Drug Testing:
A White Paper of the American Society of Addiction Medicine (ASAM)

October 26, 2013

DRUG TESTING: A WHITE PAPER OF THE AMERICAN SOCIETY OF ADDICTION MEDICINE

Adopted by the Board of Directors 10/26/2013

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Development Process

Multiple drafts of the Drug Testing White Paper were developed by the ASAM Drug Testing White Paper Writing Committee. Inputs were collected and integrated into each subsequent draft. Four teleconferences of the Writing Committee were held to explore controversial and/or unresolved issues in the White Paper.

This final draft of the White Paper was reviewed by the ASAM Public Policy Committee and ASAM Chapters Council. The Writing Committee integrated the feedback collected from these groups into the culminating White Paper which was reviewed and approved by the ASAM Board of Directors.

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I. Preface

Recognizing that drug testing is vastly underutilized throughout health care, the American Society of Addiction Medicine (ASAM), the nation's largest organization of physicians specializing in the prevention and treatment of addiction, has produced this White Paper to highlight the wide range of applications in which drug testing can promote prevention, early detection, and lifelong recovery*[1] from addiction*[2] in the interests of individual and public health. ***This paper describes the uses of drug testing as a primary prevention, diagnostic, and monitoring tool to identify the presence or absence of drugs of abuse* or therapeutic agents related to addiction management in multiple settings.***

Drug tests identify a chemical compound – a "drug"* – in body fluids or tissues. A test is "positive" if the specific compound is present in the sample at a concentration at or above the limit of detection*[3] for that compound. The identification of a drug in a drug test provides evidence of exposure to that drug. In many settings drug testing also includes alcohol testing.

This White Paper encourages wider and "smarter" use of drug testing within the practice of medicine and, beyond that, broadly within American society. Smarter drug testing means 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

[1] All terms followed by an asterisk (*) are defined in the glossary.
[2] "Addiction" is a widely used term but is not a diagnosis in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5). The DSM-5 chapter on "substance-related and addictive disorders" includes substance use disorders measured on a continuum (mild, moderate or severe) for each specific substance, and includes non-substance-related disorders, specifically gambling disorder. "Drugs of abuse" are chemicals that produce brain reward – either producing good feelings (positive reward) or relieving bad feelings (negative reward) – within seconds to minutes after administration. Many people use these drugs in ways and in amounts that cause problems, including substance use disorders. The brain reward process responds not only to drugs of abuse but to other behaviors and substances that produce pleasure or remove bad feelings (e.g. food, exercise, work). Many serious problems caused by drug use occur in people who are not addicted, that is, who do not have a substance use disorder. People with no personal history of a substance use disorder can die from a drug overdose or be impaired and cause a fatal motor vehicle crash. For this reason while we use "addiction" in this White Paper to refer to the presence of a substance use disorder, specifically in "addiction treatment", we commonly also use the more objective and comprehensive terms "drug use", "drug users", and "drugs of abuse."
[3] See the glossary for differences in the related *limit of detection*, *limit of quantitation* and *cut-off*.

drugs rather than only testing for the traditional five-drug panel[4] 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.

This White Paper explains the science and current practice of drug testing in various contexts and outlines the ways in which drug testing can be used more effectively in medical practice. We focus on ways that physicians, other health care providers, and others can use drug testing to discourage nonmedical drug use* and diversion* of controlled substances,* to encourage appropriate entry into addiction treatment,* to identify early relapse and to improve outcomes of addiction treatment through the use of long-term post-treatment monitoring.*

This White Paper is not a textbook on drug testing. Instead, it relies on and references abundant primary sources, including a recent publication from the Center for Substance Abuse Treatment (CSAT).[5] This document describes what is new and what is largely neglected by other publications: promising areas in which drug testing is currently either unused or underused. The White Paper focuses on the science and the principles of drug testing. It encourages the new generation of practice-oriented drug testing research which is needed to guide decisions to achieve the best outcomes at affordable costs in the wide variety of settings in which drug testing is useful.

Drug testing is a rapidly evolving technology that can identify the use of specific drugs. Importantly, drug testing can also reveal the absence of prescribed medications, opening a

[4] Often referred to as the "SAMHSA-5" (of the Substance Abuse and Mental Health Services Association) or the "DOT-5" (of the Department of Transportation), this drug test panel is part of federal requirements for federally mandated workplace testing discussed in greater detail later in this paper.

[5] Center for Substance Abuse Treatment. (2012).Clinical drug testing in primary care. *Technical Assistance Publication (TAP) Series, 32*. DHHS Publication No. (SMA) 12-4668. Rockville, MD: Substance Abuse and Mental Health Services Administration; Center for Substance Abuse Treatment. (2006). Detoxification and substance abuse treatment: *Treatment Improvement Protocol (TIP) Series, No. 45*. DHHS Publication No. (SMA) 06-4225. Rockville, MD: Substance Abuse and Mental Health Services Administration.

differential diagnosis which may include hoarding,* binge use,* pseudoaddiction,* various other forms of misuse,[6] diversion that is often a component of the disease of addiction, as well as a possible diagnosis of a substance use disorder* (SUD). ***Drug tests provide information about recent use of drugs, but drug tests do not identify substance use disorders or physical dependence.*** Identifying the use of drugs through drug testing is especially important because many people who use drugs conceal their drug use. An unexpected positive drug test result[7] or, in some cases, an unexpected negative drug test result necessitates a careful evaluation including a discussion with the patient. In many situations, lack of a legitimate medical explanation for the test result is a signal for swift, meaningful and sustained intervention. Drug testing results can inform and improve communication between the health care provider and the patient or other party who is the subject of drug testing, such as a participant in a monitoring program for licensed health professionals or a person working in a safety-sensitive occupation. Talking with an individual who has tested positive, rather than reflexively taking action, can prevent inappropriate reactions to a positive test result and begin a collaborative effort to solve a problem.

Drug testing is not the only way to identify drug use, misuse, diversion or a suspected substance use disorder or relapse.* Valuable information can be obtained by asking individuals about their drug use. Interviewing collateral sources of information such as family members (with patient consent in health care contexts) can also provide important information about drug use. However, because it is common for drug users to minimize or deny drug use, it is important to use drug testing as an objective assessment tool and patient advocacy/support tool.

This White Paper is not a compendium of all the guidance needed to use or interpret drug tests. It is a thoughtful summary of the current state of drug testing. Its authors recognize that drug testing is an important technology of medical practice that can be successfully used in many medical and nonmedical settings to promote individual and public health and safety. We begin by describing the experience of drug testing today and encouraging expanded drug testing, especially by physicians specializing in addiction medicine, addiction psychiatry, pain medicine, emergency medicine, and primary care, among many others.

[6] The term “misuse” is used in this paper for the purpose of brevity to refer to non-addictive drug use that is harmful or a risk for the user. This can include nonmedical use of prescription drugs and illicit drug use.
[7] Unexpected positive test results include the presence of: illicit drugs, controlled substances for which the individual is not prescribed, or levels of prescribed controlled substances that are inconsistent with medical treatment.

In this White Paper, ASAM reviews the current use of and considerations related to drug testing in many medical specialties and important nonmedical settings. In a separate document ASAM will develop specific recommendations for drug testing in addiction medicine. ASAM will be pleased to work with the leaders in other medical organizations to develop specific recommendations for the use of drug testing in other specialties and other medical settings.

II. The Science of Drug Testing

Drugs of abuse are chemicals that produce specific effects in the user's brain, particularly in the reward circuitry of the brain. In general, drugs of abuse either produce good feelings (positive reward) or relieve bad feelings (negative reward) within seconds to minutes after administration. ***The most important contribution of the scientific study of addiction in the last half century has been the new understanding of the neurobiology of brain reward.*** The power of brain reward is demonstrated both by the high prices that drug users pay to acquire drugs and the risks to health, family, livelihood, and life itself that they take to repeatedly experience drug effects. Drug-induced brain reward is not specific to the human brain but is also seen in other animals, from fruit flies to monkeys.[8] When animals that have learned to use drugs are given access to them, they self-administer these drugs and work hard to repeat the experience, often working harder for drugs than for natural rewards such as food and sex.[9] Many drugs influence the brain but do not produce brain reward and thus do not induce drug-seeking behavior. For example, antidepressants and mood stabilizers, such as fluoxetine, amitriptyline, and lithium, profoundly affect the brain but do not produce brain reward. Thus, they are not drugs of abuse.

Drugs can be administered by many routes, including inhalation (including smoking); nasal insufflation ("snorting"); oral (buccal or sublingual) absorption; oral ingestion; subcutaneous, intramuscular or intravenous injection; and, by transdermal, vaginal and rectal absorption. Experienced drug users generally prefer routes of administration that produce the most rapidly rising brain concentrations of drugs, especially smoking, snorting and intravenous injection. While the specific circuits of brain reward are the targets of all drugs of abuse, drugs are distributed throughout the body and are metabolized to breakdown products (primarily in the

[8] DuPont, R. L., Madras, B. K., & Johansson, P. (2011). Drug policy: A biological science perspective. In J. H. Lowinson & P. Ruiz (Eds.) *Substance Abuse: A Comprehensive Textbook* (5th ed., pp. 998-1010). Philadelphia, PA: Lippincott Williams & Wilkins.

[9] Galaj, E., Cruz, I., Schachar, J., Koziolek, M., & Ranaldi, R. (2013). Differential effects on natural reward processing in rats after repeated heroin. *Psychopharmacology (Berl)*. [Epub ahead of print]

liver), facilitating their elimination (mostly in urine and feces). Drug metabolites may be present in biological matrices* in higher concentrations and for longer periods of time than the parent drugs themselves, and thus, when they are analyzed in drug testing sometimes serve as specific and superior markers of drug use.

Drug tests do not detect drug use "in general." Instead, drug tests identify specific drugs or drug classes as well as drug metabolites in biological matrices that are represented in particular test panels.* Drugs can be identified in any matrix; the most common matrices for typical testing purposes include urine, blood, oral fluid, hair, nails, sweat and breath. However, because of the distinctive physicochemical characteristics of each drug (and its metabolites), its concentration may vary greatly among these matrices. Because drug testing technology is rapidly improving in sensitivity* and specificity*, it may soon be possible to test for additional compounds in breath, as is now possible for alcohol. With the growing use of synthetic cannabinoids[10] (e.g. "K2" or "spice"), synthetic cathinones[11] (known as "bath salts"), and other novel compounds,[12] drug testing has become even more challenging. The range of widely misused drugs dramatically increased in recent years, in part to evade detection by drug tests. These new synthetic drugs are commonly called "designer drugs"* because they are designed to produce psychoactive effects similar to compounds familiar to drug users but to elude drug tests and drug laws.

[10] Center for Substance Abuse Research. (2013, April 29). Synthetic marijuana third most reported substance used by U.S. high school students. *CESAR Fax, 22*(17). Available: http://www.cesar.umd.edu/cesar/cesarfax/vol22/22-17.pdf

[11] Prosser, J. M. & Nelso, L. S. (2012). The toxicology of bath salts: a review of synthetic cathinones. *Journal of Medical Toxicology, 8*(1), 33-42. Available: http://link.springer.com/article/10.1007/s13181-011-0193-z

[12] Fattore, L., & Fratta, W. (2011). Beyond THC: the new generation of cannabinoid designer drugs. *Frontiers in Behavioral Neuroscience, 5*(60),1-12.

Box 1: Forensic Drug Testing Versus Clinical Drug Testing

In forensic* drug testing, safeguards are in place so that every result can stand up to legal challenges. False positives* are a serious concern so properly constructed forensic testing programs are designed to virtually eliminate such results. Standards for federally-mandated workplace forensic testing address specimen chains of custody*, split specimens*, confirmation of all presumptive positive* or non-negative* test results in laboratories certified by the Department of Health and Human Services (DHHS)/Substance Abuse and Mental Health Services Administration (SAMHSA), review of test results by a Medical Review Officer,* as well as other issues.

Unlike forensic drug testing where the test results must be able to meet rules of evidence in administrative, civil or criminal proceedings, clinical drug testing* is part of a patient examination performed by a clinician with whom the patient is in a therapeutic relationship. The testing is used for the purposes of diagnosis, treatment, and the promotion of long-term recovery. Clinical drug test results must meet the established standards of medical practice and benefit the therapeutic relationship, rather than meeting the formal legal requirements of forensic testing. Drug testing in medicine employs the same sound procedures, safeguards, and systems of information management that are used for all other health-related laboratory tests, tests on which life-and death medical decisions are commonly made.

The majority of drug testing done today includes elements of forensic and clinical drug testing. For example, one might assume that drug testing of individuals on probation or parole in the criminal justice system is performed according to the requirements of forensic testing; however, this drug testing does not follow the rigorous federal standards for workplace drug testing programs and is not forensic in nature.

1. The Evolution of Drug Testing

The contemporary history of drug testing can be divided into three overlapping generations of technology, the details of which are described in detail in the next section, ***2. Drug Testing Technologies***. The history of drug testing in the United States provides a useful background for understanding how drug testing conducted today and the future opportunities for drug testing.

Drug testing was first widely used in the U.S. in the 1950s in hospital emergency rooms in order to rapidly diagnose and guide the treatment of patients who had overdosed. Testing was also important in death investigations. In cases of poisoning, the testing was appropriately referred to as toxicology testing (thus, the phrase “tox screens”). Most of this early drug testing used blood as the testing matrix. Not until the 1960s, with the development of thin layer chromatography,* did testing for drugs of abuse in urine become feasible in large populations.

In the 1970s, the development of sensitive and automated immunoassay* (IA) technologies conducted in laboratories permitted large scale urine drug testing in addiction treatment and in the criminal justice system. IA technology is widely used today in some circumstances as a stand-alone technique either through laboratory or point-of-collection* (POC) options. Immunoassay methodologies were the first drug testing technology to be automated, permitting high volume testing and lower costs per test. Particularly in addiction treatment and corrections settings, further analysis or "confirmation" of presumptive positive IA test results was seldom performed because the pre-test probability of positive results was usually high, tests were performed serially, and severe consequences generally did not ensue as a result of a single positive test.

In the 1970s, drug testing became routine in methadone maintenance treatment* (MMT), one opioid treatment program* (OTP), that was established throughout the country. Drug testing validated a program's success in reducing opioid and other nonmedical drug use. The rate of negative drug test results, a marker for cessation of drug use, became a central quality measure in assessing treatment outcomes in methadone-based OTPs developed under the regulatory authority of the Food and Drug Administration (FDA), the Substance Abuse and Mental Health Services Administration (SAMHSA), and Drug Enforcement Administration (DEA).

The first U.S. military drug testing also used IA technology and took place in 1971 in Vietnam, when American soldiers were commonly using heroin and other illegal drugs.[13] Drug testing screened soldiers before they were approved to return home after their tours of duty. Soldiers who tested positive were held behind until they produced negative drug test results. Not only did drug testing permit objective evidence of drug use and identify the most commonly used drugs among soldiers, but it also provided an incentive for soldiers to refrain from illicit drug use in order to hasten their return home. In 1974, a random drug testing protocol was implemented by the military to identify and refer drug users to treatment.[14]

The second generation of drug testing, IA testing with presumptive positive results confirmed by gas chromatography-mass spectrometry* (GC-MS), was introduced in the military in the early 1980s and shortly thereafter adopted by private industry, the federal government, and federally regulated industries (e.g. commercial drivers). Workplace drug testing remains

[13] U.S. Department of Defense. (n.d.) Military program historical timeline. (updated 2012). Available: http://prhome.defense.gov/RFM/READINESS/DDRP/timeline.aspx
[14] Ibid.

the most widespread model for forensic drug testing and continues to dominate the drug testing industry.

Drug testing following the 1981 crash of an aircraft aboard the USS Nimitz led to the recognition that illicit drug use was prevalent among Navy personnel. Shortly thereafter the Department of Defense recognized that illegal drug use was prevalent in all the military services. This led, in the same year, to the mandatory random drug testing of all active-duty military personnel. Positive test results commonly led to referral to substance use disorder treatment. Repeated drug use by enlisted personnel, and any drug use by officers after the military's initial attempt at rehabilitation, led to punitive actions, including less-than-honorable discharge and loss of veterans' benefits. This was the first large-scale use of drug testing as a drug use deterrence and prevention strategy.

In the 1980s, in the context of the cocaine epidemic in the U.S., drug testing became widespread in the civilian workforce to discourage drug use that could impair workforce productivity and safety. For example, following a series of highly publicized crashes, drug testing became a universal procedure for commercial drivers and others in safety-sensitive positions, including aircraft pilots and railroad engineers. In some workplace settings a positive test of an employee led to immediate termination. In others a positive drug test was a trigger for intervention, referral to addiction treatment, and follow-up drug testing to ensure continued abstinence.

The introduction of drug testing into the workplace produced controversy over privacy issues, leading to two Supreme Court decisions.[15] The controversy was intense because the consequence of a single confirmed positive test was often termination or denial of employment. Prescribed controlled substances were becoming increasingly common in the workplace and thus, needed to be addressed in order to balance legitimate medical treatment with workplace safety concerns. These challenges led to mandatory federal workplace drug testing guidelines enforced by explicit action of the U.S. Congress for interstate truck drivers regulated by the federal Department of Transportation (DOT) under 49 CFR Part 40 in the Code of Federal Regulations.[16] These guidelines specified every aspect of drug testing, including 1) the panel of

[15] Skinner v. Railway Labor Executives' Association, 1989; National Treasury Employees Union v. Von Raab, 1989.
[16] 49 CFR Part 40, Procedures for Transportation Workplace Drug and Alcohol Testing Programs. Information can be found online at the United States Department of Transportation Office of Drug & Alcohol Policy and Compliance at: http://www.dot.gov/odapc

five drugs (or drug classes) to be tested (the "SAMHSA-5"), 2) the confirmation of all presumptive positive IA results with highly specific and sensitive GC-MS testing, and 3) the use of Medical Review Officers (MRO) to evaluate all confirmed positive test results. Workplace drug tests were generally limited to pre-employment settings and to safety-sensitive employees, including an estimated 10 million commercial drivers. These efforts deterred illicit drug use in the workplace, especially among commercial drivers, where studies demonstrated a reduction in fatalities after the widespread implementation of drug testing.[17] [18] An imperative in workplace testing was to minimize false positive results, even at the cost of many false negative* results. Because workplace drug testing quickly dominated the drug testing market, the federal drug panel and the use of urine as the test matrix of choice became the standard drug testing procedure in virtually all settings. Clinicians hoping to use drug testing in health care were sometimes frustrated because commercial laboratories steered them to the very limited testing panel employed by the Department of Transportation.

In the 1990s, building on the military and workplace experiences of drug testing as a prevention tool, random student drug testing (RSDT) was extended to secondary schools. Again, conflicts arose over privacy issues, leading to two Supreme Court decisions.[19][20] Support for RSDT from the courts was based on the recognition that public schools were responsible, in part, for maintaining the safety and health of students while they participated in school-related activities. The federal government expanded the use of RSDT as part of comprehensive, non-punitive drug prevention strategies not to expel drug-using students but to keep them in schools.[21] [22]

In the first decade of the 21st century, drug testing became increasingly widespread in highway safety, as drug testing was added to alcohol testing for drivers arrested for being impaired and drivers involved in serious and fatal accidents. ***Promoting the increased use of drug testing now is part of a new national effort, led by the Office of National Drug***

[17] Jacobson, M. (2003). Drug testing in the trucking industry: The effect on highway safety. *Journal of Law and Economics, 46*(1), 131-156.
[18] Swena, D., & Gaines, W. (1999). Effect of random drug screening on fatal commercial truck accident rates. *International Journal of Drug Testing, 2*(1), 1-13. Available: https://www.criminology.fsu.edu/journal/drugscreen.pdf
[19] Vernonia School District 47J v. Acton, 1995.
[20] Board of Education of Independent School District No. 92 of Pottawatomie County, et al, Petitioners v. Lindsay Earls et al, 2002.
[21] Office of National Drug Control Policy. (2002). What You Need to Know about Drug Testing in Schools. NCJ publication no. 195522. Washington, DC: Office of National Drug Control Policy.
[22] Office of National Drug Control Policy. (2004). What You Need to Know about Starting A Student Drug-Testing Program. NCJ Publication no. 206126. Washington, DC: Office of National Drug Control Policy.

Control Policy and the Department of Transportation, to respond to the serious, and previously largely overlooked, problem of drugged driving.[23] The recent reduction or elimination of prohibitions against marijuana use in many states related to medical use, decriminalization, and legalization is leading to more marijuana use and is increasing the threat to highway safety posed by the use of this drug.[24]

Within the past few years an additional confirmation testing option has become available, liquid chromatography-mass spectrometry* (LC-MS) or tandem mass-spectrometry (LC-MS/MS). LC-MS/MS is increasingly an alternative to GC-MS to identify specific drugs or metabolites that are present in a specimen through a POC or laboratory IA test. GC-MS and LC-MS/MS tests "confirm" drugs that were identified on the initial IA test.

Historically, screening by immunoassay and confirmation by GC/MS was the standard. More recently, advances in analytical sciences allowed some laboratories to offer definitive* or identification testing* without initial screening of the specimen. This reflects the third generation of drug testing technology, one that uses LC-MS/MS as an initial testing technique to rapidly identify a far larger number of drugs than is possible with IA including opioids and other medicines for chronic pain treatment and other medical conditions. Definitive testing methods, such as LC-MS/MS and similar methods, may offer significant advantages over screening/confirmation strategies. This is called drug identification because there is no previous test on the specimen to confirm. When warranted, an initial LC-MS/MS test screening for many drugs can be confirmed by another different LC-MS/MS method.

Testing for drugs of abuse in medical practice today is rapidly increasing in the area of pain management because the increased use of opioids to treat chronic pain is paralleled by increases in opioid and other drug diversion, as well as morbidity and mortality related to the misuse of these drugs. The problem of prescription drug abuse* and resulting overdose deaths was labeled an "epidemic" by the U.S. Centers for Disease Control and Prevention.[25] [26] ***The***

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[23] Office of National Drug Control Policy. (2012). National Drug Control Strategy, 2012. Washington, DC: Office of National Drug Control Policy. Available: http://www.whitehouse.gov/sites/default/files/ondcp/2012_ndcs.pdf

[24] American Society of Addiction Medicine. (2012). White Paper on State-Level Proposals to Legalize Marijuana. Chevy Chase, MD: American Society of Addiction Medicine. Available: http://www.asam.org/docs/publicy-policy-statements/state-level-proposals-to-legalize-marijuana-final2773DD668C2D.pdf?sfvrsn=2

[25] Centers for Disease Control and Prevention. (2012). CDC grand rounds: prescription drug overdoses – a U.S. epidemic. *Morbidity and Mortality Weekly Report, 61*(1), 10-13. Available: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6101a3.htm

relatively recent dramatic rise in the misuse and diversion of prescription medications, as well as in rates of addiction and overdose deaths, prompted increases in drug testing, which are now spreading into other areas of medicine outside addiction treatment and pain management. The integration of drug testing into all segments of health care is a trend that this White Paper encourages and one that this White Paper seeks to shape for the benefit of the nation's public health.

The IA and GC-MS paradigm of workplace drug testing worked reasonably well in medical settings in the 1990s, when nearly all patients with substance use disorders used a fairly limited menu of drugs. As a growing array of prescription drugs and designer drugs became available, the drug testing challenge was no longer to identify a handful of drugs, but rather to identify the scores of continually evolving compounds taken by drug users. The development of IA drug tests to identify all of these new drugs is not commercially feasible, nor is GC-MS easily adaptable to detection of the wide range of emerging drugs of abuse. This new trend in drug use and the challenges it poses to drug testing are in their early stages. Today the higher cost of the new technology limits its use. The far wider use of expanded IA screens with flexible, rotating panels may offer many benefits at lower costs. It is instructive that the earliest adopters of the LC-MS/MS technology as an identification drug test were in pain medicine.

Although beyond the scope of this paper, which focuses on currently available drug testing technologies and practices, it is important to recognize that there is a continually evolving discussion in drug testing science about appropriate analyte* selection for detecting a drug and the quantity and timing of drug administration. Some drug users obtain prescriptions for legal drugs to mask their illegal drug use such as obtaining a prescription for dronabinol (Marinol®) to disguise marijuana use. In such a case, it would be helpful to test for THCV, a homologue of THC, the active ingredient in marijuana. THCV is present in some marijuana strains but not Marinol® and could serve as a marker for use of marijuana.[27] Scientific developments may eventually result in strategies that generate more information about dose and time of administration from a single sample collection. This is not possible today. However, in many settings, especially in those involving a drug-free standard (such as in most criminal justice and addiction treatment monitoring settings), evidence of recent drug use is all that is

[26] Manchikanti, L., Helm, S., Fellows, B., Janata, J. W., et al. (2012). Opioid epidemic in the United States. *Pain Physician, 15*(3 Suppl), ES9-ES38.
[27] ElSohly, M.A., deWit, H., Wachtel, S. R., Feng, S., & Murphy, T. P. (2001). Delta9-tetrahydrocannabivarin as a marker for the ingestion of marijuana versus Marinol: results of a clinical study. *Journal of Analytical Toxicology, 25*(7), 565-571.

necessary, and for this purpose current technology is adequate. The practice of drug testing in specific contexts is discussed in detail below in Section **IV. Current Applications of Drug Testing and Promising New Opportunities**.

Today, it is important not to let the best in drug testing become the enemy of the good, and to not embrace technologies merely because they are available and before their potential for improving patient care has been fully assessed. ***The most important challenge in drug testing today is not the identification of every drug that we are technologically capable of detecting, but to do medically necessary and accurate testing for those drugs that are most likely to impact clinical decisions.*** Choices of technology should be based on the clinical situation and patient risk. Cost must be considered in the choice of drug testing in balance with the clinical goals for each patient. The major need today is the wider and smarter use of the currently available drug testing technologies and practices. This White Paper is focused on the currently available drug testing options. This paper does not recommend adoption of specific testing technology or matrix over another; each drug testing technology and each matrix has important benefits that must be weighed against disadvantages, and costs, in the specific settings in which they are used.

2. Drug Testing Technologies

For decades, virtually all drug test samples were sent to laboratories with results returned days or even weeks later. More recently, point-of-collection* (POC) testing became ubiquitous, permitting detection of some drugs and/or their metabolites within minutes of collection. In clinical settings, such as outpatient clinics and residential addiction treatment programs, the term POC means ”point of care” testing, performed at the clinical site where the sample was collected, rather than performed at an off-site laboratory. POC testing, relying on IA technology, is currently limited to a relatively narrow range of drug classes and a few specific drugs (usually 15 or less) and to urine and oral fluid samples. IA drug tests are incapable of distinguishing among specific drugs within a class (e.g. amphetamines, barbiturates, benzodiazepines, opioids), are variably reactive with drugs within a class, and are vulnerable to cross-reactivity with other, sometimes unrelated, molecules. Laboratory-based immunoassays are available for scores of drugs, but because the technology requires an antibody and not all drugs elicit an antibody response (i.e. small molecules such as alcohol or ethyl sulfate), immunoassays are not available for all drugs. In addition, because of the costs associated with

the development of antibodies, IA test antibodies are developed only for drugs for which there is a large drug testing market.

Confirmation of presumptive positive results (and at times presumptive negative results) from laboratory or POC immunoassay tests is sometimes performed, potentially by GC-MS. Gas chromatography separates the different drugs or metabolites in a specimen, and mass spectrometry definitively identifies specific drugs or metabolites.[28] GC-MS analysis typically focuses on a select group of related compounds and to achieve this selectivity may involve cumbersome and time-consuming extraction and chemical derivatization processes.

LC-MS/MS, like GC-MS, can confirm immunoassay results.[29] LC-MS/MS uses the separation technique with two mass spectrometers placed in tandem to detect a drug's unique ions secondary to fragmentation of characteristic precursor ions. The two-stage mass fragmentation process significantly improves identification of drugs and metabolites when coupled with liquid chromatographic separation. As a confirmatory test of IA presumptive positive results, LC-MS/MS is easier and quicker to perform than GC-MS since it does not necessarily require derivatization prior to analysis. LC-MS/MS confirmation of an IA test can be reported as positive or negative based on a predetermined cut-off concentration for a drug, or alternatively, with the specific concentration of the drug or metabolite, commonly referred to as "quantification"*.

Although POC testing has great utility in providing rapid results, there are limitations with regard to specificity and accuracy compared to mass-spectrometry methods, see **Box 2: LC-MS/MS Drug Testing Technology**.

[28] Gourlay, D. L., Heit, H. A.. Caplan, Y. H. (2012). Urine Drug Testing in Clinical Practice: The Art & Science of Patient Care. John Hopkins University School of Medicine (5th edition). Available: http://www.udtmonograph.com/

[29] Willette, R. E., Kadehjian, L. J. (2002). Drugs of abuse test devices. In A. J. Jenkins & B. A. Goldberger (Eds). On-Site Drug Testing. Totowa, NJ: Humana Press.

Box 2: LC-MS/MS Drug Testing Technology

LC-MS/MS can independently of immunoassay (IA) tests identify a multitude of drugs and their metabolites. A common list of drug tests available for LC-MS/MS of urine and oral fluid from a well-established laboratory provides clinicians a choice of up to 65 specific drug analytes to test, including opioids, stimulants, benzodiazepines, muscle relaxants, barbiturates, tricyclic antidepressants, SSRIs, sedatives/hypnotics, and illicit and other non-prescription drugs.[30] The more drugs that are included in a single LC-MS/MS test, the less sensitive and specific the results. Some laboratories that use LC-MS/MS only may run an initial LC-MS/MS test with a large drug test panel and then a second LC-MS/MS confirmation test with a smaller panel of the drugs detected on the initial test.

LC-MS/MS offers several advantages over IA, including greater sensitivity, greater specificity, and the ability to rapidly detect multiple drugs at one time, including opioids and adjunctive medications for treating people with chronic pain and other medical conditions. The ability of LC-MS/MS to detect low concentrations of drugs in small matrix volumes makes it ideally suited for the rapidly emerging field of oral fluid drug testing. Even an LC-MS/MS analysis screening for 65 (or more) drugs fails to detect many of the literally hundreds of drugs currently used in the United States (see Figure 3 under ***9. What Drugs to Test***).

One examination of LC-MS/MS results following immunoassay POC testing in addiction treatment settings found high rates of clinically false negatives, that is, samples tested by POC were reported negative but LC-MS/MS results were positive.[31] Twenty-nine percent of opioids other than methadone identified by LC-MS/MS were missed by POC tests; 28% methadone, 43% amphetamines, 35% benzodiazepines, 40% cocaine and 20% marijuana. Additionally, investigators found rates of office-based false positive results including 22% of opioids other than methadone identified as positive on POC but negative on LC-MS/MS, 46% methadone, 21% amphetamines, 61% benzodiazepines, 12% cocaine and 21% marijuana.

LC-MS/MS in clinical drug testing is still relatively new. The LC-MS/MS instruments are expensive and the technology is offered by relatively few laboratories at the writing of this White Paper. The LC-MS/MS analysis requires assay development. According to the Food and Drug Administration (FDA), the LC-MS/MS assay is a laboratory-developed test* (LDT) and thus is subject to guidelines from FDA and the Clinical Laboratory Improvement Amendments (CLIA). Each laboratory develops methods based on their own testing requirements, while reading and interpreting of the mass spectrum takes training and expertise. There are also many different types and brands of LC-MS/MS instruments.

Costs of LC-MS/MS tests are highly variable but usually higher than IA tests followed by GC/MS confirmation. Check with individual laboratories offering this test to determine prices.

The difference in accuracy between various testing technologies demonstrates the importance of carefully reviewing all elements of drug testing, beginning with purpose of the test

[30] Alere Toxicology. (2013). Drug detection and monitoring chart: Common drug of abuse.
[31] Passik, S., Heit, H., Rzetelny, A., Pesce, A., Mikel, C., & Kirsh, K (2013). Trends in drug and illicit use from urine drug testing from addiction treatment clients. Proceedings of the International Conference on Opioids. Boston, MA.

and what specific information is needed from results. For example, it may be desirable to have more sensitive and specific results (e.g. an immunoassay test followed by confirmation GC-MS or LC-MS or stand-alone LC-MS/MS testing) when making difficult-to-reverse clinical decisions (e.g. treatment discharge, major changes in medication therapies, changes in legal status).

Recent developments in drug testing technology and the emergence of widespread testing in medicine, especially in pain management, focused on a broader range of drugs and on the fact that tests with smaller drug panels and lower sensitivity and specificity fail to detect drugs that are present in many samples. This can lead to high rates of false negative results. The fact is that even the most sensitive tests with the broadest drug panels do not detect all drugs use all the time. Many drug users "pass" drug tests because they have not used a drug in the few days before the test was administered, the particular drugs they were using were not present, even on an extended panel they have adulterated their urine sample to mask the presence of drugs or drank large quantities of fluids to reduce drug concentrations.

3. The Costs of Drug Testing

Drug testing is expanding rapidly with dramatically improved technology and intense competition. In parallel, drug testing applications are expanding rapidly with innovative testing strategies in different populations. Because the costs of drug tests vary widely, it is important to clarify the purpose of testing, select a testing strategy that matches this purpose, and to ensure that the cost of testing aligns with the expected benefits.

Drug testing in a population without a high prevalence of substance use disorders commonly involves infrequent, inexpensive IA testing for a relatively small panel of commonly abused drugs, followed by confirmatory testing of presumptive positive results. This type of testing is typically found in workplace and school settings. Because of both the competition in this area of drug testing and the relative simplicity of the testing methodology, costs for this type of testing decreased steadily in recent years.

The costs of testing in these settings are not limited to the tests alone, i.e. costs of laboratory analysis or the purchasing of POC materials. Costs of facilitating the testing process include those related to specimen collection, designing and implementing random specimen collection schedules, providing notification of results to specific parties and the preparation of special reports, data storage and information management systems, and managing unexpected results, all of which may be substantial. These costs are exclusive of common costs in

workplace drug testing such as medical review and administrative fees (although the costs to the employer may be mitigated by reduced worker's compensation insurance premiums in some states when Medical Review Officers are included in the drug testing program).

Testing in a population of drug users in whom determination of adherence with treatment is a significant concern sometimes requires more frequent testing, more extensive test panels, and more sensitive and specific testing techniques, although in many settings relatively inexpensive tests are useful. Similar considerations apply in parole, probation and other correctional populations at high risk of substance use. The increasing use of designer drugs, such as synthetic hallucinogens and synthetic cannabinoids, often used instead of marijuana to avoid detection by IA test devices[32], can only be detected with more advanced and expensive drug testing technologies.

Testing in other specialized settings, such as pain management, addiction treatment programs, and professional health monitoring programs also may necessitate the use of larger and more extensive drug testing panels that require more advanced and expensive testing technologies. Laboratory fees for larger panels vary widely between laboratories. With laboratory revenue and profit this high, not surprisingly, the number of laboratories providing specialized types of testing is increasing dramatically. Unfortunately, at this writing, competition between these laboratories has not yet had the same cost containment effect observed in workplace and other programs. In treatment populations with a high percentage of presumptive positive (and, often, negative) IA results requiring confirmation, the costs are higher than in other populations where the rate of presumptive positive results is lower and where presumptive negative IA results do not receive further analysis. Physicians requiring specialized testing need to select biological matrices and drug test panels that maximize the value of the tests and that produce clinically useful results.

While routine 5-drug POC IA test panels for urine, oral fluid and sweat are inexpensive, tabletop analyzers for POC urine IA tests cost much more. Hair tests for the same limited panel of analytes also cost more than POC IA test panels. Regardless of the biological matrix chosen, as the number of analytes increases, the cost increases. As the amount of information requested increases (e.g. quantitative values of analytes and their metabolites), the costs increase dramatically because of the sensitivity and specificity of the technology required to

[32] Center for Substance Abuse Research. (2013). Synthetic cannabinoid users report using the drug to avoid positive drug tests; return to marijuana use when not being tested. *CESAR Fax, 22*(27).

acquire the information. Clinicians should have a medical necessity for each test ordered. Laboratory requisition forms should allow clinicians to order medically necessary tests for each patient. The practice of routinely ordering large, arbitrary drug testing panels with the request for LC-MS/MS screening at low cut-offs, and confirmation and quantification of all presumptive positive and negative results is a significant driver in the rapidly increasing costs of drug testing.

Programs that test larger numbers of individuals may be able to negotiate cost bundling with their laboratories. Costs are lower where bundled billing is allowed as in many workplace settings and treatment and monitoring programs. In health care settings where bundling cannot be done, the billing process is opaque and complex. The costs of drug testing are passed on to third party payers and sometimes to patients. Health insurance claims for drug testing use a formalized set of billing codes and controlled prices, many of which parallel the Centers for Medicare & Medicaid Services (CMS) reimbursement fee schedule. The details of billing and coding are complex and frequently change. A discussion is beyond the scope of this White Paper. It is important, however, for physicians to consider costs to patients and to insurers when ordering drug tests. The costs described here are estimates, and vary by matrix, methodology, test panel composition, confirmatory testing practices, payer, and laboratory.

It is ASAM policy that the elements of drug testing (e.g., matrix, drug test panel, testing technology) be determined by the ordering physician based on patient-specific medical necessity.[33] Arbitrary limits on reimbursement and restrictions on drug testing can interfere with a physician's judgment and instill discriminatory limits on addiction care.

There are also costs of drug use that extend into the overall cost of health care. For example, annual health care costs of persons with opioid addiction are eight times those for persons without this diagnosis.[34] The consequences and costs of not doing drug testing, or doing inadequate testing, may be substantial, if indirect, as clinicians will forfeit potentially important information about their patients' health status.

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[33] American Society of Addiction Medicine. (2010). Public Policy Statement On Drug Testing as a Component of Addiction Treatment and Monitoring Programs and in other Clinical Settings. Adopted July 2002, revised October 2010. Chevy Chase, MD: ASAM. Available: http://asam.org/docs/publicy-policy-statements/1drug-testing---clinical-10-10.pdf?sfvrsn=0

[34] White, A. G., Birnbaum, H.G., Mareva, M. N., Daher, M., Vallow, S., Schein, J., & Katz, N. (2005). Direct costs of opioid abuse in an insured population in the United States. *Journal of Managed Care Pharmacy, 11*(6), 469-469.

4. When to Use Laboratory Definitive Testing

In some settings, a POC or laboratory-based IA for a limited number of the most commonly used drugs, without definitive testing to confirm presumptive positive results, is sufficient. Physicians using POC testing in clinical practice should reference the POC package insert in order to determine the device's capabilities, especially for specific members of drug classes (e.g. benzodiazepines, opiates), because physicians may otherwise – and incorrectly – assume that they identify all members of a drug class. For example, in pain practice it may be important to identify a specific opioid and not just the class. In such cases, definitive testing for specific drugs of interest can be accomplished with highly specific techniques such as GC-MS or LC-MS/MS.

Although there often are clinical and financial advantages to POC testing, there are also limitations. POC IA test results are *presumptive*. The panels used for POC tests are more limited and the sensitivity and specificity of POC tests, while improving, are often not as good as those of laboratory-based IA or confirmation techniques by GC-MS or LC-MS/MS. POC tests have variable, and often limited, sensitivities for detecting synthetic and semi-synthetic members of certain drug classes. In addition, all IA tests are vulnerable to cross-reactivity from prescription, over-the-counter, and herbal medications, although such cross-reactivity is far less common today now that the more specific antibodies are in use. For this reason, the potential for false positive and false negative results on POC (and even on laboratory-based IA tests) must be considered, because there are instances where immunoassay IA tests produces negative results despite continued drug use. For example, clonazepam and lorazepam and their metabolites have poor cross-reactivity with many benzodiazepines IAs, and hydromorphone and hydrocodone have poor cross-reactivity with most opiate IAs.

It is possible to compare the results from two different brands of POC tests and between two different laboratories. While these comparisons can be useful, it must be remembered that if neither of the tests detect a given drug that is present in the sample, this can mean that they are in agreement, but both are wrong. It is therefore important not only to consider the actual costs of the tests and confirmation but the "costs" of missing drugs that may be in the sample and thus missing the drug use that exists in that donor.

Workplace drug testing protocols have specific standards set by the Substance Abuse and Mental Health Services Administration (SAMHSA). The workplace drug testing model is

built for deterrence and expects and accepts a low percentage of false negatives but not false positives. Therefore, workplace testing can use a POC or laboratory-based IA and only confirm presumptive positive drugs. The clinical drug testing model is built for detection and may require confirmation of both presumptive positive and presumptive negative test results. In any testing setting is good practice to send about 5% of presumptive negative tests to the laboratory for confirmation testing.

There is no universal standard today in clinical drug testing for medication monitoring or for drug testing in addiction treatment. This also is the case in chronic disease management where professional treatment visits occur in the outpatient setting over a span of months or even years. Over the last few years laboratories have developed a variety of testing protocols. The workplace model was adapted with success in some clinical settings so that the laboratory routinely conducts an IA test and then confirms presumptive positive results by GC/MS or LC-MS/MS. This may not be suitable in other clinical settings because of high cut-offs and because not all of the individual drugs in a class have sufficient cross-reactivity with the IA.

Some laboratories offering clinical services analyze specimens by LC-MS/MS without an initial IA screen because of the larger number of drug classes and metabolites detected and the potential savings in not using and billing the IA step. LC-MS/MS specificity and sensitivity is improved when confirming individual drugs identified on an initial screen. The LC-MS/MS assay is less susceptible than IA testing to adulteration and dilution. LC-MS/MS can detect instances in which drug, but not metabolite, is present in urine, suggesting that an individual has feigned drug administration by adding a drug directly to the urine specimen or there may be a pharmacogenetic abnormality for an individual patient that will not allow them to metabolize that medication into its metabolites.

A useful confirmation of a presumptive positive IA test result is admission of drug use by the donor. In nonclinical settings, admission of drug use in response to a positive IA test may obviate the need for a confirmation test. Similarly, in clinical settings, the clinician may decide that testing is unnecessary if a patient admits to drug use prior to collection of the sample; however, in both clinical and nonclinical settings, admissions of drug use commonly minimize extent of the drug use and all drugs being used. The practice of obtaining an appropriately observed urine collection in such situations reduces the risk of dilution or substitution but when IA technologies are employed, testing may fail to detect the drug an individual admitted to using

and/or to detect other drugs that the individual did not disclose. A history of recent drug use should not in and of itself preclude the need for testing.

5. Quantification Using GC-MS or LC-MS/MS

When presumptive positive IA test samples are submitted for confirmatory testing by GC-MS or LC-MS/MS, results are quantitative. In many settings results are reported simply as "positive" or "negative" depending on whether the analyte of interest is present or not present at or above a predetermined cut-off concentration. Quantitative concentrations of specific analytes are often provided by laboratories by GC/MS or LC-MS/MS upon request at no extra cost.

The following are examples of drug testing situations in which quantification of specific analytes by GC-MS or LC-MS/MS can be helpful:

1) In workplace testing, Department of Health and Human Services (HHS)-certified laboratories must report quantitative values to the MRO on all Department of Transportation results. Quantitative values are also required in some collective bargaining situations and by some courts; lawyers and judges sometimes want them. Having quantitative values available in court-mandated testing sometimes shortens the discovery process in an otherwise protracted legal procedure. Substance Abuse Professionals* (SAPs) also frequently ask for them. This interest in quantification on the part of parties requesting drug testing, especially in legal settings, may reflect an analogy the requestor is making to alcohol testing, a setting in which quantification is useful and familiar. While quantitative values may be required or requested in workplace testing they are rarely useful.

2) There is some interest in using quantification to clarify whether or not a positive drug test resulted from incidental or unintentional exposure to drugs. Poppy seeds contain morphine and codeine, coca tea (which is illegal to import into the U.S.) contains small amounts of cocaine, and there are amounts of alcohol present in many foods and hygiene products.

In this last case, quantitative results can be useful in the review of results for the ethanol metabolites ethyl glucuronide (EtG) and ethyl sulfate (EtS) to help distinguish incidental ethanol exposure from the ingestion of beverage alcohol. If the cut-offs are either low or at the limits of detection (LOD) this can be a problem. The use of a 500 ng/ml EtG cut-off

and a 100 ng/ml EtS cutoff largely, but not fully, obviates the need for specific quantitative results. EtG and EtS testing are discussed in more detail below under the section ***10. Alcohol Testing***.

However, it is impossible to use quantitative values to distinguish between more remote use of a drug and more immediate innocent drug exposure. For example, quantification cannot distinguish between relatively remote ingestion of morphine and more immediate consumption of poppy seeds. On the other hand, quantitative values exceeding certain limits can prove actual recent drug use. For example, the difference between 100 ng/ml morphine and 15,000 ng/ml morphine is of significant value in differentiating an instance of poppy seed consumption from morphine or heroin use.

3) In specific clinical contexts, creatinine*-corrected quantitative results for marijuana metabolites – and possibly other analytes with long detection periods – may be monitored serially in order to verify that drug use has ceased. The alternative in many clinical settings is simply to test over time and observe the results. If chronic marijuana use has stopped, testing should yield negative results within a few weeks or, in the case of chronic frequent smokers, within a few months; however, when tested repeatedly over time with no additional marijuana use some donors will test positive after testing negative because of varying urine concentrations. Hence, many clinicians insist on having THC/creatinine ratio data before taking any action on a patient's treatment plan.

4) Quantitative values are sometimes helpful in opioid testing in pain management settings. For example, a review of data from a laboratory conducting mass-spectrometry drug testing for pain management practitioners showed that for 16% of specimens, quantitative values of drug concentrations were crucial for accurate interpretation.[35] In pain management very high values of a prescribed opioid may be seen with much lower values of a non-prescribed and thus, unexpected, opioid. Such a result could arise from (1) use of another opioid, (2) production of minor metabolites of the prescribed opioid, or a (3) pharmaceutical impurity in the prescribed opioid. The most common examples of minor metabolites are the small amount of hydromorphone seen in the presence of more than 5000 ng/mL of morphine and the small amount of hydrocodone that may be seen in

[35] DePriest, A. Z., Black, D. L., Robert, T., Caplan, Y. H., & Cone, E. J. (2013). Technical note: qualitative or quantitative testing? Relative value in pain management testing. *SOFT ToxTalk, 37*(2), 16-17.

the presence of more than 5000 ng/mL codeine.[36] [37] For one commercial laboratory, hydromorphone and hydrocodone must be present at less than 15% of the total values of the far larger morphine and codeine values for the tests to be reported as negative in order to support these explanations. This limit is considerably higher than existing data support, and the clinician is well advised to discuss criteria with the chosen laboratory. There is no guarantee in these cases that only one drug was administered, but if the concentrations fit this criterion and the patient claims only taking one drug, the physician should give credence to the patient's claim.

5) Clinicians may find quantification useful to aid in the identification of patients who are rapid metabolizers of opioids, including methadone (as described in *Principles of Addiction Medicine*[38]). Such quantification is for the specific metabolite and a one-time study. Clinicians often order peak and trough blood drug concentrations as an aide to evaluate metabolism should there be a valid observed urine report discrepancy.

6) If high concentrations of parent drug in absence of metabolites are observed, tampering (e.g. post-collection addition of the drug to the sample in order to appear adherent with prescribed treatment) should be suspected and follow-up assessment conducted. This is an under-appreciated problem in pain management and has not typically been a risk factor in other areas where drug testing is employed (e.g., criminal justice settings, workplace settings, etc.). Careful monitoring of urine sample collection reduces this risk. Caution is needed before making this assumption since pharmacogenetic abnormalities can also result in a parent drug being detected without a metabolite.

In cases in which quantification is utilized, the testing laboratory should provide clinicians with explanations of potentially confusing or unusual findings. If concentrations are by definition statistical outliers and exceed those typically observed with human excretion (for a large population, independent of dose), then further patient assessment to rule out misuse may be warranted.

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[36] Gourlay, D. L., & Heit H. A. (2009). Commentary on unexpected urine drug testing results in a hospice patient on high dose morphine therapy. *Clinical Chemistry*, *55*(10), 1769.

[37] Cone, E. J., Heit, H. A., Caplan, Y. H., & Gourlay, D. (2006). Evidence of morphine metabolism to hydromorphone in pain patients chronically treated with morphine. *Journal of Analytical Toxicology, 30*(1), 1-5.

[38] Martin J, Zweben J.E., & Payte J.T. (2009). Opioid maintenance treatment. In: R. Ries (ed.). *Principles of Addiction Medicine* (pp. 675-676). Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins.

6. Drug Testing Matrices (Body Fluids/Tissues Analyzed in Drug Tests)

Drugs and their metabolites are distributed throughout the body, which means that nearly any biological matrix can be used for drug testing. Each matrix has particular strengths and weaknesses when it comes to various analytes. When selecting a test matrix, the physician should match the matrix to the information that is being sought. The matrices most commonly used are urine, oral fluid (saliva), hair, blood and sweat, while breath is most commonly used for alcohol testing. Fundamental issues in the choice of a matrix for drug testing include sample collection procedures, costs, windows of drug detection (see Figure 1), and degree of incorporation of drugs and metabolites into the biological matrix.

Advancements in drug testing technology in the 1970s changed the default testing matrix from blood to urine, because urine is copious, easily and noninvasively collected, and does not require elaborate sample preparation before testing. [39] Today, urine remains the most commonly used drug testing matrix as it has the advantage of familiarity, is typically the least expensive to analyze, and offers a wide range of drugs for inclusion on test panels. The primary problem with urine testing is that it is vulnerable to subversion or "cheating", especially in unmonitored collection situations and when donors know that they will be tested and thus can aggressively hydrate themselves, substitute “clean” specimens, or otherwise adulterate their specimens. There are innumerable strategies for subverting urine drug tests, some of which can be effective. The risk of subversion is lowered with careful monitoring of specimen collection and close supervision and/or a narrow time frame between notification of testing* and the time of specimen collection.* After a single episode of drug use, the window of detection* for most drugs in urine is 1-3 days depending upon the pharmacological characteristics of the drug. Detection periods, however, are variable and also depend on sensitivity and cutoffs of the assay, physicochemical characteristics of the drug or metabolite (e.g. lipid solubility), pattern of drug use (e.g. dose, frequency, and chronicity of use), and urine concentration.

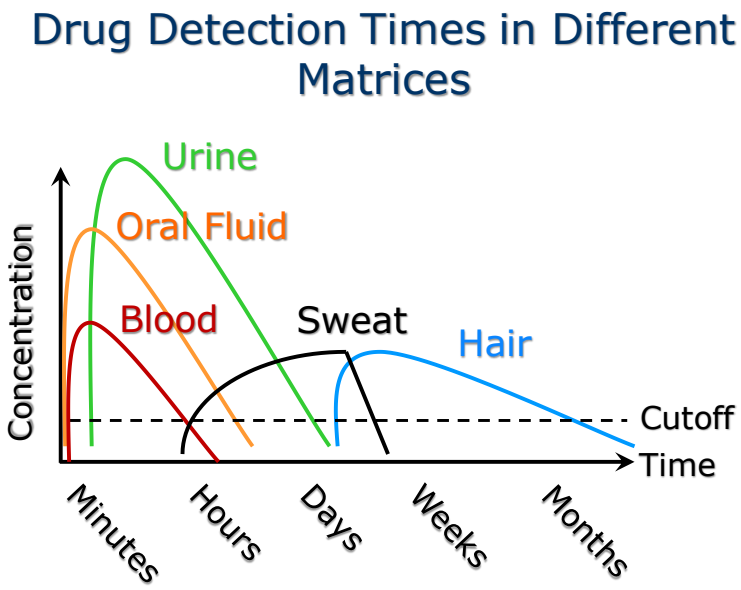
During the past decade oral fluid testing has become more widespread. This shift has been made possible by improvements in both immunoassay and mass spectrometric technologies, which are now capable of achieving the sensitivities necessary to detect many drugs in oral fluid. Oral fluid testing, like urine testing, is widely available for POC testing, and the costs are comparable. Commercially available POC oral fluid testing generally offers fewer

[39] Heit, H. A., & Gourlay, D. L. (2004). Urine drug testing in pain medicine. *Journal of Pain and Symptom Management, 27*(3), 260-267.

analytes on test panels beyond the most commonly used drugs, although broader panels are becoming commercially available. The window of detection for drugs in oral fluid is generally 12 to 48 hours, somewhat shorter than for urine. At this point, POC oral fluid tests are less sensitive to THC than oral fluid samples analyzed using laboratory-based methods, although technology is improving. Sensitivity to prescription drugs is largely unknown.

Hair and nail testing is more expensive than urine or oral fluid testing but as “repository matrices”* the typical window of detection can be as long as 90 days, depending on the length of the hair or nails – making these by far the longest windows of detection of all drug test matrices. With hair testing there may be no record of drug use in the 5-7 day period before sample collection because it takes that long for the hair to emerge from the follicle in the skin where the hair is produced. Hair and nails are metaphoric tape recordings of drug use from the time they are produced. Because head hair grows at a rate of about 0.5 inches per month, the standard 1.5 inch hair sample has information about drug use over the prior 90 days. The current fashion of men shaving their heads limits availability, and the habit of women to color their hair causes modest degradation of drugs in the matrix, diminishing somewhat the value of hair testing. In these situations it may be possible to get a nail sample. Nails are thicker than hair and appear to be less readily affected by external exposure to dyes or chemicals. Hair testing is useful in settings where testing is scheduled, because of the longer detection window. It is easy for some persons with substance use disorders or other drug users to abstain from drug use for a few days when facing a scheduled oral fluid or urine drug test. It is far more difficult for most drug users to refrain from drug use for 90 days in order to pass a hair test. However, one distinct disadvantage to hair testing is that some drug classes (e.g. benzodiazepines) are poorly detected in hair.

Figure 1. Drug Detection Times in Different Matrices[40]



Sweat patch testing is an artificial repository testing method that is used far less often than urine or oral fluid. A patch is applied to the skin for a period of 7-10 days and then removed and sent to a laboratory for immunoassay testing. The cost of sweat patch testing is similar to laboratory immunoassay testing of urine and oral fluid. Today only the minimum 5-drug panel (discussed in ***9. What Drugs to Test***) is available for sweat testing. Unlike urine, sweat testing may be more resistant to subversion because patches visibly pucker when tampered with, making attempts to subvert the test clearly visible. However, unintentional or accidental damage or lifting of a patch can occur from showering and local trauma, setting up the possibility of misidentification of intentional adulteration.

There are many laboratories conducting urine and oral fluid testing, while there are fewer laboratories conducting hair or nail testing, and only one known laboratory as of 2013 offering sweat testing.

Although blood is infrequently collected in many testing settings, it is important to understand drug disposition in this matrix. The primary mode of entry of drugs and metabolites into other biological matrices is through the bloodstream. On average, an adult human male weighing 70 kilograms has a blood volume of approximately 5 L. Following drug absorption into

[40] Cone, E. J. (2011). Oral Fluid Drug Testing Workshop: Pain Management. Society of Forensic Toxicology/The International Association of Forensic Toxicologists (SOFT/TIAFT). September 25-30, 2011. San Francisco, CA.

the bloodstream, changes in blood concentrations initially reflect changes that occur as a result of distribution and uptake by tissues. After administration, drug concentration in blood approaches equilibrium with drug sequestered in tissues. Once equilibrium is established, drug concentration declines as a result of metabolism and elimination.

The appearance of drug metabolites in blood is influenced by the route of administration. The liver is the major site of drug metabolism. Absorption of drugs from the gastrointestinal tract depends on the drug's ability to pass across intestinal cell membranes and resist metabolism in the liver (first-pass effect*). During absorption, significant metabolism may occur, so that only a fraction of the administered drug may reach the bloodstream after passing through the liver. Drug administration by non-oral routes, e.g., intravenous, transmucosal, transalveolar, and transdermal, may partially or totally bypass the liver and avoid the first-pass effect.

The detection time for drugs in blood is typically shorter than for oral fluid and urine. Detection time for opioids, cocaine, and amphetamines in blood is approximately 24 hours or less.

Breath is the standard matrix for alcohol testing because alcohol is volatile and substantially excreted through the lungs. Today, there are no commercial tests for other drugs using breath; however, because drugs and drug metabolites are present in breath and the condensate from breath, albeit at very low concentrations, as testing technologies become more sophisticated, breath testing for various drugs will become available in the future.[41] [42] [43]

The matrices have different detection windows and sensitivities. Different laboratories have different capabilities depending on their choice of immunoassay and confirmatory mass-spectrometry tests. Depending on the testing context, it can be useful to rotate the use of urine, oral fluid, and hair or nail testing so test subjects do not know what matrix will be tested. This strategy will vary by clinical setting as most clinical applications require frequent enough testing to be included within the window of detection of urine and oral fluid. Additionally, such rotation

[41] Beck, O., Leine, K., Palmskog, G., & Franck, J. (2010). Amphetamines detected in exhaled breath from drug addicts: a new possible method for drugs-of-abuse testing. *of Analytical Toxicology, 34*(5), 233-237.
[42] Beck, O., Sandqvist, S., Eriksen, P., Franck, J, & Palmskog G. (2011). Determination of methadone in exhaled breath condensate by liquid chromatography–tandem mass spectrometry. *Journal of Analytical Toxicology, 35*(3), 129 -133.
[43] Beck, O., Sandqvist, S., Dubbelboer, I., & Franck, J. (2011). Detection of Δ9-Tetrahydrocannabinol in Exhaled Breath Collected from Cannabis Users. *Journal of Analytical Toxicology, 35*(8), 541-544.

may be staff intensive. Clinicians should understand the advantages and disadvantages of each matrix before considering rotational strategies.

Oral fluid increasingly is being used as a specimen in numerous venues of drug testing including the criminal justice system, the workplace, and clinical settings such as pain management. Oral fluid tests have been shown to produce results that are equivalent to urine testing. For example, Table 1 compares results of over 340,000 general workforce oral fluid tests to over 2,500,000 general workforce urine tests and over 860,000 federally mandated urine tests.[44] Similarly, Figure 2 shows more recent data on positivity rates from over 18,000,000 urine and 600,000 oral fluid tests, in data gathered over a one-year period from specimens collected from varied testing applications.[45]

Table 1. Positivity Rates of General Workforce Laboratory-Based Oral Fluid, General Workforce Urine, and Federally Mandated Workforce Urine Drug Tests

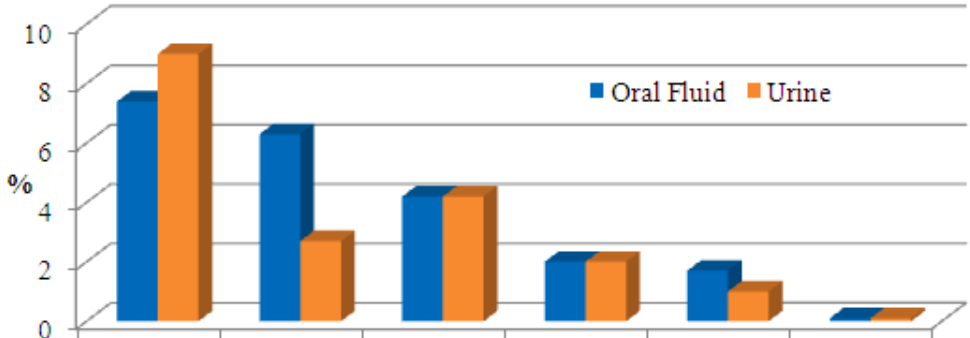
Drug Category	General Workforce Oral Fluid Drug Testing January-June 2012 (N>340,000)	General Workforce Urine Drug Testing January-June 2012 (N>2,500,000)	Federally Mandated, Safety-Sensitive Workforce, Urine Drug Testing January-June 2012 (N>860,000)
6-Acetylmorphine	-	0.018	0.015
Amphetamines	0.38	0.86	0.47
Methamphetamine	0.15	-	-
Cocaine	0.35	0.25	0.29
Marijuana/THC	3.4	2.0	0.65
MDMA	-	0.001	0.003
Opiates	0.88	0.42	0.17
PCP	0.02	0.01	0.03
Total (%)	**5.0**	**4.1**	**1.7**

Data from Quest Diagnostics'' Drug Testing Index for workplace drug tests performed January to June 2012. Available: http://www.questdiagnostics.com/home/physicians/health-trends/drug-testing.html

[44] Quest Diagnostics. (2013, March 7). Pre-employment drug test positives increase more than 5%, according to new data from Quest Diagnostics Drug Testing Index. Quest Diagnostics. Available: http://www.questdiagnostics.com/home/physicians/health-trends/drug-testing.html

[45] Redwood Toxicology Laboratories, Santa Rosa, CA – will be updated with peer-reviewed journal article citation.

Figure 2. Comparison of Laboratory-Based Oral Fluid and Urine Test Positivity Rates



	THC-THCA	AMPS	Opiates	Benzos	COC-BZE	PCP
Oral Fluid	7.4	6.3	4.2	2	1.7	0.1
Urine	9	2.7	4.2	2	1	0.1

Several organizations have accepted oral fluid as a matrix for analysis, have proposed cut-off concentrations, and are in the process of establishing testing guidelines. The European Workplace Drug Testing Society released recommendations for oral fluid testing in 2011[46] and in the United States, SAMHSA, the predominant agency for workplace test guidance, first released proposed guidelines for oral fluid testing in 2004[47] and in 2012 recommended that oral fluid be permitted as a specimen for mandated federal workplace testing.[48]

7. Collection and Storage of Samples

Sample collection (i.e. collection of body fluids and tissues) and storage can be problematic. Although urine collection is common in medical settings, it is less common in many other settings including mental health care and at the roadside. In settings where urine sample collection is common for urinalyses, it is easy to add drug testing to the laboratory checklists. Unmonitored urine collections are the rule in clinical practice since most urine analysis is for microbiology and clinical chemistry testing, not drug testing. The potential for adulteration and substitution of urine samples in unmonitored collection for drug testing must be considered. The collection of oral fluid and hair samples is easy in many settings, including addiction treatment

[46] Cooper, G., Moore, C., George, C., & Pichini, S. (2011). Guidelines for European workplace drug testing in oral fluid. *Drug Testing and Analysis, 3*(5), 269-276.
[47] Department of Health and Human Services, SAMHSA. (2004). Proposed revisions to mandatory guidelines for federal workplace drug testing programs. *Federal Register*, 69, 19673-19732. Available: http://www.gpo.gov/fdsys/pkg/FR-2004-04-13/pdf/04-7984.pdf
[48] SAMHSA's Drug Testing Advisory Board (DTAB) recommended that SAMHSA include oral fluid as an alternative specimen in the Mandatory Guidelines for Federal Workplace Drug Testing Programs. Recommendations approved January 26, 2012, available: http://www.datia.org/resources/DTAB+recommendation+memo+signed.pdf

and criminal justice. Specimen collection, a crucial component of drug testing, must be carefully designed and actively managed to ensure that valid results are generated. Additionally, the storage of samples, particularly urine, may be challenging if testing is delayed for a number of days. If the delay between collection and testing is substantial, appropriate storage is needed to help prevent drug degradation. Many clinic office staff members are untrained in collection and storage procedures, exacerbating the opportunity for patient donors to adulterate or substitute specimens or for drug degradation. Some laboratories may place trained collection technicians in clinics to reduce these threat to the integrity of the test results. It is useful to discuss these issues with the testing laboratory.

In settings in which specimen collection is not routine, there is an important alternative to be considered. State physician health programs (PHPs), that test blood, breath (for alcohol), hair, oral fluid, and urine, do not perform the collections themselves. Instead, they use commercial laboratories (and their network of collection sites) with which they have relationships. In addition there is a robust market for third party administrators* (TPAs) that are able to manage drug testing and random monitoring schedules for organizations and individuals (including PHPs) who want to establish drug testing systems for specimen collection, analysis, interpretation, and reporting, freeing them from these processes. To date, the use of TPAs has been primarily for forensic testing such as in the workplace and in random student drug testing (RSDT), rather than in clinical settings, but as monitoring of the status of a patient's remission of addiction becomes more widespread, and as the standard of care for addiction evolves toward chronic disease management, clinicians may become more interested in contracting with TPAs for specimen collection and information management services.

A chain-of-custody protocol provides a paper trail documenting the handling of a specimen from collection through analysis and reporting of laboratory results. All federal workplace drug testing requires meticulous chain-of-custody, though many other testing programs use such a protocol. Chain-of-custody includes proper labeling and security measures to ensure that the specimen belongs to the individual identified on the federal chain-of-custody form and that the specimen is transported and stored appropriately.

8. Validity Testing of the Specimen

Clinicians who suspect dilution, substitution or adulteration of a specimen, particularly urine, may consider ordering validity testing. In clinical settings, an unexpected finding on

validity testing may indeed be the first finding that leads to a dialogue with the patient and the beginning of changes in clinical management.

Characteristics of Urine. The characterization of a urine specimen is based on its appearance, temperature, pH, urinary creatinine concentration, and specific gravity (See Table 2).[49] [50] [51] Aberrant test results should be discussed with the patient and/or the laboratory, as necessary. The color of a urine specimen is related to the concentration of its constituents. Concentrated urine samples are generally more reliable than dilute samples. A urine specimen may be colored because of endogenous/exogenous substances derived from food pigments, medications, or disease states that produce excessive analytes. Urine can appear colorless as a result of excess hydration due to diet, medical condition, or deliberate volume loading. In the absence of underlying renal pathology, patients who repeatedly provide dilute urine samples should be advised to decrease water intake prior to testing and to provide samples in the early morning when urine samples are likely to be most concentrated. The ability of the patient to produce periodic concentrated specimens reduces the likelihood of any chronic renal pathology causing a dilute specimen.

Table 2: Normal Characteristics of a Urine Specimen

Temperature within 4 minutes of voiding 90ºF to 100ºF [a]
pH 4.5 to 8.0
Urinary creatinine >20 mg/dL
Specific gravity >1.003
[a] If the sample is of sufficient volume (30 mL or more) and the patient is normothermic [b] Sample degradation, due to improper storage or prolonged transportation, even in the absence of sample adulteration, can result in sample pH in excess of 9.0.

[49] Cook, J. D., Caplan, Y. H., LoDico, C. P., & Bush, D. M. (2000). The characterization of human urine for specimen validity determination in workplace drug testing: a review. *Journal of Analytical Toxicology, 24*(7), 579-588.
[50] Cook, J. D., Strauss, K. A., Caplan, Y. H., LoDico, C. P., & Bush, D. M. (2007). Urine pH: the effects of time and temperature after collection. *Journal of Analytical Toxicology, 31*(8), 486-496.
[51] Gourlay, D. L., Heit, H. A., Caplan, Y. H. (2012). Urine Drug Testing in Clinical Practice: The Art & Science of Patient Care. John Hopkins University School of Medicine (5th edition). Available: http://www.udtmonograph.com/

9. What Drugs to Test

Single drugs can be tested for in drug testing, but usually multiple drugs or drug classes are tested for simultaneously. This broadens the scope of testing from a single drug and provides operational efficiencies and cost savings when information is desired about more than a single drug. Drug testing panels identify the use of only the specific drugs, drug classes, or drug metabolites built into the particular test panel. However, clinicians should have the choice of what drugs to test for each patient based on their assessment of that patient and risk history. Unlike forensic testing, clinical testing should be individualized to each patient situation and not determined by a forced panel of drugs.

The most common immunoassay drug test panel includes the SAMHSA-5: amphetamines (various stimulant drugs as a drug class), marijuana metabolites (THC), cocaine metabolites, opiates (natural opiates such as codeine and morphine, a metabolite of heroin but *not* other opioids such as oxycodone, hydrocodone, buprenorphine and methadone), and phencyclidine (PCP). As previously noted, the history of the SAMHSA-5 drug test panel dates back to 1988 when U.S. Congress passed the Drug-Free Workplace Act requiring testing of commercial truck drivers. The five drugs specified in the law were the five classes of drugs most commonly used by truck drivers at that time. Thus, while the SAMHSA-5 is something of an anachronism, it is the law for federally-mandated drug testing. Revisions to the original law call for confirmatory testing for specific drugs, including some stimulants including hallucinogenic amphetamines and specific opioids. Using the updated SAMHSA- panel, federally mandated drug testing procedures call for the confirmation of positive IA test results with specific tests for marijuana, cocaine, amphetamine, methamphetamine, MDMA, MDA, MDEA, codeine, morphine, 6-AM (heroin) and PCP. Most commercially available IA drug test panels can be extended beyond this standard panel, often to include benzodiazepines, some of the semi-synthetic opioids such as buprenorphine, hydrocodone, and oxycodone, and some of the synthetic opioids such as meperidine and methadone. Many laboratories offer a “10-drug panel” for immunoassay tests. Often these broader panels are only marginally more expensive than the SAMHSA-5 drug panels.

Because there are hundreds of drugs that have rewarding and addictive properties, it is not practical to test for all of them. Moreover, once individuals know for which drugs they will be tested, some drug users can switch to drugs that they know will not be detected (e.g. workplace testing), or switch to similar drugs that may not react to the drug class for which the

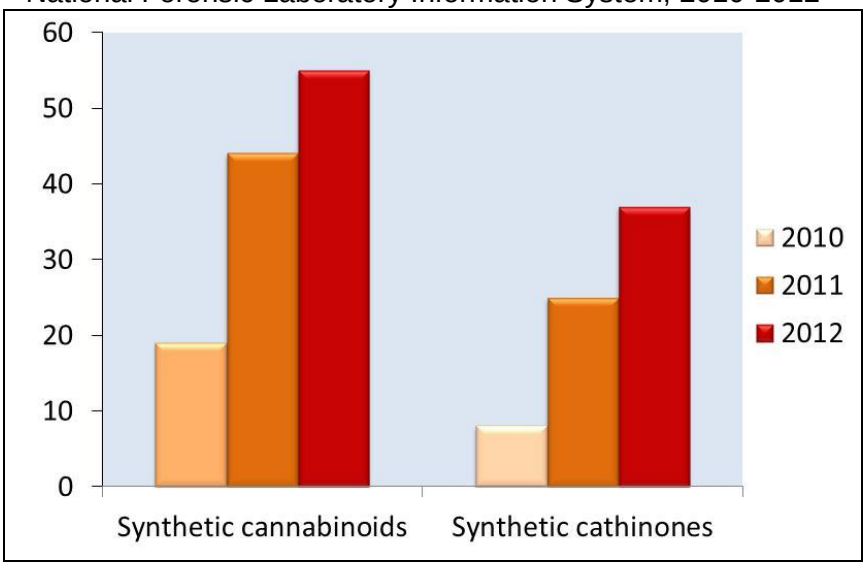
immunoassay is designed. For example, a patient who is abusing dextroamphetamine may switch to methylphenidate knowing that this drug, which produces similar effects, differs structurally and will not be detected by an amphetamine immunoassay. Many websites are available to drug users to inform them about chemistry, laws and laboratory procedures. With this resource they can choose which compounds to select to produce the effects that they desire.

As illicit drug designers have focused on drug laws and drug testing, a large segment of the illegal drug industry has developed a new category of drugs, termed "designer drugs." These drugs are designed to evade detection by drug tests and drug laws.[52] Although many synthetic drugs are now classified as Schedule I in an amendment to the Controlled Substances Act,[53] drug suppliers typically sell designer drugs until they are widely identified, tested for, and outlawed. At that point the suppliers shift to a new drug, often only slightly modified from the earlier drug, which has not yet been identified on drug tests or made illegal. As Figure 3 shows, the Drug Enforcement Administration has identified a vast and growing array of new synthetic drugs in recent years. Laboratories recently have begun to test for a few of the most commonly used designer drugs including a few of the literally hundreds of synthetic cannabinoids and synthetic cathinones now being sold and used. The increasing proliferation of drugs designed to evade drug laws and drug tests is a significant challenge to drug testing.

[52] Madras, B. (2012). Designer drugs: An escalating public health challenge. *Journal of Global Drug Policy and Practice, 6*(3). Available: http://www.globaldrugpolicy.org/Issues/Vol%206%20Issue%203/Designer%20Drugs%20FINAL%20V6%20formatted.pdf

[53] Drug Enforcement Administration, DEA Public Affairs. (2012, June 19). Congress agrees to add 26 synthetic drugs to Controlled Substances Act. Washington, DC: Drug Enforcement Administration. Available: http://www.justice.gov/dea/divisions/hq/2012/hq061912.shtml

Figure 3. Unique Synthetic Drugs Identified by the National Forensic Laboratory Information System, 2010-2012[54]



Although it is possible for individuals to use only drugs that are not typically included in test panels, most individuals who use less commonly used drugs also use commonly used drugs.[55] [56] [57] In such cases, the more commonly used drugs will be detected, while the less commonly used drugs may go undetected. Moreover, 55% of individuals admitted to state-funded treatment in 2010 for a substance use disorder reported polydrug use[58], demonstrating the overlap in substance misuse.

Because patterns of illicit drug use and addiction prevalence vary geographically and by specific populations, it is desirable to periodically add or rotate additional, less frequently used drugs into drug test panels. Rotating the choice of drugs tested permits the identification of new patterns of substance use and addiction. The unpredictability of the set panels can deter drug use in general, including those drugs that are not represented on most drug panels. The U.S.

[54] Graph provided by Bertha K. Madras, Ph.D., created using data from U.S. Drug Enforcement Administration, Office of Division Control, National Forensic Laboratory Information System, 2012.
[55] Scholey, A. B., Parrott, A. C., Buchanan, T., Heffernan, T. M., Ling, J. & Rodgers, J. (2004). Increased intensity of ecstasy and polydrug usage in the more experienced ecstasy/MDMA users: a WWW study. *Addictive Behaviors, 29*(4), 743-752.
[56] Wish, E. D., Fitzelle, D. B., O'Grady, K.E., Hsu, M. H., & Arria, A. M. (2006). Evidence for significant polydrug use among ecstasy-using college students. *Journal of American College Health, 55*(2), 99-104.
[57] Darke, S. & Hall, W. (1995). Levels and correlates of polydrug use among heroin users and regular amphetamine users. *Drug and Alcohol Dependence, 39*(3), 231-235.
[58] Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. Treatment Episode Data Set (TEDS): 2000-2010. (2012). *National Admissions to Substance Abuse Treatment Services*. DASIS Series S-61, HHS Publication No. (SMA) 12-4701. Rockville, MD: Substance Abuse and Mental Health Services Administration.

military no longer rotates drugs and instead uses a standard panel of amphetamine, methamphetamine, MDA, MDMA, cocaine, marijuana, codeine, morphine, heroin (6-AM), hydrocodone, hydromorphone, oxycodone, oxymorphone and benzodiazepines. The military still has the option of testing for all other drugs on a case-by-case basis, including all synthetic cannabinoids.

Rotation of test panels cannot overcome one of the most challenging problems facing drug testing today: the dramatic proliferation of drugs of abuse. The epidemic of misuse of and addiction to prescribed controlled substances (referred to many as "prescription drug abuse") creates an especially daunting challenge to effective drug testing. This includes sedatives and psychostimulant drugs, not only opioid analgesics.

10. Alcohol Testing

Alcohol is readily identified in breath because it is volatile and present in much higher concentrations than other drugs of abuse. Although alcohol testing has been used for years through detection of Blood Alcohol Concentration (BAC), there are newer, more sensitive tests for ethanol metabolites: ethyl glucuronide (EtG) and ethyl sulfate (EtS).[59] These metabolites can extend the detection window of alcohol in urine to 72 hours or longer, depending on the amount of alcohol consumed (as opposed to a detection window of approximately 6 hours for blood testing and about 12 hours for older methods of urine alcohol testing) and timing of the test (alcohol is metabolized at a rate of about half a standard drink per hour).[60] EtG can be identified on an immunoassay test or by GC-MS or, better, by LC-MS/MS, whereas there is no immunoassay available at this time for EtS, which must be quantified by LC-MS/MS. These tests do not measure the amount of alcohol that was consumed, nor do they determine the time of use. Regrettably some addiction treatment programs today are using EtG and EtS testing to try to determine the level of drinking or the severity of the alcohol use disorder. For such purposes, these tests represent a source of misinformation and a waste of resources. These tests are, however, useful in identifying recent alcohol use in settings where use is strictly prohibited.

[59] Ethylglucuronide (EtG) and Ethylsulfate (EtS). http://etg.weebly.com/
[60] Substance Abuse and Mental Health Services Administration. (2012). The role of biomarkers in the treatment of alcohol use disorders, 2012 Revision. *SAMHSA Advisory*, 11(2). Available: http://store.samhsa.gov/shin/content//SMA12-4686/SMA12-4686.pdf

The EtG immunoassay test is prone to *analytical* false positives,* likely due to cross-reactivity with other urinary glucuronides; thus, EtG test results should be confirmed with more specific LC-MS/MS testing in forensic settings. EtG is also prone to *clinical* false positives* on both immunoassay and confirmatory tests, due to exposure to alcohol in the environment. This so-called incidental or extraneous alcohol exposure to non-beverage alcohol has caused concern. Products such as over-the-counter cough syrup, food cooked with alcohol, communion wine, "alcohol-free" wine and beer, hand sanitizers and mouthwashes, etc., can cause positive EtG and EtS tests. Setting high cut-off concentrations for EtG and EtS tests reduces, but does not eliminate, clinical false positives due to incidental exposures. Cut-off concentrations now commonly in use range between 100ng/ml and 1,000ng/ml, the most common being 500ng/ml. The more alcohol a person consumes, the longer these alcohol metabolites are excreted in the urine.

Post-collection fermentation can occur in a sample, creating ethanol, particularly among diabetic patients when a sugar source is present with yeast and bacteria. This fermentation process can create the EtG biomarker and bacteria can break down EtG degrading the sample. This issue presents a significant concern in clinical practice when diabetes is undiagnosed.

EtG and EtS testing is also available for hair and nails, and since the threshold concentration necessary to yield positive results appears to require more significant and/or chronic alcohol use, there is no problem of clinical false positives resulting from of incidental exposure to alcohol. The longer detection period provided by hair and nail testing allows for the accumulation of analyte over time. There appears to be a linear relationship between the total amount of beverage alcohol consumed and the concentration of EtG detectable in hair and nails, permitting estimates of the intensity of alcohol use.[61] Additional hair testing for Fatty Acid Ethyl Esters (FAEEs) improves the reliability of such consumption estimations, because EtG and FAEEs in hair provide very complementary data and have different biological sources.[62] International interpretive standards have already been promulgated,[63] and the EU and UK

[61] Appenzeller, B. M., Agirman, R., Neuberg, P., Yegles, M., & Wennig, R. (2007). Segmental determination of ethyl glucuronide in hair: a pilot study. *Forensic Science International, 173*(2-3), 87-92.
[62] Society of Hair Testing. (2011). Consensus on the Society of Hair Testing on hair testing for chronic excessive alcohol consumption 2011. Available: www.soht.org/pdf/Revised%20Alcohol%20marker%20Consensus.pdf
[63] Pragst, F., Rothe, M., Moench, B., Hastedt, M., Herre, S., & Simmert, D. (2010). Combined use of fatty acid ethyl esters and ethyl glucuronide in hair for diagnosis of alcohol abuse: interpretation and advantages. *Forensic Science International, 196*(1-3), 101-110.

routinely employ hair testing for EtG and FAEEs in family law cases, civil procedures, rehabilitation and abstinence compliance monitoring.

Testing for another new and useful alcohol marker, blood phosphatidylethanol (PEth), has recently become commercially available. It has been shown that PEth tests are accurate using fingerstick blood on filter paper. This makes obtaining and submitting samples more convenient than traditional specimen collection of blood via venipuncture. PEth is a phospholipid formed only in the presence of ethanol via the action of phospholipase D (PLD).[64] [65] Initial reports found PEth positive in alcoholics and suggested that a threshold of total ethanol intake yielding detectable PEth seems to be around 1000 g over the previous three weeks, with a mean daily intake of about 50 g (i.e. about four "standard drinks").[66] [67] [68] PEth remains positive for two to three weeks or longer after detection.[69] Additionally, no gender differences have been found[70] and several studies have reported no false positive results.[71] [72] [73] [74] Finally, a linear correlation between amount of ethanol consumed and PEth values is probable.[75] [76] [77]

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[64] Gustavsson, L. & Alling, C. (1987). Formation of phosphatidylethanol in rat brain by phospholipase D. Biochemical and Biophysical Research Communications 142(3), 958-963.
[65] Kobayashi M., & Kanfer, J. N. (1987). Phosphatidylethanol formation via transphosphatidylation by rat brain synaptosomal phospholipase D. *Journal of Neurochemistry, 48*(5), 1597-1603.
[66] Hansson, P., Caron, M., Johnson, G., Gustavsson, L. & Alling, C. (1997). Blood phosphatidylethanol as a marker of alcohol abuse: levels in alcoholic males during withdrawal. *Alcoholism: Clinical and Experimental Research 21*(1), 108-110.
[67] Varga, A., Hansson, P., Lundqvist, C., & Alling, C. (1998). Phosphatidylethanol in blood as a marker of ethanol consumption in healthy volunteers: comparison with other markers. *Alcoholism: Clinical and Experimental Research 22*(8), 1832-1837.
[68] Varga, A., Hansson, P., Johnson, G., & Alling, C. (2000). Normalization rate and cellular localization of phosphatidylethanol in whole blood from chronic alcoholics. *Clinica Chimica Acta, 299*(1-2), 141-150.
[69] Wurst, F. M., et al. (2010). Phosphatidylethanol: normalization during detoxification, gender aspects and correlation with other biomarkers and self-reports. *Addiction Biology, 15*(1), 88-95.
[70] Ibid.
[71] Wurst, F. M., Vogel, R., Jachau, K. et al. (2003). Ethyl glucuronide discloses recent covert alcohol use not detected by standard testing in forensic psychiatric inpatients. *Alcoholism, Clinical and Experimental Research 27*(3), 471-476.
[72] Wurst, F. M., Alexson, S., Wolfersdorf, M. et al. (2004) Concentration of fatty acid ethyl esters in hair of alcoholics: comparison to other biological state markers and self reported-ethanol intake. *Alcohol and Alcoholism 39*(1), 33-38.
[73] Wurst, F. M., et al. (2012). Characterization of sialic acid index of plasma apolipoprotein J and phosphatidylethanol during alcohol detoxification--a pilot study. *Alcoholism, Clinical and Experimental Research 36*(2), 251-257.
[74] Hartmann, S., Aradottir, S., Graf, M., et al. (2007). Phosphatidylethanol as a sensitive and specific biomarker: comparison with gamma-glutamyl transpeptidase, mean corpuscular volume and carbohydrate-deficient transferrin. *Addiction Biology, 12*(1), 81-84.
[75] Aradottir S, Asanovska G, Gjerss S, et al. (2006). Phosphatidylethanol (PEth) concentrations in blood are correlated to reported alcohol intake in alcohol-dependent patients. *Alcohol and Alcoholism, 41*(4), 31-37

In a recent drinking experiment, 11 participants, on five successive days, consumed an amount of ethanol leading to an estimated blood alcohol concentration of approximately 1000 mg/kg.[78] In 10 of 11 volunteers, detectable PEth-16:0/18:1 (molecular alcohol biomarker) values were found one hour after the start of drinking. Over the following days, concentrations of PEth increased, reaching the maximum concentrations between days three and six. The highest concentration found was 237 ng/ml.

An additional benefit to PEth testing is that blood is not subject to the confounding effects of concentration that complicates urine testing. These facts, and the time spectrum of detection, make blood PEth a potential confirmation test for alcohol consumption. There is no large scale study, however, examining the effect of coincident medications, illnesses, and/or variations among individuals with regard to kinetics of PEth. Because it is a new test its use should be limited to non-forensic applications at this time.

11. Tobacco Testing

Nicotine is the addicting chemical in tobacco. It produces brain reward and dependence the way other drugs of abuse do, but it is not impairing and does not produce overdose deaths. Unlike alcohol and other drugs, tobacco deaths are mostly limited to older users with a history of use, typically sparing the young but ultimately producing more deaths than all other drugs combined.[79] Nicotine is metabolized to cotinine, which is readily identified in urine, hair, and oral fluid for several days after last exposure.[80] Cotinine testing is common in health insurance applications, in order to determine whether the applicant is a smoker. Cotinine testing is also required by some practitioners treating patients in long-term opioid therapy. (Smoking is significantly more prevalent among patients in long-term opioid therapy than the general

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[76] Stewart, S. H., et al. (2009). Preliminary evaluation of phosphatidylethanol and alcohol consumption in patients with liver disease and hypertension. *Alcohol and Alcoholism, 44*(5), 464-467.
[77] Stewart, S. H., et al. (2010). Phosphatidylethanol and alcohol consumption in reproductive age women. *Alcoholism, Clinical and Experimental Research 34*(3), 488-492.
[78] Gnann, H., Weinmann, W., & Thierauf, A. (2012). Formation of phosphatidylethanol and its subsequent elimination during an extensive drinking experiment over 5 days. *Alcoholism, Clinical and Experimental Research 36*(9), 1507-1511.
[79] Centers for Disease Control and Prevention. (2008). Annual smoking-attributable mortality, years of potential life lost, and productivity losses—United States, 2000-2004. *Morbidity and Mortality Weekly Report, 57*(45), 1226-1228. Available: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5745a3.htm
[80] Benowitz, N. L., Hukkanen, J., & Jacob III, P. (2009). Nicotine chemistry, metabolism, kinetics and biomarkers. *Handbook of Experimental Pharmacology,* (192), 29-60.

public,[81] and opioid-dependent smokers have higher rates of mortality than opioid-dependent non-smokers.[82]) It must be noted that nicotine replacement products cause positive cotinine test results.

In addition to cotinine testing to identify nicotine use, carbon monoxide, a product of smoking, can be detected in breath to determine an individual's smoking status.[83] [84] Unlike cotinine testing, nicotine replacement products do not produce positive carbon monoxide results, nor do e-cigarettes. Carbon monoxide is produced by smoking tobacco as well as smoking marijuana.[85] The technology to detect expired air carbon monoxide levels is similar to breath testing for alcohol in that it is quick and easy to administer, inexpensive and is resistant to subversion.

12. Summary

All of the commonly used drug tests use the same basic, reliable, and rapidly evolving technologies, each of which has advantages and disadvantages related to sensitivity, specificity, and cost, among other factors. There are also advantages and disadvantages to each of the available matrices: urine, breath, oral fluid, hair, nails, blood, and sweat. Breath testing technology, widely used in alcohol testing, is under development for the detection of other drugs. Urine, while familiar and widely available, suffers from two serious drawbacks: the "bathroom problem" which makes collection awkward and opens the door to the second problem, subversion, the Achilles heel of urine testing. Available drug test panels vary among the testing technologies as does the sensitivity among matrices. All available testing matrices and technologies should be considered when developing or evaluating a drug testing program.

[81] Dunn, K. E., Sigmon, S. C., Reimann, E. F., Badger, G. J., Heil, S. H., & Higgins, S. T. (2010). A contingency-management intervention to promote initial smoking cessation among opioid-maintained patients. *Experimental Clinical Psychopharmacology, 18*(1), 37-50.
[82] Hser, Y. I., McCarthy, W. J., & Anglin, M, D. (1994). Tobacco use as a distal predictor of mortality among long-term narcotic addicts. *Preventative Medicine, 23*(1), 61–69.
[83] Jarvis, M. J., Belcher, M., Vesey, C., & Hutchinson, D. C. (1986). Low cost carbon monoxide monitors in smoking assessment. *Thorax, 41*(11), 886-887.
[84] Middleton, E. T., & Morice, A. H. Breath carbon monoxide as an indication of smoking habit. *Chest, 117*(3), 758-763.
[85] Hecht, E., & Vogt, T. M. (1985). Marijuana smoking: effect on expired air carbon monoxide levels. *Internal Journal of Addiction, 20*(2), 353-361.

III. The Practice of Drug Testing

The selection of drug testing technology, matrix and testing panel do not alone define a drug testing program or individual procedure for patients. The practice of drug testing includes identifying the tested population and the actions taken in response to drug test results.

1. Whom to Test and Privacy Considerations

Drug testing is appropriate in settings in which the use of drugs of abuse is prohibited; however, defining drug testing populations may be contentious. Obvious examples of appropriate drug testing settings include the criminal justice system and addiction treatment. Less obvious, and more controversial, settings include health care, workplace, highways, schools and home, all of which are addressed in **IV. Current Applications of Drug Testing and Promising New Opportunities**.

Privacy should be considered in all drug testing settings. The acquisition of information about a person's drug use has created a controversy at the core of drug testing. Drug use puts the individual at risk, warranting surveillance for drug use in many settings including, for example, clinical practice, drug treatment, and criminal justice. Drug use also puts others at risk, warranting surveillance in the workplace and on the roadways. Early detection of and intervention for drug use can prevent subsequent drug and alcohol use disorders, which is one rationale for the implementation of drug testing in some school settings.

In forensic settings, like highway testing, drug testing is a "search" under the United States Constitution (and some state constitutions). The constitutional protection against an "unreasonable" search is limited to government actions and does not apply to private non-governmental situations. For this reason the Supreme Court decisions on drug testing in the workplace and school-based drug testing were limited to government-mandated workplace drug testing and drug testing in public schools. The legal standard governing what is unreasonable is a balance between the privacy invasion of the search and the public interest in the search. Private schools and private employers usually are not bound by these laws; however, there are also state and local laws to consider, which is why, before beginning any drug testing protocol of any population, it is necessary to assess the legal status of the testing, whether it is a government action or a private action.

A particular privacy concern relates to the use of prescription drugs. Individuals in some settings (e.g. workplace) may object to others knowing what prescription drugs they take. In the federal workplace confirmatory process, a Medical Review Officer (MRO) verifies that confirmed positive results are consistent with administration of drug(s) for which the sample donor has current, valid prescription(s). The MRO may communicate with a prescribing physician and/or pharmacy and in such a case the MRO-verified test result is reported to the workplace authorities as "negative," thus protecting the donor's privacy. However, if MROs, in their medical judgment, believe that use of the prescription medication poses a safety risk to the employee or to anyone else, they include a safety warning to the employer.

In clinical settings, drug tests are used for diagnostic and therapeutic purposes and do not represent a search any more than other medical tests do. A patient can refuse to cooperate with a drug test. The physician can make a reasonable effort to address the medical implications of such refusal, including the physician's and patient's understanding that doing so could result in reduced treatment options which may result in sub-standard medical care. In clinical settings, identification of prescription drugs is of particular importance.

The invasiveness of the specimen collection is an important consideration in both forensic and clinical drug testing. Monitored or directly observed urine collections reduce test subversion, but may be awkward for the donor and the collector. If urine collections are not monitored or directly observed, it is helpful to use POC validity testing – such as temperature, pH, specific gravity, and presence of oxidizing agents – which is available on many inexpensive collection cups. Validity testing can reduce, but cannot eliminate, successful test subversion. Urine should be promptly tested after collection or be placed in refrigerated storage if there is a lag between collection and testing. Other matrices can complement or, if necessary, substitute for urine. It is important to note that practitioners who order testing of donor samples using two matrices that both usually will not be paid by health insurers.

2. Scheduled Versus Random Drug Testing

When drug tests are administered at predictable, scheduled times, it is easier for the donor to cheat and the tests are more easily "passed", both because of the brief detection windows of urine (1 to 3 days) and oral fluid (12 to 48 hours) and because of the typically limited and predictable drug test panels commonly employed. Knowing when a drug test is scheduled, some drug users abstain from the drugs in the test panel for the few days necessary to pass the

test or they figure out how to subvert the test. It is harder to cheat on hair or nail testing with their 90-day detection windows. However, some drug users, such as those who are dependent on opioids, face painful withdrawal symptoms when they stop drug use, even for a few days. In addition, chronic marijuana users will continue to test positive on many matrices even if they do stop drug use for a few days or weeks.

When possible, random urine or oral fluid testing schedules are preferred to fixed testing schedules. Random testing involves notifying the individual of an immediate testing time and often involves escorting the individual to an observed testing site for specimen collection. While important in some settings, it is not feasible in others.

3. Testing High-Risk Populations and Populations with Substance Use Disorders

Testing among populations at risk for substance use is generally infrequent but random. The random aspect of such testing increases the value as donors do not know when they will be tested. This testing is intended to deter substance use and when drug use is detected to provide an opportunity for appropriate intervention. Such tested populations include criminal offenders under community supervision, youth, and medical patients treated with chronic administration of opioids, among others. The U.S. military is the model for testing large populations, as this testing is both random and relatively frequent (see ***3.2 United States Military*** under **IV. Current Applications of Drug Testing and Promising New Opportunities**).

Among populations with known substance use problems, such as those in addiction treatment and those with diagnosed substance use disorders, random drug testing is much more frequent. In such medical settings, intervention often includes structured efforts to help patients achieve and sustain a drug-free status including intensive long-term monitoring.

The physician health programs (PHPs) are the model for long-term monitoring of people with known, serious substance use problems (see **Box 3: The Physician Health Programs** under **IV. Current Applications of Drug Testing and Promising New Opportunities**). These programs conduct frequent random drug and alcohol testing with immediate intervention for detected use.

4. Understanding a Positive Drug Test Result

A common criticism of drug testing in is that it is often presented, or operated, as a stand-alone solution to a drug problem identified in a particular setting or population. Drug testing clearly is not a panacea. Drug tests miss infrequent drug use and are subject to subversion. A negative drug test never guarantees absence of drug and says nothing about the use of drugs that are not tested for. A positive drug test does not "diagnose" addiction. Drug tests do identify drug use and must be successfully linked to interventions appropriate to the specific settings.

There has historically been little education of physicians in interpretation of specific drug tests. Evidence suggests that many clinicians lack the adequate understanding of the complexities of drug testing and incorrectly interpret test results.[86] [87] [88] This can result in inappropriate patient care. For example, a physician may think a negative benzodiazepine POC immunoassay test indicates their patient prescribed lorazepam is non-adherent, or potentially diverting, and may act on the incorrect assumption that lorazepam will be detected in the test. The increased use of drug testing requires physicians to become better educated about the specific drug testing techniques used in their practices and associated facilities. ASAM recommends physicians contact the professionals at the testing laboratories if they have any questions about interpreting a test result.

It is of particular importance for all involved in drug testing to understand the implications of a positive random drug test. According to the National Survey on Drug Use and Health, in 2011, 47.0% of Americans age 12 and older reported using an illicit drug in their lifetime, 14.9% reported past year use, and 8.7% reported past month use.[89] Although frequent drug use is relatively uncommon among the general population, most of the problems resulting from drug use occur among those individuals who use drugs frequently. Random testing is most effective in identifying frequent users. A random drug test result is often misunderstood as likely to come

[86] Reisfield, G.M., Webb, F. J., Bertholf, R. L., Sloan, P.A., & Wilson, G. R. (2007). Family physicians' proficiency in urine drug test interpretation. *Journal of Opioid Management 3*(6), 333-337.
[87] Reisfield, G. M., Salazar, E., & Bertholf, R. L. (2007). Rational use and interpretation of urine drug testing in chronic opioid therapy. *Annals of Clinical and Laboratory Sciences, 37*(4), 301-314.
[88] Starrels, J. L., Fox, A. D., Kunins, H. V., & Cunningham, C. O. (2012). They don't know what they don't know: Internal medicine residents' knowledge and confidence in urine drug test interpretation for patients with chronic pain. *Journal of General Internal Medicine, 27*(11), 1521-1527.
[89] Substance Abuse and Mental Health Services Administration. (2012). Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-44, HHS Publication No. (SMA) 12-4713. Rockville, MD: Substance Abuse and Mental Health Services Administration.

from a person who uses drugs only occasionally. It is common for individuals with a positive test to claim that they only used the detected drug once. The reality is far different. Positive random drug tests are unlikely to come from occasional drug users because the detection windows of both urine and oral fluid are brief, and it takes multiple drug uses in the prior 90 days to produce a positive hair test.

To demonstrate this point, a study of drug testing in the workplace estimated that among illicit drug users, 55% used only in the past year, 37% used in the past month and 8% used daily.[90] Analysis showed that, among drug users identified by positive random drug tests, 52% would be daily users, 41% would be monthly users, and only 7% would be annual users.

5. Responding to Unexpected Positive Drug Test Results

All physicians (and others) involved in drug testing should determine the questions the tests are intended to answer before the testing is administered and should have a plan for what to do with the results. The response to an unexpected positive drug test result is related to the circumstances of the test. In some cases, an unexpected positive test serves as the beginning of a discussion. For example, in routine medical settings, an unexpected positive drug test may lead to further screening for substance use problems. In other cases, a single unexpected positive drug test often produces profound consequences. In the workplace, a single positive test in an airline pilot or commercial driver may lead to termination of employment. Alternatively, an employee who produces an unexpected positive drug test result may be referred to an employee assistance program* (EAP). A job applicant who tests positive on a pre-employment test is not likely to be hired.

In most other settings, including health care, unexpected positive test results should lead to further evaluation, interventions including counseling the patient and treatment if necessary, as well as to follow-up testing to monitor for ongoing drug use. In addiction treatment, the consequence of an unexpected positive drug test should generally be intensification of treatment, at least initially. Suspension of treatment or dismissal from treatment in response to a single positive drug test result counterproductive and is not an appropriate clinical response. Military personnel who test positive on a drug test risk discharge but may also be referred for

[90] DuPont, R. L., Griffin, D. W., Siskin, B. R., Shiraki, S. & Katze, E. (1995). Random drug tests at work: The probability of identifying frequent and infrequent users of illicit drugs. *Journal of Addictive Diseases, 14*, 1-17.

evaluation and treatment, especially if it is a first positive test and if the person testing positive is not an officer.

There are few situations when a single positive drug test leads to a draconian outcome. An exaggerated perception of the negative consequences of a drug test may produce hostility towards testing and discourage the implementation of valuable testing programs. This is why it is important that each setting in which drug testing is done maintains clear, thoughtful and appropriate protocols for follow-up with individuals who have unexpected positive or negative drug test results.

There is an important tradeoff in handling drug test results: the more lenient, delayed, and uncertain the consequences of an unexpected positive test, the less deterrence drug testing provides against continuing drug use or relapse to addiction. As briefly noted, and discussed in more detail in Section **IV. Current Applications of Drug Testing and Promising New Opportunities**, the physician health programs (PHPs) and similarly structured criminal justice system programs offer important models for responses to positive drug tests. In the PHPs, the response to a single use of alcohol or other drugs is an immediate and comprehensive reassessment. Use of alcohol or other drugs can lead to removal from medical practice and intensified treatment, often at the residential level of care, and often lasting for several months. In Hawaii's HOPE probation program and South Dakota's 24/7 Sobriety program, the response to a single positive test for drugs or alcohol is immediate brief incarceration, lasting at most a few days. The lesson to be taken from these experiences is that the deterrence power of testing is best achieved by swift, certain and meaningful, but usually not draconian, responses for any use of alcohol or other drugs.

Whether any adverse action should be taken in response to an unexpected IA positive test absent a confirmatory test can be complex. Whenever there are serious consequences for positive test results, especially for random tests in nonclinical settings where legal challenges are possible, both confirmation of presumptive positive immunoassay test results and involvement of a Medical Review Officer (MRO) are important. The role of medical review of laboratory confirmed positive results in clinical testing is much broader than it is in workplace testing and includes not only determination of legitimate medical explanations for positive results. The clinical MRO is also frequently asked to give an opinion on whether or not the positive test result indicates alcohol or drug use that violates the requirements of the individual's treatment or monitoring program. Even in the many settings in which an MRO is not required,

or as a practical matter is unavailable or unaffordable, it is important to establish the validity of the test and the fact that the test result corresponds to the identified subject. It is also important to determine if the drug use identified in the drug test reflected appropriate medical treatment, as opposed to unhealthy behavior on the part of the person who tested positive. ASAM has held a longstanding leadership role in information on MROs in drug testing, with an annual comprehensive course.[91]

Individuals subject to drug testing should know, in advance of testing (and preferably in writing), what the consequences will be of an unexpected positive result, with specifications related to the reason for performing the drug test. In workplace settings in particular, it is common for consequences of positive "for cause"* drug tests to be different, and usually more severe, than consequences of positive random drug tests. In general, it is desirable to take actions that promote both prevention of, and recovery from, substance use disorders. This is not to say that every drug user identified by a drug test needs treatment; this is certainly not the case. However, taking no action after a positive drug test signifies tolerance of continued drug use, misses an opportunity for effective intervention, and undermines the preventive value of the drug test. Conversely, a positive drug test in a medical or psychiatric treatment setting should not lead to discharge from the physician's care anymore than non-adherence to a diabetic diet should immediately lead to discharge. Data gained from this testing, as with any testing in a medical setting, should be used by treating physicians to engage the patient in appropriate treatment planning.

6. General Principles of Drug Testing Applications

In settings in which drug testing is done routinely for many people, ASAM encourages using the full range of biological matrices; both POC and laboratory-based tests. In settings where testing is now seldom or never done, ASAM encourages using drug tests that are easily adopted, such as urine or oral fluid testing. When testing is done in high-risk populations, such as addiction treatment, the criminal justice system, and return-to-work settings after addiction treatment, ASAM encourages the use of random rather than scheduled drug tests. The frequency of the random tests can be varied to fit the needs of the tested population just as frequency of testing in clinical settings changes with clinical indications. For example, more frequent testing at the outset may be used until stable abstinence is achieved, followed by less

[91] American Society of Addiction Medicine, Comprehensive MRO (Medical Review Officer): http://www.asam.org/education/comprehensive-mro-(medical-review-officer)

frequent testing as abstinence is maintained. This approach to random testing increases the effectiveness of the testing in promoting recovery and is far less expensive. Moreover, testing is most intense for the subjects at highest risk of drug use.

In scheduled tests, consideration should be given to matrices more resistant to subversion, especially hair and oral fluid. Random, directly-observed testing with the donor accompanied to the restroom directly after notification of the test is the most effective way to reduce subversion with urine tests, but balancing this with privacy concerns and other practicalities should be case- and/or context-specific. When subversion of a urine drug test is proven or suspected, it is incumbent to perform an immediate recollection under monitored conditions. In many clinical settings oral fluid would be a common secondary matrix to test. Though not offered by as many laboratories, a hair test could be used as it is more resistant to subversion and offers an extended detection window, although it will not detect very recent use and to detect marijuana, use must be frequent and sustained.

The concept of "smarter" drug testing includes ordering testing based upon clinical need as well as the use of a core panel of the most commonly used drugs, complemented by a rotation of less-commonly used drugs.[92] This approach can be used in settings where testing is frequent to permit assessment of the prevalence of use of many drugs in the tested population. Further, the use of a rotating panel has greater prevention power because the tested population does not know which drugs will be tested. In populations where testing is less frequent, it may be more helpful to use a wider drug test panel.

IV. Current Applications of Drug Testing and Promising New Opportunities

This section explores a range of settings in which drug testing is used. Each application includes a description of common testing patterns and a discussion of the potential for improving testing. ASAM encourages wider and smarter drug testing. Although this White Paper includes the current practices and potential expansions of drug testing in a range of settings, its focus is on drug testing in medical settings, where testing is not commonly used. In a previous public policy statement, ASAM specifically endorsed the use of drug testing in clinical diagnostic settings, addiction treatment settings and for monitoring and, separately, for medical-

[92] DuPont, R. L. & Graves, H. (2005). *Smarter student drug testing*. Rockville, MD: Institute for Behavior and Health, Inc.

legal purposes.[93] Drug tests are valuable tools for health care professionals to use as part of a comprehensive evaluation of patients in order to reach the correct diagnosis and to develop appropriate treatment, and monitoring plans. They are tools that can improve diagnosis and treatment, just as laboratory testing is a central component of most areas of health care to improve clinical accuracy and outcomes. Increasing the use of drug testing in both medical and nonmedical settings has the potential to improve public health by discouraging unhealthy or illicit drug use and by promoting early identification of substance use disorders. Drug testing provides opportunities for appropriate therapeutic interventions.

Indications for drug testing depend upon treatment setting and clinical purpose (primary, secondary, or tertiary prevention). Drug testing can be used in primary care settings for screening and brief intervention, often in combination with standardized substance use and addiction screening questionnaires. Testing can assist in early identification in high-risk populations, such as patients with histories of substance use and adolescents being treated for mood, anxiety, or attention deficit disorders. Drug testing is also a valuable diagnostic procedure in the assessment of patients presenting with symptoms of psychiatric conditions, in which aberrant behavior, perceptions, thought processes, or affective states could be attributable to a primary psychiatric condition, to the effects of a psychoactive substance or to both. Testing for drugs and alcohol is appropriate in the assessment and treatment of medical conditions such as chronic pain, gastrointestinal complaints, neuropathies, liver disease, anemia, traumatic conditions, musculoskeletal disorders, and sleep disorders. As many as 20% of patients in medical clinics have alcohol use disorders although, regrettably, most typically go unrecognized.[94] In a recent study, 9.7% of individuals receiving opioid therapy for chronic noncancer pain in primary care settings met criteria for a substance use disorder.[95]

An issue in all medical settings is whether or not confirmation of an immunoassay result is necessary. As discussed earlier in this paper, there is no simple answer. While in some clinical situations, the immunoassay results are sufficient, with the knowledge and acceptance of their higher rates of false negatives and positives; however, there are other settings in which

[93] American Society of Addiction Medicine. (2010). Public Policy Statement On Drug Testing as a Component of Addiction Treatment and Monitoring Programs and in other Clinical Settings. Adopted July 2002, revised October 2010. Chevy Chase, MD: ASAM. Available: http://asam.org/docs/publicy-policy-statements/1drug-testing---clinical-10-10.pdf?sfvrsn=0

[94] Cleary, P. D., Miller, M., Bush, B. T., Warburg, M. M., Delbanco, T. L., & Aronson, M. D. (1988). Prevalence and recognition of alcohol abuse in a primary care population. *American Journal of Medicine, 85*(4), 466-471.

[95] Fleming, M. F., Balousek, S. L., Klessing, C. L., Mundt, M. P. & Brown, D. D. Substance use disorders in a primary care sample receiving daily opioid therapy. *Journal of Pain, 8*(7), 573-582.

additional information is needed. When definitive information is needed there are two options to consider. The first is to confirm the immunoassay presumptive positive or negative result using GC-MS or LC-MS/MS methods. The second option is to bypass the immunoassay test altogether and subject the sample to a screening LC-MS/MS analysis. This has the advantage of testing for more drugs than any immunoassay can identify, but as well as providing the option for retesting via LC-MS/MS with a more focused panel to improve sensitivity and specificity. It has also been noted in this White Paper that a disadvantage of LC-MS/MS testing is that it may be more expensive than alternative analytical methods. These decisions cannot be made through simple rules. They require clinical judgment in each specific clinical situation with careful consideration of the costs and benefits of testing. These concerns are not specific to any medical specialty or setting.

1. Drug Testing in Addiction Treatment

Drug testing is currently used, and can be employed in ways to markedly improve care in three phases of addiction treatment: 1) screening and diagnostic evaluation, 2) formal treatment, and 3) long-term monitoring after initial intensive phases of addiction treatment.

1.1. Addiction Screening and Diagnostic Evaluation

An obvious occasion to employ drug testing in addiction medicine is as part of the initial assessment. Patients presenting for evaluation, and those initially seen for consultation in an emergency department or on in an inpatient hospital unit, should receive a thorough clinical evaluation to establish a diagnosis, including the possibility of a substance use disorder. However, a clinical interview and examination alone should not be considered sufficient, just as the history and physical examination of a patient with a possible diagnosis of diabetes would not be considered sufficient if it did not include laboratory testing. Drug testing provides an objective source of information to compare to the patient's self-report. In cases where there is a discrepancy between the patient's subjective report and the objective drug test result, the clinician is in a position to engage the patient over this discrepancy, using motivational interviewing techniques,* with the goal of enhancing accuracy of the diagnosis and the appropriateness of the treatment plan. Moreover, drug testing is an important clinical tool to assist the evaluating physician, counselor, or other health care professional to determine the risk the individual manifests for acute withdrawal and the indication for withdrawal management ("detoxification"). Just as a single laboratory assessment is insufficient for detection and

management of diabetes or hypertension, monitoring for substance use, including drug testing when indicated, should occur throughout the course of medical treatment for a substance use disorder.

The reality in addiction treatment is that drug testing is currently underutilized. Many initial assessments, conducted by a counselor or even by an addiction specialist physician, do not include information available from drug testing. Formal programs of intensive treatment, such as partial hospitalization programs or residential programs, as a rule collect specimens for drug testing periodically; however, among patients in general outpatient care, it is the exception rather than the rule that data from drug testing is gathered in a random basis, over the course of treatment. This is particularly the case in programs serving patients in public sector treatment settings. Initial and ongoing evaluation of a patient's status in addiction treatment can be accompanied by initial and periodic drug testing.

Drug testing should be a key component of assessment and treatment planning, especially when integrated with other clinical information gathering, such as a substance use history, physical and mental status examinations, withdrawal severity scores, and standardized laboratory assessments of metabolic, neurologic, and psychiatric status. A knowledgeable clinician can use drug testing to verify self-reports, confirm diagnoses, identify denial and minimization of drug and alcohol use, enhance motivation for treatment, measure biological adaptation, assist in development of treatment planning, monitor treatment response, document treatment effectiveness and outcomes, support patient advocacy by validating abstinence from alcohol and drug use, and validate adherence in taking prescribed controlled substances.

Before discussing in more detail the applications of drug testing in addiction treatment, it is important for clinicians to recognize that the response to a positive drug test is critical in setting the goals of care.

1.2. Responding to Positive Tests During Various Phases of Treatment

A fundamental goal of addiction treatment is for patients to achieve abstinence from the use of alcohol and other drugs of abuse. In this context, an unexpected positive test result signals continued use of non-prescribed drugs of abuse by tested patients. In medication-assisted treatment (MAT), a test result that fails to confirm the patient's use of the prescribed medicine (e.g. methadone or buprenorphine) (an unexpected negative test result) also is a

significant finding because it signals non-compliance and possible diversion. In the context of MAT, the identification of prescribed medications is not a violation of the abstinence standard.

Ignoring positive test results undermines treatment goals. Discharging a patient from treatment for an initial positive test is seldom, if ever, appropriate. Positive test results signal the need to intensify or alter current care. There are many options to consider in response to positive test results, including more frequent testing and specialized interventions for non-compliant patients. In MAT, a positive test for opioid use may reflect the need for a higher dose of medication.

Continued positive test results, after the intensification of treatment, raise the question of the value of treatment and may justify discharging the patient from treatment. Each patient's situation should be taken into account as a clinician determines what changes should be made to the treatment plan in the patient's best interests in response to positive test results.

1.3. Intensive Addiction Treatment

Drug testing is used in the initial, often intensive, phase of addiction treatment, sometimes referred to as "primary treatment." Primary treatment includes intensive psychosocial services to assist patients in establishing abstinence; psychoeducational activities to assist patients in understanding their disease; psychotherapeutic interventions to help them overcome shame and guilt and to accept their circumstances without minimization, denial, or bargaining; and cognitive-behavioral interventions to help patients manage cravings and identify drug-use triggers. Primary treatment is offered in residential, partial hospitalization, and intensive outpatient settings, depending on the severity of illness and the medical necessity for a given intensity of treatment services, using objective criteria such as those found in *The ASAM Criteria.*[96] Random and frequent drug testing should always be an important component of primary addiction treatment.

In residential primary treatment, drug testing helps to ensure that the integrity of the drug-free therapeutic environment has not been compromised by smuggled contraband. For patients, the establishment and maintenance of abstinence from the use of alcohol or other drugs is a fundamental goal of traditional recovery-oriented primary treatment. Drug testing can

[96] Mee-Lee, D. (Ed.). (in press). *The ASAM Criteria: Treatment Criteria for Addictive, Substance-Related, and Co-Occurring Conditions*. Chevy Chase, MD: American Society of Addiction Medicine. http://asamcriteria.org/

detect difficulties patients experience in reaching and maintaining this fundamental and early treatment goal. Most patients who use unauthorized substances in treatment do not volunteer this information to staff, so drug testing is necessary to detect such events.

In outpatient primary treatment settings, the opportunities for the use of alcohol or other drugs are much greater. Thus, the need for frequent random drug testing is greater than for patients in residential treatment. The detection of substance use in an outpatient setting should be used to revise treatment plans, including using additional strategies to help the patient establish and maintain a drug-free state. Termination from treatment is seldom appropriate for a single positive drug test, but repeated positive tests are incompatible with continuing in many outpatient treatment programs. Just as new information about disease severity in the treatment of another chronic medical or psychiatric illness would lead to treatment plan adjustments (usually intensification and addition of new elements), positive drug test results are a manifestation of the severity of illness, or the inadequacy of treatment, and signals the need to reevaluate and readjust treatment plans.

In outpatient OTPs, after an initial period of adjustment to the prescribed medicine (e.g. methadone or buprenorphine), drug test results are commonly used to determine the gain or loss of take-home medication privileges. Drug testing is also an indicator of adequacy of the dispensed medication dose, as adequate doses of methadone or buprenorphine generally block the rewarding effects of opioid use, therefore extinguishing the use of other opioids. Additional responses to positive drug tests may include more frequent visits with counselors, including more intensive group or individual counseling, revising treatment plans, increased engagement in 12-step recovery programs, and increasing the frequency of drug testing. An option with particular appeal is to require patients with repeated positive tests to participate in weekly or even daily group sessions specifically designed to assist those who repeatedly engage in drug use while receiving their daily maintenance pharmacotherapy. Thus, alcohol and drug using patients are not terminated from treatment, but their continued treatment is contingent on participation in this more intensive and highly focused intervention. All of these responses help patients work toward establishing and maintaining abstinence. While discharge from services is the last option to be considered for initial and subsequent positive tests in OTPs and other addiction treatment programs, there are patients who do not benefit from treatment and for whom discharge is the appropriate step, especially if they decline a recommended referral to a more intense (e.g. residential) level of care. A “therapeutic discharge” often sets the stage for

the patient's later return to treatment with more determination to meet the program's expectations.

Drug testing also can be useful in harm reduction settings to provide objective feedback to patients and to their clinicians regarding frequency of use and whether, over time, progress is being made. Moreover, drug testing provides information about discordance between patients' self-reports and their actual drug use. The therapeutic alliance is generally strengthened when there can be frank discussions about the presence of, and the psychological motivations underlying, falsified communications from the patients to their healthcare providers.

A setting of addiction care where medical components of treatment, including physician visits and drug testing, are rarely employed is the longer-term, lower-intensity residential level of care, generally referred to as halfway house or sober living placement. Such patients may be seen in intensive outpatient programs, in general outpatient addiction care, or even in intensive community support programs (assertive community treatment [ACT] models) for the most recalcitrant patients with addiction. Most halfway or sober living residences strive to maintain a drug-free recovery environment for their residents, but many are unable to do so. However, even relatively low cost POC testing is rarely used in these settings to verify abstinence. (Note: the funding challenges for addiction treatment, especially in the public sector, are well known and beyond the scope of this White Paper).

Of course, nonmedical use of drugs in such populations can occur when individuals are off-site from their sober living placement, but some drug use in these circumstances is due to contraband brought into the facility, which *de facto* compromises the recovery environment itself for *all* residents of the facility. It is not unreasonable to consider weekly random testing as appropriate in these settings, both to verify abstinence of the individual and to maintain the integrity of the sober residence for the group. In general, in outpatient settings (where patients reside at home), a positive drug test result should be used to revise patient treatment plans rather than terminate treatment. Similarly, for residents of halfway houses or sober living residences (which provide even less structure than halfway houses), while the integrity of the facility as a safe recovery environment may require immediate expulsion from the facility of persons who evidence relapse, even by self-report, expulsion from the facility should not mean that they are expelled from their ongoing therapeutic relationship with their outpatient addiction treatment professionals.

1.4. Monitoring in Addiction Treatment

Chronic disease management of other health conditions often involves having patients return for professional contacts to monitor their status of remission. The monitoring phase after formal addiction treatment has been completed can last for varying lengths of time; however, at the center of this phase is continued random drug and alcohol testing. After primary addiction treatment, patients should be followed using models of chronic disease management, with the treatment goal of long-term, even lifetime, recovery that includes abstinence from alcohol and drug use. As an intermediary step, programs often seek to reduce the frequency and severity of relapses, and to minimize functional impairment should any substance use resume. Relapse is most common in the first 90 days after completion of primary treatment. When patients are still engaged with a clinician and they return to alcohol or other drug use, they are often too embarrassed or ashamed to admit it. Drug testing can help both the patient and the clinician operate with the "facts." It is unfortunate when clinicians or case managers view drug testing as appropriate only during phases of active treatment and not as an approach that can have great utility after intensive phases of treatment are no longer needed.

Box 3: The Physician Health Programs

Physician Health Programs (PHPs) maintain the absolute no-use standard for use of drugs of abuse, including alcohol, with frequent random drug testing over long periods of time, typically 5 years or longer. In PHP care management, physicians and other licensed health professionals at the outset receive evaluation and, when needed, intensive treatment after which they are required to make regular use of 12-Step and other community support programs. While formal treatment is usually brief, seldom more than 90 days, the monitoring and the support of the PHPs are continuous for the duration of each licensee's participation. PHPs typically require participants to check online or by telephone every day to see if they must submit a sample for drug testing that day. If they are to be tested, the participants must be present at a designated collection site that same day. Failure to provide a specimen when it is required, producing a positive test result, or producing an adulterated specimen each are violations of the physicians' written contracts with their PHPs, contracts which explicitly spell out in advance all of the consequences of violations. Participants who violate the monitoring requirements of their PHPs, including relapsing to the use of alcohol or other drugs, are subject to an intensification of the treatment required under their participation contract with the PHP; violating monitoring requirements also places the licensee at risk of being reported to their licensure board resulting in possible loss of their license to practice their profession. At the outset of monitoring, the frequency of random drug testing is high, commonly once a week, while after a few months of producing negative drug and alcohol tests, the frequency of random testing is gradually reduced, often to once a month. Any detected alcohol or other drug use or suspicious drug test result leads to more frequent testing and/or testing with alternative matrices.

PHPs produce impressive results: A study of 904 physicians participating in 16 state PHPs found that, over the course of monitoring periods of five years or longer, 78% of participants never tested positive for either alcohol or other drugs.[97] Of those who produced at least one positive test over the monitoring period, two thirds did not produce a second positive test. Of participants with known outcomes at 5-year follow-up, 64% completed their participation contracts with the PHP, 16% extended their contracts, and only 19% failed to complete their contracts.

In PHPs and in other random drug testing protocols including in community-based addiction treatment settings, a patient who is tested today may be tested tomorrow, because every day the selection for testing is random. This strategy provides a strong incentive to remain abstinent from drugs and alcohol throughout the monitoring period.

PHPs generally use immunoassay testing of urine followed by GC-MS or LC-MS/MS confirmation of the drugs identified on the initial test. PHPs also test hair and blood samples. LC-MS/MS is used for EtG and EtS alcohol tests. Recently the PHPs have begun exploring using LC-MS/MS as a screening test in selected cases but high costs of this test have limited its potential.

While physicians or other licensed health professionals enrolled in PHPs are distinctive among patients with addiction (being more highly educated and with greater access to pharmaceuticals in their workplace than other populations), these same principles have been widely used in dramatically different populations, such as in the criminal justice system with comparable results. As discussed in 3.3. Criminal Justice System, programs using frequent random drug tests with a zero tolerance standard for any use of alcohol and other drugs also produce outstanding long-term results.

While the generalizability of the PHP results remains to be determined, the outstanding outcomes produced by this system of care management suggest that using similar strategies can produce similar good long-term outcomes in many other populations and settings.

[97] McLellan, A. T., Skipper, G. E., Campbell, M. G. & DuPont, R. L. (2008). Five year outcomes in a cohort study of physicians treated for substance use disorders in the United States. *British Medical Journal, 337*:a2038.

1.5. Frequency and Duration of Drug Testing in Addiction Treatment.

When drug testing is used in addiction treatment settings, it is best to use random, rather than scheduled, testing and to set the frequency of the random testing higher at the start of treatment, when patients are known to more frequently engage in continued drug use. When the patient has attained a substantial period of stable abstinence from drug use, the frequency of random drug testing can be lowered; however, random testing less frequently than once a month in addiction treatment is seldom wise, even for patients with established abstinence. It is important that the testing be unpredictable, even if it is infrequent, so the patient can be tested at any time, even the day after the prior test. It is also wise to vary the drug testing panels and the matrix used for the testing. These should be as unpredictable to the participant as the date and time of the test itself.

Cost-benefit analysis and risk stratification is necessary in deciding the frequency of drug test monitoring, balancing laboratory science (i.e. chromatographic testing) and behavioral science (i.e. to address deficits in self-monitoring in patients with substance use disorders). The emerging “best clinical practice” means increased cost of testing. The cost to society of not detecting a “slip” or “relapse” is unknown. Monitoring schedules and frequency of testing balance several considerations that constitute an individualized cost-benefit analysis for each patient. Risk and cost of failing to detect non-adherence and relapse is a consideration for the patient, healthcare professional and for society as a whole.

Even though drug testing is a central component of years-long monitoring programs for licensed health professionals, there is no agreed-to standard among states regarding frequency or duration of testing in such programs. This lack of standardization is, in part, a reflection of the reality that most PHPs have some connection with state regulatory and licensing authorities and professional licensure is a state-based function under specific oversight with substantial variation among the states. The PHP model is continuing to evolve, with differences between the states crucial to this evolution. Standardization would slow if not stop innovation, which has been a hallmark of the PHP experience. In general, most PHPs set the frequency of random testing at once a week early in their monitoring. The frequency of testing is reduced to twice a month and then once a month after long-term sobriety is achieved. It is essential to recognize that in random testing a donor who is tested today can be tested again tomorrow – even if the random testing is set for only once a month. This means that donors who are being monitored cannot predict when they will be tested, regardless of the nominal frequency of the drug and

alcohol testing. The duration of drug testing in monitoring programs for licensed health care professionals also varies from state to state, but the evolving consensus is that the duration of monitoring for physicians who have received addiction treatment should be at least five years. The PHPs find that when the mandate for monitoring has expired, many physicians participating in the PHP voluntarily request to continue monitoring by their state program, including drug testing. They do this for two reasons. First, it promotes their recoveries. Second, the continued random monitoring validates that they remain alcohol- and drug-free. This objective validation is useful to these physicians in dealing with their malpractice carriers, hospital medical staff credentials committees, licensing boards and, not surprisingly, also with their families.

2. Drug Testing in Various Medical Specialties

Today, drug testing is an underutilized and misapplied tool in patient care.[98] [99] Moreover, testing for alcohol and drug use is often fraught with patient mistrust and suspicion. Despite these problems, drug testing can facilitate good medical care and help to solve complex patient management problems. The value of clinical drug testing in the general medical populations not showing an elevated risk of substance use may be questioned because of the costs incurred by the patient, the practitioner, and the health care system as a whole. However, given the high prevalence of substance use disorders, including among medical patients, drug testing can facilitate improved patient outcomes. When applied thoughtfully to any patient population, especially those at high risk of substance use disorders, drug test results can lead to a useful clinical discussion between patients and their physicians that would otherwise never occur whether the test results are positive or negative. Drug testing, like testing for blood sugar and blood pressure, provides clinically useful information that can inform and improve patient care and provides an opportunity for health education by the physician or other healthcare provider.

Drug testing can be successfully integrated into many aspects of health care. Physicians are in an excellent position to work with patients to identify and to intervene with problematic drug and alcohol use, and to manage patient care during and after treatment, parallel to the management of patients with hypertension and diabetes. Currently, drug testing is underutilized

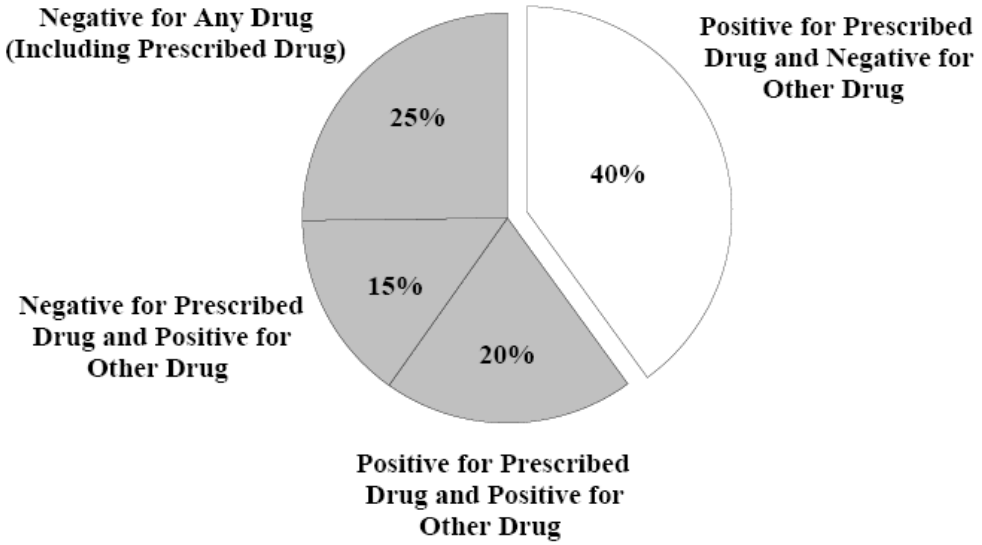
[98] Starrels, J.L., Becker, W. C., Weiner, M.G., Lis, X., Heo, M., & Turner, B. J. (2011). Low use of opioid risk reduction strategies in primary care even for high risk patients with chronic pain. *Journal of General Internal Medicine, 26*(9), 958-964.
[99] Reisfield, G.M., Webb, F. J., Bertholf, R. L., Sloan, P.A., & Wilson, G. R. (2007). Family physicians' proficiency in urine drug test interpretation. *Journal of Opioid Management 3*(6), 333-337.

in most health care settings, including pain management and primary care, even when controlled substances are prescribed. Exceptions include those emergency departments, pain management programs, and psychiatric crisis centers, where testing is used to identify recent drug use and thus guide differential diagnosis and immediate treatment.

Data from Quest Diagnostics' prescription drug monitoring service indicates that 60% of drug test specimens from patients referred by their physicians had results inconsistent with the controlled substances prescribed (See Figure 4).[100] Only 40% of patients tested positive for prescribed medications and negative for other drugs. Twenty five percent of patients tested negative for all drugs, including medications prescribed by their physician, 15% were negative for the prescribed drug and positive for another un-prescribed drug, and 20% were positive for both the prescribed medications and other drugs. Marijuana, present in 26% of specimens, was the most frequently detected non-prescribed drug among patients with inconsistent test results.[101] Additionally, individuals in this study who tested positive for marijuana were more likely to test positive for non-prescribed pharmaceuticals (45%) than individuals negative for marijuana use (36%). Following marijuana, the most common non-prescribed drug classes identified in this study included opiates (22%), benzodiazepines (16%), oxycodone (14%), cocaine (8%), and methadone (6%). The conclusion from this study is that when drug testing is not employed, physicians lack essential information about their patients' pattern of drug use, missing both the use of non-prescribed drugs and the misuse and diversion of prescribed drugs.

[100] Center for Substance Abuse Research. (2013, June 3). Lab test results suggest majority of patients do not take prescription drugs as prescribed. *CESAR Fax, 22*(22).
[101] Quest Diagnostics. (2013). Prescription Drug Misuse in America: A Report on Marijuana and Prescription Drugs. Quest Diagnostics Health Trends: Prescription Drug Monitoring Report 2013. Available: http://www.questdiagnostics.com/dms/Documents/health-trends/2013_health_trends_prescription_drug_misuse.pdf

Figure 4. Percentage of Patients Referred to Quest Diagnostics Laboratories for Drug Testing by Their Physicians Testing Positive and Negative for Drugs Prescribed for Them, 2012.[102]



Drug testing can also be used in both hospital and outpatient settings, including pain medicine, palliative medicine, general psychiatry, obstetrics, geriatrics, adolescent medicine and primary care. While this is not an exhaustive list, the following discussion of drug testing in these settings provides a good introduction to drug testing in general health care and in specific medical settings. The use of drug testing in pain management is an area of medicine which is undergoing a very important revolution, largely because of the growing recognition of the importance of opioid misuse, a problem that has reached an epidemic level.[103] The field of pain management is now wrestling with the challenges of promoting effective relief of pain while identifying substance misuse and diversion in this high-risk patient population.[104]

2.1 Pain Medicine

Long-term opioid therapy for the management of chronic non-cancer pain (CNCP) has gained widespread clinical acceptance over the past two decades. In recent years many unintended consequences have become apparent. As prescriptions for opioids have

[102] Center for Substance Abuse Research. (2013, June 3). Lab test results suggest majority of patients do not take prescription drugs as prescribed. *CESAR Fax, 22*(22).
[103] Manchikanti, L., Helm, S., Fellows, B., Janata, J. W., et al. (2012). Opioid epidemic in the United States. *Pain Physician, 15*(3 Suppl), ES9-ES38.
[104] Volkow, N. D., & McLellan, T. A. (2011). Curtailing diversion and abuse of opioid analgesics without jeopardizing pain treatment. *JAMA, 305*(13), 1346-1347.

dramatically increased, opioid-related treatment episodes, emergency room visits, and drug-related deaths have increased in parallel.[105]

There continues to be a role for long-term opioid therapy in selected patients with CNCP, but it is clear that careful, ongoing monitoring for opioid-related problems is an essential component of that care. Monitoring techniques include speaking with patients about their drug use and their lives; investigating and discerning the meaning of aberrant drug-related behaviors; querying state prescription drug monitoring program (PDMP) databases at the onset of opioid prescribing and for the duration of a plan of care for chronic non-cancer pain; and performing drug testing.[106]

Patients are sometimes untruthful about their drug use[107] [108] and behavioral monitoring is of limited value in identifying patients who use drugs.[109] [110] The clinician's "hunch" and the identification of aberrant behaviors on the part of patients have been shown to correlate poorly with the actual presence of addiction in a given patient. Thus, there is no substitute for drug testing combined with good clinical judgment. Selected evidence indicates that drug testing in pain management may improve patient adherence.[111] [112] [113] Finally, drug testing in pain medicine is recommended in several clinical guidelines, including those of the American Pain Society, the American Academy of Pain Medicine, the American Society of Interventional Pain Physicians, the Federation of State Medical Boards, among others.[114] [115] [116] [117] [118] [119] Drug

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[105] Centers for Disease Control and Prevention. (2012). CDC grand rounds: prescription drug overdoses – a U.S. epidemic. *Morbidity and Mortality Weekly Report, 61*(1), 10-13. Available: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6101a3.htm

[106] Volkow, N. D., & McLellan, T. A. (2011). Curtailing diversion and abuse of opioid analgesics without jeopardizing pain treatment. *JAMA, 305*(13), 1346-1347.

[107] Fishbain, D. A., Cutler, R. B., Rosomoff, H. L., & Rosomoff, R. S. (1999). Validity of self-reported drug use in chronic pain patients. *Clinical Journal of Pain, 15*(3), 184-191.

[108] Berndt, S. Maier, C., & Schutz, H. W. (1993). Polymedication and medication compliance in patients with chronic nonmalignant pain. *Pain, 52*(3), 331-339.

[109] Katz, N., & Fanciullo, G. J. (2002). Role of urine drug toxicology testing in the management of chronic opioid therapy. *Clinical Journal of Pain, 18*(4 Suppl), S76-S82.

[110] Wasan, A. J., Butler, S. F., Budman, S. H., Benoit, C., Fernandez, K., & Jamison, R. N. (2007). Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. *Clinical Journal of Pain, 23*(4), 307-315.

[111] Manchikanti, L., et al. (2006). Does random urine drug testing reduce illicit drug use in chronic pain patients receiving opioids? *Pain Physician, 9*(2), 123-129.

[112] Pesce A, et al. (2011). Illicit drug use in the pain patient population decreases with continued drug testing. *Pain Physician, 14*(2), 189-193.

[113] Starrels, J. L., Becker, W. C., & Weiner, M. G. (2011). Low use of opioid risk reduction strategies in primary care even for high risk patients with chronic pain. *Journal of General Internal Medicine, 26*(9), 958-964.

[114] Owen, G. T., Burton, A. W., Schade, C. M., & Passik, S. (2012). Urine drug testing: current recommendations and best practices. *Pain Physician, 15*(3), ES119-ES133.

testing comprises a number of sophisticated analytic techniques and its ordering and interpretation can, at times, be complex. The ethical application of drug testing imposes an obligation on the physician to order tests, interpret the results, and respond clinically with requisite knowledge and skill.

The use of drug testing in pain management has increased exponentially over the past decade.[120] This fact conceals three important realities. First, drug testing remains underutilized in pain management. A recent survey of physician members of the American Pain Society, the American Academy of Pain Medicine, and the American Society of Regional Anesthesia and Pain Medicine found that only 59% of respondents order random urine drug testing.[121] Second, drug testing is highly skewed by medical specialty. Medicare data shows that anesthesiologists (who comprise 74% of pain specialists) ordered nearly as many drug tests in 2009 (636,880) as family practice physicians (258,132), internal medicine physicians (241, 431), neurologists (128,713), and general practitioners (70,031) combined. A recently published study of a large primary care health system found that only 8% of patients receiving long-term opioid therapy – and only 24% of the highest risk patients – were evaluated via urine drug testing.[122] Third, evidence indicates that, regardless of specialty, many physicians who employ drug testing are not proficient in interpreting test results.[123] [124] [125]

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[115] Chou, R., et al. for American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. (2009). Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *Journal of Pain, 10*(2), 113-130.

[116] Trescot, A. M., et al. (2008). Opioids in the management of chronic non-cancer pain: an update of the American Society of the Interventional Pain Physicians' (ASIPP) guidelines. *Pain Physician, 11*(2 Suppl), S5-S62.

[117] Federation of State Medical Boards of the United States, Inc. (2013). Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain. Washington, DC: Federation of State Medical Boards. Available: http://www.fsmb.org/pdf/pain_policy_july2013.pdf

[118] Gourlay, D. L., & Heit, H. A. (2009). The art and science of urine drug testing. *Clinical Journal of Pain 26*(4), 267-358.

[119] Federation of State Medical Boards of the United States, Inc. (2013). Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain. Washington, DC: Federation of State Medical Boards. Available: http://www.fsmb.org/pdf/pain_policy_july2013.pdf

[120] Collen, M. (2012). Profit-driven drug testing. *Journal of Pain and Palliative Care Pharmacotherapy, 26*(1), 13-17.

[121] Benzon, H. T., Kendall, K. C., Katz, J. A., et al. (2012). Prescription patterns of pain medicine physicians. *Pain Practice*. doi: 10.1111/papr.12011. [Epub ahead of print]

[122] Starrels, J. L., Becker, W. C., & Weiner, M. G. (2011). Low use of opioid risk reduction strategies in primary care even for high risk patients with chronic pain. *Journal of General Internal Medicine, 26*(9), 958-964.

[123] Reisfield, G.M., Webb, F. J., Bertholf, R. L., Sloan, P.A., & Wilson, G. R. (2007). Family physicians' proficiency in urine drug test interpretation. *Journal of Opioid Management 3*(6), 333-337.

[124] Reisfield, G. M., Salazar, E., & Bertholf, R. L. (2007). Rational use and interpretation of urine drug testing in chronic opioid therapy. *Annals of Clinical and Laboratory Sciences, 37*(4), 301-314.

Specifics of testing. Drug testing does not lend itself to a one-size-fits-all approach. Each aspect of testing must be individualized.

•Testing frequency. Frequency of testing should be matched to patient risk. Every patient poses some, however small, risk for drug misuse, addiction, or diversion. Risk should be assessed for every patient prior to and throughout opioid therapy. Patients with added risk factors for opioid misuse – personal or family history of substance use disorders, psychiatric co-morbidities, and younger age (particularly males[126]) – may warrant more frequent testing. Likewise, those patients who display problematic behaviors should be tested for-cause. It is reasonable for stable, low-risk patients to be tested infrequently but randomly.

•Testing schedule. Patients should not be privy to testing schedules. For patients who misuse, are addicted to, or divert their medications, to be forewarned is to be forearmed. Nearly anyone can temporarily change their drug-use behaviors or subvert a drug test if they know they will be tested. Rather, testing should be unpredictable or for-cause.

•Testing panels. Testing panels in pain management vary widely, and there is no single ideal pain management panel. Rather, testing should be patient-centered. Panels should include but not be limited to prescribed controlled substances. For individuals with histories of substance misuse or substance use disorders, panels should be more comprehensive and should include drugs that have been problematic for the patient in the past. Consideration should also be given to testing for substances that are endemic to the region. There are advantages for health care providers to have an option of ordering customized panels to reduce costs and reflect substances of most clinical importance to that patient in that region.

•Type of collection. Urine collection in pain management is generally unobserved and unmonitored. Evidence from one large study indicated a specimen adulteration incidence of approximately 2.5%.[127] In order to balance privacy concerns with specimen integrity concerns, it is reasonable to have patients follow a basic collection protocol: leave jackets, purses, hats, and

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[125] Starrels, J. L., Fox, A. D., Kunins, H. V., & Cunningham, C. O. (2012). They don't know what they don't know: Internal medicine residents' knowledge and confidence in urine drug test interpretation for patients with chronic pain. *Journal of General Internal Medicine, 27*(11), 1521-1527.

[126] Substance Abuse and Mental Health Services Administration. (2004). Results from the 2003 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-25, DHHS Publication No. SMA 04-3964). Rockville, MD.

[127] Michna, E., Jamison, R. N., Pham, L. D., et al. (2007). Urine toxicology screening among chronic pain patients on opioid therapy: frequency and predictability of abnormal findings. *Clinical Journal of Pain, 23*(2), 173-179.

other items in an examination room and show the contents of pockets. Collection devices should have built in integrity checks, measuring temperature, pH, specific gravity, and presence of oxidizing agents. (Specimen integrity can also be gauged in the laboratory by measuring random urine creatinine.) If, based on sample appearance or integrity checks, there is a suspicion of adulteration, patients should provide a second, monitored specimen and both specimens should be sent for analysis.

Definitive testing. Definitive (also: “confirmatory” or "identification” testing) testing, which involves chromatography and mass spectrometry, incurs additional expense and thus should be done for specific indications. In general, a previously agreed upon protocol should be in place such that definitive testing is performed based upon rational clinical indicators.

Definitive testing following positive immunoassay (IA) results. In general, positive IA results need only be subjected to definitive testing when the results conflict with patients’ account of their drug use or when drug specificity is needed in class-specific assays (i.e. amphetamines, benzodiazepines, opiates). In a pain practice it is sometimes, but not always, important to identify the specific drug, not just the class of the drug.

Definitive testing following negative immunoassay results. In clinical practice there is no compelling rationale for subjecting all negative IA results to definitive testing. Although mass-spectrometry-based testing offers state-of-the-art sensitivity, thus turning some analytical false-negative IA results into true-positive definitive results, the clinical value of this additional information must be balanced by the costs associated with its acquisition. However, when the unexpected absence of a prescribed drug on an IA test is at odds with the patient’s account of medication use, definitive testing of the specimen is strongly suggested. In a patient with a history of misuse or substance use disorder, periodic definitive testing of negative IA test results for specific drugs or metabolites is warranted.

For some drugs of abuse – including synthetic cannabinoids and cathinones – immunoassays are under development. Although for some laboratories these drugs are only detectable by means of mass spectrometry methods, there are several laboratories using enzyme multiple immunoassay test (EMIT) technology, and the U.S. military now employs a commercial IA test.

Quantification should not be used to determine adherence with a specific dosage or formulation regimen. There are, however, some specific reasons for obtaining quantitative data.

For example, when several opioids are present in the urine of a patient prescribed a single opioid, quantification can help the clinician decide whether the presence of the other opioids is consistent with metabolism of the prescribed opioid or with contamination from the opioid manufacturing process, or if more than one drug within a class is being used. As well, in the setting of illicit drug use, serial creatinine-corrected quantitative values can help the clinician distinguish cessation of drug use from continued drug excretion from ongoing drug use.

Oral fluid testing. Recent advances in enzyme-linked immunosorbent assay* (ELISA) and LC-MS/MS have made the accurate measurement of low concentrations of multiple drug and drug metabolites in small oral fluid volumes possible. Oral fluid offers the advantage of observed collection, dramatically decreasing the possibilities for test subversion. A recent study of paired oral fluid and urine samples of long-term opioid patients found substantial agreement between the matrices: about 5% of analytes that were found in the oral fluid were not found in the urine, while nearly 10% of analytes found in urine were not found in oral fluid.[128] Lower detection rates in oral fluid compared to urine were reported for benzodiazepines, hydromorphone, and oxymorphone. Continued advances in knowledge and technology could narrow – but probably not close – the gap between oral fluid and urine, particularly for highly-protein bound or highly-water soluble analytes.[129]

Testing for marijuana. Some physicians, especially those in states that have passed medical marijuana laws, request laboratories to remove THC metabolites from drug testing panels. Regardless of the rationale, this practice has potential risks. First, marijuana remains a federal Schedule I drug under the Controlled Substance Act. Second, it has been shown to be impairing after use and it is unclear how its impairing effects are affected by concomitant use of opioids and other sedating drugs, such as benzodiazepines. Third, the medico-legal implications are uncertain if physicians come under investigation by legal or regulatory agencies or if there is evidence of patient harm or injury to others, as in highway crashes or workplace incidents and accidents.[130] ASAM supports testing for marijuana on all routine drug tests including drug testing in addiction treatment.

[128] Heltsley, R., DePriest, A., Black, D. L., et al. (2012). Oral fluid drug testing of chronic pain patients. II. Comparison of paired oral fluid and urine specimens. *Journal of Anal Toxicology, 36*(2), 75-80.
[129] Ed Cone, PhD, personal communication, March 28, 2013
[130] Jennifer Bolen, personal communication, March 8, 2013.

The bottom line for clinicians, regardless of the drug test used, is to understand the strength and limitations of each test to do effective monitoring in a patient-centered fashion. Drug testing is done *for* the patient not *to* the patient.[131]

2.2 Palliative Medicine

It is clear that physicians inadequately identify and assess substance use disorders.[132] This appears to be especially true in the context of palliative care, where high-stakes medical issues must be negotiated without offending patients who are facing terminal illnesses, or their family members. Patients with life-limiting illnesses are not exempt from the problems of drug misuse and addiction. The prevalence of substance use disorders in this population likely reflects the prevalence of these disorders in society at large.[133]

In one of the few studies that examined the prevalence of substance use disorders at the end of life, researchers reported a prevalence of alcohol dependence of 27% in patients admitted to a tertiary care palliative care unit.[134] In more recent years, the increased prescribing of opioids and the earlier referral to hospice and palliative care programs have led to increasing concerns about substance use including nonmedical use of prescription controlled substances.[135] In this case, an essential medication can be both the solution and the problem. With adequate training of health care professionals these co-occurring problems can often be successfully managed.[136]

Among physicians and nurses without an understanding of substance use disorders, there is sometimes a sense of futility about treating substance use disorders at the end-of-life. The attitude, “Oh, well, he’s going to die anyway; let him enjoy himself; there’s no point in addressing his addiction now” is all-too-common. This is a dehumanizing misconception of the

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[131] Gourlay, D., & Heit, H. A. (2013). You ordered the urine drug test: now what? *Practical Pain Management, 13*(7). Available: http://www.practicalpainmanagement.com/treatments/pharmacological/opioids/you-ordered-urine-drug-test-now-what

[132] O'Connor, P.G., Nyquist, J. G., & McLellan, A. T. (2011). Integrating addiction medicine into graduate medical education in primary care: the time has come. *Annals of Internal Medicine, 154*(1), 56-59.

[133] Reisfield, G. M., Paulian, G. D., & Wilson, G. R. (2009). Substance use disorders in the palliative care patient. *Journal of Palliative Medicine, 12*(5), 475-476.

[134] Bruera, E., et al. (1995). The frequency of alcoholism among patients with pain due to terminal cancer. *Journal of Pain and Symptom Management 10*(8) 599-603.

[135] Childers, J.W., & Arnold, R. M. (2012). "I feel uncomfortable 'calling a patient out'": educational needs of palliative medicine fellows in managing opioid misuse. *Journal of Pain and Symptom Management, 43*(2), 253-260.

[136] Gourlay, D. L., & Heit, H. A. (2008). Pain and addiction: managing risk through comprehensive care. *Journal of Addictive Diseases, 27*(3), 23-30.

nature of substance use disorders and the suffering they impose upon the individual and their loved ones, all of whom are adversely affected when these common and highly treatable disorders are present. For individuals in recovery from substance use disorders, continued recovery is commonly a central part of their identity, a matter of substantial pride. For individuals with active addiction, the establishment of recovery can be a foundation for important end-of-life work, in which self-esteem can be restored and fractured relationships can be mended. In both cases, the stress associated with advanced, life-limiting illness can be a serious and ongoing threat to recovery.[137] This threat is heightened by relatively unfettered access to opioids, benzodiazepines, and other psychotropic medications. There are several other problems related to poorly managed substance use disorders in this population, including[138]:

1. Adversely affected patient engagement in active treatment often results in a diminished quality of life due to difficulty in identifying and treating mood and anxiety disorders and difficulty in effectively treating pain and other physical symptoms;
2. Elevated risk of adverse medication interactions;
3. Stressors on psychosocial support systems;
4. Impaired trust in vital patient-physician and patient-nurse relationships; and,
5. Promotion of "chemical coping"[139], during a period of important decision-making and other end-of-life business.

While the role of drug testing in palliative care remains largely unstudied, drug testing is an important component of patient-centered care and can contribute to safer and more effective opioid prescribing and optimal end-of-life care. Patient-centered drug testing means that drug test results are used to help drug using patients and not to reject or abandon them. Drug test results are used to facilitate therapeutic discussion and problem resolution. Expected drug test results can provide positive reinforcement, support recovery, increase the confidence of treating physicians and nurses, and strengthen other relationships. Unexpected drug use identified by drug tests can identify lapses or relapses, allowing these to be addressed early to the benefit of

[137] Koob, G. F., & Le Moal, M. (2001). Drug addiction, dysregulation of reward, and allostasis. *Neuropsychopharmacology, 24*(2), 97-129.
[138] Reisfield, G. M., Paulian, G.D., & Wilson, G. R. (2009). Substance use disorders in the palliative care patient #127. *Journal of Palliative Medicine, 12*(5), 475-476.
[139] Bruera, E., et al. (1995). The frequency of alcoholism among patients with pain due to terminal cancer. *Journal of Pain and Symptom Management 10*(8) 599-603.

patients. Where necessary, when substance misuse is identified, treatment can be restructured to optimize safety and efficacy for the patient.

Best practices for drug testing in palliative medicine have not been defined formally but should be determined on a patient-by-patient basis using respectful clinical judgment. The moral imperative inherent in end-of-life care must not result in suspension of sound clinical principles and should not limit the compassionate use of the full spectrum of treatment options, including the prescribing of controlled substances and the provision of addiction treatment when these are indicated.

2.3 Emergency Medicine

Drug testing is frequently used in emergency departments to assist in the diagnosis of and immediate treatment decisions for patients. This is especially true of patients presenting with suspected adverse reactions to drugs (including unresponsive patients and those with acute psychiatric presentations), patients with trauma, and patients presenting with chronic pain. In this setting, immunoassay drug tests are used routinely because they rapidly identify the presence of multiple drugs or drug classes. More sophisticated confirmatory testing is rarely needed in the emergency or urgent care setting unless the patient disputes the results or unless there are unusual complicating factors that require more sophisticated testing.

2.4 Psychiatry

Psychiatrists and primary care physicians managing psychiatric problems can successfully incorporate drug testing into their routine treatment plans. Psychostimulants prescribed for attention deficit/hyperactivity disorder (ADHD) or depression, and benzodiazepines, prescribed for anxiety disorders and other conditions, are subject to misuse, addiction, and diversion. Physicians and other professionals with prescribing authority too often initiate authorizations for these classes of drugs without conducting even cursory screening for risk of misuse. This failure of vigilance contributes to the widespread misuse and diversion of these drugs. Patients provided with prescriptions for controlled substances including stimulants, sedative-hypnotics including benzodiazepines, and opioids are at risk of using illicit drugs and/or alcohol along with their prescription medications, putting their health and safety at risk as well as posing a risk of diversion. Just as informed consent between the prescriber and the patient is a useful component of high-quality health care when opioids are prescribed, so is it a component of high-quality health care when psychostimulants or benzodiazepines are prescribed. This

approach incorporates the concept of "universal precautions"[140] [141] to minimize the risk of misuse of prescription medications. Written treatment agreements signed by both the prescriber and the patient used in mental health treatment settings, as they are in pain management settings, call for wider use random drug tests. Adolescents and young adults, who are more prone to poor judgment and poor impulse control, are at higher risk for the development of addiction when they do use drugs of abuse. The highest rates of substance use disorders occur in the late teens and the twenties.[142] In addition, there is a high level of psychiatric and addiction comorbidity in these age groups with patients often minimizing or denying drug use to their physicians. For this reason, it is appropriate to consider periodic random drug testing for all psychiatric patients, and especially young patients and those with a history of substance use disorders, particularly when they have been prescribed psychostimulants and benzodiazepines. This should become part of the standard treatment planning of private psychiatric practices, community health (and mental health) centers, and other primary care practices where patients are prescribed psychopharmacological agents with the potential for misuse.

2.5 Obstetrics

The incidence of neonatal abstinence syndrome (i.e. opioid withdrawal in the newborn) increased almost 300% from 2000 to 2009.[143] During the same time period, the incidence of pregnant women physically dependent on opioids at the time of delivery increased almost 500%.

In the past three decades, first trimester use of prescription medications has increased more than 60%. The use of four or more medications during pregnancy has more than tripled.[144]

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[140] Gourlay, D., Heit, H. A., & Almahrezi, A. (2005). Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. *Pain Medicine, 6*(2), 107-112.
[141] Gourlay, D., & Heit, H. A . (2009). Universal precautions revisited: managing the inherited pain patient. *Pain Medicine, 10*(S2), S115-S123.
[142] Substance Abuse and Mental Health Services Administration. (2012). ***Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings***, NSDUH Series H-44, HHS Publication No. (SMA) 12-4713. Rockville, MD: Substance Abuse and Mental Health Services Administration.
[143] Patrick, S. W. Schumacher, R. E., Benneyworth, B.D., Krans, E. E., McAllister, J. M., & Davis, M.M. (2012). Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. *Journal of the American Medical Association, 307*(18), 1934-40.
[144] Mitchell, A. A., et al. (2011). Medication use during pregnancy, with particular focus on prescription drugs: 1976-2008. *American Journal of Obstetrics and Gynecology, 205*(1), e1-e8.

Illicit drug use during pregnancy may involve the use of prescription drugs or street drugs. In the case of opioids, it is likely that the illicit use began prior to conception.

Obstetric patients underreport their use of medications, drugs of abuse, and alcohol. In a study of electronic medical records versus self-reporting, 50% of patients did not report the use of opioids and 50% of patients did not report the use of antidepressants. Reliability was good for the use of diabetes, thyroid, and asthma medications. Sociodemographic and reproductive health characteristics were not predictive of medication use.[145] Because of the underreporting of opioids and benzodiazepines, it is often helpful for the obstetrician to use drug testing to complement patient history.

The American College of Obstetricians and Gynecologists (AGOC) and ASAM have jointly recommended that all obstetrical patients be routinely asked about their use of alcohol and other drugs.[146] [147] Screening may include the use of urine drug tests when patient consent is obtained and the patient understands the purpose of the test and how the results will be used, including any mandatory state reporting requirements.[148] [149] [150] [151] Although ACOG states that laboratory drug testing "is not appropriate for routine well-women care,"[152] the organization recommends the use of drug testing when substance use is suspected.[153] [154]

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[145] Sarangarm, P., et al. (2012). Agreement between self-report and prescription data in medical records for pregnant women. *Birth defects research. Part A, Clinical and molecular teratology, 94*(3), 153-161.
[146] American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. (2011). Committee Opinion No. 479: Methamphetamine abuse in women of reproductive age. *Obstetrics and Gynecology, 117*(3), 751-755.
[147] American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women and the American Society of Addiction Medicine. (2012). Committee Opinion No. 524: Opioid abuse, dependence, and addiction in pregnancy. *Obstetrics and Gynecology, 119*(5), 1070-1076
[148] Ibid.
[149] American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. (2011). Committee Opinion No. 479: Methamphetamine abuse in women of reproductive age. *Obstetrics and Gynecology, 117*(3), 751-755.
[150] American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. (2012). Committee Opinion No. 538: Nonmedical use of prescription drugs. *Obstetrics and Gynecology, 120*(4), 977-982.
[151] American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. (2008). Committee Opinion No. 422: At-risk drinking and illicit drugs use: ethical issues in obstetric and gynecologic practice. *Obstetrics and Gynecology, 112*(6), 1449-1460.
[152] American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. (2012). Committee Opinion No. 538: Nonmedical use of prescription drugs. *Obstetrics and Gynecology, 120*(4), 977-982.
[153] American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. (2011). Committee Opinion No. 479: Methamphetamine abuse in women of reproductive age. *Obstetrics and Gynecology, 117*(3), 751-755.

It is of particular importance to identify among obstetric patients the use of alcohol, and specific opioids and benzodiazepines. POC urine testing has limitations because it will not identify alcohol or certain opioid(s) and/or their metabolites.[155] While benzodiazepines are generally detected by POC immunoassay, not all benzodiazepines are equally detected by all reagents.[156] Since polypharmacy is common, especially in more complicated pregnancies, it may be clinically useful to identify the specific drug being used and to extend the range of drugs being identified by using a laboratory–based immunoassay test followed by confirmation using GC-MS or LC-MS/MS, or alternatively, in specific cases, using LC-MS/MS alone. The use of laboratory-based immunoassay testing, as opposed to POC testing, may reduce the likelihood of false positive or false negative test results, while providing greater specificity in drug identification. These benefits may be offset by the extra cost and the delayed timeframe for the clinician receiving the test result.

Patient-centered drug testing enhances physician awareness of medication/drug use and possible misuse and it provides the physician an opportunity to educate and motivate behavioral change. This is an opportunity for collaboration and building a trusting patient-provider relationship. Drug tests should not be used to screen drug-using obstetric patients out of the physician's practice any more than they should be used to reject or abandon any patient.

Two studies in the Kaiser Health System in 2003 and 2008 encompassed nearly 50,000 obstetrical patients.[157] Women were screened as possible substance users by both patient questionnaires and urine drug tests. Patients who screened positive, with positive responses to questionnaires and positive drug test results, were placed in an early intervention program. These patients had virtually the same outcomes as the control group, who screened negative for substance use, with regard to neonates requiring assisted ventilation, low birth weight, preterm delivery, placental abruption, and intrauterine fetal demise. Patients who screened positive for drug use and did not participate in any treatment had risk outcome ratios 2-16 times higher than the controls. The worst results were with intrauterine fetal demise. This study suggests that, in at least this complicated population of obstetrical patients, drug testing and

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[154] American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women and the American Society of Addiction Medicine. (2012). Committee Opinion No. 524: Opioid abuse, dependence, and addiction in pregnancy. *Obstetrics and Gynecology, 119*(5), 1070-1076

[155] Gourlay, D., Heit, H., & Caplan, Y. H. (2012). *Urine Drug Testing in Clinical Practice: The Art and Science of Patient Care* (5th ed.). Baltimore, MD: Johns Hopkins University School of Medicine.

[156] Ibid.

[157] Goler, N. C., Armstrong, M. A., Taillac, C. J., & Osejo, V. M. (2008). Substance abuse treatment linked with prenatal visits improves perinatal outcomes: a new standard. *Journal of Perinatology, 28*(9), 597-603.

patients' self-reporting can assist in effective resource allocation to improve maternal and fetal outcomes.

Best practices in obstetrics require utilization of a comprehensive substance use assessment, including patient-centered drug testing. Sadly, the obstetrical population is no less likely to suffer from substance use disorders than the general population. Recognizing this reality, drug testing is an underutilized tool in the optimum care and management of this important and vulnerable patient population.

2.6 Geriatrics

The geriatric population is growing as baby boomers, a generation known for its wide acceptance of psychotropic drug use, enter old age.[158] Drug testing can do more than detect and monitor substance use; it can be used as a clinical tool to improve patient care,[159] particularly among the elderly patient population. Geriatric patients with a history of alcohol or drug use earlier in their lives are at higher risk of substance use disorders in their senior years.[160]

Altered mental status as a result of drug use – exhibited for example by prescription drug use from an unidentified source (e.g. "borrowing from a friend or family member") and/or unreported attendance at the ER, walk-in clinics or other health care providers – is difficult to identify in the brief period of time typically available to a busy clinician. A discussion of drug testing can quickly open up this avenue of inquiry and broadens the differential diagnosis to include treatable drug interaction problems and pharmacologically-induced cognitive impairment.

Drug testing is useful in the monitoring of treatment adherence among geriatric populations. Is an apparent treatment failure the result of the wrong course of therapy, or failure to adhere to a potentially efficacious therapeutic regimen? Is the wrong drug being used or does the patient need more encouragement/monitoring to take the medication as prescribed? In

[158] Koechl, B., Unger, A., & Fischer, G. (2012). Age-related aspects of addiction. *Gerontology, 58*(6), 540-541.
[159] Heit, H. A., & Gourlay, D. L. (2004). Urine drug testing in pain medicine. *Journal of Pain and Symptom Management, 27*(3), 260-267,
[160] Center for Substance Abuse Treatment. Substance Abuse Among Older Adults. (1998). Treatment Improvement Protocol (TIP) Series, No. 26. HHS Publication No. (SMA) 12-3918. Rockville, MD: Substance Abuse and Mental Health Services Administration.

some cases, the absence of a prescribed medication or its metabolite in a drug test result may be the only indication that the patient may not be fully adhering to treatment.

Diversion of prescription drugs is used by some elderly patients to cope with poverty or demoralization. The geriatric population has been the target of drug dealers, who may even take them to medical appointments and then trade prescriptions for cash. Moreover, family members may misappropriate patients' medications for profit or to support their own nonmedical drug use patterns. Here again, an unexpected negative drug test can be a useful point of conversation with a patient.[161]

With a drug test, there is a potential to open up a dialog with the patient that might not otherwise have occurred, in response to the presence or absence of certain drugs in a drug test result. Polypharmacy is a particularly challenging problem for the elderly.[162] The use of over-the-counter medications, health food store supplements, and multiple prescribing clinicians may go undetected if these specific points are not discussed with the patient. A drug test result can provide the opportunity for such a discussion. While routine drug testing in the general geriatric population may have a low therapeutic yield, drug testing in specific clinical situations or in an identified higher risk population is in the geriatric patients' interests.

2.7 Adolescent Medicine

The American Academy of Pediatrics (AAP) recommends routine screening of all adolescent patients for substance use yearly, at minimum, using a standardized, validated interview tool appropriate for this age group. Recognizing that adolescents, especially those with serious substance use disorders, may underreport or deny drug use, the AAP recommends drug testing as part of an assessment of behavioral or mental health symptoms.[163] Drug testing also is important for monitoring youth during and after treatment for substance use disorders. Parental involvement is essential to the success of substance use treatments.

[161] Inciardi, J. A., Surratt, H. L., Cicero, T.J., & Beard, R. A. (2009). Prescription opioid abuse and diversion in an urban community: the results of an ultrarapid assessment. *Pain Medicine, 10*(3), 537-548.
[162] Ghusn, H. (2012). Polypharmacy: what clinicians need to know while caring for an elder. *Le Journal Médical Libanais, 60*(4), 207-213.
[163] American Academy of Pediatrics. (in press/embargoed). Testing for drugs of abuse in children and adolescents. Washington, DC: American Academy of Pediatrics.

Forthcoming AAP guidelines detail recommended uses of drug testing in pediatric care, and information on interpreting results and managing adolescent patients.[164] Drug testing is clearly outlined by the AAP as a component of overall clinical assessment rather than a stand-alone assessment for drug use. The AAP recognizes the importance of information that can be obtained through drug testing and the need to carefully interpret test results. The AAP recommends that the collection of samples for drug testing require patient consent, although it also states that "refusal to consent to a drug test should not prematurely conclude an evaluation of a substance use problem or disorder."[165]

The AAP does not recommend that parents perform home drug testing to detect drug use by their adolescent children because of the complexity of the procedure and possible misinterpretation of the results.[166] The AAP "encourages parents who are concerned that their child may be using drugs or alcohol to consult their child's primary care physician or other health professional rather than rely on school-based drug testing or use home drug testing products,"[167] two areas discussed in more detail in ***3. Non-Clinical Applications of Drug Testing***. Further, the AAP recommends that "health care professionals who obtain drug tests or assist others in interpreting the results of drug tests be knowledgeable about the relevant technical aspects and limitations of the procedures."

2.8 Primary Care

The use of drug testing in primary care has been thoughtfully addressed in a Technical Assistance Publication (TAP) by the federal Center for Substance Abuse Treatment (CSAT).[168] There are several other guidelines developed by medical organizations and state medical

[164] American Academy of Pediatrics. (in press/embargoed). Testing for drugs of abuse in children and adolescents. Washington, DC: American Academy of Pediatrics.
[165] Ibid.
[166] Ibid.
[167] American Academy of Pediatrics Committee on Substance Abuse and Council on School Health. (2007). Testing for drugs of abuse in children and adolescents: addendum – testing in schools and at home. *Pediatrics, 1119*(3), 6270630. Available: http://pediatrics.aappublications.org/content/119/3/627.full
[168] Center for Substance Abuse Treatment. (2012).Clinical drug testing in primary care. *Technical Assistance Publication (TAP) Series, 32*. DHHS Publication No. (SMA) 12-4668. Rockville, MD: Substance Abuse and Mental Health Services Administration. Available: http://www.kap.samhsa.gov/products/manuals/pdfs/TAP32.pdf

societies including the Johns Hopkins University School of Medicine's continuing medical education monograph on urine drug testing in clinical practice for physicians.[169]

Screening for unhealthy levels of alcohol use and non-prescribed drug use through brief questions and motivational interviewing has been shown to be effective in identifying and helping patients with problems.[170] SBIRT is a key feature of the Patient Protection and Affordable Care Act (PPACA). Physicians are encouraged to ask all adolescent and adult patients about their use of alcohol and drugs. During the screening process, physicians ask patients if, in the past year they have ever consumed five or more standard drinks in a single sitting; if they have used any illegal drugs; if they have used prescription drugs without a valid prescription; and if they have used a prescription drug in ways not consistent with the recommendations of the prescribing physician. A "yes" answer to any element of this screen leads to further evaluation, which may include a POC or laboratory IA test for alcohol and other drugs.

Drug testing is especially important in primary care when dealing with patients who are at high risk of substance misuse or addiction. Recognizing that substance use is widespread, there are few if any unaffected patient populations. Nevertheless, it is wise to focus initially on the patient populations most at risk for substance misuse, including patients with a personal history of use, patients who have been treated for complications of substance use, including accidents, overdoses and infectious diseases, and patients with family histories of addiction.

Drug testing among high-risk populations includes routine testing to identify patients who are drug users, to assist in assessment of potential substance use disorders (SUDs), and to monitor recovery in patients with histories of SUDs. When patients are diagnosed with SUDs it is essential that the diagnosis not be a reason to withhold medical treatment in primary care; rather, it is an opportunity to intensify medical care and offer interventions. SUDs are commonly lifelong problems that require medical monitoring as part of health promotion and to identify relapses. SUDs are often treatable in primary care settings. For those patients whose SUDs cannot be managed successfully in these settings, referral to a specialized addiction clinician is indicated. Even then, however, it is important for primary care providers to remain involved in

[169] Gourlay, D., Heit, H. A., & Caplan, Y. H. (2012). *Urine Drug Testing in Clinical Practice: The Art & Science of Patient Care*. John Hopkins University School of Medicine. Available: http://www.udtmonograph.com/

[170] Lundahl, B. W., Kunz, C. Brownell, C., Tollefson, D., & Burk, B. L. (2010). A meta-analysis of motivational interviewing: twenty-five years of empirical studies. *Research on Social Work Practice, 20*(2), 137-160.

the ongoing care and monitoring of their patients, especially after they return from a specialty care setting to the care of the primary care provider.

The emergence of accountable care organizations (ACOs) and other payment reforms, and the emergence of medical homes and other primary care delivery system reforms, underscore the importance of not only the recognition of SUDs as major public health problems but also their long-term management within the medical context in both private sector and public sector settings. Drug testing should become a routine part of the ongoing testing process for SUDs in all primary care settings so as to discourage unauthorized drug use and to detect such use when it occurs, in order to allow for early intervention. The preventive and early diagnostic functions of drug testing are at the core of its wider use in health care settings.

Drug testing is important in primary care settings when physicians need to know about drug use prior to starting a medication or treatment in which drug use could be a critical determinant of outcome. For example, some neurosurgeons test patients for tobacco use before spinal surgery and may refuse surgery if the patient is positive for cotinine, and some orthopedic surgeons have imposed similar requirements on their patients before joint surgery. Additionally, when considering prescribing controlled substances, it is helpful to determine ongoing drug use. In such cases, a patient may refuse the drug test, but that may decrease the treatment options and the clinician may decide to withhold the prescribing of the controlled substance. The most important reason for such a protocol is safety. A drug-addicted person may seek additional drugs through prescription, which would increase their risk of overdose. Testing is also important in older patients who may have sleep apnea, chronic obstructive pulmonary disease, or other medical conditions that could make overdose or other adverse effects of opioid use more likely.

Drug testing can also prevent unnecessary prescribing in primary care. Drug use may cause the symptoms patients are seeking to treat. For example, students seeking stimulants to treat attention deficit hyperactivity disorder (ADHD), without symptoms of the disorder present in childhood may exhibit ADHD symptoms as adults after marijuana or other drug use.[171] Proper initial treatment of such a patient would involve discontinuing stimulant use to determine if the ADHD symptoms resolve. Similarly, some patients seek benzodiazepines from a physician because of anxiety and insomnia, but the actual cause of the symptoms might be stimulant

[171] Fergusson, D. M., & Boden, J. M. (2008). Cannabis use and adult ADHD symptoms. *Drug Alcohol Depend*, 95(1-2): 90-96.

misuse. Unfortunately, physicians who do not use drug testing in practice may prescribe multiple controlled substances to patients whose condition is caused by illegal drug use. New prescriptions may only make the problems worse. Much of this behavior may be preventable by routine drug testing in primary care.

Drug testing is appropriate in monitoring patients on prescribed controlled substances. An example of a safety concern is prescribing oxycodone to a patient who begins to use alprazolam or methadone purchased on the street. Drug testing can also help detect patients who are not taking their medications at all. Although such drug tests are voluntary it is acceptable medical practice that they be required if the physician is going to prescribe medications. A physician would not continue to prescribe a blood thinner such as warfarin to a patient who refused a prothrombin time test. Similarly, an oncologist would not continue chemotherapy for a patient who refuses white blood cell counts or liver function tests. Drug testing is voluntary but is linked to voluntary treatment, be it use of warfarin to treat blood clots, chemotherapy to treat cancer, long-term opioids to treat pain or amphetamine to treat ADHD.

In spite of the difficulties in doing drug testing in primary care, there are many surprise results that can impact treatment. The key to success is accuracy, confirmation and a positive, therapeutic attitude on the part of the physician and staff.

3. Non-Clinical Applications of Drug Testing

There are many non-patient populations in which drug testing is utilized, the lessons from which can inform other areas of drug testing, including health care testing.

3.1 Workplace

There are a variety of drug testing contexts in the workplace. Pre-employment drug tests are common and are usually scheduled events. Pre-employment tests serve as a basic screening tool for drugs in the workplace, though it usually only requires a few days of abstaining from drugs to produce a negative urine or oral fluid test result.

Random drug testing in the workplace is part of the mandatory federal drug testing program for employees in safety-sensitive positions[172] but may also be implemented more

[172] United States Department of Transportation Federal Motor Carrier Safety Administration. (n.d.). Alcohol and drug rules. Washington, DC: Federal Motor Carrier Safety Administration. Available: http://www.fmcsa.dot.gov/rules-regulations/topics/drug/engtesting.htm

widely in non-federal settings. The U.S. Department of Transportation has required random testing rates for drugs and for alcohol for each agency. For example, in 2013, the annual testing rate for the Federal Motor Carrier Safety Administration for random drug tests is 50% and for random alcohol tests is 10% (see Table 3).

Table 3. Department of Transportation Random Testing Rates 2013[173]

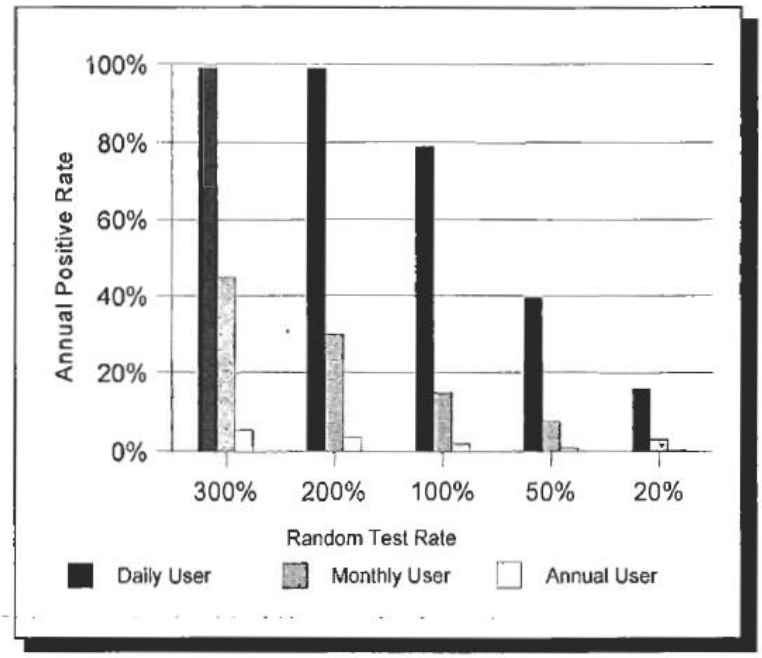
DOT Agency	Random Drug Testing Rate	Random Alcohol Testing Rate
Federal Motor Carrier Safety Administration (FMCSA)	50%	10%
Federal Aviation Administration (FAA)	25%	10%
Federal Railroad Administration (FRA)	25%	10%
Federal Transit Administration (FTA)	25%	10%
Pipeline & Hazardous Materials Safety Administration (PHMSA)	25%	N/A
United States Coast Guard (USC)	25%	N/A

Random drug tests most frequently identify regular drug users rather than one-time or occasional drug users.[174] The probability of identifying many daily, monthly, and annual illicit drug users is dependent on random drug testing rates. As Figure 5 shows, for example, an annual random urine drug testing rate of 100% (that is, conducting 100 tests per 100 workers in a year) would identify over the course of the year 79% of daily drug users, less than 20% of monthly drug users, and less than 5% of annual users.

[173] United States Department of Transportation. (2013). Current random testing rates: 2013 DOT random testing rates. Washington, DC: Department of Transportation. Available: http://www.dot.gov/odapc/random-testing-rates

[174] DuPont, R. L., Griffin, D. W., Siskin, B. R., Shiraki, S. & Katze, E. (1995). Random drug tests at work: The probability of identifying frequent and infrequent users of illicit drugs. *Journal of Addictive Diseases, 14*, 1-17.

Figure 5. Probability of Detection by User Type and Random Test Rate[175]



For-cause drug tests are typically conducted when employees appear to be impaired or are involved in work-related accidents. A recently proposed protocol to address workplace impairment includes immediate comprehensive for-cause drug testing with an expanded drug testing panel to better identify prescription and synthetic drugs and use of multiple testing matrices, followed by a thorough physician evaluation.[176]

Employees often are drug tested when returning to work after formal addiction treatment. ”Return to duty” testing is used to monitor the employee’s progress in maintaining abstinence and to identify relapses for re-referral to treatment and/or other resources. Workplaces may use Employee Assistance Programs (EAPs) to monitor drug and alcohol use and provide necessary interventions and provide treatment plans with employees.[177]

In a public policy statement on workplace drug testing, ASAM states that a positive drug test result should not be considered evidence of functional impairment or addiction. If there is

[175] DuPont, R. L. (1996, July/August). Do random workplace drug tests primarily identify casual or regular drug users? *MRO Update*, 5-7.
[176] Reisfield, G. M., DuPont, R. L., Demery, J. A., & Shults, T. F. (2013). A protocol to evaluate drug-related workplace impairment. *Journal of Pain and Palliative Care Pharmacotherapy, 27*(1), 43-48.
[177] U.S. Department of Health & Human Services, Federal Occupational Health. (n.d.) Employee assistance Program. Bethesda, MD: Federal Occupational Health. Available: http://www.foh.dhhs.gov/services/eap/eap.asp

suspected impairment, the drug test panel should include both prescription and illegal controlled substances. ASAM recommends the use of MROs to minimize erroneous interpretations of test results. Finally, ASAM notes the importance of the workplace employers, rather than MROs or physicians acting in clinical roles, in specifying penalties for employees as a consequence of a positive drug test result. If penalties are directly linked to test results, ASAM recommends forensic procedures, including witnessed specimen collection, chain-of-custody specimen handling, and laboratory confirmation of presumptive positive immunoassay test results.[178]

[178] American Society of Addiction Medicine. (2005). Public Policy Statement On Drug Testing in Workplace Settings. Adopted October 2002. Chevy Chase, MD: ASAM. Available: http://asam.org/docs/publicy-policy-statements/1drug-testing---workplace-10-021.pdf?sfvrsn=0

3.2 United States Military

The U.S. military is the model for the use of drug testing to prevent drug use. All active-duty personnel are frequently, randomly tested with observed collection. Unlike other settings, which typically use small drug test panels, military panels include the following core drugs: marijuana, cocaine, amphetamines (methamphetamines/MDMA/MDA), heroin (morphine/codeine/6 MAM), PCP and oxycodone/oxymorphone, plus recent additions of selected benzodiazepines, hydrocodone, and hydromorphone.[1] They have also recently added the potential for testing several synthetic cannabinoids. By using this more frequent and sophisticated strategy, the military assesses the extent of use of many drugs over time in various populations and geographic locations.

In 1980, 27.6% of all active duty military personnel used an illegal drug in the past month.[179] The military drug testing program began in 1982, and from 1980 to 1988 the rate of illegal drug use dramatically declined and through 1998 to 2.7%.[180] Past month illegal drug use among active duty personnel increased from 5% in 2005 to 12% in 2008, largely due to the nonmedical use of prescribed controlled substances; however, the use of purely illegal drugs has not changed in recent years.[181] Most recently, in 2011, 1.4% of active duty personnel reported past-year use of purely illicit drugs while 1.3% reported nonmedical use of prescription drugs.[182]

In 2011, nearly 90% of active duty personnel reported being drug tested within the past year and 28% reported being tested in the prior month.[183] Although it is not practical to test most populations with a high level of intensity, the U.S. military drug testing program provides useful lessons for drug prevention about the effectiveness of smarter random drug testing.

3.3 Criminal Justice System

Most offenders in community corrections on parole and probation are subject to prolonged supervision, often several years or longer. Typically offenders are subject to infrequent, usually scheduled, drug testing. Often the results are not sent to their probation or parole officers for days or weeks after sample collection. This is the “Old Paradigm” of

[179] Bray, R.M., et al. (1999). *1998 Department of Defense Survey of Health Related Behaviors Among Military Personnel*. RTI Institute.
[180] U.S. Department of Defense, Office of the Assistant Secretary of Defense. (1999, May 13). DOD releases results of 1998 Survey of Health Related Behaviors. Available: http://www.defense.gov/releases/release.aspx?releaseid=2085
[181] Bray, et al. (2009). *2008 Department of Defense Survey of Health Related Behaviors Among Active Duty Military Personnel*. RTI Institute. Available: http://www.tricare.mil/2008HealthBehaviors.pdf
[182] Barlas, F. M., Higgins, W. B., Pfieger, J. C., & Diecker, K. (2013). *2011 Department of Defense Health Related Behaviors Survey of Active Duty Military Personnel, Executive Summary.* Department of Defense. Available: http://tricare.mil/tma/dhcape/surveys/coresurveys/surveyhealthrelatedbehaviors/downloads/Final%202011%20HRB%20Active%20Duty%20Survey%20Exec%20Summary.pdf
[183] Ibid.

community corrections. Typically, there are no meaningful consequences when offenders miss drug tests or test positive for illegal drugs, even though drug use is a violation of the requirements of their community supervision. Only after repeated infractions is a sanction finally imposed. This unpredictable, delayed, and seemingly arbitrary and often draconian punishment has little effect on offender behavior. Often that sanction is prolonged incarceration based on the original criminal offense.

The use of infrequent scheduled drug tests is an ineffective strategy to identify drug use. Combined with long-delayed, unpredictable, and draconian consequences, this paradigm is a poor way to change offender behavior. With an estimated national recidivism rate of 40% and substantial numbers of individuals re-incarcerated due to technical violations of community corrections,[184] this is a promising area for reducing drug use, criminal recidivism, and the high costs in dollars and lives of prolonged incarceration.

Dramatically different from the "Old Paradigm," a New Paradigm is now used by innovative criminal justice programs. The New Paradigm in community corrections administers frequent random drug tests to enforce the no-use standard. Any drug use or other program violation, such as missed appointments with probation or parole officers is met with swift, certain and meaningful – but not draconian – consequences, i.e. brief incarceration. The New Paradigm recognizes that not every offender with substance use problems requires treatment, thus saving scarce treatment resources for those who need it most. It sets a new standard for community corrections.

In Hawaii's HOPE Probation, probationers are subject to intensive random drug testing for up to six years. Any drug use or other program violation (e.g. missed appointments) is met with immediate short-term incarceration. These sanctions are swift and certain, but not oppressive. Formal treatment is provided to probationers who request it and to those who demonstrate a need for it through continued drug use under monitoring alone.

In a one-year, randomized, controlled study of HOPE Probation compared to standard probation, HOPE participants were 55% less likely to have been arrested for new crimes, 72% less likely to have used drugs, 61% less likely to have missed appointments with probation

[184] Pew Center on the States. (2011). *State of Recidivism: The Revolving Door of America's Prisons.* Washington, DC: The PEW Charitable Trusts. Available: http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/Reports/sentencing_and_corrections/State_Recidivism_Revolving_Door_America_Prisons%20.pdf

officers, and 53% less likely to have had their probation revoked.[185] Over the course of one year, 61% of HOPE participants never had a single positive drug test, 20% had only one positive, 9% had two positives, and 10% had three or more positives.

South Dakota's 24/7 Sobriety, a program focused on repeat Driving Under the Influence (DUI) offenders, utilizes a combination of mandatory twice-daily alcohol breath testing and random drug testing or, alternatively, a combination of continuous alcohol monitoring ankle bracelets and sweat testing patches to identify any recent alcohol or drug use. Any evidence of alcohol or other drug use is met with immediate arrest and a short jail stay. Forty-eight percent of participants had three or more prior DUI convictions. Over the average estimated 111 days of participation in the program, 55% of participants did not fail a single alcohol or drug test, 17% had one positive, 12% had two positives, and 16% had three or more positives.[186] The 24/7 Sobriety Project has expanded across South Dakota and new programs are emerging nationally using this model, which is applicable to the 1.4 million drivers arrested each year for DUI.

The New Paradigm, embodied by these and similar programs, has been shown to significantly reduce drug use, criminal recidivism, and incarceration. The foundation of this approach is frequent, random drug testing.

3.4 Highway Safety

Drugged driving is now a leading cause of crashes, injuries, deaths, and associated financial losses – on scale with the better known problem of drunk driving.[187] New efforts to curb drugged driving are based on wider use of drug testing of drivers identified as impaired.[188] Additionally, the standardization of drug testing methodologies for laboratories conducting analysis in highway safety is another federal focus to address the drugged driving problem. As drug testing has become more common in highway safety it has become more important to develop forensically defensible drug tests for many drugs of abuse both at the roadside and the police station.

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[185] Hawken, A., & Kleiman, M. (2009). Managing drug involved probationers with swift and certain sanctions: Evaluating Hawaii's HOPE. National Institute of Justice, Office of Justice Programs, U.S. Department of Justice. Award number 2007-IJ-CX-0033.

[186] South Dakota Office of the Attorney General. (2012). 24/7 Sobriety Program. Available: http://apps.sd.gov/atg/dui247/247ppt.pdf

[187] More information about drugged driving can be found at: www.StopDruggedDriving.org, www.StopDUID.org, and www.WeSaveLives.org

[188] Office of National Drug Control Policy. (2012). National Drug Control Strategy, 2012. Washington, DC: Office of National Drug Control Policy. Available: http://www.whitehouse.gov/sites/default/files/ondcp/2012_ndcs.pdf

In 2009, 63% of all fatally injured drivers were drug tested using whole blood, though the percentage of drivers tested varies dramatically by state. Increasing drug testing of fatally and seriously injured drivers will dramatically improve the limited drugged driving knowledge base.[189]

Drug testing currently conducted in highway settings is largely an adjunct to efforts to detect alcohol-impaired drivers.[190] Typically only when drivers arrested for impairment who do not produce a blood alcohol concentration (BAC) at or above 0.08 g/dL are they tested for drugs using matrices of urine or blood.

In 2010, 1.2 million drivers were arrested for DUI;[191] these drivers who are educated after arrest should be tested for alcohol and drugs. As in the case of alcohol-impaired driving, the process of drug testing and prosecution of drug-impaired drivers can expand the pathway into addiction treatment and recovery. The aforementioned 24/7 Sobriety Project provides an inspiration for a new generation of programs to manage DUI offenders, one that holds the promise of deterring alcohol and other drug use and reducing the high rate of recidivism in this high-risk population.[192] A comprehensive research agenda for drugged driving has recently been published by the National Institute on Drug Abuse.[193]

Drug testing is a crucial part of drugged driving identification and enforcement. The successful use of administrative license revocation (ALR) to quickly remove drunk drivers off the road[194] provides a model for new laws to address drugged drivers. Under current ALR laws, drivers that test at or above 0.08 g/dL BAC lose their licenses immediately; these laws have

[189] DuPont, R. L., Logan, B. K., Shea, C. L., Talpins, S. K., & Voas, R. B. (2011). Drugged driving: A white paper. Institute for Behavior and Health, Inc. Drugged Driving Committee. Bethesda, MD: National Institute on Drug Abuse.
[190] DuPont, R. L., Voas, R. B., Walsh, J. M., Shea, C., Talpins, S. K., & Neil, M. M. (2012). The need for drugged driving per se laws: A commentary. *Traffic Injury Prevention, 13*(1), 31-42.
[191] U.S. Department of Justice, Federal Bureau of Investigation. (2012). Crime in the United States, 2011. Persons arrested. Available: http://www.fbi.gov/about-us/cjis/ucr/crime-in-the-u.s/2011/crime-in-the-u.s.-2011/persons-arrested/arrestmain_final.pdf
[192] Kilmer, B., Nicosia, N., Heaton, P., & Midgette, G. (2013). Efficacy of frequent monitoring with swift, certain, and modest sanctions for violations: insights from South Dakota's 24/7 Sobriety Project. *American Journal of Public Health, 103*(1), e37-e43.
[193] DuPont, R. L., Logan, B. K., Shea, C. L., Talpins, S. K., & Voas, R. B. (2011). Drugged driving: A white paper. Institute for Behavior and Health, Inc. Drugged Driving Committee. Bethesda, MD: National Institute on Drug Abuse.
[194] Nelson, T. F., Xuan, Z., Babor, T. F., Brewer, R. D., Chaloupka, F. J., et al. (2014). Efficacy and the strength of evidence of U.S. alcohol control policies. *American Journal of Prevention Medicine, 45*(1), 19-28.

reduced alcohol-related fatal crash involvement.[195] Under an ALR law for drugs, drivers arrested for suspicion of impaired driving who test positive for drugs would have their licenses suspended.

3.5 Education

Because children spend much of their time in school, school is an environment in which substance use can be identified and where appropriate interventions can take place. Early substance use is an important risk factor for later addiction.[196] There is a bidirectional relationship between substance use and academic failure and dropout in high school and college.[197] [198] Academic failure and dropout on the one hand, and substance use on the other, are closely linked. Youth in recovery from substance use disorders report increased academic performance and school attendance.[199] If paired with constructive interventions, drug testing of at-risk youth could increase early identification and management of drug use and other high-risk behaviors and improve educational outcomes.

Many schools have for-cause drug testing policies for students who appear intoxicated. Such tests are typically tied to school-wide substance use policies in which evidence of drug use or impairment at school results in disciplinary action. In addition some schools have implemented random student drug testing (RSDT) programs as part of comprehensive drug and alcohol use prevention programs.[200] RSDT has two explicit goals: to prevent student drug use and, failing prevention, to provide an intervention, including engaging the student's family and referral to clinical services in order to help the student become and stay drug-free.[201] In schools

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[195] Wagenaar, A. C., & Maldonado-Molina, M. M. (2007). Effects of drivers' license suspension policies on alcohol-related crash involvement: long-term follow-up in forty-six states. *Alcoholism, Clinical and Experimental Research, 31*(8), 1399-1406.

[196] Chen, C., Storr, C. L., & Anthony, J. C. (2009). Early-onset drug use and risk for drug dependence problems. *Addictive Behaviors, 34*(3), 319-322.

[197] DuPont, R. L., Caldeira, K. M., DuPont, H. S., Vincent , K. B., Shea, C. S., & Arria, A. M. (2013). America's Dropout Crisis: The Unrecognized Connection to Adolescent Substance Use. Rockville, MD: Institute for Behavior and Health, Inc.

[198] Arria, A. M., Caldeira, K. M., Bugbee, B. A., Vincent, K. B., & O'Grady, K. E. (2013). The Academic Opportunity Costs of Substance Use During College. College Park, MD: Center on Young Adult Health and Development.

[199] DuPont, R. L., Caldeira, K. M., DuPont, H. S., Vincent , K. B., Shea, C. S., & Arria, A. M. (2013). America's Dropout Crisis: The Unrecognized Connection to Adolescent Substance Use. Rockville, MD: Institute for Behavior and Health, Inc.

[200] More information about RSDT can be found at: www.PreventionNotPunishment.org

[201] DuPont, R. L., Merlo, L. J., Arria, A. M., & Shea, C. L. (2012). Random student drug testing as a school-based drug prevention strategy. *Addiction, 108*(5), 839-845.

with RSDT, a positive random drug test result, in contrast to a positive for-cause drug test result, should never lead to student suspension or expulsion from school.

Two Supreme Court cases affirmed schools' drug testing of students engaged in athletics and other extracurricular activities.[202] When students in the testing pool test positive on random drug tests, their families are informed and the students are evaluated to determine if referral for outside help is needed. Students are typically temporarily removed from extracurricular activities until they produce a negative drug test result, demonstrating abstinence from drugs. Follow-up testing may be used to help motivate the student to remain drug-free. Although RSDT is designed to be non-punitive,[203] a survey of school coordinators indicated that some do not follow federal guidelines and may implement consequences for random tests that are more appropriate to "for-cause" testing contexts, [204] further adding to the controversy of RSDT. An estimated 25% of all U.S. school districts with middle or high schools reported having student drug testing policies in 2006, with half of those conducting random drug testing of specific student populations.[205] A recently published study showed that, compared to students who knew they were not in the random drug testing pool at their school, students who knew they were subject to random testing were less likely to use illegal drugs and had more positive views of testing.[206]

The American Academy of Pediatrics (AAP) does not endorse the use of RSDT in schools due to a paucity in evidence of their efficacy to reduce drug and identify individuals with substance use disorders. However, the AAP recognizes that schools play an important role in the prevention and reduction of adolescent substance use.[207] There is a general concern that RSDT programs target students who are at lower risk for substance use than their peers who do

[202] Vernonia School District 47J v. Acton, 1995; Board of Education of Independent School District No. 92 of Pottawatomie County, et al, Petitioners v. Lindsay Earls et al, 2002.
[203] Office of National Drug Control Policy. (2002). What You Need to Know about Drug Testing in Schools. NCJ publication no. 195522. Washington, DC: Office of National Drug Control Policy; Office of National Drug Control Policy. (2004). What You Need to Know about Starting A Student Drug-Testing Program. NCJ Publication no. 206126. Washington, DC: Office of National Drug Control Policy.
[204] Ringwalt C., Vincus A. A., Ennett S. T., Hanley S., Bowling J. M., Yacoubian G. S. Jr., et al. (2009). Responses to positive results from suspicionless or random drug tests in U.S. public school districts. *Journal of School Health, 79*(4), 177–83.
[205] Jones, S. E., Fisher, C. J., Hertz, M. F., & Pritzl, J. (2007). Healthy and safe school environments part I: results from the School Health Policies and Programs Study 2006. *Journal of School Health, 77*(8): 522–43.
[206] DuPont, R. L., Campbell, M. D., Campbell, T. G., Shea, C. L., & DuPont, H. S. (2013). Self-reported drug and alcohol use and attitudes toward drug testing in high school with random student drug testing. *Journal of Child & Adolescent Substance Abuse, 22*(2), 104-119.
[207] American Academy of Pediatrics. (in press; embargoed). Adolescent drug testing policies in schools. Washington, DC: American Academy of Pediatrics.

not participate in extracurricular activities or athletics. It is stressed by the AAP that drug testing should not be instituted in place of other support services for students. Those engaged in education, prevention, and pediatric care agree that rigorous long-term research on the current practices and efficacy of RSDT in schools is needed.[208]

3.6 Home/Family

Like school, home is a crucial environment for youth drug prevention and for the identification of alcohol and drug use. Parental expectations about alcohol and drug use are an important factor in youth drug use.[209] It is vital for parents to clarify their expectations and to exercise their authority to prevent youth from using alcohol, tobacco, and other drugs, the use of which is both illegal and particularly harmful to the still-developing adolescent brain.

While not recommended by the American Academy of Pediatrics (AAP) (see 2.7. Adolescent Medicine under ***2. Drug Testing in Various Medical Specialties***), some families use POC drug testing kits at home to deter and detect drug use by family members as part of a family policy on drug and alcohol use.[210] Parents monitoring for signs and symptoms of substance use can seek an evaluation by a health care professional including the use of drug testing. Supervision of drug testing by a knowledgeable health care professional in the administration and interpretation of drug tests results is helpful as parents may not understand the limitations of a drug test or the full implications of a result. Various matrices may be used depending on the reason for and scope of the testing. For example, hair tests will detect drug use over a period of months while oral fluid tests will detect drug use over the previous hours, to a day, or more (e.g. THC-COOH has been identified in heavy chronic marijuana users for three weeks[211]).

Positive drug tests provide an opportunity for family intervention and may lead to further evaluation and treatment by health care professionals. How parents handle positive drug tests

[208] DuPont, R. L., Merlo, L. J., Arria, A. M., & Shea, C. L. (2012). Random student drug testing as a school-based drug prevention strategy. *Addiction, 108*(5), 839-845.
[209] Substance Abuse and Mental Health Services Administration, Office of Applied Studies. (2009, May 28). The NSDUH Report: Parental Involvement in Preventing Youth Substance Use. Rockville, MD: Substance Abuse and Mental Health Services Administration. Available: http://www.oas.samhsa.gov/2k9/159/ParentInvolvementHTML.pdf
[210] DuPont, R.L., & Bucher, R.H. (2012). Guide to Responsible Family Drug and Alcohol Testing. Rockville, MD: Institute for Behavior and Health, Inc.
[211] Bergamaschi, M. M., Karschner, E. L., Goodwin, R. S., Scheidweiler, K. B., Hirvonen, J., Queiroz, R. H., & Huestis, M. A. (2013). Impact of prolonged cannabinoid excretion in chronic daily cannabis smokers' blood on per se drugged driving laws. *Clinical Chemistry, 59*(3), 519-526.

can be problematic. Physicians can be helpful in managing how parents respond to positive drug tests. It is important to fit the testing into the family values and to establish the circumstance under which testing will be done and the consequences for both positive and negative tests. A paper is available to help parents think through these issues.[212]

V. Conclusions

Drug testing, the technology of addiction medicine, identifies the use of specific drugs with the potential for misuse and addiction. Drug test results do not identify or diagnose substance use disorders, or establish the presence of impairment or physical dependence. Although drug testing is not a magic bullet that solves all of the problems associated with substance use disorders, drug testing is essential for the identification of recent drug use in all settings in which drug – and in many cases, alcohol – use is problematic.

Drug tests are not the only way to identify drug use. It is also valuable to speak with people, since self-report identifies the use of drugs not included on test panels and covers a far longer period of time than do drug tests, and reports from others (e.g. family members, workplace supervisors, etc.) can provide useful information as well. Self-report permits detailed questions related to the pattern of drug use, consequences arising from that use, and efforts that have been made to cut down or stop use. Thus, self-report is complementary to drug testing. It is wise to use both.

The most basic and crucial questions about drug testing involve whom to test, what drugs to test for, what matrix to use (which body fluid or tissue to test), and what to do with the test results. These questions must be answered in each specific application of drug testing.

Today drug testing is dramatically evolving to become more effective at the same time that the modern drug epidemic is evolving to become more complex. A generation ago, drug testing meant almost exclusively testing urine or blood. Now drug testing matrices includes oral fluid, hair, nails, sweat and breath. Similarly, in years past, drug testing meant the identification of the recent use of a relatively small number of widely-used, mostly agriculturally-produced, drugs. Now the dramatic and deadly increase in the misuse of prescription controlled substances presents a significant challenge to testing. While standard drug testing practice

[212] DuPont, R.L., & Bucher, R.H. (2012). Guide to Responsible Family Drug and Alcohol Testing. Rockville, MD: Institute for Behavior and Health, Inc. Available: http://www.preventionnotpunishment.org/pdfs/GuidetoResponsibleFamilyDrugandAlcoholTesting.pdf

historically included testing for a small number of widely used drugs, such a narrow focus has become less useful today especially with the emergence of the ever-changing, synthetic "designer" drugs that are designed to evade detection through drug tests and to evade drug laws. Unlike drugs from earlier generations, today's drugs of abuse are often created in chemistry laboratories and not grown on farms; nor are neither they exclusively distributed through well-established criminal channels. Designer drugs, for example, are produced in clandestine laboratories all over the world and sold in convenience stores and gas stations or sent by global delivery services. In addition, prescription drugs associated with misuse and addiction usually originate with legal prescriptions written by physicians.

Most drug testing panels today include less than 20 drugs, often as few as five. The available testing panels change much more slowly than the rapid changes in the patterns of drug use. The efforts to thwart drug testing are dramatically more sophisticated, better organized, and more available than was true even a decade ago.

Looking forward, drug testing technology will become increasingly sensitive and easier to use, possibly leading to the development of breath testing for drugs of abuse, as is now done for alcohol. The move to from urine testing to oral fluid testing reduces privacy concerns and minimizes the subversion problems that bedevil urine testing. Drug testing practices in the future must include identification of a far larger number of drugs. Drug testing must become less expensive and more resistant to subversion. Drug tests must rapidly identify newly emerging drugs of abuse. Important as these technical challenges are in drug testing, the challenge that is directly addressed by this White Paper, while different, is no less important. Today's most urgent need is for broader use of drug testing, especially in clinical settings, and for smarter approaches to drug testing, especially by physicians working in addiction medicine and all medical specialties.

ASAM's principal goal in drug testing is for today's impressive drug testing technology to be far more widely used, particularly within health care. Wider, smarter, and more appropriate use of drug testing holds the promise of deterring drug use and minimizing its adverse consequences, including addiction, crime, infectious diseases, drug-impaired driving, drug-drug interactions, overdoses, and death. In particular, wider use of drug testing in health care is needed to identify patients with substance use problems and to get them the help they need to become and to stay drug-free. Patients with substance use disorders need to be tested in health care over long periods of time to discourage and to identify relapses. Drug testing needs

to become as common in medical practice as clinical diagnostic testing is in the management of hypertension and diabetes.

Patients may refuse to allow drug testing. Both denial that there are any problems related to substance use and resistance to drug testing sometimes greet drug testing requests by physicians. Patients may feel they have been singled out inappropriately. They may feel they are being accused of drug misuse. They may jealously guard their scheduled prescriptions for pain and anxiety, especially if they misuse the medications. Patients may become angry or anxious and avoid any meaningful discussions about the issues related to their substance use. They may even express a desire to switch physicians or health care professionals.

For nonclinical populations, there is usually leverage that is used to override resistance to drug testing. In many settings where testing is being conducted there is the potential for loss of current or desired employment, or threatened loss of or restrictions on a professional or commercial license, or legal and forensic necessity is usually persuasive. In clinical settings the leverage is in the relationship between the physician or health care professional and the patient. The development of this traditional relationship, even with a first visit, is enhanced by conducting a thorough patient history and physical examination. The rationale for drug testing (and other testing procedures) naturally flows from the results of these evaluations and is usefully related to other tests commonly done to guide diagnosis and treatment. Subsequent discussions and explanations approached in a calm, non-accusatory matter-of-fact manner can help reduce resistance to drug testing. The thoughtful compassionate and persuasive skills of the physician, all in the patients' interests, can reassure patients that testing is done *for* them to enhance their health and safety and not just something done *to* them to embarrass or harm them. It is incumbent on physicians and other health care professionals to assist patients to conclude drug testing is in the patients' interests.

The identification of drug use in all clinical settings permits appropriate interventions to promote health and to reduce the high rate of health problems associated with drug and alcohol use. It is to the achievement of this goal, especially within health care, that this White Paper is dedicated.

VI. Glossary

Terminology in drug testing must be used by all stakeholders and be consistent with current with basic science and best clinical practices. The following defined terms are relevant to the practice and technology of drug testing and are referred to throughout the text. Many of these terms appear in the glossaries of other ASAM publications, including *The ASAM Criteria* and ASAM's comprehensive textbook, *Principles of Addiction Medicine*. Note that some terms included in this glossary are terms which ASAM has recommended to not be used any longer, such as the terms "misuse" and "substance abuse." An asterisk [*] denotes a definition that has been formally adopted by the ASAM Board of Directors.

This glossary is written to assist readers of this White Paper. It is not an official glossary of ASAM. The meanings of many of the terms used here continue to be controversial and to evolve with new meanings in new contexts. Like any dictionary, the definitions here are subject to change over time in the evolving settings in which they are used.

Abstinence*: Intentional and consistent restraint from the pathological pursuit of reward and/or relief that involves the use of substances and other behaviors. These behaviors may involve, but are not necessarily limited to, gambling, video gaming, spending, compulsive eating, compulsive exercise, or compulsive sexual behaviors. In cases related to substance use or substance use disorders, abstinence refers to the absence of use of **drugs of abuse**, including alcohol. Abstinence does not preclude the use of prescription drugs used as directed by the prescribing physician.

Abuse: *This term is not recommended for use in clinical or research contexts.* Abuse can be synonymous with harmful use of a specific psychoactive substance. The term abuse also applies to one category of psychoactive substance-related disorders in previous editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) of the American Psychiatric Association. While recognizing that the term "abuse" is part of past diagnostic terminology, ASAM recommends that an alternative term be found for this purpose because of the pejorative connotations of the word "abuse."

Addiction*: A primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits, caused by prior repeated drug use, leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. Addiction is

characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

Addiction-credentialed physician: Predetermined set of standards, such as certification, establishing that the physician has achieved professional recognition in the treatment of addiction. Physicians can be certified for their expertise in addiction by two pathways. Any physician may either complete an Addiction Medicine fellowship or meet other eligibility criteria and then by examination, receive certification and Diplomate status from the American Board of Addiction Medicine. A second pathway is exclusive to psychiatrists. A psychiatrist may complete a fellowship in Addiction Psychiatry, and then by examination become certified by the American Board of Psychiatry and Neurology, a member board of the American Board of Medical Specialties. In situations where a certified addiction physician is not available, physicians treating addiction should have had some specialty training and/or experience in addiction medicine or addiction psychiatry and if treating adolescents, experience with adolescent medicine.

Addiction Psychiatrist. A physician who specializes in addiction psychiatry and is Board Certified in this subspecialty by the American Board of Psychiatry and Neurology.

Addiction Specialist Physician: A general term that encompasses **addictionist** and **addiction psychiatrist**.

Addiction treatment*: Treatment is the use of any planned, intentional intervention in the health, behavior, personal and/or family life of an individual suffering from alcoholism or from another drug dependency designed to enable the affected individual to achieve and maintain sobriety, physical and mental health, and a maximum functional ability. There are many components of treatment including, but not limited to, physical and psychiatric evaluations, detoxification, counseling, self-help support, treatment for co-morbid physical or behavioral complications, and medication-assisted treatment. For a more complete discussion on treatment modalities, read ASAM's Public Policy Statement on Treatment for Alcoholism and Other Dependencies.

Addictionist (also, addictionologist):* A physician who specializes in addiction medicine (usually someone certified by the American Board of Addiction Medicine (ABAM) or the American Board of Psychiatry and Neurology (ABPN) in addiction psychiatry).The preferred term is **addictionist** or **addiction specialist physician**, rather than the older term "addictionologist."

Addictive Disorder: Clinical presentations due to addictive behaviors such as gambling that demonstrate sufficient signs or symptoms to substantiate a diagnosis of an addictive disorder in the DSM-5 of the American Psychiatric Association. Consistent with ASAM's definition of addiction, ASAM makes no distinction between the individual pathologically pursuing reward and/or relief by substance use and other behaviors. Thus "addictive disorders" involve both substance use disorders and addictive behaviors that meet diagnostic criteria, e.g., gambling disorder.

Adulteration: Any process used to attempt to alter the results of a drug test. For example, adding a chemical to a urine sample. Adulteration is an example of **subversion**.

Analyte: A substance (drug or drug metabolite) or chemical component that is the target of analysis. It is the compound that is "tested for" and the compound that, when present in a sample, results in a test result being reported as "positive."

At-risk Use (alternately: Risky Use): See ***Hazardous Use***

Binge or ***binge drinking.*** *This term not recommended for use in clinical or research contexts.* These terms can be useful in public health discourse because a "binge" is often understood to be a heavy drinking episode. [Note: The United States Centers for Disease Control and Prevention uses the term to mean heavy drinking episode; however, because it is used variably with different meaning it is not generally preferred.] The general public often uses the terms "binge" and "bender" interchangeably to describe heavy use of drugs of abuse during a short period of time or a days-long episode of heavy drinking.

Chain-of-custody: A legal term that refers to a process that identifies and documents all individuals involved with the collection, transport, testing and reporting of a drug test result and the "hand-off's" of a sample from one individual to another.

Clinical drug testing: Refers to the use of drug testing by physicians and other health care treatment providers to help determine the medical condition of a patient and to inform care of that patient.

Confirmation testing: Confirming the results of a preliminary drug test using a highly specific mass spectrometry technique such as **gas chromatography-mass spectrometry** or **liquid chromatography-mass spectrometry**. A **confirmation test**, sometimes referred to as an **identification test** or a **definitive test**, is often used to validate an initial, less specific **screening test**.

Controlled substance: A substance subject to statutory control under the federal Controlled Substances Act or comparable state legislation; includes illicit drugs and medications that can be obtained legally only with a valid prescription. Controlled substances are listed in the Controlled Substances Schedules maintained by the federal Drug Enforcement Administration; thus, the terms “scheduled drug” and “controlled substance” are often used interchangeably.

Creatinine: A breakdown product from creatinine phosphate in muscle which is primarily filtered out of the blood through the kidneys at a fairly constant rate; often used as part of the process to conduct **validity testing** (see definition below) on urine drug test samples.

***Cut-off*:** The drug concentration above which an assay reports a positive result and below which the result is reported as “negative.”

Definitive testing: See ***identification testing***.

Designer drugs: An informal term for psychoactive drugs discovered through research on, or experimentation upon, existing ***drugs of abuse***. Small modifications to known psychoactive drugs—such as their structural analogues, stereoisomers, and derivatives—yields drugs that may differ greatly in effects from their “basis” drug (e.g. showing increased potency, or novel psychoactive effects, or decreased side effects). In some instances, designer drugs are developed that have similar subjective effects to other drugs, but have completely dissimilar chemical structures. Designer drugs are synthesized in order that a novel psychoactive compound may be available for sale and use that can evade detection through drug tests and can evade law enforcement consequences for the user, seller or manufacturer of the drug.

Diversion: The act of diverting drugs from their lawful medical purpose.

Donor: The individual providing a specimen for drug testing.

Drug: A natural or artificial substance that is used to treat, diagnose, mitigate the effects of or prevent disease, or is used to produce brain reward.

Drug of abuse: Chemicals that produce brain reward and are associated with cases of **addiction**; such compounds generally appear under **controlled substance** schedules, though technically legal substances such as ethanol and nicotine are "abusable" drugs as well. **Drugs of abuse** are the substances used by persons with **substances user disorders**. While the term **abuse** is not recommended for use in clinical research contexts (see above), as the term can be considered synonymous with **harmful use** of a specific psychoactive substance and the terms **substance abuse** and **drug abuse** are considered by ASAM to be antiquated (given changes in the DSM-5), pejorative and stigmatizing, the term "substance abuse" still has wide currency, especially in governmental, research, and policy settings. While the **non-medical drug use** or **unhealthy use** of drugs can represent both aberrant behavior that can produce adverse health consequences, or place a user at risk for such consequences, and also can be associated with **addiction**, and while terms such as "addictive drug" or "psychoactive drug" or "euphoriant" may be less stigmatizing than the term "drug of abuse," most health professionals understand what is meant by the term **drug of abuse** and this term is used in this White Paper in the service of brevity and familiarity.

Drug use: Use of ***drugs of abuse***. Use can be isolated and infrequent, or frequent and risky, or harmful to the user or collaterals. Use can produce no identifiable harm or risk; thus, **drug use** occurs in many cases of **addiction** but also occurs in many situations by persons who do have addiction. **Drug use** is often unhealthy but is not necessarily so.

Drug abuse: *This term is not recommended for use in clinical or research contexts (see **abuse**).* Alternate, more appropriate terms are preferred such as **nonmedical drug use**, **unhealthy use**, **harmful use,** or **substance use disorder**.

Drug misuse: *This term is not recommended for use in clinical or research contexts.* Alternate, more appropriate terms are preferred such as **nonmedical drug use**, **harmful use,** or **at-risk use**.

Drug test panel: A single diagnostic procedure ordered by a physician or licensed independent practitioner which includes several **analytes**. Drug test panels are constructed to allow for the

testing of several analytes that are likely to represent drugs used by a given patient population. Panels are often less expensive (and thus more cost-effective for clinicians and patients) than ordering separate drug tests for individual analytes. A drug test panel can also specify which technologies will be used.

Employee assistance program (EAP): Serves organizations and their employees in multiple ways, ranging from consultation at the strategic level about issues with organization-wide implications to individual assistance to employees and family members experiencing personal difficulties. EAPs are workplace program designed to assist: (1) work organizations in addressing productivity issues, and (2) "employee clients" in identifying and resolving personal concerns, including health, marital, family, financial, alcohol, drug, legal, emotional, stress, or other personal issues that may affect job performance

Enzyme-linked immunosorbant assay (ELISA): Assay test used to detect the presence of antibodies or antigens in a liquid or wet sample such as blood, urine or oral fluid.

False negative: The analytical failure to detect the presence of a drug or drug metabolite that is present in the specimen. A false negative on a **screening immunoassay test** can be discovered by **confirmation testing** using **GC-MS** or **LC-MS/MS** testing when these tests are used on samples that have been screened as negative.

False positive: The reporting of a positive drug or drug metabolite that is not present in the specimen. A false positive on a **screening immunoassay** test is often discovered by **confirmation testing** using **GC-MS** or **LC-MS/MS** testing.

> ***Clinical false positive:*** A positive test result caused by incidental or extraneous exposure to a substance.
>
> ***Analytical false positive:*** A positive test result caused by changes in the sample which may be related to physical disease or conditions of the donor or improper or delayed storage, etc.

First-pass effect: The initial metabolism of drugs which have been orally ingested and absorbed by the upper gastrointestinal tract; this term refers to the biological actions applied to drugs as they pass through the liver on their way to distribution into the general circulation. First-pass metabolism often involves oxidative metabolism via the cytochrome P450 enzyme system in the liver.

For-cause drug test: A drug test ordered as a result of an observed behavior that may be the result of the use of alcohol or other drugs. For example, testing after a workplace or highway accident or after an employee at work or operator of a motor vehicle appears to be impaired.

Forensic drug testing: Refers to the practice of using drug testing to identify drug use in non-medical settings, particularly legal contexts and in the workplace. Forensic drug testing uses standardized procedures related to informed consent, specimen collection, chain-of-custody and use of medical review. **Forensic drug testing** involves analytical techniques and specimen collection and handling processes that will allow for test results to comport with rules of evidence in criminal and similar procedures.

Gas chromatography-mass spectrometry (GC-MS): An analytic technique used to separate and identify a compound based on its molecular structure and properties. **GC-MS** typically involves extraction of the drug or drug metabolite from the biological **matrix** prior to analysis. The **analyte** is separated from other analytes or adulterants via gas chromatography and then is identified as a unique compound (rather than as a member of a pharmacological class of compounds) via mass spectrometry.

Harm reduction*: A treatment and prevention approach that encompasses individual and public health needs, aiming to decrease the health and socio-economic costs and consequences of addiction-related problems, especially medical complications and transmission of infectious diseases, without requiring or even aiming for abstinence. **Abstinence**-based treatment approaches are themselves a part of comprehensive harm reduction strategies. A range of recovery activities may be included in every harm reduction strategy. (For example, providing clean needles and/or syringes to injection drug users to reduce the spread of HIV and hepatitis infections reduces the medical harm associated with the route of drug self-administration even as the drug user continues to use drugs intravenously.)

Harmful (substance) use*: Use with health consequences in the absence of **addiction**.

Hazardous (substance) use or ***at-risk*** use: Substance use that increases the risk for health consequences.

Hoarding: Instead of using a prescribed drug as prescribed, stockpiling it for possible future use (for example, patients prescribed methadone who fear losing access to it may store take-home methadone doses); this is one form of **nonmedical use**.

Identification testing or ***definitive testing:*** Identifying a specific drug or metabolite by a specific test such as **GC-MS** or **LC-MS/MS**. This term is in contrast to a "**screening test**" which often identifies not a specific drug but a class of drugs (for example, after a positive **immunoassay** screening test has identified the presence of a compound from the pharmacological class of opioids whereas the "identification test" can identify the specific opioid such as morphine or codeine).

Immunoassay: A technique based on competitive binding between an antibody and an antigen that are targeted towards a specific drug or drug metabolite. An immunoassay drug test is designed to classify substances as either present or absent in a specimen based on a predetermined cutoff threshold; thus, it is an example of **qualitative testing**.

Laboratory-developed test: A test developed and performed by a laboratory; in distinction to a **point-of-collection test**.

Limit of Detection (LOD): The lowest amount of drug or metabolite that a laboratory can reliably identify in a specimen. The limit of detection varies depending on the methodology and the laboratory. The LOD is a laboratory-based standard driven by consensus guidelines for forensic and/or clinical analytical identification criteria for which the concentration provided is known to not be within +/- 20% of the true value (up to 35% depending on the method).

Limit of Quantitation (LOQ): A value that is driven by consensus guidelines on the acceptable "signal to noise" required to provide both identification and quantitation (quantification) that meet forensic and/or clinical defensibility standards.

Liquid chromatography-mass spectrometry (LC-MS): An analytic technique used to separate and identify a compound based on its molecular structure and properties. Liquid chromatography is used to separate the different components in a specimen and mass spectrometry is used to specifically identify the components. **LC-MS/MS** typically does not involve extraction of the drug or drug metabolite from the biological **matrix** prior to analysis.

Maintenance treatments: pharmacotherapy on a consistent schedule for persons with addiction, usually with an agonist or partial agonist, which mitigates against the pathological pursuit of reward and/or relief and allows for remission of overt addiction-related problems. Maintenance treatments of addiction are associated with the development of a pharmacological steady-state in which receptors for substances are occupied, resulting in relative or complete

blockade of central nervous system receptors such that addictive substances are no longer sought for reward and/or relief. Maintenance treatments of addiction are also designed to mitigate against the risk of overdose. Depending on the circumstances of a given case, a care plan including maintenance treatments can be time-limited or can remain in place life-long. Integration of pharmacotherapy via maintenance Treatments with psychosocial treatments generally is associated with the best clinical results. Maintenance treatments can be part of an individual's treatment plan in abstinence- based recovery activities or can be a part of harm reduction strategies. (A common example is **methadone maintenance treatment**, often abbreviated as MMT.)

Matrix (matrices): The sample used for analysis in a drug test. Examples include blood, urine, oral fluid, hair, nails, sweat, and breath.

Medical Review Officer (MRO): A physician trained and certified to interpret drug test results and to validate the testing process.

Medication-assisted recovery (MAR) or ***medication assisted treatment (MAT):*** These are transitional terms (terms that are still in current use and are useful today but may not be in use in the future) to help the general public, recipients of health care services, and professional health care service providers understand that pharmacotherapy can be helpful in supporting recovery. The manifestations of addiction-related problems are addressed in their biological, psychological, social, and spiritual dimensions during addiction treatment, in treatment approaches that are abstinence-based, and in treatment approaches that are harm-reduction-based. MAR is one component of the treatment and recovery process. **Medication-assisted treatment (MAT)**, another variation on the concept of MAR, may involve pharmacotherapy alone. It is essential that addiction treatment and recovery approaches address the various aspects of biological, psychological, social, and spiritual dimensions for optimum health and wellness. It is hoped that as the public and professionals recognize that recovery and treatment need to be holistic, appropriate pharmacotherapy would be well accepted as part of treatment and recovery, such that the terms MAR and MAT would be deemed unnecessary.

Metabolite: A biological transformation of a drug by the body to a form that facilitates excretion of the drug; the colloquial understanding of **metabolite** is that this term refers to a "breakdown product" of an original compound.

Methadone maintenance treatment program (MMTP): See ***maintenance treatment***.

Motivational enhancement therapy: A patient-centered counseling approach for initiating behavior change by helping patients to resolve ambivalence about engaging in treatment and stopping substance use or gambling. This approach employs strategies to evoke rapid and internally motivated change in the patient, rather than guiding the patient stepwise through the recovery process. It is an empathic, supportive counseling style that supports the conditions for change. Practitioners are careful to avoid arguments and confrontation, which tend to increase a person's defensiveness and resistance.

Misuse: *This term not recommended for use in clinical or research contexts.* Misuse refers to any use of a prescription drug that varies from accepted medical practice. It can also refer to unhealthy use of alcohol outside the context of addiction. (Note: The WHO Lexicon defines misuse as use for a purpose not consistent with legal or medical guidelines, and notes that the term "misuse" may be less pejorative than the term "abuse"). The term non-medical use is often the term that can be used to covey the concepts that some include in the term "misuse."

Motivational Interviewing: includes the following definitions for the layperson, practitioner and a technical definition:

> Layperson: a collaborative conversation style for strengthening a person's own motivation and commitment to change.
>
> Practitioner: a person-centered counseling style for addressing the common problem of ambivalence about change.
>
> Technical: a collaborative, goal-oriented style of communication with particular attention to the language of change. It is designed to strengthen personal motivation for and commitment to a specific goal by eliciting and exploring the person's own reasons for change within an atmosphere of acceptance and compassion.

Nonmedical drug use: use of an illicit drug or the use of a prescribed medicine for reasons other than the reasons intended by the prescriber, e.g., to produce positive reward or negative reward. Nonmedical use of prescription drugs often includes use of a drug in higher doses than authorized by the prescriber or through a different route of administration than intended by the prescriber, as well as for a purpose other than the indication intended by the prescriber (for example, the use of methylphenidate prescribed for Attention Deficit Hyperactivity Disorder [ADHD] to produce euphoria rather than to reduce symptoms or dysfunction from ADHD).

Non-negative: See ***presumptive positive***

Notification of testing: The process of informing an individual that he or she is subject to a drug test.

Opiate: An historical term, still in use in drug testing processes, referring specifically and solely to naturally occurring alkaloids derived from opium (morphine, codeine, 1,6-diacetyl morphine [commonly referred to as heroin]).

Opioid**:** A current term for any psychoactive chemical that resembles morphine in pharmacological effects, including opiates and synthetic/semisynthetic agents that exert their effects by binding to highly selective receptors in the brain where morphine and endogenous opioids effect their actions.

Opioid substitution therapy (OST): See ***maintenance treatment***

Opioid treatment program (OTP): An **addiction treatment** service that is specifically licensed by federal and state agencies to offer **maintenance treatments**, generally with methadone or buprenorphine.

Physical dependence: A state of adaption that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation or rapid dose reduction of a drug and/or by administration of an agonist. It is *not* synonymous with **substance dependence** or with **addiction**.

Point-of-collection / point-of-care (POC): A drug test performed at the site where the biological specimen is collected using either instrumented or non-instrumented commercial devices (e.g. a chromatography or immunoassay test strip or some modification on a test strip in lieu of a mechanical analysis instrument); in distinction to a **laboratory-developed test**. (A **POC test** is often referred to as an “instant test”; “home drug test” kits purchasable by laypersons are also **POC** tests).

Prescription drug abuse: The **nonmedical use** of prescribed **controlled substances**.

Presumptive positive or ***non-negative:*** Refers to a positive result on an immunoassay test.

Post-treatment monitoring: Drug and alcohol testing done after successful completion of addiction treatment (note that monitoring can also involve monitoring of functional/workplace behaviors and monitoring of adherence to treatment; in the context of drug testing, post-treatment monitoring refers to laboratory monitoring to determine if abstinence is being maintained, after a phase of active addiction treatment has been suspended).

Problem use: see **harmful use**. *This term not recommended for use in clinical or research contexts.* The term is not preferred because when used with patients it has connotations that are not helpful and can be seen as pejorative if the patient is viewed as being the problem or having a problem, as opposed to the substance being a problem.

Program: A generalized term for an organized system of services designed to address the treatment needs of patients.

Pseudoaddiction*: A term that has been used to describe patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may "clock watch," and may otherwise seem inappropriately "drug seeking." Even such behaviors as illicit drug use and deception can occur in the patient's efforts to obtain relief. Pseudoaddiction can be distinguished from true addiction in that the behaviors resolve when pain is effectively treated. (Another example of pseudoaddiction involves an appearance of addiction when addiction is not present, e.g. when patients taking benzodiazepines therapeutically display symptoms of withdrawal when benzodiazepine use is abruptly stopped and a layperson or a health professional believes incorrectly that the person as addiction.)

Random testing: drug testing determined by random selection rather than on a predictable pattern so that on any particular day donors in the drug testing pool are subject to testing even if they were tested the prior day; in distinction to **scheduled testing**.

Recovery: A process of sustained action that addresses the biological, psychological, social, and spiritual disturbances inherent in addiction. This effort is in the direction of a consistent pursuit of abstinence, addressing impairment in behavioral control, dealing with cravings, recognizing problems in one's behaviors and interpersonal relationships, and dealing more effectively with emotional responses. Recovery actions lead to reversal of negative, self-defeating internal processes and behaviors, allowing healing of relationships with self and others. The concepts of humility, acceptance, and surrender are useful in this process.

Note: ASAM continues to explore, as an evolving process, improved ways to define Recovery. In practice, the judgment about whether a patient is in a "state of recovery" must be made on clinical grounds, based on the most complete assessment possible of the state and seriousness of the initial illness and the quality and length of remission.

Relapse: A process in which an individual who has established abstinence or sobriety experiences recurrence of signs and symptoms of active addiction, often including resumption of the pathological pursuit of reward and/or relief through the use of substances and other behaviors. When in relapse, there is often disengagement from recovery activities. Relapse can

be triggered by exposure to rewarding substances and behaviors, by exposure to environmental cues to use, and by exposure to emotional stressors that trigger heightened activity in brain stress circuits. The event of using or acting out is the latter part of the process, which can be prevented by early intervention.

Qualitative drug testing: Drug testing which reports a results as "positive" or "negative" based on a **cut-off value,** rather than reporting a quantitative result**.**

Quantitative drug testing: Drug testing which specifies and report a result with a specified numerical value for the concentration of the **analyte** in the sample; i.e., drug testing which employs **quantification**.

Quantification: The determination of drug concentration in the matrix with a specific numerical value. For example: THC 50 ng/ml in urine. Also referred to as quantitation.

Scheduled drug: See ***controlled substance***

Scheduled testing: Testing done at a routine time; in distinction to **random testing**. For example, persons on probationers through the criminal justice system are tested each time they meet with their probation officer. Testing done based on a set schedule allows for a person using substances to engage in **subversion** of the testing process.

Screening test**:** A drug test that is designed to be rather sensitive affordable; the results have lower specificity than a confirmatory test. This term, though imprecisely used to describe an initial immunoassay test to identify the presence of classes of prescribed and non-prescribed medications and **drugs of abuse** rather than devoting the more rigorous and expensive technologies of **confirmatory testing**.

Sensitivity: Also called the "true positive rate", or the "recall rate" in some fields, that measures the proportion of actual positives which are correctly identified as such (e.g. the percentage of sick people who are correctly identified as having the condition). **Sensitivity** refers to the likelihood that a given test is able to detect the presence of a drug or metabolite that is actually in the specimen.

Specificity: Measures the proportion of negatives which are correctly identified as such (e.g. the percentage of healthy people who are correctly identified as not having the condition, sometimes called the "true negative rate"). **Specificity** refers to 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 falsely.

Specimen collection: the process of collecting a biological specimen for analysis. For example, in urine collection, the sample may be collected with or without direct observation of the **donor** in the act of urinating.

Split specimen: term used to describe a process where a biological specimen (most often urine) is collected from an individual and then split into two containers. These two containers are often referred to as 'A' and 'B' bottles. Both containers are sent to the testing laboratory where bottle A is tested. Should there be a challenge to a positive test result, bottle 'B' can be sent to another laboratory for independent testing.

Substance abuse: *This term not recommended for use in clinical or research contexts.* **Abuse** is synonymous with **harmful use** of a specific psychoactive substance. The term **Substance Abuse** applies to one category of psychoactive substance-related disorders in previous editions of the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association (DSM) but has been supplanted by the newer term, **substance use disorder**. While recognizing that the term **abuse** is part of past diagnostic terminology, ASAM recommends that an alternative term be found for this purpose because of the pejorative connotations of the word "abuse." *See also* **abuse** *and* **substance use disorder**.

Substance Abuse Professional (SAP): an individual who evaluates employees who have violated a federal drug and alcohol workplace program regulation and makes recommendations concerning education, treatment, follow-up testing and ongoing care.

Substance dependence: *This term not recommended for use in clinical or research contexts.* **Substance dependence** is *not* synonymous with the term **physical dependence. Substance dependence** applies to one category of psychoactive substance-related disorders in previous editions of the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association (*DSM*) but has been supplanted by the newer term, **substance use disorder**.

Substance-related disorder*:* Include disorders related to the taking of alcohol/tobacco or another addictive drug, to the side effects of a medication, and to toxin exposures. **Substance-related disorders** include substance use disorders, substance intoxication, substance withdrawal, and substance- induced disorders, as defined in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (*DSM-5*) of the American Psychiatric Association.

Substance use disorder (SUD): Substance use disorder is marked by a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues to use alcohol, tobacco, and/or other drugs despite significant related problems. Specific diagnostic criteria are given in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (*DSM-5*) of the American Psychiatric Association. **Substance use disorder** is the new nomenclature for what previously included **substance dependence** and **substance abuse** in the previous edition of the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*) of the American Psychiatric Association.

Substitution: when a previously collected biological specimen is used in place of a specimen collected at the time of the drug test. For example, if a donor provides previously collected urine (from themself or someone else, or even non-human urine) in place of their own urine at the time of the test.

Subversion: any intentional action by a person who is the subject of drug testing designed to interfere with the generation of valid results from testing; this includes **substitution** of specimens, **adulteration** of specimens, dilution of specimens, over-hydration in anticipation of being required to produce a specimen, etc.

Technologies (in drug testing): The method of analysis performed on the analyte, e.g., gas chromatography-mass spectrometry, liquid chromatography-mass spectrometry, thin-layer chromatography, etc.

Thin layer chromatography (TLC): a chromatography technique used to separate non-volatile mixtures. Thin layer chromatography is performed on a sheet of glass, plastic, or aluminum foil, which is coated with a thin layer of adsorbent material, usually silica gel, aluminum oxide, or cellulose. This layer of adsorbent is known as the stationary phase.

After the sample has been applied on the plate, a solvent or solvent mixture (known as the mobile phase) is drawn up the plate via capillary action. Because different analytes ascend the TLC plate at different rates, separation is achieved.

Third Party Administrator (TPA): an organization that manages the collection and processing of drug tests including determination of when to test in random testing programs, how and where collection is done, and how the sample is tested.

Tolerance*: state of adaptation in which exposure to a drug induces changes that result in diminution of one or more of the drug's effects over time.

Turnaround time: the time required by the laboratory to provide final results after receipt of the specimen to be tested.

Validity Testing: refers to testing of a specimen to ensure that it has not been **adulterated** or compromised. Usually refers to testing of the specimen for some combination of **creatinine**, specific gravity, nitrates, glutaraldehyde, pH and oxidants.

Window of detection: a term used to describe how long a substance may be detected in a biological sample.

Unhealthy substance use*: any use of alcohol or other drug that increases the risk or likelihood for health consequences (**hazardous use**) or has already led to health consequences (**harmful use**).

Appendix: Writing Committee Member Disclosures

Author	Commercial Interest	Nature of Relevant Financial Relationship (Include all those that apply)	
		What was received	**For what role?**
Andrea Barthwell, MD	Millennium Laboratories Alere	Travel Reimbursement Consulting Fee	Laboratory visit Consultation on policy matter
Louis E. Baxter, Sr., M.D., FASAM	I have NO relevant relationships to disclose.		
Al Beaubier	Bensinger, DuPont & Associates (provided drug test management services)	Annual salary	Senior Vice-President
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Jack Croughan, M.D.	I have NO relevant relationships to disclose.		
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Robert L. DuPont, M.D.	Bensinger, DuPont & Associates Prescription Drug Research Center (BDA subsidiary)	Owner/Employment	Executive Vice President Chairman

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M.P. George, MS	Alere Toxicology	Salary	Management position
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Bruce Goldberger, Ph.D.	I have NO relevant relationships to disclose.		
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Christine Moore, PhD	Employee of Immunalysis	Salary	Discussion of immunoassays for drug testing
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