Drugs of Abuse in Oklahoma: Trends and Testing Technologies

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Agenda

Drug prevalence in the State of Oklahoma throughout 2016

Drug screening technologies

Efficacy of screening vs. confirmatory testing

Case studies
Seized drugs in Oklahoma - 2016

Drugs Submitted to OSBI

### Throughout 2016

<table>
<thead>
<tr>
<th>I illicit (weight)</th>
<th></th>
<th>Prescription (tablets)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>2722.0 lbs.</td>
<td>Alprazolam (Xanax) 14,939</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>268.0 lbs.</td>
<td>Hydrocodone (Lortab, Norco) 6,979</td>
</tr>
<tr>
<td>Cocaine</td>
<td>25.7 lbs.</td>
<td>Oxycodone (Percocet) 4,434</td>
</tr>
<tr>
<td>Heroin</td>
<td>19.4 lbs.</td>
<td>Clonazepam (Klonopin) 2,887</td>
</tr>
<tr>
<td>PCP</td>
<td>100 g.</td>
<td>Diazepam (Valium) 2,771</td>
</tr>
</tbody>
</table>
Opioid-Prescribing Rates by Specialty

Benefits of drug testing

Drug testing provides information that:

- detect patient use of illicit substances
- can increase safety of prescribing medications
- identify pregnant women who are misusing drugs
- monitor substance abstinence
- can affect clinical decisions; influencing other medical decisions


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Screening technology – Immunoassay

Several different formats

- Cup
- Dipstick
- Cartridge
- Instrumental
  - CEDIA
  - KIMS
  - DRI
  - ELISA
  - QMA
Know your tests
 Screening Cut-off

Federally mandated Department of Transportation (DOT) guidelines for drug testing of safety-sensitive transportation employees have established the following cutoffs for abused drugs and metabolites:

<table>
<thead>
<tr>
<th>Initial Test Analyte</th>
<th>Initial Test Cutoff Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana metabolites</td>
<td>50 ng/mL</td>
</tr>
<tr>
<td>Cocaine metabolites</td>
<td>150 ng/mL</td>
</tr>
<tr>
<td>Opiate metabolites</td>
<td></td>
</tr>
<tr>
<td>Codeine/Morphine</td>
<td>2000 ng/mL</td>
</tr>
<tr>
<td>6-Acetylmorphine</td>
<td>10 ng/mL</td>
</tr>
<tr>
<td>Phencyclidine</td>
<td>25 ng/mL</td>
</tr>
<tr>
<td>Amphetamines</td>
<td></td>
</tr>
<tr>
<td>AMP/MAMP</td>
<td>500 ng/mL</td>
</tr>
<tr>
<td>MDMA</td>
<td>500 ng/mL</td>
</tr>
</tbody>
</table>

DOT Required Screen Concentrations vs Point of Care Product Inserts

Comparison of Screening Methods

<table>
<thead>
<tr>
<th>Drug</th>
<th>DOT</th>
<th>Cup 1</th>
<th>Cup 2</th>
<th>Cup 3</th>
<th>Cup 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine</td>
<td>150</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>100</td>
</tr>
<tr>
<td>Opiates</td>
<td>2,000</td>
<td>2,000</td>
<td>2,000</td>
<td>2,000</td>
<td>100</td>
</tr>
<tr>
<td>6-AM</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PCP</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Amph</td>
<td>500</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
<td>300</td>
</tr>
<tr>
<td>MDMA</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>-</td>
<td>40</td>
</tr>
<tr>
<td>Marijuana</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

All concentration levels in ng/mL.
POC testing criticized for the high rate of false positives

A review article describes false positives in the following drug classes.

- Amphetamines: bupropion, chlorpromazine, dimethylamylamine, labetalol, metformin, ofloxacin, promethazine, trazodone
- Benzodiazepines: sertraline, Efavirenz
- Cannabinoids: Efavirenz, ibuprofen, naproxen, niflumic acid
- Buprenorphine: amisulpride, sulpiride, codeine, morphine, dihydrocodeine, tramadol
- Methadone: diphenhydramine, creatinine, tapentadol, verapamil
- Morphine: levofloxacine, enoxacine
- Heroin: pentazocine


Product Inserts

Non-cross reactive compounds

- Not reactive at 100µg/mL

T-Cup product insert
Product Inserts

More than just the instructions

<table>
<thead>
<tr>
<th>Drug concentration</th>
<th>THC</th>
<th>MTD</th>
<th>mAMP</th>
<th>MDMA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>0% Cut-off</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>-50% Cut-off</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td>-25% Cut-off</td>
<td>30</td>
<td>12</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td>Cut-off</td>
<td>30</td>
<td>1</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>-25% Cut-off</td>
<td>30</td>
<td>1</td>
<td>29</td>
<td>2</td>
</tr>
<tr>
<td>+50% Cut-off</td>
<td>30</td>
<td>0</td>
<td>30</td>
<td>0</td>
</tr>
</tbody>
</table>

Product Inserts

Cross reactivity

The following Benzodiazepine-related substances yield positive results for Benzodiazepines:

- Oxazepam: 300
- Alprazolam: 400
- Bromazepam: 2,000
- Chlordiazepoxide: 8,000
- Clorazepate: 400
- Clonazepam: 5,000
- Diazepam: 2,000
- Estazolam: 20,000
- Flunitrazepam: 1,000
- Lorazepam: 4,000
Product Inserts

Cross reactivity

The following Opiates/Morphine-related substances yield a positive result for Opiates/Morphine at 2000 ng/ml cut-off level:

- Morphine .......................... 3000 ng/ml
- Morphine Sulfate Pentahydrate .......................... 2000 ng/ml
- Morphine-3-β-D Glucuronide .......................... 2000 ng/ml
- Codeine ................................ 2000 ng/ml
- Heron ................................ 2000 ng/ml
- Levorphanol .......................... 1000 ng/ml
- Ranitidine ................................ 100,000 ng/ml
- 6-Acetylmorphine .......................... 50 ng/ml

The following Oxycodone-related substances yield positive results for Oxycodone at 100 ng/ml cut-off level:

- Oxycodone-2HCl .......................... 100 ng/ml
- Codeine ................................ 700 ng/ml
- Hydrocodone .......................... 500 ng/ml
- Hydromorphone .......................... 1,500 ng/ml
- Morphine-Sulfate .......................... 7,000 ng/ml
- Morphine-3,4-Dihydroxyacetyl .......................... 40,000 ng/ml
- Norcodeine .......................... 40,000 ng/ml
- Oxymorphone .......................... 300 ng/ml

Evaluation – Screen vs. Confirmation
Comparative Evaluation of POC to LC/MS/MS

Opioids and Illicit Drugs

<table>
<thead>
<tr>
<th>Test</th>
<th>False Negative %</th>
<th>False Positive %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td>7.8</td>
<td>6.9</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>24.6</td>
<td>7.7</td>
</tr>
<tr>
<td>Marijuana</td>
<td>9.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>60*</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Benzodiazepine assay compared to LC/MS/MS

Point of care cup

- Study evaluated benzodiazepine POC results against LC/MS/MS confirmation.
  - 99 false negatives out of 410 samples (24.1%) were found
  - A false positive rate of 10.5% (10 of 95 results)
  - The total efficacy of the test was 78.4%.
Difficulties in detection of benzodiazepines

Laboratory immunoassay instrument

- False negative rates for three different immunoassay technologies were unacceptably high
  - HS-CEDIA - 22%
  - KIMS - 45%
  - CEDIA - 53%
- Highest sensitivity - alprazolam (Xanax)
- Lowest sensitivity – lorazepam (Ativan) and clonazepam (Klonopin)
- There were no false positives were found.
Interpretation

- Cocaine positive case study
- Amphetamine & methamphetamine
- Methylphenidate
- Opiates positive

Tricking the Test

- Medication substitution
- Pill shaving


Reference Lab Confirmatory Testing Cutoff

Comparison of Confirmation

<table>
<thead>
<tr>
<th>Drug</th>
<th>DOT Confirm</th>
<th>Lab 1</th>
<th>Lab 2</th>
<th>Lab 3</th>
<th>Lab 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>15</td>
<td>10</td>
<td>2</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Cocaine</td>
<td>100</td>
<td>50</td>
<td>50</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Opiates</td>
<td>2,000</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>6-AM</td>
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<td>---</td>
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<td>10</td>
<td>10</td>
</tr>
<tr>
<td>PCP</td>
<td>25</td>
<td>10</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>250</td>
<td>100</td>
<td>50</td>
<td>125</td>
<td>250</td>
</tr>
<tr>
<td>MDMA</td>
<td>250</td>
<td>100</td>
<td>50</td>
<td>---</td>
<td>200</td>
</tr>
</tbody>
</table>
Sources

1. Substance Abuse Testing in Primary Care Technical Assistance Publication (TAP) 32. HHS Publication Number (SMA) 12-4668. Rockville, MD; Substance Abuse and Mental Health Services Administration, 2012.

2. 49 CFR Part 40 Section 40.87


4. KIMS, CEDIA and HS-CEDIA Immunoassays are Inadequately Sensitive for Detection of Benzodiazepines in Urine from Patients Treated for Chronic Pain, Pain Physician 2014; 17:359-366.
