1000 – 1661 Portage Avenue
Winnipeg, MB R3J 3T7
Tel: (204) 774-4344 Fax: (204) 774-0750
Toll Free (MB only) 1-877-774-4344
www.cpsm.mb.ca

MANITOBA OPIOID AGONIST THERAPY RECOMMENDED PRACTICE MANUAL

1.7 Recommendations for the Use of Urine Drug Testing in the Management of Opioid Use Disorder

GENERAL CONSIDERATIONS

Urine drug testing (UDT) is an important clinical tool in the management of patients with opioid use disorder (OUD) who are treated with opioid agonist therapy (OAT). UDT is considered a standard of care in OAT[1] and has the potential to enhance patient and public safety. When used appropriately, UDT helps to confirm or refute patient compliance with the treatment plan and helps assess the overall risk posed by ingested substances. It forms the basis for demonstrating the stability needed for patients to earn take-home doses in OAT. UDT can also help providers understand local drug use patterns and raise red flags for diversion.

However, routine use of UDT should be balanced against the cost to the healthcare system, as well as some associated harms. For example, UDT can undermine the patient's sense of autonomy and trust in providers[2]. A 2014 systematic review of the use of UDT in OAT concluded that there was insufficient evidence to demonstrate the usefulness of the practice[3]. A critical review of the literature from 2019 supported the use of UDT as a standard of care, but added that the area requires further research[4].

This chapter outlines recommendations for the use of UDT for OAT providers in Manitoba, based on evidence, cost-benefit balance, and local clinical expertise.

While the principles of UDT identified here may be useful in other clinical situations, the scope is limited to the management of OUD in the outpatient setting with OAT. Recommendations for UDT in the context of polypharmacy and polysubstance use in OUD are reviewed briefly, where clinical overlap is a common challenge. This chapter does not specifically address an approach to patients using opioids for chronic pain exclusively, and is not for application in emergency or palliative care settings.

SPECIFIC CONSIDERATIONS

A PATIENT-CENTERED APPROACH TO UDT

A patient-centered approach to care is essential in the management of substance use disorders, as it leads to improved treatment retention and health outcomes[5], two of the main goals of OAT. The process of UDT can be stigmatizing and damaging to the development of a therapeutic relationship[2]. As UDT is often perceived negatively by patients, clinicians should take active steps to help patients understand and accept its role in treatment.

From the first visit, OAT providers should ensure that patients understand UDT as a routine practice and that its intent is to optimize their safety. Providers should encourage frank discussion and explain the role of UDT in earning take-home (carry) doses, and the loss of carry doses, according to the clinic policy. Other potential impacts on the management plan should be explained during visits, such as reducing dispensing intervals of other prescribed medications in the interest of patient safety.

Reiterate that any changes in the management plan triggered by UDT results are intended to support patients toward increased clinical stability, not as punishment for bad behavior. It can be helpful to reinforce that OUD is not viewed as a moral failing, but rather as a chronic disease, in which relapse and periods of instability are common and manageable. Clinicians should avoid referring to test results using judgmental terms such as “clean” and “dirty”, preferring neutral terms such as “positive” or “unexpected results”.

Patients can be given the opportunity to disclose drug use prior to providing a sample or reviewing the results, to avoid the appearance that the provider is trying to “catch them in the act”. **Finally, clinicians should exercise extreme caution before accusing patients of dishonesty or implementing punitive measures due to UDT findings alone**. UDT results are subject to false positives and false negatives[6]. Clinicians often make errors in interpretation that can have very unfortunate outcomes if therapeutic relationships break down and patients leave treatment.

Patients should be assured that their UDT results will not be used to withhold OAT treatment. Diversion can be difficult to prove even with regular use of UDT. However, if it becomes clear that patients are not engaged with OAT and are likely diverting their prescription (by using information gathered from UDT, clinical assessment, and/or collateral history), it may be necessary to discontinue prescribing. In these rare cases, where the benefits of continued prescribing are outweighed by the risks to the patient or the community, every attempt should be made to engage the patient in harm reduction strategies and extend the offer of treatment in the future. Treatment agreements are effective tools to review the role of UDT and behavioural/safety expectations with patients when initiating OAT and throughout care, particularly if concerns arise that may warrant withdrawal of treatment. See the Comprehensive Assessment chapter section on treatment agreements and Discontinuing Treatment for further guidance on these topics.

TESTING METHODOLOGIES AVAILABLE

The two types of UDT used in the management of OUD with OAT are **immunoassays** and **liquid chromatography high-resolution mass spectrometry** (also known as a comprehensive urine drug screen or C-UDS). Immunoassay testing is available in two formats: point-of-care (POC) kits used in clinic or Immunoassay Drug Screens. The latter is commonly known as a "Street Drug Screen" on older versions of the UDT requisition and is performed at Westman Laboratory and St. Boniface Laboratory, with testing done 24/7. Comparatively, C-UDS is significantly more expensive than POC testing. Therefore, when available and clinically appropriate to do so, POC tests should be used preferentially. In general, comprehensive testing should be reserved for specific clinical scenarios, as detailed below.

Point-of-Care Tests

For most purposes, POC is the preferred method of testing as it provides immediate results that can be shared with the patient and used in the development of a timely management plan[1]. It should be ordered upon initiation of treatment and for follow-up testing.

Disadvantages of POC tests include the cost to the provider/clinic and the lack of specificity of information that is sometimes required (see *Interpretation of Results* below). Immunoassays often detect a class of drugs (e.g., opioids, benzodiazepines) rather than a specific drug. They are often *not* equipped to detect semi-synthetic opioids (oxycodone, hydromorphone), synthetic opioids (fentanyl), some common benzodiazepines, or the metabolites of drugs of abuse. Because they are based on antibody detection, there is potential for cross-reactivity (false positives) with other drugs. Where POC testing gives an unexpected result, laboratory confirmation with C-UDS is recommended if it will impact the clinical management of the patient[7].

There are many POC tests available, and it is important to be familiar with the features of the test used in your practice. Clinicians should consider cost and local drug use patterns in determining the best POC test for their clinical setting. Basic assays usually include some combination of benzodiazepines, amphetamines, methamphetamine, cocaine, opioids (naturally occurring, such as heroin, morphine, and codeine), methadone and its metabolite EDDP, THC and PCP. Since class tests will likely miss semi-synthetic and synthetic opioids, it is **recommended to purchase POC tests that will specifically look for hydromorphone, oxycodone, fentanyl, and buprenorphine for use in the OAT patient population**.

Comprehensive Urine Drug Screens

C-UDS is recommended when initiating OAT therapy. Confirmatory testing with C-UDS is also recommended in the case of unexpected POC test results, either positive or negative, when further information is needed to formulate an appropriate treatment plan for a patient.

It is *not* recommended to use C-UDS routinely for the follow-up of OAT patients, including for the routine determination of clinical stability[7].

For providers with limited or no access to POC testing, an Immunoassay or "Street Drug Screen" rather than a comprehensive screen can be ordered for this purpose (see the provincial Urine Drug Screen Requisition Form).

Occasionally, when a patient is known to use a substance that cannot be specified on POC testing, C-UDS will need to be used in place of POC for routine monitoring. As an example, heroin cannot be distinguished from morphine by POC, as both will test positive for naturally occurring opioids. For a patient on slow-release oral morphine (SROM), whose drug of choice is heroin, C-UDS will be needed for monitoring.

The main disadvantage of C-UDS, other than the cost to the healthcare system, is that results can take up to one week and are therefore less helpful in timely treatment planning.

The list of medications which are routinely screened for in a comprehensive drug screen by Diagnostic Services was reduced, as of June 2021, to contain costs. A specific list of the approximately **80 substances** tested for on a comprehensive screen is available **here**. This specific panel of drugs is intended to balance clinical utility with a cost-effective approach to testing. **This is essential information for prescribers to correctly interpret C-UDS results in the interest of patient care**.

Physicians are encouraged to document all prescription and illicit substances known to be used by the patient and to formulate a clear clinical question on the laboratory requisition. If a physician is interested in the presence or absence of a specific compound not included in the routine test, Diagnostic Services may be able to add the substance of interest to the test. They can only do this if the request is clearly written on the requisition.

The College of Physicians and Surgeons of Manitoba (CPSM) is taking the lead on providing ongoing feedback to Diagnostic Services regarding the list of reported compounds and welcomes feedback from registrants on drugs of interest to be added to the list. To offer feedback, prescribers can contact Dr. Marina Reinecke, Medical Consultant to the CPSM Prescribing Practices Program, at 204-774-4344.

INTERPRETATION OF RESULTS

UDTs should always be interpreted by a clinician who is familiar with the patient's clinical situation and knowledgeable about the tests used. Caution should be used before making impactful treatment decisions based on results of UDT, such as removal of carries or an involuntary taper from OAT.

In general, a pattern of unexpected results is more reliable than a single aberrant test.

False negatives can occur when:

- The drug is present below the threshold of the test,
- The drug is not detected by the test,
- The test occurs outside the window of exposure, or
- Occasionally, there are individual variabilities in metabolism, such as in the case of certain prescribed medications or medical illnesses.

False positives can occur when:

- Substances cross-react with other drugs,
- The supply is contaminated with an unexpected substance,
- A patient intentionally tampers with the sample in an attempt at diversion, or
- Rarely, in the case of passive exposure.

It is important to note that cross-reactivity is only possible with immunoassays; *not* with C-UDS. Commonly prescribed medications known to cause false positives for opioids on a POC test strip include trazodone, risperidone, paliperidone, quetiapine, and verapamil[1].

The Nature of Detection

Generally, most substances will test negatively if the patient abstains for 2-3 days prior to testing, with some common exceptions. Methadone can be detected up to a week. THC can be detected for days to months, depending on duration and amount used. With chronic use of fentanyl, it can remain detectable in the urine for up to 4 weeks due to its lipophilic properties. Diazepam used in the context of alcohol withdrawal (large quantities administered over days in hospital) will also remain detectable for up to six weeks, depending on the amount used. Therefore, a positive test for these medications does not necessarily mean ongoing use[8].

POC tests are not quantitative and C-UDS results are not reported quantitatively. Results are reported as the presence or absence of a substance, above a specified threshold level, and therefore cannot be used to determine how much or how often a substance was used. As such, chronic vs. sporadic use (e.g., a single episode of relapse) can only be demonstrated by repeated tests. Additionally, diversion of a portion of the prescribed medication, or supplementing with an illicit supply of the same prescribed medication, cannot be proven or disproven with UDT, since the amount taken cannot be determined.

Metabolites

C-UDS panel includes the metabolites of many drugs of abuse. Results of confirmatory testing must be interpreted cautiously, so that patients are not accused falsely of taking medications that are in fact metabolites of drugs they are known to be using.

For example, codeine breaks down to morphine, and diazepam breaks down into temazepam and oxazepam. Similarly, morphine metabolism includes a small amount of hydromorphone production. A positive result for hydromorphone may be due to high doses of morphine, typical of SROM, and not indicative of hydromorphone use.

C-UDS panel also includes some agents used to "cut" street drugs. The presence of levamisole, an anthelmintic, for example, is indicative of cocaine use. It is commonly used to increase the weight of the cocaine, and unfortunately can cause vasculitis, leading to necrosis of the digits.

CLINICAL INDICATIONS FOR UDT IN OAT

UDT should be used along with clinical assessment (history and focused physical examination) for the monitoring of OAT, to:

- Confirm opioid use during initial assessment prior to initiating therapy.
- Assess clinical stability by:
  - Screening for ongoing non-prescribed or over-the-counter medication use, as well as illicit substance use. Special attention is paid to the use of illicit opioids, as ongoing use may indicate a need for an OAT dose increase.
  - Confirming that prescribed medication is being taken in patients with carry doses.
- Support decision making regarding carry doses.
- Identify local trends in compound availability and use patterns.

Initial Assessment

POC testing is usually performed at the first visit, to confirm recent opioid use. However, false negatives can result if the patient uses in small amounts, intermittently, or uses a semi-synthetic or synthetic opioid not found on the POC test. UDT would also not detect opioids in patients with a recent period of abstinence, such as incarceration or residential treatment.

Providers practicing remotely may not have access to POC tests at the time of presentation of the patient. Clinicians must use clinical judgement in these cases as to whether it is safe to start OAT with a convincing history and physical exam, but a negative or absent POC test. In most cases, the harms of delaying treatment outweigh the risks of starting OAT in the absence of UDT results. **Buprenorphine is strongly preferred over methadone and SROM in this situation**.

In cases where there is no POC available or it is negative for opioids, AND the clinician has doubt as to whether opioids are currently being used, it is strongly recommended to collect a urine sample for C-UDS and await results prior to starting OAT.

In select cases, where POC is not available, lab immunoassays can be ordered *in addition to* C-UDS. Both Westman Laboratory (Brandon) and St. Boniface Laboratory perform immunoassay

UDT. Most rural testing is conducted at Westman Laboratory, where turnaround time for immunoassay results is faster than for C-UDS. Confirming opioid use sooner can facilitate earlier induction. In such cases, C-UDS results may then serve to confirm the immunoassay results and provide a broader analysis of other prescribed and illicit drugs used by the patient.

C-UDS is also recommended at the first visit or shortly thereafter. This panel will provide an accurate picture of the illicit substances being used, as well as any prescribed and over-the-counter medications the patient is currently taking. Results should be compared to the patient's medication record (DPIN) and self-reported substance use history. Ideally, a DPIN record including all medication entries over the preceding six months should be reviewed together with the patient.

Common drugs of concern that are not identified on POC tests include gabapentinoids, dimenhydrinate, tramadol, trazodone, antidepressants, antipsychotics, and Z-drugs. **Each of these may contribute to patients' overall risk and will need to be addressed individually, whether prescribed or illicitly obtained**. This is an opportunity for the provider to engage in harm reduction conversations with patients and to review their overall treatment goals. Safety measures may be instituted when appropriate, such as daily dispensing of psychoactive and/or sedating medications to reduce overdose risk or a monitored taper of unnecessary or contraindicated medications.

The section AN APPROACH TO POLYPHARMACY IN THE CONTEXT OF OAT in Managing Polypharmacy, Benzodiazepines, Alcohol, & Polysubstance Use provides useful recommendations to support medication reviews. The Comprehensive Assessment chapter also provides guidance on collecting a detailed substance history.

The presence of other high-risk substances (including benzodiazepines) is not an absolute contraindication to initiation of OAT, given the relative safety of OAT compared to ongoing opioid abuse, but should always be addressed in the management plan.

The UDT policy of the practice setting should be explained to patients at the first visit, including how unexpected results will be handled. Treatment agreements also present an opportunity to provide a written explanation of the UDT policy, with attention to literacy level. See the Comprehensive Assessment section on treatment agreements for further guidance. For most patients, any opioid use unless prescribed by a provider, presence of non-prescribed medications with sedative/psychoactive properties and/or abuse potential, or any illicit drug use would be considered a positive test.

Assessment of Clinical Stability

The determination of clinical stability is never based on UDT results alone. Clinicians should rely on patient history, collateral information, and direct observation/clinical examination, which is augmented by information collected from UDT, to formulate treatment plans in partnership with the patient.

Clinicians should monitor for a consistent pattern of presence of the treatment drug(s) and absence of other opioids/drugs of abuse in the urine, together with improvement in overall health status and quality of life. These findings in combination suggest the patient is on an effective management plan. Once the pattern is established, patients can start to receive take-home doses and require less frequent UDT monitoring and clinical follow-up.

Ideally, POC UDT that includes a dedicated buprenorphine strip should be used. If buprenorphine is absent on POC, it is often due to a limitation of the POC test itself and can be clarified with C-UDS.

Historically, C-UDS in Manitoba did not reliably detect buprenorphine. The C-UDS panel now contains the glucuronides of both buprenorphine and norbuprenorphine and can accurately detect these drugs (parent drug and metabolite). For clinical interpretation, however, it may be useful to note that C-UDS *primarily* detects buprenorphine-glucuronide and norbuprenorphine-glucuronide, not the parent compounds.

Absence of the treatment drug, particularly in the case of methadone or morphine, is concerning for diversion in patients with carries. **Return to daily witnessed dosing is indicated in the interest of patient and public safety**. Furthermore, if patients are diverting a portion of their doses, loss of tolerance can rapidly develop, often requiring a fifty percent or more dose reduction and increased clinical follow-up. Close communication with the pharmacist is also recommended.

After an initial dose reduction, frequent follow-up will allow for appropriate and safe OAT dose adjustments (up or down) depending on how the clinical situation evolves. Where a pattern of repeated attempts at diversion is clear, together with lack of engagement in treatment goals, involuntary withdrawal of treatment may be necessary. See Discontinuing Treatment for further guidance on these topics.

POC testing is also used to monitor for substances of concern:

- **Ongoing opioid use or intermittent relapses** should prompt non-judgemental discussion about adjustments to the treatment plan. Clinicians should exercise clinical judgement regarding the most appropriate response in each circumstance, such as an OAT dose increase or a different OAT medication for patients experiencing ongoing withdrawal and cravings.

  Referral for additional supports for patients experiencing psychosocial stress, or alternate pain management approaches for patients with concomitant pain, may also need to be considered. Returning to previous levels of monitoring and removal or reduction in carries in response to relapse is standard in most settings (see *Decision Making Regarding Take-home Doses* below).

- **Use of stimulants, such as methamphetamine or cocaine**, for example, can undermine patient stability and may require implementation of other strategies, such as referral for residential treatment (treatment intensification).

  Amphetamines, as a rule, have the highest number of false positives of any class of drug on **immunoassay testing only** (POC UDT and lab immunoassays). A positive result for "amphetamine" on the immunoassay can possibly mean that the analyte detected was amphetamine, MDMA, MDA, MDEA, methamphetamine, etc. Cross-reactivity can also occur with aripiprazole, bupropion, chlorpromazine, fluoxetine, trazodone, and venlafaxine[1]. When a POC test is positive for amphetamine, it is essential to compare the results to DPIN and to inquire about use of illicit prescription medications, including those used in the treatment of ADHD.

  However, on **C-UDS**, amphetamine, MDMA, MDA, MDEA and methamphetamine, can be identified individually. Only ephedrine and pseudoephedrine cannot be distinguished. Aripiprazole, bupropion, chlorpromazine, fluoxetine, trazodone, and venlafaxine can also be differentiated from amphetamine and methamphetamine with C-UDS. There is no cross-reactivity with this methodology.

- **Benzodiazepines/Z-drugs are of particular concern in terms of patient safety and overdose risk**[1]. Presence of benzodiazepines/Z-drugs is not a contraindication for starting or continuing OAT, but clinicians should review the type of benzodiazepine/Z-drug used (prescribed vs. illicit), consider the diagnosis of sedative-hypnotic use disorder, and initiate a taper if indicated.

  In patients with benzodiazepines detected on POC testing, C-UDS is required to determine which drugs are being taken. As noted, diazepam breaks down into temazepam and oxazepam, so these three cannot be distinguished even on comprehensive testing. Alprazolam and clonazepam each have unique metabolites and can be identified on C-UDS. Note that lorazepam is not currently reliably detected on C-UDS, as lorazepam-glucuronide is not currently tested for. Most benzodiazepines are highly metabolized, so it may be missed if the metabolite is not tested for on C-UDS.

  When following patients on a prescribed taper it is recommended to monitor for supplemental benzodiazepine use with regular C-UDS. Some common benzodiazepines, such as alprazolam and clonazepam, are routinely missed on POC tests[6]. Novel compounds, which are typically ordered online, will be missed on both tests. For identification of novel compounds that may be suspected based on patient history, consultation with the lab is recommended. **Clinicians can contact the Shared Health Duty Chemist on-call** (**phone 431-276-0131**), available Monday to Friday, 8 am to 4 pm.

In general, a pattern of consistent presence in UDT of substances that are not prescribed should result in continued frequent monitoring of the patient and will preclude authorization of carries.

See Managing Polypharmacy, Benzodiazepines, Alcohol, & Polysubstance Use for further recommendations.

Presence of THC, now legal, may not be of concern to the OAT provider in the context of a patient who uses cannabis recreationally and who has no cannabis use disorder. Patients who use recreational cannabis may still be granted carries if they are otherwise clinically stable. Of note, most POC tests do not test for alcohol, a substance that should not be ignored in the overall assessment of a patient's stability and should be part of routine history taking.

Decision Making Regarding Take-Home Doses

Patients on OAT, in most cases, start with daily witnessed dosing and progress to take-home doses with demonstrated stability, supported by UDT results. See take-home (carry) recommendations for Buprenorphine and Methadone as applicable.

In the case where UDT identifies relapse to opioid or other substance use, reduction and eventual removal of carries has the potential to help restabilize patients by increasing their contact with a healthcare provider (nurse, pharmacist), improving the consistency with which the OAT medication is taken, and reducing risk of diversion.

However, an overly aggressive policy that does not attend to individual patient circumstances (e.g., issues of work, childcare, travel restrictions, or sense of self-efficacy) can have a negative impact on treatment retention. Recently published Canadian data, arising from the COVID-19 pandemic, revealed that loosening restrictions on take-home doses did not increase harm to patients, but did improve retention rates in OAT programs[9]. **Some flexibility in enforcing a policy of carry reduction in response to UDT results is reasonable, especially when overall improvement in stability and attainment of treatment goals is demonstrated. Rationale for decisions to deviate from the policy should be documented**.

Identification of Local Trends

Patients are often unaware of the drugs present in the substances they are using. Many illicitly sourced drugs are pressed using pill presses to appear pharmaceutical grade and marketed as a particular drug, while containing a cocktail of other psychoactive medications. When POC testing is inconsistent with patient history, C-UDS may help identify local trends. Sharing these findings with patients is an important step to establish trust and to engage them in keeping themselves and their community safe.

Some circumstances warrant increased harm reduction planning on the part of local health providers, such as when opioids are found in drugs marketed as stimulants and could result in accidental overdose in opioid-naïve patients. Drugs sourced from the internet may contain substances that do not appear in either POC or C-UDS tests because they are novel. In such cases, providers may need to consult with the provincial laboratory to identify new substances.

RECOMMENDATIONS FOR FREQUENCY OF UDT

UDT, consisting of both a POC and C-UDS, should be collected upon initiation of OAT whenever possible. POC testing provides immediately useful information for safe induction planning. Despite the delayed result, C-UDS can then provide additional and more complete information about the prescribed, over the counter, and illicit substances that a patient is consuming. This comprehensive testing informs appropriate medication management, ongoing treatment planning, and overall risk management.

Subsequently, urine samples for POC testing should be collected when results will affect the management plan, most commonly for the purpose of establishing sufficient stability to authorize carries or to monitor the patient's use of other drugs.

The frequency of UDTs should not interfere with a stable patient's responsibilities to family and work. UDT can be obtained without necessitating a medical appointment.

UDT Frequency for Buprenorphine/naloxone

A minimum of **one C-UDS** is recommended in all patients on buprenorphine during the first three months of treatment. After that, further C-UDS should be based on clinical need/indication.

A **minimum of monthly POC testing** is recommended for all patients during the **first three months** of treatment with buprenorphine/naloxone. However, some stable patients treated with buprenorphine may wish to supply **weekly** samples initially, in order to rapidly earn take-home doses as follows:

- After participating in daily witnessed dosing for the first two weeks of treatment, patients should demonstrate a minimum of **two weeks of clinical stability and two appropriate POC results, 7-10 days apart, per each additional carry earned,** up to **once-weekly witnessed dosing**. A clinically stable patient can thereby attend the pharmacy for witnessed dosing once weekly (i.e., a maximum of six take-home doses) after 12 weeks. After that, UDT may be reduced in frequency to align with opportunities to increase take-home dosing further (see Buprenorphine Take-home (Carry) Dosing Recommendations for details).
- After a further three months of clinical stability (total of six months in treatment) with once-weekly witnessed dosing, and two appropriate POC tests done 7-10 days apart, patients can receive **biweekly witnessed doing**.
- After one year of clinical stability with biweekly witnessed dosing, and two more follow-up POC tests done 7-10 days apart, patients can receive **once-monthly witnessed dosing**.

The presence of illicitly obtained opioids or other drugs of abuse in a sample should result in stepping back to the previous carry level. If clinical assessment and collateral information indicates an ongoing relapse or use of high-risk opioids (e.g., fentanyl), removal of all carries may be indicated. Patient and public safety must be the primary considerations in these situations.

During such periods of relapse or clinical instability, UDT frequency should be increased to monthly. If patients report that their illicit use is under control and wish to rapidly re-earn carries, more frequent testing (every 7-10 days) may be considered to facilitate the patient's request (if geographically possible).

For patients stabilized on buprenorphine/naloxone with **once-monthly witnessed dosing, a minimum of three to four POC tests per year (approximately every three to four months) is acceptable** to continue the established maximum carry schedule.

For patients with significant barriers to UDT, such as those living remotely or having transportation challenges, less frequent UDT is acceptable but clinical rationale must be documented. Local nursing stations and labs may be able to assist with sample collection, and such opportunities should be explored.

For patients who have no interest in earning carries, or who self-disclose use of other substances and who are therefore ineligible for carries, the frequency of UDT can be reduced. The frequency of testing in this situation, after the first three months of treatment, is determined by the stability of the patient and is at the clinician's discretion. Intermittent monitoring of the urine can encourage discussion regarding high-risk findings and reinforce treatment goals.

Non-judgemental discussion regarding UDT findings can also move patients towards healthy behavior change with substance use overall. Conversely, repeated conversations about ongoing drug use with a patient who is pre-contemplative about change can also be counter productive. **Hence the importance of clinical discretion**.

UDT Frequency for Extended-Release Buprenorphine

For patients on Sublocade® (buprenorphine extended-release injection) or Probuphine® (buprenorphine implant) frequency of UDT is at the clinician's discretion. For example, unstable patients may still require regular monthly UDT to assist with management of other substance use disorders. In a stable patient using Sublocade® or Probuphine® it is reasonable to conduct a UDT two or three times per year during follow-up visits.

Given that co-occurring substance use disorders are common and can arise at any time, the prospect of UDT may encourage disclosure and engage a patient in a new care plan before a clinically evident decline.

UDT Frequency for Methadone & SROM

Patients prescribed methadone and SROM should have **POC UDT every 7-10 days during the induction and stabilization phase of treatment**. Frequency can gradually be reduced as patients demonstrate clinical stability, to a minimum of every two months. Frequency should increase during periods of clinical deterioration.

A minimum of **one C-UDS** is recommended in all patients on methadone and SROM during the first three months of treatment. After that, further C-UDS and POC should be based on clinical need/indication:

- Patients using methadone and SROM are **not eligible for take-home doses for the first two months of therapy**, except under specific circumstances (see sections in Methadone Induction, Titration, & Stabilization regarding daily witnessed ingestion, and take-home (carry) recommendations for Methadone and SROM for specific guidance).
- After that period, once stability is established, a minimum of **three appropriate POC tests (7-10 days apart) is required to earn one additional carry dose per calendar month**, up to the **maximum** allotted carry doses of **six per week for methadone** and **four per week for SROM**.
- Due to the less favorable safety profiles compared to buprenorphine, methadone or SROM demands a **minimum of six UDTs** per year in clinically stable patients who have achieved maximum carries.

RECOMMENDATIONS FOR COLLECTING URINE SAMPLES

Refusal to comply with UDT requirements can be regarded as a positive urine drug screen, with the same consequences. Opioids can cause urinary hesitancy, so having water available can facilitate obtaining samples. Long wait times in the waiting room may result in patients needing to void before seeing clinic staff, so providing patients with an opportunity to give a sample for UDT upon arrival in clinic may be useful.

Given the significant potential consequences of positive UDT results, **clinical judgement should be exercised in enforcement of clinic policies**, considering real-world barriers to compliance.

Tampering with urine samples will be rare if the use of UDT is perceived as supportive to safe patient care and non-punitive. However, when a patient is diverting medications or attempting to mask their results for other reasons, they may use tactics such as substituting another individual's sample, diluting the sample, or adding compounds to the sample that are known to mask the presence of drugs of abuse. To reduce risk of swapping samples, clinics are encouraged to provide containers that are labeled with the patient's name and to have samples directly passed back to clinic staff. Patients may be asked to leave jackets and bags outside the washroom area.

POC tests are also often equipped with pH, specific gravity, and temperature strips to help detect attempts at tampering. The methadone metabolite, EDDP, will help ensure patients are ingesting carries of methadone, rather than diverting their doses and adding a small amount directly to their own or another individual's sample in order to test positive.

However, sophisticated kits can be purchased online to facilitate a patient providing a warm sample from another patient directly into an appropriately labeled container. It is important to keep in mind that UDT is only one component of assessing stability.

Direct observation of the sample collection is NOT indicated (i.e., witnessed urination)[7]. Indicators of a tampering can be considered a positive sample and clinicians should discuss concerns frankly with the patients before proceeding with changes to the treatment plan/carry dosing, as appropriate under the circumstances.

True random sampling, which consists of calling patients in without warning, is the most clinically useful way to conduct UDT but is impractical in most clinical circumstances. If this is practiced, it is reasonable to give patients 24-48 hours to present for the test to account for work, travel, and childcare needs[1].

Most clinicians collect samples when patients attend for in-person visits and allow patients to drop in to give samples as able, without a medical visit, when trying to earn carries. In most settings this is preferable to random sampling from a practicality standpoint and achieves most of the objectives of UDT.

Third Party Requests

It is generally advised that patients should not share UDT results with third parties. Patients can be assured that their test results are private and will not be shared with third parties without their explicit consent unless the provider is legally obliged to do so through a court order.

OAT programs do not utilize "chain of custody" capable labs for UDT and requests to do so can be declined, as it is expensive and runs counter to the therapeutic intent of the test.

Organizations such as employers, treatment programs, and Child and Family Services should be instructed to conduct their own testing. However, patients are entitled to a copy of their results upon request. Patient education is important to help them understand the potential risks of sharing their results with third parties.

When in doubt, physicians can consult with the Canadian Medical Protective Association (CMPA) regarding how to proceed with a request for UDT results.

IN SUMMARY

- In general, UDT should not be used without a clear clinical reason[7], as outlined in this guidance document.
- UDT should be accompanied by discussion with the patient about their substance use and the treatment plan, using non-stigmatizing language to discuss testing and the results[1].
- POC testing, if available, should be performed on initiation of OAT to confirm presence of opioids, and is the preferred UDT for follow-up tests. In circumstances were POC is not available prior to induction, providers can use clinical judgment to ensure timely access to treatment *if OAT is indicated*. UDT should be arranged as soon as it is feasible.
- C-UDS should be performed on initiation of OAT to establish other medication and illicit substance use that may add risk and warrant discussion with the patient, and to clarify uncertainty when POC yields an unexpected result, if it will affect the treatment plan.
- UDT results should be interpreted by a skilled clinician, familiar with both the patient's situation and the strengths and pitfalls of the test used.
- Results should not be used punitively, but rather in the context of promoting patient and community safety, and as a tool to improve stability and achieve shared goals of therapy.
- Direct observation of sample collection for UDT is not necessary and is considered invasive by patients[7].
- As a general principle, more frequent UDT is indicated at the beginning of treatment and when patients display a change in clinical status.
- Patients receiving maximum take-home doses should have a minimum number of UDT per year (three to four annually for buprenorphine; six annually for methadone and SROM).

References

1. British Columbia Centre on Substance Use (BCCSU). *Urine Drug Testing in Patients Prescribed Opioid Agonist Treatment – Breakout Resource*. BCCSU, BC Ministry of Health, and Ministry of Mental Health and Addictions; 2021. Available at: https://www.bccsu.ca/wp-content/uploads/2021/07/Urine-Drug-Testing-Breakout-Resource.pdf
2. Incze MA. Reassessing the role of routine urine drug screening in opioid use disorder treatment. *JAMA Intern Med.* 2021;181(10): 1282-1283. doi:10.1001/jamainternmed.2021.4109

3. Dupouy J, Mémier V, Catala H, Lavit M, Oustric S, Lapeyre-Mestre M. Does urine drug abuse screening help for managing patients? A systematic review. *Drug and Alcohol Dependence*. 2014;136:11-20. doi:10.1016/j.drugalcdep.2013.12.009

4. McEachern J, Adye-White L, Priest KC, et al. Lacking evidence for the association between frequent urine drug screening and health outcomes of persons on opioid agonist therapy. *Int J Drug Policy*. 2019; 64:30-33. doi: 10.1016/j.drugpo.2018.08.006.

5. Barrio P, Gual A. Patient-centered care interventions for the management of alcohol use disorders: a systematic review of randomized controlled trials. *Patient Prefer Adherence*. 2016;10:1823- 1845. doi: 10.2147/PPA.S109641.

6. Kale N. Urine drug tests: Ordering and interpreting results. *Am Fam Physician*. 2019;99(1):33-39.

7. Canadian Society of Addiction Medicine. Choosing Wisely Canada Website: Addiction Medicine. 2022. https://choosingwiselycanada.org/recommendation/addiction-medicine/. Accessed January 2023.

8. Huhn AS, Hobelmann JG, Oyler GA, Strain EC. Protracted renal clearance of fentanyl in persons with opioid use disorder. *Drug Alcohol Depend*. 2020;214:108147 doi: 10.1016/j.drugalcdep.2020.108147

9. Gomes T, Campbell T, Kitchen S, et al. Association between increased dispensing of opioid agonist therapy take-home doses and opioid overdose and treatment interruption and discontinuation. *JAMA.* 2022;327(9):846-855. doi:10.1001/jama.2022.1271