

A Positive Immunoassay Is a Presumptive Result: Not a Diagnosis

Clinical Scenario

A patient enrolled in your opioid treatment program submits a urine sample that screens positive for amphetamines on the point-of-care cup. You have no record of a stimulant prescription, and the patient denies use. Do you document a positive result and initiate a clinical response?

The Pearl

Immunoassay (IA) screens, including point-of-care cups, lateral flow strips, and laboratory-based analyzers, detect drug classes by antibody cross-reactivity, not by identifying a specific compound. A positive IA result means only that *something in the sample triggered the antibody*. It does not confirm the presence of an illicit drug, identify a specific molecule, or distinguish a prescribed medication from a controlled substance.

Liquid chromatography-tandem mass spectrometry (LC-MS/MS) is the confirmatory standard. It identifies the **specific compound** present, quantifies the concentration, and is the only result that can reliably support a clinical or legal action.

Why It Matters

Acting on an unconfirmed IA result can have serious consequences:

- A patient may be wrongly accused of illicit drug use in a treatment or drug court setting.
- A clinically appropriate medication may be discontinued or withheld without justification.
- Legal or regulatory action may be initiated on the basis of a result that would not survive confirmation.

Many commonly prescribed medications are known to cause false positive IA results. Bupropion (prescribed for depression and smoking cessation) is a well-documented cause of false positive amphetamine screens on multiple platforms. Quetiapine has been associated with false positive methadone results. Diphenhydramine can trigger a false positive PCP result. These are not rare edge cases; they are documented, clinically reproducible cross-reactivities that occur in everyday practice.

Platform Note

Cross-reactivity profiles vary significantly by immunoassay manufacturer and analyzer platform. A compound that triggers a false positive on one platform may test negative on another. When investigating a discordant or unexpected result, request the cross-reactivity data directly from your testing laboratory or the assay manufacturer, and always confirm with LC-MS/MS before taking clinical or legal action.

Bottom Line: Never act on a positive immunoassay alone. Confirmatory LC-MS/MS identifies the specific compound and is the only defensible basis for a clinical or legal action.

References

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3. Dasgupta A. *Beating Drug Tests and Defending Positive Results: A Toxicologist's Perspective.* Humana Press; 2010.

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