Drug Testing: Practical Interpretation Beyond the Urine Cup

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Learning Objectives

- Interpret the limitations of urine, oral fluid, hair, and sweat testing in various settings.
- Recognize how misinterpretation of confirmatory or quantitative results may lead to clinical or legal harm, and identify safeguards to prevent misuse.
- Evaluate the current role of CLIA-waived and point-of-care tests, including regulatory considerations, emerging technologies, and public health implications.

Why this matters

- Drug supply variations
- Adulterants
- Incomplete data guiding clinical decisions
- Regulations
- Misinterpretations
  - Harm, stigma, legal consequences

Potential Harms of Misinterpreting Drug Tests

- Wrong conclusions about **recent use or impairment**
- **False accusations** (legal, workplace, custody)
- **Inappropriate treatment decisions**
- Loss of **trust and treatment engagement**
- **Safeguards**
  - Confirm unexpected results
  - Interpret tests in clinical context
  - Distinguish **clinical vs legal standards**

How to choose?

- Clinical Question first→ Test second
- Recent use? Pattern over weeks? Current levels? Diversion?
- Results interpretation: timing, route, dose, physiology, assay limits

Legal vs Clinical Contexts

- **Legal / Forensic questions**
  - Parole or probation violations
  - Motor vehicle impairment
  - Workplace intoxication or injury
  - Proof of **recent use of specific substances**

- **Clinical questions**
  - Is substance use contributing to **current symptoms or intoxication?**
  - What **treatment modality or level of care** is needed?

- **Key point:**
  Testing standards and interpretation differ when results guide patient care vs legal decisions.

	Blood	Breath	Oral Fluid	Urine	Sweat	Hair
Best use in treatment setting	Determination of acute impairment or intoxication for alcohol	Determination of acute impairment or intoxication for alcohol	Short-term detection in ongoing addiction treatment	Intermediate-term detection in ongoing addiction treatment	Medium-term prospective monitoring	Long-term monitoring
General detection period (varies)	1-48 hours	~1 hour per standard drink	1-48 hours	1-4 days	Continuous, usually for 1-4 weeks	7-100 days
Primarily detects	Parent drug; blood alcohol concentration	Parent drug; blood alcohol concentration	Parent drug	Drug metabolite	Parent drug	Parent drug

Technology Basics

- Immunoassay (Presumptive)
  - Enzyme common
  - Rapid
  - Cut-off levels
  - False positives/false negatives
- Confirmatory (Definitive)
  - Mass spectrometry, chromatography
  - Specific
  - Still based on reference library

Moeller KE, Lee KC, Kissack JC.
Urine drug screening: practical guide for clinicians.
Mayo Clin Proc. 2008;83(1):66–76

Why Urine Dominates

- Widely available, cheaper, multiple menus
- Available for many substances

- Limits
  - Does not detect current intoxication
  - Tampering/substitution risk
  - Analyte availability
  - False positives/false negatives

Urine pitfalls

- Detection window limits
- Concentration does not equal dose
- Immunoassay vs definitive
- Metabolism logic errors

Alternative Matrices

- Oral fluid
  - Recent use, observed collection
- Hair
  - Longer-term pattern of use
- Sweat
  - Continuous collection
- Blood
  - Current levels
- Breath
  - Alcohol, cannabinoids
- Nails
  - Long window of detection

Oral Fluid Testing: Applications in Clinical Addiction Medicine

Detection & Clinical Utility

- Short detection window: 12-48 hours post-use
- ASAM-endorsed alternative to urine testing
- Reflects parent drug concentrations vs. metabolites
- Ideal for frequent monitoring of acute drug use in high-risk patients
- Direct observation minimizes adulteration risk

ASAM, 2017; Desrosiers, 2019; SAMHSA, 2024

Detection Windows Comparison

Drug Class	Oral Fluid	Urine
Cocaine	1–2 days	2–4 days
Amphetamines	1–2 days	2–5 days
Opioids	6–48 hours	2–4 days
THC (Cannabis)	6–24 hours (Oral contamination first 30min)	3–30 days

Ref: Bosker & Huestis, *Clin Chem* 2009; DOT 49 CFR Part 40

Oral Fluid Testing: Applications in Clinical Addiction Medicine

Collection & Limitations

- Non-invasive swab collection under tongue
- No private facilities required - clinic-friendly
- Xerostomia (dry mouth) can compromise validity
- Limited detection of benzodiazepines/barbiturates
- Best used in complementary strategy with urine testing

Enables real-time clinical decision-making with 48-hour turnaround for treatment continuity

ASAM, 2017; Desrosiers, 2019; SAMHSA, 2024

Ensuring Integrity in MOUD Clinics

- **Case evidence underscores the effectiveness of oral fluid testing:**
  - Identifies sample substitution and illicit drug use that urine tests might overlook.

- **Illustration from a buprenorphine treatment program:**
  - Oral fluid testing revealed amphetamine use and the absence of buprenorphine.
  - Urine tests inaccurately showed buprenorphine presence, c/w sample tampering.

- **Benefits of oral fluid testing:**
  - Collection is supervised, ensuring sample authenticity.
  - Supports precise compliance monitoring.
  - Allows for prompt and effective intervention.

https://innovation.premierbiotech.com/adulteration-a-case-study/

Case: Conermann *et al.*, 2014

Utility of Oral Fluid in Compliance Monitoring of Opioid Medications

Pain Physician 2014; 17:63-70

Design: Single-center academic pain clinic study
Goal: Compare efficacy of oral fluid (OF) vs. urine testing for opioid compliance monitoring

Comparison: Paired samples analyzed for prescribed & illicit substances

92%

Methadone Detection

Oral fluid detected methadone in 92% of cases vs. 91% in urine (Comparable efficacy)

Superior Fentanyl Sensitivity

Oral fluid detected fentanyl missed by urine testing due to low urine concentrations

Clinical Implication: Oral fluid may be superior for detecting transdermal/buccal medications and complements urine for MOUD monitoring.

Ref: Conermann T et al. *Pain Physician* 2014;17:63-70

Proposed MOUD Oral Fluid Drug Testing Panel

- **Fentanyl / Norfentanyl** (Synthetic Opioid)
- **6-AM (Heroin) / Morphine** (Opioids)
- **Oxycodone / Oxymorphone** (Prescription Opioids)
- **Buprenorphine / Norbuprenorphine** (MOUD)
- **Methadone / EDDP** (MOUD)

Ref: SAMHSA OFMG; Bosker & Huestis, *Clin Chem* 2009;55(11):1910-31.

Case: THC Detection vs Ongoing Use

History

- Social Worker used vaporized cannabidiol (CBD) for pain
- Frequency: 2–4 times per week
- Product later found to contain small amounts of THC
- Stopped use 1 month prior

Testing Scenario

- Workplace: random drug testing
- Employee requested oral fluid testing
- Request declined
- Urine drug test performed

Result: Urine positive for THC metabolite (THCCOOH) 30 days after last use

Key Point

Urine THC testing detects inactive metabolite (THCCOOH) and may remain positive for weeks, while oral fluid detects acute use.

Regulatory Framework Overview

Substance Abuse and Mental Health Services Administration (SAMHSA) Oral Fluid Mandatory Guidelines **2023**

DOT Part 40 oral fluid 2024

HHS lab certification needed Zero HHS-certified oral fluid labs as of March 2026 Requirement for two certified labs before DOT testing begins

Clinical vs. workplace rules

Ref: DOT Part 40 Procedures; SAMHSA Mandatory Guidelines for Federal Workplace Drug Testing Programs using Oral Fluid (OFMG), 88 FR 70814 (Oct 2023)

Clinical vs. Workplace Testing

Clinical

- **CLIA/CAP** standards
- **Medical care** & diagnosis
- **Physician orders** required
- **Patient consent** based
- **Variable cutoffs** allowed

Workplace

- **SAMHSA/DOT** rules
- **Deterrence** & safety
- **Employer mandated**
- **Chain of custody** strict
- **Standardized cutoffs**

Ref: DOT 49 CFR Part 40; SAMHSA Mandatory Guidelines for Federal Workplace Drug Testing Programs using Oral Fluid (OFMG)

CLIA-Waived and Point-of-Care Testing: What They Can and Cannot Do

- **Clinical testing: CLIA/state lab rules**
  - **CLIA: Clinical Laboratory Improvement Amendments of 1988**
  - **Useful for clinical care when rapid screening helps engagement or immediate decisions**
  - **Screening tests, not definitive tests**

- **Federal workplace testing:** Substance Abuse and Mental Health Services Administration (**SAMHSA)/Department Of Transportation (DOT) rules**
  - **Oral fluid in DOT/federal program: specific collector/lab/MRO requirements**
  - **Public-health upside**: easier observed collection, less tampering, more acceptable collection in some patients
  - **Public-health downside**: misuse when screening tests are treated as proof of impairment, relapse, or legal violation

SAMHSA's **Mandatory Guidelines for Federal Workplace Drug Testing Programs using Oral Fluid** (2023)

Interpretation Pitfalls

- Oral contamination
- Immunoassay cross-reactivity
- Dose–timing variability
- Metabolite ratios matter; oral pH
- Document meds, last use, food/oral products

Ref: Bosker & Huestis (Clin Chem 2009); DOT Part 40 Procedures

Specimen Validity Criteria

- Device within expiry
- Volume indicator observed
- Split A/B documented
- Seals initialed, intact
- CCF complete, legible

Ref: SAMHSA Oral Fluid Specimen Collection Handbook 2024.

Oral Fluid Testing Summary

- Uses: clinical monitoring and spot testing where supervised collection and recent use detection are priorities
  - Specificity high for targeted assays; cross-reactivity risk with some immunoassays
  - Common invalid samples: insufficient volume, contamination, oral blood, recent food or drink
  - Best for detecting recent use of stimulants, some opioids, cannabis, but not benzodiazepines
  - Pitfalls: do not rely for long-term abstinence verification; confirm positives with laboratory GC-MS or LC-MS/MS

- Collection process: observe donor, avoid recent oral intake, use validated collection device, label immediately

- Summary: rapid, noninvasive, clinically useful for recent-use screening when collection integrity is ensured

Hair and Nails

Case - Hair Testing Pitfall

Employee in workplace monitoring program has hair test positive for cocaine.

Patient denies use and works as a bartender with frequent environmental exposure.

Hair tests reflect exposure over weeks–months.

External contamination from drug-containing environments may occur despite washing.

- Ref: Kintz P. Forensic Sci Int. 2017.

Teaching point: Hair testing may detect environmental exposure and does not always prove ingestion.

Hair/Nails

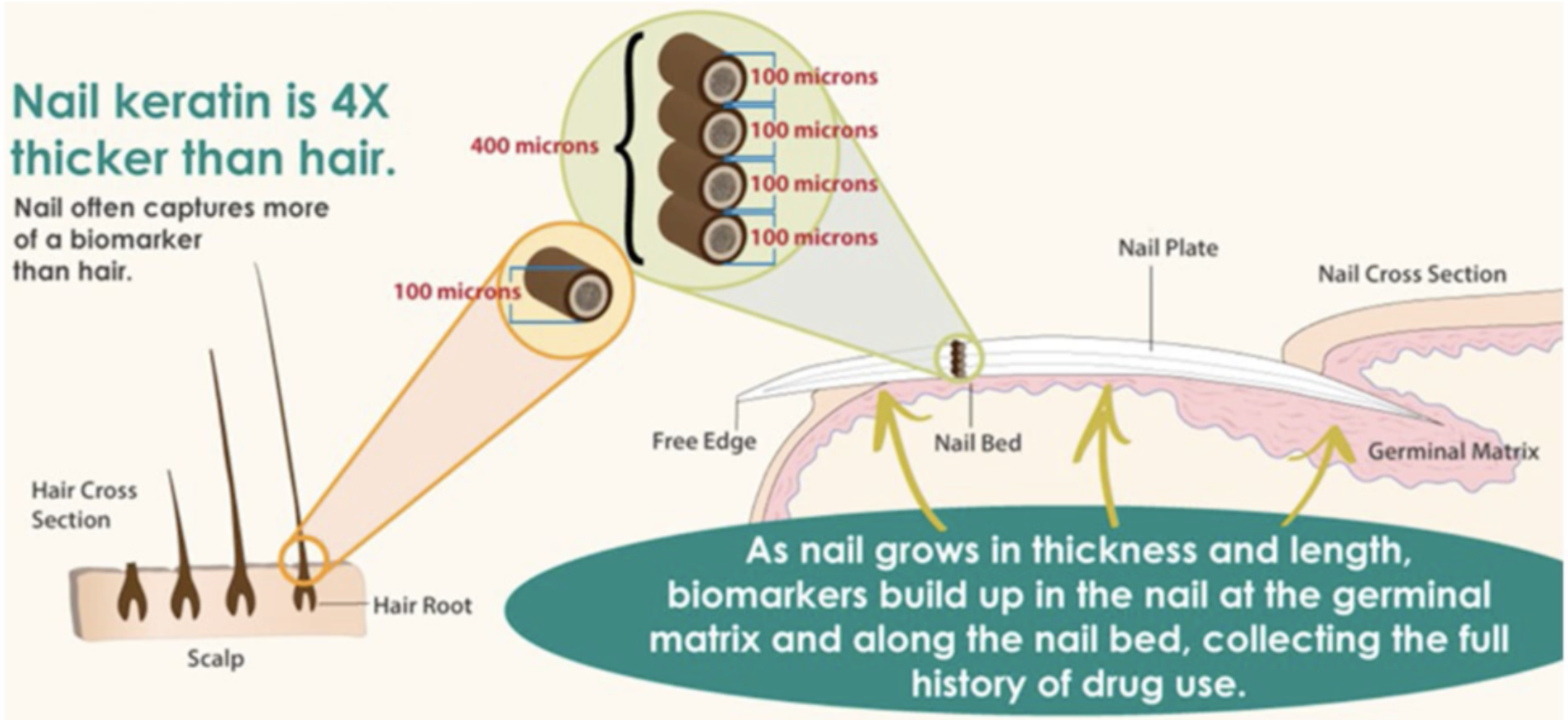
- Keratinized matrices → long-term detection window
  - Drugs accumulate over time via blood flow to hair follicle and nail bed

- Hair
  - Scalp hair → 3 months (most common)
  - Body hair → 12 months

- Nail
  - Fingernails → 3-8 months (fingernails)
  - Toenails → 4-12 months

Cooper et al., 2012; Palamar et al., 2019

Hair and Nail



Drug Testing Lab. United States Drug Testing Laboratories. May 5, 2018. https://www.usdtl.com/

Hair/Nail: Drug Incorporation and Preparation

- Basic drugs incorporated at a higher rate than neutral/acidic drugs
- Concentrations reflect cumulative exposure
  - Not dose/frequency
- For most drugs → hair > nail, fingernail > toenail
- Preparation:
  - Decontamination/washing → pulverization/incubation → extraction and analysis via LC-MS/MS

Daniel et al, 2004; Bandoli et al, 2024

Hair/Nails

Reliably detects

- Amphetamines, cocaine, opioids, PCP, MDMA

Unreliably detects

- THC, BZD

Kinetic wash analysis helps mitigate false results

- Measuring drug concentrations in sequential wash solutions

Morie et al, 2024; Cobo-Golpe et al, 2021

Hair/Nails

Advantages

- Does NOT detect recent use
  - 7-10 days
- Hair cosmetics affect drug levels
  - Degradation from dying/bleaching
- External contamination
- Cannot detect low-level or infrequent use patterns
- Nail methodologies lack standardization
  - Cut-off values undefined
- Costly

Limitations

Extended detection period

- 3-12 months

Easy, non-invasive collection

Stability at room temperature

Less susceptible to tampering

Segmental hair analysis

- Provides timeline of drug use

Palamar et al, 2019; Pating et al, 2017; Solimini et al, 2017; Cooper et al, 2012

Testing Characteristics: Urine, Hair, and Nails

Feature	Urine	Hair (90-day, 1.5")	Nail (Fingernail)
Detection Window	2–7 Days	~90 Days	3–6 Months
Sensitivity (Single Use)	High	Low/Moderate	Low
Sensitivity (Chronic Use)	Moderate	High	Very High
Specificity	High	High (>90%)	Very High (>90%)
Tamper Resistance	Low	High	Very High
Common Use Case	Post-accident, recent use	Pre-employment, long-term	Long-term compliance

Palamar et al, 2019; Pating et al, 2017; Solimini et al, 2017; Cooper et al, 2012

Hair/Nails

- Compared to urine; hair has lower sensitivity, higher specificity

- Hair/nail testing **complements** urine/blood testing
  - It is NOT a replacement

- Clinical/social settings:
  - Child custody cases to help establish long-term use patterns to determine parental fitness/child safety
  - Comparison of hair results within families
  - Usually not appropriate in SUD treatment settings

Pating et al, 2017; Palamar et al, 2019

Hair/Nails: Regulation

- No comprehensive federal regulatory framework

- Patchwork of the following:
  - Federal guidelines
  - Professional society standards
  - Laboratory accreditation requirements

Bush DM. The U.S. Mandatory Guidelines for Federal Workplace Drug Testing Programs: current status and future considerations. *Forensic Sci Int*. 2008

Sweat

Sweat

- Detect substances while worn up to 7 days
  - Allows water vapor to escape
- Detection Mechanism:
  - Passive diffusion from bloodstream into the sweat glands
  - Direct deposition in stratum corneum
- Detection duration
  - Metabolism dependent
  - 1-48 hours after use

Chawarski et al, 2013

Sweat

Clinical Applications: Rarely used

- Child Protection Services cases
- Parole departments
- Other government settings

Advantages

- Swab or Patch for different utility
- Non-invasive
- Difficult to adulterate
- Tamper resistance
  - Can't be removed and reapplied without clear evidence

Hadland and Levy, 2016

Sweat

- Insufficient evidence per ASAM guidelines (2017)
- Limitations
  - Patch loss
  - Skin contamination
    - Precautionary methods are not completely reliable
  - Validation concerns: mixed results
  - Unknown effects of variable sweat excretion

Jarvis, Margaret, et al. "Appropriate use of drug testing in clinical addiction medicine."*Journal of addiction medicine* 11.3 (2017): 163-173.

Case - Sweat Patch Monitoring

Patient on probation wears a sweat patch for 7 days.

Patch returns positive for cocaine.

Patient denies use but attended a gathering where cocaine was present.

Sweat patches collect drug exposure over several days.

- Ref: Kidwell DA, Smith FP. J Anal Toxicol. 2001.

Teaching point: Sweat patch results reflect exposure during the wear period but cannot determine timing or impairment.

Fingerprint

- Modified Sweat Test
- Detects metabolites in sweat
- 10 minutes
- Similar accuracy to urine and blood tests
- Used in multiple clinic settings but notably
  - Airport border control (detecting drug mules)
  - Mortuaries for cause of death

Hudson 2018

Breath

Breath

- First studied in 1924 by Dr. Emil Bogen
- 1931 Drunkometer was developed followed by Alcometer and Intoximeter
- Even in late 1960's below 0.15 BAC was not considered prosecutable
  - Not the same elsewhere
- 1967 first electronic breath test with infrared spectroscopy

Breath

- Current validated use is limited to alcohol
- Proxy for blood alcohol level
  - Typically a 1:2100 ratio
- Requires 1.1 to 1.5 liters of breath
  - Typically 5-6 seconds of exhaling
- Mouth alcohol
  - Regurgitation from, belching or recent intake
  - Requires at least 15 min

Hadland and Levy, 2016

Breath

- Advantages
  - Well-established
  - Readily available
- Disadvantages
  - Only established for alcohol
  - Short window of detection
  - Not widely clinically available
  - Almost exclusively used as punitive and may not reflect level of intoxication as intended

Hadland and Levy, 2016

Item	Use	Alcohol (%)
Listerine Antiseptic Mouthwash	Mouthwash	26.9
Dilaudid Cough Syrup	Cough suppressant, Analgesic	5
Colgate Mouthwash	Mouthwash/gargle	15.3
Vicks Nyquil	Decongestant, cough	25
Vicks Formula 44	Cough suppressant	20
Tylenol Adult Liquid Pain Reliever	Analgesic	7
Phenergan Syrup-Plain	Antihistamine	7

American Academy of Pediatrics
Kauffman RE, et al. *Ethanol content of medications.* **Pediatrics. 1984;73(3):405–407**

Breath

- Emerging Uses
  - THC
    - Recent legalization in many states
    - Detectable roughly 2 hours to several days
    - Considering two test standard within 1 hour to determine falloff
    - Small studies
    - Cannabinoid derivatives

- Not established trials include:
  - Amphetamine
  - Methamphetamine
  - Methylphenidate
  - Buprenorphine
  - Cocaine
  - Diazepam
  - Tramadol
  - 6-acetylmorphine
  - benzoylecgonine

Goodman, 2024; Beck 2013

Blood

Blood

- Often considered definitive test for intoxication
- Helpful in emergency situations
- THC
  - Often detected if someone is acutely intoxicated within 6 hours
  - Can be present for up to 30 days
- Measures parent drug

Lillsunde et al, 2024

Blood

- Advantages
  - Screening in recent use
  - Emergency situations
  - Established
- Disadvantages
  - Limited window
  - Invasive
  - Infection risk
  - Venous access

Hadland and Levy, 2016

Blood

- Dried blood spot
  - Have been used in several settings historically
    - Newborn screening!!!
    - Case management
    - Clinical investigations
    - Epidemiologic studies
  - Easy transportation
  - Can be stored at room temperature for up to years
  - Promising but needs more research

Ververi et al, 2023

Meconium/Cord Blood

- Detected in newborn's first several stools/umbilical cord
- Detects maternal substance use in third trimester
  - Up to months of detection
- Can have critical consequences for guardianship
  - Not diagnostic of active substance use disorder
- Not routine substance use disorder treatment applications
- May help with detection of neonatal abstinence syndrome

Hadland and Levy, 2016

Substances/Matrix

•American Society of Addiction Medicine. *Appropriate Use of Drug Testing in Clinical Addiction Medicine*, 2017 ; Substance Abuse and Mental Health Services Administration. *Clinical Drug Testing in Primary Care (TAP 32)* ; Verstraete AG. *Ther Drug Monit.* 2004 ; Moeller KE et al. *Mayo Clin Proc.* 2008 ; Kintz P. *Clin Chem.* 2012

Substance/	Urine	Oral Fluid	Blood	Breath	Sweat	Hair/Nail	Key Clinical Notes
Alcohol	⚠ (EtG/EtS)	⚠	✓	✓ **Best**	✗	✗	Breath = real-time impairment; urine detects past use only
Cannabis (THC)	⚠ (long window)	✓ **Recent**	✓	✗	⚠	⚠	Urine ≠ impairment; oral fluid/blood better for recency
Cocaine	✓	✓	✓	✗	⚠	✓	Parent drug in oral fluid/blood; metabolites in urine
Amphetamines	✓	✓	✓	✗	⚠	✓	Reliable across most matrices
Opioids (general)	✓	✓	✓	✗	⚠	✓	Good detection; interpret in context of timing
Fentanyl	✗*	✓ **Best**	✓	✗	⚠	⚠	Missed on routine urine; must order specifically
Buprenorphine	⚠	**((compliance)**	⚠	✗	✗	⚠	Urine vulnerable to spiking; oral fluid confirms adherence
Benzodiazepines	⚠	⚠	✓	✗	⚠	✓	Many missed on immunoassay (e.g., lorazepam, clonazepam)
Ketamine	⚠	✓	✓	✗	✗	⚠	Short window; oral fluid better for recent use
Dextromethorphan	⚠	⚠	⚠	✗	✗	⚠	Often not included in standard panels
Nicotine	✓	✓	✓	✗	⚠	✓	Cotinine widely detectable across matrices
Synthetic cannabinoids	✗	⚠	⚠	✗	✗	⚠	Frequently missed unless specialized testing
Inhalants	✗	✗	⚠	⚠	✗	✗	Poor detection in standard clinical testing

CLIA waived Point of Care

Matrix	Point-of-Care	CLIA-waived
Urine	Yes	Yes
Oral fluid	Limited	Some
Breath (alcohol)	Yes	Yes
Blood	Rare	No
Hair	No	No
Sweat	No	No
Nail	No	No

- **Only urine and breath alcohol currently has widespread CLIA-waived point-of-care testing across addiction clinics.**
- Oral fluid is **emerging**, while **hair and sweat remain laboratory-only matrices**

Centers for Medicare & Medicaid Services (CMS).
Clinical Laboratory Improvement Amendments (CLIA).
42 CFR Part 493.

Clinical Versus Legal Context

- In clinical toxicology:
  - Library match + calibration + QC → reported concentration
- In forensic/legal:
- Must meet:
  - Retention time tolerance
  - Ion ratio tolerance
  - Signal threshold
  - Chain of custody
  - Validated reference standard
- This is why immunoassay ≠ definitive.

Scientific Working Group for Forensic Toxicology (SWGTOX).
Standard practices for method validation in forensic toxicology.
Journal of Analytical Toxicology. 2013;37(7):452–474.
doi:10.1093/jat/bkt054

Safeguards to Prevent Misuse of Drug Testing

- **Use the right test for the question**:
  - recent use, long-term pattern, current intoxication, or treatment monitoring are not interchangeable.
- **Do not act on an unexpected immunoassay alone**
  - confirm with LC-MS/MS or GC-MS when stakes are high or the story and screen differ.
- **Do not over-interpret concentrations**
  - concentration does not equal dose, timing, or impairment.
- **Document context**
  - meds, route, timing, last use, food/oral products, and matrix limitations.
- **Separate clinical care from legal/punitive use**
  - different standards, different consequences.
- **Use non-stigmatizing, trauma-informed communication and informed consent whenever possible.**

Jarvis M, Williams J, Hurford M, et al.
Appropriate use of drug testing in clinical addiction medicine.
Journal of Addiction Medicine. 2017;11(3):163-173.
doi:10.1097/ADM.0000000000000323

Lab Collaboration

- Know matrix offerings and cutoffs
- Which analytes are included/excluded
- Turnaround times
- Confirmation thresholds
- Consulting with lab toxicologist

Matrix Summary

- Recent use/observed collection-->oral fluid
- Long term pattern-->hair (not routine)
- Treatment monitoring: urine
- Current ingestion: blood
- Sweat: not recommended for routine addiction treatment

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