

Urine Drug Testing in Patients Prescribed Opioid Agonist Treatment

Breakout Resource

We would like to respectfully acknowledge that the land on which we work is the unceded territory of the Coast Salish Peoples, including the territories of the $x^wm \partial \theta kw \partial \phi m$ (Musqueam), Skwxwu7mesh (Squamish), and solií iliwota?4 (Tsleil-Waututh) Nations.

We recognize that the ongoing criminalization, institutionalization, and discrimination against people who use drugs disproportionately harm Indigenous people, and that continuous efforts are needed to dismantle colonial systems of oppression.

We hope that this guidance document helps to reduce the harms faced by people who use drugs and for those who choose to maintain recovery.

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Target Audience: Physicians, nurses and nurse practitioners, pharmacists, policy makers, health care administrators, allied health care professionals, and all other clinical and non-clinical personnel with and without specialized training in addiction medicine, who are involved in the care and management of individuals with opioid use disorder who receive opioid agonist treatment.

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ABOUT THE BC CENTRE ON SUBSTANCE USE

The BC Centre on Substance Use (BCCSU) is a provincially networked organization with a mandate to develop, help implement, and evaluate evidence-based approaches to substance use and addiction. The BCCSU seeks to improve the integration of best practices and care across the continuum of substance use through the collaborative development of evidence-based policies, guidelines, and standards. With the support of the Province of BC, the BCCSU aims to transform substance use policies and care by translating research into education and care guidance, thereby serving all British Columbians. The BCCSU seeks to achieve these goals through the integrated activities of its three core functions: research and evaluation, education and training, and clinical care guidance.

Research—Leading an innovative multidisciplinary program of research, monitoring, evaluation and quality improvement activities to guide health system improvements in the area of substance use.

Education and Training—Strengthening addiction medicine education activities across disciplines, academic institutions, and health authorities, and training the next generation of interdisciplinary leaders in addiction medicine.

Clinical Care Guidance—Developing and helping implement evidence-based clinical practice guidelines, treatment pathways, and other practice support documents.

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When exercising clinical judgment in the treatment of opioid use disorder, health care professionals are expected to take this document fully into account, alongside the individual needs, preferences and values of patients, their families and other service users, and in light of their duties to adhere to the fundamental principles and values of the Canadian Medical Association Code of Ethics, especially compassion, beneficence, non-maleficence, respect for persons, justice and accountability, as well as the required standards for good clinical practice of the College of Physicians and Surgeons of BC, the BC College of Nurses and Midwives, and any other relevant governing bodies. The application of the guidance in this document does not override the responsibility of health care professionals to make decisions appropriate to the circumstances of an individual patient, in consultation with that patient and their guardian(s) or family members, and, when appropriate, external experts (e.g., specialty consultation). Nothing in this document should be interpreted in a way that would be inconsistent with compliance with those duties.

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1.0 About this Document

This breakout resource was developed in response to calls from clinicians for more guidance on urine drug testing (UDT) in the clinical management of opioid use disorder (OUD). Although the BCCSU and Ministry of Health's *Guideline for the Clinical Management of Opioid Use Disorder* provides high-level UDT guidance, including recommended frequency, it does not provide an in-depth review of indications for UDT, how and when to order and interpret UDT, or recommended approaches for managing unexpected results. This breakout resource expands upon the guidance included in the 2017 *OUD Guideline* with some important updates. The UDT guidance contained herein effectively replaces the UDT information in the 2017 *OUD Guideline*.

Content in this breakout resource is based on a structured review of the academic and grey literature (e.g., existing guidelines and best practice documents from other regions) relating to UDT in the management of OUD and expert consultation. Consultation was sought from physicians and nurse practitioners who specialize in addiction medicine, registered nurses, and people with lived experience. In addition, a laboratory scientist reviewed the document and provided feedback to ensure information aligned with available provincial lab services and requisition requirements. Following drafting of the document, the clinical committee for the forthcoming update to the *Guideline for the Clinical Management of Opioid Use Disorder* was invited to review and provide feedback on the breakout resource. The document was also shared with the Provincial Opioid Agonist Treatment Support Program Steering Committee for review and feedback, and circulated to all of the opioid agonist treatment (OAT) prescribers in BC along with a survey to solicit feedback.

Key guidance in this breakout resource includes:

- Describing clinical scenarios where UDT is indicated
- Emphasizing that UDT should be used when the results will impact clinical management of the patient and that results should not be used punitively
- Underscoring the importance of discussing the purpose of performing UDT with patients, including how unexpected results will be addressed
- Clarifying that confirmatory testing should only be ordered when the results would change the clinical management of the patient
- Recommending that clinicians give patients 24–48 hours to present for a random drug test
- Recommending supervised UDT but not witnessed UDT
- Recommending increased clinical discretion regarding frequency of UDT
 - o For example, for take-home dosing: 2–4 per year for buprenorphine, and 6–8 for methadone and slow-release oral morphine
- Providing instructions for sample collection procedures and confirming temperature of sample
- Conducting UDT through virtual care
- Interpreting and managing unexpected UDT results
- Providing information about false-positive and false-negative results

The guidance in this document also updates the guidance on urine drug testing provided in the BCCSU's <u>Guidance for Injectable Opioid Agonist Treatment for Opioid Use Disorder</u>. This document should be referred to when providing urine drug testing in the context of injectable opioid agonist treatment (iOAT).

1.1 BACKGROUND AND SCOPE

According to provincial practice standards set by the BCCSU and Ministry of Health's <u>Guideline for the</u> <u>Clinical Management of Opioid Use Disorder</u>, UDT is considered an essential component of the clinical management of patients with OUD who are prescribed oral OAT, and promotes both patient and public safety by potentially helping to identify clinical instability and diversion and informing treatment plan modifications.

This document reviews the current evidence for UDT, provides an overview of the use of UDT in the primary care management of patients with OUD who are receiving **oral** OAT (buprenorphine/naloxone, methadone, or slow-release oral morphine), and offers guidance and general practices for ordering, collecting, and interpreting UDT. Brief guidance on the use of UDT for patients who are receiving iOAT is also provided.

2.0 EVIDENCE SUMMARY

Urine drug testing at regular intervals is the standard of care in the provision of OAT and can be a useful tool in the medical management of patients prescribed OAT. For example, UDT can support comprehensive assessment, including determining patient adherence to treatment, validating self-reported use of opioids or other substances, detecting the use of other substances that may affect safety (e.g., benzodiazepines), and evaluating treatment response and outcomes (e.g., abstinence from fentanyl or other opioids).

Despite widespread use of UDT and clinical guidance that recommends that UDT should be widely used in opioid use disorder care,¹ the utility of UDT is unclear.^{2,3} A 2019 critical review of the literature supporting the use of UDT as a standard of care for individuals on OAT found that this area of clinical care has been under-researched.² The authors concluded that there is insufficient evidence to determine effectiveness for both patient and community health outcomes, and called for more research to determine the relationship between UDT frequency and health outcomes.² This finding accords with a 2014 systematic review that examined the use of UDT in OAT and found insufficient evidence to demonstrate the utility of carrying out UDT for medical management of individuals receiving OAT.³ Additionally, a 2012 cross-sectional study of general practitioners in France who use UDT with patients on buprenorphine or methadone found that the most common practitioner responses to unexpected UDT results included increased counselling (71%), referral to a specialist (48%), and/or discontinued OAT (29%). This study demonstrates both the benefits of UDT as a component of care for OUD, as UDT results can be used to inform necessary changes in clinical care, as well as the potentially negative consequences, such as discontinuing OAT due to unexpected results.⁴

3.0 GENERAL PRACTICES FOR USING URINE DRUG TESTING

This section provides guidance on general practices for UDT, including indications for use, patient-centred care, non-punitive approaches, discussing testing with patients, and management of unexpected results.

3.1 Indications for Urine Drug Testing

Urine drug testing should be used along with collateral information, self-report, and clinical assessment for the monitoring of treatment.⁵ In the absence of clearer evidence supporting the use of UDT for individuals receiving OAT, UDT should be used for specific purposes, such as:

- Confirming illicit opioid use during baseline assessment
- Supporting decision-making regarding take-home doses
- Confirming that the medication is being taken
- Screening for ongoing non-prescribed or illicit opioid use, which may indicate the patient is undertreated or needs additional support
- Detecting the presence of other substances, including substances the patient may be unaware they have ingested
- Evaluating treatment response and outcomes

Information about urine drug testing, including purpose, how the results will be used, and general collection procedures, should be included in treatment agreements and clearly articulated to patients.⁵

All UDT should be accompanied by a discussion with the patient about their substance use and care plan and should be based on the principles of improved patient care and outcomes. For example, to support decision-making for take-home doses of methadone, UDT can be used to help inform assessment of clinical stability. Conversely, UDT likely provides little additional information for patients who selfreport ongoing fentanyl use while they are prescribed methadone, unless there is additional clinical rationale for ordering UDT. Clinicians should consider the patient's clinical and social stability, safety, and perceived risks, taking into consideration the patient's autonomy and other factors that might influence their ability to provide a urine sample on short notice, such as employment or childcare needs.

Table 1: Clinical Scenarios for UDT

Clinical scenarios in which UDT may be indicated	 To confirm opioid use at baseline screening To help inform assessment of clinical stability before and during prescription of take-home doses To ensure medications are being taken To screen for illicit opioid use or other substances during treatment, if necessary, including substances the patient may not be aware they were exposed to
Clinical scenarios in which UDT may not be indicated	 To test without clinical rationale To test when results will not impact clinical management of the patient To screen for ongoing substance use by a patient who self-reports ongoing substance use, where confirmation of ongoing substance use will not change clinical management

3.2 Patient-Centred Care

Research evidence suggests that incorporating patient-centred approaches in the clinical management of substance use disorders can improve retention in care, treatment satisfaction, and health outcomes.⁶⁻⁸ In addition to recognizing the unique needs, values, and preferences of each patient, patient-centred care involves listening to, informing, and empowering patients as experts in their own care. Practical strategies for incorporating patient-centred care in the context of UDT may include¹⁰:

- Collaboratively developing treatment plans and setting patient-provider expectations
- Discussing the purpose of UDT with your patient
- Using a shared decision-making framework to select treatment options or interventions (e.g., frequency of UDTs)
- Only using UDT when it may alter clinical management
- Ensuring there is a clear understanding of the rationale for and impacts of UDT to avoid patient perception of punitive treatment decisions (e.g., clear expectations regarding the degree of clinical stability needed for take-home dosing of full agonist OAT medications, and the impacts of UDT results that may affect take-home doses)
- Avoiding punitive approaches to treatment monitoring (e.g., automatically discontinuing OAT due to ongoing illicit opioid use rather than discussing with patient and adjusting treatment plan)
- Discussing with patient how UDT results may impact care (e.g., consistently positive for prescribed medication and negative for illicit substances may lead to increased take-home dosing, while the opposite may lead to daily witnessed ingestion and other strategies to increase clinical stability)
- Being open to and respectful of patient agency and choice

Clinicians should also be aware of the language they use and its potential to contribute to the stigmatization of people who use drugs. Accordingly, clinicians should strive to use "people-first" language, non-judgmental medical terminology, and language that promotes recovery in routine practice and when interacting with patients, families, colleagues, and healthcare professionals. In the context of UDT, clinicians should avoid referring to test results using colloquial terms, namely "dirty" or "clean," as these reinforce the concept that substance use is a moral failing.¹ For more information, clinicians are encouraged to review <u>Respectful Language And Stigma: Regarding People Who Use Substances</u>, a resource jointly developed by the Provincial Health Services Authority (PHSA), the BC Centre for Disease Control (BCCDC), and the BCCDC's <u>Toward the Heart</u>.

3.3 Use Urine Drug Testing Non-Punitively

Clinicians should emphasize—and ensure that patients understand—that UDT is performed for all patients prescribed OAT and that the intention is not to police or punish patients, but to provide them with the safest and most effective care possible, including identifying unexpected substances, evaluating treatment response, and collaboratively making changes to the treatment plan as necessary.¹ Clinicians should discuss general strategies for managing unexpected UDT results (see <u>Managing Unexpected Urine</u> <u>Drug Testing Results</u>) with their patients and reassure them that unexpected UDT results—for example, positive for non-prescribed opioids or other substances or negative for the prescribed OAT—will not be used punitively or as sole grounds to discontinue treatment, but may be used to inform changes to their clinical management (e.g., modifications to take-home dosing in response to decreased clinical stability).

3.4 Use Urine Drug Testing When Results Will Change Clinical Management

Clinicians should use UDT when test results may impact clinical management for a given patient; however, UDT results should not be the only factor considered when making shared treatment decisions. Before initiating changes to the patient's treatment plan, clinicians should review the treatment plan and patient goals, and inquire about any underlying circumstances or changes that may be occurring in the patient's life (e.g., changes in housing, financial security, relationships, or social circumstances) that may be relevant. This conversation can be used as an opportunity to discuss with patients how UDT results can affect their treatment plan. For example, ongoing substance use or diversion of prescribed medication may affect eligibility for or continuation of take-home doses of OAT.

A pattern of tests positive for the prescribed medication and negative for unexpected substances suggests a treatment plan is effective, whereas the opposite indicates the need for treatment plan adjustments.⁵ Treatment plan adjustments should be discussed with the patient and may include discontinuation of take-home doses, increased psychosocial interventions and support (which may be provided on-site or referred out to), a higher level of care, increased patient education, a dose increase, more frequent or more random UDT schedule, or trialing a different medication option based on patient preference (e.g., switching to buprenorphine/naloxone if the patient prefers take-home dosing).⁵

3.5 Discussing Urine Drug Testing with Patients

Before initiating OAT, clinicians should provide their patients with relevant information regarding UDT,

including an overview of urine sample collection procedures, expectations regarding the frequency of UDT, and an explanation of random versus scheduled UDT. Completion of an <u>OAT Prescriber–Patient</u> <u>Agreement</u> may be used to ensure that patients know what to expect during treatment. The use of this form—or any patient contract—should be based on clinical need (for example, helping to set expectations for someone new to OAT). Some individuals (e.g., those with low literacy or who are otherwise not able to sit long enough to go through the document) may find the use of such an agreement overly onerous, while others (e.g., those with significant experience on OAT) may already be familiar with the expectations.

In conversation, clinicians may describe UDT as an objective and unbiased tool used in combination with patients' self-reported information (e.g., symptoms, response to treatment, ongoing substance use) and clinical assessment to provide a complete picture of treatment effectiveness.¹

3.6 Managing Unexpected Urine Drug Testing Results

In order to ensure an accurate and up-to-date understanding of what substances each patient may be exposed to and to ensure the treatment plan continues to be safe and effective, clinicians should review medical records and PharmaNet, as well as discussing recent substance use with the patient, prior to discussing UDT results.

Clinicians should review UDT results with the patient, using a non-judgmental and collaborative approach that gives the patient the opportunity to ask questions about test results and discuss any challenges they are experiencing. It may be helpful to ask the patient if and why they think their UDT could have unexpected results and to explore potential reasons for an unexpected result with the patient. Clinicians should review the treatment plan and goals, emphasizing that UDT results are one factor in making shared treatment decisions and inquire if the treatment plan is meeting their needs (e.g., adequately controlling withdrawal symptoms with minimal side effects). Clinicians should also ask about any underlying circumstances or changes that may be occurring in the patient's life (e.g., changes in housing, financial security, relationships, or social circumstances).¹

If UDT results indicate ongoing—or return to—illicit opioid use, the clinician should promptly follow up with the patient and determine if the current treatment plan is meeting their needs. For example, ongoing use or return to use might signal the need to intensify treatment, alter approach, or transition to an alternative OAT medication, depending on the circumstances and patient preference.

Patients should be actively engaged in this decision making. Ongoing use or return to illicit opioid use should not be considered an absolute indication to discontinue treatment, especially in the context of the ongoing overdose public health emergency, but may indicate a need to reassess the patient's treatment plan.

Point-of-care UDT results should be confirmed with laboratory testing, for example, in cases in which there are unexpected and unexplained results and confirmation would have a significant impact on clinical management.¹ If clinicians are interested in testing for opioids that cannot be detected on a standard immunoassay (e.g., tramadol) and confirmation would have a significant impact on patient management, they should consult a laboratory.

Clinicians can reduce the number of "unexpected" UDT results by maintaining open communication

with patients and working to ensure patients feel comfortable disclosing ongoing use or return to use.¹ Clinicians should also be aware of the limitations of point-of-care UDT (e.g., false-negative and false-positive results, detects only classes of some substances). This can reduce or prevent misinterpretation of UDT results, conflicts with patients, and loss of trust (e.g., false-positive test results). The main goal is to retain patients in care.

Examples of specific types of unexpected results, possible explanations, and the recommended actions can be found in <u>Appendix 1.11</u>

3.6.i Managing Unexpected Urine Drug Testing Results that Indicate Diversion

A UDT result that is negative for the prescribed OAT medication or a UDT result indicative of sample adulteration or substitution may indicate diversion, and should prompt follow up and reassessment of a patient's treatment plan. In particular, the clinician should ask the patient if the treatment is working for them—for example, whether they are experiencing any withdrawal symptoms, undesirable side effects, or challenges attending the pharmacy regularly if prescribed witnessed doses. If take-home ("carry") doses are prescribed, the clinician should weigh the risks and benefits of returning to daily witnessed ingestion at a pharmacy. Diversion of full agonist OAT medications (i.e., methadone and slow-release oral morphine) presents a risk of fatal overdose if taken by an individual with a lower opioid tolerance or in combination with other opioids and may warrant discontinuation or reduction of take-home doses. Diversion, particularly the first documented instance, should not be considered an absolute indication to discontinue treatment. If applicable, the clinician should discuss any underlying reasons for diversion of OAT.

If the patient's UDT result is negative for the prescribed OAT, it's likely they have missed doses and may require dose reduction and titration. Given that some patients on slow-release oral morphine or methadone can experience loss of tolerance after just 1 and 3 days of missed doses, respectively, it may be dangerous to resume treatment at the same dose. Meanwhile, the risks related to interruption of buprenorphine are smaller, with patients requiring dose adjustment only after ≥5 consecutive days of missed doses.

The clinician may consider treatment intensification, for example, if the patient is using illicit opioids to manage withdrawal symptoms or ongoing cravings and providing substituted urine or diverting their prescribed medication. Treatment intensification may include:

- Increasing the frequency of clinical visits in order to provide more intensive support, monitoring, and assessment
- Increasing the daily dosage of oral OAT
- For patients prescribed injectable OAT, prescribing an additional dose of oral OAT, or if already prescribed, increasing the daily dosage of oral OAT
- Providing information about and referrals to psychosocial treatment interventions, and community and recovery supports
- Discussing with patients whether transitioning to an alternate OAT option (e.g., from oral OAT to injectable OAT; from methadone to slow-release oral morphine) would be right for them

If a patient does not benefit from treatment intensification or optimization, or if there are significant safety concerns, the clinician should use their best judgement in terms of appropriate follow-up. While not recommended, there are some situations in which discontinuing OAT might be necessary if the risks of

continuing treatment outweigh the benefits. For example, if—despite attempts to intensify and optimize treatment—a patient is not benefiting from OAT (including improvements in physical health, mental health, or social stability) and continued treatment poses serious personal safety risks or if there are continued or repeated diversion attempts, the clinician and patient may need to consider cessation of OAT. In such cases, the clinician should ensure that the patient remains connected to care and health services; has access to psychosocial, community, and recovery supports; and harm reduction supplies including naloxone kits, and knows that they can return to treatment at any time if their circumstances change. Clinicians should clearly document the rationale for any changes to the patient's treatment plan, including treatment discontinuation. Please refer to the BC Centre on Substance Use and Ministry of Health's *Guideline for the Clinical Management of Opioid Use Disorder* for more information.

4.0 Performing Urine Drug Testing

4.1 Uses of Urine Drug Testing

Urine drug testing can be used to:

- Confirm illicit opioid use prior to initiating OAT^a
- Support decision-making regarding take-home doses
- Assess adherence to OAT through the presence of prescribed medication in urine²
- Confirm the self-reported use of non-prescribed opioids or other substances that might adversely affect patient safety or increase overdose risk²
- Confirm the presence of substances the patient may be unaware they have ingested (e.g., benzodiazepines present in what was expected to be fentanyl)
- Evaluate treatment response and outcomes¹²

4.2 Types of Urine Drug Testing used Alongside Opioid Agonist Treatment

There are two main types of UDT: (1) immunoassay-based tests and (2) confirmatory testing,¹³ both of which are described below. See <u>Point-of-Care vs. Laboratory Urine Drug Testing</u> for more information.

4.2.i Immunoassay-based Screening Tests

Immunoassay-based screening tests use antibodies to detect the presence of a substance or class of substances in a sample.¹³ "Point-of-care" UDT most often refers to qualitative-based tests that can be performed in the clinical setting where a patient is receiving care, rather than in an off-site laboratory (as is the case for confirmatory testing). Point-of-care immunoassay-based UDT is the preferred approach for patients prescribed OAT (see <u>Point-of-Care vs. Laboratory Urine Drug Testing</u>). Immunoassay-based UDT can also be done in a laboratory; however, this causes a delay in receiving test results due to transport, processing, analysis, and reporting time.

Point-of-care immunoassay-based UDT is convenient and provides rapid results; however, it has some limitations. Although useful when the specific drug is unknown, immunoassays usually detect a class of drugs (e.g., opiates, benzodiazepines) rather than a specific type of drug (e.g., heroin, diazepam).^{13,14} In addition, because immunoassay tests are based on antibody detection, there is potential for cross-reactivity with other, sometimes unrelated, molecules (see <u>Common Causes of False-Positive and False-Negative Urine Drug Tests</u>).^{1,15} Given the potential for false-positive or false-negative results with immunoassay-based testing, laboratory confirmation is recommended if immunoassay-based UDT yields an unexpected result and the results will impact clinical management of the patient.¹³

Immunoassay-based tests are not quantitative; that is, results are reported as detecting the presence or absence of a substance or class.^{1,12} Therefore, immunoassay-based tests cannot be used to determine when exactly a substance was last used, how much was used, or how often it was used; in addition, one-

^a Opioid use disorder can also be confirmed in the absence of UDT (e.g., using past hospital records, a clinical history where the patient describes intoxication, euphoria, and/or withdrawal). Confirmation of OUD and the initiation of OAT without UDT should be documented, including the clinical rationale for not ordering UDT.

time or infrequent use cannot be distinguished from ongoing use.¹² In some instances, immunoassaybased UDT can test for either the specific substance or, preferably, its metabolite, rather than only the class of drugs. The metabolite is preferred because it is formed as the body metabolizes the substance and, therefore, testing is less vulnerable to adulteration or substitution of the sample. With these limitations in mind, immunoassay-based tests can be used to determine recent use of a substance. See <u>Appendix 3</u> for approximate timelines for detection.

4.2.ii Confirmatory Testing

Confirmatory testing using gas chromatography/mass spectrometry or liquid chromatography/mass spectrometry is the gold standard for definitive drug testing, offering greater sensitivity, specificity, and accuracy, as well as providing (often) quantitative results compared to immunoassay-based tests.¹ Briefly, chromatography is first used to separate the components of a sample and mass spectrometry is then used to identify specific components on the basis of their mass/charge ratio.^{1,13} Unlike immunoassay-based screening tests, confirmatory testing is generally performed in an off-site external laboratory, meaning that results are not provided as quickly, making it primarily useful for confirmation of immunoassay-based test results, which may include verifying the presence of expected metabolites.

The major strength of confirmatory over immunoassay-based screening tests is that confirmatory testing can determine the presence of specific drugs, particularly semi-synthetic and synthetic opioids. As such, confirmatory testing can be used to identify drugs that are not included in immunoassay panels or are not detectable in immunoassay panels (e.g., tramadol).¹⁶ In addition, because confirmatory testing provides both qualitative and quantitative information about the presence of specific drugs, it can be used to resolve cases of false-positive results.¹ Its specificity is also useful in cases in which a patient is prescribed more than one opioid or is prescribed an opioid that has active metabolites.¹⁴

Generally, gas chromatography/mass spectrometry or liquid chromatography/mass spectrometry should only be used to confirm immunoassay-based test results when results would impact clinical management of the patient, due to both the delay in results and higher cost per test.¹

Furthermore, the results of confirmatory testing must be interpreted cautiously, given that some opioids have active metabolites.¹⁴ For example, the presence of morphine according to confirmatory testing may be due to the metabolism of codeine, an over-the-counter opioid, rather than heroin or a non-prescribed opioid.^{1,14} Similarly, a positive result for hydromorphone may be due to high levels of morphine^b (e.g., in patients prescribed slow-release oral morphine) and does not necessarily indicate hydromorphone has been taken.

4.2.iii Characteristics of Immunoassay-based and Confirmatory Urine Drug Testing

There are several important characteristics of immunoassay-based and confirmatory UDT that clinicians should consider when ordering UDT, including test setting, availability, sensitivity and specificity, use, and cost.

^b Morphine is metabolized to hydromorphone by a minor pathway. With low doses of morphine, the amount of hydromorphone may not be detectable. However, individuals prescribed slow-release oral morphine for the treatment of OUD are prescribed relatively high doses, which can lead to concentrations of hydromorphone well above the cut-off being detected in their urine.

Table 2: Immunoassay vs. Confirmatory Testing

	Immunoassay ¹	Confirmatory ¹
Test setting	Point-of-careLaboratory (screening)	Laboratory only (confirmatory)
Availability	 Immediate results if point-of-care 	 Delayed results (due to transport, processing, analysis, and reporting time)
Sensitivity for opioid detection	 Variable, depending on test used Opiate panel: low to null for detection of semi-synthetic^c and synthetic opioids (e.g., fentanyl, oxycodone, buprenorphine, and methadone) 	• High
Specificity for opioid detection	 Variable depending on test used Can result in false-positive or false-negative results 	• Absolute
Use	 Qualitative Can determine presence/absence of drug classes (i.e., opiates, benzodiazepines, amphetamines) Limited number of tests for specific substances 	 Qualitative & quantitative Detects specific substances and concentration present in sample
Cost	Inexpensive	Expensive; should only be used if clinically necessary

4.3 Scheduled vs. Random Urine Drug Testing

Urine drug testing can be scheduled at predetermined appointments or on random, unscheduled dates, with random testing preferred over scheduled testing.⁵ Random urine drug testing involves contacting the patient and requesting that they present to a clinic (preferred) or local laboratory facility for UDT within 48 hours. The reasoning for utilizing random UDT should be discussed with the patient. Random UDT is considered more likely to yield accurate results as it reduces the likelihood of sample adulteration or behavioural changes that could occur in anticipation of a scheduled UDT. However, random UDT involves advance coordination by clinic staff, might not always be feasible for patients (e.g., due to work or parenting commitments), and may be perceived by patients as punitive and stigmatizing.

Patients who miss their appointment for random or scheduled UDT should be reassessed, as this may indicate risk of return to use, non-medical use, or diversion. Patients should not face treatment discontinuation or other punitive measures on the sole grounds of being unable or unwilling to provide a random UDT sample at 48 hours' notice. Clinicians should be aware that requesting random UDTs can cause ongoing stress for patients, and providing random UDTs can be burdensome for

^c Although hydromorphone is a semi-synthetic opioid, most immunoassay opiate panels are able to detect it.

many patients, requiring a range of arrangements such as requesting time off from work, organizing childcare, or changing travel plans. In such cases, clinicians are advised to follow up with the patient as soon as possible after the missed or declined test to determine if there are any underlying circumstances that would indicate the need to re-evaluate their treatment plan, such as return to illicit opioid use, or barriers such as those described above, which require more flexibility or a longer window to provide a sample. Using a collaborative and patient-centred approach, the patient and clinician can decide if and how a treatment plan should be adjusted to better meet the patient's needs.

4.4 Urine Drug Testing Frequency for Patients Prescribed Opioid Agonist Treatment

Determining the frequency of random versus scheduled UDT should be at the discretion of the prescribing clinician. Urine drug testing frequency should be guided by therapeutic need, with an understanding that there is insufficient evidence to suggest that more frequent testing affects substance use.⁵ Clinicians should aim to balance patient safety, convenience, and autonomy. Clinicians should also rely on clinical assessment, interview, and patient self-report to supplement UDT or, when appropriate, in lieu of frequent UDT, in order to appropriately monitor treatment adherence or illicit substance use.

A general principle of more frequent testing at the beginning of treatment may be followed. Generally, UDT should be performed at baseline and when patients display a change in clinical status.⁵ During initiation and dose escalation, urine drug testing should be performed monthly or more or less frequently as required when clinically indicated and at the discretion of the clinician to confirm self-reported abstinence from illicit opioid use and/or when the treatment plan changes to include take-home dosing and when UDT results would change clinical management. There may be circumstances in which UDT may be difficult to complete (e.g., virtual/telehealth appointment,^d patients in rural or remote settings, patients with barriers such as limited transportation, medical conditions), in which case the clinical rationale for less frequent UDT should be documented. More frequent urine drug tests are not necessarily required if ongoing substance use is fully disclosed by the patient; however, UDT can be used in this situation to determine which substance(s) the patient may have unknowingly used (e.g., unknowingly using benzodiazepines due to the adulterated illicit opioid supply). Following initiation, and once a patient has stabilized on a given dose of OAT, UDT should be performed when the results would change clinical management. It is recommended that patients receiving take-home doses should have a minimum number of random UDTs per year (2-4 for buprenorphine; 6-8 for methadone and slow-release oral morphine), or more frequent as required if there are safety concerns (e.g., return to use, diversion).

Physicians are compensated through the Medical Services Plan (MSP; fee code P15039) for performing and interpreting point-of-care UDT as part of opioid agonist treatment up to a maximum of 26 UDT per patient per year; however, UDT should be performed for a specific purpose and according to therapeutic need. For that reason, many patients will require fewer than 26 UDT per year.

Note: The guidance in this document supersedes the guidance provided in the BCCSU and Ministry of Health's <u>Guideline for the Clinical Management of Opioid Use Disorder</u> on urine drug testing. Recommendations for UDT frequency depending on treatment stage and type of OAT medication have been updated and can be found in Table 3.

^d See <u>Urine Drug Testing and Virtual Care</u>, in this document, for more information.

Table 3: Recommended urine drug testing for opioid agonist treatment medications

Treatment stage	UDT schedule	
Initial confirmatory testing	Performed to confirm illicit opioid use prior to initiating OAT	
Buprenorphine/naloxor	ne	
Induction and stabilization	Monthly or more or less frequently as required and when clinically indicated ^e	
Maintenance	When clinically indicated	
Take-home doses	At least 2–4 random tests per year or more frequently if there are any safety concerns Frequency of scheduled UDT is as required when clinically indicated	
Methadone		
Initiation, titration, and stabilization	Monthly or more or less frequently as required and when clinically indicated. In circumstances where UDT is occurring less than monthly, patient safety can be increased with daily witnessed ingestion. ^f	
Maintenance	When clinically indicated	
Take-home doses	At least 6–8 random tests per year or more frequently if there are any safety concerns Frequency of scheduled UDT is as required when clinically indicated	
Slow-release oral morphine		
Initiation, titration, and stabilization	Monthly or more or less frequently as required and when clinically indicated. In circumstances where UDT is occurring less than monthly, patient safety can be increased with daily witnessed ingestion. ^f	
Maintenance	When clinically indicated	
Take-home doses	At least 6–8 random tests per year or more frequently if there are any safety concerns Frequency of scheduled UDT is as required when clinically indicated	

^e Although best practice, there may be situations in which it is reasonable to forgo UDT prior to initiating buprenorphine/naloxone specifically (e.g., telehealth in a remote setting with significant collateral information, where requiring UDT would constitute an unreasonable barrier; emergency department induction with significant collateral information; a patient who has been abstinent but is at risk of relapse; outreach settings with significant collateral information, where requiring UDT would constitute an unreasonable barrier). The clinical rationale, including buprenorphine/naloxone's superior safety profile and decreased risk of diversion, should be recorded. It is not generally appropriate to forgo UDT prior to initiating methadone or slow-release oral morphine; however, in the context of the COVID-19 pandemic it may be appropriate (for example, for individuals self-isolating). See <u>Risk Mitigation in the Context of Dual Health Emergencies: Interim Clinical Guidance</u> for more information.

^f For example, during the COVID-19 pandemic, monthly UDT may not be utilized, in which case daily witnessed ingestion through delivery could increase patient safety in the absence of regular UDT.

4.4.i Urine Drug Testing Frequency for Patients Prescribed Injectable Opioid Agonist Treatment

Note: The guidance in this document supersedes the guidance on urine drug testing provided in the BCCSU's *Guidance for Injectable Opioid Agonist Treatment for Opioid Use Disorder*.

Unlike with oral OAT, where regular and random UDT are considered standard of care, scheduled and random UDT are not considered standard care for iOAT, due to both the low risk of diversion and the high frequency of contact with care providers.¹⁷ Clinicians should use their discretion when ordering UDT for iOAT patients.

During initial screening, UDT should be performed to confirm illicit opioid use. Other than these initial confirmatory UDTs, there is no required number for individuals on iOAT. Point-of-care UDT may be useful for providing immediate feedback to patients, making prompt treatment decisions when unexpected and potentially harmful substances are detected (e.g., substances patients are unaware they have consumed due to adulteration of the illicit drug supply), informing discussions of harm reduction and safety, and monitoring trends (such as decreased illicit substance use). Patients who are showing signs of instability or who disclose ongoing illicit substance use may benefit from using UDT to guide more intensive follow-up and reassessment.¹⁷ Given the risk of fentanyl contamination in illicit substances—including both opioids and non-opioids—it is recommended that point-of-care tests include fentanyl any time a UDT is ordered for iOAT patients.¹⁷

Injectable OAT ¹⁷		
Initiation, titration, and stabilization	Initial confirmatory UDT	
Maintenance	When clinically indicated	
Take-home/carry prescriptions	Not applicable. Take-home doses are not provided.	

Table 4: Recommended urine drug testing for injectable opioid agonist treatment

4.5 Procedures for Collecting Urine Samples for Urine Drug Testing

Urine samples should be collected following the procedures for supervised UDT in clinical settings. During a supervised UDT, the patient produces a sample in a designated collection area without being witnessed. Patients should not be asked to provide witnessed UDT (i.e., where the patient provides the sample under direct visual observation). Many patients perceive witnessed UDT as a violation of trust, respect, and privacy. In addition, they may be traumatizing or retraumatizing for patients,¹ especially those who have experienced psychological or sexual trauma.

4.5.i Before a Patient Provides a Urine Sample

- Emphasize that this is a routine part of OAT. For example, tell patients: *"I do this for all my patients on OAT."*
- Emphasize that UDT results will not be used punitively or as grounds to discontinue treatment. For example, tell patients that:
 "You will not be punished or forced to end treatment based only on the results of the UDT."
- Take a detailed history of any substances used in the past week. For example, ask patients: "Is there anything I should expect to see in your results?" or "Is there anything you expect to see in your results?"

4.5.ii General Procedures and Standards for Supervised Urine Collection:

- Securely store sample containers away from the collection area
- Have the responsible staff member confirm the patient's identity before providing a sample container^g
- Provide patients with a pre-labeled container prior to entering the collection area
- Before patients enter the collection area, request that they remove extra clothing, such as coats or bulky sweaters, and leave any parcels, bags, or purses behind in a secured and supervised area^h
- Provide patients with instructions on how to provide a sample. Instructions (written and visual) should be available in the collection area
- Respect trans, non-binary, and gender non-conforming patients' dignity and needs by:
 - o Providing single-stall and gender-neutral washrooms and collection areas, when possible
 - o Adding signs to existing washrooms that state that trans people are welcome
 - o Ensuring all staff are aware that no staff or other patients should be commenting on or checking which bathroom patients use based upon their perceived gender
- Ensure patients with disabilities can safely access washrooms and collection areas
 - o Install mobility aids to assist patients (e.g., handrails, security poles)
 - o Ensure the collection area is wheelchair accessible
- Use hand on outside of container to determine that sample is warm or check temperature of sampleⁱ
- Several possible actions may be taken if the patient is unable to provide a urine sample:
 - If the patient has not started OAT, wait to begin OAT until a urine sample can be provided.
 If the patient has a known history of opioid use or known tolerance, UDT may be omitted if it would present a barrier to beginning OAT. Clinicians can also use collateral sources (e.g.,

^g Staff members can support patient dignity and confidentiality by avoiding identification of a patient in front of other patients and, where possible, directing the patient to a collection area outside the view of the reception area and other patients.

^h Some patients (e.g., patients experiencing paranoia, patients experiencing homelessness, patients with histories of trauma) may be reluctant to leave their belongings behind. In these situations, the responsible staff member should assure patients that their belongings will be securely stored. If the requirement to leave their belongings is presenting a significant barrier, the clinician may use clinical discretion and collaborative decision making to determine how best to resolve the issue; a patient's desire to keep their belongings with them should not present a barrier to starting or continuing OAT.

It is not required to measure the temperature of the urine sample. However, it may be appropriate or preferred in some instances. In these cases, measure the temperature of the urine sample within 4 minutes of production (recommended volume \geq 45mL) with an attached temperature-sensitive strip; the sample should be within the range of 32.2–37.7°C (90–100°F).' Defective temperature-sensitive strips are extremely rare.

Meditech, Cerner, or CareConnect) or consultation with another treating clinician (e.g., the patient's primary care provider) to determine if a patient has previously been diagnosed with OUD or has a history of opioid overdoses or opioid-positive UDTs.

- o If the patient is on OAT and receives daily witnessed ingestion, offer water and ask them to provide a sample. If they are still unable to provide a sample, the UDT may be postponed until the next scheduled UDT at the clinician's discretion.
- o If the patient provides a sample that has been substituted or adulterated, discuss the reason for these results with the patient, as well as the expectations for UDT that had been discussed and agreed to at treatment initiation.
- If the patient has been prescribed take-home dosing, inability to provide a sample 0 or providing a substituted or adulterated sample may be managed in the same way as a positive UDT result for illicit opioids. Inability to provide a sample or providing a substituted or adulterated sample, particularly the first documented attempt, should not be considered an absolute indication to discontinue treatment. If a patient is unable to provide a sample or provides a substituted or adulterated sample, discuss any underlying circumstances or changes that may be occurring in the patient's life (e.g., changes in housing, financial security, relationships, or social circumstances) or any barriers they may be experiencing in accessing take-home doses of OAT (e.g., difficulty going to the pharmacy frequently, need for child care, other medical conditions). If there has been a pattern of inability to provide a sample, clinicians can consider switching from take-home doses to daily witnessed ingestion. Clinicians should exercise caution if the patient may have been diverting take-home doses, as their tolerance may have decreased. Clinicians should consider a gradual titration of daily witnessed ingestion doses while decreasing or discontinuing the number of take-home doses.

4.6 Urine Drug Testing and Virtual Care

Virtual care (e.g., telehealth, video conferencing software) is increasingly being used in OUD care. This can help reduce barriers for individuals who have to travel to see their prescriber (e.g., in rural and remote locations), as well as reducing the risk of viral transmission during the COVID-19 pandemic. There are several options for clinicians to consider when ordering UDT for patients through virtual health.

- Clinicians can request the patient present to a local laboratory to provide a urine sample.
- Patients can be directed to a clinic location that has staff available to conduct a UDT and the prescribing clinician can then follow up on the results with the patient.
- If the patient is staying in a shelter or supported housing, the staff in the shelter may be able to conduct the UDT and support the patient to connect with the prescribing clinician.
- Clinicians can also use collateral sources (e.g., Meditech, Cerner, or CareConnect) if a patient has recently had a UDT ordered by another clinician.

It is important for clinicians to consider each patient's circumstances when ordering UDT through virtual health. Clinical judgement should be used to determine when virtual UDT is appropriate, prioritizing patient safety and the avoidance of unreasonable barriers for patients.

5.0 POINT-OF-CARE VS. LABORATORY URINE DRUG TESTING

Point-of-care UDT is preferable to laboratory UDT because it provides rapid results, which allow for immediate review with patients, supporting real-time discussions and shared decision-making (for example, same-day dose adjustments or prescription of take-home doses).¹ All point-of-care UDT products used for clinical purposes must be approved by Health Canada (see <u>Health Canada's Medical Devices Active License Listing</u> for a list of Health Canada-approved UDT products).

Laboratory confirmatory testing uses gas chromatography/mass spectrometry or liquid chromatography/ mass spectrometry. While confirmatory testing is costly, it has higher sensitivity and absolute specificity compared to immunoassays.¹ Therefore, clinicians are advised to use confirmatory testing when the results would significantly impact the clinical management of the patient. Careful interpretation of test results (including consideration of false-positive or false-negative results when warranted; see <u>Common Causes of</u> <u>False-Positive and False-Negative Results in Urine Drug Testing</u>)^{13,15} and patient-centered approaches are critical to maintaining the clinician-patient relationship and retaining patients in care.

5.1 Point-of-Care Urine Drug Testing

Point-of-care immunoassay-based tests are typically available for the following substances:

- Opiates (unspecified)
- Oxycodone
- Buprenorphine
- Methadone metabolite (EDDP)
- Fentanyl
- Hydromorphone

- Benzodiazepines (unspecified)
- Amphetamines (unspecified)
- Cocaine metabolite
- Cannabinoids
- Alcohol

Vendors typically offer a standard panel that includes tests for several substances. Clinicians should review what is included in standard panels prior to ordering and request additional single-agent test strips if a substance of interest is not included in the panel (e.g., buprenorphine, fentanyl).

It is important to note that **the immunoassay opiate test strip panel is designed to detect naturally derived opiates** including heroin, morphine, codeine. The immunoassay opiate test strip cannot reliably detect synthetic and semi-synthetic opioids such as buprenorphine, methadone, oxycodone, or fentanyl. Individual tests for semi-synthetic and synthetic opioids are available but must be ordered separately.



Availability and accuracy of tests vary by product and manufacturer. Clinicians should carefully review the manufacturer's product insert to determine which drugs within a class are detected. A point-of-care UDT for a particular drug class (e.g., benzodiazepines or opiates) should not be assumed to include all possible drugs within that class. Test strip cut-offs should also be noted, as cut-offs can differ based on test settings (e.g., for medical monitoring, opiates have a standard cut-off of 300ng/mL, while the standard cut-off for workplace testing is 2000ng/mL).

Unexpected point-of-care UDT results do not necessarily indicate ongoing illicit use, return to illicit use, or diversion.¹ If there is doubt and the result will impact clinical decision-making—for example, if point-of-care UDT results are discordant with patient self-report—clinicians should consider confirmatory laboratory UDT or a consultation with laboratory staff.¹

5.2 Detection of Substances in Point-of-Care Urine Drug Testing

The substances that should be tested for in a UDT point-of-care strip, dipstick, or collection cup panel will depend on the OAT medication prescribed and the treatment plan for that particular patient.

Table 5: Substances recommended for inclusion when performing urine drug testing
alongside OAT

Recommendation	Substance
Recommended for all patients prescribed OAT	 Prescribed OAT medication (buprenorphine or methadone metabolite, see <u>Interpreting Urine Drug</u> <u>Testing Results</u> for guidance on slow-release oral morphine) Opiates (unspecified; check product insert and verify cut-off is 300ng/mL) Fentanyl Benzodiazepines Amphetamines Cocaine metabolite
At prescribing clinician's discretion	 Oxycodone Buprenorphine (if patient is prescribed a different OAT medication) Methadone metabolite (if patient is prescribed a different OAT medication) Hydromorphone (if not prescribed): not recommended for slow-release oral morphine patients unless clinical suspicion is high, in order to avoid false positive results due to metabolism of morphine.
Not required	Cannabinoids/THCAlcohol

5.2.i Opioids

Urine drug testing should always include specific immunoassay tests for the prescribed OAT medication (e.g., specific immunoassays for buprenorphine, methadone metabolite). Refer to <u>Interpreting Urine Drug</u> <u>Testing Results</u> for guidance on slow-release oral morphine-based OAT.

To verify patient self-report and/or detect non-prescribed opioid use, a standard opiate strip panel (i.e., codeine, morphine, and heroin) should be included as well as a specific test for fentanyl. Clinicians should be aware that, with regular fentanyl use, fentanyl can persist in urine for up to 4 weeks or longer following consumption due its lipophilic properties.¹⁸ Urine drug tests conducted during this time frame will screen positive for fentanyl—this does not necessarily indicate ongoing fentanyl use by the patient. Clinicians may consider including specific tests for semi-synthetic and synthetic opioids as appropriate or indicated (e.g., oxycodone, buprenorphine, hydromorphone, and methadone). Clinicians should be aware that patients may have a positive UDT result for hydromorphone if morphine levels are high (e.g., in patients prescribed slow-release oral morphine); however, this does not necessarily indicate hydromorphone has been taken.

Including other non-opioid substances in the UDT test strip panel is done at the prescribing clinician's discretion and may depend on treatment approach or individual treatment plans.

5.2.ii Benzodiazepines

Benzodiazepines should be included in UDT panels for all patients prescribed OAT, due to a significantly increased risk of respiratory depression, overdose, and death when co-prescribed or used concurrently.¹⁹⁻²² While co-prescription of benzodiazepines is not a contraindication for starting or continuing OAT according to the *Guideline for the Clinical Management of Opioid Use Disorder*, the prescribing clinician should review the indication for benzodiazepine use, assess and diagnose any underlying sedative use disorder, and initiate a taper.^{23,24} In addition, the clinician should monitor such patients closely, conduct ongoing assessment of risks and benefits, and educate patients about the increased safety risks. Consult the *Guideline for the Clinical Management of Opioid Use Disorder* for more information on managing co-occurring benzodiazepine use.

Clinicians should be aware that point-of-care UDT can identify only some families of benzodiazepines. Some commonly used benzodiazepines, such as clonazepam, lorazepam, and alprazolam, are not reliably detected on point-of-care UDT. Urine drug testing results that indicate illicit use of benzodiazepines, particularly repeated positive results, warrant prompt discussion with patients about safety, risk, and overdose prevention, as well as strategies for reducing illicit benzodiazepine use and optimizing OAT. Clinicians should discuss with their patients how unexpected UDT results that indicate benzodiazepine use will be addressed when initiating OAT. Clinicians should also consider the nature of the benzodiazepine (e.g., diverted pharmaceuticals or novel illicit compounds) in view of the growing prevalence of novel illicit compounds such as etizolam, flualprazolam, and flubromazolam.

The street opioid supply in BC is increasingly adulterated with benzodiazepines and benzodiazepine analogues.²⁵⁻²⁸ Several novel benzodiazepine analogues have been identified in drug samples that were sold as opioids, including etizolam, bromazolam, flualprazolam, and flubromazepam.^{28,29} These benzodiazepine analogues can be significantly more potent than pharmaceutical-grade benzodiazepines such as diazepam (Valium) and alprazolam (Xanax).²⁹ Guidance for care considerations—including implications for starting OAT—for individuals exposed to benzodiazepines through the illicit opioid supply can be found in the BCCSU's <u>Clinical Bulletin: Benzodiazepines and Opioids</u>.

5.2.iii Stimulants

Stimulants such as amphetamines and cocaine should be included in point-of-care UDT. Any immunoassay for cocaine metabolite is extremely reliable; however, all amphetamine immunoassays (both point-of-care and laboratory) are prone to false-positive results. It should be noted that concurrent use of illicit stimulants (e.g., methamphetamine and cocaine) is not a contraindication to starting or continuing OAT according to the provincial *Guideline for the Clinical Management of Opioid Use Disorder*. However, as concurrent stimulant use can affect treatment outcomes as well as the clinical and social stability of patients prescribed OAT, it is recommended that reduction or cessation of stimulant use should be discussed and included in a patient's treatment plan when appropriate, particularly if this is a patient-identified treatment goal. The prescribing clinician should provide regular assessment, monitoring, counselling, and general support (e.g., medical management) for achieving treatment goals as standard of care. Clinicians should discuss with their patients how unexpected UDT results that indicate illicit stimulant use will be addressed when initiating OAT, noting that ongoing stimulant use will not be used as grounds to discontinue or reduce OAT, but may impact the treatment plan (e.g.,

reducing or discontinuing take-home doses of slow-release oral morphine or methadone based on clinical discretion).

5.2.iv Tetrahydrocannabinol

Inclusion of tetrahydrocannabinol (THC) test strips in point-of-care UDT is not required and is at the prescribing clinician's discretion, bearing in mind that positive THC UDT results may persist for weeks after use. Inclusion of THC test strips should be based on a clear clinical rationale and be documented. The clinical rationale and utility of these findings should be considered in addition to a patient's individualized treatment plan, which may or may not include abstinence from cannabis use.

5.2.v Alcohol

Inclusion of alcohol test strips in point-of-care UDT is not required and is at the prescribing clinician's discretion. Point-of-care UDT are available for alcohol and its metabolite, ethyl glucuronide. The clinical utility of UDT findings should be considered in the context of known limitations of this test (i.e., non-quantitative results and short detection window) as well as a patient's individualized treatment plan, which may or may not include abstinence from alcohol.

Because of the increased risk of overdose associated with the combined use of alcohol and opioid medications, clinicians should routinely assess alcohol use through clinical assessment and patientclinician discussion. While concurrent alcohol use and alcohol use disorder are not contraindications to starting or continuing OAT according to the provincial *Guideline for the Clinical Management of Opioid* <u>Use Disorder</u>, such patients should be monitored more closely, with ongoing assessment of risks and benefits, and education of patients about the increased risks related to combining alcohol and opioid medications.

If alcohol test strips are included in point-of-care UDT, clinicians should discuss with their patients how unexpected UDT results that indicate alcohol use will be addressed when initiating OAT.

5.3 Common Causes of False-Positive and False-Negative Point-of-Care Urine Drug Testing Results

Clinicians should not automatically assume a false-positive or false-negative result if the patient is prescribed one of the medications listed below. This cross-reactivity table does not provide definitive answers as to the reason for a positive or negative UDT result. Clinicians are advised to request confirmation testing if there is an unexpected result and the result will impact clinical management.

Table 6: Possible causes of false-positive and false-negative results in urine drug testing

	False-negative results	Check product insert carefully. False-negative results can occur when immunoassays do not reliably detect the following semi-synthetic or synthetic opioids ¹ :	
		Oxycodone ¹³ Buprer Hydromorphone ³⁰ Fentar	yl ¹³ Methadone ¹³ yl ¹³ Meperidine ¹
	False-positive results	Cross-reactivity and false-positive results can occur with compounds that have a similar chemical and physical structure.	
		Substances Cross-react with:	
Opioids		Fluoroquinolones ¹³ Poppy seeds ¹³ Dextromethorphan ¹³ Diphenhydramine ¹³ Quinine ¹³ Rifampin ³¹	Morphine Codeine Heroin metabolite
		Trazodone ³² Risperidone ³³ Paliperidone ³⁴	Fentanyl
		Quetiapine ¹⁵ Verapamil ^{13,15}	Methadone metabolite
Benzodiazepines	False-negative results	Check product insert carefully. Some benzodiazepines have distinct metabolic pathways and may not adequately cross-react on immunoassays. "Z-drugs" are not detected in benzodiazepine immunoassay panels. ³⁵	
		Lorazepam ³⁵ Alpraz Clonazepam ³⁶ Zopicl	olam ³⁵ Zolpidem ³⁵
	False-positive results	Cross-reactivity and false-posit have a similar chemical and ph	ive results can occur with compounds that ysical structure.
		Sertraline ¹⁵ Oxap	rozin ³¹
	False-negative results	Not applicable	
	False-positive results	Amphetamines have the highest degree of cross-reactivity of any substance and thus the highest rate of false-positive results. ¹⁵	
		Substances	
Amphetamines		Amantadine ¹³ FenproAripiprazole ³⁷ FluoxeBupropion ¹⁵ L-MethChlorpromazine ¹⁵ LabetaClobenzorex ¹⁵ MethylDesipramine ¹³ PhenteEphedrine ¹⁵ Phenyl	porex38Phenylpropanolamine15tine13Promethazine13amphetamine13Pseudoephedrine13lol31Ranitidine15phenidate13Thioridazine13ermine13Trazodone15ephrine35Venlafaxine31
		Lactate dehydrogenase and lactate, in patients with lactic acidosis ³⁹	
	False-negative results	Check product insert carefully. Synthetic cannabinoids are very unlikely to cross-react and are typically present at very low concentrations. ⁴⁰	
	i also negative results	Nabilone ⁴¹	
THC	False-positive results	Cross-reactivity and false-positive results can occur with compounds that contain THC or cannabidiol, or with compounds that have a similar chemical and physical structure.	
		Sativex ³² Efavire Dronabinol ¹³ NSAID	nz ¹³ Proton pump inhibitors ¹³ s ^{13,15} Baby soap ^j or shampoo ⁴²

^j Topical use of commercial baby soaps may cause false positive results.

5.4 Laboratory Testing

5.4.i Laboratory Immunoassay-based Urine Drug Testing

For immunoassay-based testing, in-office, point-of-care UDT is preferred, as results are available immediately for review with the patient, which supports patient–clinician discussions and shared decision-making.¹ Providing urine samples for testing while attending appointments at their primary care or OAT clinic may also be more convenient, discreet, and potentially less stigmatizing for patients.

If point-of-care UDT is unavailable or infeasible because of low patient volume or cost considerations, patients can be referred or urine samples collected in clinic can be sent to a local laboratory service for immunoassay-based UDT.

When requisitioned from a local laboratory, the standard immunoassay urine drug screen covered by MSP includes only the following: opiates (i.e., morphine, codeine, and heroin), hydromorphone, amphetamines, benzodiazepines, cocaine metabolite, and methadone metabolite. Clinicians must individually and explicitly request additional tests for synthetic and semi-synthetic opioids (i.e., fentanyl, oxycodone, and buprenorphine).⁴³ For example, if testing for buprenorphine and hydromorphone is required, "test for buprenorphine and hydromorphone must be written on the requisition.

5.4.ii Confirmatory Testing

The Ministry of Health provides MSP coverage for confirmatory testing only in cases in which the presence of the drug would significantly impact the clinical management of the patient. Because confirmatory testing is expensive, it should only be requested when clinically indicated and when accurate test results are required to make important treatment decisions.

Clinicians must specifically indicate confirmatory testing after a positive test result on the laboratory requisition. For example, if confirmation of fentanyl is required from an initial fentanyl-positive screen, write "confirm fentanyl if positive."

Clinicians can refer to the <u>Medical Services Commission Fee Schedule ("General Services—</u><u>Miscellaneous" p. 3-5</u>) for information about the standard immunoassay urine drug test that is available and covered by MSP in BC for patients who are receiving OAT. Clinicians can refer to the <u>Laboratory</u><u>Services Schedule of Fees ("Chemistry Fee Items" p. 3-20 to 3-21</u>) for a list of additional immunoassay and confirmatory tests that are available and covered by MSP in BC, which may be ordered if medically necessary. Clinicians should be aware that confirmatory testing requests may be subject to a laboratory medicine physician's approval or alteration based on clinical expertise or practice guidelines and protocols.

5.5 Ordering Laboratory Urine Drug Testing

Availability, cost, and general processes for requesting UDT for specific substances should be confirmed with local laboratory services. Laboratory-based testing is significantly more costly than office-based point-of-care testing, and should be used judiciously.

As different laboratories may have different testing protocols, clinicians are encouraged to contact the laboratory prior to sending samples if they are uncertain of how to order UDT or confirmatory testing. In most cases, if a non-specific "urine drug test" is ordered, an immunoassay will be performed as the default option. Tests for specific substances using immunoassay or confirmatory testing using gas-chromatography/mass spectrometry or liquid chromatography/mass spectrometry will only be done if explicitly requested and should only be used if the test result would significantly impact patient management. Clinicians can request confirmation (or any other tests) be added to their initial requisition and are advised to confirm how long the laboratory retains samples.

Ideally, a requisition will have limited text and should not include broad lists of compounds or specific methods. For example,

- "Urine drug screen (methadone)*, fentanyl"
 - o Tests performed: amphetamines, benzodiazepines, cocaine metabolite, opiates, methadone metabolite, fentanyl
- "Urine drug screen (methadone)*, fentanyl, confirm opiates if positive"
 - o Tests performed: amphetamines, benzodiazepines, cocaine metabolite, opiates, methadone metabolite; confirmation for morphine/codeine/heroin metabolite if opiate screen is positive

* Specifying methadone is helpful to the laboratory to ensure that methadone metabolite is included in the UDT.

6.0 INTERPRETING URINE DRUG TESTING RESULTS

Clinicians should exercise caution when interpreting immunoassay-based UDT results as these tests use threshold values that are designed to have higher sensitivity and lower specificity (i.e., false-positives are more likely to occur).¹ Immunoassay-based UDT only provides information on the presence or absence of a particular substance or metabolite at a single point in time using a pre-determined threshold value. Results do not provide accurate information on the time of last use or the quantity or frequency of use, and unexpected results do not necessarily confirm ongoing use, a substance use disorder, physical dependence, or diversion (see <u>Appendix 3</u> for more information on detection timelines).⁴⁴ When interpreting UDT test results, clinicians should note which substances are present or absent, both expected and unexpected. In addition to positive and negative results, clinicians should consider⁴⁵:

- The purpose of the UDT
- Limitations of the test
- Drug or drug metabolite(s) being detected and those not being detected
- Potential cross reactivities
- Limitations of the selected matrix when interpreting results

A pattern of tests positive for the prescribed medication and negative for unexpected substances suggests a treatment plan is effective, whereas the opposite can indicate the need for treatment plan adjustments.⁵ These may include⁵:

- Discontinuation or reduction of take-home doses
- Increased psychosocial interventions and support
- A higher level of care (e.g., more frequent appointments, increased psychosocial supports)
- Increased patient education
- A dosage increase
- More frequent or more random UDT schedule
- Trialing a different medication option

See <u>Appendix 1</u> for more information on interpreting UDT results. For laboratory UDT, clinicians are encouraged to contact their local laboratory if they have any questions or uncertainty in interpreting test results.

See Appendix 4 for an example UDT report

6.1 Interpreting Urine Drug Testing Results for Patients Prescribed Slow-release Oral Morphine-based Opioid Agonist Treatment

For patients treated with slow-release oral morphine, standard point-of-care opiate test strips and panels will be positive for morphine metabolites. Clinicians should be aware that patients prescribed slow-release oral morphine may have a positive UDT result for hydromorphone due to high morphine levels; however, this does not necessarily indicate hydromorphone has been taken. Morphine is metabolized to hydromorphone by a minor pathway. With low doses of morphine, the amount of hydromorphone may not be detectable. However, individuals prescribed slow-release oral morphine for the treatment of OUD are prescribed relatively high doses, which can lead to concentrations of hydromorphone well above the cut-off being detected in their urine. In addition, it is impossible to distinguish illicit heroin use from prescribed slow-release oral morphine using these tests.¹ Clinicians can consider using specific point-of-care UDT for fentanyl to assess illicit opioid use as needed to supplement clinical assessment and further patient–clinician discussion of ongoing substance use.

Monitoring of patients on slow-release oral morphine is best requested on the requisition form as "urine drug screen (methadone): confirm opiates if positive," with the results interpreted as follows:

Substance	UDT Result Profile ⁴⁶
Heroin	Variably high morphine combined with 5–10% codeine The short-lived heroin metabolite 6-monoacetylmorphine (6-MAM) confirms heroin but might not always be present.
Acetaminophen with codeine (Tylenol #3)	High codeine, relatively low morphine
Slow-release oral morphine	Very high morphine (>10,000 ng/mL), trace levels of codeine (<100ng/mL)

Table 7: Interpreting confirmatory testing results for slow-release oral morphine

7.0 RESOURCES

The following resources may be helpful for clinicians who provide OUD care and order UDT as a component of OAT:

- The BCCSU and Ministry of Health's *Guideline for the Clinical Management of Opioid Use* <u>Disorder</u>
 - o Provincial guideline for the management of OUD in BC
- Provincial Opioid Addiction Treatment Support Program
 - o Includes an educational module on UDT that is available to all health care providers
- The BCCSU's 24/7 Addiction Medicine Clinician Support Line
 - Provides telephone consultation for physicians, nurse practitioners, nurses, mid-wives, and pharmacists who provide addiction and substance use care. Clinicians can consult the 24/7 Line if they would like assistance in interpreting UDT results. It is available 24/7, 365 days a year. Call 778-945-7619. More information can be found at www.bccsu.ca/24-7
- The California Academy of Family Physicians' <u>Urine Drug Testing In Clinical Practice</u>
 o Provides information on conducting UDT in clinical settings
- Mayo Clinic Proceedings' Clinical Interpretation of Urine Drug Testing
 - o Provides information on immunoassay and confirmation testing and interpretation

Appendix 1: Managing Unexpected Urine Drug Testing Results

Table 8: Managing unexpected urine drug testing results

UDT result	Possible explanation	Recommended actions
Negative for prescribed OAT ¹¹	False-negative result Missed doses or non- adherence Diversion (particularly if UDT repeatedly negative) Very low dose <u>and</u> unusually dilute urine	 Ask the patient if they have been taking their medication, missed any doses, or given their medication to others Review results with the patient Order a confirmatory test and/or consult pathologist, if necessary Consider checking with the patient's pharmacy to confirm witnessed ingestion of doses Review/revise treatment plan—patients who have not been taking their OAT medication may require re-initiation of treatment If the patient is prescribed take-home doses, weigh risks and benefits of returning to daily witnessed ingestion at a pharmacy Repeated diversion at a pharmacy
Positive for non-prescribed opioids or benzodiazepines ¹¹	False-positive result Patient has acquired opioids or benzodiazepines from other sources	 Review PharmaNet to determine if the patient is being prescribed these medications by another clinician Ask the patient if they accessed opioids or benzodiazepines from other sources, including other clinicians or if they could have been unintentionally exposed to benzodiazepines through the illicit opioid supply Review results with the patient Discuss risks of concurrent benzodiazepine and opioid use Discuss any circumstances in the patient's life that may be affecting ongoing substance use Review/revise treatment plan Offer support and referrals if the patient is interested Send sample to lab for confirmation, especially if patient has not self-reported drug use
Positive for other non-prescribed or illicit drugs ¹¹	False-positive result Might indicate concurrent substance use	 Concurrent use of stimulants is not a contraindication to starting or continuing OAT and a positive result for stimulants should not be used as grounds to discontinue or reduce OAT, but may impact treatment plan Ask the patient if they have been prescribed medications by another clinician Review PharmaNet to determine if the patient is being prescribed medications by another clinician Review results with the patient Discuss any circumstances in the patient's life that may be affecting ongoing substance use Assess the patient for other substance use disorders Offer support and referrals if the patient is open to treatment Continue to monitor and follow-up. Send sample to lab for confirmation, especially if patient has not self-reported drug use
Lab reports sample as "substituted" or "adulterated"	Water has been added to sample Synthetic or another person's urine provided Substance (e.g., methadone, buprenorphine/naloxone) added to sample Other substance (e.g., chemicals) added to sample	 Ask the patient if they provided a substituted or adulterated sample Review results with patient A substituted or adulterated sample for a patient on takehome doses may be considered a positive UDT Discuss any circumstances in the patient's life that may be affecting ongoing substance use Discuss the rationale for ordering UDT, and re-establish expectations regarding unexpected results Repeat UDT if the results will change clinical management, otherwise wait until the next scheduled UDT Review/revise treatment plan Consider a return to daily witnessed ingestion from takehome doses

Appendix 2: Billing for Urine Drug Testing

Clinicians are compensated through MSP (fee code: P15039) for performing and interpreting point-of-care UDT as part of OAT management up to a maximum of 26 UDTs per patient per year.

Note: Fee code 15040 should be used for patients who are not enrolled in OAT.

Appendix 3: Timelines for Detection of Substances

Table 9: Timelines for detection of substances in immunoassay urine drug testing^k

Substance	Length of Time Detectable
Alcohol	6–8 hrs
Amphetamines	2–5 days ^{38,47}
Benzodiazepines	Days to weeks ¹
Short-acting	1–2 days ¹
Intermediate-acting	1–5 days ¹
Long-acting	≤30 days (regular use)¹
Cocaine	≤1 day¹
Benzoylecgonine (cocaine metabolite)	≤4 days³º
Opioids	
Morphine or codeine	2–5 days ⁴⁸
Heroin metabolite (6-MAM)	<1 day
Fentanyl—short-term use	≤3 days¹
Fentanyl—chronic use ^l	Up to 4 weeks ¹⁸
Hydromorphone	≤3 days¹
Buprenorphine	≤7 days¹
Methadone	≤3 days¹
EDDP (metabolite) ^m	≤6 days¹
ТНС	
Single use	1–3 days ³⁸
Chronic Use	≤30 days¹

^k Substances are present in urine from within minutes of use to several days after. Detection times for substances may vary depending on the specific substance; quantity ingested; amount of substance-free urine in the bladder at the start of substance use; the patient's hepatic, cardiac, and renal function; and state of hydration. Substances that are smoked or injected can be detected in urine almost immediately, while substances taken orally will not be detected in urine for several hours.⁴⁵

¹ Fentanyl persists in urine for up to 4 weeks due to its lipophilic properties, not due to its duration of action (i.e., fentanyl is not a long-acting opioid).

^m Clinical experience suggests that EDDP may be detected in urine for longer than 5 days, in the context of long-term use at high doses.

Appendix 4: Example Urine Drug Testing Report

The following UDT report is provided as an exampleⁿ. Reports from different laboratories may include different information. If clinicians have any questions or concerns regarding a UDT report, they should contact the laboratory for more information.



[&]quot; The BCCSU acknowledges, with gratitude, LifeLabs for providing this example UDT report.

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