## Appendix D: Urine Drug Testing for Monitoring Opioid Therapy

i. **Monitoring opioid therapy with urine drug testing (UDT)**

ii. **UDT algorithm for monitoring opioid therapy**

iii. **UDT clinical vignettes**

iv. **Frequently Asked Questions (FAQs) about UDT**

## i. Using Urine Drug Testing (UDT) to Monitor Opioid Therapy for Chronic Non-cancer Pain[47-49]

The purpose of drug testing is to identify aberrant behavior, undisclosed drug use and/or abuse and verify compliance with treatment. If a decision has been made to prescribe opioids for chronic non-cancer pain, the prescriber should get a baseline UDT and screen all patients for risk level to develop an appropriate monitoring plan as well as a basis for consultation or referral. Although UDT and other screening tools are helpful in identifying aberrant behavior, it is also important for prescribers to use their clinical judgment in the development of a monitoring plan. The Prescriber should repeat random UDT based on the patient's risk category. There are several validated screening tools available to assess risk of aberrant behavior. The Opioid Risk Tool (ORT) provides a brief questionnaire that can easily be used in the primary care setting (see Appendix B).

Prior to drug testing, the prescriber should inform the patient of the reason for testing, frequency of testing and consequences of unexpected results. This gives the patient an opportunity to disclose drug use and allows the prescriber to modify the drug screen for the individual circumstances and more accurately interpret the results.

| Risk Category | UDT Frequency | Drugs or Drug Classes to Test | Consideration |
|---|---|---|---|
| Low Risk by ORT | Periodic (e.g. up to 1/year) | • Drug you are prescribing if not listed<br>• Amphetamines<br>• Opiates<br>• Cocaine<br>• Benzodiazepines<br>• Alcohol<br>• Barbiturates<br>• Oxycodone<br>• Methadone<br>• Fentanyl<br>• Marijuana<br><br>Testing for all drug classes may not be necessary, depending on clinical situation. | Typically, the initial (screening) drug test uses an immunoassay method to identify the presence of a drug (presumptive positive). Because of cross-reactivity and different sensitivity and specificity between immunoassays, **a second confirmatory test is required** unless result is expected or the patient has disclosed drug use. Confirmatory drug tests use gas chromatography/mass spectrometry or liquid chromatography/tandem mass spectrometry (GC/MS or LC/MS/MS) to verify a presumptive positive result.<br><br>**Contact the laboratory director, toxicologist or a certified Medical Review Officer (MRO) in your area for questions about drug testing or result.**<br><br>If a point-of-care (POC) device is used, contact technical support from the manufacturer for questions. |
| Moderate Risk by ORT | Regular (e.g. up to 2/year) | | |
| High Risk by ORT **or** opioid doses >120 mg MED/d | Frequent (e.g. up to 3-4/year) | | |
| Aberrant Behavior (lost prescriptions, multiple requests for early refills, opioids from multiple providers, unauthorized dose escalation, apparent intoxication, etc.) | At time of visit<br><br>(Address aberrant behaviors in person, not by telephone) | | |

### UDT Results

Interpreting UDT results can be challenging, especially when the parent drug can be metabolized to other commonly prescribed drugs. The table on the next page may aid prescribers when interpreting UDT results. The following UDT results should be viewed as a "red flag", requiring confirmation and intervention:

- Negative for opioid(s) you prescribed
- Positive for drug (benzodiazepines, opioids, etc) you did NOT prescribe or have knowledge of
- Positive for amphetamine or methamphetamine
- Positive for alcohol
- Positive for cocaine or metabolites

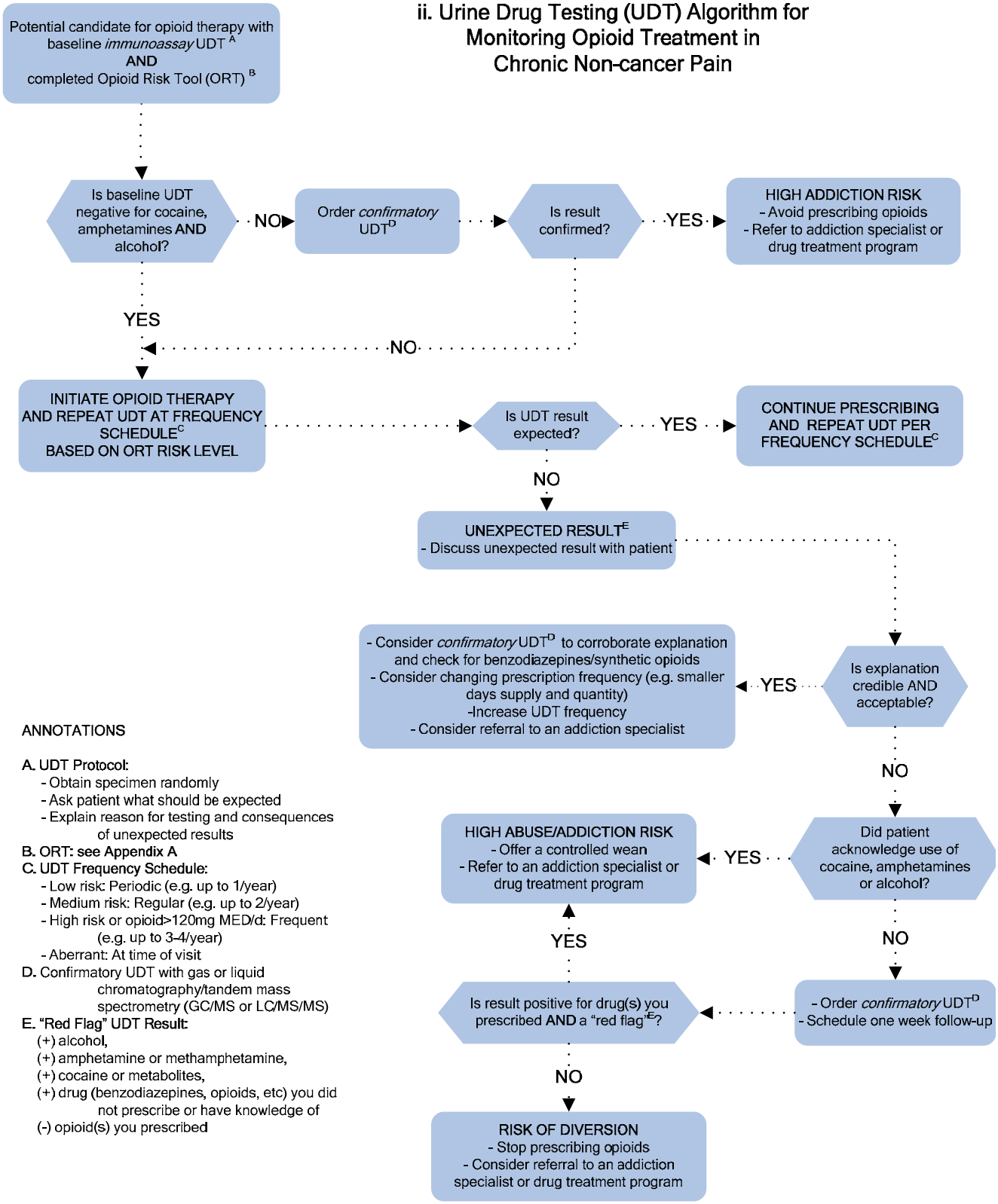
If a **confirmatory drug test** substantiates a "red flag" result AND is:

- **Positive for prescribed opioid(s)**, prescriber should consider a controlled taper and a referral to an addiction specialist or drug treatment program depending on the circumstances.
- **Negative for prescribed opioid(s)**, prescriber should stop prescribing opioid(s) and consider a referral to an addiction specialist or drug treatment program depending on the circumstances.

| Drugs or Drug Classes | Detection Time in Urine* | Test to Order | Expected Results | Consideration |
|---|---|---|---|---|
| ***Opioids or "opiates" – Natural (from opium)*** | | | | |
| Codeine (Tylenol #2/3/4) | 1-3 days | Opiates Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates Immunoassay – positive<br>GC/MS or LC/MS/MS – codeine, possibly morphine & hydrocodone | Immunoassays for "opiates" are responsive for morphine and codeine but do not distinguish which is present. Confirmatory testing is required to reliably identify drug(s) present. Since codeine is metabolized to morphine and small quantities to hydrocodone, these drugs may be found in the urine. Also, morphine may metabolize to produce a small amount (<10%) of hydromorphone. |
| Morphine (Avinza, Embeda, MS Contin, Kadian) | 1-3 days | | Opiates Immunoassay – positive<br>GC/MS or LC/MS/MS – morphine, possibly hydromorphone | |
| ***Opioids – Semisynthetic (derived from opium)*** | | | | |
| Hydrocodone (Lorcet, Lortab, Norco, Vicodin) | 1-3 days | Opiates Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates Immunoassay – positive<br>GC/MS or LC/MS/MS – hydrocodone, possibly hydromorphone | "Opiates" immunoassays may also detect semisynthetic opioids depending on their cross-reactivity pattern. However, a negative result does not exclude use of semisynthetic opioids. Confirmatory testing (GC/MS or LC/MS/MS) is required to verify compliance with the prescribed semisynthetic opioid(s).<br><br>Since hydrocodone is metabolized in small amounts to hydromorphone, both may be found in the urine. Likewise, oxycodone is metabolized to oxymorphone, so these may both be present in the urine of oxycodone users. However, the reverse is not true. In other words, hydromorphone and oxymorphone use does not result in positive screens for hydrocodone and oxycodone, respectively. |
| Hydromorphone (Dilaudid, Exalgo) | 1-3 days | Opiates Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates Immunoassay – positive<br>GC/MS or LC/MS/MS –hydromorphone | |
| Oxycodone (Roxicet, OxyContin) | 1-3 days | Oxycodone Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates Immunoassay – positive<br>GC/MS or LC/MS/MS – oxycodone possibly oxymorphone | |
| Oxymorphone (Opana) | 1-3 days | Opiates or Oxycodone Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates or Oxycodone Immunoassay – positive<br>GC/MS or LC/MS/MS – oxymorphone | |
| ***Opioids – Synthetic (man-made)*** | | | | |
| Fentanyl | 1-3 days | GC/MS or LC/MS/MS Fentanyl | GC/MS or LC/MS/MS – fentanyl & norfentanyl | **Current "opiates" immunoassays do not detect synthetic opioids.** Thus confirmatory testing (GC/MS or LC/MS/MS) is needed to identify these drugs. If the purpose is to document compliance with treatment, the laboratory can be instructed to remove the cutoff concentration so that the presence of lower concentrations can be identified. |
| Meperidine (Demerol) | 1-3 days | GC/MS or LC/MS/MS Meperidine | GC/MS or LC/MS/MS – normeperidine, possibly meperidine | |
| Methadone (Methadose) | 3-7 days | Methadone Immunoassay + GC/MS or LC/MS/MS Methadone | Methadone Immunoassay – positive<br>GC/MS or LC/MS/MS – methadone & EDDP | |
| Propoxyphene (Darvon, Darvocet) | 1-3 days | Propoxyphene Immunoassay + GC/MS or LC/MS/MS Propoxyphene | Propoxyphene Immunoassay – positive<br>GC/MS or LC/MS/MS – propoxyphene & norpropoxyphene | |
| ***Others*** | | | | |
| Alcohol | Up to 8 hours | Alcohol | Alcohol – see Consideration | Additional testing for alcohol metabolites, ethyl glucuronide (EtG) or ethyl sulfate (EtS), can identify alcohol up to 80 hours after consumption. |
| Amphetamines | 2-3 days | Amphetamines, Methamphetamines or MDMA Immunoassay + GC/MS or LC/MS/MS Amphetamines | Amphetamines, methamphetamines or MDMA Immunoassay – see Consideration<br>GC/MS or LC/MS/MS – amphetamine, methamphetamine or MDMA | Amphetamines immunoassays are highly cross-reactive so results should be interpreted cautiously, and may require consultation with the lab. They may detect other sympathomimetic amines, such as ephedrine, pseudoephedrine or selegiline. Confirmatory testing can identify which amphetamine is present. |
| Barbiturates | 1-3 days w/short-acting; up to 30 days w/long acting | Barbiturates Immunoassay | Barbiturates Immunoassay – see Consideration | The clearance half-life of intermediate-acting barbiturates averages 24 hours. It takes about 5 to 7 half-lives to clear 98% of a drug dose. Thus, the presence of an intermediated-acting barbiturate indicates exposure within 5-7 days. |
| Benzodiazepines | 1-3 days w/short-acting; up to 30 days w/long-acting | Benzodiazepines Immunoassay | Benzodiazepines Immunoassay – see Consideration<br>GC/MS or LC/MS/MS – alprazolam, diazepam, clonazepam, lorazepam, etc. | Immunoassays for benzodiazepines have a 28% overall false negative rate and vary in cross-reactivity. Certain benzodiazepines (clonazepam and alprazolam) have limited detectability by most available immunoassays. Confirmatory testing is needed when use is expected or suspected. |
| Cocaine or benzoylecgonine | 2-4 days | Cocaine Metabolites Immunoassay | Cocaine Metabolites Immunoassay – see Consideration | Cocaine immunoassays do not cross-react with other topical anesthetics that end in "caine" (e.g. lidocaine) and are highly specific for cocaine use. |
| Marijuana | 2-4 days; up to 30 days w/chronic heavy use | Cannabinoids (THC) Immunoassay | Cannabinoids Immunoassay – see Consideration<br>GC/MS or LC/MS/MS – THC | THC may be an indicator of the patient's risk category. Prescribers should have an office policy, discuss with the patients reason for use and adjust monitoring plan accordingly. |

*detection time for most drugs depends on the drug, dose, frequency of use and individual metabolism

## ii. Urine Drug Testing (UDT) Algorithm for Monitoring Opioid Treatment in Chronic Non-cancer Pain




ANNOTATIONS

A. UDT Protocol:
- Obtain specimen randomly
- Ask patient what should be expected
- Explain reason for testing and consequences of unexpected results

B. ORT: see Appendix A

C. UDT Frequency Schedule:
- Low risk: Periodic (e.g. up to 1/year)
- Medium risk: Regular (e.g. up to 2/year)
- High risk or opioid>120mg MED/d: Frequent (e.g. up to 3-4/year)
- Aberrant: At time of visit

D. Confirmatory UDT with gas or liquid chromatography/tandem mass spectrometry (GC/MS or LC/MS/MS)

E. "Red Flag" UDT Result:
(+) alcohol,
(+) amphetamine or methamphetamine,
(+) cocaine or metabolites,
(+) drug (benzodiazepines, opioids, etc) you did not prescribe or have knowledge of
(-) opioid(s) you prescribed

## iii. UDT Clinical Vignettes in Chronic Non-cancer Pain

| Case Studies | Discussion |
|---|---|
| **New Patient:** A 31-year-old female with low back pain from an injury 2 months ago. She wants to establish care. According to the patient, she was initially prescribed naproxen and hydrocodone in the emergency room. She is currently taking naproxen OTC, but no reported opioids. Her other medical conditions include depression for which she takes citalopram. You are considering prescribing opioid(s) and your suspicion for drug abuse is low. What should you do? | IF you have decided to initiate chronic opioid therapy AND prior to prescribing, you should:<br>1. Obtain a baseline UDT (see drug or drug classes to test, page 1);<br>2. Assess risk of aberrant behavior with ORT;<br>3. Assess psychiatric status (e.g. PHQ-9);<br>4. Obtain a signed opioid agreement;<br>5. Establish treatment goals including improvements in both function and pain;<br>6. Describe expectations for behavior related to use of opioids (take as prescribed, use one pharmacy, one prescriber, no early refills, no self escalation, no sharing of drugs, etc)<br>7. Develop a follow-up plan to monitor treatment, including the frequency of UDT's based on ORT |
| **New Patient on Opioids:** A 45-year-old male presents with severe neck pain from a motor vehicle accident 2 years ago. He has been treated with OxyContin 30mg BID and oxycodone 5mg 1 tab Q3H PRN (MED = 150mg/day). He reports no history of substance abuse. Due to "personality differences" with previous provider, he would like you to assume care and continue prescribing OxyContin and oxycodone for his neck pain. You have no medical records to confirm previous treatment. What should you do? | **Do not prescribe opioids at initial visit since records are unavailable:**<br>• Comprehensively evaluate the patient (see Guideline – *Before you decide to prescribe opioids for chronic pain*),<br>• Order a baseline UDT,<br>• **Inform patient that a signed release of information form is required prior to prescribing opioids**. Also request medical records from previous provider(s) or consider contacting the previous prescriber for information on treating this patient and<br>• Schedule a follow-up visit for when UDT results and medical records are available.<br>On follow-up visit, if UDT is consistent and prior medical records show improved pain and function with no history of aberrant behaviors, follow steps 2 – 7 above before prescribing. |
| **Compliance Testing in a patient on < 120mg MED/day:** A 55-year-old male with chronic knee pain comes in for a routine visit. His opioid regimen consists of methadone 5mg QID and hydrocodone/acetaminophen 5/500mg 1 tab Q6H PRN (MED = 100mg/day). He has moderate risk on ORT and last random UDT was a year ago. What should you do? | Assess the risks and benefits of current opioid therapy (see Guideline – *Assessing effects of opioid therapy*). Discuss with the patient reason for testing, frequency of testing and consequences of unexpected results, order an immunoassay test for the drug classes below, and follow the UDT algorithm.<br>• Amphetamines<br>• Opiates<br>• Cocaine metabolites<br>• Methadone<br>• Benzodiazepines<br>• Alcohol<br>• Oxycodone |
| **Unexpected Results:** The immunoassays from the above vignette were positive for methadone, opiates and cocaine metabolites but negative for the remainder of the drug classes tested. Confirmatory testing with GC/MS was done per laboratory protocol. The confirmatory results show methadone, hydrocodone and benzoylecgonine (cocaine metabolite). What should you do? | Discuss the unexpected results with the patient and offer a controlled taper and referral to an addiction specialist. |

| | |
|---|---|
| **Point of Care Testing:** A 47-year-old male with rotator cuff tendonitis has chronic shoulder pain managed with morphine SR 30mg TID and oxycodone/acetaminophen 5/325mg 1 tab Q4H PRN (MED = 135mg/day). He reports no other drug therapy. A treatment agreement has been signed by you and the patient recently. You perform a random UDT using a point-of-care testing kit. The immunoassays are positive for opiates but also positive for benzodiazepines. What should you do? | Discuss the unexpected results with the patient:<br>• If explanation is credible (e.g. receiving treatment for anxiety from another provider), you may want to send the urine sample to laboratory to confirm his story. You may also want to discuss future expectations with the patient and request records from other treating providers for possible specialty consultation.<br>• If explanation is not accepted (e.g. patient admits benzodiazepine use that is not prescribed for the patient), confirmatory testing is not necessary but offer a controlled taper and/or referral to an addiction specialist depending on the circumstances.<br>• If result cannot be explained, send original urine sample to laboratory for confirmatory testing. |

## iv. UDT Frequently Asked Questions (FAQ)

Q **Drug screening implies that I don't trust my patients. How do I get around this?**

A Self-report of drug use has limited validity, and monitoring behavior alone can fail to detect problems revealed by UDTs. Creating a UDT policy in advance and applying it consistently to all patients on opioids may help de-stigmatize the testing. Inform patients that drug testing is a routine procedure for all patients starting or maintained on opioid therapy and it is an important tool for monitoring the safety of opioid therapy. Possible language for explaining to patient includes:

- "Ensures my capacity to provide treatment for your pain while balancing the need for safety."
- "Provides critical information needed to assess the success of your therapy."
- "Prescription medications are a common form of treatment for chronic pain. However, each person reacts differently to them. UDT enables us to identify individual risks related to your medications and avoid problems."
- "Our clinic uses 'universal precautions' in opioid prescribing, which includes UDT. This is the same as wearing gloves on all patients when drawing blood."

Q **Can I tell whether my patient has taken the dose of opioid(s) I prescribed?**

A No. It is very difficult to correlate urine drug concentration with a patient's dose. UDT can detect the parent drug and/or its metabolite(s) and demonstrate recent use of prescribed drugs and illegal substances. However, it CANNOT determine the amount of drug used and when the last dose was taken, nor can it identify the source of the drug.

Q **My patient says he is a "high metabolizer" and that is why the expected drug is not found in the urine. Is this possible?**

A A small percentage of persons are ultrarapid metabolizers. They metabolize specific drugs more rapidly than typical patients. It would be rare to take an opioid as prescribed and have a totally negative UDT. It is important that you use testing that is specific to the medication of interest and with cutoff thresholds that are extremely low.

Q **How do I deal with marijuana?**

A This is a complex issue. Marijuana is currently classified as a Schedule I drug by the DEA. For that reason, many providers will not prescribe opioids to patients using cannabis. Other providers reference State "Medical Marijuana" laws (**http://apps.leg.wa.gov/RCW/default.aspx?cite=69.51A&full=true**) and feel comfortable prescribing opioids to cannabis users. Some providers adopt a "don't ask, don't tell" policy, and request the lab to remove marijuana from the UDT so that positive results are not seen. Do your homework and create an office policy. Then disclose this policy to your patients.

Q **Would short-acting opioids show up in UDT?**

A Urine testing typically has a 1 to 3-day window of detection for most drugs depending on dose and individual differences in drug metabolism. Short-acting opioids can be detected if the lab removes the cutoff concentration so that the presence of lower concentrations is detected. If the laboratory uses LC/MS/MS, then it will have a lower limit of detection (LOD) with less interference.

Q **Why confirm results?**

A Immunoassays used in drug screening can cross-react with other drugs and vary in sensitivity and specificity. Thus, confirmation with a more accurate method may be required for clinical decision making. Confirmatory drug testing (GC/MS or LC/MS/MS) of the original specimen is recommended for unexpected results, or in cases where patients are known to be high risk. However, on occasion, even confirmatory testing requires expert assistance for interpretation. Consider consultation with the lab before discussing/confronting the patient with unexpected test results and discontinuing opioid therapy.

**Q Should I use temperature and adulteration strips?**

A It depends. Drug testing for clinical compliance, unlike employment testing, does not require a strict "chain-of-custody". However, if tampering is a concern, the specimen should be monitored for temperature and/or adulterants. Normal human urine should have a temperature between 90°F – 100°F, pH between 4.5 – 8.5 and creatinine >20mg/dL. Be aware that there are multiple websites and devices devoted to getting a "clean" urine drug screen.

**Q Should I perform a drug screen on every visit for patients using opioids for chronic pain?**

A No. Random screening based on the frequency recommended in the guideline should suffice for most patients. Those patients who you feel require drug screening on every visit, are perhaps not candidates for chronic opioid therapy.