Appropriate Use of Drug Testing in Clinical Addiction Medicine

Expert Panel Members (in alphabetical order)
Louis Baxter, Sr., MD, DFASAM
Lawrence Brown, MD, MPH, DFASAM
Matthew Hurford, MD, *Expert Panel Moderator*
William Jacobs, MD
Kurt Kleinschmidt, MD
Marla Kushner, DO, DFASAM
Lewis Nelson, MD
Michael Sprintz, DO, FASAM
Mishka Terplan, MD, MPH, FASAM
Elizabeth Warner, MD
Timothy Wiegand, MD, FACMT, FAACT

ASAM Quality Improvement Council
(in alphabetical order)
John Femino, MD, DFASAM
Kenneth Freedman, MD, MS, MBA, DFASAM
Barbara Herbert, MD, DFASAM
Margaret Jarvis, MD, DFASAM, *Chair*
Margaret Kotz, DO, DFASAM
David Pating, MD, FASAM
Sandrine Pirard, MD, PhD, MPH, FAPA, FASAM
Robert Roose, MD, MPH, FASAM
Brendan McEntee, *ASAM Staff*
Penny Mills, MBA, ASAM, *Executive Vice President*
Taleen Safarian, *ASAM Staff*

Special External Reviewer
Michael Miller, MD, DFASAM, FAPA

IRETA Team Members (in alphabetical order)
Peter Cohen, MD, *Medical Advisor*
Leila Giles, BS
Matthew Hurford, MD, *Expert Panel Moderator*
Piper Lincoln, MS
Dawn Lindsay, PhD
Peter Luongo, PhD
Jessica Williams, MPH

Disclosure information for the **ASAM Expert Panel Members and Quality Improvement Council** is available in **Appendix 6**.

INTRODUCTION

Purpose

The purpose of the *Appropriate Use of Drug Testing in Clinical Addiction Medicine* is to provide guidance about the effective use of drug testing in the identification, diagnosis, treatment, and promotion of recovery for patients with, or at risk for, addiction. This document draws on existing empirical evidence and clinical judgment on drug testing with the goal of improving the quality of care that people with addiction receive.

By focusing on the identification, diagnosis, treatment, and promotion of recovery for patients with, or at risk of, addiction, the appropriateness document:

- Identifies current clinical practice and disagreement regarding the use of drug testing.
- Utilizes the Research and Development/University of California Los Angeles (RAND/UCLA) Appropriateness Method, which combines existing empirical evidence and clinical expertise to develop recommendations for appropriate practice.
- Compiles recommendations in a comprehensive document for use by a variety of providers who utilize drug testing.

Background

Drug testing uses a biological sample to detect the presence or absence of a specific drug (or drugs) as well as drug metabolites within a specific window of time. No universal standard exists today in clinical drug testing for addiction identification, diagnosis, treatment, medication monitoring, or recovery.

The American Society of Addiction Medicine (ASAM) recognizes that the absence of guidance creates a vacuum. Even in the context of limited research about how to approach a given clinical practice, providers and payers make decisions about what kind of care patients should and do receive. This appropriateness document is intended to guide provider decisions about drug testing to improve the quality of care that patients with addiction receive.

It is ASAM policy that the elements of drug testing (eg, matrix, drug panel, testing technology) be determined by the provider based on patient-specific needs, not by arbitrary limits from insurance providers [1]. However, most physicians and other providers employing drug testing in addiction care have operated without authoritative guidance about how this therapeutic tool should be utilized effectively in treatment.

ASAM has produced 2 key documents related to drug testing: ''Public Policy Statement on Drug Testing as a

• Adopted by the ASAM Board of Directors April 5, 2017
Endorsed by the American College of Medical Toxicology.

Component of Addiction Treatment and Monitoring Programs and in other Clinical Settings'' and ''Drug Testing: A White Paper of the American Society of Addiction Medicine'' [1,2]. Neither document provides specific guidance and neither was developed using a rigorous methodology to develop practice recommendations.

In its 2010 policy statement, ASAM recognized drug testing as part of medical care for people being treated for addiction. The Statement expressed ASAM policy that drug testing should not face undue restrictions; decisions about the types and frequency of testing should be made by the ordering physician; and arbitrary limits on reimbursement by payers interfere with the physician's judgment and violate federal parity laws. The Statement provided a brief review of drug testing purposes, practices, and procedures that are recommended by ASAM.

The White Paper provided extensive background regarding the science and current practices of drug testing in various contexts, as well as broad suggestions for ways to improve drug testing in clinical practice. However, the White Paper acknowledged that more specific clinical guidance was needed and would be forthcoming from ASAM.

In the White Paper, ASAM advocates for the use of ''smarter'' drug testing as follows:

> Smarter drug testing means the increased use of random testing rather than the more common scheduled testing, and it means testing not only urine but also other matrices such as blood, oral fluid (saliva), hair, nails, sweat and breath when those matrices match the intended assessment process. In addition, smarter testing means testing based upon clinical indication for a broad and rotating panel of drugs rather than only testing for the traditional five-drug panel that was designed not by practicing physicians or researchers, but by the federal government for government-mandated testing such as that required of commercial drivers. Smarter testing means improved sample collection and detection technologies to decrease sample adulteration and substitution. Designing appropriate steps to respond to the efforts of individuals trying to subvert the testing process must be considered when evaluating the costs/benefit ratio of different testing matrices, recognizing that such countermeasures may have a dramatic impact on the usefulness of testing. Smarter drug testing means careful consideration of the financial costs of testing in relationship to the value and in many cases, medical necessity, of the test results. It means considering the advantages and limitations of the many testing technologies available today. [2]

This appropriateness document is designed to guide providers toward ''smarter'' drug testing.

Addiction treatment is increasingly delivered in primary care offices, with the proliferation of addiction medications such as buprenorphine and naltrexone. Drug-testing technology using matrices such as oral fluid (saliva), sweat, and hair is becoming increasingly sophisticated. Although urine is still by far the most common matrix, an evidence base is building for alternatives. And finally, the availability of synthetic drugs (some designed specifically to evade detection by drug testing) has grown dramatically and will continue to do so. According to ASAM's White Paper, the dramatic proliferation of potentially addictive drugs is one of the most challenging problems facing drug testing today [2]. Consistent with the ''smarter'' drug testing paradigm, the ASAM White Paper states, ''The most important challenge in drug testing today is not the identification of every drug we are technologically capable of detecting, but to do medically necessary and accurate testing for those drugs that are most likely to impact clinical outcomes.''

Cost Considerations

This document is designed to convey statements about drug testing as part of appropriate clinical care. It is not an analysis of the cost benefits of drug testing using various technologies or under various circumstances. However, ASAM is acutely aware that this document will be released in a context where a lack of clarity about the appropriate use of drug testing has led not only to inconsistent clinical practice, but also unethical and/or fraudulent activities.

The inappropriate use of drug testing can have extraordinary costs to third-party payers, taxpayers, and at times the patients who are receiving care. Though non-monetary, this has also cost the addiction treatment field because of loss of credibility. Examples of inappropriate and often-costly drug-testing practices are (1) the routine use of large, arbitrary test panels, (2) unnecessarily frequent drug testing without consideration for the drug's window of detection, and (3) the confirmation and quantification of all presumptive positive and negative test results [3,4].

It is ASAM's position that these and other inappropriate drug-testing practices are harmful not only because they waste valuable resources but because they do not fit the standards of appropriate clinical care. Providers have an obligation to ensure the highest possible quality of treatment for all patients, which includes the appropriate use of clinical drug testing. One of the purposes of this document is to clarify appropriate clinical use of drug testing and, in so doing, shine a light on drug-testing practices that are clearly outside of these boundaries. The delineation of appropriate treatment practices will confer multiple benefits; most importantly, it will improve patient care. At the same time, it will reduce waste and fraud.

How to Use This Document

Unlike clinical guidelines that typically focus on either more generalized or disease-specific recommendations, this appropriateness document determines when, where, and how often a drug test should be performed for the identification, diagnosis, treatment, and recovery of patients with, or at risk for, addiction.

Providers

This document contains practical information to guide the appropriate use of drug testing to help identify, diagnose, treat, and support recovery for patients with or at risk of addiction. Providers are encouraged to utilize this appropriateness document to improve their quality of care, recognizing that it will be necessary to seek supplemental information when questions arise that this document does not comprehensively address. For example, providers seeking specific guidance for interpreting drug test results should consider

consulting with a laboratory or a physician with Medical Review Officer (MRO) certification.

Payers

The primary audience for this document are providers who utilize drug testing in clinical settings. It is not designed as a template for payer policies. For example, it would be inappropriate to translate the statement that ''during the initial phase of treatment, drug testing should be at least weekly'' into a payer policy that will not reimburse drug tests that are more frequent than weekly.

Administrators

Healthcare administrators in residential, outpatient, and other settings should reference this document as a guide for appropriate practice related to drug testing. This document may inform policy decisions related to establishing or improving a drug-testing program in a variety of clinical settings.

Scope of Project

This document focuses on clinical drug testing for identification, diagnosis, treatment, and recovery of patients with, or at risk for, addiction. ASAM recognizes that drug testing is used in other contexts (eg, criminal justice, workplace, and pain management settings). ASAM's intent with this document, however, is to focus primarily on patients in addiction treatment and recovery, where drug testing is used to assess the patient for indicators of a substance use disorder (SUD), monitor the effectiveness of the treatment plan, and support recovery, and to also focus on selected special populations at risk for addiction. Although ASAM acknowledges that these recommendations may be applied to other settings where drug testing is utilized, note that the materials reviewed and methodology used were restricted to the populations and settings described.

Included and Excluded Settings

Inasmuch as the scope of the project includes the recognition of addiction, which often occurs in general healthcare settings, these settings are included briefly in this context. This document excludes recommendations for federally mandated workplace forensic testing, which are regulated by Substance Abuse and Mental Health Services Administration (SAMHSA). Drug testing in the contexts of criminal justice and pain management is also outside the scope of this document.

Types of Tests

This document will address considerations involved in the timing and selection of presumptive and definitive drug testing. Also, while urine drug testing (UDT) is the most common type of test utilized in the identification, diagnosis, treatment, and monitoring of patients with addiction, ASAM recognizes that drug test technology utilizing biological matrices such as oral fluid, hair, and sweat is becoming increasingly advanced and widespread.

Settings

This document includes recommendations about the frequency and duration of drug testing according to ASAM levels of care (eg, Outpatient and Residential) and includes a section on considerations for Opioid Treatment Services (OTS), including Opioid Treatment Programs (OTP) as well as Office-Based Opioid Treatment (OBOT). Also, while not an ASAM level of care, the document also includes recommendations for patients in recovery residences. In cases where no specific guidance was recommended for a particular level of care, the reader is directed back to the general principles section regarding appropriate clinical practice.

Special Populations

This document includes considerations for the following special populations: adolescents, pregnant women, people in recovery, and health and other professionals. For adolescents, the focus is in general healthcare settings and not in addiction treatment settings because there are unique considerations for drug testing adolescents in general healthcare settings. For pregnant women, the focus is also primarily in general healthcare settings for pregnant and postpartum women.

Intended Audience

This appropriateness document is intended for addiction specialists and for all providers utilizing drug testing in the context of the identification, diagnosis, treatment, and monitoring of patients with, or at risk for, addiction. This document will also be useful for physicians and other providers concerned about the possibility of addiction in their patient population.

Qualifying Statement

This document is intended to aid providers in their clinical decision-making and patient management. The document strives to identify and define clinical decision-making junctures that meet the needs of most patients in most circumstances. Recommendations in this document are not intended to substitute for independent clinical judgment based on the particular facts and circumstances presented by individual patients. Clinical decision-making should involve consideration of the quality and availability of expertise and services in the community wherein care is provided. In circumstances in which the document is being used as the basis for regulatory or payer decisions, improvement in quality of care should be the goal. Because lack of patient understanding and adherence may adversely affect outcomes, providers should make every effort to promote the patient's understanding of, and adherence to, prescribed and recommended pharmacological and psychosocial treatments and any associated testing. Patients should be informed of the risks, benefits, and alternatives to a particular treatment or test, and should be an active party to shared decision-making whenever feasible. Recommendations in this document do not supersede any federal or state regulation.

Terminology and Key Terms

Below are brief definitions of select key terms and explanations of how they are used in this document. For example, the term ''provider'' is used throughout this document to refer to any individual or organization who may utilize clinical drug testing for identification, diagnosis, treatment, and recovery of patients with, or at risk for, addiction.

This includes addiction treatment clinicians, addiction treatment programs, drug treatment programs and primary or general healthcare physicians. Please refer *Appendix 2: Glossary and Terms* to clarify the use of other specific terms. *Appendix 1: Abbreviations and Acronyms* provides further clarification.

Analyte: The component of a biological sample that is identified and measured. In drug testing, both parent drugs and the products of drug metabolism are targeted. Their presence indicates exposure to a substance or family of substances.

Definitive testing: In contrast to presumptive testing, testing performed using a method with high sensitivity and specificity that is able to identify specific drugs, their metabolites, and/or drug quantities. Definitive testing is likely to take place in a laboratory and each individual test can be expensive. Gas or liquid chromatography combined with mass spectrometry is the gold standard method in definitive drug testing.

Expected test results: In the context of addiction treatment that includes medication (eg, buprenorphine) an expected test result is positive for prescribed medication and negative for other addictive substances.

Matrix (plural matrices): The biological material used for analysis in a drug test. Examples include blood, urine, oral fluid (spit/saliva), hair, nails, sweat, and breath.

Negative test result: The result reported by a test that fails to detect the presence of a target substance in a sample. This can indicate either a complete lack of the drug or drug metabolite or a level too low to be detected by the test. In this document, a ''negative test result'' refers to a test result showing no use of non-prescribed addictive substances. However, in the context of addiction treatment that includes medication, the terms positive and negative have been replaced with ''unexpected'' and ''expected.''

Patient: Anyone who receives care for an addiction in a specialty addiction treatment center or other healthcare setting.

Point of collection test/point of care test (POCT): A drug test performed at the site where the sample is collected using either an instrumented or non-instrumented commercial device (eg animmunoassay test strip or dipstick or a machine-based immunoanalyzer with optical reader).

Positive test result: The result reported by a test that detects the presence of a target substance in a sample. In this document, a ''positive test result'' refers to a test result showing the use of non-prescribed addictive substances. However, in the context of addiction treatment that includes medication, the terms positive and negative have been replaced with ''unexpected'' and ''expected.''

Presumptive testing: In contrast to definitive testing, testing performed using a method with lower sensitivity and/or specificity, which establishes preliminary evidence regarding the absence or presence of drugs or metabolites in a sample.

Provider: Used throughout the appropriateness document, this term is intentionally broad. It encompasses anyone (an individual or organization) who participates in providing care to patients with addiction, including staff at specialty addiction treatment centers or other healthcare settings that provide addiction treatment.

Unexpected test results: In the context of addiction treatment that includes medication (eg, buprenorphine), an unexpected test result could be (a) negative for prescribed medication, (b) positive for other addictive substance, or (c) both.

Window of detection: The range of time that a substance can be detected in a sample. It refers both to the time to detection (time to be absorbed and distributed to sample material) and time to clearance (time to be metabolized/eliminated/excreted). Each matrix and analyte has a different window of detection, ranging from minutes to months.

PART 1: PRINCIPLES OF DRUG TESTING IN ADDICTION TREATMENT

Clinical Value of Drug Testing

Principles of Biological Detection of Substance Use

Drug tests are tools that provide information about an individual's substance use. Any practitioner involved with the care of patients with addiction should understand what information drug testing can and cannot convey. Drug testing has been referred to as ''the technology of addiction treatment'' [5], but like any technology, its value depends on whether it is utilized correctly. Drug testing is an effective technology when the right test is selected for the right person at the right time.

Drug tests are designed to detect whether a substance has been used within a particular window of time. The test involves collecting a biological sample, also called a specimen, which is tested for the presence or absence of a specific substance or substances. While it can be a powerful tool, a drug test is designed to answer a rather narrow question: is substance X detected in sample Y? The answer is limited to the substance or substances that are targeted by the test, the individual sample which was tested (representing the patient's biological state at the time of collection), and the detection method used by the test. If the answer is yes, the result is labeled ''positive'' and if no, the result is labeled ''negative.''

A positive drug test result indicates that the patient providing the sample had a detectable amount of the targeted substance(s) in his or her system when the sample was collected. The timing of sample collection is important. Substances have a constant rate of elimination from the body, but the rate varies across biological sample type, or matrix. Some drug tests may be better or worse at detecting a substance in a particular matrix, which means it is important for a provider to understand the test's sensitivity and specificity to gauge the possibility of false negatives or positives. But even the most effective test under ideal circumstances can only measure the presence of a substance within the window of time it remains detectable in the body, also called the window of detection.

A positive drug test is not sufficient evidence for a diagnosis of an SUD. It does not explain whether a patient's symptoms are caused by the presence of a substance. In most cases, a drug test does not measure impairment and in most cases a drug test does not measure patterns of use over time.

It is important not to over-interpret a negative test result. A negative result does not mean that a patient has not used substances; it merely means that the patient has not used the substance(s) targeted by the test within the window of detection or used an amount less than the test is capable of detecting. Not only does an accurate negative test result not rule out substance use, it also does not rule out SUD, which can be present without recent substance use.

Drug Testing and Self-Reported Substance Use

If the appropriate interpretation of a drug test result is so narrow, why test at all? Drug testing provides another source of information to complement self-report, collateral report, and provider assessment. Having an additional, alternative means of assessing a patient's recent substance use is important to treatment planning and ongoing treatment adjustment.

Because individuals with addiction pathologically pursue reward and/or relief by substance use, some patients will give inaccurate or incomplete histories. Therefore, it behooves providers to verify self-report with biological testing. In contrast to a patient's self-report, biological test results are considered ''objective'' in that they are not subject to limitations caused by memory, social acceptability, or missing information. For example, a patient might not accurately remember his or her substance use history, may try to minimize or overstate his or her past use, and may not be aware of the composition of the substances he or she has consumed, especially as synthetic drugs increase in prevalence.

Patients facing potential negative consequences if substance use is detected, such as increased sanctions or legal action, may be less likely to self-report accurately. For example, a multisite trial of patients with prescription drug use disorders concluded that ''self-reports of substance use are most likely to be valid when participants believe that they will not suffer negative consequences'' as a result of their report [6]. In situations where substance use may result in these consequences, the combination of self-reported use and drug test results may lead to a more accurate picture of recent substance use.

Due to its inherent limitations, drug testing should not be relied upon as the sole measure of a patient's substance use. All drug testing should be accompanied by a discussion with the patient about his or her substance use. A patient's self-report provides additional clinically relevant information that drug testing cannot. In the event that a patient's self-reported substance use differs from the results of a drug test, the provider should use the discrepancy as a springboard for therapeutic discussions.

Drug Testing and Patient Outcomes

The decision to use any tool in health care should be grounded in the principles of improved patient care and outcomes. Although evidence is limited that the use of drug testing in addiction treatment improves patient outcomes, the expert panel cited extensive clinical experience supporting the use of drug testing to improve patient outcomes.

Moreover, two 2014 studies illuminated the currently unrealized role of drug tests in addiction treatment. Blum et al [7] looked at whether drug test results are useful indicators of patients' progress in treatment and concluded that testing for both prescribed addiction medications and illicit drug use can improve a provider's ability to determine the effectiveness of the current treatment approach. However, a systematic review of patient charts concluded that drug testing does not appear to change the way patients are managed by their treatment providers, although it was unclear whether these results were due to provider behavior or actual lack of effect of drug testing on management or outcome of patients in addiction treatment [8]. Together, these results suggest that drug testing has the potential to improve patient outcomes if used correctly and consistently to monitor and adjust treatment plans. Drug testing should be used widely in addiction treatment settings and its use should be integrated into the process of making treatment decisions.

Drug Testing and Evidence-Based Therapy

Although drug testing in addiction treatment settings is common, providers have heretofore received very limited guidance on how drug testing should be integrated with evidence-based addiction treatment.

The most extensively researched behavioral therapy used in conjunction with drug testing is contingency management. Contingency management can involve tying behavioral incentives to the result of a drug test and has been shown to be an effective approach to addiction treatment [9]. It is clear that the contingency management model fits well with drug testing [10] and the expert panel recommends combining the 2. When using drug testing as part of contingency management, providers should also seek self-reported information from patients about substance use.

Clinical Use of Drug Testing

Therapeutic Tool

Drug testing should be used as a tool for supporting recovery rather than exacting punishment. Every effort should be made to persuade patients that drug testing is a therapeutic, rather than punitive, component of treatment. This process may require time and multiple conversations. If drug testing is used in such a way that it creates an ''us versus them'' mentality, it is at odds with the therapeutic alliance. In fact, drug testing can be thought of as a tool to improve the therapeutic alliance in that it transfers the role of detector from the provider to the test.

Using drug testing as a therapeutic tool means addressing test results as a part of therapy. Drug testing should be used to explore denial, motivation, and actual substance use behaviors. Test results that do not align with a patient's self-report should generate therapeutic discussion with the patient. If a patient refuses to undergo a drug test, that refusal should be an area of focus for the patient's treatment plan. Some of the value of using drug test results as a topic of therapeutic discussion has been demonstrated by 2 qualitative studies that showed favorable responses to drug test discussions among some patients in treatment [11,12].

In addition to measuring treatment efficacy, drug testing may also serve as a source of motivation and reinforcement for abstinence [13]. Providers should use negative test results as a source of encouragement.

Assessment

Drug testing should be a key component of assessment for SUD and should be used to assist in treatment planning.

Test results should always be combined with patient history, psychosocial assessment, and a physical examination during an assessment. According to ASAM's *Principles of Addiction Treatment*, ''Laboratory testing in the clinical setting is intended to guide diagnosis and treatment planning...the provider must combine the findings from the history and physical examination with that of the laboratory testing for accurate interpretation and management'' [14]. The results of the medical and psychosocial assessment generate valuable information (eg, types of substances used) that should inform the provider's decision about drug testing (see *Choosing a Test*, p. 7).

It is recommended that treatment providers include drug testing at intake. Drug test results at intake have been determined to be a useful predictor of treatment outcomes [15,16]. Patients who submit a positive drug test at intake may benefit from different approaches to treatment than patients who submit a negative test [17].

Drug testing as part of an initial assessment provides additional benefits. For example, test results can help illuminate any links between substance use and psychiatric or medical symptoms a patient is experiencing. For a patient presenting with altered mental status, a negative drug test result may support differentiation between intoxication and/or presence of an underlying psychiatric and/or medical condition that should be addressed in treatment planning. Drug testing can also verify a patient's substance use history or demonstrate a discrepancy between self-reported use and test results. Finally, drug tests may be used to help determine optimal placement in a level of care using *The ASAM Criteria*, particularly in assessing Dimension 1 (Acute Intoxication and/or Withdrawal Potential), Dimension 4 (Readiness to Change), and Dimension 5 (Relapse, Continued Use, or Continued Problem Potential).

Drug testing may also assist providers in re-assessing patient needs while the patient is receiving treatment. For example, it is appropriate to conduct drug tests when patients display a change in clinical status, such as apparent sedation/ataxia/agitation or other behavior change that might indicate recent drug exposure.

Monitoring

Drug testing should be used to monitor the effectiveness of a patient's treatment plan. If a goal of treatment is to reduce or eliminate substance use, drug testing can be thought of as an ongoing measure of treatment performance. A pattern of tests that are positive for expected prescribed medications and negative for other unexpected substance use, in combination with other indicators, suggest a patient's treatment plan is effective. In contrasts, tests that are positive for unexpected substance use (and/or negative for expected prescribed substances) suggest that the treatment plan should be adjusted. If a provider is making treatment adjustments, test results can be helpful in determining optimal placement in a level of care. Providers should note that immediate cessation of substance use early in treatment may not be a realistic treatment goal. The section on *Responding to Test Results* provides more detail on the appropriate response to test results.

Drug testing is only one measure of one treatment goal and it should not be the only method of detecting substance use or monitoring treatment outcomes; results should be interpreted in the context of collateral and self-report and other indicators.

Summary of Recommendations

Clinical Value of Drug Testing

Principles of Biological Detection of Substance Use

- Providers should understand that drug tests are designed to measure whether a substance has been used within a particular window of time.

Drug Testing and Self-Reported Substance Use

- Drug testing should be used in combination with a patient's self-reported information about substance use.
- Drug testing is an important supplement to self-report because patients may be unaware of the composition of the substances(s) they have used.
- Drug testing is particularly appropriate for patients facing negative consequences if substance use is detected, who are therefore less likely to provide accurate self-reported substance use information.
- Discrepancy between self-report and drug tests results can be a point of engagement for the provider.

Drug Testing and Patient Outcomes

- Because evidence suggests that drug testing assists with monitoring adherence and abstinence in treatment and can improve patient outcomes, drug testing should be used widely in addiction treatment settings.

Drug Testing and Evidence-Based Therapy

- Contingency management is most extensively researched behavioral therapy used in conjunction with drug testing. When utilizing contingency management therapy to encourage abstinence, providers should consider incorporating drug testing.

Clinical Use of Drug Testing

Therapeutic Tool

- Drug testing is recommended as a therapeutic tool as part of evidence-based addiction treatment.
- Providers should utilize drug testing to explore denial, motivation, and actual substance use behaviors with patients.
- If drug-testing results contradict self-reports of use, therapeutic discussions should take place.
- Providers should present drug testing to patients as a way of providing motivation and reinforcement for abstinence.
- Providers should educate patients as to the therapeutic purpose of drug testing. To the extent possible, persuade patients that drug testing is therapeutic rather than punitive to avoid an ''us versus them'' mentality.

- If a patient refuses a drug test, the refusal itself should be an area of focus in the patient's treatment plan.

Assessment

- Treatment providers should include drug testing at intake to assist in a patient's initial assessment and treatment planning.
- Results of a medical and psychosocial assessment should guide the process of choosing the type of drug test and matrix to use for assessment purposes.
- Drug test results should not be used as the sole determinant in assessment for SUD. They should always be combined with patient history, psychosocial assessment, and a physical examination.
- Drug testing may be used to help determine optimal placement in a level of care.
- Drug testing can serve as an objective means of verifying a patient's substance use history.
- Drug testing can demonstrate a discrepancy between a patient's self-report of substance use and the substances detected in testing.
- For a patient presenting with altered mental status, a negative drug test result may support differentiation between intoxication and/or presence of an underlying psychiatric and/or medical condition that should be addressed in treatment planning.
- Drug testing can be helpful if a provider is required to document a patient's current substance use.

Monitoring

- Drug testing should be used to monitor recent substance use in all addiction treatment settings.
- Drug testing should be only one of several methods of detecting substance use or monitoring treatment; test results should be interpreted in the context of collateral and self-report and other indicators.

PART 2: PROCESS OF DRUG TESTING IN ADDICTION TREATMENT

Choosing a Test

When choosing a test, providers will make decisions about the following factors:

- The information they wish to gain from testing
- The substance or substance(s) targeted
- Matrix sample collected
- The reliability/usefulness of the result
- Cost

"Smarter" drug testing means that providers actively address these factors in the process of choosing a drug test, rather than defaulting to perceived organizational or industry norms [2].

Clinical Necessity and Value

Tests should be chosen based on the information they are expected to reveal. All tests are designed to answer certain questions and all tests have limitations. Providers should first determine the purpose of the test—what question it needs to answer—and choose the test best able to provide that answer.

Test selection should be individualized based on a patient's clinical needs and their self-reported substance use (see *Drug testing and self-reported substance use*, p. 5). When possible, it is recommended that providers conduct a drug test after obtaining a patient's self-report. Admitted use and knowledge of preferred substances can guide the provider's process of choosing a drug test.

Individualization of testing does not mean that every patient will get a different test, but that he or she *can* if the circumstances warrant it. The expert panel concluded that the use of a routine test panel is generally acceptable practice. However, this should not block the ability of providers to use alternative matrices and tests, individualized to the patient's needs.

Identifying Substance(s) of Interest

The substances targeted in a patient's routine drug test should be adjusted based on the patient's drug of choice, prescribed medications, and drugs commonly used in the patient's geographic location and peer group.

It is generally useful for addiction treatment programs/providers to establish a routine panel based on the most commonly used substances in their treatment population with consideration for regional patterns of use.

Substance use trends vary considerably by region. Providers should be aware of which drugs tend to be prevalent in their region and attentive to new substance use trends and emerging drugs (many of them synthetic) that may become available to their patient population for the first time. Note that an important area for future research is when and how to identify novel synthetic drugs, such as cannabinoids and cathinones, for various patient populations.

Because emerging drugs will continue to proliferate, providers will always be playing catch-up when trying to detect substance use. Test panels should be updated regularly to address local substance use trends. A testing laboratory can be a valuable resource regarding information related to changes in substance use at the local level. Medical toxicologists can also provide information on regional variations in drug use or on local trends.

Providers should not rely on a 5-panel screen known as the NIDA-5 (or SAMHSA-5) as a routine drug panel. This panel is intended for workplace drug testing; the substances targeted and their associated cutoff levels are not appropriate for the clinical care of patients with addiction.

Providers should be aware that some drugs share common metabolites. For example, codeine and heroin are both metabolized to morphine. The detection of morphine indicates that an individual has been exposed to one of these opioids, but that result by itself cannot determine if the drug that was consumed was morphine, codeine or heroin. Detecting which opioid requires a test for either a parent drug (eg, heroin) or an analyte specific to that substance (eg, 6-monoacetylmorphine [6-MAM]).

Matrix Advantages and Disadvantages

Urine, blood, exhaled breath, oral fluid (saliva), sweat, and hair are some biological samples (known as matrices) that

are used in drug testing. As defined by ASAM, ''smarter'' drug testing means using the matrix best able to answer the clinical question at hand. Although urine is the best established matrix in addiction treatment settings, other matrices provide different levels of sensitivity and specificity over different windows of detection. For example, heroin is rapidly converted to 6-MAM and subsequently to morphine. Heroin or 6-MAM must be detected to specifically confirm heroin rather than general opiate use. While 6-MAM remains present at detectable concentrations in oral fluid for longer than urine, the subsequent metabolic products remain detectable in urine for longer than oral fluid.

A main consideration in matrix choice is also its varying susceptibility to sample tampering. Rotating matrices can reduce the potential for tampering with samples. However, providers should understand the advantages and disadvantages of each matrix before considering such strategies.

The use of an alternative matrix is also appropriate if a particular sample type cannot be collected (eg, patients on dialysis, who are bald or have dry mouth or shy bladder) or when a sample collection technique is too invasive (such as direct observed urine testing for a patient with sexual trauma). If a given sample is likely to be prone to confounds, providers should choose an alternative matrix. For example, heavily chemically treated hair is not appropriate for drug testing.

Clinical considerations that pertain to matrices are covered more fully in *Part 4: Biological Matrices.*

Presumptive and Definitive Tests

Drug testing can be divided into 2 classes: presumptive and definitive. Presumptive tests generally have lower sensitivity and/or specificity compared to definitive tests.

The primary benefit of presumptive testing methods is a much faster turnaround time to receive results, which allows for a more rapid therapeutic response that can more meaningfully link substance use and behavior. Therefore, presumptive tests should be used when it is a priority to have more immediate (although potentially less accurate) results. If a patient disputes the results of a presumptive test, the test should be confirmed using a definitive method. If a patient confirms that he or she used a substance detected by a presumptive test, it is not necessary to perform a definitive test to confirm the result. Presumptive testing should be a routine part of initial and ongoing assessment of a patient's use of substances.

Definitive testing should be used whenever a patient disputes the findings of a presumptive test, when a provider wants to detect a specific substance not adequately identified by presumptive methods (eg, heroin rather than opiates) or when the results will inform a decision with major clinical or non-clinical implications for the patient (eg, treatment transition, changes in medication therapies, changes in legal status).

If a provider expects the result of a presumptive test to be positive (eg, a patient reports recent use), and information regarding specific substance and/or quantity is desired, it may be appropriate to skip the presumptive test in favor of a definitive test. When ordering a definitive test, providers should advise the testing laboratory of suspected or expected substance(s) in the specimen. Providers should be aware that many laboratories do not automatically perform definitive testing on positive presumptive results (known as ''reflex testing'') and may require an additional order for such testing to occur.

Use of Specific Terms

Presumptive and definitive tests are often referred to using terminology, which actually describe differences in analytical method (eg, immunoassay vs. chromatography/mass-spectrometry), test setting (eg, the point of care or in a laboratory) or underlying purpose (eg, screening or confirmation). While some of these differences may have fallen neatly within the category of presumptive and definitive testing in the past, advances in technology have made these generalizations increasingly inaccurate. Table 1 illustrates a number of terms often used interchangeably to refer to presumptive and definitive tests.

In this document, the terms ''presumptive'' and ''definitive'' are used, except when referring to a specific aspect of a test (eg, Point of Care Tests).

Immunoassay Versus Chromatography/Mass Spectrometry

For the most part, presumptive testing uses immunoassay technology and definitive testing uses a combination of various chromatography and mass spectrometry techniques. However, there are some immunoassays, which can be used as definitive tests (eg, Immunoassays for cocaine metabolites are quite specific).

Immunoassays use antibodies designed to bind with a specific drug (eg, methadone), metabolite (eg, 6-MAM) or class of compounds (eg, opiates, which detects morphine) in a sample. If no drug compounds are present in a sample, the antibodies will instead bind with a conjugate compound and register as a colored line in the test readout area. Immunoassays have varying degrees of sensitivity and specificity depending on the particular antibodies and the cutoff value used. A cutoff value is the amount of substance that needs to be detected in a sample for it to be considered positive. Test results are positive if there is enough drug or metabolite present in a sample to react with a predetermined threshold of antibodies in the assay.

TABLE 1. Terms Often Used Imprecisely to Refer to Presumptive and Definitive Tests

Presumptive	Definitive
Qualitative	Quantitative
Preliminary	Confirmatory
Immunoassay	Chromatography/mass-spectrometry
Point of care/in-office/lab-based	In-office/lab-based
Screen	Confirmation
Semi-quantitative/quasi-quantitative	Absolute level/creatinine-corrected
Simple (cup/strip/dipstick/cassette)	Complex
Class or category test	Specific drug identification

Reference 146.

Gas or liquid chromatography combined with mass spectrometry are the gold standard methods of drug testing. Chromatography is used to separate a specimen into its component parts and mass spectrometry to identify those parts. These methods are both highly sensitive and highly specific. This testing is likely to take place in a laboratory and each individual test can be expensive.

Screening Versus Confirmation

The terms ''screening'' and ''confirmation'' refer to the purpose of the test. A common practice in testing is to first screen samples using an inexpensive test to rule out likely negative samples and then confirm potential positive results using a highly specific test. Often, immunoassay methods are used to screen samples and positively screened samples are confirmed using a chromatography/mass-spectrometry method or an immunoassay using a lower cutoff value and/or one targeting specific substances within a class.

When using a cutoff, a negative result does not exclude the presence of a drug or metabolite in a sample, but reflects it was not a sufficient amount to cross the cutoff limit. Screening tests often use cutoffs chosen to minimize the incidence of false positives. This, consequently, increases the incidence of false negatives. Many laboratories and point of care tests (POCTs) use screening cutoff levels calibrated for workplace or law enforcement drug testing. These cutoffs may be set very high to identify individuals which use large amounts of a substance and minimizes false positives from accidental environmental exposure (eg, from second-hand marijuana smoke); therefore, they may not be appropriate for clinical use. Providers should know the cutoff concentration used for immunoassay when interpreting a presumptive or definitive test result of ''no drug present.''

Class or Category Test Versus Specific Substance Test

A drug ''screen'' can also refer to an immunoassay, which reacts to the presence of a class of drugs. The specific substance is then ''confirmed'' using a test method, which can identify a specific substance or metabolite. It is often only possible to test for specific substance using chromatography/mass-spectrometry, but immunoassays are also available that are highly targeted and specific to individual substances.

The degree of an immunoassay's specificity depends on the extent to which antibodies will bind specifically with a target compound while excluding structurally related compounds, also known as cross-reactivity. The less specific an immunoassay is for a single substance, the higher the cross-reactivity is for other substances. For example, standard opiate immunoassays target morphine-like molecules and best detect morphine and codeine. They show moderate cross-reactivity with the morphine-derived semi-synthetics hydrocodone and hydromorphone, and poor cross-reactivity with thebaine-derived semi-synthetics oxycodone and oxymorphone. Fentanyl, meperidine, methadone, and buprenorphine have negligible to no cross-reactivity with a standard opiate immunoassay. Semi-synthetic opioids less structurally similar to morphine and fully synthetic opioids are better detected with immunoassays that use different antibodies that are specific to these analytes.

Qualitative Versus Quantitative

A qualitative test is one that detects the presence or absence of a particular compound in a sample. A quantitative test is one that measures the quantity of a particular compound in a sample. Immunoassays are qualitative tests. Most chromatography/mass-spectrometry techniques are quantitative. Quantitative results are reported as the concentration within a sample. The concentrated amount should be used cautiously when interpreting the dose or timing of substance use because of individual differences in metabolism.

POCT Versus Laboratory

While definitive testing used to be the performed exclusively in the lab, the line is becoming increasingly blurry due to enhancements in the quality and availability of point of care testing (POCT). Although simple POCTs, such as urine dipstick technologies, are prone to lower accuracy and precision, newer POCT analyzers have significantly greater quality control and rival central laboratory analysis in terms of their sensitivity and specificity. For routine clinical use, POCT (including newer urine dipstick testing) is more efficient and economical and provides reliable results. For high stakes testing (eg, testing that will inform an irreversible clinical decision), formal laboratory analysis remains the ''gold standard'' testing methodology (Table 2).

Cost

Providers should always consider cost both to patients and insurers when choosing drug tests. Smarter drug testing means careful consideration of the financial costs of testing in

TABLE 2. Definitions of Sensitivity and Specificity

	Sensitivity	Specificity
Definition	The likelihood that a given test is able to detect the presence of a drug or metabolite that is actually in the specimen	The likelihood that a given test is able to identify the specific drug or metabolite of interest in the specimen and not to erroneously label other drugs or metabolites
Determined by	Ability to avoid false negatives, where the presence of a drug is missed in a positive sample	Ability to avoid false positives, when an analyte is misidentified as the target in a negative sample
Calculated by	Number of false negatives/number of positive samples	Number of false positives/Number of Negative samples
Utility	A negative result in a test with high sensitivity is useful for ruling out substance use, since positive samples are rarely missed	A positive result in a test with high specificity is useful for ruling in substance use, since negative samples are rarely mislabeled

Adapted from American Society of Addiction Medicine [2].

relationship to the value and in many cases, medical necessity, of the test results [2].

Responding to Test Results

According to the ASAM White Paper, ''All physicians (and others) involved in drug testing should determine the questions the test are intended to answer before the testing is administered and should have a plan for what to do with the results'' [2]. It is important for providers to attach a meaningful response to test results, both positive and negative, and deliver it as quickly as possible. Although negative and positive test results can provide valuable information about recent substance use, providers should be aware that a positive drug test does not diagnose a SUD and a negative test result does not rule out a SUD (see *Clinical Value of Drug Testing*, p. 4).

Drug testing should function as a therapeutic tool (see *Clinical Use of Drug Testing*, p. 5), so a provider's response to test results should not be confrontational. This approach can perpetuate an ''us versus them'' mentality that reduces the effectiveness of drug testing to support recovery.

Providers may also be compelled to make significant, sometimes irreversible, clinical decisions on the basis of drug test results. For example, a provider may consider whether a patient should be transferred to a higher level of care after multiple positive test results. Providers are encouraged to consider all relevant factors when making a significant clinical decision, rather than drug test results exclusively, keeping in mind that immediate abstinence may not be a realistic goal for patients in the early stages of treatment.

Providers should also be aware that all tests have some rate of false-positive and false-negative outcomes (Table 3). False positives occur when a negative sample is incorrectly labeled as positive. This can occur if the target analyte is present in the sample, but for reasons other than a patient knowingly consuming an addictive substance. Perhaps the most infamous example of false positives of this kind comes from consuming poppy seeds, which produce a detectable amount of morphine in the body. The amount produced, however, results in a much lower body tissue concentration of morphine than that resulting from typical recreational or medicinal opioid use. Samples can also become contaminated through handling collection containers after the use of alcohol-containing hygiene products or hand sanitizers. The use of a detection threshold, or cutoff limit, is meant to reduce false-positive results from unintentional, incidental contact with a substance by effectively decreasing the sensitivity of a test.

Of greater concern are false positives resulting from the misidentification of a similar substance for the target. The list of potential sources of false positives is too extensive to list here, but a few noted examples include; cough suppressants resulting in positive opioid results, ephedrine in cold medicine resulting in positive result for amphetamines, and antidepressants resulting in positive opioid results. Comprehensive reviews of sources of false positives have been published for UDT [18,19], but providers should be aware that new examples of false positives are continuously detected for various tests, and tests are continuously updated and refined to address these limitations. Providers without formal toxicology training can participate in available courses, and/or should collaborate with a medical toxicologist, a toxicologist from the testing laboratory, or a physician certified as an MRO. Providers could consider MRO training and/or certification through organizations including the American Association of MROs and/or the Medical Review Office Certification Council.

False negatives occur when a positive sample is incorrectly labeled as negative. Sometimes this is the result of the use of a cutoff limit. In this case, a negative result does not exclude the presence of a drug or metabolite, but reflects it was not a sufficient amount to cross the cutoff limit.

Unclear Test Results

When test results are unclear, providers should communicate with the testing laboratory to properly interpret them. It is important that the relationship between an addiction treatment provider and a testing laboratory be collaborative (see *Choosing a laboratory*, p. 14) to enable proper interpretation of test results. Providers may also consider consulting with a medical toxicologist or MRO for assistance in interpreting unclear test results. Sometimes test results are unclear because of tampering (dilution, substitution, or adulteration). When a provider suspects tampering may have occurred, he or she may have the option to retain the sample for additional testing (including specimen validity testing), use a different matrix, or change/add to the test panel. The original sample should not be discarded; instead, it should be retained to help investigate whether and how tampering occurred. Note that urine is the matrix most prone to sample tampering; see *Urine*, p. 17, for more detail on avoiding and responding to tampering with urine samples.

Presumptive Test Results

There are 2 possible outcomes to a presumptive test: positive and negative.

Positive presumptive test results should be referred to as ''presumptive positive'' results until confirmed by a definitive test, although it is not always necessary to perform a definitive test on a presumptive positive sample (see *Presumptive and definitive tests*, p. 12). An appropriate response to a

TABLE 3. Possible Test Outcomes

	Positive sample	Negative sample
Positive test result	True positive Test correctly identified the presence of target analyte.	False positive Test misidentified an analyte as target analyte.
Negative test result	False negative Test missed the presence of target analyte.	True negative Test correctly did not identify any target analyte.

presumptive positive test result includes speaking with the patient, discussing possible cross-reactivity related to medications or food, and ordering a definitive test if the patient's self-report is not consistent with the presumptive test result. Providers may also want to consult with their testing laboratory for assistance interpreting the presumptive positive result.

Presumptive tests are often called ''qualitative tests'' because they are designed to measure the presence or absence of the target drug/analyte, rather than the amount. Because presumptive tests use cutoff values and are designed to have high sensitivity and lower specificity, providers should use caution when interpreting and responding to presumptive test results.

Particularly in the case of presumptive tests, providers should remember that a negative test result does not rule out substance use (which could have occurred outside the window of detection, below the cutoff value or been excluded from the test panel) or SUD (which is a clinical diagnosis). If presumptive test results are negative, but the patient exhibits signs of use (eg, through signs of intoxication or withdrawal), it is appropriate to confirm using a definitive test with greater sensitivity. Providers may also want to expand the drug panel to include previously untargeted substances.

Definitive Test Results

The results of a definitive test can be taken as conclusive. In the event of a positive definitive test, providers should consider adjusting the patient's treatment plan. The patient may benefit from intensified treatment or the addition of an adjunctive treatment element.

Even if the result of a definitive test is quantitative, providers should use caution when using test results to draw conclusions about the amount or pattern of a patient's substance use. There are some tests and methods that are better at correlating the quantity of drug measured in a sample with amount used. For example, a blood or breath test for ethanol or hair test for the metabolite ethyl glucuronide (EtG) can indicate point-in-time or average-over-time alcohol use. The concentration of ethanol or EtG in urine, however, is dependent on additional factors such as hydration and metabolic health (see *Comparing Matrices*, p. 35). For questions about interpreting a positive test result, providers should consult with their testing laboratory.

In the event of a negative definitive test, providers should be mindful of the limitations of drug testing (see *Clinical Value of Drug Testing*, p. 4) and not over-interpret its significance. A patient whose definitive test results are negative may still have engaged in substance use (outside of the window of detection of the test) or have an SUD (which is a clinical diagnosis).

Test Scheduling

Test schedule is an area of interest for providers and payers. There is very little guidance about clinically appropriate test schedules, which has led to both an over- and under-utilization of drug testing, and generally, an approach to test scheduling that does not meet the standards of ''smarter'' testing.

Test Frequency

For patients in addiction treatment, frequency of testing should be dictated by patient acuity and level of care. For recommendations related to specific level of care, see *Part 5: Settings*.

There is no magic formula for determining the test frequency a patient should receive. The expert panel strongly disagreed with statements about specific numerical limitations on drug test frequency. For example, the panel agreed that the following statement is inappropriate: ''Drug testing should be scheduled no more than 24 times per year.''

In accordance with the principle of ''smarter'' drug testing, the provider's therapeutic questions should dictate the frequency of drug testing. In formulating questions, providers should be aware that there is currently insufficient evidence that more frequent testing leads to decreased substance use. Based on these questions, providers should look to the tests' detection capabilities and windows of detection to help determine the frequency of testing. (*See Appendix 4: Windows of Detection Table* for a chart describing matrices and windows of detection for various target analysis.)

As a general principle, drug testing should be scheduled more frequently at the beginning of treatment. The Expert Panel recommends that a patient in early recovery be tested at least weekly. As the patient becomes more stable in recovery, the frequency of drug testing should be decreased, but performed at least on a monthly basis. Individual consideration may be given for less frequent testing if a patient is in stable recovery.

If the patient returns to substance use after a period of abstinence, the provider should resume the early recovery testing schedule, possibly in conjunction with an adapted or intensified treatment plan.

Random Testing

Whatever the frequency, clinical consensus favors unannounced drug testing over scheduled drug testing and random testing schedules to fixed testing schedules [2,13,20]. A fixed schedule (eg, every Monday) offers patients increased opportunity to engage in sample tampering. Even if the frequency is within a test's normal window of detection (eg, a urine immunoassay screen for amphetamines every Monday and Thursday) it is possible for a patient to engage in substance use on Thursday night and not produce a positive result on Monday morning. Although not always possible to implement, a random testing schedule can eliminate such strategic workarounds by making patients unaware of when exactly they will be tested.

Providers should note that the way randomization is applied to scheduling in a clinical setting can make it more or less effective. The purest form of randomization is to have a set probability (eg, 15%) that a patient could be tested on any given day. This is akin to rolling a die every day and testing whenever a 6 appears. While this eliminates known safe periods, the length of time a patient may go between testing can be quite long.

To avoid unknown testing intervals, many addiction treatment providers randomly select a day from a fixed interval [21]. Once the day is selected, however, no testing

will occur until the start of the next interval, leaving the problem of known non-testing periods if the selected day occurs early within the interval (eg, Monday from a weekly interval). Instead, providers can randomly select the interval from a set of allowable days between testing (eg, 2, 3, . . . 6, 7 days). This limits both the maximum interval between tests and known non-testing periods.

Summary of Recommendations

Choosing a Test

Clinical Necessity and Value

- Before choosing the type of test and matrix, providers should determine the questions they are seeking to answer and familiarize themselves with the benefits and limitations of each test and matrix.
- Test selections should be individualized based on specific patients and clinical scenarios.
- Patients' self-reported substance use can help guide test selection.

Identifying Substance(s) of Interest

- Drug-testing panels should be based on the patient's drug of choice, prescribed medications, and drugs commonly used in the patient's geographic location and peer group.
- Addiction treatment programs/providers should establish a routine immunoassay panel.
- Providers should not rely on the NIDA 5 (also known as the SAMHSA 5) as a routine drug panel.
- Test panels should be regularly updated based on changes in local and national substance use trends. Providers should collaborate with the testing laboratory when determining the preferred test selections to obtain information about local and demographic trends in substance use.

Matrix Advantages and Disadvantages

- Providers should understand the advantages and disadvantages of each matrix before considering rotational strategies.
- If a particular specimen cannot be collected (eg, due to baldness, dry mouth, shy bladder), providers should consider collecting an alternative specimen.
- If a given sample is likely to be prone to confounds, providers should choose an alternative matrix. For example, heavily chemically treated hair is not appropriate for drug testing.

Presumptive and Definitive Tests

- Presumptive testing should be a routine part of initial and ongoing patient assessment.
- Presumptive testing should be used when it is a priority to have more immediate (although less accurate) results.
- Providers should know the cutoff threshold concentrations that their laboratory uses when interpreting a report of "no drug present."
- Federal cutoff threshold concentrations used for occupational testing are not appropriate for clinical use.
- Definitive testing techniques should be used whenever a provider wants to detect specific substances not identified by presumptive methods, quantify levels of the substance present, and refine the accuracy of the results.
- Definitive testing should be used when the results inform clinical decisions with major clinical or non-clinical implications for the patient (eg, treatment transition, changes in medication therapies, changes in legal status).
- If a patient disputes the findings of a presumptive test, a definitive test should be done.
- When ordering a definitive test, providers should advise the testing laboratory if the presence of any particular substance or group of substances is suspected or expected.
- Because not all laboratories automatically perform a definitive test of positive presumptive results (the common term for this is "reflex" testing), providers should be aware that laboratories may require a specific order for definitive testing.

Cost

- Providers should always consider cost both to patients and insurers when utilizing drug testing.

Responding to Test Results

- Providers should attach a meaningful therapeutic response to test results, both positive and negative, and deliver it to patients as quickly as possible.
- Providers should not take a confrontational approach to discussing positive test results with patients.
- Providers should be aware that immediate abstinence may not be a realistic goal for patients early in treatment.
- When making patient care decisions, providers should consider all relevant factors surrounding a case rather than make a decision based solely on the results of a drug test. Considering all relevant factors is particularly important when using drug test results to help make irreversible patient care decisions.

Unclear Test Results

- Providers should contact the testing laboratory if they have any questions about interpreting a test result or to request information about the laboratory procedures that were used.
- Providers may consult with a medical toxicologist or a certified MRO for assistance in interpreting drug test results.
- If the provider suspects the test results are inaccurate, he or she should consider repeating the test, changing the test method, changing/adding to the test panel, adding specimen validity testing, or using a different matrix.
- If tampering is suspected, samples should not be discarded. Rather, further testing should be performed to help identify whether and how tampering occurred.
- Providers should consider samples that have been tampered with to be presumptive positive.

Presumptive Test Results

- Positive presumptive test results should be viewed as "presumptive positive" results until confirmed by an independent chemical technique such as gas chromatography mass spectrometry (GC-MS) or liquid chromatography-mass spectrometry (LC-MS).

- An appropriate response to positive presumptive test results includes speaking with the patient.
  - Providers should seek definitive testing if the patient denies substance use.
  - Providers should review all medications, herbal products, foods, and other potential causes of positive results with the patient.
- An appropriate response to positive presumptive test results may include speaking with the laboratory for assistance in interpreting the test results.
- Because presumptive tests may use cutoff values, a negative presumptive test result should not be over-interpreted. It does not rule out substance use or SUD, as the latter is a clinical diagnosis.
- It is appropriate to consider ordering a definitive test if presumptive test results are negative, but the patient exhibits signs of relapse.

Definitive Test Results

- In the event of a positive definitive test result, consider intensifying treatment or adding adjunctive treatments.
- An appropriate response to positive definitive test results may include speaking with the laboratory for assistance in interpretation.
- Providers should use caution when using drug test results to interpret a patient's amount or frequency of substance use. Individual metabolism and variability in absorption should be considered.
- Providers should not over-interpret a negative definitive test result. It does not rule out substance use or SUD, as the latter is a clinical diagnosis.

Test Scheduling

Test Frequency

- For people in addiction treatment, frequency of testing should be dictated by patient acuity and level of care.
- Providers should look to tests' detection capabilities and windows of detection to determine the frequency of testing.
- Providers should understand that increasing the frequency of testing increases the likelihood of detection of substance use, but there is insufficient evidence that increasing the frequency of drug testing has an effect on substance use itself.
- Drug testing should be scheduled more frequently at the beginning of treatment; test frequency should be decreased as recovery progresses.
- During the initial phase of treatment, drug testing should be done at least weekly. When possible, testing should occur on a random schedule.
- When a patient is stable in treatment, drug testing should be done at least monthly. Individual consideration may be given for less frequent testing if a patient is in stable recovery. When possible, testing should occur on a random schedule.

Random Testing

- Random unannounced drug tests are preferred to scheduled drug tests.
- A random-interval schedule is preferable to a fixed-interval schedule because it eliminates known non-testing periods (eg, if Monday is randomly selected from a week interval, the patient knows they will not be tested Tuesday-Saturday) and it is preferable to a truly random schedule because it limits the maximum number of days between tests.

PART 3: ADDITIONAL CONSIDERATIONS FOR DRUG TESTING IN ADDICTION TREATMENT

Documentation and Confidentiality

Addiction treatment providers and programs should have testing procedures in writing and share these with patients. One way to do this is to incorporate information about drug testing into patients' treatment agreements. Providers should also carefully document drug-testing procedures and rationale for individual patients. Documentation should include:

- Rationale for drug test types
- Rationale for drug-testing decisions
- Potential sources of cross-reactivity, including various foods and current medications
- Particular characteristics of the sample with potential to lead to problems with interpretation (eg, hair that has been chemically treated)
- Test results

Sometimes providers are asked to share test results with outside entities, such as social services agencies or the criminal justice system. The expert panel suggests that providers keep test results confidential to the extent permitted by law and use caution when sharing test results with outside entities. Providers should ensure that the patient has given informed consent for sharing test results; however, even when patients have authorized the release of test results, providers should be mindful that the aims and methods of employment-related drug testing and forensic drug testing are different from the aims and methods of clinical drug testing. Optimally, test results should be confirmed with a definitive test, although it may be appropriate to share presumptive results when they are negative. When sharing presumptive test results, ensure that they are clearly labeled "presumptive." Providers are responsible for providing patient education about confidentiality, consent, and sharing test results with outside entities.

Practitioner Education and Expertise

Knowledge and Proficiency

The accuracy of any drug test is predicated on the use of valid testing procedures, which include sample collection, analysis, and interpretation of results. Inadequate provider proficiency can result in inaccurate test results. The outcomes of a drug test can have serious consequences for patients; therefore, providers have a responsibility to ensure that they and their staff have the knowledge and proficiency necessary to carry out their roles in the drug-testing protocol.

A provider's necessary level of knowledge and proficiency about drug testing depends on his or her role in the

testing process. Providers who order tests should primarily be aware of the limitations of testing, common sources of false-positive and false-negative results, and tradeoffs between testing methods. They should:

- Be familiar with the limitations of presumptive testing
- Be familiar with the potential for cross-reactivity in drug testing (see *Responding to Test Results*, p. 10)
- Be familiar with the potential for sample tampering to obscure test results (see *Urine sample integrity*, p. 17)
- Understand the benefits of alternative matrices to urine (eg, oral fluid, hair, etc)
- Be aware of the costs of different test methods

Interpretation of drug test results is usually not extensively covered in medical school. Individuals who interpret test results should have some knowledge of toxicology and other issues related to proper interpretation. Providers without formal toxicology training can participate in available courses, and/or should collaborate with a medical toxicologist, a toxicologist from their laboratory, or a physician certified as a MRO. Providers could consider MRO training and/or certification through organizations including the American Association of MROs and/or the Medical Review Office Certification Council.

Language and Attitude

Successfully sending the message that drug testing is a therapeutic tool rather than a punitive measure will depend on providers and programs using therapeutic language and a proactive attitude towards testing and test results. Providers should use neutral terminology that does not further stigmatize addiction and its symptoms. Test results should be referred to using the terms ''positive'' or ''negative'' as opposed to ''clean'' or ''dirty.'' These terms are consistent with a growing body of research literature and clinical guidance about non-stigmatizing language [22,23].

Furthermore, staff attitudes toward drug testing and drug test results should remain consistent throughout the organization. If some members of the treatment team convey the message that drug testing is an important part of proactively addressing continued symptomatology while other members are dismissive, patients will benefit less from drug testing as a therapeutic tool.

Test Facilities and Devices

Addiction treatment providers can choose to conduct their own testing on-site, send samples to a qualified laboratory, or both. These choices involve tradeoffs in quality, turnaround time for results, availability of test technology, and cost.

Point of Care Tests

Some addiction treatment providers perform on-site drug testing using Point of Care Tests (POCTs). There are advantages and disadvantages to POCTs. The most significant advantage of POCTs is the short turnaround time for results, which can be available within minutes. This allows providers to respond to a patient's use of substances quickly and meaningfully (see *Responding to Test Results*, p. 10).

However, it is important to recognize that many POCTs use immunoassay technology, which (varying by the substances being detected and the matrix being used), can have drawbacks. POCTs may be vulnerable to cross-reactivity, detect classes of drugs rather than specific drugs, and require confirmation by a definitive test. Another major disadvantage of POCTs is that despite internal quality control measures, improper sample handling can result in inaccurate results. It has been said that ''the single most important quality issue surrounding POCT devices is the initial and ongoing training of the individual(s) performing the testing to maintain competency'' [24].

Ongoing staff training and quality control are essential. Individuals who collect, store, and interpret POCTs should be educated about the devices' sensitivity, the spectrum of analytes detected, the potential for cross-reactivity, cutoff values, and the nomenclature of the device being used. Users of POCTs should refer to the POC package insert or the manufacturer to determine the device's capabilities.

To ensure POCTs are being used effectively, providers should conduct individual- and organization-level evaluations of staff proficiency by comparing POCT results to the results of a qualified laboratory. POC testing can be implemented comprehensively or on a more limited basis. For example, one provider may use POCTs to conduct all presumptive testing while another uses POCTs only to confirm self-reported substance use that could be detected by the test's panel. Depending on the extent of POCT use, cost should be a consideration when deciding whether to use a POCT protocol. There are costs associated with the extra staff time and space as well as the equipment and supplies necessary to perform the test, staff training, quality assurance procedures, and documentation of POC testing.

Office based testing is most practically done utilizing Clinical Laboratory Improvement Amendments (CLIA)-waived tests. CLIA-waived tests are POCTs defined by the FDA as ''simple'' and having an ''insignificant risk for an erroneous result.'' More information from the FDA can be found on the website: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.htm. Additional resources, including online training and recommendations for the use of CLIA-waived tests can be found on the CMS website: https://www.cms.gov/regulations-and-guidance/legislation/clia/downloads/waivetbl.pdf. When considering a CLIA waiver, providers should keep in mind that some states have regulations that differ from the federal guidelines pertaining to waivers to perform this type of POCT procedure.

Choosing a Laboratory

Regardless of whether a provider uses POCTs, the selection of an appropriate laboratory is an important component of an effective drug-testing protocol. It is important to choose carefully. Providers should contact the director or a medical toxicologist at the prospective laboratory directly to discuss panels, types of drug tests, testing procedures, and technical assistance. Some laboratories are geared toward workplace testing; this is not ideal for an addiction treatment setting. It is more appropriate to work with a laboratory that

has experience working with addiction treatment settings. Also look for a laboratory that allows providers to order specific tests for each patient because drug testing in addiction treatment should be individualized.

The ability to consult with laboratory staff when needed is an important consideration in choosing a laboratory. The relationship between the testing laboratory and the addiction treatment center should be collaborative. Providers should be able to communicate with the testing laboratory about test panels, detecting sample tampering, test result interpretation, and regional drug use trends.

Certification requirements should be reviewed. Laboratories that perform forensic drug testing for federal agencies and federally regulated industries are required to maintain a national certification overseen by the Department of Health and Human Services (HHS). Typically, it is not necessary for a laboratory working with an addiction treatment provider to have an HHS certification. However, it is important to confirm that the laboratory follows established federal and state regulations. The CLIA of 1967 and of 1988 set forth conditions that all laboratories must meet to be certified to perform testing on biological specimens. Additionally, state clinical laboratory programs operate under individual state laws; these state programs are usually authorized through the Centers for Medicare & Medicaid Services. Providers should investigate whether state law requires a specific certification for a testing laboratory working with an addiction treatment provider. A list of state CLIA contacts is available on the Centers for Medicare and Medicaid Services website (https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA).

Summary of Recommendations

Documentation and Confidentiality

- Addiction treatment programs should provide written drug-testing procedures to patients. Procedures should be reviewed with the patient at the start of his or her treatment.
- Providers should document the rationale for the drug tests they order and the clinical decisions that are based upon drug test results.
- Providers should ask patients about and document potential sources of cross-reactivity, including various foods and current medications.
- Particular characteristics of a sample with the potential to lead to problems with interpretation (eg, hair that has been chemically treated) should be documented at the time of collection.
- Test results should be documented.
- Test results should be kept confidential to the extent permitted by law. Providers should thoroughly explain to patients all rules regarding confidentiality, consent, and sharing test results with outside entities.
- In general, providers should use caution when sharing test results with outside entities such as justice settings or employers. When sharing test results with outside entities, it is optimal that positive results be verified with a definitive test.

Practitioner Education and Expertise

Knowledge and Proficiency

- Providers responsible for ordering tests should be familiar with the limitations of presumptive and definitive testing.
- Providers responsible for ordering tests should be familiar with the potential for cross-reactivity in drug testing.
- Providers responsible for ordering tests should consider the possible impact of tampering on test results. Providers should note that tampering is more likely in settings where consequences for substance use are severe, such as discharge from treatment.
- Providers responsible for ordering tests should understand the potential benefits of alternative matrices to urine (eg, oral fluid, hair, etc).
- Providers responsible for ordering tests should be aware of the costs of different test methods.
- If the provider responsible for making clinical decisions based on test results does not have training in toxicology, he or she should collaborate with a medical toxicologist, a toxicologist from the testing laboratory, or an individual with MRO certification, as needed.

Language and Attitude

- Providers should communicate with patients about drug testing using non-stigmatizing language. For example, results should be discussed as ''positive'' or ''negative'' as opposed to ''clean'' or ''dirty.''
- Providers should exhibit a consistent and positive attitude toward drug testing. Ambivalent attitudes toward drug testing among staff can be a barrier to its effective use.

Test Facilities and Devices

Point of Care Tests

- Staff training and demonstrated proficiency is particularly important for organizations that use point of care tests (POCTs).
- Providers performing POCTs should be evaluated for their proficiency. POCTs should be performed only by providers who demonstrate adequate proficiency with the drug test in question. Facilities using POCTs should periodically evaluate the accuracy of their system in comparison to a qualified laboratory.
- Users of POCT devices need to be educated about the tests.
  - They need to understand the statistical and analytical sensitivity of the device.
  - They need to understand the spectrum of analytes (drugs and metabolites) detected by the device.
  - They need to understand any known interferences from drugs or metabolites that could affect interpretation of results.
  - They need to understand the nomenclature of the device.
- Users of POCTs should refer to the POC package insert and/or the manufacturer to determine the device's capabilities.
- Cost issues should be considered when deciding to initiate a POCT protocol. These include costs associated with additional staff time and training, space to perform testing,

quality assurance procedures, and documentation of POCT results.

Choosing a Laboratory

- Providers should seek to work with a laboratory that has expertise in drug testing in addiction treatment settings.
- When selecting a laboratory, providers should investigate whether state law requires a specific certification.
- It is important to work with a laboratory qualified to perform accurate tests and assist in the interpretation of results.
- Providers should work to create a collaborative relationship with the laboratory; important areas for collaboration are test panel selection, detecting sample tampering, interpreting test results, and regional drug use trends.
- When selecting a laboratory, providers should contact the toxicology director or a medical toxicologist at the laboratory to discuss panels, types of drug tests, testing procedures, and technical assistance.
- Because drug testing should be individualized, laboratories should allow providers to order specific tests for each patient.

PART 4: BIOLOGICAL MATRICES

Comparing Matrices

Urine, blood, exhaled breath, oral fluid (saliva), sweat and hair are some biological samples that are used in drug testing. Smarter testing involves choosing the matrix best capable of detecting the substance of interest within the desired window of detection, and this often involves making tradeoffs in terms of test capabilities. See Table 4 for information about relative advantages and disadvantages of available matrices. *Appendix 4: Windows of Detection Table* contains detection windows for specific parent drugs and metabolites in urine, blood and oral fluid.

Biological drug testing detects the presence or absence of parent drug compounds and/or their metabolites, which remain in the body for longer periods of time, in a biological sample. Drugs and their metabolites become present in the body primarily by being absorbed into the bloodstream and then distributed to other matrices via mechanisms such as passive diffusion and ultrafiltration. Specific mechanisms will be discussed in the section for each matrix addressed in this document.

The physiological distribution of drugs implies a varying relationship between the concentration a drug or metabolite has in different matrices depending on properties such as lipid solubility, acid dissociation (pK_a) and protein binding tendency. For example, drugs that are more acidic (eg, benzodiazepines) will have higher concentrations in fluids with higher pH (eg, plasma/blood) while more basic drugs (eg, amphetamines and opiates) will have higher concentrations in fluids with lower pH (eg, saliva/oral fluid).

The relationship between concentration and matrix depends on (a) the pharmacokinetic profile of the drug; (b) the consumer's underlying health functioning; and (c) the pattern, dose and route of drug administration. These factors influence the absorption, distribution, and elimination of the

TABLE 4. Comparing Testing Characteristics Across Matrices

	Blood	Breath	Oral Fluid	Urine	Sweat	Hair
General detection period	<24 hours [2] 1–8 hours [25] 1–48 hours [26]	~1 hr per standard drink	<24 hours [2] 12–24 hours [27] 1–36 hours [28] 5–48 hours [29] 12–48 hours [25]	1.5–4 days [29] 1–3 days [25,26,30]	Continuous, usually 1–4 weeks [2,26]	7–90 days [2] 7–100 days [26]
POCT/On-site immunoassay available	Yes, primarily used for alcohol	For alcohol	Yes	Yes	No	No
Primarily detects	Parent drug compound; blood alcohol concentration	Parent drug compound; blood alcohol concentration	Parent drug compound	Drug metabolite	Parent drug compound	Parent drug compound
Best use in treatment setting	Determination of acute impairment or intoxication for alcohol	Determination of acute impairment or intoxication for alcohol	Short-term detection in ongoing treatment	Intermediate-term detection in ongoing treatment	Medium-term prospective monitoring	Long-term monitoring; 3-month drug use history
Ease of collection	Requires staff trained in phlebotomy	Easily collected	Easily collected	Requires specialized collection facility (restroom)	Easily collected	Easily collected
Intrusiveness of collection	High for intravenous access	Low	Low	High	Low	Low
Resistance to tampering	High	High	High, but some uncertainty	Low	High, but some uncertainty	High when chemically untreated
Retesting same sample	Difficult	Generally not possible	Difficult	Possible	Possible depending on patch used	Easy

TABLE 5. General Windows of Detection Across Matrices

	Minutes	Hours	Days	Weeks	Months
Blood	■	■			
Breath	■	■			
Oral Fluid	■	■	■		
Urine		■	■		
Sweat		■	■	■	
Hair				■	■

Adapted from Substance Abuse and Mental Health Services Administration [53].

drug and ultimately determine their window of detection. For example, tetrahydrocannabinol (THC), the primary compound in cannabis, is highly lipid soluble and binds to fat cells in the body. A person who uses cannabis once may only test positive for 24 hours, while a person who has used chronically may test positive for a month or longer after cessation as stored THC continues to be eliminated from the body [31] (Table 5).

In general, the longest windows of detection occur in hair, followed by sweat, urine, oral fluid and blood [29]. But maximum detection time is not the only important criteria for choosing a test. Other factors to consider include:

- Time to detection
- Time to obtain results (availability of POCT)
- Ease of collection (need for trained personnel, collection facilities)
- Invasiveness/unpleasantness of collection
- Availability of the sample (eg, renal health, shy bladder, baldness, dry mouth)
- Susceptibility of the sample to tampering

The accuracy of any drug test is predicated on obtaining a valid specimen. The nature of addiction may lead some patients to try to mask continued substance use or relapse. The pressure to do so may depend on the severity of the consequences they will face if detected, such as increased sanctions, or legal action. (see *Drug testing and self-reported substance use*, p. 5).

Urine

Basics of Urine Drug Testing

As the kidneys filter the bloodstream, waste and other by-products including metabolites are extracted and eliminated along with water from the body as urine. It takes approximately 2 hours after use for a substance to be detected in urine, a longer time to detection than for other bodily fluids such as saliva and breath [32]. The window of detection for most substances of interest is 1–3 days and up to 4 days in some cases and is dependent on factors such as fluid intake and urinary pH. The concentration of a drug or its metabolites in urine represents the amount, which has accumulated in the bladder since the last void.

See Table 4 for more information about the advantages and disadvantages of UDT in comparison to alternative matrices.

Use of Urine Drug Testing in Addiction Treatment

At this time, urine is the most well-established and well-supported biological matrix for presumptive detection of substance use in addiction treatment settings. Urine is the most commonly used biological specimen for drug and alcohol testing in clinical settings [33]. Urine is also the best established matrix in POC testing. UDT represents a mature technology; because of its popularity, the drug-testing industry has focused development on producing more rapid and less expensive technologies for testing urine. This means there are many testing options available, generally at lower cost compared to other matrices.

Disadvantages of Urine Drug Testing

There are 2 major drawbacks to UDT: (1) the ease of sample tampering through substitution, dilution, and adulteration, and (2) the invasiveness and resource intensity of witnessed sample collection, the primary means of countering sample tampering.

If appropriate measures to reduce urine sample tampering are not able to be taken and tampering is of high concern, providers should consider testing an alternative specimen. The use of alternative matrices to complement UDT could take place in a number of ways, including on a clinic-wide basis by rotating the collection of specimen types (see *Matrix advantages and disadvantages*, p. 7) or on an individual collection-by-collection basis.

Urine Sample Integrity

Urine is the specimen most prone to sample tampering. UDT can be circumvented through sample substitution, dilution and adulteration by ingesting something prior to a test (in vivo) or adding something to a sample (ex vivo) with the purpose of obscuring the test results. A substituted sample is one that replaces the patient's urine with another sample, either urine or some other liquid. Diluting a urine sample makes it less likely that a drug or its metabolite(s) can be detected above the cutoff threshold of an immunoassay test. Adulteration involves the use of a masking agent that destroys the presence of drugs in urine or interferes with the enzymatic reactivity of an immunoassay test.

There are measures that can be taken to mitigate the risk of urine sample tampering and ensure sample integrity, described in the following sections. Providers should choose a urine sample collection method that will protect patients' dignity and privacy while minimizing opportunities for tampering. Each clinic should have clear specimen tampering and diversion control strategies in place and these should be discussed with patients. In order for sample tampering policies to have their intended effect, providers should be trained appropriately in these measures.

Observed Urine Sample Collection

The primary method used to prevent urine sample tampering is direct observation of urination by a staff member of the same gender during collection. Observation prevents several common ex vivo methods of substitution, dilution and adulteration at the time of collection. For example, substitution generally requires a patient to carry the replacement sample in a container with them to the bathroom. A patient can dilute a sample by adding liquids such as water or colored fluids (apple juice, lemonade) to the sample container. Adulterants that are added to a sample container include many household chemicals. The most commonly used chemicals include table salt (sodium chloride), vinegar, Drano, dish soap, hand soap, liquid laundry bleach, denture cleansing tablets, lemon juice, ascorbic acid, hydrogen peroxide, and rubbing alcohol (isopropyl alcohol) [34].

If there are concerns about urine sample tampering, or if a provider suspects sample tampering has occurred, sample collection should be observed. (See *Signs of urine sample tampering* for a discussion of what constitutes reasonable concern or suspicion regarding tampering). If collection was previously unobserved, this change should be explained to the patient and described as being undertaken in their best interest. This may provide an opportunity for therapeutic discussion about the patient's health and well-being, which underlie the decision to change collection procedure.

Limitations of Observed Urine Sample Collection

There are a few problems with singular reliance on observed sample collection as a tampering mitigation strategy. First, observed urine collection does not completely prevent sample tampering. Supervised collection addresses ex vivo, but not in vivo methods of sample tampering. For example, urine can be made dilute by rapidly consuming large amounts of fluid approximately 1 to 2 hours prior to the test (water loading) or taking diuretics. Adulterants taken prior to providing a sample include oxidizing agents such as nitrites or agents, which affect urine pH such as soda crackers.

Routine observed collection may not be feasible, even when tampering is suspected, due to staffing issues. Same-sex staff might not be available to supervise patients or a patient/staff member's gender identity may not fit into the traditional male/female dyad, which can complicate the issue of same-sex observation. Direct observation of urination is potentially embarrassing and uncomfortable for both the patient and person supervising collection. Staff may avoid very close observation and miss the use of commercially available sample substitution devices.

Direct observation of urination can be seen by patients as a perceived violation of trust and respect and patients frequently indicate they would prefer an alternative specimen be collected if available [35]. Consider the use of unobtrusive sample collection method for patients with a history of psychological trauma, particularly sexual trauma. Observed urination may be distressing for these patients.

Given these limitations, providers should utilize other strategies—either in addition to or instead of—observed collection to mitigate urine sample tampering.

Unobserved Urine Sample Collection

Having a well set up bathroom collection area can remove some opportunities for sample tampering during unobserved collection. Although all of the following may not be possible in all facilities, providers should employ appropriate measures to decrease the likelihood of urine sample tampering during unobserved collection. Do not allow patients to carry personal items with them into the collection area. Ensure that potential adulterants, such as soap, ammonia, or bleach are not readily available in the collection area. Place blue dye in the toilet and turn off the water source to the collection area during collection. Provide an alternative hand cleansing option to patients as they exit the bathroom.

Specimen Validity Testing

Urine sample integrity can be verified through specimen validity testing. Specimen validity testing indicates that a sample has been tampered with by detecting the presence of adulterants or the absence of biological indicators of normal human urine. Specimen validity testing can detect both in vitro and in vivo methods of tampering. However, not all adulterants can be detected in standard adulterant test, including Visine eye drops and newer adulterants such as Urine Luck, UrinAid, Klear, and Whizzies [34].

Definitive testing should always include specimen validity testing which measures creatinine concentration, pH level and specific gravity. At the presumptive testing stage, not all samples need to be tested for specimen validity. However, some POCT devices include specimen validity tests for specific gravity and pH.

If a sample is suspected of having been tampered with then it should be tested for specimen validity, including creatinine concentration, pH level, specific gravity and adulterants. (See *Signs of urine sample tampering*, p. 18 for a discussion of what constitutes reasonable concern or suspicion regarding tampering.)

Signs of Urine Sample Tampering

There are differing opinions on what criteria best indicate that urine sample tampering may have occurred. SAMHSA's guidelines for urine sample verification in federal workplace testing programs are a useful reference point [20]. With regard to sample integrity, most of the SAMHSA guidelines are considered appropriate in the addiction treatment context with the exception of universal presumptive specimen validity testing. This would be difficult to undertake given the cost and currently available technology.

Unusual Specimen Characteristics

All urine samples should be inspected for unusual characteristics that indicate that tampering may have occurred. Characteristics include:

- Unexpected temperature
- Unusual color
- Unusual smell
- Soapy appearance, cloudiness or particles floating in the liquid

A recently provided sample should be within expected body temperature range, approximately 90 to 100 degrees within 4 minutes of production. This can be evaluated using a heat sensitive strip on the outside of a collection cup. A sample that is too cold suggests that a substitute sample or cold liquid was added to the sample. A sample that is too hot suggests that a chemical heat pack like a hand warmer was used to try to mask the addition of a cold liquid.

A visual inspection can indicate that a sample may be dilute or adulterated. Dilute urine is lighter in color than normal urine, which ranges from light/pale yellow to dark/deep amber. Nitrites also tend to make the color of urine dark. Urine that has been diluted with liquids such as vinegar, ascorbic acid and rubbing alcohol can sometimes be detected by their distinct smell. Table salt (sodium chloride) and denture tablets may be visible as undissolved granules. Dish and hand soap will give the sample a soapy appearance.

If the sample exhibits unusual specimen characteristics, perform specimen validity testing. Sample inspection should not be relied upon solely as evidence of sample tampering, but as an indication of the need for further testing [36,37]. Abnormal urine appearance can also be the result of a urinary tract infection, kidney stones, yeast infection, diet (eg, beets, asparagus) and the use of over-the-counter vitamins and medications (eg, ex-lax, Vitamin B) [38].

Requiring a minimum volume sample can help to increase the reliability of temperature readings and visual inspection as well as ensure there will be enough specimen available for testing.

Unusual Behavior

The expert panel advised broad use of clinical judgment in identifying behavioral signs that a patient may have tampered with a urine sample.

If a patient's behavior suggests that he or she has recently used an illicit substance, but continues to produce negative urine test results, sample collection should be observed and specimen validity testing conducted. A patient may also continue to produce negative urine test results for reasons that are related to the testing procedure including the use of a substance not targeted in the test or is using an amount below the threshold of detection for the cutoff used by the test. The provider could adjust the test panel or order a more sensitive test (see *Choosing a Test*, p. 7) (Table 6).

Responding to Specimen Validity Test Results

Samples are considered substituted or invalid if they fail some aspect of specimen validity testing. It is appropriate for practitioners to consider samples that have been tampered with to be presumptive positive. Providers should respond as they would to a presumptive positive drug test result and rapidly involve the patient in therapeutic discussion (see *Responding to Test Results*, p. 10).

If a specimen is invalid, most labs will stop the testing process on the assumption that the concentration of a drug or metabolite as measured in the sample will be uninterpretable.

TABLE 6. Components of Urine Specimen Validity Testing

Characteristic	Description
Creatinine	Creatinine is the product of muscle metabolism and is produced at a fairly constant rate by the body. Creatinine is used clinically as an indicator of renal health, with very high or very lowconcentrations indicating abnormal kidney function as in Diabetes Insipidus. Creatinine will be very low if an individual has over-hydrated, and very high concentrations can result from the use of some adulterants. SAMHSA has set criteria for normal creatinine concentrations in urine, with <20 mg/dL indicating a dilute sample. This limit is meant to screen out probable instances of attempted tampering among the general workplace population. Creatinine concentrations can be used to normalize drug concentrations if practitioners want to continue with definitive testing of a dilute sample.
Specific gravity	Specific gravity is a measure of the concentration of dissolved particles in a liquid by comparing its density to the density of water. The specific gravity of normal human urine is between 1.003 and 1.030. While a urine specific gravity of 1.000 is essentially water and suggest dilution, higher specific gravity values can indicate that an adulterant has been added to a sample. For example, the amount of table salt needed to produce a false-positive results in specific gravity over 1.035 [34]. Most sources recommend that specific gravity need only be checked if creatinine is <20 mg/dL.
pH	pH is a measure of acid-base and ranges between 4.5 and 8.0 in urine. It greatly affects the concentration and stability of some drug and drug metabolites in urine and therefore the likelihood that they will be detected. The pH of the sample may influence the enzymatic action and performance of immunoassay screens. Abnormal pH can indicate that a sample is dilute or adulterated. Bleach, acid, soap, detergent and vinegar all alter pH to outside the normal human range [34]. Abnormal pH can also be the result of a kidney or urinary tract infection as well as diets extremely high in protein or low in carbohydrates.
Immunoglobulin (IgG)	IgG is the most common antibody in the bloodstream. Concentrations <0.5 μg/ml suggest that a sample was substituted with synthetic or animal urine. While IgG is discussed in the literature and is available as part of a specimen validity test at many lab facilities, the expert panel had mixed opinions regarding the appropriateness of its inclusion in specimen validity testing, with some commenting that it was not commonly used in their practice.
Adulterants	Testing for the presence of adulterants such as glutaraldehyde, pyridium chlorochromate and nitrites can be done on-site or in a laboratory [39]. However, not all adulterants can be detected in standard adulterant test, including Visine eye drops and newer adulterants such as Urine Luck, UrinAid, Klear, and Whizzies [34].

Adapted from Kirsh KL, Christo PJ, Heit H, et al. [154].

In the case of dilute urine, however, the creatinine concentration of the sample can be used to normalize drug concentrations.

Dilute Urine Samples

Dilution is the most common cause of an invalid sample. A combination of low creatinine (below 20 mg/dL) and specific gravity is used to indicate that a sample is dilute. Expert panel members commented that dilution is usually the result of deliberate water loading. Practitioners can employ a number of solutions to decrease the likelihood of collecting a dilute sample. For patients with a history of dilute urine samples, providers should:

- Advise the patient to decrease water intake prior to sample collection
- Collect samples first thing in the morning
- Collect samples before work or on days off (if a patient's occupation involves the need to hydrate heavily)
- Consider the use of an alternative matrix

There are some health conditions, primarily kidney ailments and diabetes, which can lead to unusually high or low specific gravity and low creatinine levels [40]. However, a dilute urine sample resulting from an underlying health condition, such as Diabetes Insipidus, is very rare. Providers should first advise patients with a dilute sample about apparent tampering and evaluate for an underlying etiology only if the trend continues.

Urine Testing for Specific Substances

Urine is the most well-established and well-supported biologic matrix when conducting drug testing for patients with addiction, but its utility depends on the substance of interest and the information the provider needs. Providers should consider the questions they are seeking to answer when conducting a urine test for a substance of interest and be aware of known detection issues. For example, THC is detectable in urine, but it is difficult to distinguish when the substance was used. See *Appendix 4: Windows of Detection Table* for window of detection for specific substances in urine as compared to oral fluid and blood.

Alcohol

Alcohol use can be detected through the direct measurement of ethyl alcohol (EtOH) or one of its metabolites. EtOH has a very short detection window of approximately 10–12 hours and varies considerably by consumption pattern, hydration level and individual metabolism. If providers are interested in detecting such recent alcohol consumption, a breath test may be more convenient than urine EtOH.

Instead of EtOH, providers are encouraged to use tests of ethyl metabolites, which are detectable in urine for longer periods of time. The expert panel primarily encouraged the use of direct alcohol metabolites EtG and/or ethyl sulfate (EtS), detectable in urine for up to 1 to 2 days and widely available in testing. The expert panel also briefly reviewed the use of phosphatidyl ethanol (PEth) and found its extended window of detection to have promising clinical applications; however, most panel members expressed that they were not yet familiar with this technology and it is not yet widely available. No existing recommendations were found regarding testing of fatty acid ethyl ester (FAEE) in urine. FAEEs are formed by the reaction of ethanol with free fatty acids and their amount does not correlated with the amount of alcohol consumed [41]. EtG, EtS, PEth, and FAEEs are considered direct biomarkers of alcohol use because there are present only when alcohol has been consumed. Indirect markers including carbohydrate-deficient transferrin and gamma glutamyl transferase are used primarily to evaluate chronic excessive alcohol consumption, rather than the clinical determination of recent alcohol consumption, and were not reviewed by the panel.

Although rare, it is possible for exposure to ethanol-containing products such as hand sanitizer to result in a positive EtG or EtS test [42]. Patients should be advised to avoid the use of ethanol-containing products before an EtG or EtS test.

Amphetamines

Urine testing is helpful when assessing a patient's amphetamine use. However, there are known limitations to urine immunoassays for amphetamines and providers should be cautious when interpreting their results. Standard amphetamine immunoassays target amphetamine, which is also a direct metabolite of methamphetamine. Amphetamine immunoassays are also subject to many false-positives compared to other drug class assays. For example, Adderall and Benzedrine contain amphetamine, Vicks Inhalers contain methamphetamine, and Bupropion is known to result in positive methylenedioxymethamphetamine (MDMA) test results. Providers should know the sensitivity and specificity of the test being used for each of the amphetamine variants. The testing laboratory will have this information.

Benzodiazepines

Urine testing is helpful when assessing a patient's benzodiazepine use. There are known limitations to urine immunoassays for benzodiazepines and providers should be cautious when interpreting their results. Most general benzodiazepine assays have very low sensitivity to clonazepam and lorazepam. Some assay tests perform better than others, however, and depend on the antibodies used by the manufacturer. Providers should know the sensitivity and specificity of the test being used for each of the benzodiazepine variants. The provider's laboratory will have this information.

Immunoassays are generally not sensitive to therapeutic doses of benzodiazepines. Providers should know the cutoff limits of the test being used. If a patient's benzodiazepine immunoassay is negative, but the patient states that he or she is taking their medication as prescribed, providers can request a definitive test if they wish to confirm use.

Opiate/Opioids

Urine testing is helpful when assessing a patient's opioid use. There are known limitations to urine immunoassays for opiate use and providers should be cautious when interpreting their results. Providers should carefully review the testing report produced by the laboratory to ensure they

understand which opiates and opioids a test is capable of detecting. Semi-synthetic and synthetic opioids may not be included in a test for opiates using immunoassay technology.

A standard opiate immunoassay will detect the use of morphine, codeine (which is metabolized to morphine) and heroin (which is metabolized to 6-MAM and subsequently to morphine) and return a positive opiate result. Metabolites specific to codeine must be detected to confirm codeine use. Heroin or 6-MAM must be detected to confirm heroin use. Hydrocodone and hydromorphone (a metabolite of hydrocodone) are also detected in most standard opiate immunoassays.

Oxycodoneand oxymorphone (a metabolite of oxycodone) are detected in a few but not most standard opiate immunoassays depending on the antibodies used by the manufacturer. One author listed the cross-reactivity of standard opiate immunoassays with oxycodone as ranging between 1% and 10% in 2012 [34]. Providers should be aware of the cross-reactivity of the assay they are using.

Meperidine, methadone, buprenorphine, and fentanyl will not be detected in a standard opiate immunoassay and require their own test.

Although rare, the consumption of poppy seeds can result in a positive opiate immunoassay test result and patients should be instructed to avoid the consumption of poppy seeds. The cutoff designated by SAMHSA for use in the Federal Workplace Guidelines is designed to eliminate positive opiate results from poppy seed consumption. Providers who use a lower cutoff for their clinical population may have an increased risk of positives from this type of exposure (see *Presumptive and definitive tests*, p. 8).

Cocaine

Cocaine use can be detected in urine. Urine testing targets the cocaine metabolite benzoylecgonine (BZE) as cocaine itself has a very short half-life. Compared with opiate, benzodiazepine, and amphetamine tests, presumptive tests for cocaine are more sensitive and specific because they target a specific analyte.

Cannabis

Cannabis use can be detected in urine. Urine testing targets THC metabolite THC-9-carboxylic acid (THC-COOH).

Blood

Basics of Blood Testing

Blood is mainly composed of plasma, serum, white blood cells and red blood cells. Although whole blood samples are sometimes analyzed, more often they are filtered and only plasma or serum is analyzed. Blood testing allows for the precise measurement of drug concentration levels and can be used to interpret dose or timing, which can be very useful in emergency situations.

See Table 4 for more information about the advantages and disadvantages of blood testing in comparison to other matrices.

See *Appendix 4: Windows of Detection Table* for windows of detection for various substances in blood as compared to urine and oral fluid.

Use of Blood Testing in Addiction Treatment

The relevance of blood testing is limited mostly to emergency situations where there is a need to assess impairment and degree of intoxication, and is primarily used to assess alcohol use. Drawbacks to blood testing include the need for staff to be trained in phlebotomy, the invasiveness of drawing blood, and the fact that collected blood samples are hazardous to handle.

Breath

Basics of Breath Testing

Drugs are detected in exhaled breath as aerosolized particles formed from the fluid lining of the lungs. In the context of alcohol testing, a breath test represents the amount of alcohol present in exhaled breath, which is diffused into the air held in the lungs from pulmonary capillary blood. Breath alcohol concentration (BrAC) can then be used to estimate blood alcohol concentration (BAC).

See Table 4 for more information about the advantages and disadvantages of breath testing in comparison to other matrices.

Use of Breath Testing in Addiction Treatment

Breath testing has primarily been directed at the detection of recent alcohol use and impairment; it currently represents the most used matrix for POC alcohol testing. Such devices have largely been developed for roadside and other forensic testing environments. This means that while such devices will be relatively simple to use and provide rapid results, cutoff levels may be optimized to identify degree of intoxication or use above a legal limit and may be of less value when applied to a clinical population or setting. Similarly, remote breath monitoring for alcohol use, while a promising technology, was outside the scope of the current project and was not considered.

Two known drawbacks of breath testing are sample contamination from food or oral hygiene products, which contain alcohol and insufficient breath volume [34]. Some devices require larger sample volumes than others and getting a sufficient breath volume is necessary for devices to work properly.

Researchers have begun to expand the substances detected in breath beyond alcohol. In a recent study, testing patients in an outpatient addiction treatment program for amphetamine, benzodiazepine, cannabis, cocaine, buprenorphine, methadone and opioid use, using definitive breath testing was determined to be viable and preferred by patients over urine testing [43].

Oral Fluid

Basics of Oral Fluid Testing

Drugs are present in oral fluid primarily through passive diffusion from the bloodstream to salivary glands and through absorption and excretion by mucous membranes in the oral cavity during ingestion or inhalation. Because oral fluid testing is primarily blood-based, oral fluid drug concentrations generally correlate with plasma concentrations and

provide a good indication of parent drug presence and impairment [44]. However, if a substance is consumed orally, it will often be present at very high concentrations due to direct contact with mouth surfaces, which make it difficult to correlate concentration and intoxication for a period of about 2 hours after dosing.

See Table 4 for more information about the advantages and disadvantages of oral fluid testing in comparison to other matrices.

See *Appendix 4: Windows of Detection Table* for more information about oral fluid's window of detection for various substances in comparison to urine and blood.

Use of Oral Fluid Testing in Addiction Treatment

Oral fluid testing is appropriate for presumptive detection of substance use in addiction treatment settings. Oral fluid has gained attention as a possible replacement for urine as the matrix of choice in drug testing [45]. The expert panel did not prefer its use over UDT at this time, but suggested that oral fluid may have certain advantages which can be capitalized on in clinical practice.

Although oral fluid offers a shorter window of detection than urine (12–48 hours for most substances), it is unobtrusively collected, does not require the same staff and bathroom facility resources, and so far, does not suffer from the same sample tampering problems that urine has. Oral fluid is also more likely to contain detectable concentrations of parent drug compounds, making it possible to identify the drug consumed, while urine typically targets metabolites, which may be shared across drug class. For example, 6-MAM, a direct marker for heroin, is present in oral fluid at high concentrations but quickly degrades in urine.

Like breath testing, oral fluid has been primarily developed and evaluated for use in roadside and other forensic settings, although it is being increasingly studied in clinical applications [44]. Oral fluid has also been the focus of a great deal of POCT device development.

Drawbacks to oral fluid testing include difficulty with sample collection due to dry mouth, sample contamination from smoking and eating, and oral cavity contamination from recently consumed drugs. Also, while a 2008 study found that commercially available adulterants designed to mask positive results are less effective than those found for urine testing, adulteration methods for oral fluid may become more sophisticated as the technology becomes more widely used [44].

Collection of Oral Fluid Samples

One benefit of oral fluid testing is that sample collection is observed, but is unobtrusive. Oral fluid is collected with a device such as an absorbent pad that is held in the mouth for 30 to 60 seconds before placing the pad into a container. Oral fluid collection with a device such as a pad is preferable to direct expectoration into a container. The pad serves to filter contaminants such as food particles, making them a more precise measurement tool than expectoration [46]. The pad can also help stimulate saliva production, although this may affect pH level and skew analyte concentrations. Dry mouth is a common side effect of the use of many illicit drugs such as cannabis and amphetamines as well as prescription medications. Small oral fluid sample volumes mean there may not be enough specimen available for analysis and prevents retesting of the same sample for validity or subsequent definitive testing [47].

Contamination from food particles can interfere with test results. Providers should encourage patients to abstain from eating for 15 to 60 minutes prior to sample collection. Contamination of the oral cavity from recently consumed drugs can skew quantitative results. If a patient recently took a drug by mouth (ingestion or inhalation), it is recommended that practitioners wait at least 2 hours before collecting an oral fluid sample. Qualitative detection of recent use, however, will still be valid [28].

Sweat

Basics of Sweat Testing

The mechanism by which drugs are incorporated into sweat is not fully understood and several potential mechanisms have been proposed, including diffusion from blood vessels passing by sweat glands or through sebaceous glands also present on the surface of the skin, which primarily excrete lipids [32].

Sweat is collected continuously by an absorbent pad or "sweat patch" that is held close to the skin with an adhesive area, similar to a Band-Aid. Drug concentrations represent an individual's accumulated use of substances over the period the patch was worn, usually 1 to 2 weeks, but can be up to 4 weeks. Drawbacks to this method include possible external contamination and the loss of patch adhesion over time, which can result in the sweat patch falling off for some patients [24,48].

See Table 4 for more information about the advantages and disadvantages of sweat testing in comparison to other matrices.

Use of Sweat Testing in Addiction Treatment

As a new technology, little research exists regarding the use of sweat testing in addiction treatment settings. At this time, there is insufficient evidence to support the routine use of sweat testing in addiction treatment. More research is needed before sweat testing can be recommended over urine testing in clinical settings.

An overview of sweat testing literature considers the practice to be promising [32]. A wide detection window that captures any substance use may be advantageous for some patients, although that window comes with the tradeoff of delay between use and therapeutic response. Sweat testing is also a form of prospective detection, that is, the device is applied prior to the activity that it is supposed to detect. For patients who view testing as having a helpful deterrent effect, prospective testing methods may be additionally beneficial (see *Clinical Use of Drug Testing*, p. 5). The sweat patch also offers a passive collection technique that does not require intensive staff training.

Hair

Basics of Hair Testing

Hair can be thought as a continuous collection device which absorbs compounds as blood passes through the hair

follicle and as sweat gathers and is absorbed around the base of a growing hair shaft. Scalp hair is the most commonly tested sample, but pubic, armpit and facial hair can be also be used. Head hair provides a window of detection of approximately 3 months; body hair, which grows much more slowly, can be used to detect use up to 12 months [49,50]. Hair testing does not detect recent use or impairment. Hair takes approximately 8 days to grow from the follicle to above the scalp, making it possible to collect. Drug and metabolite compounds in hair also begin to degrade over time, limiting interpretation to segments of hair grown in the prior 3 months. Chemical treatments such as dyeing, bleaching, perming, and straightening can alter the structure of hair and degrade drug compounds that may be present [51].

The literature on hair testing shows variability in drug absorption based on hair's characteristics, including pigmentation, texture and porosity, which may lead to incidental racial discrimination [42,52]. Drug compounds are incorporated into dark and thick hair at greater concentrations compared to lighter or thinner hair, although large sample studies suggest these differences do not lead to a significant race effect.

Hair testing appears to be useful for detecting amphetamines, cocaine, opioids, phencyclidine, and MDMA, but less so for marijuana [53].

See Table 4 for more information about the advantages and disadvantages of hair testing in comparison to other matrices.

Use of Hair Testing in Addiction Treatment

The routine use of hair testing is not appropriate for most addiction treatment settings. While the primary advantage of hair testing is the wide window of detection, hair testing is costly, and interpretation of hair test results is potentially discriminatory and can be confounded by passive external contamination.

The window of detection for hair testing is clinically relevant in a few situations. Practitioners may want to know about a patient's past 3-month substance use when assessing a patient and creating a treatment plan. Hair testing may also be useful during long-term monitoring. The cost may be prohibitive, however, if repeated tests are needed over a long period of time.

Collection of Hair Samples

If hair is collected, patients should be asked about their use of chemical hair treatments (eg, dying, bleaching, perming, and relaxers) at the time of sample collection. Use of chemical hair treatments should be recorded and non-head hair (ie, pubic, arm, beard) or an alternative specimen should be collected if possible.

Summary of Recommendations

Urine

Use of Urine Drug Testing in Addiction Treatment

- Urine should be considered the most well-established and well-supported biological matrix for presumptive detection of substance use in a clinical setting.
- Urine should be considered the best established matrix for POCTs.
- If tampering is of high concern or appropriate measures to reduce the likelihood of tampering cannot be taken, providers should consider using an alternative specimen type.

Urine Sample Integrity

- Urine should be considered the matrix most prone to sample tampering through dilution, adulteration and substitution.
- Providers should choose collection methods that protect patients' dignity and privacy while minimizing opportunities for tampering.
- Observed sample collection can deter urine sample tampering; if there are concerns about tampering, collection should be observed by a same-gender staff member.
- Observed urine sample collection does not completely prevent sample tampering; providers should consider other strategies to mitigate urine sample tampering.
- Providers should consider the use of an unobtrusive sample collection method for patients with a history of psychological trauma, especially sexual trauma.
- Providers should employ appropriate measures in the facility where patients provide specimens to decrease the likelihood of urine sample tampering during unobserved collection.
  - Do not allow personal items in the collection area.
  - Ensure that potential adulterants, such as soap, ammonia, or bleach are not readily available in the collection area.
  - Consider placing blue dye in the toilet and turn off the water source to the collection area during collection.
- If a provider suspects that a patient has engaged in substance use but continues to produce negative urine test results, sample collection should be observed and specimen validity testing should be conducted.
- If a sample is suspected of having been tampered with, it should be tested for specimen validity including creatinine concentration, pH level, specific gravity and adulterants.
- All samples undergoing definitive testing should be tested for creatinine concentration, pH level and specific gravity (if creatinine is low).

Signs of Urine Sample Tampering

- All urine samples should be checked for unusual specimen characteristics. Characteristics include:
  - Temperature outside expected range of 90–100 degrees within 4 minutes of production (This can be checked using a heat sensitive strip).
  - Unusual color or smell, soapy appearance, cloudiness or particles floating in the liquid.
- If a urine sample exhibits unusual specimen characteristics, the sample should undergo specimen validity testing to help identify whether and how tampering occurred.

Responding to Specimen Validity Test Results

- Providers should consider samples that have been tampered with to be presumptive positive.