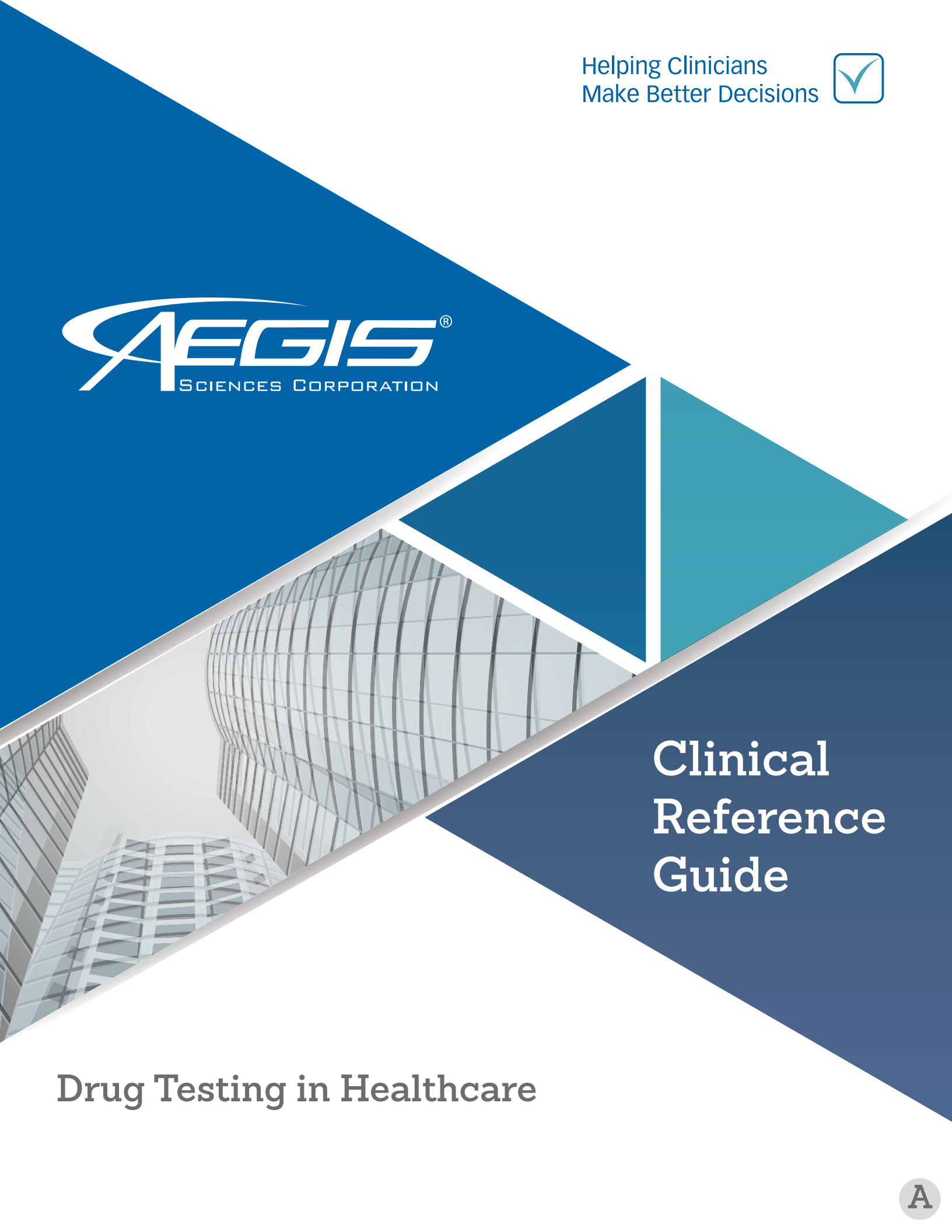


Helping Clinicians
Make Better Decisions



Clinical Reference Guide

Drug Testing in Healthcare

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Drug testing provides objective and valuable information when evaluating and monitoring patient risk for substance abuse.

A. Prevalence and Cost of Drug Abuse

On an individual and societal basis, drug abuse is highly prevalent and costly. One in ten individuals in the U.S. over the age of 12 currently uses illicit drugs.¹ The rate of drug overdose deaths has more than doubled in the past decade,² and poisoning, mostly due to drug overdose, is the leading cause of injury death.³ The annual costs to society from substance abuse (tobacco, alcohol, and illicit drugs) is estimated to be over \$740 billion; this includes costs associated with crime, lost work productivity, and healthcare expenses.⁴

In 2016, 6.2 million individuals (2.3% of the 12 or older U.S. population) misused prescription medications, with 3.3 million of these abusing prescription opioids. Misuse of prescription opioids is second only to marijuana among substances abused illicitly.¹ Although the U.S. makes up 4.6% of the global population, the U.S. consumed 69% of the world's supply of opioids in 2014; this includes 99.7% of the hydrocodone supply and 73.1% of the oxycodone supply.⁵ More than six out of ten drug overdose deaths are attributed to opioids, and it is estimated that 115 Americans die every day from an opioid overdose.⁶ Opioid abusers are estimated to contribute over \$14,000 per abuser in excess healthcare costs compared to those not abusing opioids.⁷

B. Toxicology Findings in Literature

A patient's report of their own misuse or diversion of prescription drugs and/or illicit substances is often unreliable, and behavioral signs may not always be present. Therefore, drug testing can provide an objective method to assist with identification of aberrant behaviors.⁸⁻¹⁰ Many providers are surprised at the prevalence of unexpected findings once they initiate drug testing in their practice. Reported prevalence data from the literature regarding unexpected findings from urine drug testing (UDT) can be found in Table 1.1.

C. Drug Testing as a Standard of Care

Drug testing offers an objective way to determine use of illicit or nonprescribed drugs, as well as identify the absence of prescribed controlled medications.^{10,18} Drug testing plays a valuable role in the initial assessment and ongoing adherence monitoring in patients prescribed chronic opioid therapy and is recommended in guidelines published by the American Pain Society (APS), American Academy of Pain Medicine (AAPM), American Society of Interventional Pain Physicians (ASIPP), American Association for Clinical Chemistry (AACC), Federation of State Medical Boards (FSMB), and the Centers for Disease Control and Prevention (CDC).^{5,9,10,18,19} Some states require drug testing with opioid prescribing; therefore, checking with your state licensing board and local laws is recommended.

Abnormal findings may lead to necessary conversations between the patient and provider, changes in treatment, and/or referrals to specialized treatment programs.^{5,8} Additionally, drug testing is often utilized by providers to improve adherence and deter misuse of nonprescribed drugs or diversion of prescribed medications.^{5,8} In a study by Knezevic et al of a small group of patients (n=77) with previously unexpected results, repeated UDT was associated with improved adherence in 64% of patients.¹⁴ Drug testing should be performed as part of a comprehensive treatment plan, involving other tools such as clinical and behavioral assessments, past medical and family history review, treatment agreements, prescription drug monitoring programs (PDMPs), and pill counts.^{5,20}

D. Assessing Risk and Testing Frequency

Clinical guidelines for chronic opioid prescribing recommend assessment of patient risk for substance abuse, diversion, or adverse outcomes before initiating chronic opioid therapy. Assigned risk may change over time based on observations during patient monitoring. Drug testing is recommended as part of risk assessment, risk mitigation, and ongoing monitoring.^{5,10,18,21} Screening

Table 1.1: *Prevalence of Unexpected Toxicology Findings*

POPULATION	% UNEXPECTED	CRITERIA	TESTING METHOD
Cancer Center ¹¹	44%	Positive for illicit drug, nonprescribed drug or alcohol	Unknown
Chronic pain (non-cancer) ¹²	45%	Negative for prescribed drug; or positive for a nonprescribed or illicit drug; or adulterated	Definitive
Chronic pain (non-cancer) ¹³	29%	Positive for illicit drug, nonprescribed drug or alcohol	Definitive
Chronic pain (non-cancer) ¹⁴	23%	Negative for prescribed drug; or positive for a nonprescribed or illicit drug	Definitive
High risk primary care (FQHC) ¹⁵	22% ^a	Positive for unreported drug	POCT
High risk primary care ¹⁶	40%	Positive for unreported drug	POCT
Addiction treatment ¹⁷	52%	Negative for prescribed drug; or positive for a nonprescribed or illicit drug	Definitive

Abbreviations: FQHC: federally qualified health center; POCT: Point of Care Testing (Immunoassay)

^aOnly patients with a positive UDT were included in this study; % based on lack of self-report of positive finding

tools that assess risk are available such as the Opioid Risk Tool (ORT), Screener and Opioid Assessment for Patients with Pain (SOAPP), Diagnosis, Intractability, Risk, Efficacy (DIRE) instrument, and others.¹⁰ Although assessing risk is consistently viewed as beneficial, the confidence in tools/methods to predict risk varies;^{5,18} therefore, utilizing multiple methods to determine risk such as PDMPs, UDT, accurate history, and psychological evaluations is recommended.⁵

Recommendations in guidelines for testing frequency in patients receiving opioids for chronic pain are ambiguous and highly dependent on the provider's clinical judgment and patient's assigned risk.^{5,10,18,20} A summary of recommendations by guideline for chronic pain and addiction treatment can be found in Tables 1.2a and 1.2b, respectively. Random testing is preferred over scheduled testing.^{8,9,19,20} ASIPP, CDC, and Official Disability Guidelines (ODG) recommend POCT/immunoassay when presumptive testing is adequate; however, definitive testing is recommended when more specific testing is needed (e.g., POCT results are unexpected, a specific drug needs to be identified vs. class of drug, if POCT does not detect the drug in question).^{5,17,20} The Veterans Affairs (VA) guidelines offer direction for when definitive testing is needed based on the drug or drug group of interest.²¹ Federal guidelines for opioid treatment programs (OTPs) note that POCTs "have a place in clinical decision making, but are not by themselves adequate to satisfy the regulatory requirements for drug use testing services."²²

AACC recommends qualitative definitive testing over immunoassay when possible due to "superior sensitivity and specificity".¹⁹ Additional recommendations may be available in state-specific or local guidelines and are not included in the table below. Referring to guidelines and regulations regarding drug testing in your local area of practice is recommended prior to performing drug testing.

E. Drugs Included in Testing

There are a variety of drugs that may be tested to identify substance abuse or risk for adverse effects in a patient. The decision for which drugs to test should be patient specific and based on individual patient assessment and risk.⁸ Current and regional abuse trends should also be considered. Table 1.3 lists substances commonly tested in healthcare along with the rationale for testing.

F. Responding to Unexpected Results

Some unexpected results may be explained by patient dosage/frequency of dosing, medication dosage form, nonadherence due to adverse effects or misunderstanding of dose instructions, complexity of drug metabolism, disease states, pharmaceutical impurities, and food ingestions. While other times, unexpected results may indicate nonadherence to the treatment plan or diversion. Developing a thorough understanding of drug testing interpretation and a plan to respond to results is recommended when utilizing

drug testing.^{5,8,18} Having the ability to consult a toxicology expert specializing in drug testing interpretation when encountering unexpected results is recommended.^{9,19,21} Additionally, unexpected results should be discussed with the patient.^{9,18} Simply dismissing a patient from care due to an unexpected drug test result is not recommended and may be harmful to the patient;^{5,8,18} care of the patient should continue whether through altering the treatment plan or referral to other care such as addiction treatment.^{9,10} Drug testing results should not stand alone; they should be considered as a tool along with other clinical information.²⁰ If aberrant behaviors are present, including those confirmed by drug testing, follow-up actions are based on the provider’s discretion and may include discussions with the patient, more frequent monitoring, tapering off or decreasing dose of controlled medications, offering naloxone, substance abuse screening, counseling, and/or referral to addiction treatment.^{10,18,53} Table 1.4 provides examples of aberrant behaviors and indicators of misuse. A provider’s response to unexpected drug testing results will depend on the provider and the

unique clinical picture of the patient. Examples from the literature that provide suggestions for dealing with unexpected results can be found below.

- “Responsible, Safe, and Effective Prescription of Opioids for Chronic Non-Cancer Pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines” (Pain Physician. 2017;20:S3-92)⁵
 - o Table 12, pg S50: “Interpreting unexpected results of urine drug screens”
 - o Fig. 18, pg S59: “Algorithmic steps in urine drug testing in chronic pain”
- “Recommendations for Urine Drug Monitoring as a Component of Opioid Therapy in the Treatment of Chronic Pain” (Pain Medicine. 2012;13:886-96)⁵⁵
 - o Figure 2, pg 893: “Potential actions based upon the differential diagnoses presented in section 4.”
 - o Pg 893-4: “Key Question 5. How to Handle Discrepancies in Test Results”

Table 1.2a: *Chronic Noncancer Pain-Recommendations for Testing*

SOURCE	FREQUENCY
AACC ¹⁹	Initiation + random testing at minimum of 1-2 times per year for low risk, with increasing frequency for higher risk
APS/AAPM ¹⁰	Periodically*
ASIPP ⁵	Initiation + subsequent use as adherence monitoring
CDC ¹⁸	Initiation + at least annually
FSMB ⁹	"Periodic and unannounced...clinical judgement trumps recommendations for frequency of testing"
ODG ²⁰	Initiation + ongoing based on risk: Low risk: test again within 6 months, then yearly Moderate risk: 2-3 times per year High risk: as often as once per month
VA ²¹	Initiation + periodically

*UDT or "other information to confirm adherence"

Table 1.2b: *Addiction Treatment-Recommendations for Testing*

SOURCE	FREQUENCY
Federal Guidelines for OTPs ²²	Maintenance: at least eight random tests per year Short-term detox: at least one initial test Long-term detox: initial and monthly random tests
ASAM: "Appropriate use of drug testing in clinical addiction medicine" ²³	Early recovery: at least weekly More stable: less frequent but at least once per month
FSMB ⁹	"As frequently as necessary to ensure therapeutic adherence"

Table 1.3: *Substances Frequently Tested in Healthcare*

Alcohol	<ul style="list-style-type: none"> · 34% of past month heavy alcohol users (defined as binge drinking on ≥ 5 days of the past 30 days) reported use of an illicit drug in the past month compared to 5% of non-users in a national survey.²⁴ · Alcohol was involved in 12% – 22% of drug overdose deaths involving fentanyl, heroin, hydrocodone, morphine, oxycodone, alprazolam, diazepam, or cocaine in 2014.²⁵ · Alcohol can be dangerous when combined with commonly prescribed medications; therefore, some providers may instruct their patients to completely abstain from its use and monitor this abstinence by drug testing.
Amphetamines	<ul style="list-style-type: none"> · Amphetamines are commonly abused. Methamphetamine ranked first, and amphetamine ranked tenth in drugs seized during law enforcement actions against illegal use of drugs/trafficking in 2017.²⁶ · In 2016, over 5 million individuals over the age of 12 reported misuse of amphetamine products.²⁴ · The rate of overdose deaths that involved psychostimulants, such as amphetamines, increased by 33% from 2015 to 2016.²⁷
Barbiturates	<ul style="list-style-type: none"> · Barbiturates are prescribed in combination products for headache or irritable bowel syndrome and alone for seizures or as a sleep aid. Providers may drug test to ensure adherence or identify abuse of these agents. · A national survey found that 60,000 adults reported misuse of a barbiturate in 2016.²⁴
Benzodiazepines	<ul style="list-style-type: none"> · A study combining Drug Abuse Warning Network (DAWN) data from 2005 to 2011 discovered almost a million ED visits involved benzodiazepines alone or in combination with opioid pain relievers or alcohol.²⁸ · The number of deaths involving benzodiazepines increased by over 500% from 2002 to 2016.² · Over 30% of opioid overdoses involve benzodiazepines.²⁹ · The Food and Drug Administration (FDA) has required boxed warnings on benzodiazepine labeling related to the dangers of combining benzodiazepines and opioids.³⁰
Buprenorphine	<ul style="list-style-type: none"> · A 2015 study described the use of buprenorphine in opioid treatment programs as increased due to a surge in the number of Drug Addiction Treatment Act (DATA)-waived physicians, particularly in rural areas.³¹ · Buprenorphine ranked in the top 10 most frequently seized drugs by law enforcement in 2017 and was the fourth most frequently seized opioid.²⁶ · A national survey found that 694,000 adults reported misuse of buprenorphine in 2016.²⁴ · Buprenorphine is tested to determine both adherence, especially in opioid treatment programs, and nonprescribed use.
Carisoprodol	<ul style="list-style-type: none"> · The highly dangerous combination of an opioid, benzodiazepine, and carisoprodol is referred to as “The Holy Trinity” and is sought after by drug abusers.³² · A national survey found that 436,000 adults reported misuse of carisoprodol in 2016.²⁴ · Carisoprodol is often prescribed in pain management and tested to ensure adherence and identify abuse of nonprescribed carisoprodol.
Cocaine	<ul style="list-style-type: none"> · From 2010 to 2017, there was a 3.5-fold increase in overdose deaths involving cocaine.² · In 2016, 978,000 individuals 18 years of age or older used cocaine for the first time.²⁴ · In 2016, nearly 5 million adults (2% of the U.S. adult population) reported use of cocaine in the past year.²⁴ · Cocaine ranked third behind methamphetamine and marijuana in drugs seized by law enforcement in 2017.²⁶
Fentanyl	<ul style="list-style-type: none"> · The primary source of fentanyl products for abuse is from clandestine labs versus prescription sources. Fentanyl is over 50 times more potent than heroin and commonly mixed with heroin products or formed into counterfeit prescription pills, with contents often unknown to the user.^{33,34} · According to the DEA, “fentanyl is the most prevalent and the most significant synthetic opioid threat to the United States”.³⁵ · Reported law enforcement drug seizures involving fentanyl more than doubled from 2015 to 2016 with over 34,000 reports.³⁶ · Fentanyl and related synthetic opioids are the top group of drugs associated with overdose deaths, comprising nearly 30,000 of over 72,000 total overdose deaths in 2017.² · There was a 22-fold increase in deaths associated with fentanyl and related synthetic opioids from 2002 to 2017.²
Gabapentin/ Pregabalin	<ul style="list-style-type: none"> · Gabapentin has been reported to be abused typically in individuals with a past history of substance abuse.³⁷ · A study found that 12.1% of urine specimens from patients with opioid addiction were positive for pregabalin without a medical indication.³⁸ · A study of 196 opioid dependent patients seeking detoxification revealed 11% used gabapentin without a prescription; 36% of those with a prescription used higher than the prescribed dose.³⁹ · U.S. Poison Control Center data illustrated a 4.3-fold increase in abuse of gabapentin or pregabalin from 2006 to 2014.⁴⁰ · Gabapentin and pregabalin are both commonly prescribed in pain management. They may be tested to ensure adherence with non-opioid pain treatments in addition to monitoring for abuse.
Heroin	<ul style="list-style-type: none"> · Heroin is second only to fentanyl and related synthetic opioids in contributing to overdose deaths.² · Overdose deaths associated with heroin increased over 5-fold from 2010 to 2017.² · Heroin ranked in the top 5 most frequently seized drugs by law enforcement in 2017.²⁶

Continue Table 1.3: *Substances Frequently Tested in Healthcare*

Marijuana	<ul style="list-style-type: none"> · Marijuana is the most commonly abused illicit drug and is used by 84% of current illicit drug users.¹ · A national survey found that 8.9% of individuals aged 12 or older have used marijuana in the past month.¹ · In 2016, approximately 1.5% of individuals aged 12 or older had a marijuana use disorder.¹ · Positive UDT results for marijuana have been associated with current and future opioid misuse.^{41,42}
Meperidine	<ul style="list-style-type: none"> · A national survey found that 91,000 adults reported misuse of meperidine in 2016.²⁴
Methadone	<ul style="list-style-type: none"> · A national survey found that 324,000 adults reported misuse of methadone in 2016.²⁴ · Methadone was involved in over 3,200 overdose deaths in 2017.² · Methadone is prescribed both for pain management and medication-assisted treatment for opioid addiction and may be tested to determine adherence with prescribed therapy or abuse of nonprescribed methadone.
Nicotine	<ul style="list-style-type: none"> · 25.8% of past month cigarette smokers reported use of an illicit drug compared to 7% of nonsmokers in a national survey.²⁴ · Cigarette smoking is highly prevalent in opioid treatment programs with a reported prevalence of 77-98%.⁴³⁻⁴⁷ · In a cohort study of individuals with a substance use disorder, smoking-related conditions contributed to 36-49% of deaths in this population.⁴⁸ · Providers may test for nicotine to determine nicotine use/smoking status or to monitor adherence with smoking cessation efforts.
Opiates (codeine, hydrocodone, hydromorphone, morphine, oxycodone, oxymorphone)	<ul style="list-style-type: none"> · In 2016, approximately 3.3 million people aged 12 or older were current misusers of pain medications, which accounts for 1.2% of the total U.S. population.¹ · In 2017, approximately 15,000 overdose deaths involved prescription opiates.² · Oxycodone, hydrocodone, morphine, and codeine were among the top 25 drugs most frequently seized by law enforcement in 2017.²⁶ · Of narcotic analgesics seized by law enforcement in 2017, oxycodone, hydrocodone, and morphine made up 19%, 12%, and 3% of reports, respectively.²⁶ · As opiates are commonly prescribed in pain management, they are included in testing to ensure adherence and to assess potential diversion or abuse.
Synthetic Cannabinoids	<ul style="list-style-type: none"> · Synthetic cannabinoids are similar to marijuana in effects but are often much more potent with inconsistent content leading to increased risk of harm.⁴⁹ · In August 2018, over 70 individuals overdosed in Connecticut in a one day period as a result of receiving a synthetic cannabinoid laced with fentanyl.⁵⁰ · 1,958 exposures to synthetic cannabinoids were reported to the American Association of Poison Control Centers in 2017.⁵¹ · In 2017, 24,501 reports of synthetic cannabinoid identifications, representing 2% of all drugs reported, were submitted by laboratories testing for law enforcement.²⁶
Tramadol	<ul style="list-style-type: none"> · Tramadol ranked in the top 25 most frequently seized drugs by law enforcement in 2017.²⁶ · Tramadol prescriptions increased 88% from 2008 to 2013.⁵² · In 2016, over 1.5 million adults reported misuse of tramadol in the past year in a national survey.²⁴

Table 1.4: *Examples of Aberrant Behaviors and Indicators of Misuse*^{5,9,54}

Aggressive complaining	Non-adherence with non-opioid treatments
Alcohol use	No relief from opioid treatment
Altering/forging prescriptions	Obtaining opioids from friends/relatives
Asking for early refills	Observed intoxication
Combining controlled drugs with alcohol	Refusal to bring in medication for pill counts/inaccurate pill counts
Decrease in functioning	Repeated ED visits to obtain opioids
Doctor shopping	Self-escalation of prescribed dose
Drug seeking	Selling prescription drugs
Family reports of overuse	Stealing drugs
Harassing office staff/threatening behaviors	Taking illicit or nonprescribed drugs
Losing/stolen prescriptions	Unscheduled clinic appointments
Negative affective state	Using a different route of administration than prescribed

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