SIEMENS

# Syva®

# *Emit*® *II Plus* Opiate Assay

See shaded sections:
Updated information from 2017-04 version.

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## Opiate Assay

### 1 Intended Use

The Emit® II Plus Opiate Assay is a homogeneous enzyme immunoassay with a 300 ng/mL or 2000 ng/mL cutoff (SAMHSA initial test cutoff level).[1] The assay is intended for use in the qualitative and semiquantitative analyses of opiates in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.

***The Emit® II Plus Opiate Assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method.[2] Other chemical confirmation methods are available. Clinical consideration and professional judgment should be applied to any drug-of-abuse test result, particularly when preliminary positive results are used.***

### 2 Summary and Explanation of the Test

Opiates are a class of compounds that includes morphine, codeine, and heroin. Morphine and codeine are naturally occurring alkaloids that are found in opium, a substance exuded from the unripe seed pod of the opium poppy *Papaver somniferum.* Heroin is a semisynthetic derivative of morphine.[3,4]

Morphine is a potent analgesic. Codeine is used in analgesic preparations and as a cough suppressant. Heroin is an even more potent analgesic than morphine. Both morphine and codeine are legitimate drugs. Heroin is a drug of abuse that may be snorted, smoked, or dissolved and injected subcutaneously or intravenously.

Opiates are absorbed rapidly. Heroin is converted almost immediately to morphine, which is excreted in urine both unchanged and as a glucuronidated metabolite. Excretion takes place over a period of a couple of days. Codeine is excreted in urine as a glucuronidated conjugate, as free and conjugated norcodeine, and as morphine. The presence of opiates in the urine indicates the use of heroin, morphine, and/or codeine.

The Emit® II Plus Opiate Assay tests for morphine, morphine-3-glucuronide, and codeine in human urine and gives a positive result if any of these opiates are present. It also detects synthetic opiates related to morphine, such as hydromorphone, and high concentrations of the analgesic meperidine and the narcotic antagonist nalorphine. Positive results for specimens containing other compounds structurally unrelated to opiates have not been observed.

Methods historically used for detecting opiates in biological fluids include thin-layer chromatography, gas chromatography, high-performance liquid chromatography, fluorometry, microcrystallography, enzyme immunoassay, and radioimmunoassay.[5]

While confirmation techniques other than GC/MS may be adequate for some drugs of abuse, GC/MS is generally accepted as a vigorous confirmation technique for all drugs, since it provides the best level of confidence in the result.[2]

### 3 Principle

The Emit® II Plus Opiate Assay is a homogeneous enzyme immunoassay technique used for the analysis of specific compounds in human urine.[6] The assay is based on competition between drug in the specimen and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the sample can be measured in terms of enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that is measured spectrophotometrically. Endogenous serum G6PDH does not interfere because the coenzyme NAD functions only with the bacterial *(Leuconostoc mesenteroides)* enzyme employed in the assay.

### 4 Reagents

| REF | Product Description | Volume |
|---|---|---|
| 9B039UL/ | **Emit® II Plus Opiate Assay** | 29 mL/ |
| 9B309UL/ | **Antibody/Substrate Reagent 1** | 115 mL/ |
| 9B329UL | Sheep polyclonal antibodies to morphine (4.2 µg/mL),* G6P (10 mM), NAD (6 mM), bovine serum albumin, preservatives, and stabilizers | 1000 mL |
| | **Enzyme Reagent 2** | 11 mL/ |
| | Morphine labeled with bacterial G6PDH (0.47 U/mL),* Tris buffer, bovine serum albumin, preservatives, and stabilizers | 50 mL/ 435 mL |

****The antibody titer and enzyme conjugate activity may vary from lot to lot.***

***Note: Reagents 1 and 2 are provided as a matched set. They should not be interchanged with components of kits with different lot numbers.***

For *in vitro* diagnostic use.

**Preparation and Storage of Assay Components**

**Reagents:**

The Emit® II Plus Opiate Assay reagents are provided ready to use and may be used directly from the refrigerator. Close the reagent bottles when not in use.

***Note: Caps must always be replaced on the original containers.***

When not in use, store reagents at 2–8°C (36–46°F), upright and with screw caps tightly closed. If stored as directed, reagents are stable until the expiration date printed on the label. Refer to the analyzer-specific protocols for on instrument stability information. Do not freeze reagents. Avoid prolonged exposure to temperatures above 32°C. **Improper storage of reagents can affect assay performance.**

### 5 Specimen Collection and Preparation

- Urine specimens may be collected in plastic (ie, polypropylene, polycarbonate, polyethylene) or glass containers. Some plastics can adsorb certain drugs.
- Internal testing has shown that, if not analyzed immediately, specimens may be stored unrefrigerated for up to 7 days. Specimens may be stored refrigerated for 30 days before analysis. After 7 days unrefrigerated or 30 days refrigerated, samples should be stored frozen.
- Frozen specimens must be thawed and mixed thoroughly prior to analysis.
- Specimens with high turbidity should be centrifuged before analysis.
- The recommended pH range for urine specimens is 3.0–11.0.
- Adulteration of the urine specimen may cause erroneous results. If adulteration is suspected, obtain another specimen.
- Human urine specimens should be handled and treated as if they are potentially infectious.

### 6 Procedure

**Materials Provided**

Emit® II Plus Opiate Assay
Reagent 1
Reagent 2

**Materials Required But Not Provided**

| | |
|---|---|
| 9A509UL | Emit® Calibrator/Control Level 0 |
| 9A529UL | Emit® Calibrator/Control Level 1 |
| 9A549UL | Emit® Calibrator/Control Level 2 |
| 9A569UL | Emit® Calibrator/Control Level 3 |
| 9A609UL | Emit® Calibrator/Control Level 5 |

Commercially available controls (see Quality Control, Semiquantitative Analysis)

**Instruments**

Siemens Healthcare Diagnostics provides instructions for using this assay on a number of chemistry analyzers. Contact the Technical Assistance Center in the USA or your local Siemens representative for application sheets.

Analyzers must be capable of maintaining a constant reaction temperature, pipetting specimens/reagents and measuring enzyme rates precisely, timing the reaction accurately, and mixing reagents thoroughly.

**Daily Maintenance**

Refer to the instrument operator's manual for maintenance instructions.

**Assay Sequence**

To run the assay, see the instrument operator's manual and the analyzer-specific protocol from Siemens.

**Calibration**

***Note: These reagents are qualified for use with these calibrators only. However, other material may be used for quality control purposes.***

**Table 1 — Emit® Calibrators/Controls for Use in Qualitative or Semiquantitative Analysis**

| Desired Cutoff Level (ng/mL) | Required Calibrators/Controls for Qualitative Analysis (ng/mL) | Required Calibrators/Controls for Semiquantitative Analysis (ng/mL) |
|---|---|---|
| 300 | Level 0 (0)<br>Level 1 (300)<br>Level 5 (4000) | Level 0 (0)<br>Level 1 (300)<br>Level 2 (1000)<br>Level 3 (2000) |
| 2000 | Level 0 (0)<br>Level 3 (2000)<br>Level 5 (4000) | Level 0 (0)<br>Level 2 (1000)<br>Level 3 (2000)<br>Level 5 (4000) |

***Note: For any individual cutoff level, a calibrator/control is used either as a calibrator or as a control when the assay is used for qualitative analysis. When a calibrator/control is used as a calibrator for an individual cutoff level, the other level calibrators/controls (above or below it, as listed above) are used as controls.***

*Qualitative Analysis*

**300 ng/mL CUTOFF**

Run the Emit® Calibrator/Control Level 1 (300 ng/mL) in duplicate. Validate the calibration by running controls (see Quality Control). Refer to the Emit® Calibrators/Controls instructions for use and the analyzer-specific protocol for additional information and instrument settings. Recalibrate as indicated by control results.

**2000 ng/mL CUTOFF**

Run the Emit® Calibrator/Control Level 3 (2000 ng/mL) in duplicate. Validate the calibration by running controls (see Quality Control). Refer to the Emit® Calibrators/Controls instructions for use and the analyzer-specific protocol for additional information and instrument settings. Recalibrate as indicated by control results.

*Semiquantitative Analysis*

**300 ng/mL CUTOFF**

Prepare a calibration curve by running Emit® Calibrators/Controls Level 0 (0 ng/mL), Level 1 (300 ng/mL), Level 2 (1000 ng/mL), and Level 3 (2000 ng/mL). Validate the calibration by running controls (see Quality Control). Refer to the Emit® Calibrators/Controls instructions for use and the analyzer-specific protocol for additional information and instrument settings. Recalibrate as indicated by control results.

**2000 ng/mL CUTOFF**

Prepare a calibration curve by running Emit® Calibrators/Controls Level 0 (0 ng/mL), Level 2 (1000 ng/mL), Level 3 (2000 ng/mL), and Level 5 (4000 ng/mL). Validate the calibration by running controls (see Quality Control). Refer to the Emit® Calibrators/Controls instructions for use and the analyzer-specific protocol for additional information and instrument settings. Recalibrate as indicated by control results.

**Quality Control**

*Qualitative Analysis*

**300 ng/mL CUTOFF**

Validate the calibration by assaying controls. Ensure that the result from Emit® Calibrator/Control Level 0 (0 ng/mL) or Emit® Calibrator/Control Level 5 (4000 ng/mL) relates appropriately to the result from Emit® Calibrator/Control Level 1 (300 ng/mL). That is,

- If Emit® Calibrator/Control Level 0 (0 ng/mL) was run, ensure that the result is negative relative to Emit® Calibrator/Control Level 1 (300 ng/mL).
- If Emit® Calibrator/Control Level 5 (4000 ng/mL) was run, ensure that the result is positive relative to Emit® Calibrator/Control Level 1 (300 ng/mL).

Once the calibration is validated, run urine specimens.

**2000 ng/mL CUTOFF**

Validate the calibration by assaying controls. Ensure that the result from Emit® Calibrator/Control Level 0 (0 ng/mL) or Emit® Calibrator/Control Level 5 (4000 ng/mL) relates appropriately to the result from Emit® Calibrator/Control Level 3 (2000 ng/mL). That is,

- If Emit® Calibrator/Control Level 0 (0 ng/mL) was run, ensure that the result is negative relative to Emit® Calibrator/Control Level 3 (2000 ng/mL).
- If Emit® Calibrator/Control Level 5 (4000 ng/mL) was run, ensure that the result is positive relative to Emit® Calibrator/Control Level 3 (2000 ng/mL).

Once the calibration is validated, run urine specimens.

*Semiquantitative Analysis*

**300 ng/mL CUTOFF**

Validate the calibration curve by assaying commercial controls. Ensure that control results fall within acceptable limits as defined by your laboratory.

Once the calibration curve is validated, run urine specimens.

**2000 ng/mL CUTOFF**

Validate the calibration curve by assaying commercial controls. Ensure that control results fall within acceptable limits as defined by your laboratory.

Once the calibration curve is validated, run urine specimens.

*Qualitative and Semiquantitative Analysis*

1. Follow government regulations or accreditation requirements for quality control frequency. At least once each day of use, analyze two levels of Quality Control (QC) material with known Morphine concentrations. Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.
2. Refer to the instrument operator's manual for appropriate instrument checks.

## 7 Results

*Qualitative Analysis*

**300 ng/mL CUTOFF**

The Emit® Calibrator/Control Level 1 (cutoff), which contains a concentration of 300 ng/mL morphine, is used as a reference for distinguishing "positive" from "negative" specimens.

**Positive Results.** A specimen that gives a change in rate value equal to or higher than the Emit® Calibrator/Control Level 1 rate value is interpreted as positive: The specimen contains opiates.

**Negative Results.** A specimen that gives a change in rate value lower than the Emit® Calibrator/Control Level 1 rate value is interpreted as negative: Either the specimen does not contain opiates or opiates are present in concentrations below the cutoff level for this assay.

**2000 ng/mL CUTOFF**

The Emit® Calibrator/Control Level 3 (cutoff), which contains a concentration of 2000 ng/mL morphine, is used as a reference for distinguishing "positive" from "negative" specimens.

**Positive Results.** A specimen that gives a change in rate value equal to or higher than the Emit® Calibrator/Control Level 3 rate value is interpreted as positive: The specimen contains opiates.

**Negative Results.** A specimen that gives a change in absorbance rate value lower than the Emit® Calibrator/Control Level 3 rate value is interpreted as negative: Either the specimen does not contain opiates, or opiates are present in concentrations below the cutoff level for this assay.

*Semiquantitative Analysis*

The semiquantitation of positive results enables the laboratory to determine an appropriate dilution of the specimen for confirmation by GC/MS. Semiquantitation also permits the laboratory to establish quality control procedures and assess control performance. Refer to the Analytical Recovery section for the semiquantitative range.

Using the Emit® II Plus Opiate Assay, it is possible to make semiquantitative determinations of opiates. See Table 1, Emit® Calibrators/Controls for Use in Qualitative or Semiquantitative Analysis, for requirements. Refer to the analyzer-specific protocol for further instructions.

Results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation and other findings.

Siemens has validated use of these reagents on various analyzers to optimize product performance and meet product specifications. User defined modifications are not supported by Siemens as they may affect performance of the system and assay results. It is the responsibility of the user to validate modifications to these instructions or use of the reagents on analyzers other than those included in Siemens Application Sheets or these instructions for use.

## 8 Limitations

- The assay is designed for use only with human urine.
- A positive result from the assay indicates the presence of opiates but does not indicate or measure intoxication.
- Poppy seeds can contain opiates, and ingestion of products containing poppy seeds can cause a positive test result at the 300 ng/mL cutoff.[7]
- Boric acid is not recommended as a preservative for urine.
- Other substances and/or factors not listed (eg, technical or procedural errors) may interfere with the test and cause false results.
- Interpretation of results must take into account that urine concentrations can vary extensively with fluid intake and other biological variables.
- Immunoassays that produce a single result in the presence of a drug and its metabolites cannot fully quantitate the concentration of individual components.

## 9 Expected Values

When the Emit® II Plus Opiate Assay is used as a qualitative assay, the amount of drugs and metabolites detected by the assay in any given specimen cannot be estimated. The assay results distinguish between positive and negative specimens—positive indicating specimens that contain opiates.

When used semiquantitatively, the assay yields an approximate concentration of the drug detected by the assay (see Section 7, Results).

## 10 Specific Performance Characteristics

The data appearing in this section were collected on the SYVA®-30R Biochemical System using the Emit® II Plus Opiate Assay and the Emit® II Opiate Assay (300 ng/mL) or the Emit® II Opiates 300/2000 Assay. Positive specimens were confirmed by GC/MS.

**300 ng/mL CUTOFF**

**Accuracy**

*Qualitative Results*

Both the Emit® II Plus Opiate Assay and the Emit® II Opiate Assay (comparative method) use a cutoff level of 300 ng/mL.

One hundred five (105) specimens were analyzed by the Emit® II Plus Opiate Assay and by the comparative method.

Fifty-one (51) specimens showed positive results by both methods; 54 specimens showed negative results by both methods. All specimens that showed positive results by both methods were confirmed by GC/MS to contain opiates. The GC/MS method used has a limit of detection (LOD) for morphine of 50 ng/mL.

All specimens that showed positive results by both methods were confirmed by GC/MS to contain between 246 and greater than 2000 ng/mL opiates. These specimens were tested by GC/MS for the following opiates: morphine and codeine.

No drug was detected by GC/MS in 20 negative specimens that were randomly selected from the 54 negative specimens.

Data are summarized in Table 2.

**Table 2 — Accuracy of Qualitative Results for the 300 ng/mL Cutoff**

| | | Emit® II Plus Opiate Assay | |
|---|---|---|---|
| | | Comparative Method | |
| | | + | – |
| Emit® II Plus Opiate Assay | + | 51 | 0 |
| | – | 0 | 54 |

**Analytical Recovery**

*Qualitative Results*

In qualitative spike analysis, the Emit® II Plus Opiate Assay correctly identified the mean rate of spiked specimens containing less than 300 ng/mL morphine as negative and the mean rate of spiked specimens containing greater than 300 ng/mL morphine as positive.

*Semiquantitative Results*

Negative human urine specimens were spiked with concentrations of morphine at levels throughout the semiquantitative range of 75 to 1800 ng/mL. For each known concentration, drug recovery was calculated using the average concentration obtained by the Emit® II Plus Opiate Assay. Semiquantitative results are shown in Table 3.

**Table 3 — Accuracy by Analytical Recovery of Semiquantitative Results for the 300 ng/mL Cutoff**

| Nominal Morphine Concentration (ng/mL) | Average Morphine Concentration by Emit® II Plus Opiate Assay (ng/mL) | Recovery (%) |
|---|---|---|
| 75 | 86 | 115 |
| 150 | 147 | 98 |
| 225 | 224 | 100 |
| 270 | 279 | 103 |
| 330 | 364 | 110 |
| 375 | 409 | 109 |
| 450 | 519 | 115 |
| 500 | 565 | 113 |
| 600 | 684 | 114 |
| 700 | 820 | 117 |
| 800 | 876 | 110 |
| 1000 | 1036 | 104 |
| 1500 | 1513 | 101 |
| 1800 | 1921 | 107 |

**Precision**

Qualitative analysis of precision was determined by assaying calibrators and controls on 20 days, 2 runs per day in replicates of 3 (N = 120). Semiquantitative precision was determined by assaying calibrators and controls on 20 days, 2 runs per day in replicates of 3 (N = 120). Precision data were calculated according to the National Committee of Clinical Laboratory Standards (NCCLS) Guideline EP5-A (February 1999). Results are summarized in Tables 4 and 5.

**Table 4 — Qualitative Analysis of Precision for the 300 ng/mL Cutoff**

| Calibrator or Control | Mean (mAU/min) | SD | CV (%) |
|---|---|---|---|
| **Within-Run Precision** | | | |
| 0 ng/mL Calibrator | 197.8 | 0.9 | 0.5 |
| Control Level 1 (225 ng/mL) | 244.5 | 1.4 | 0.6 |
| 300 ng/mL Calibrator | 266.3 | 1.7 | 0.6 |
| Control Level 2 (375 ng/mL) | 288.7 | 1.4 | 0.5 |
| **Total Precision** | | | |
| 0 ng/mL Calibrator | 197.8 | 1.5 | 0.8 |
| Control Level 1 (225 ng/mL) | 244.5 | 2.1 | 0.9 |
| 300 ng/mL Calibrator | 266.3 | 2.1 | 0.8 |
| Control Level 2 (375 ng/mL) | 288.7 | 2.2 | 0.8 |

**Table 5 — Semiquantitative Analysis of Precision for the 300 ng/mL Cutoff**

| Calibrator or Control | Mean (ng/mL) | SD | CV (%) |
|---|---|---|---|
| **Within-Run Precision** | | | |
| Control Level 1 (225 ng/mL) | 212.7 | 5.3 | 2.5 |
| 300 ng/mL Calibrator | 302.3 | 7.3 | 2.4 |
| Control Level 2 (375 ng/mL) | 409.5 | 7.5 | 1.8 |
| **Total Precision** | | | |
| Control Level 1 (225 ng/mL) | 212.7 | 9.8 | 4.6 |
| 300 ng/mL Calibrator | 302.3 | 11.9 | 3.9 |
| Control Level 2 (375 ng/mL) | 409.5 | 16.0 | 3.9 |

**Specificity**

The Emit® II Plus Opiate Assay detects morphine and morphine-3-glucuronide (the major metabolites of heroin) and codeine in human urine.

Table 6 gives the compounds this assay detects and the levels at which the compounds have been found to give a response approximately equivalent to that of the cutoff calibrator (Emit® Calibrator/Control Level 1). Each concentration represents the reactivity level for the stated compound when it is added to a negative urine specimen. If a specimen contains more than one compound detected by the assay, lower concentrations than those listed in Table 6 may combine to produce a rate approximately equivalent to or greater than that of the cutoff calibrator.

Therapeutic doses of ofloxacin (Floxin) or levofloxacin (Levaquin), non-opiates, may produce positive results with this assay. A positive result from an individual taking ofloxacin or levofloxacin should be interpreted with caution and confirmed by another method.

**Table 6 — Concentrations (ng/mL) of Opiate Compounds That Produce a Result Approximately Equivalent to the 300 ng/mL Cutoff**

| Compound | Concentration (ng/mL) at 300 ng/mL Cutoff |
|---|---|
| Codeine | 102–306 |
| Dihydrocodeine | 291 |
| Ethylmorphine | 240 |
| Hydrocodone | 247 |
| Hydromorphone | 498 |
| Levallorphan | 3740* |
| Levorphanol | 480 |
| Meperidine | > 15000† |
| 6-Acetylmorphine | 435 |
| Morphine-3-Glucuronide | 626 |
| Nalorphine | 2130* |
| Naloxone | 360000 |
| Oxycodone | 3340 |
| Oxymorphone | 9300 |

***Therapeutic or toxic urinary levels of levallorphan and nalorphine are not reported in the literature.***

***†Meperidine urinary concentrations of 150000 ng/mL have been measured in cases of fatal meperidine overdosage.[8]***

Table 7 lists the concentrations of compounds that show a negative response to the Emit® II Plus Opiate Assay at a 300 ng/mL cutoff level.

**Table 7 — Concentrations of Compounds Showing a Negative Response to the 300 ng/mL (0.3 µg/mL) Cutoff**

| Compound | Concentration Tested (µg/mL) |
|---|---|
| Acetaminophen | 1000 |
| L-α-Acetylmethadol (LAAM) | 25 |
| *N*-Acetylprocainamide (NAPA) | 400 |
| Acetylsalicylic Acid | 1000 |
| Amitriptyline | 7 |
| D-Amphetamine | 1000 |
| Benzoylecgonine | 1000 |
| Buprenorphine | 1000 |
| Caffeine | 1000 |
| Cimetidine | 1000 |
| Clomipramine | 2.5 |
| Clonidine | 1000 |
| Cotinine | 100 |
| Cyclobenzaprine | 63 |
| Desipramine | 25 |
| Diphenhydramine | 500 |
| Doxepin | 10 |
| 2-Ethylidene-1,5-dimethyl-3, 3-diphenylpyrrolidine (EDDP) | 1000 |
| Fluoxetine | 500 |
| Glutethimide | 500 |
| Ibuprofen | 1000 |
| Ketamine | 100 |
| Ketorolac Tromethamine | 1000 |
| Lormetazepam | 1 |
| LSD | 10 ng/mL |
| D-Methamphetamine | 35 |
| Methaqualone | 1500 |
| Nalbuphine | 1000 |
| Naproxen | 1000 |
| Nortriptyline | 250 |
| Oxazepam | 300 |
| Phencyclidine | 1000 |
| Phenytoin | 1000 |
| Promethazine | 2 |
| Propoxyphene | 1000 |
| Ranitidine | 900 |
| Scopolamine | 500 |
| Secobarbital | 1000 |
| Tapentadol | 45 |
| 11-nor-$\Delta^9$-THC-9-COOH | 100 |
| Thioridazine | 100 |
| Tramadol | 1000 |
| Tyramine | 100 |
| Zidovudine (AZT) | 2 mg/mL |
| Zolpidem | 100 |

**Sensitivity**

The sensitivity level of the Emit® II Plus Opiate Assay using the 300 ng/mL cutoff is less than 16 ng/mL. This level represents the lowest concentration of opiate that can be distinguished from 0 ng/mL with a confidence level of 95%.

**2000 ng/mL CUTOFF**

**Accuracy**

*Qualitative Results*

Both the Emit® II Plus Opiate Assay and the Emit® II Opiates 300/2000 Assay (comparative method) use an optional cutoff level of 2000 ng/mL for distinguishing between positive results and negative results.

One hundred twenty (120) specimens were analyzed by the Emit® II Plus Opiate Assay and by the comparative method.

Fifty-four (54) specimens showed positive results by both methods, and 65 specimens showed negative results by both methods. All specimens that showed positive results by both methods were confirmed by GC/MS to contain opiates. The GC/MS method used has a limit of detection (LOD) for morphine of 50 ng/mL.

All specimens that showed positive results by both methods were confirmed by GC/MS to contain between 575 and greater than 4000 ng/mL opiates. These specimens were tested by GC/MS for the following opiates: morphine and codeine. Four (4) samples were confirmed positive by GC/MS for 6-acetylmorphine above the 10 ng/mL confirmation level.

One (1) specimen showed a borderline negative result by the Emit® II Plus Opiate Assay and a borderline positive result by the comparative method. This specimen was confirmed by GC/MS to contain morphine at a concentration of 1826 ng/mL.

No drug was detected by GC/MS in 20 negative specimens that were randomly selected from the 65 negative specimens.

Data are summarized in Table 8.

**Table 8 — Accuracy of Qualitative Results for the 2000 ng/mL Cutoff**

| | | Emit® II Plus Opiate Assay | |
|---|---|---|---|
| | | Comparative Method | |
| | | + | – |
| Emit® II Plus Opiate Assay | + | 54 | 0 |
| | – | 1* | 65 |

***Shown to contain morphine at a concentration of 1826 ng/mL.***

### Analytical Recovery

*Qualitative Results*

In qualitative spike analysis, the Emit® II Plus Opiate Assay correctly identified the mean rate of spiked specimens containing less than 2000 ng/mL morphine as negative and the mean rate of spiked specimens containing greater than 2000 ng/mL morphine as positive.

*Semiquantitative Results*

Negative human urine specimens were spiked with concentrations of morphine at levels throughout the semiquantitative range of 500 to 3800 ng/mL. For each known concentration, drug recovery was calculated using the average concentration obtained by the Emit® II Plus Opiate Assay. Semiquantitative results are shown in Table 9.

**Table 9 — Accuracy by Analytical Recovery of Semiquantitative Results for the 2000 ng/mL Cutoff**

| Nominal Morphine Concentration (ng/mL) | Average Morphine Concentration by Emit® II Plus Opiate Assay (ng/mL) | Recovery (%) |
|---|---|---|
| 500 | 582 | 116 |
| 600 | 661 | 110 |
| 700 | 778 | 111 |
| 800 | 820 | 103 |
| 1000 | 1012 | 101 |
| 1500 | 1554 | 104 |
| 1800 | 1866 | 104 |
| 2200 | 2216 | 101 |
| 2500 | 2529 | 101 |
| 3000 | 2993 | 100 |
| 3600 | 3560 | 99 |
| 3800 | 3750 | 99 |

### Precision

Qualitative analysis of precision was determined by assaying calibrators and controls on 20 days, 2 runs per day in replicates of 3 (N = 120). Semiquantitative precision was determined by assaying calibrators and controls on 20 days, 2 runs per day in replicates of 3 (N = 120). Precision data were calculated according to the National Committee of Clinical Laboratory Standards (NCCLS) Guideline EP5-A (February 1999). Results are summarized in Tables 10 and 11.

**Table 10 — Qualitative Analysis of Precision for the 2000 ng/mL Cutoff**

| Calibrator or Control | Mean (mAU/min) | SD | CV (%) |
|---|---|---|---|
| **Within-Run Precision** | | | |
| 0 ng/mL Calibrator | 205.6 | 1.0 | 0.5 |
| Control Level 1 (1500 ng/mL) | 297.8 | 1.6 | 0.5 |
| 2000 ng/mL Calibrator | 323.4 | 1.9 | 0.6 |
| Control Level 2 (2500 ng/mL) | 340.9 | 1.5 | 0.4 |
| **Total Precision** | | | |
| 0 ng/mL Calibrator | 205.6 | 1.3 | 0.6 |
| Control Level 1 (1500 ng/mL) | 297.8 | 2.4 | 0.8 |
| 2000 ng/mL Calibrator | 323.4 | 3.0 | 0.9 |
| Control Level 2 (2500 ng/mL) | 340.9 | 2.9 | 0.9 |

**Table 11 — Semiquantitative Analysis of Precision for the 2000 ng/mL Cutoff**

| Calibrator or Control | Mean (ng/mL) | SD | CV (%) |
|---|---|---|---|
| **Within-Run Precision** | | | |
| Control Level 1 (1500 ng/mL) | 1529.4 | 25.0 | 1.6 |
| 2000 ng/mL Calibrator | 2005.2 | 40.0 | 2.0 |
| Control Level 2 (2500 ng/mL) | 2463.5 | 47.0 | 1.9 |
| **Total Precision** | | | |
| Control Level 1 (1500 ng/mL) | 1529.4 | 44.5 | 2.9 |
| 2000 ng/mL Calibrator | 2005.2 | 84.3 | 4.2 |
| Control Level 2 (2500 ng/mL) | 2463.5 | 92.1 | 3.7 |

### Specificity

The Emit® II Plus Opiate Assay detects morphine and morphine-3-glucuronide (the major metabolites of heroin) and codeine in human urine.

Table 12 gives the compounds this assay detects and the levels at which the compounds have been found to give a response approximately equivalent to that of the cutoff calibrator (Emit® Calibrator/Control Level 3). Each concentration represents the reactivity level for the stated compound when it is added to a negative urine specimen. If a specimen contains more than one compound detected by the assay, lower concentrations than those listed in Table 12 may combine to produce a rate approximately equivalent to or greater than that of the cutoff calibrator.

**Table 12 — Concentrations (ng/mL) of Opiate Compounds That Produce a Result Approximately Equivalent to the 2000 ng/mL Cutoff**

| Compound | Concentration (ng/mL) at 2000 ng/mL Cutoff |
|---|---|
| Codeine | 660–1980 |
| Dihydrocodeine | 1872 |
| Ethylmorphine | 1570 |
| Hydrocodone | 1545 |
| Hydromorphone | 5349 |
| Levallorphan | 101000* |
| Levorphanol | 7680 |
| Meperidine | >400000† |
| 6-Acetylmorphine | 2100 |
| Morphine-3-Glucuronide | 6167 |
| Nalorphine | 67200* |
| Naloxone | >3500000 |
| Oxycodone | 48000 |
| Oxymorphone | >100000 |

***Therapeutic or toxic urinary levels of levallorphan and nalorphine are not reported in the literature.***

***†Meperidine urinary concentrations of 150000 ng/mL have been measured in cases of fatal meperidine overdosage.[8]***

Compounds that produce a negative result by the Emit® II Plus Opiate Assay are listed in Table 13, Concentrations of Compounds Showing a Negative Response to the 2000 ng/mL (2 µg/mL) Cutoff. These compounds were tested at the 2000 ng/mL cutoff level.

**Table 13 — Concentrations of Compounds Showing a Negative Response to the 2000 ng/mL (2 µg/mL) Cutoff**

| Compound | Concentration Tested (µg/mL) |
|---|---|
| Acetaminophen | 1000 |
| L-α-Acetylmethadol (LAAM) | 25 |
| *N*-Acetylprocainamide (NAPA) | 400 |
| Acetylsalicylic Acid | 1000 |
| Amitriptyline | 7 |
| D-Amphetamine | 1000 |
| Benzoylecgonine | 1000 |
| Buprenorphine | 1000 |
| Caffeine | 1000 |
| Cimetidine | 1000 |
| Clomipramine | 2.5 |
| Clonidine | 1000 |
| Cotinine | 100 |
| Cyclobenzaprine | 63 |
| Desipramine | 25 |
| Diphenhydramine | 500 |
| Doxepin | 10 |
| 2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP) | 1000 |
| Fluoxetine | 500 |
| Glutethimide | 500 |
| Ibuprofen | 1000 |
| Ketamine | 100 |
| Ketorolac Tromethamine | 1000 |
| Lormetazepam | 1 |
| LSD | 10 ng/mL |
| D-Methamphetamine | 35 |
| Methaqualone | 1500 |
| Nalbuphine | 1000 |
| Naproxen | 1000 |
| Nortriptyline | 250 |
| Oxazepam | 300 |
| Phencyclidine | 1000 |
| Phenytoin | 1000 |
| Promethazine | 2 |
| Propoxyphene | 1000 |
| Ranitidine | 900 |
| Scopolamine | 500 |
| Secobarbital | 1000 |

| Compound | Concentration Tested (µg/mL) |
|---|---|
| Tapentadol | 45 |
| 11-nor-$\Delta^9$-THC-9-COOH | 100 |
| Thioridazine | 100 |
| Tramadol | 1000 |
| Tyramine | 100 |
| Zidovudine (AZT) | 2 mg/mL |
| Zolpidem | 100 |

**Sensitivity**

The sensitivity level of the Emit® II Plus Opiate Assay using the 2000 ng/mL cutoff is less than 140 ng/mL. This level represents the lowest concentration of morphine that can be distinguished from 0 ng/mL with a confidence level of 95%.

**Non-Interfering Substances**

The following compounds, when added to urine at ±25% concentration of the cutoff, do not yield a false response relative to the 300 and 2000 ng/mL cutoff levels:

**Table 14 — Non-Interfering Substances**

| Compound | Concentration |
|---|---|
| Acetone | 1.0 g/dL |
| Ascorbic Acid | 1.5 g/dL |
| Bilirubin | 0.25 mg/dL |
| Creatinine | 0.5 g/dL |
| Ethanol | 1.0 g/dL |
| Gamma Globulin | 0.5 g/dL |
| Glucose | 2.0 g/dL |
| Hemoglobin | 115 mg/dL |
| Human Serum Albumin | 0.5 g/dL |
| Oxalic Acid | 0.1 g/dL |
| Riboflavin | 7.5 mg/dL |
| Sodium Chloride | 6.0 g/dL |
| Urea | 6.0 g/dL |

## 11 Risk and Safety

H317
P280, P272, P302 + P352, P333 + P313, P501
**Warning!**
May cause an allergic skin reaction.

Wear protective gloves/protective clothing/eye protection/face protection. Contaminated work clothing should not be allowed out of the workplace. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Dispose of contents and container in accordance with all local, regional, and national regulations.

**Contains:** 5-chloro-2-methyl-3(2h)-isothiazolone mixture with 2-methyl-3(2h)-isothiazolone.

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare

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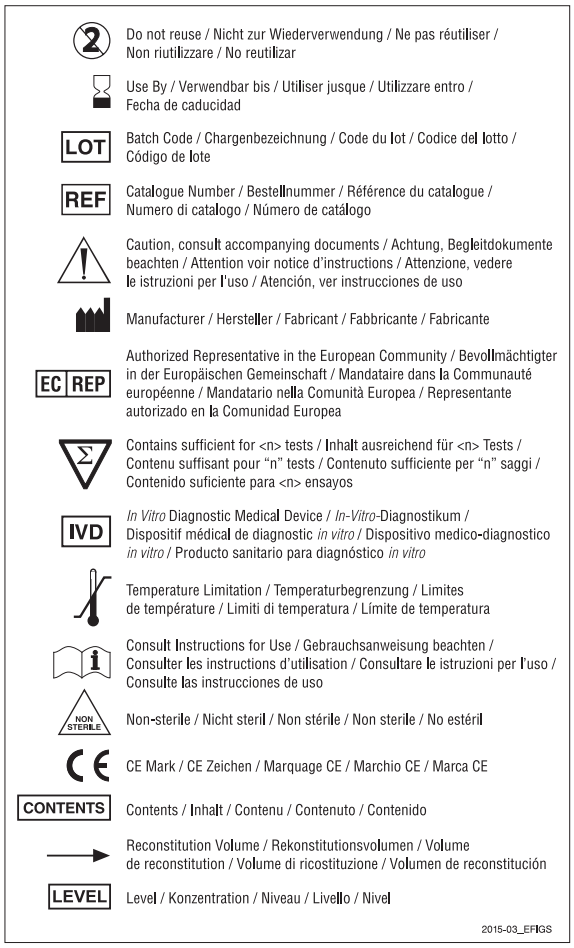
## 13 Symbols Key

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