MINISTRY MEDICAL GROUP – Managing Pain, Improving Lives

Previous pain updates provided information on interpretation of immunoassay (IA) urine drug test results. You should recall that positive IA results should be considered presumptive until confirmed by gas or liquid chromatography-mass spectrometry (GC-MS/LC-MS), although it is not always necessary to confirm all positive results. GC/LC-MS provides highly-specific results through identification and quantification of the individual drugs or metabolites within a specimen. GC/LC-MS also provides highly sensitive results due to lower cutoff levels for detection. Refer to Testing Methods for Urine Drug Screening for an overview of GC/LC-MS testing.

Interpretation of confirmatory urine drug test results:

1. Correct interpretation of confirmatory test results requires a basic understanding of metabolic pathways, particularly for opioids and benzodiazepines, in order to understand which metabolites will be present and which metabolites should not be present, based on the patient’s prescribed medication.

Opioid Metabolic Pathways:

![Image of Opioid Metabolic Pathways]

Benzodiazepine Metabolic Pathways:

![Image of Benzodiazepine Metabolic Pathways]


2. Metabolites should be present; absence suggests potential adulterated sample (SAMHSA, 2012; page 47-49)

3. Opioids are metabolized in a linear sequence
   a. Heroin is rapidly converted to 6-MAM and then to morphine; there is minimal metabolism to hydromorphone. Rarely will heroin or 6-MAM be present due to heroin’s very short half-life.
   b. Codeine is metabolized to morphine; therefore both substances may be present after codeine use.
Confirmatory Urine Drug Testing

i. Codeine alone is possible because a small proportion of patients (<10% of Caucasians) lack the enzyme needed to convert codeine to morphine.

ii. Codeine may be metabolized to small quantities (generally <15%) of hydrocodone; this should not be interpreted as hydrocodone use when high concentrations of codeine are present.

c. Morphine is metabolized to 3-morphine-glucuronide and 6-morphine-glucuronide and to a small extent (<5%) to hydromorphone.

i. Morphine does not metabolize to codeine; presence of morphine only is consistent with use of morphine or heroin.

d. Hydrocodone may be metabolized to small quantities of hydromorphone; this should not be interpreted as hydromorphone use when high concentrations of hydrocodone are present.

e. Synthetic opioids e.g., oxycodone, methadone, and fentanyl, have limited metabolism.

i. Oxycodone is metabolized to noroxycodone and oxymorphone. If the concentration of oxycodone is greater than oxymorphone, use of oxycodone is likely.

ii. Oxymorphone does not produce any metabolites that could be mistaken for another opioid.

4. Benzodiazepine metabolism is complex; providers should refer to metabolic pathways for anticipated metabolites.

5. THCA quantification can demonstrate abstinence through decreasing levels.

a. May be present in urine for more than 3 months in chronic high users

b. Levels may increase if a patient has lost significant weight despite being abstinent

c. Passive smoke inhalation does not produce appreciable amounts of THCA in a urine specimen to explain positive marijuana results

6. Amphetamines are minimally metabolized but frequently cross react; therefore, confirmatory testing is needed to identify which substances are present.

7. A methamphetamine positive result requires chiral analysis to differentiate between two isomers: d-methamphetamine and l-methamphetamine

a. Any d-methamphetamine present is from an illicit source.

b. If 100% of the isomer is l-methamphetamine (aka l-desoxyephedrine), the source is likely from a Vicks inhaler or a metabolite of selegiline.

8. Confirmatory tests provide quantitative concentrations of drugs and their metabolites; however, there is currently no broadly accepted, scientifically validated relationship between the concentrations reported in the urine and the doses taken of any drug.

a. Interpretation of quantitative concentrations is difficult and requires more specialized training

b. Providers with questions about interpretation should speak with a pain or addiction specialist experienced with interpretation.

9. Confirmation of all positive IA results is not clinically indicated and not cost effective.

a. If a patient admits drug use when informed of a positive test result, a confirmatory test is generally not needed.

b. If the IA test is highly specific to a drug with limited cross-reactivities e.g., cocaine, confirmation is generally not needed.

c. Refer to the tables Drugs of Abuse Testing – Illicit Drugs and UDT – Prescribed Medications to help determine when confirmation is necessary.
Confirmatory testing with chromatography and spectrometry of positive urine drug testing by IA is complicated and contains many opportunities for miscommunication and misunderstanding. This guide is intended to provide a broad overview of the most common pitfalls that providers are likely to encounter. Refer back to this and the other articles in this series often to ensure a clear understanding of the test results when discussing them with patients. Any questions can be referred to a pain or addiction specialist experienced with interpretation and clinical application of findings.

For additional information:

- Testing Methods for Urine Drug Screening
- Managing Unexpected UDT Results – Illicit Substances
- Managing Unexpected UDT Results – Prescription Medications

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References:


Substance Abuse and Mental Health Services Administration. (2012). Clinical Drug Testing in Primary Care, Technical Assistance Publication (TAP) 32. Retrieved from SAMHSA: