# Common Interferences in Drug Testing

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**KEYWORDS**

• False positive • False negative • Drugs • Toxicology • Forensic • Workplace • Laboratory

**KEY POINTS**

- Interferences relating to laboratory toxicology testing refer to results which differ from their true value and are often encountered in the setting of a drug screen compared with confirmatory testing results.
- Interferences fall into two general categories; those that cause false positive results (when a drug screen is positive but confirmatory testing is negative) and those that cause false negative results (when a drug screen is negative when in reality the sample donor has ingested the tested substance).
- Interferences can result from differences in laboratory testing methodology, reagent and analyte cross reactivity, limits of analyte detection, instrument resolution, reporting cutoff, sample processing, tissue type and sample adulteration among others.
- Awareness of the possible causes of such interferences are integral to proper laboratory result interpretation and patient management.

Interferences with toxicology testing fall into two categories: those that cause false-positive results and those that cause false-negative results. The terms *false positive* and *false negative* in the context that follows refers to the screening test result as compared with the true result; that is, a false-positive result is a result that is screen positive for a particular class of drugs, when in reality, the donor has not ingested any of those substances. Conversely, a false-negative result is when a sample screens negative for a class of drugs, when in reality, the donor has ingested one of the tested substances.[1]

False-positive screen results are not a major concern for most toxicology laboratories, as confirmatory testing will resolve the screening discrepancy. Conformation

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testing is always more sensitive and specific than the initial screening test. False-negative results are a significant concern, however, as a sample that screens negative will not be sent for confirmatory testing. This issue becomes a concern because if the donor has intentionally masked the ingestion of a drug, the testing will not reveal it.

It should be noted that interferences only occur with the initial testing, which is usually immunoassay. Mass spectrometry confirmation tests are not affected by interfering substances or cross-reacting drugs.[2]

## FALSE POSITIVE

False-positive interferences are usually drugs or other substances that are often structurally related to the class of drugs that is being screened for. Antibodies in the screening reagent are designed to detect common epitopes, particularly in drug classes with many substances (opioids, benzodiazepines, sympathomimetic amines). This design allows the test to be able to detect the many different drugs within a particular class. However, sometimes substances may be structurally similar to the intended class and, thus, are inadvertently detected by the assay. There is most often no intent on the part of the sample donor to cause a false-positive result.[3,4] **Table 1** describes commonly known drug interferences.[4,5]

## FALSE NEGATIVE

False-negative interferences may or may not be intentionally ingested to attempt to mask the ingestion of a drug patients do not want to be detected. False-negative tests are more of a concern because, based on most toxicology laboratories' testing scenarios, negative screening samples are not investigated further.

### *Dilution*

The simplest of these interferences involves diluting one's urine to the point that the concentration of the drug is less than the detection limits of the test. Patients either add additional liquid to the urine sample or drink something that causes their urine to be very dilute. Although this is a very effective technique, it is easily detected by the testing facility when they test the creatinine and specific gravity or observe the collection process. A normal urine has a creatinine greater than 20 mg/dL, along with a specific gravity that is greater than 1.030. If a urine specimen has both creatinine and specific gravity values less than these cutoffs, the urine is considered to be dilute.[6]

### *Substitution*

Patients can attempt to substitute their urine with either someone else's urine or with a urinelike liquid. This type of interferences is detected with an observed collection, recording the temperature of the urine immediately after collecting, and/or the testing facility testing the creatinine and specific gravity of the sample. A sample that is not between 90°F and 100°F is not humanly possible and should be questioned as to the source of the specimen (Nuclear Regulatory Commission, Regulations Title 10, Code of Federal Regulations, part § 26.111). Additionally, a creatinine that is less than 2 mg/dL with a specific gravity that is less than or equal to 1.0010 or greater than or equal to 1.030 is not physiologically possible and is, thus, considered to be substituted.[6]

### *Adulterated*

Another way a sample can be tampered with is by the addition of a substance that interferes with screening test that is causing the antibody to not bind to the drug. Specimen validity testing for oxidative substances and the pH of the sample usually detects