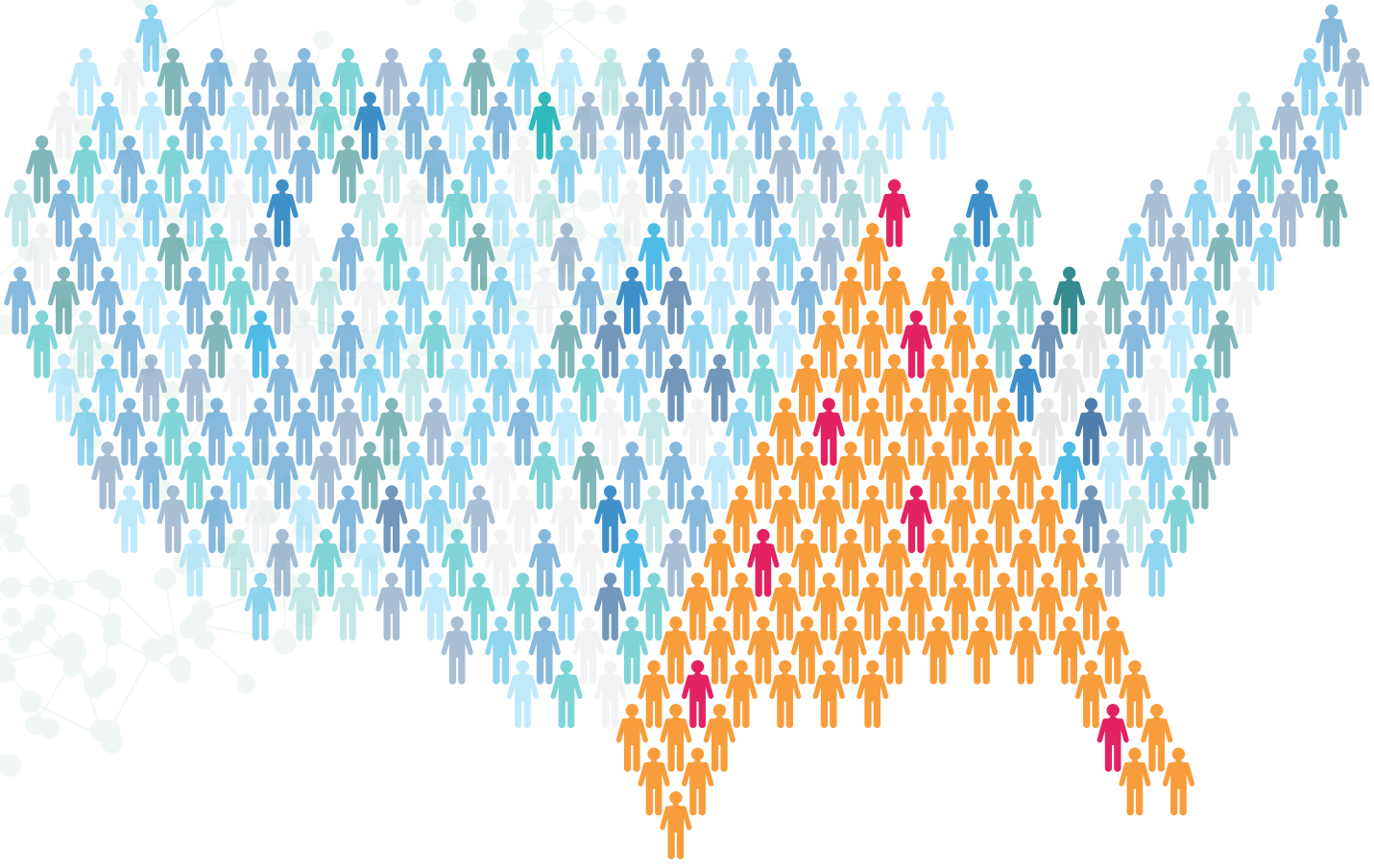
Acūtis

What Immunoassay Presumptive Screens Miss: **Raising the Bar with a High-Sensitivity Presumptive Screen**



Acūtis=Accūracy

Why High Sensitivity Presumptive Screening **Matters in Addiction Care**

Acutis High Sensitivity Screen vs Traditional Immunoassay

Presumptive drug screening is the first and often only gateway to detecting substance use before a reflex to confirmatory testing can be performed. When a presumptive result is positive or inconsistent with the expected outcomes, it is typically reflexed to a more sensitive and specific method, most commonly LC-MS/MS (liquid chromatography-tandem mass spectrometry), to precisely identify and quantify the compounds involved. Yet across the industry, outdated immunoassay methods are routinely missing key drug use events due to high cutoff thresholds, poor cross-reactivity, and inconsistent performance.

> ***Drugs such as buprenorphine, amphetamines, benzodiazepines, and cocaine/ heroin yield false negative immunoassay [screen] results due to low cross reactivity and non-reactivity...***

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In spite of its inadequacies, there is a critical dependency on presumptive screening. When the presumptive test fails to detect drug use, the opportunity for a reflex to confirmation, and for clinical action, is lost. Conversely, a false positive result can lead to confrontational or accusatory discussions between patient and counselor, damaging trust and consuming valuable time and resources in response to a result that ultimately proves inaccurate.

> ***We have solved an industry wide problem with a high sensitivity presumptive screen.***

Marjorie Bon Homme
PhD, DBACC, Chief Scientist

The Problem **with Traditional Immunoassay Screens**

Laboratories still rely on enzyme immunoassay (EIA) for presumptive testing. EIA was never designed to keep up with today's drug landscape, and it has several well-documented limitations:

- ✖ **High Cutoff Thresholds** → Traditional EIAs have relatively high detection limits, meaning low-level or recent drug use often goes undetected, resulting in false negatives.
- ✖ **Poor Cross-Reactivity** → EIAs are often not optimized for many commonly prescribed or abused medications. For example, widely used benzodiazepines such as lorazepam, clonazepam, alprazolam (Xanax), and midazolam frequently go undetected.
- ✖ **Unintended Cross-Reactions** → Conversely, some non-target drugs may trigger a positive result, leading to false positives and unnecessary consequences for the patient.

Acutis High Sensitivity Screen: **A New Standard**

To address these limitations, Acutis has developed a **high-sensitivity presumptive screen** that redefines what early-stage testing can achieve:

- ✔ **Lower Cutoff Thresholds** → Our screens are calibrated to detect lower concentrations of drugs, significantly reducing the risk of false negatives.
- ✔ **Enhanced Drug Coverage** → We've optimized our screen to detect a wider range of benzodiazepines and other challenging drug classes that traditional assays miss.
- ✔ **Reduced False Positives** → Better target specificity means more reliable results, and less unnecessary reflex testing or confrontation with patients.

This advancement bridges the gap between rapid screening and definitive testing, ensuring that critical cases don't slip through the cracks.

Closing the Gap

Our scientists have analyzed the most common failure points in traditional immunoassay-based drug screening. Acutis research has identified key areas where standard presumptive tests often fall short in sensitivity, specificity, and cross-reactivity across high-risk drug classes. In response, we developed a proprietary high-sensitivity presumptive screen that directly addresses these limitations. This enhanced screening method is designed to detect lower drug concentrations and capture compounds that are frequently missed or misidentified in conventional screens. The result is a more accurate, reliable first-line test that supports timely clinical decisions and improves patient care outcomes.

Benzodiazepine Analysis

Amongst a patient population of 6,000 samples tested using the Acutis high sensitivity presumptive screen, **46% of the samples contained a formulation of Benzodiazepines that are not picked up in traditional immunoassay- based screens due to poor cross reactivity.** Results for our high sensitivity presumptive test for benzodiazepines shows that we are detecting drugs such as lorazepam, clonazepam, alprazolam (Xanax), and midazolam that frequently go undetected in immunoassay presumptive screens.

Comparative Detection: Standard EIA Vs. Acutis High-Sensitivity Screen

Benzodiazepines	Detected by Standard EIA	Acutis Detection Rate	Relative Use Amongst Benzo Positive Patients*	Notes
Diazepam (Valium)	GOOD ✔	Concordance with Confirmatory	8%	Strong cross-reactivity via oxazepam/nordiazepam
Lorazepam (Ativan)	POOR ⚠		3%	Glucuronidated metabolite poorly detected by EIA
Clonazepam (Klonopin)	POOR ✖		19%	7-aminoclonazepam not picked up on most EIAs
Alprazolam (Xanax)	POOR ✖		23%	α-hydroxyalprazolam has low EIA cross-reactivity
Midazolam	VERY POOR ✖		1%	Undetectable via EIA, often missed entirely

* Percentage (%) indicates the prevalence of the drug as a percentage of all positive benzodiazepine samples that were detected using the Acutis high sensitivity presumptive screen. Data illustrates what is likely missed with the industry standard EIA presumptive screen.

Cocaine Analysis

Cocaine use is rising. This is especially in combination with other substances like opioids and alcohol, driving an increase in overdose deaths and relapse events. Despite its high addiction potential and severe health risks, traditional presumptive screening methods are often failing to detect cocaine use in time for intervention due to the inadequate detection cutoff thresholds.

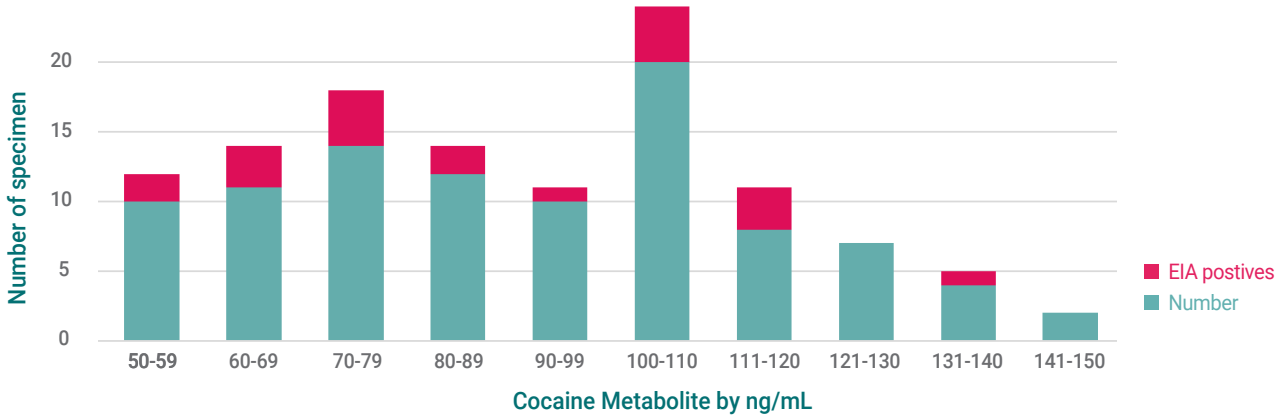
Standard immunoassay screens typically use a cutoff of 150 ng/mL for the cocaine metabolite benzoylecgonine. Acutis analysis shows that **32% of positive cocaine cases are missed** at this threshold compared to a more sensitive 50 ng/mL cutoff.

32% of Positive Samples Missed at 150 ng/mL

Presumptive Screen	Cutoff (mg/mL)
Immunoassay	150
High Sensitivity	50

In fact, nearly **80% of all cocaine-containing samples that fall between 50–150 ng/mL go undetected** by conventional screens.

Cocaine Containing Samples Between 50-150 ng/mL Not Detected By Immunoassay



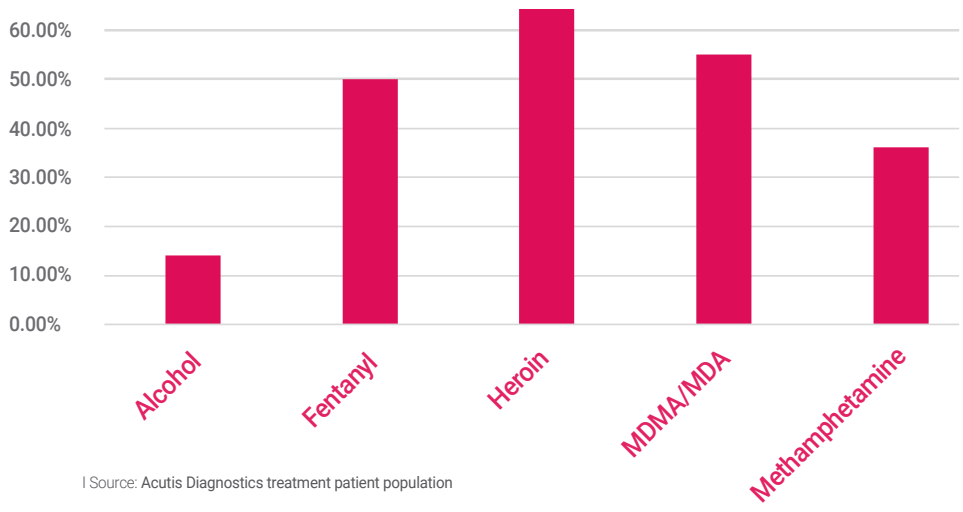
| Source: Acutis Diagnostics treatment patient population

Cocaine has a relatively short detection window in urine, especially when screened at higher cutoff levels. Traditional immunoassays with a 150 ng/mL threshold may miss use that occurred more than 3 to 4 days prior. By lowering the cutoff to 50 ng/mL, the detection window is extended, allowing clinicians to identify use that would otherwise be overlooked. This extended window is critical in treatment settings where timely insight into relapse or co-use can shape immediate clinical decisions.

Cocaine co-use

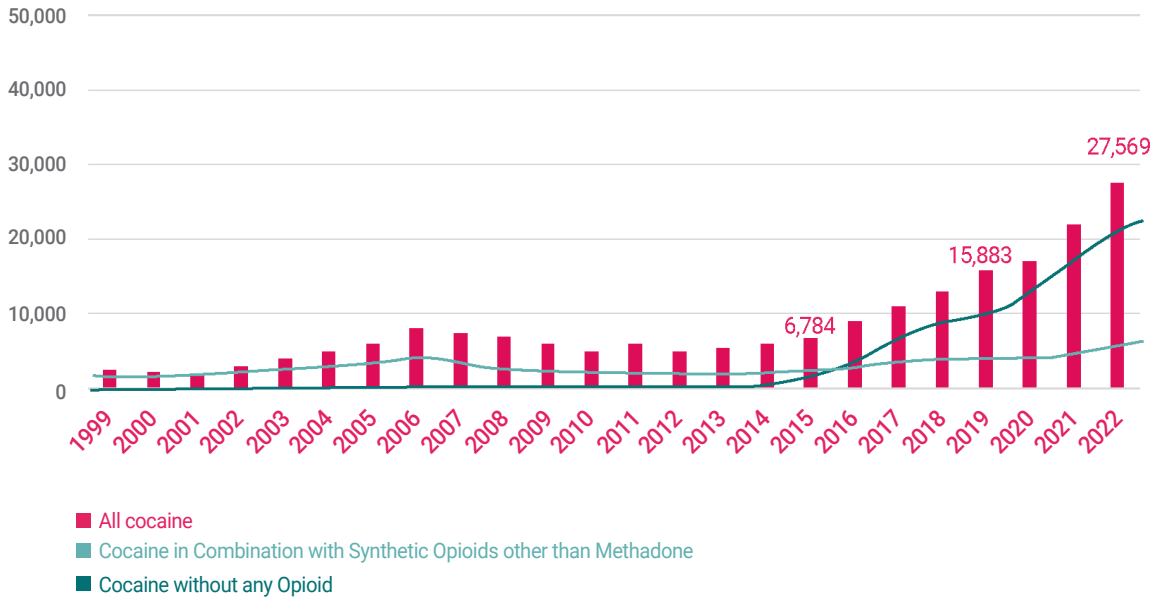
Cocaine use is of increased concern due to its co-use with other substances, particularly opioids, alcohol, and amphetamines. Data from the CDC and Acutis Diagnostics show that **overdose deaths involving cocaine have sharply risen when combined with opioids**, underscoring the danger of poly-substance use.

Rate of co-use with cocaine



| Source: Acutis Diagnostics treatment patient population

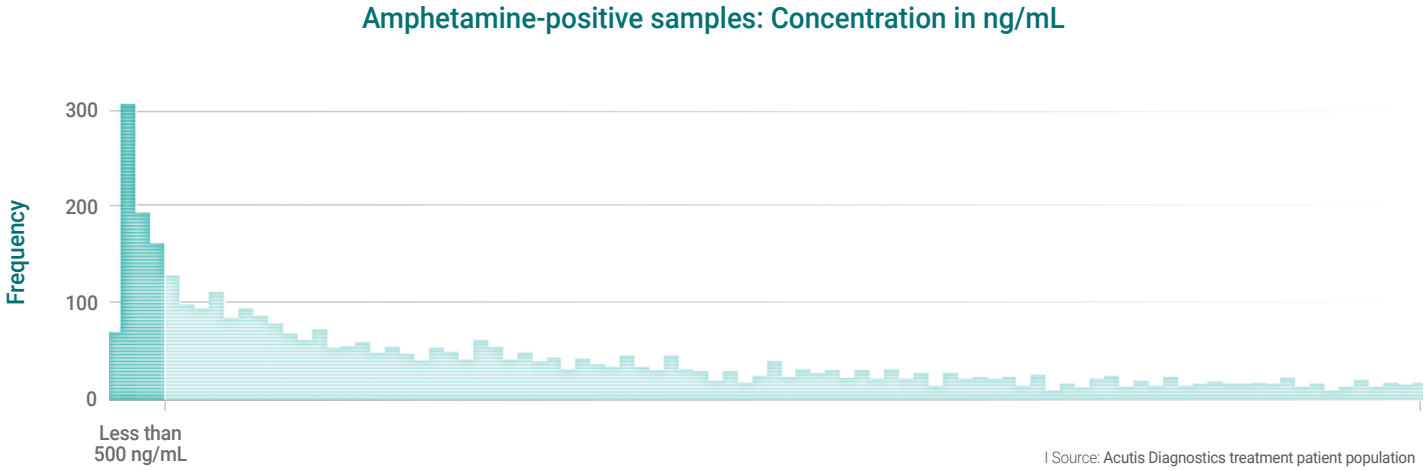
U.S. Drug Overdose Deaths Involving Cocaine*, by Opioid Involvement, 1999-2022



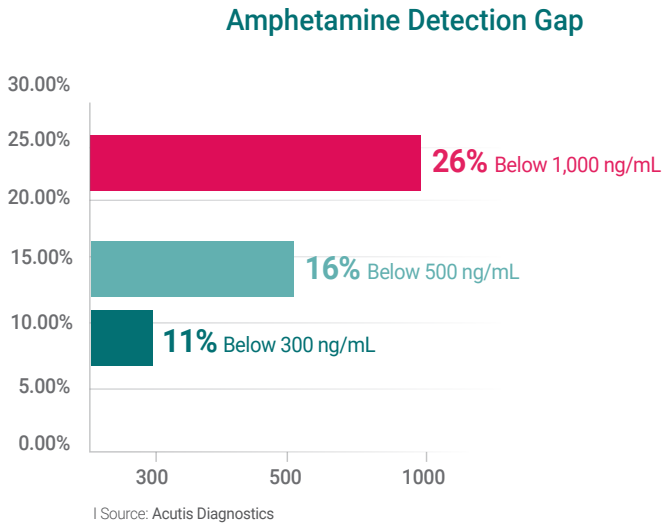
* Among deaths with drug overdose as the underlying cause, the cocaine category was determined by the T40.5 ICD-10 multiple cause-of-death code.
| Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024

Amphetamine Analysis

Amphetamines, encompassing both prescribed medications like Adderall and illicit substances such as methamphetamine, are prevalent in various patient populations. A primary concern with traditional immunoassay presumptive screens is the high cutoff thresholds commonly employed, in some cases as high as 1,000 ng/mL, which can miss lower concentrations of amphetamines present in patients' systems. Moreover, the structural diversity of amphetamine compounds contributes to detection challenges.



Internal analysis at Acutis reveals that **26% of amphetamine-positive samples fall below the 1,000 ng/mL cutoff**, with **16% below 500 ng/mL** and **11% below 300 ng/mL**. These statistics underscore a significant detection gap in conventional screening methods.



Opiates Analysis

Immunoassay-based presumptive screening for "Opiates" is primarily optimized for morphine, the classical target molecule. This leads to a common misconception that an "Opiates" screen is equally sensitive for other opioids, such as hydrocodone, hydromorphone, oxycodone, and oxymorphone. However, the reality is that cross-reactivity varies significantly across different opioids.

The table below, excerpted from a leading manufacturer's published specificity data, illustrates the approximate equivalent concentrations (in ng/mL) required to generate a positive result at the assay cutoff level of 300 ng/mL. Detection of semi-synthetic opioids (hydrocodone, oxycodone, oxymorphone, hydromorphone) requires much higher concentrations to generate a positive result. For example, at a 300 ng/mL cutoff, oxycodone requires approximately 10,500 ng/mL to trigger a presumptive positive, while oxymorphone requires approximately 37,000 ng/mL.

The specificity of the assay was evaluated using 300 ng/mL and 2000 na/mL as cutoff calibrators.
The following tables summarize the results.
The compounds in the table below produced a result approximately equivalent to the cutoff calibrator.

Compound	300 ng/mL Cutoff Concentration	200 ng/mL Cutoff Concentration
6-Monoacetyl Morphine	280	2500
Codeine	180	1200
Dihydrocodeine	650 ⚠	4500
Heroin	380	2400
Hydrocodone	650 ⚠	6500
Hydrocodone	1400 ⚠	13000
Levorphanol	10500 ⚠	87000
Morphine	300	2000
Morphine-3-Glucuronide	600 ⚠	5000
Morphine-6-Glucuronide	270	1350
Oxycodone	10500 ⚠	9000
Oxymorphone	37000 ⚠	30000
Ranitidine	50000 ⚠	300000

Conclusion

Improving the accuracy of the outdated industry wide immunoassay presumptive drug screening isn't just a technical upgrade. Our high sensitivity presumptive screen is a necessary evolution in patient care. By identifying and addressing the limitations of traditional methods, Acutis has developed a more sensitive, clinically aligned approach that ensures providers have the information they need when it matters most. As substance use patterns shift and co-use risks rise, testing strategies must keep pace. Our high sensitivity screen is designed to do exactly that.

Comparative Detection: Acutis High-Sensitivity Screen vs.Traditionnal EIA Cutoff

Drug Class	Acutis Screen Cutoff (ng/mL)	Traditionnal EIA Cutoff (ng/mL)	Clinical Impact *
Amphetamine	100 ✔	500 ⚠	Traditional EIA often produces **false negatives** due to excessively high thresholds. An estimated 16% of samples are missed with traditional immunoassay screens at 500 ng/mL.
Benzodiazepines	50 ✔	150 ⚠	Traditional EIA often results in **false negatives**; not optimized for most commonly prescribed benzodiazepines
Cocaine	50 ✔	150 ⚠	**1 in 3 cocaine users** are missed at the EIA threshold of 150 ng/mL and as much as 50% are missed at 300 ng/mL. Cocaine is a fast metabolizer and increasingly co-used with sedatives
Heroin Metabolite	10 ✔	300 ⚠	EIA may miss low-level heroin exposure; Acutis enables earlier detection
Hydrocodone	50 ✔	300 ⚠	21% of samples have concentration values below 300 ng/mL
Opiates	50 ✔	300 ⚠	EIA is optimized for morphine with poor sensitivity for other common Opiates
Oxycodone	50 ✔	100 ⚠	Lower cutoff improves detection of recent or low-dose oxycodone use

*Acutis Analysis

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