What is Urine Drug Testing (UDT)?

UDT:
- Is a method which involves the analysis of a urine specimen to detect the presence or, in some cases, the absence of a drug and/or the metabolite(s) at or above a predetermined threshold
- Plays a key role in safely managing a chronic pain patient, to:
  - Stratify individual risk
  - Identify relapse or drug misuse
  - Assist in monitoring for compliance with the agreed upon treatment plan
  - Advocate for the pain patient with family, workplace, and other relevant third parties

Important to note:
- Thresholds and testing strategies in federally regulated UDT make the assumption that most participants are non-drug users. In the chronic pain population, most participants “are appropriate users” of prescription drugs
- UDT can be regulated (ie, workplace testing) and non-regulated (ie, clinical testing)
- Regulated UDT was not designed for use in the chronic pain patient population. The SAMHSA-based testing model was never meant to be used clinically. It was designed to be used primarily to identify inappropriate drug use in the workplace
- Regulated urine drug screening immunoassay tests are designed to detect illicit drug use in a population pool of largely non-drug users
- Regulated urine drug detection thresholds are usually set at high levels consistent to minimize false-positive results
- No one standard UDT exists for all drug testing scenarios. UDT does not test for every drug, hence, a “testing strategy” must be in place to insure that the tests ordered meet the patient/clinicians’ needs

Utility of UDT

UDT results may be used:
- As an objective data point to support baseline patient data collection
- To assess patient adherence with the treatment plan/treatment agreement
- To show recent previous exposure to a drug(s) or its metabolite(s), or to members of certain classes of drugs
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Limitations of UDT

*UDT cannot provide information about:*

- Motivation behind exposure, eg, legitimate medical exposure to cocaine as a topical anesthetic vs. illicit use of cocaine. Both will result in a positive UDT for benzoylecgonine and/or cocaine parent
- Amount of drug used
- Time of last drug use
- Source of drug (licit or illicit)
- Confirmation of addiction, physical dependence, or impaired function
- Synthetic or semi-synthetic opioid use
  - Immunoassay urine methods have a low sensitivity for semi-synthetic opioids
  - “Opiate” immunoassay screens will not detect synthetic agents like fentanyl or methadone unless the assay is specific for the particular molecule
  - Immunoassay UDTs are sensitive for naturally occurring opiates such as codeine/morphine and less reliably for semi-synthetic agents like oxycodone, hydrocodone, oxymorphone or hydromorphone
  - Specific immunoassay tests are available for some synthetic or semi-synthetic agents such as methadone or oxycodone
  - GC/MS and other more sophisticated laboratory tests do detect these and many other molecules
- Negative opiate immunoassay results do not preclude use of semi-synthetic or synthetic opioids
- Drug-specific testing is available; communicate with the laboratory regarding availability and costs of drug-specific testing and their particular need
- Remember to alert the laboratory to the drug(s) in question to identify the parent and/or the metabolite(s) in question, if possible

*Important to note:*

- Order the appropriate test
- Always consider UDT results in context with drug metabolism and comprehensive patient data
- Metabolite pathways can produce positive results for analytes that might appear to indicate drug abuse when in reality, it is simply the detection of a metabolic pathway, eg, codeine may result in a positive for hydrocodone (please refer to the pathway of opioid metabolism on page 5)
- Communication with the laboratory, especially with unexpected results, is critical to the proper interpretation of laboratory data. In some cases, the “expected” result may be misleading, ie, where a patient is prescribed an opioid such as fentanyl and is positive for “opiates.” This appears to be “as expected,” but because fentanyl is a synthetic opioid, it cannot explain the positive opiate results. A call to the laboratory is essential unless the patient’s clinical story is consistent with the results

Factors Affecting UDT Results

- Integrity of urine sample
- Type of drug and pharmacokinetics
- Cross-reactivity of other agents
- Last time and amount of drug used
- Patient metabolism and genetic profile
- Laboratory or human error

*Always re-test the original specimen if there is any doubt regarding the initial tests results.*
## Urine Drug Testing

### Urine Sample\(^1,3,4,7,16-19\)

- Concentrated sample is best if practical
- Unobserved collection is acceptable
- Use colorant in toilet water and limit availability to other water sources to limit potential for sample dilution
- Sample should be consistent with human urine:
  - Temperature 90-100 degrees Fahrenheit within 4 minutes of collection in a suitable sample volume (ie, \(\geq 30\) mL)
  - pH 4.5-8.0
  - Random urinary creatinine greater than 20 mg/dL; less than 20 mg/dL is considered dilute and less than 5 mg/dL is not consistent with human urine

### Testing Options: Strengths and Limitations\(^4,16\)

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Results TAT</th>
<th>Costs</th>
<th>Test Results</th>
<th>Appropriate Use</th>
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</table>
| POC or IA     | Immediate   | $$\text{Including personnel time to perform testing}$$ | IA testing, done at POC or laboratory, use essentially the same reagents, however, the cutoff points may be different especially for opioids, which are 300 ng/mL therapeutically, but regulated tests are at 2,000 ng/mL | • If results will alter course of therapy or are in dispute; may want to confirm with additional testing using GC/MS or LC/MS  
• The biggest advantage to POC is the immediacy of the test result and the ability of the clinician to target specific therapeutic interventions based on POC results  
• The biggest disadvantage to POC is responsibility for testing quality lies with testing site, accuracy and/or cost |
| IA Laboratory | Fast; usually \(< 24\) hours | $$\text{QA is performed by the laboratory}$$ | Detects classes of drug/metabolite per panel selection if ordered  
High sensitivity | Order separate test for semi-synthetic/synthetic opioid drug detection, ie, fentanyl, methadone |
| GC/MS or LC/MS| Time consuming; complex sample preparation | $$$\text{High specificity}$$ | Detects specific drug and/or drug metabolite; thresholds can often be set lower than with IA testing  
Reliable true-positives; true-negatives  
QA is performed by the laboratory | Confirmatory testing after a positive finding from IA, if disputed by patient |

POC = point of care/collection; GC/MS = gas chromatography-mass spectrometry;  
LC/MS = liquid chromatography-mass spectrometry; QA = quality assurance; IA = immunoassay;  
TAT = turnaround time
UDT: Frequency and Timing\textsuperscript{2,6,8-15}

**UDT may be ordered:**

- In line with your particular practice’s “risk strategy” for UDT assessment. If your practice has high-risk patients, then monitoring requirements would be substantially different from a practice where the majority of patients are NOT at high risk for substance use disorders.

- Prior to treatment; as part of the baseline assessment in opioid-naïve patients or in those previously or currently prescribed opioid therapy.

- Throughout course of treatment; based on results of initial and ongoing risk assessments and patient need, in response to display or reports of aberrant drug-related behaviors.

- The frequency of scheduling UDT should be based on the treatment agreement boundaries and the level of risk for each patient (ie, low-risk patients may only be required to be tested 1-2 times a year, whereas a high-risk patient may need to be tested more frequently).

- As needed (ie, in response to an aberrant drug-related behavior; at times of treatment modification; in response to third-party assertions of illegal or aberrant drug-taking behavior).

- Randomly, for patients who are in recovery.

**Important to note\textsuperscript{10-12}:**

- A UDT strategy minimizes profiling based upon clinician bias – the decision to test should be based on the overall strategy, not based on the “look” of a patient.

- UDT is only one part of Universal Precautions, risk management requires looking at the patient as a whole.

- Sole reliance on patient self-report may result in missing a significant number of illicit drug users.

- Reductions in illicit drug use by routine use of UDT in chronic pain patients have been reported.

- Stigma associated with UDT may be minimized if UDT is ordered rationally.

Confounding Factors in Clinical Testing

**The following information is useful for the doctor to record in the patient’s chart prior to ordering a UDT for later comparison.** “Crystallize the moment” (personal communication Dr. Douglas Gourlay) with these details so that UDT results can be discussed meaningfully with the patient/laboratory at a later date if the results do not match the clinical findings.

- All prescribed medications and duration of opioid therapy.

- Time of last dose as stated by the patient.

**Compliance algorithms based on this information are currently not ready for clinical use\textsuperscript{20,21}:**
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**Morphine: Positive Finding**\(^4,22-24\)

- Morphine is a metabolite of both codeine and heroin (diacetylmorphine)
- Hydromorphone can be a minor metabolite of morphine
- Very low concentrations of hydromorphone may be detected in the urine of patients prescribed high-dose morphine therapy

**Oxycodone or Other Semi-synthetic or Synthetic Opioids: False-Negative Finding**\(^25,26\)

- Immunoassays, including those specifically for oxycodone, have relatively high thresholds and may not detect low concentrations as sometimes seen with dilute samples. Confirmation of negative immunoassay results using GC/MS or LC/MS may be necessary
- “No limit testing”/“no threshold testing” is recommended when the apparent absence of prescribed medications or their metabolites may adversely affect patient care

**Opioid Metabolism**\(^4\)

This is not a comprehensive pathway but may help the clinician to explain the presence of drugs which they have not directly prescribed.

**Conclusion**

UDT can be a simple and valuable tool for pain management clinicians in the initial and ongoing assessment of chronic pain patients. It is imperative to communicate with your testing laboratory or test kit provider to accurately utilize and interpret UDT results. It is also imperative to build mutual trust and honesty in the doctor-patient relationship by explaining the rationale behind UDT as stated in a treatment agreement. An effective and patient-centered UDT strategy combined with accurate interpretation of the test results can be used as part of a comprehensive risk management strategy to reduce stigma and improve patient care.
Glossary

**Compliance testing** – Urine specimen testing to determine if patients with chronic pain are adhering to appropriate use of their prescribed controlled substance medication and not using non-prescribed medications or illicit drugs.

**Confirmatory testing** – Use of a test with greater specificity to validate an initial positive screen test result. Confirmatory testing is a term more in-line with forensic workplace testing. Pain clinicians are interested in specific identification rather than confirmation since they need to know ‘which’ drug is giving the class-positive test result.

**Cut-off** – The concentration of a drug in urine, usually in nanograms per milliliter (ng/mL), used to determine whether a specimen is positive (at or above the cut-off) or negative (below the cut-off) for the drug in question. This may be arbitrarily set.

**Drug-detection threshold** – The minimum concentration used to determine a positive finding as established by the manufacturer or a laboratory based on analytical performance of a specific method.

**Federally-regulated urine drug testing** – Workplace testing limited to the ‘Federal Five’ (THC, cocaine, PCP, opiates, amphetamine/methamphetamine); Department of Health and Human Services and Department of Transportation strictly regulate all facets of process and do not permit testing for other drugs.

**Gas chromatography/mass spectrometry (GC/MS) urine drug testing** – GC/MS is a highly sensitive and specific technique usually performed to confirm a positive screening result (ie, from an immunoassay) or to identify a specific drug; GC/MS combines the physical separation capability of GC with MS and identifies the presence of a particular substance based on characteristic fragmentation patterns (fingerprint) at specific retention times.

**Immunoassay (IA)** – A technique used to measure substances in a specimen, including drugs of abuse in urine. In immunoassays, an antibody to the drug/drug class is used to detect the presence of that drug/drug class at or above a defined threshold or cut-off. Some IAs, such as those for opiates and benzodiazepines, are designed to detect only a limited number of drugs in the drug class and may not detect some clinically important drugs. The antibodies used in the IAs may also cross-react with other compounds that have a similar structure.

**Liquid chromatography/mass spectrometry (LC/MS)** – LC/MS is an analytical chemistry technique that combines the physical separation capabilities of liquid chromatography (or HPLC) with the mass analysis capabilities of mass spectrometry as with GC/MS.

**Metabolite** – A chemical substance produced in the process (metabolism) by which the body breaks down (eg, via liver enzymes) and converts drugs to similar but different substances. The product produced may be pharmacologically active (and act as a drug) or not (no effect).

**Non-regulated urine drug testing** – UDT for clinical and non-forensic uses. Consult with laboratory prior to testing to determine best test mix (profile) for the information desired.

**Point of care urine drug testing** – Immunoassay-based testing performed at the site of patient care; testing may be performed by health care provider or a technician. Similar in technology to that used in screening in laboratory testing, only on a smaller scale and more dependent on operator training and skill.

**Specimen validity testing** – Tests conducted by the laboratory to determine if a urine sample has been diluted with water (in vitro or in vivo), or has been adulterated with a foreign substance.

**Treatment agreement** – This is a document outlining conditions under which opioids will be prescribed (ie, one physician, one pharmacist) in which physicians need to document overall improvement in pain and function, and patient’s responsibilities need to be described. It should include the utilization of unscheduled UDT, consequences of agreement breech, and conditions of treatment discontinuation.

**Universal Precautions in Pain Medicine** – This is a term coined in a paper published by Gourlay/Heit that recommends an approach to the chronic pain patient that includes a strategy of risk management that improves care, reduces risk and eliminates stigma.
Urine Drug Testing

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For further information on UDT, please visit [www.EmergingSolutionsinPain.com](http://www.EmergingSolutionsinPain.com) today!

**References**


