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Global Division

Siemens Healthcare
Diagnostics Inc.
1717 Deerfield Road
Deerfield, IL 60015-0778
USA
www.siemens.com/diagnostics

Siemens Global Headquarters

Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

**Global Siemens
Healthcare Headquarters**

Siemens AG
Healthcare Sector
Henkestrasse 127
91052 Erlangen
Germany
Telephone: +49 9131 84 - 0
www.siemens.com/healthcare

www.usa.siemens.com/diagnostics

**Test Result
Interpretation**

EMIT Drug Abuse Assays: How Accurate Are They?

Answers for life.

SIEMENS

Syva has been a leading developer and manufacturer of drugs-of-abuse tests for more than 30 years.

Now part of Siemens Healthcare Diagnostics, Syva® boasts a long and successful track record in drugs-of-abuse testing, and leads the industry in the production of enzyme immunoassays. In addition to drugs-of-abuse assays, Syva has been a key player in the development and manufacture of therapeutic drug monitoring assays.

Syva products are sold in more than 45 countries worldwide.

Syva EMIT® immunoassays are the most widely used and scientifically documented screening tests for drugs of abuse. No other drugs-of-abuse screening tests have a longer or more reliable record. EMIT test results have been upheld in numerous court decisions and at the highest level of the American judicial system: the United States Supreme Court.

This brochure is one in a series designed to keep customers informed on a variety of relevant topics.

This brochure describes the rigorous process used to ensure the reliability and accuracy of all EMIT assays and reviews some scientific literature, which documents the accuracy and reliability of EMIT drugs-of-abuse assays.

Built-in Reliability Ensures Accuracy

Syva builds reliability into each one of its tests. Each EMIT assay must pass a rigorous testing protocol to show that it can consistently distinguish between negative (drug-free or containing drug levels below the EMIT assay cutoff) and positive (containing drug levels above the EMIT assay cutoff) samples. The results of these studies are confirmed by independent laboratories. Overall, thousands of hours of testing are required before a new assay is ready to be marketed.

Once an assay is on the market, each newly manufactured lot must pass additional testing procedures. A production lot is not released unless it meets performance criteria during quality assurance testing.

Each EMIT assay is repeatedly tested on drug-free urine samples and samples containing known drug concentrations. In addition, EMIT assays are subjected to multiple tests performed on different instruments by different operators. All results are compared to reference methods, including gas chromatography/mass-spectrometry (GC/MS).

False Positives or Unconfirmed Results?

In drug testing, a false-positive result means that a drug or drug metabolite is reported in a sample when it is not actually present. The majority of suspected false-positives are, in fact, unconfirmed positive results; that is, the drug is actually present, but the confirmation method does not bear this out.

This may occur for two different reasons:

1. The confirmation test may be detecting different (or fewer) metabolites of the target drug than the EMIT assay detects.

Some EMIT assays detect a class of drugs. For example, the EMIT opiate assays detect several opiates and metabolites in addition to morphine. A positive EMIT result does not specify which opiate is present, only that the opiates in the sample exceed the assay cutoff.

If the confirmatory method detects only the presence of codeine and morphine, it is possible that some EMIT opiate positives will not be confirmed. Unconfirmed specimens may contain hydromorphone (Dilaudid, a commonly abused street narcotic), oxycodone (a commonly abused prescription narcotic), or any of several other opiate drugs.

Other examples of class assays are the EMIT barbiturate assays, the EMIT benzodiazepine assays, and the EMIT amphetamine assays. If there is a need to determine which specific drug is present from a class, suitable confirmation techniques are available.

Other EMIT assays (such as the cannabinoids) may cross-react with several metabolites of a specific drug. Cross-reactivity of this type is useful when the abused drug has more than one urinary metabolite. However, EMIT assay results may be difficult to confirm when the alternative method detects only one drug metabolite. This is sometimes the case when a highly sensitive but selective test such as GC/MS, which detects only one of the several substances detected by the EMIT assay, is used for confirmation.

2. The confirmation test may not detect the drug or drug metabolite(s) in question at as low a concentration as does the EMIT assay.

Because EMIT assays are so sensitive to their target drugs, low or borderline EMIT results are sometimes difficult to confirm by less sensitive procedures such as thin-layer chromatography (TLC) and, sometimes, gas chromatography (GC) and high-pressure liquid chromatography (HPLC).

Poppy Seeds and Opiate Assays

Poppy seeds are obtained from an opium producing plant (*Papaver somniferum*), and most varieties contain morphine and codeine, which are excreted in the urine. Ingesting poppy seeds can produce positive responses with opiate assays. These positive responses are sometimes referred to as “false-positive” results, when, in fact, the assays have accurately detected opiates.

Cannabinoid Assays

More than 30 metabolites of THC (Δ^9 -tetrahydrocannabinol) have been identified in human urine. The EMIT cannabinoid assays detect a large number of THC (tetrahydrocannabinol) metabolites. This ability to cross-react with many THC metabolites was built into the assays to maximize their ability to detect marijuana use.

Some drug-testing techniques detect only the principal active ingredient of marijuana, THC, and/or its major urinary metabolite, 11-nor- Δ^9 -THC-9-carboxylic acid (carboxy THC or THC-COOH). The concentration of carboxy THC in urine can range from less than 10% to more than 60% of the total mixture of THC metabolites. A confirmation test that measures only carboxy THC may not confirm EMIT results.

Most commercial laboratories follow the Substance Abuse and Mental Health Services Administration (SAMHSA) recommendations for a GC/MS cutoff of 15 ng/mL. This concentration is almost always low enough to confirm the presence of carboxy THC in urine samples found positive by EMIT assays with cutoffs of 50 ng/mL or higher. However, in some cases, confirmation by GC/MS may still be difficult in samples that contain a low concentration of carboxy THC or in samples that fall close to the cutoff of the EMIT assay.

Reviewing the Literature

Numerous published studies compare EMIT assay results with those of other analytical methods. Following are brief summaries of a few of these journal articles. For the sake of brevity, we report only the findings related to the EMIT assays.

Detection Times of Marijuana Metabolites in Urine by Immunoassay and GC/MS. Huestis MA, Mitchell JM, Cone EJ. J Anal Toxicol. 1995;19:443-449.

The authors investigated the detection time of various cannabinoid assays. Six subjects each smoked a single marijuana cigarette (placebo, 1.75, or 3.55% Δ^9 -tetrahydrocannabinol [THC]) each week on three separate occasions over a period of 4-6 weeks. Nine hundred fifty-seven (957) individual urine specimens were collected throughout the three-week study and analyzed by RIA, immunoassay, and GC/MS (15 ng/mL cutoff). In addition to several other immunoassays, five different EMIT immunoassays were used in the

study: EMIT® II Cannabinoid 50 ng and 100 ng Assays, and EMIT® d.a.u.™ 20 ng, 50 ng, and 100 ng Assays.

The authors found that the window of detection for marijuana is narrower (less than 1-2 days in most cases) than the 1 week that is usually assumed. The size of the window varies widely by individual, but is also dependent on the amount of drug ingested; the cut off level of the assay; and the sensitivity and specificity of the assay. Relative to other immunoassays, EMIT cannabinoid assays have long overall detection times, and, because of their sensitivity to many THC metabolites, they yield more positive results.

The best correlation with GC/MS detection time was by the EMIT d.a.u. Cannabinoid 20 ng Assay. Mean detection times for the EMIT d.a.u. 20 ng/mL cutoff assay and GC/MS were 51.0 and 33.7 hours, respectively, at the low dosage, and 92.6 and 88.6 hours, respectively, at the high dosage.

Evaluation of Phencyclidine by EMIT d.a.u. Utilizing the ETS® Analyzer and a 25-ng/mL Cutoff Sneath TC, Jain NC J Anal Toxicol. 1992;16:107-108.

These authors evaluated the EMIT d.a.u. Phencyclidine Assay on the ETS System for detecting concentrations of ≥ 25 ng/mL phencyclidine in urine. More than 1600 urine specimens were analyzed by the EMIT assay at the 25 ng/mL cutoff. Of the 1600 specimens, 53 gave positive results; 52 of which were confirmed positive by GC/MS. The one discordant sample was reanalyzed by the EMIT assay, with negative results.

The authors concluded that the EMIT d.a.u. Phencyclidine Assay on the ETS System accurately detects phencyclidine at 25 ng/mL

Use of over-the-counter Vicks™ inhalers, which contain l-methamphetamine (l-desoxyephedrine), have been found to cause positive responses in urine specimens being screened by some amphetamine/methamphetamine assays.

The following two studies evaluated possible cross-reactivity of l-methamphetamine in three EMIT amphetamine assays: EMIT II Monoclonal Amphetamine/Methamphetamine Assay, EMIT d.a.u. Monoclonal Amphetamine/Methamphetamine Assay, and EMIT d.a.u. Amphetamine Class Assay.

**Response of the EMIT II Amphetamine/
Methamphetamine Assay to Specimens Collected
Following Use of Vicks Inhalers**
Poklis A, Jortani SA
J Anal Toxicol. 1993;17:284–286.

The authors of this study evaluated the EMIT II Monoclonal Amphetamine/Methamphetamine Assay for possible cross-reactivity caused by Vicks inhalers. They collected urine specimens from seven subjects using Vicks inhalers: four subjects using the inhaler every two hours for five days, and three subjects using the inhaler every hour for three days. Both regimens were well above the manufacturer's recommended use of the inhaler.

A total of 150 urine specimens were collected and analyzed by the EMIT II assay on a Hitachi 717[®] analyzer. Specimens yielding a response close to the cutoff calibrator (1000 ng/mL d-methamphetamine) were quantitated by GC/MS.

The use of Vicks inhalers did not cause positive results in urine specimens tested by the EMIT II Monoclonal Amphetamine/Methamphetamine Assay. All specimens tested negative. Two specimens showing absorbance rates close to the assay's cutoff calibrator yielded concentrations of 1290 and 1390 ng/mL l-methamphetamine when analyzed by GC/MS. A third specimen showing an absorbance rate of 22 units less than the cutoff calibrator rate yielded 740 ng/mL l-methamphetamine.

The authors concluded that the use of Vicks inhalers as recommended by the manufacturer, or even double the dose, will not cause positive results with the EMIT II Amphetamine/Methamphetamine Assay.

**Response of EMIT Amphetamine
Immunoassays to Urinary Desoxyephedrine
Following Vicks Inhaler Use**
Poklis A, Moore KA
Ther Drug Monit. 1995; 17:89–94.

This study evaluated the EMIT d.a.u. Monoclonal Amphetamine/Methamphetamine Assay and the EMIT d.a.u. Amphetamine Class Assay (a polyclonal assay) for cross-reactivity in urine specimens collected from six subjects using Vicks inhalers. Four subjects used the inhaler every two hours for five days, and two subjects used the inhaler every hour for three days. All voided urine was collected (132 specimens total) and analyzed by both assays. Specimens testing positive were confirmed by GC/MS.

None of the 132 urine specimens tested positive (100% accuracy) by the EMIT d.a.u. Monoclonal Amphetamine/Methamphetamine Assay. With the EMIT d.a.u. Amphetamine Class Assay, 17 specimens tested positive (87% accuracy). Six of the 17 positive specimens came from one subject using the inhaler every two hours, and 11 came from the two subjects using the inhalers every hour. The EMIT d.a.u. Amphetamine Class Assay, which contains polyclonal antibodies, is designed to detect structurally related amphetamines. Because Vicks inhalers contain a structurally related amphetamine (l-methamphetamine), some urine specimens from persons using the inhalers can test positive with the EMIT d.a.u. Amphetamine Class Assay. Use of Vicks inhalers did not cause positive results with the EMIT d.a.u. Monoclonal Amphetamine/Methamphetamine Assay.

Urinary Screening for Adinazolam and Its Major Metabolites by the EMIT d.a.u. and FPIA Benzodiazepine Assays with Confirmation by HPLC.

**Fraser AD, Isner AF, Bryan W
J Anal Toxicol. 1993;17:427–431.**

This laboratory evaluated the accuracy of the EMIT d.a.u. Benzodiazepine Assay for detecting adinazolam, its major metabolite, N-desmethylnadinazolam, and a minor metabolite, estazolam. Adinazolam is a benzodiazepine structurally similar to alprazolam and triazolam.

Six volunteers were given adinazolam in single oral doses of 10, 30, and 50 mg. Multiple urine specimens were collected from each participant during the 36 hours following administration of the drug. The results were confirmed by high-performance liquid chromatography (HPLC).

All specimens produced positive results every two hours until 36 hours after dosing. The EMIT assay yielded responses equivalent to the cutoff calibrator (300 ng/mL) at 100 to 200 ng/mL for the metabolites, N-desmethylnadinazolam and estazolam, and at 200 ng/mL for the parent drug, adinazolam. The authors concluded that the EMIT d.a.u. Benzodiazepine Assay is an acceptable method of detecting adinazolam in urine.

Urinary Screening for –OH triazolam by FPIA and EIA with Confirmation by GC/MS

**Fraser A, Bryan W, Isner AF
J Anal Toxicol. 1992;16:347–350.**

These authors evaluated the capability of the EMIT d.a.u. Benzodiazepine Assay to detect –OH triazolam, the major metabolite of triazolam, in urine. The authors collected urine specimens from patients receiving triazolam and prepared standard concentrations of –OH triazolam ranging from 100 to 10,000 ng/mL in drug-free urine. Samples that tested positive by the EMIT assay were confirmed by GC/MS.

Nine out of nine urine specimens collected from individuals receiving triazolam were positive

according to the EMIT assay. The assay gave a response equivalent to the cutoff calibrator (300 ng/mL oxazepam) at levels of 100 ng/mL to 200 ng/mL –OH triazolam.

The authors concluded that EMIT d.a.u. Benzodiazepine Assay is an acceptable method of screening urine specimens for triazolam.

Substance Abuse Testing of Urine by GC/MS in Scanning Mode Evaluated by Proficiency Studies, TLC/GC, and EMIT.

**Gibb RP, Cockerham H, Goldfogel GA, Lawson GM, Raisys VA.
J Foren Sci. 1993; 38:124–133.**

This study evaluated gas chromatography/mass spectrometry (GC/MS) analysis as a screening technique for drugs of abuse in urine specimens and compared the results with those from EMIT assays and thin-layer chromatography. The EMIT assays were performed on a Boehringer Mannheim/Hitachi 717 analyzer.

Of the 590 urine samples analyzed, 161 were confirmed positive for drugs of abuse. EMIT assays and GC/MS were in agreement on 142 of the 161 positive results. Of the 19 discrepant results, three samples containing 4496 ng/mL lorazepam, 334 ng/mL oxazepam, or 75 ng/mL THC were found positive by GC/MS, but tested negative by EMIT assay; and 16 samples were positive according to the EMIT assays, but negative by GC/MS.

Virtually all of these 16 samples contained some drug—eight of which contained drug concentrations above the calibrator cutoffs for EMIT assays, but below threshold levels for GC/MS. Hence, the results from these eight samples can be considered unconfirmed positive, increasing the overall accuracy of EMIT assays to 93%. That is, 150 of 161 samples containing amphetamines, barbiturates, benzodiazepines, cocaine, marijuana, or opiates were correctly identified by EMIT assays. Phencyclidine was not detected in any of the samples by EMIT assays or by GC/MS.

External Quality Assessment of Techniques for the Detection of Drugs of Abuse in Urine.

Wilson JF, Smith BL, Toseland PA, Williams J, Burnett D, Hirst AD, Watson ID, Horn AN. *Ann Clin Biochem.* 1994; 31:335–342.

In order to examine the quality of drugs-of-abuse testing, the United Kingdom National External Quality Assessment Scheme for Drugs of Abuse in Urine (UKNEQAS) evaluated testing data accumulated during a two-year period at 133 laboratories throughout Europe and the Near East. UKNEQAS evaluated results of five chromatographic techniques: thin-layer chromatography kits, in-house TLC tests, gas chromatography, gas chromatography/mass spectrometry, and high-performance liquid chromatography; and six immunoassays: EMIT d.a.u. assays, EMIT[®] st[™] assays on the Qst[®] instrument, fluorescence polarization immunoassay, polarization fluoroimmunoassay, radioimmunoassay, and Boehringer Corp. London (BCL) assays.

UKNEQAS supplied participating laboratories with aliquots from 25 freeze-dried urine specimens. The specimens contained either no drug or one of three (low, medium, or high) concentrations of six drugs: amphetamines, barbiturates, benzodiazepines, benzoyllecgonine, methadone, and morphine. Other analytes were present in the specimens as well. UKNEQAS specified cutoffs of 1000 ng/mL for all analytes except cocaine metabolite, which was specified as 300 ng/mL.

Of 1035 reported test results, 29.9% came from EMIT d.a.u. assays—the most widely used of all methods studied. Overall sensitivity for the EMIT d.a.u. assays was 87.9%, the highest sensitivity reported. Overall sensitivity for EMIT st assays on the Qst was 86.9%. If the results from samples containing <150 ng/mL benzoyllecgonine are excluded, since EMIT cocaine assays are not designed to detect the metabolite at concentrations below 300 ng/mL, overall sensitivity increases significantly. Overall sensitivities for EMIT d.a.u. assays and EMIT st assays increase to 92.7% and 91.5%, respectively. Overall specificity for the EMIT d.a.u. assays was 98.9% and for EMIT st assays, 98.6%.

The following values are the mean of percent sensitivities.

Amphetamines: Sensitivities at medium concentrations of amphetamines (1500 ng/mL) were 96.7% for the EMIT d.a.u. Amphetamine Assay and 100% for the EMIT st Amphetamine Assay.

Barbiturates: EMIT d.a.u. Barbiturate Assay sensitivities for samples containing medium and high levels of drug were 86.9% and 97.8%, respectively. EMIT st Barbiturate Assay sensitivities at medium and high levels were 91.2% and 97.6%, respectively. At low concentrations, immunoassays showed reduced cross-reactivity. This was attributed to the barbiturate in the samples, amylobarbitone (amobarbital), which is more commonly prescribed in the UK. EMIT assays are designed to detect quinalbarbitone (secobarbital), the most frequently used barbiturate in the U.S.

Benzoyllecgonine: Immunoassays were more sensitive than GC, GC/MS, or TLC for the cocaine metabolite. Sensitivities for specimens containing 500 ng/mL benzoyllecgonine were 97.0% for the EMIT d.a.u. Cocaine Metabolite Assay and 100% for the EMIT st Cocaine Metabolite Assay.

Benzodiazepines: Sensitivities at medium drug concentrations for the EMIT d.a.u. Benzodiazepine Assay and EMIT st Benzodiazepine Assay were 99.1% and 100%, respectively.

Methadone: Sensitivities at medium drug concentrations of methadone for the EMIT d.a.u. Methadone Assay and the EMIT st Methadone Assay were 98.8% and 96.3%, respectively.

Morphine: For specimens containing 1500 ng/mL morphine, the EMIT d.a.u. Opiate Assay and EMIT st Opiate Assay sensitivities were 99.1% and 97.8%, respectively.

Drug Testing Confirmation

Drugs-of-abuse testing involves the serious consideration of social, legal, and technical issues. Positive results from urine samples screened for drugs of abuse should be confirmed by a more specific alternate method, such as gas chromatography/mass spectrometry. GC/MS is generally considered to be the most conclusive method of confirming the presence of a drug in urine.

At Siemens Healthcare Diagnostics, our goal is to be a technical resource for our customers. Our company's worldwide sales and service network includes technical experts who, in addition to providing day-to-day technical assistance, help customers design and implement drug testing programs, set up laboratories for testing, and train laboratory personnel.

If you have specific questions about confirming positive test results or other questions about testing for drugs of abuse with EMIT assays, please call our Siemens Technical Solutions Center at 1-800-227-8994 in the United States.