

Curbing Drug Addiction and the Opioid Crisis

**The Role of Toxicology Laboratories in
Diagnosis, Treatment, and Prevention**



The National Independent Laboratory Association

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Definitions

Laboratory: a facility that provides controlled conditions in which scientific or technological research, experiments, and measurements may be performed.

Clinical laboratory: a facility that performs laboratory testing on specimens obtained from humans for the purpose of providing information for health assessment and for the diagnosis, prevention, or treatment of disease.

High complexity tests: testing that requires clinical laboratory expertise beyond normal automation and require a higher level of knowledge, training and experience; special handling of reagents and materials preparation; close monitoring of operational testing; a high level of specialized knowledge and maintenance; and extensive independent interpretation to perform the testing process.

Mass spectrometry: an analytical technique that determines the mass-to-charge ratio of an analyte and can be used to identify and/or quantitate drugs, poisons and their metabolites. It can be performed on many specimen types (blood, serum, tissues, urine) in the clinical laboratory.

Point-of-care drug screen: a drug screen performed near or at the point of patient care (in a doctor's office, at a clinic, etc.). Often performed on urine, they are simple tests that produce a rapid, semi-qualitative result (presence or absence of a chemical, but not the amount).

Toxicology: a multidisciplinary study of chemicals (e.g., drugs, poisons, etc.) aimed to correlate the quantitative and qualitative relationships between them and their physiological and behavioral effects in living systems.

Toxicology laboratory: a clinical and forensic laboratory that performs high complexity testing utilizing a host of highly specific instruments, including mass spectrometry to identify and/or quantitate compounds of toxicological interest.

CLIA-certified laboratory: a clinical laboratory regulated by the Centers for Medicare & Medicaid Services under the Clinical Laboratory Improvement Amendments (CLIA).

Parent drug: the non-biotransformed (metabolized, degraded, etc.) substance that individuals are exposed to. For example, aspirin is the parent drug for the metabolite salicylic acid.

Drug metabolites: substances formed through biotransformation processes that take place in the body after exposure to or ingestion of a parent drug.

The Essential Role of Toxicology Laboratories in the Drug Addiction and Opioid Crisis

Since 2006, there has been a steady rise in drug-related deaths in the U.S. with no signs of reversing course. In 2016, referencing the most recent data available, more than 63,000 people died from a drug overdose, and more than half of these drug-related deaths were from opioids.¹ Provisional data suggest that nearly 72,000 overdose deaths occurred in 2017.² While there has been an increase in deaths due to prescribed opioids, today a majority of opioid overdose deaths are caused by illicitly manufactured chemicals such as fentanyl (and its derivatives) and extremely potent synthetic substances, such as carfentanil and U-47700, that have little to no known use in humans. In addition to opioids, other novel psychoactive substances, such as synthetic cannabinoids, can cause severe illness, health problems, and death. In both cases, illicitly synthesized drugs appear to produce similar psychoactive effects as licitly synthesized drugs or other traditional drugs of abuse and are effective at eluding routine drug detection methods. The adverse effects of these abused substances on individuals, families, society, and health care costs are devastating. While this public health crisis is recognized and well-publicized, with federal and state governments investing billions of dollars in an attempt to end the opioid epidemic, there is still much progress to be made toward ending these preventable deaths.³

One of the most important tools available to health care providers managing patients who require chronic opioid therapy is periodic drug monitoring to ensure patients comply with treatment. Drug testing has become an essential tool to help achieve the goal of reducing opioid abuse in this country. The importance of this testing is rarely discussed and often misunderstood, but toxicology laboratories using mass spectrometry to perform drug testing are essential to physicians, health care providers, and law enforcement agencies. For example, drug tests are used to determine if a patient is taking opioids or other pain medications as prescribed or to determine if a patient is abusing other substances. While many health care professionals often rely on point-of-care drug screens that are convenient and inexpensive, these tests can produce higher incidences of false positives and false negatives. A lack of confidence in test results can endanger patients' lives by wrongly discharging them from pain management and addiction recovery programs or by continuing to supply them with prescription drugs when their treatment protocol should be altered. Given such concerns by the medical community and a desire to have more nuanced information, many physicians seek results from toxicology laboratories. This type of high complexity drug testing conducted

"Urine drug testing is one of the most important tools that I have in monitoring chronic pain patients who require chronic opioid therapy. This test provides completely objective information and ensures patient compliance with our prescribing."

-Dr. David Kloth, a chronic pain specialist

¹ Centers for Disease Control and Prevention. *U.S. drug overdose deaths continue to rise; increase fueled by synthetic opioids*, 2018, <https://www.cdc.gov/media/releases/2018/p0329-drug-overdose-deaths.html>.

² Centers for Disease Control and Prevention. *Vital Statistics Rapid Release: Provisional Drug Overdose Death Counts*, 2018, <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>.

³ U.S. Senate. *S.2680, The Opioid Crisis Response Act of 2018*, <https://www.help.senate.gov/imo/media/doc/S.2680%20Summary.pdf>.

by toxicology laboratories is a necessary additional step to point-of-care drug screens because it provides clinicians and law enforcement with qualitative and quantitative results and reduces the incidence of false positives and false negatives. While mass spectrometry testing costs more and requires highly trained staff, the results are more accurate and are essential for physicians to confidently treat persons with drug dependencies and addictions. The purpose of this paper is to highlight the essential role that toxicology laboratories play in managing the opioid crisis.

*Figure 1. Characteristics of Laboratories Involved in Testing for Drugs of Abuse**

| Toxicology Laboratories | Clinical Laboratories | Point-of-Care Drug Screens |
|--|--|--|
| <ul style="list-style-type: none">• CLIA-certified high complexity laboratories• Subject to routine regulatory oversight• Require a laboratory director with a doctoral degree• Specialize in mass spectrometry technology to identify drugs of abuse• Can test a range of specimens including urine, blood, serum and tissues• Have an extensive menu of analytes that are included in testing protocols• Require trained laboratory personnel to perform and interpret tests | <ul style="list-style-type: none">• CLIA-certified laboratories• Can perform high or moderate complexity testing• Subject to routine regulatory oversight• Perform diagnostic testing for a range of different clinical specimens to aid in diagnosis, treatment and prevention of disease• Require trained laboratory personnel to perform and interpret tests• Not specialized to perform high complexity drug testing using mass spectrometry• May provide point of care drug screening | <ul style="list-style-type: none">• Often CLIA-waived technology (e.g., urine dipsticks)• Not subject to routine regulatory oversight• Can be performed outside of the laboratory at the bedside or in the field• Limited to urine or oral fluid specimens• Inexpensive (~\$5 per test)• Do not require trained laboratory personnel to perform testing• Can provide information when used in the field or in the emergency department to help understand clinical condition of a patient• Produce semi-qualitative results |

**This list is not comprehensive of all types of laboratories and is intended to provide examples of laboratories performing testing for drugs of abuse*

Toxicology laboratories have long played an integral role in the health care continuum by providing health care providers with data to monitor effective pain management and to evaluate patients struggling with drug abuse. These types of laboratories are distinct from federal, state and municipal public health laboratories in that they are independent entities that conduct testing largely for clinical diagnostic purposes in order to direct a patient's clinical care. The Centers for Disease Control and Prevention (CDC) and the American Association for Clinical Chemistry (AACC) recommend drug screening for substance use and abuse before and during the course of opioid prescription.^{4,5} This is a critical component of patient monitoring and an essential tool in curbing the opioid epidemic. In addition, numerous states have guidelines and recommendations that require urine drug testing as a component of the spectrum of treatment.⁶ However, with the rise of prescribed and illicit synthetic opioids, which typically cannot be detected with routine point-of-care drug screening, the toxicology laboratory's role of detecting opioid misuse, monitoring patients, and providing data on emerging synthetic drugs has become even more critical.

The opioid epidemic is a complex problem with no single solution and little objective data to support clinical decision-making and treatment protocols. Strategic partnerships whereby toxicology laboratories provide objective data to public health officials, scientists, addiction specialists, psychiatrists, pain management physicians, pharmacists, and law enforcement officials must be formed to develop best practices, nationwide policies and innovative medical management solutions. By partnering across this diverse set of stakeholders, toxicology laboratories can provide key data elements to help develop coordinated and multi-faceted strategies to combat and solve the opioid crisis.

Toxicology Laboratories Produce High Quality Data

Testing conducted in toxicology laboratories is distinct from the initial point-of-care drug screening that is conducted in non-specialized laboratories or in a doctor's or health care provider's office. A point-of-care drug screen provides a presumptive result and must be confirmed by additional tests, as point-of-care drug screens are prone to cross reactivity, false positives, and false negatives. It is critical for clinicians and health care providers to rely on accurate results performed by high-complexity tests because this data directly affects day-to-day clinical decision-making. Laboratory data is also invaluable for epidemiological studies to target prevention efforts, detect and track emerging synthetic drugs, and direct policy changes. Community-based toxicology laboratories that are in close proximity to the at-risk patient population work in conjunction with health care providers to design specific testing schemes that are often geographically focused and based on the observed and reported abuse in that specific

⁴ Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. DOI: <http://dx.doi.org/10.15585/mmwr.rr6501e1>.

⁵ American Association of Clinical Chemistry. *Using Clinical Laboratory Tests to Monitor Drug Therapy in Pain Management Patients*, 2017, <https://www.aacc.org/science-and-practice/practice-guidelines/using-clinical-laboratory-tests-to-monitor-drug-therapy-in-pain-management-patients>.

⁶ Lutz, J. Affirm Health. *Opioid Prescribing Guidelines: A State-by-State Overview*, 2018, <https://www.affirmhealth.com/blog/opioid-prescribing-guidelines-a-state-by-state-overview>.

region. While point-of-care drug screening is inexpensive and plays a role in immediate clinical settings, it has several disadvantages when it is relied on for clinical decision-making, surveillance, law enforcement, and prescription drug monitoring programs. Namely, point-of-care testing:

1. Relies on the presence of an antibody, but not all drugs elicit an antibody response, limiting the number of drugs detected. For example, some opioids, such as fentanyl, buprenorphine, tapentadol, and tramadol, are not routinely detected;
2. Lacks comprehensive quality assessment controls and does not require highly trained laboratory personnel to perform or interpret the testing;
3. Does not provide quantitative results;
4. Can produce false positive results due to cross-reactivity with structurally related and other compounds from prescriptions, herbal compounds and over-the-counter drugs, or false negative results due to lack of cross-reactivity with newer, emerging novel psychoactive substances, all of which can result in poor patient care and incorrect data that skew national statistics.

Alternatively, testing performed by a toxicology laboratory offers the following advantages:

1. Provides qualitative and quantitative results with highly specific and sensitive results;
2. Guarantees the use of quality assessment controls and requires trained laboratory personnel to perform and interpret the test results;
3. Produces accurate and high-quality data that can improve treatment and prevention efforts;
4. Detects a wide range of drugs and differentiates between classes of drugs, providing specific data to clinicians, public health agencies, and law enforcement;
5. Produces data reflecting medication compliance or lack thereof;
6. Effectively monitors emerging synthetic drugs, providing information to public health and safety agencies about the factors driving the drug abuse epidemic;
7. Accurately identifies potentially dangerous drug interactions, such as benzodiazepines and alcohol, that can lead to an overdose or death, so that health care providers can intervene.

Point-of-care testing does not detect the presence of alcohol or its metabolites in the urine, and since mixing prescribed medications with alcohol is one of the most common causes of unintentional overdose, this information is very important to the prescriber.

Staying Ahead of the Evolving Designer Drug Landscape

A large contributing factor to the spike in overdose-related deaths and the overall opioid epidemic is the increasing popularity of highly addictive drugs, such as fentanyl and other novel opioids, synthetic cannabinoids, etc. These synthetic substances are collectively known as novel psychoactive substances. These substances are created in illegal, clandestine laboratories, either locally or abroad, and are designed to mimic the effect of scheduled licit or illicit drugs but often escape regulation or clinical detection due to minor changes to the chemical structure. Novel psychoactive substances present additional health care, societal, law enforcement and scientific challenges and often have morbidity and mortality not associated with the compounds they are meant to mimic. For example, bath salts, representing a class of synthetic stimulants, can be swallowed, smoked, inhaled or injected, and have been linked to a range of violent incidents and increases in emergency department visits since they became popular.⁷ Synthetic cannabinoids, often known as K2 or Spice, dominated the news recently after more than 70 people overdosed in a single day in New Haven, Connecticut, resulting in a public health crisis.⁸ Toxicology tests revealed the synthetic cannabinoid responsible for the outbreak was found to be laced with fentanyl. While no deaths have been linked to the New Haven incident, synthetic cannabinoids can cause hospitalization, psychosis, acute kidney failure, respiratory failure, heart attacks and death.

The rapidly changing landscape of such substances can only be identified by highly trained staff, using state-of-the-art laboratory instruments, who are dedicated to staying abreast of the diverse array of emerging drugs circulating within communities. The information produced by toxicology laboratories not only leads to the development and innovation of faster and more accurate diagnostic tests, but also provides critical information to stakeholders, such as health departments and health care providers. Without these efforts, newer novel psychoactive substances will go undetected and have significant detrimental impacts on public health and safety.

The value of toxicology data is highlighted in a recent, multi-state outbreak of severe bleeding due to the use of synthetic cannabinoids laced with rat poison.⁹ Rat poison contains a chemical known as brodifacoum, which is a long acting anticoagulant that is thought to extend the synthetic cannabinoid's high. In this particular case, three people died and at least one hundred individuals experienced symptoms requiring treatment.¹⁰ The use of rat poison in these synthetic cannabinoids required high-complexity toxicology testing to detect the substance that would otherwise not be normally

⁷ National Institutes of Health. National Institute of Drug Abuse. *Synthetic Cathinones ("Bath Salts")*, 2018, <https://www.drugabuse.gov/publications/drugfacts/synthetic-cathinones-bath-salts>

⁸ Schmidt, S. Washington Post. 'It is taking people out': More than 70 people overdose on K2 in a single day in New Haven, 2018, www.washingtonpost.com/news/morning-mix/wp/2018/08/16/it-is-taking-people-out-more-than-70-people-overdose-on-k2-in-a-single-day-in-new-haven/?utm_term=.343f3e5b5776.

⁹ Powell, D. Scientific American. *The Spice of Death: The Science behind Tainted "Synthetic Marijuana*, 2018, <https://www.scientificamerican.com/article/the-spice-of-death-the-science-behind-tainted-synthetic-marijuana/>.

¹⁰ Ibid.

considered.¹¹ Results from this toxicology testing provided clinicians with critical data to guide patient care.

High Quality Testing and Data Require Adequate Reimbursement

Despite the important role of toxicology laboratories in direct patient care and in providing critical data for law enforcement officials and policy makers, toxicology laboratories struggle to receive adequate reimbursement for their services. In 2014, Congress passed the Protecting Access to Medicare Act (PAMA), which intended to move clinical laboratory reimbursement to a market-based system.¹² Upon implementation, the Centers for Medicare and Medicaid Services (CMS) ignored congressional intent and captured less than one percent of the laboratory market in its data collection.¹³ This extremely skewed data resulted in deep cuts to Medicare's Clinical Laboratory Fee Schedule (CLFS) upon which many private pay fee schedules are based. The implemented reductions have led to significant losses and the restructuring of laboratories capable of performing drug testing.

The National Independent Laboratory Association (NILA) is a trade association for community, regional and health system clinical laboratories. NILA's members serve small and medium-sized communities (many in rural areas) and multi-state regions. NILA members perform a range of diagnostic testing, and not all NILA members perform toxicology work.

Additionally, PAMA is stifling laboratory innovation and hindering the ability of toxicology laboratories to respond to the opioid epidemic. In the National Independent Laboratory Association's (NILA's) study on the impact of PAMA, laboratories indicate the ability to innovate and stay ahead of emerging novel psychoactive substances has suffered due to cuts in reimbursement. The already small profit margins of many regional and community toxicology laboratories limit their ability to reinvest into faster, more accurate technologies to improve opioid testing practices, and the laboratory community is falling behind.

As toxicology laboratories aim to continue to perform such services, they have had to commit significant financial resources to develop new methods and purchase new equipment to reach a balance between current reimbursement rates and the needs of health care providers, public health, and law enforcement agencies. Such stresses on laboratory infrastructure will continue to reduce the number of performing laboratories to the detriment of local communities, health care in general, abuse deterrence, and law enforcement officials.

¹¹ Ibid.

¹² Root C.B. American Association for Clinical Chemistry. *Challenging Times for Mass Spectrometry Reimbursement*, 2016, <https://www.aacc.org/publications/cln/articles/2016/may/challenging-times-for-mass-spectrometry-reimbursement>.

¹³ Centers for Medicare & Medicaid Services. *Summary of Data Reporting for the Medicare Clinical Laboratory Fee Schedule Private Payor Rate-Based System* 2017, <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/CY2018-CLFS-Payment-System-Summary-Data.pdf>.

NILA is aware of the ongoing issues of fraudulent activities conducted by laboratories that submit unnecessary claims to obtain higher reimbursement from insurance companies, Medicare, and Medicaid. Unfortunately, the poor decisions made by these laboratories have cast a pall over the type of testing that is essential to combating the opioid epidemic. Toxicology laboratories that employ quality standards that meet or surpass those expected, that belong to organizations dedicated to quality-based testing, and that continue to perform the critical testing needed should not be confused with these other laboratories, many of which have been shut down or are subject to ongoing investigations. Nor should these actions by this subset of laboratories diminish the importance of toxicology testing and the need for higher reimbursement in order to safely and effectively combat the opioid crisis.

Forging Strategic Partnerships

Success in combating the opioid epidemic requires a multifaceted, collaborative approach, of which toxicology laboratory data is a critical component. NILA members are interested in developing strategic partnerships with federal agencies, state and local health agencies, associations, law enforcement officials, health care providers and others to leverage the data collected by clinical laboratories to use for treatment and prevention efforts. Toxicology laboratories have the ability to work in conjunction with health care providers and state and local agencies to design specific methods and patterns of testing that are often geographically focused and based on the observed and reported abuse in that specific region. Additionally, toxicology laboratories have the ability to assist health care providers in developing and managing individualized patient risk protocols and implementing testing policies that reduce cost, utilization and frequency while simultaneously improving patient care and outcomes.

NILA supports the creation of a database to enable data sharing where HIPAA-compliant, de-identified, anonymous toxicology laboratory data on drugs of abuse trends can be accessed by key stakeholders. NILA sees tremendous value in such a database for a wide array of partners including public health departments, health care providers, payors such as Medicare and Medicaid, federal agencies such as CDC, the Substance Abuse and Mental Health Services Administration (SAMHSA), the Department of Justice (DOJ), and local law enforcement agencies. An undertaking of this magnitude requires significant resources in time and planning to determine core data elements, event identifiers and technical guidelines. NILA recommends that a formal discovery process be conducted to establish and communicate a clear understanding of the objectives and success metrics for maximizing value from the high-quality opioid testing data that is available but currently under-utilized for public health purposes. This discovery process can distill the essence of the project into actionable goals, and prioritize and determine the quickest path to a minimum viable product (MVP) to opioid data sharing.

A Call to Action

The U.S. is confronted with an ongoing health care crisis of drug abuse. Without toxicology laboratories that provide accurate information vital to confronting the ongoing public health and public safety crises, there will be an escalation in the opioid epidemic and a lack of reliable surveillance data that is key for public health prevention and monitoring and allocating limited resources appropriately and effectively. With the support of its members, NILA invites the broader stakeholder community that has an investment in curbing the addiction and opioid crisis to:

Call to Action

Educate Partners

- Educate policymakers, public health partners, federal government partners, law enforcement agencies and others about the role of toxicology laboratory testing in curbing the opioid epidemic, including differences in types of tests

Ensure Adequate Reimbursement

- Ensure adequate reimbursement for toxicology laboratories to preserve the complex laboratory infrastructure that is essential to addressing public health crises, including the opioid epidemic

Enable Data Sharing

- Assemble stakeholders to undertake a formal discovery process to determine core elements of a data-sharing strategy to inform public health and surveillance efforts

Foster Collaboration

- Leverage existing relationships and catalyze new partnerships to collaboratively address the addiction and opioid epidemic and ensure the inclusion of toxicology laboratory experts

Ultimately, the goal is to reduce addiction and opioid-related deaths through stakeholder collaboration. NILA is committed to working with all interested parties to curb the nation's addiction and opioid epidemic through high quality, toxicology laboratory services.

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