More Effective Drug Testing: 
Tools, Interpretation, and Challenges 

Dr. Leo Kadehjian 
Palo Alto, California 

Pharmacokinetics 
Dose → Blood → Receptors → Effects 
Absorption 
Distribution 
Metabolism 
Elimination → Urine, sweat, oral fluid, hair, …

Correlating Test Results to Effects: What Can Be Said?

Body fluid levels 
Blood levels → Brain levels → Receptor levels 
Likelihood of impairment → Degree of impairment 

Forensic Challenges: Specimens, Technologies

- Urine: Adulteration, substitution, dilution, interpretation 
- Oral fluid: Adulteration, interpretation 
- On-site: Subjectivity, performance 
- Hair: Contamination, bias, ADA, standards 
- Sweat: Contamination, tampering, standards 
- Oculomotor: Science, standards 

Forensic Issues for Laboratories / Toxicologists

- Admissibility of evidence 
  Legal standards: peer review, known error rate, standards, … 
- Evidentiary weight 
  Chain of custody, laboratory performance, interpretation, … 
- Legal requirements for decisionmaking 
  Beyond a reasonable doubt, preponderance, … 
- Laboratory liability 
  Duty owed, negligence, privacy of records/HIPAA … 
- Expert liability 
  Peer oversight 

Admissibility of evidence 
Evidentiary weight 
Legal requirements for decisionmaking 
Laboratory liability 
Expert liability 

100% 
Beyond a reasonable doubt 

50% 
Preponderance of the evidence 

0% 
Mere suspicion 

Dowling, 1976
### Qualitative vs. Quantitative

**Qualitative**

(positive, negative)

**Quantitative**

(ng/mL, immunoreactive equivalents, rate units)

“Semi-quantitative”

(no such thing!?)

### Antibody Specificity: Cross-Reactivity

**Antibody Specificity:** Cross-Reactivity

**Antibody Specificity**

- **Cross-reactants**
- **No cross-reactivity**

**Assay response**

- **Positive sample**
- **Cut-off**
- **“Negative” sample**

**Estimated concentration**

- **Cut-off**
- **Estimated concentration**

### Limit of Detection (LOD)

Level established administratively at or above which a result is reported as “positive” and below which is reported as “negative”

### Limit of Quantitation (LOQ)

Level at which a result may be reported as a quantitative value (e.g. ng/mL) with acceptable accuracy (e.g. ±95%)

### Cutoff

Level at which a result can be clearly distinguished from the range of results for “drug-free” specimens
**San Mateo County "Truth in Testing"**

- Standard immunoassay screening cutoffs
- FDA-cleared immunoassay screening device
- Limit of quantitation GC/MS confirmation testing
- Federally-certified (SAMHSA) laboratory
- Established scientific methods and procedures
- Regulatory recognition (SAMHSA policy)
- Case law support

**SAMHSA “Drug Presence” Criteria**

Mandatory Guidelines for Federal Workplace Drug Testing Programs
Subpart B–Scientific and Technical Requirements
Section 2.4 Laboratory Analysis Procedures

(j) Retesting a Specimen for Drugs.

(2) Because some drugs or drug metabolites may deteriorate during storage, the retest of an aliquot of a single specimen or the test of a split (Bottle B) specimen is not subject to a specific drug cutoff requirement, but must provide data sufficient to confirm the presence of the drug or metabolite.

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**U.S. v. Klimek (SDNY, 3/2/04)**

- Drug use violation of supervised release
- "Positive" on-site immunoassay (300 ng/mL cut-off)
- "Negative" laboratory screening immunoassay (181 ng/mL)
- "Negative" GC/MS confirmation (118 ng/mL BE)
- Creatinine 29.6 mg/dl.
- s.g. 1.003 = “diluted, invalid”
<table>
<thead>
<tr>
<th><strong>U.S. v. Klimek (SDNY, 3/2/04)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;The results of a drug test … shall be subject to confirmation only if the results are positive, …&quot;</td>
</tr>
<tr>
<td>A drug test confirmation shall be a urine drug test confirmed using gas chromatography/mass spectrometry techniques …</td>
</tr>
<tr>
<td>18 U.S.C. §3563(e) (probation)</td>
</tr>
<tr>
<td>18 U.S.C. §3583(d) (supervised release)</td>
</tr>
<tr>
<td>&quot;The program shall include such standards and guidelines as the Director may determine necessary to ensure the reliability and accuracy of the drug testing programs …&quot;</td>
</tr>
<tr>
<td>18 U.S.C. §3608</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th><strong>U.S. v. Klimek (SDNY, 3/2/04)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;However, the test result did not mean that Klimek did not have cocaine in his system.&quot;</td>
</tr>
<tr>
<td>&quot;Here, a GCMS test was performed, and it confirmed that cocaine metabolite was present in Klimek's system.&quot;</td>
</tr>
<tr>
<td>&quot;It should go without saying that it violates the terms of Klimek's supervised release to have ANY cocaine metabolite in his system.&quot;</td>
</tr>
<tr>
<td>&quot;Even if I assume that the fixing of a &quot;cut-off&quot; level for GCMS represents the Director's conclusion that Klimek's test result is questionable, that is simply a factor going to the weight of the drug testing evidence before me.&quot;</td>
</tr>
</tbody>
</table>

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<th><strong>U.S. v. Klimek (SDNY, 3/2/04)</strong></th>
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</thead>
<tbody>
<tr>
<td>&quot;… there is nothing magical about the cut-off level selected by the AO; equally reputable organizations involved in drug testing specify lower cut-off levels.&quot;</td>
</tr>
</tbody>
</table>
| "The results of the specimen validity test strongly suggest an effort to beat the test and are most persuasively interpreted in that way."

<table>
<thead>
<tr>
<th><strong>U.S. v. Klimek, 2nd Cir., 6/8/05</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Even more significantly, the confirmation test performed on defendant's sample—once it was &quot;normalized&quot; for dilution—would have evinced a cocaine metabolite concentration of 406 nanograms per milliliter, well above the cutoff level of 150 nanograms per milliliter.&quot;</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th><strong>U.S. v. Klimek, 2nd Cir., 6/8/05</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;We need not decide at this time whether Sections 3583(d) and 3608 preclude a district court from revoking a defendant's supervised release based solely on a test result that fell below the cutoff level.&quot;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>“Negative”</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>does NOT mean</strong></td>
</tr>
<tr>
<td><strong>“No drug”</strong></td>
</tr>
</tbody>
</table>
**Abused Prescription Drugs**

<table>
<thead>
<tr>
<th>Opioids</th>
<th>CNS Depressants</th>
<th>Stimulants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine, codeine, etc.</td>
<td>Benzodiazepines</td>
<td>Cocaine</td>
</tr>
<tr>
<td>Oxycodone (OxyContin)</td>
<td>Non-benzos</td>
<td>Amphetamine</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Barbiturates</td>
<td>Methamphetamine</td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
<td>Methylphenidate</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>OTC</td>
<td></td>
</tr>
<tr>
<td>Meperidine</td>
<td>Ephedrine, etc.</td>
<td></td>
</tr>
<tr>
<td>Proxpyphene</td>
<td>Dextromorphine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Antihistamines</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**United States’ Drug Consumption**

- 4.6% of world population
- Consumes 2/3 of illicit drug supply
- Consumes 80% of global opioid supply
- Consumes 99% of global hydrocodone supply

*L. Manchikanti and A. Singh, 2008*

**Past Year Initiates in Illicit Drug Use**

- Pain relievers
- Marijuana
- Tranquilizers
- Cocaine
- Stimulants
- Sedatives
- Heroin

**Increase in Abuse of Controlled Drugs**

- 542% – New teenager opioid abuse
- 212% – 12 to 17 yr. olds abusing
- 150% – Prescriptions
- 81% – Adults abusing
- 14% – U.S. Population

*L. Manchikanti, 2006*

**Retail Sales of Opioids (millions of grams)**

- Oxycodone: +732%
- Hydrocodone: +244%
- (1 prescribed drug in U.S.)
- Codeine: -25%
- Morphine: +196%
- Methadone: +1177%
- Meperidine: +128%
- Hydromorphone: +274%
- Fentanyl: +479%

*www.deaddiversion.usdoj.gov*

**Concentration**

- Abuse
- Supra-therapeutic use, misuse
- Therapeutic use
**Urine Drug Concentrations (ng/mL): 10,922 Chronic Pain Patients**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>10,163</td>
<td>3,910</td>
<td>196–93,372</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>15,674</td>
<td>1,854</td>
<td>108–329,591</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>7,599</td>
<td>2,690</td>
<td>100–341,009</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>4,930</td>
<td>1,637</td>
<td>100–188,306</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>2,953</td>
<td>1,380</td>
<td>100–405,020</td>
</tr>
<tr>
<td>Methadone</td>
<td>4,167</td>
<td>2,179</td>
<td>104–93,322</td>
</tr>
<tr>
<td>Meperidine</td>
<td>3,086</td>
<td>1,138</td>
<td>195–52,216</td>
</tr>
<tr>
<td>Normeperidine</td>
<td>3,490</td>
<td>1,575</td>
<td>124–19,908</td>
</tr>
</tbody>
</table>

*E. Cone et al., 2008*

**Amphetamine: Adderall, XR**

- Synthesized 1887
- \(d\)-isomer 3-4× CNS activity vs. \(l\)-isomer
- Dosing: Therapeutic: 5–30 mg (3–19 mg)  
  Abuse: up to 2,000 mg/d
- Therapeutic urine concentrations: 5 mg: 620–3,160 ng/mL  
  10 mg: 3,345 (602–12,191)  
  20 mg: 6,076 (1,339–15,359)  
  20 mg x 5 d: 7,739–19,172 ng/mL
- Abusers’ urine concentrations: 10,000–100,000 ng/mL
- Fatalities: 237,000 ng/mL (25,000–700,000)
- 30%–40% eliminated unchanged  
  (74% in acidic urine, 1% in alkaline urine)

**Utility of Urine Drug Levels**

- Evidence of use (“negative” vs. “no drug”)
- “Unconfirmed positive” vs. “false positive”
- Consistency of results with claims of donor
- Renewed use vs. residual
- Likelihood of dosing scenarios
- Likelihood of impairment

**Issues in the Use of Urine Drug Levels**

- Test technology
  - Immunoassay (instrumented vs. non-instrumented GC/MS)
- Laboratory reports
  - Qualitative, quantitative, “semi-quantitative”
- Interpretation
  - Use, time of use, dosing, impairment

**New Drugs of Abuse: Detection and Challenges**

Dr. Leo Kadehjian  
Palo Alto, California
### New Drugs: “Designer Drugs” “Legal Highs”

- **1980s**: Fentanyl
- **Late 1980s**: Ring-substituted phenethylamines
- **1990s**: Tryptamines (“Foxy”)
- **2000s**: Salvia divinorum, Synthetic opioids, cocaine derivatives, Synthetic cathinones, “Spice”, synthetic cannabinoids, Benzylpiperazines

### Cannabis History

- **2327 BC**: Documented use of cannabis, Nung dynasty
- **1937**: Marijuana Tax Act
- **1964**: Identification of Δ⁹-THC
- **1970**: Controlled Substances Act: Marijuana Schedule I
- **1985**: Marinol (dronabinol) FDA approved: nausea
- **1988**: CB₁ receptor identified
- **1990**: CB₁ receptor cloned
- **1992**: Endogenous ligand “Anandamide” (“Internal bliss”)
- **1993**: CB₂ receptor cloned
- **1994**: CB₁ receptor antagonist SR 141716A, Rimonabant (Acomplia)
- **1996**: Medical marijuana initiatives (CA, AZ)
- **1998**: CB₂ receptor antagonist SR 144528

### Synthetic THC Analogues

- Δ⁹-Tetrahydrocannabinol (Dronabinol)
- CP 47,497
- CP 55,940
- Δ⁹-Tetrahydrocannabinol (Dronabinol)
- Nabulone (Cesamet) anti-nausea

### “Spice” Resources

- **Synthetic Cannabinoids and "Spice" (2009)**
- **Understanding the "Spice" Phenomenon (2009)**
- **J.W. Huffman, Clemson University, SC**
  45 papers on cannabinoids, synthetics
New Drugs Resources

- NIDA: www.nida.gov
- DEA: dea.gov
- European Monitoring Centre for Drug and Drug Addiction: www.emcdda.europa.eu
  since 1997 Early-Warning System (110 substances identified)
- 2009 24 new substances
- Erowid: erowid.org
### Passive Inhalation of Crack Cocaine

<table>
<thead>
<tr>
<th>Dose</th>
<th>Space</th>
<th>Time</th>
<th>Max. BE levels</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 mg</td>
<td>4 x 5</td>
<td>1/2 hr</td>
<td>≤15 ng/mL</td>
<td>Baselt et al., 1991</td>
</tr>
<tr>
<td>100 mg</td>
<td>7 x 8</td>
<td>1 hr</td>
<td>22–123 ng/mL</td>
<td>Cone et al., 1995</td>
</tr>
<tr>
<td>200 mg</td>
<td>7 x 8</td>
<td>1 hr</td>
<td>26–107 ng/mL</td>
<td>Cone et al., 1995</td>
</tr>
<tr>
<td>87.5 mg sidestream</td>
<td>11 x 15</td>
<td>4 hr</td>
<td>0–6 ng/mL</td>
<td>Cone et al., 1995</td>
</tr>
</tbody>
</table>

### EtG: Passive Exposure: Hand Sanitizer

<table>
<thead>
<tr>
<th>n</th>
<th>Description</th>
<th>Test results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>1 mL @ 60% EtOH, 20 per d (= 10 g EtOH), 5 d</td>
<td>≤10 – 114 ng/mL</td>
<td>Rosas and Lin, 2008</td>
</tr>
<tr>
<td>3–4</td>
<td>62% EtOH, every 30, 60 min</td>
<td>neg @ 50 ng/mL</td>
<td>Rohrig, 2006</td>
</tr>
<tr>
<td>2</td>
<td>every 15 min for 8 hr</td>
<td>1/2 pos, 62 ng/mL</td>
<td>Rohrig, 2006</td>
</tr>
<tr>
<td>24</td>
<td>conditions not specified</td>
<td>pos, cutoff not</td>
<td>ASAM, 2006 (Wall St. J.)</td>
</tr>
<tr>
<td></td>
<td>repeated throughout day</td>
<td>specified</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>62% EtOH, throughout day</td>
<td>770 ng/mL</td>
<td>Wall St. J., 2006</td>
</tr>
</tbody>
</table>

### EtG: “Innocent” Oral Exposure

<table>
<thead>
<tr>
<th>n</th>
<th>Description</th>
<th>Test results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>2 x 12 oz non-alcoholic beer</td>
<td>93 ng/mL</td>
<td>AACC / Quest, 2006</td>
</tr>
<tr>
<td>9</td>
<td>1 nip communion wine (5% EtOH)</td>
<td>77 ng/mL</td>
<td>AACC / Quest, 2006</td>
</tr>
<tr>
<td></td>
<td>4 oz mouthwash (12% EtOH), gangle every 30 sec, 5 min</td>
<td>≤246 ng/mL</td>
<td>AACC / Quest, 2006</td>
</tr>
<tr>
<td>11</td>
<td>gargle 3 x, 5 d</td>
<td>1/55 ≤50 ng/mL, all &lt;100 ng/mL</td>
<td>Costantino, 2005, 2006</td>
</tr>
</tbody>
</table>
### EtG: “Innocent” Oral Exposure

<table>
<thead>
<tr>
<th>n</th>
<th>Sample Description</th>
<th>Concentration (ng/mL)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>2.5 L “non-alcoholic” beer</td>
<td>300–870</td>
<td>Thierauf et al., 2010</td>
</tr>
<tr>
<td>2</td>
<td>Baker’s yeast/sugar</td>
<td>120, 500</td>
<td>Thierauf et al., 2010</td>
</tr>
<tr>
<td>4</td>
<td>Brewer’s yeast/sugar</td>
<td>ND</td>
<td>Thierauf et al., 2010</td>
</tr>
</tbody>
</table>

“Currently, the use of an EtG test in determining abstinence lacks sufficient proven specificity for use as primary or sole evidence that an individual prohibited from drinking, in a criminal justice or regulatory compliance context, has truly been drinking. Legal or disciplinary action based solely on a positive EtG, or other test discussed in this Advisory, is inappropriate and scientifically unsupported at this time. These tests should currently be considered as potential valuable clinical tools, but their use in forensic settings is premature.”

SAMHSA, Substance Abuse Treatment Advisory, 5(4), September 2006.

### SAMHSA: Alternative Specimens

“Also, scientific advances in the use of head hair, sweat, and oral fluid in detecting drugs have made it possible for these specimens to be used in Federal programs with the same level of confidence that has been applied to the use of urine.”

SAMHSA, Federal Register, 4/13/04, 69 FR 19689

### PharmChem Sweat Patch: PharmCheck

- **Patch components:**
  - Gas–permeable polyurethane outer membrane (Tegaderm™), 0.025 mm thick
  - Release liner: cellulose tissue, 0.003 mm thick
  - Cellulose absorbent pad: 3 x 5 cm (14 cm²), 0.7 mm thick
- **Patch sweat absorption:** ~300 µL/day ≈ 2 mL/week
- **Patch wear period:** 1–2 weeks
- **Patch processing:**
  - Eluted with 2.5 mL 75/25 MeOH/0.5 M acetate buffer
  - Immun assay screen
  - LC/MS/MS confirmation
- **Sweat patch cut-off:** Cocaine, BE: 10 ng/mL = 25 ng/patch

### Sweat Patch Drug Testing: Admissibility and Evidentiary Weight

- FDA cleared collection device and immunoassays (controlled-dosing, field, procedural integrity studies)
- Over 70 supporting publications in international peer-reviewed literature (only few challenges)
- Federal regulatory recognition (SAMHSA Proposed Rule 4/04)
- Majority of case law precedents supportive (especially recent)

### Oral Fluid: Benefits and Issues

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ease of specimen collection</td>
<td>Low specimen volume</td>
</tr>
<tr>
<td>Difficult to adulterate</td>
<td>Low drug concentrations</td>
</tr>
<tr>
<td>Better correlation with effects</td>
<td>Shorter detection times</td>
</tr>
<tr>
<td>Established and growing scientific literature</td>
<td>On-site testing limited</td>
</tr>
<tr>
<td>Minimal biohazard risks</td>
<td>No formal regulatory scheme</td>
</tr>
<tr>
<td>Good specimen stability</td>
<td>No formal proficiency program</td>
</tr>
<tr>
<td>Accurate testing methods</td>
<td>Limited case law</td>
</tr>
</tbody>
</table>
Issues in Hair Testing

- Hair anatomy and physiology
- Mechanisms of incorporation of drugs
- Specimen stability
- Analytical methods
- Interpretation of results
- Donor subversion
- Admissibility and evidentiary weight

Urine Specimen Validity Tests

Department of Health and Human Services
Substance Abuse and Mental Health Services Administration
Mandatory Guidelines for Federal Workplace Drug Testing Programs

Revised Mandatory Guidelines 4/13/04
69 FR 19644–19673
Effective 11/1/04

Drug Use, Dilution, and Detection

<table>
<thead>
<tr>
<th>Positive at Limit of Detection</th>
<th>Positive at HHS cut-offs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilute</td>
<td>9.9%</td>
</tr>
<tr>
<td>Normal (758 controls)</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

- s.g. <1.003 and / or creatinine <20 mg/dL.
- National Laboratory Certification Program, Program Document #25, 1993

Required Specimen Validity Tests: Urine

- Creatinine
- Specific gravity if creatinine <20 mg/dL.
- pH
- Oxidizing adulterants (≥1)
  - Nitrates, pyridinium chlorochromate, chromium (VI), bleach, iodine, halogens, peroxidase, peroxide, others
- Additional as needed

Urine Specimen Validity Testing

- Adulterated
  - Non-normal constituent
  - Endogenous constituent at non-normal concentration
- Substituted
  - Creatinine ≤2 mg/dL AND s.g. ≤1.0010 or ≥1.0200
- Invalid
  - Inconsistent creatinine, specific gravity
  - Nitrine, pH, possible presence of other adulterants
  - Interference
  - Appearance
- Dilute
  - Creatinine ≥2 mg/dL but <20 mg/dL AND s.g. >1.0010 but <1.0030

Validity Testing Criteria: Urine

Creatinine, mg/dL

- Inconsistent = Invalid
- Dilute
- Normal
- Substituted

Specific gravity

- Inconsistent = Invalid
- 1.0010 – 1.0030
- 1.0200
**SAMHSA**

**U.S. Courts**

- **Dilute**
  - creat ≥ 2 but < 20
  - and
  - s.g. > 1.0010 but < 1.0030 or
  - s.g. 1.002 or 1.003

- **Invalid**
  - creat < 2 and
  - s.g. > 1.0010 but < 1.0020 and s.g. ≤ 1.0010
  - pH ≥ 3 but < 4.5 and pH ≥ 9 but < 11

- **Substituted**
  - creat < 2 and creat < 2
  - s.g. ≤ 1.0010 or ≥ 1.0200

- **Adulterated**
  - pH < 3 or ≥ 11
  - Non-normal substance
  - Non-normal level

---

**Urine Production Rate After Water Loading**

- **Typical:**
  - Drink 1 L water
  - Urine production rate (mL/min)

- **Cut-off:**
  - Drink 2 L water
  - Urine production rate (mL/min)

---

**Creatinine**  **Specific Gravity**

- **Typical:**
  - ~150 mg/dL
  - ~1.025

- **Cut-off:**
  - 20 mg/dL
  - 1.003

---

**Dilution: THC**

- **Typical:**
  - Cut-off: 50 ng/mL

- **Cut-off:**
  - 20000 ng/mL

---

**Dilution: Cocaine**

- **Typical:**
  - Cut-off: 5000 ng/mL

- **Cut-off:**
  - 20000 ng/mL
Effect of Water Loading on Urine Cannabinoid Levels

E. Cone et al., 1998

Urine Creatinine

D. Barr et al., 2004

Urine Creatinine: Diabetics vs. Normal Population

N. de Fine Olivarius et al., 2006

Effect of Creatine Loading on Urine Creatinine

Ropero-Miller et al., 1998
**Adjusting Cannabinoid Levels for Dilution / Concentration**

\[
\frac{\text{ng Cannabinoids}}{\text{mg Creatinine}} / \text{mL} \times 100 = \frac{\text{ng Cannabinoids}}{\text{mg Creatinine}} / \text{dL}
\]

\[
\frac{50 \text{ ng Cannabinoids}}{150 \text{ mg Creatinine}} / \text{dL (normal)} \times 100 = \frac{33 \text{ ng Cannabinoids}}{\text{mg Creatinine}}
\]

\[
\frac{50 \text{ ng Cannabinoids}}{15 \text{ mg Creatinine}} / \text{dL (dilute)} \times 100 = \frac{333 \text{ ng Cannabinoids}}{\text{mg Creatinine}}
\]

**Marijuana Detection Times for 6 Immunoassays and GC/MS**

- **Low dose**:
  - Huestis et al., 1995
  - E. Kouri et al., 1999

- **High dose**:
  - @ 100 ng/mL
  - @ 50 ng/mL
  - GC/MS @ 15 ng/mL

**Creatinine Normalized THC-COOH in Chronic Users**

- Normalized THC-COOH ng/mL ≥ 5000 doses lifetime use (= daily use for 14 years)
- Levels normalized to 100 mg/dl creatinine
- ±SE
- 5/17 (29%) negative (EMIT @ 20 ng/mL) w/i 1 week
- 9/17 (53%) negative w/i 2 weeks
- 11/17 (65%) negative w/i 3 weeks

**Renewed Use vs. Residual?**
Renewed Use or Residual?

With current immunoassays @ 50 ng/mL cut-off:

- Occasional users: positive for 1–2 days, rarely longer
- Documented chronic users: positive for 2–3 weeks, rarely longer
- Examine every positive, review intervening "negatives"
- Positive after 1 month → Renewed use (conservative)
- 50% increase in dilution-adjusted levels → Renewed use after 1 week (conservative)

Renewed Use vs. Residual Levels from Prior Use?

Issues for consideration:

- Time: between test results, from claimed last use
- Drug levels (normalized)
- Pattern: levels (normalized), time, specimen ratios
- Specimen validity: dilution, creatinine, normalization
- Donor claims, history