# Testing Methods and Standard Thresholds for Various Screening Methodology an Overview

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Standard threshold levels for screening and confirmatory tests. Detection of specific drugs using standard Immunoassay as opposed to the confirmatory test GC/MS or Gas Chromatography.

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**Standard threshold levels for screening and confirmatory tests**

| **Drug/drug class** | **Immunoassay screen (ng/mL)** | **GC/MS confirmation (ng/mL)** |
|---|---|---|
| Amphetamine and methamphetamine | 1000 | 500 |
| Barbiturates | 300 | 200 |
| Benzodiazepines | 300 | 200 |
| Cocaine metabolite (benzoylecgonine) | 300 | 150 |
| Marijuana metabolites (delta-9-tetrahydrocannabinol-9-carboxylic acid) | 50 | 15 |

Methadone

300

200

Opiates (codeine and morphine)

2,000

2,000

Phencyclidine

25

25

Propoxyphene

300

200

Abbreviation: GC-MS, Gas chromatography-mass spectrometry.

**False-Negative Results**

False negatives are uncommon but can occur as a result of low drug concentrations in the urine, tampering, and in other situations. Possible reasons for false-negative results include: 1,2

- Dilute urine (excess fluid intake, diuretic use, pediatric sample)
- Infrequent drug use
- Prolonged time since last use
- Recent ingestion
- Insufficient quantity ingested
- Metabolic factors
- Inappropriate test used
- Elevated urine lactate
- Tampering
    - Tetrahydrozoline (eye drops)
    - Bleach
    - Vinegar
    - Soap
    - Ammonia
    - Lemon juice
    - Drain cleaner
    - Table salt
    - Various chemicals (glutaraldehyde, sodium or potassium nitrate, pyridinium chlorochromate, and peroxide/peroxidase)

Understanding the UDS and ordering the appropriate test can prevent false-negative results. Results from an immunoassay or a GC-MS can be deceiving, as these tests may not be able to detect every drug in a particular drug class.2 This particularly pertains to the opiate and amphetamine/methamphetamine immunoassays. For example, a test for opiates will detect morphine and drugs that are metabolized to morphine, such as codeine and heroin. Heroin itself can only be detected for up to 8 hours after use. After 8 hours, only the morphine metabolite of heroin will be detected in the urine by immunoassay or by GC-MS. Other opiates such as fentanyl, oxycodone, methadone, hydrocodone, buprenorphine, and tramadol will not be detected and require an expanded immunoassay panel for detection.1 The amphetamine/ methamphetamine immunoassay can detect racemic compounds (dextroamphetamine, methamphetamine) and illicit analogues (methylenedioxyethylamphetamine, methylenedioxyamphetamine, and methylenedioxyethylamphetamine [MDMA]). This assay, however, has a low sensitivity for MDMA and a more specific test should be performed if MDMA is suspected.

**False-Positive Results**

Although immunoassays are very sensitive to the presence of drugs and drug metabolites, specificity and accuracy varies depending on the assay used and the substance for detection.2 This limitation may result in false-positives from substances cross-reacting with the immunoassay. Positive results seen on immunoassay need to be confirmed using the more accurate GC-MS, the forensic standard. The DHHS detection limits reduce false-positive results, but do not eliminate them. In 1998, the cut-off for opiates was raised from 300 ng/mL to 2000 ng/mL to avoid false positives from poppy seed ingestion. However, these more stringent requirements can lead to false-negatives and many laboratories continue to use the lower value for detection. For example, detectable levels of cannabinoids after ingestion of hemp-containing foods with immunoassay have been reported. Levels of cannabinoids in these samples, however, were not detectable with GC-MS. Passive marijuana or cocaine smoke inhalation has never been documented to achieve detectable urine concentrations in adults, however, passive cocaine smoke inhalation has achieved detectable levels in pediatric cases.

**GC-MS is very accurate; however, it is not without problems in drug detection**.2

As mentioned earlier, heroin and hydrocodone are metabolized into morphine and hydromorphone respectively, and GC-MS may identify the metabolites rather than the parent compound. Selegiline is metabolized to *l*-amphetamine and *l*-methamphetamine, isomers without central nervous system stimulation. Neither immunoassay nor GC-MS can differentiate between the *l* and *d* isomers and a positive result for amphetamines will be found; an alternative test, chiral chromatography, may be needed.

Many prescription and nonprescription substances have been reported to cross-react with immunoassays and cause false-positives.2 Most have only been documented in case reports. Table 3 lists substances reported to cause false-positive results using immunoassay. This list may not include all potential substances. The frequency of false-positives varies, depending on the specificity of immunoassay used and the substance under detection. Immunoassay results for cannabinoid and cocaine metabolites are associated with very few false-positives while immunoassay results for amphetamines and opiates are associated with a higher number of false-positives.

**Substances that may cause false-positives on immunoassay urine drug screens.**

**Drug/drug class**

**Interfering drug**

| **Drug/drug class** | **Interfering drug** |
| --- | --- |
| Amphetamine and | |
| Amantadine | |
| Cocaine | |
| Amoxicillin | |
| methamphetamine | |
| Brompheniramine | |
| Coca leaf teas | |
| Bupropion | |
| Tonic water | |
| Chlorpromazine | |
| Methadone | |
| Chlorpromazine | |
| Desipramine | |
| Clomipramine | |
| Desoxyephedrine | |

Diphenhydramine

Ephedrine

Doxylamine

Fluoxetine

Ibuprofen

Isometheptene

Quetiapine

Isoxsuprine

Thioridazine

Labetalol

Verapamil

Phentermine

Opiates

Dextromethorphan

Phenylephrine

Diphenhydramine

Phenylpropanolamine

Fluoroquinolonesa

Promethazine

Poppy seeds and oil

Pseudoephedrine

Rifampin

Ranitidine

Quinine

Selegiline

Phencyclidine

Dextroamphetamine

Thioridazine

Dextromethorphan

Trazodone

Diphenhydramine

Trimethobenzamide

Doxylamine

Trimipramine

Ibuprofen

Vicks inhalerb

Imipramine

Barbiturates

Ibuprofen

Ketamine

Naproxen

Meperidine

Benzodiazepines

Oxaprozin

Thioridazine

Sertraline

Tramadol

Cannabinoids

Dronabinol

Venlafaxine

Efavirenz

Tricyclic

Carbamazepine

Hemp-containing foods

antidepressants

Cyclobenzaprine

Ibuprofen

Cyproheptadine

Ketoprofen

Diphenhydramine

Naproxen

Hydroxyzine

Piroxicam

Quetiapine

Promethazine

Lyseric acid

Amitriptyline

Proton pump inhibitorsc

diethylamine (LSD)

Dicyclomine

Sulindac

Ergotamine

Tolmetin

Promethazine

Sumatriptan

a Ciprofloxacin, levofloxacin, and ofloxacin.

b Vicks inhaler due to *l*-methamphetamine content interfered with older immunoassays; interference has not been seen with new enzyme multiplied immunoassay tests (EMIT).

c Pantoprazole.

**Summary**

The strengths and limitations of UDS need to be fully understood in order to perform the correct screen and also to correctly interpret the results. Patients who are being monitored by random drug screens for a specific drug, GC-MS is not indicated for every positive result found on immunoassay due to the high cost of GC-MS and the ability of immunoassay to detect metabolites of the parent drug. An extensive medication history including prescription, nonprescription, and herbal medications should be obtained from the patient. Medication histories are important in order to anticipate false-positives as well as differentiate between drugs used for legitimate medical purposes and drugs of abuse.

**References**

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