Appropriate Interpretation of Urine Drug Screen Results

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Dr. Leppien specializes in the treatment of chronic pain, substance use disorder and psychiatric illness. Her professional and research interests include opioid and non-opioid pharmacotherapy, as well as the integration of behavioral health and substance use disorder treatment within pain management services. Dr. Leppien is an active member of the American Pharmacists Association (APhA), currently serving as the Pain, Palliative Care and Addiction SIG Coordinator.
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Mark Garofoli is a Pitt PharmD graduate, Strayer MBA graduate, Board-Certified Geriatric Pharmacist (BCGP), Certified Pain Educator (CPE), and Certified Tobacco Treatment Specialist (CTTS). His past positions include being a pharmacist leader with CVS Health, Humana, and the WV Safe & Effective Management of Pain (SEMP) Program, along with coordinating the WV SEMP Guidelines Panel.

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Financial Disclosures

Mark Garofoli, PharmD, MBA, BCGP, CPE, CTTS, Emily E. Leppien, PharmD, BCPS, BCPP, and APhA’s editorial staff declare no relevant financial relationships or commercial interests in any product or service mentioned in this activity, including grants, employment, gifts, stock holdings, honoraria.

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Conflicts of interest have been resolved through content review by Kieu Nguyen, PharmD, Director of Content Development at the American Pharmacists Association.
Target Audience

The overarching goal of PCSS is to train health care professionals in evidence-based practices for the prevention and treatment of opioid use disorders, particularly in prescribing medications, as well as for the prevention and treatment of substance use disorders.
Educational Objectives

At the conclusion of this application-based activity, participants will be able to:

1. List causes that may lead to unexpected UDS results, specifically false positives and negatives.
2. Explain how opioid and benzodiazepine metabolism impacts UDS results.
3. Interpret a UDS reading based on patient history and reported results.
4. Recommend appropriate monitoring based on patient history and UDS results.
5. Make patient-specific treatment recommendations after analyzing UDS results.
Development and Support

This accredited learning activity for pharmacists, *Appropriate Interpretation of Urine Drug Screen Results*, is developed by the American Pharmacists Association.

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Baseline Knowledge Assessment
Pre-Assessment Question 1

Which one of the following medications can possibly produce a false positive urine drug screening for methadone?

A. Ciprofloxacin
B. Naproxen
C. Quetiapine
D. Cyclobenzaprine
Pre-Assessment Question 2

A patient using morphine may also show a positive result for ________ on a confirmatory urine drug test.

A. Codeine
B. Hydromorphone
C. Oxycodone
D. Hydrocodone
Pre-Assessment Question 3

Urine drug monitoring should be performed for low-risk patients a minimum of every ________.

A. 1 month
B. 3 months
C. 6 months
D. 12 months
1. Nonopioid therapies are effective for many common types of acute pain
2. Nonopioid therapies are preferred for subacute and chronic pain
3. Utilize immediate-release (IR) before extended-release (ER) opioids
4. Start Low, Go Slow, and avoid increasing to high-risk dosage levels
5. For patients already utilizing high-risk opioid dosages: continually and carefully weigh benefits and risk, taper only if risks outweigh benefits, and when tapering ensure a gradual taper unless there is a life-threatening concern
6. When opioids are utilized in acute pain, provide only for expected duration
7. Reevaluate chronic/subacute opioid utilization at least every 3 months (within 1 to 4 weeks initially)
8. Naloxone education
9. Prescription Drug Monitoring Program (PDMP) review initially and periodically
10. **TOXICOLOGY URINE DRUG TESTING (UDT)**
11. Caution with opioid/benzodiazepine combinations (or opioids with any CNS depressant)
12. Treatment with evidenced-based medications to treat patients with opioid use disorder

Urine Drug Monitoring Goals

- Improve proper medication adherence
- Prevent medication misuse/diversion
- Detect medication misuse/diversion

## Urine Drug Monitoring Frequency

<table>
<thead>
<tr>
<th>Risk</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Annual</td>
</tr>
<tr>
<td>Moderate</td>
<td>≥ 2x/year</td>
</tr>
<tr>
<td>High</td>
<td>≥ 3x/year</td>
</tr>
<tr>
<td>Any</td>
<td>? Every Appointment ?</td>
</tr>
</tbody>
</table>

How to Assess Risk?

- Physical examination and detailed medication history
  - Past or current use of illicit substances
  - Specific opioid medications used

- Review of Prescription Drug Monitoring Program (PDMP)

- Use of concomitant medications
  - Benzodiazepines
  - Non-Benzodiazepine Receptor Agonists (NBRAs, Z-Drugs)

- Screening tools:
  - Drug Abuse Screening Test (DAST-10)
  - Opioid Risk Tool (ORT)
  - Screener and Opioid Assessment for Patients with Pain Revised (SOAPP-R)

Urine Drug Screening Strategies: Trust, But Verify

● Patient and Provider Agreement → UDM Procedures

● Random or scheduled (e.g., appointments)

● Urine samples collected in a private bathroom without running water, soap, hand sanitizer or other liquids – and with toilet water stained blue

● Urine specimen cups with temperature strips that fluoresce between 90°F to 100°F

● Urine creatinine and specific gravity can be ordered together with a drug test panel

Urine Color

- The yellow color of urine results from urobilin that is produced as a product of bilirubin degradation
- Normal urine color → light yellow

Toxicology Testing

Urine Drug Monitoring (UDM)

Urine Drug Screening (UDS)

Urine Drug Testing (UDT)
### Urine Drug Monitoring

<table>
<thead>
<tr>
<th>Urine Drug Screening (UDS)</th>
<th>Urine Drug Testing (UDT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoassay screen (e.g., cup)</td>
<td>GC-MS or LC-MS</td>
</tr>
<tr>
<td><strong>PRESUMPTIVE</strong></td>
<td><strong>DEFINITIVE</strong></td>
</tr>
<tr>
<td>In-office, point-of-care, or lab-based</td>
<td>Laboratory, highly specific and sensitive</td>
</tr>
<tr>
<td>Results within minutes</td>
<td>Results in hours or days</td>
</tr>
<tr>
<td>Various cups detect a majority of legal and illicit medications by structural class</td>
<td>Measures all drug/metabolite concentrations</td>
</tr>
<tr>
<td>Guidance for preliminary treatment decisions</td>
<td>Definitive identification and analysis</td>
</tr>
<tr>
<td>Cross-reactivity common: more false positives</td>
<td>False-positive results are rare</td>
</tr>
<tr>
<td>Higher cutoff levels: more false negatives</td>
<td>False-negative results are rare</td>
</tr>
</tbody>
</table>
| $ | $$$

**GC-MS**: gas chromatography-mass spectrometry  
**LC-MS**: liquid chromatography-mass spectrometry

### Urine Drug Monitoring
#### Cut-Off Levels (SAMHSA)

<table>
<thead>
<tr>
<th>Chemical</th>
<th>UDS Cut-Off (ng/mL)</th>
<th>UDT Cut-Off (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetrahydrocannabinol (THC)</td>
<td>50</td>
<td>15</td>
</tr>
<tr>
<td>Opiates</td>
<td>2,000</td>
<td>2,000</td>
</tr>
<tr>
<td>Hydrocodone/Hydromorphone</td>
<td>300</td>
<td>100</td>
</tr>
<tr>
<td>Oxycodone/Oxymorphone</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>6-Monoacetylmorphine (6-MAM)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Amphetamines/Methamphetamine 3,4-Methylenedioxyamphetamine (MDMA)</td>
<td>500</td>
<td>250</td>
</tr>
<tr>
<td>Cocaine (Benzoylecegonine)</td>
<td>150</td>
<td>100</td>
</tr>
<tr>
<td>Phencyclidine (PCP)</td>
<td>25</td>
<td>25</td>
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</tbody>
</table>

### Urine Drug Detection Times

<table>
<thead>
<tr>
<th>Drug</th>
<th>Detection Time After Ingestion</th>
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<tbody>
<tr>
<td>Alcohol</td>
<td>7 to 12 Hours</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>2 to 3 Days</td>
</tr>
<tr>
<td>Benzodiazepines (Short-Acting)</td>
<td>3 Days</td>
</tr>
<tr>
<td>Benzodiazepines (Long-Acting)</td>
<td>30 Days</td>
</tr>
<tr>
<td>Marijuana (Single Dose)</td>
<td>3 Days</td>
</tr>
<tr>
<td>Marijuana (4x/Week)</td>
<td>5 to 7 Days</td>
</tr>
<tr>
<td>Marijuana (Daily)</td>
<td>10 to 15 Days</td>
</tr>
<tr>
<td>Marijuana (Long-Term)</td>
<td>&gt;30 Days</td>
</tr>
<tr>
<td>Codeine</td>
<td>2 Days</td>
</tr>
<tr>
<td>Heroin</td>
<td>2 Days</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>2 to 4 Days</td>
</tr>
<tr>
<td>Methadone</td>
<td>3 Days</td>
</tr>
<tr>
<td>Morphine</td>
<td>2 to 3 Days</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>2 to 4 Days</td>
</tr>
</tbody>
</table>
**UDS Different Drug Panels**

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>5 Panel</th>
<th>7 Panel</th>
<th>10 Panel</th>
<th>12 Panel</th>
<th>13 Panel</th>
<th>14 Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>THC</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cocaine</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Opiates</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>PCP</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Barbiturates</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Quaaludes</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ecstasy</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Oxycodone</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Fentanyl</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Meperidine</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

False Positives and Negatives

Rates of False Positives & Negatives in Immunoassay Urine Drug Screens

- Opiates
- Oxycodone
- Methadone
- Benzodiazepine
- Amphetamines
- Barbiturates
- Antidepressants
- Cocaine
- Marijuana
- Methamphetamine

Percentage

# UDS False Positives

<table>
<thead>
<tr>
<th>Substance</th>
<th>UDS Cross-Reactant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>asthma inhalers and isopropyl alcohol</td>
</tr>
<tr>
<td>Amphetamine Methamphetamine</td>
<td>amantadine, bupropion, chlorpromazine, desipramine, labetalol, phentermine, phenylephrine, promethazine, pseudoephedrine, selegiline, trazodone</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>ibuprofen and naproxen</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>oxaprozin, sertraline and some herbals</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>dronabinol (synthetics), NSAIDs (ibuprofen/naproxen), efavirenz, PPIs (pantoprazole), promethazine</td>
</tr>
<tr>
<td>Opioids</td>
<td>chlorpromazine, dextromethorphan, diphenhydramine, doxylamine, poppy seeds, quinine, quinolones, rifampin, verapamil</td>
</tr>
<tr>
<td>Methadone</td>
<td>quetiapine</td>
</tr>
<tr>
<td>Tricyclic antidepressants (TCAs)</td>
<td>carbamazepine, cyclobenzaprine, quetiapine</td>
</tr>
</tbody>
</table>
Cannabinoids: Use Is on the Rise

- THC metabolite: THC-COOH
  - Carboxylic acid group added to allow for kidney excretion

- Cannabidiol (CBD) *should not* screen (+) for THC, however
  - High % of products contain other substances
  - Bonn-Miller et al. *JAMA* 2017 study:
    - 26 of 84 (~30%) CBD extracts had accurate labels
  - CBD and THC structures are very similar

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Example Patient Case 1

• JP is prescribed oxycodone ER and hydrocodone/acetaminophen. After review of his medical records, it is noted he is also prescribed cyclobenzaprine and dronabinol for pain management. Routine 12-panel UDS was positive for opiates, oxycodone, and TCAs.

• **TRUE/FALSE:** UDS results are as expected given the patient’s current medication regimen.

• What happens next?

**FALSE**
UDS False Negatives

- Dilute urine, overhydration
- Low urine drug concentration
- As needed use, with no use prior to screening
- Increased time between administration and screening time

UDS “Work-Arounds”

- Home remedies:
  - Niacin, bleach, vinegar, goldenseal root, cranberry juice
- Synthetic urine
  - Purchasing urine from a smoke shop
- Dilution
  - Decrease amount of drug present in urine
- Substitution
  - Using someone else’s urine

UDT to Confirm Results

- Unexpected or unexplained results should be confirmed with UDT
  - Unexpected positive or negative results

Copyright Permission Allowed:
UDT Negative Result: Possible Causes

- Never took medication
- ↓ oral absorption of medication
- ↓ urinary excretion of medication metabolites
- Medication taken too many hours before test for detectable level to be present
- Medication was stolen, sold, or otherwise illicitly distributed

What to Expect on UDT?  
Opiate Metabolism

# CYP450 Opioid Metabolism

<table>
<thead>
<tr>
<th>Drug</th>
<th>CYP Metabolism</th>
<th>Primary Active Metabolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>2D6</td>
<td>Morphine</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>3A4</td>
<td>--</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>3A4, 2D6</td>
<td>Hydromorphone</td>
</tr>
<tr>
<td>Methadone</td>
<td>3A4, 2D6, 2C8, 2C9, 2C19, 2B6, 1A2</td>
<td>Oxymorphone</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>3A4, 2D6</td>
<td>Oxymorphone</td>
</tr>
<tr>
<td>Tramadol</td>
<td>2D6</td>
<td>--</td>
</tr>
</tbody>
</table>

What to Expect on UDT?
Benzodiazepine Metabolism

Benzodiazepine Metabolism

Liver Metabolism

Phase I (Oxidation, CYP450s)
↓ w/age
- Diazepam
  - Triazolam
- Alprazolam

Phase II (Glucoronidation)
Minimal changes w/age
- Lorazepam
  - Temazepam
- Oxazepam
If unexpected results occur when ordering a UDT, remember that the focus is to improve patient safety. Have a plan in place for communicating results and practice the difficult conversations you may have with your patients.

**TALKING WITH PATIENTS ABOUT URINE DRUG TESTING RESULTS:**

- Always keep the focus on the patient’s well-being and safety.
- Do not jump to conclusions about unexpected results; have a candid conversation with the patient about possible explanations.
- Do not dismiss patients from care based on UDT results.
- Consider using the CDC mobile app to practice the types of conversations you may encounter with patients.

**Actions to take post-urine drug testing:**

- Discuss unexpected results with the local laboratory or toxicologist if assistance is needed with interpretation.
- Inform the patient of the test results.
- Take time to discuss unexpected results with the patient and refer to pre-UDT information the patient may have shared with you.
- Review the treatment agreement and focus conversations around patient safety.
- Determine if frequency and intensity of monitoring should be increased and keep the patient informed.

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Example Patient Case 2

- AZ is prescribed morphine ER 15 mg PO Q8h and duloxetine 60 mg PO BID for chronic pain. Routine 12-panel UDS was negative for all substances.

- Urine sample is sent to laboratory for confirmatory UDT.

- UDT reveals positive result for morphine, marijuana, and cocaine.
  - Are these results expected?
  - How do we discuss these results with the patient?
  - When should UDM be repeated?
Handling Situations: Confirmed Drug Seeking or Diversion

• Reference the patient and provider agreement/contract

• Treatment can continue with non-controlled substance therapies

• Refer to a substance-use disorder specialist or program

• Contact law enforcement if concern for safety of patient or others

• Respect for all those directly or indirectly involved in the specific patient case should be upheld, while also ensuring both a procession within federal and state laws and an appropriate level of patient care
Avoid Patient Abandonment

• Document patient encounters thoroughly
• Engage in collaborative interprofessional care
• Stress importance of continued patient care
• Submit referrals to additional healthcare professionals as appropriate

Key Messages

- Urine Drug Monitoring (UDM) includes:
  - Urine Drug Screenings (UDS) and Urine Drug Tests (UDT)
- UDS is presumptive with a concerning observed percentage of false positives/negatives
  - UDT is definitive
- To determine if a possible false positive can occur for a given substance on a UDS, one can analyze the chemical structure to review for similarities
  - This is not a concern with UDT
- Many opioids and benzodiazepines are metabolized into active metabolites
  - Metabolites may be commercially available products
- Monitoring frequency can be determined by identifying risk
  - No such thing as too frequent monitoring
  - Can also consider performing random UDM
Post-Assessment Question 1

Which one of the following medications can possibly produce a false positive urine drug screening for methadone?

A. Ciprofloxacin
B. Naproxen
C. Quetiapine
D. Cyclobenzaprine
Post-Assessment Question 2

A patient using morphine may also show a positive result for ________ on a confirmatory urine drug test.

A. Codeine
B. Hydromorphone
C. Oxycodone
D. Hydrocodone
Post-Assessment Question 3

Urine drug monitoring should be performed for low-risk patients a minimum of every ________.

A. 1 month
B. 3 months
C. 6 months
D. 12 months
PCSS Mentoring Program

- PCSS Mentoring Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder (MOUD).

- PCSS mentors are a national network of providers with expertise in 
  addictions, pain, and evidence-based treatment including MOUD.

- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.

- No cost.

For more information visit: 
https://pcssNOW.org/mentoring/
Have a clinical question?

Ask a Colleague

A simple and direct way to receive an answer related to medications for opioid use disorder. Designed to provide a prompt response to simple practice-related questions.

http://pcss.invisionzone.com/register
**PCSS** is a collaborative effort led by the American Academy of Addiction Psychiatry (AAAP) in partnership with:

<table>
<thead>
<tr>
<th>Addiction Technology Transfer Center</th>
<th>American Society of Addiction Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Academy of Family Physicians</td>
<td>American Society for Pain Management Nursing</td>
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<tr>
<td>American Academy of Pain Medicine</td>
<td>Association for Multidisciplinary Education and Research in Substance use and Addiction</td>
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<tr>
<td>American Academy of Pediatrics</td>
<td>Council on Social Work Education</td>
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<td>American Pharmacists Association</td>
<td>International Nurses Society on Addictions</td>
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<td>National Association of Community Health Centers</td>
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<td>National Association of Social Workers</td>
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<tr>
<td>American Medical Association</td>
<td>National Council for Mental Wellbeing</td>
</tr>
<tr>
<td>American Osteopathic Academy of Addiction Medicine</td>
<td>The National Judicial College</td>
</tr>
<tr>
<td>American Psychiatric Association</td>
<td>Physician Assistant Education Association</td>
</tr>
<tr>
<td>American Psychiatric Nurses Association</td>
<td>Society for Academic Emergency Medicine</td>
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Educate. Train. Mentor

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