%</td>
</tr>
<tr>
<td>Blood</td>
<td>6%</td>
</tr>
<tr>
<td>Breath Alcohol Test (BAT)</td>
<td>5%</td>
</tr>
<tr>
<td>Saliva</td>
<td>3%</td>
</tr>
<tr>
<td>Hair</td>
<td>2%</td>
</tr>
</tbody>
</table>
Cocaine Metabolites

Liver
Butyrylcholinesterase (BChE)
Cytochrome P450 3A4 (CYP3A4)
Human Carboxylesterases (hCE-1/2)

- Cocaine
- Norecgonine methyl ester
- Ecgonine methyl ester
- Benzoylecgonine
Drug Derivatization

Why: Most drugs containing polar groups (-OH, -COOH, -NH₂, -NRH, etc) are less volatile and sometimes does not pass GC columns

Goal: Convert polar/hydrophilic compounds to less polar/hydrophobic compounds

How: Chemical derivatization

Popular techniques:
Alkylation
Acylation
Silylation
# Silylation

<table>
<thead>
<tr>
<th>No.</th>
<th>Reagent&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Compounds</th>
<th>Derivatives</th>
</tr>
</thead>
</table>
| 1.  | \[
\begin{align*}
\text{CH}_3 \\
\text{H}_3\text{C} &- \text{Si} - \text{CH}_3 \\
\text{Cl} &
\end{align*}
\] (TMCS) | R−COOH |  |
| 2.  | \[
\begin{align*}
\text{CH}_3 &- \text{CH}_3 \\
\text{H}_3\text{C} &- \text{Si} - \text{N} - \text{Si} - \text{CH}_3 \\
\text{CH}_3 &- \text{CH}_3 \\
\text{H} &
\end{align*}
\] (HMDS) | R−OH | R−O−Si(CH_3)_3 |
|     |                     |           | O           |
|     |                     |           | R−C−O−Si(CH_3)_3 |
| 3.  | \[
\begin{align*}
\text{CH}_3 &- \text{CH}_3 \\
\text{H}_3\text{C} &- \text{Si} - \text{O} - \text{C}=\text{N} - \text{Si} - \text{CH}_3 \\
\text{CH}_3 &- \text{CH}_3 &- \text{CH}_3 \\
\text{R}_1 &- \text{NH} \\
\text{R}_2 &
\end{align*}
\] (BSA) | R−OH | R−O−Si(CH_3)_3 |
|     |                     | R−NH₂     | R−N−Si(CH_3)_3 |
|     |                     | R₁−NH     | R₁−N−Si(CH_3)_3 |
|     |                     | R₂        | R₂ |
|     |                     | O         | O−Si(CH_3)_3 |
|     |                     | R−C−NH₂   | R−C−N−Si(CH_3)_3 |
|     |                     | R−COOH    | R−C−O−Si(CH_3)_3 |
Silylation

4. \[
\begin{array}{c}
\text{CH}_3 \\
\text{H}_3\text{C}-\text{Si}-\text{O}-\text{C}=\text{N}-\text{Si}-\text{CH}_3 \\
\text{CH}_3 \quad \text{CF}_3 \quad \text{CH}_3 \\
(\text{BSTFA})
\end{array}
\]

Same as BSA, leaving group
\[
\begin{array}{c}
\text{O} \\
\text{H} \\
\text{F}_3\text{C}-\text{C}-\text{N}-\text{Si}-(\text{CH}_3)_3 \\
(\text{BSTFA})
\end{array}
\]
more volatile than that of BSA

5. \[
\begin{array}{c}
\text{O} \\
\text{CH}_3 \\
\text{F}_3\text{C}-\text{C}-\text{N}-\text{Si}-\text{CH}_3 \\
\text{H}_3\text{C} \quad \text{CH}_3
\end{array}
\]

Same as BSA, leaving group
\[
\begin{array}{c}
\text{O} \\
\text{H} \\
\text{F}_3\text{C}-\text{C}-\text{N}-\text{CH}_3
\end{array}
\]
is very volatile

6. \[
\begin{array}{c}
\text{N} \\
\text{CH}_3 \\
\text{N}-\text{Si}-\text{CH}_3 \\
\text{CH}_3
\end{array}
\]

(steroids)
\[
\begin{array}{c}
\text{R}-\text{OH} \\
\text{R}-\text{COOH}
\end{array}
\]

\[
\begin{array}{c}
\text{R}-\text{O}-\text{Si}(\text{CH}_3)_3 \\
\text{R}-\text{C}-\text{O}-\text{Si}(\text{CH}_3)_3
\end{array}
\]

No reaction with amines

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\(^a\) HMDS, hexamethyldisilazane; BSA, \(N,O\)-bis(trimethylsilyl)acetamide; BSTFA, \(N,O\)-bis (trimethylsilyl)trifluoroacetamide; MSTFA, \(N\)-methyl-\(N\)-trimethylsilyltrifluoroacetamide.
Silylation by BSTFA

Will do lab/demo

Benzoyllecgonine (cocaine metabolite)