SIEMENS

Syva®

Emit® II Plus Buprenorphine Assay

10872256_B

Buprenorphine Assay

1 Intended Use

The Emit® II Plus Buprenorphine Assay is a homogeneous enzyme immunoassay with a 5 ng/mL cutoff. The assay is intended for use in laboratories for the qualitative and/or semiquantitative analyses of buprenorphine in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.

The semiquantitative mode is for the purpose of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as Liquid Chromatography/ Mass Spectrometry (LC/MS) or permitting laboratories to establish quality control procedures.

The Emit® II Plus Buprenorphine Assay provides only a preliminary analytical test result. A more specific alternative chemical method(s) must be used to obtain a confirmed analytical result. Gas Chromatography/Mass Spectrometry (GC/MS) or LC/MS are the preferred confirmatory methods.[1,2] 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

Buprenorphine is a semi-synthetic opioid analgesic derived from thebaine, a component of the opium poppy Papaver somniferum. Buprenorphine structurally resembles morphine, but has both antagonist and agonist properties.[3] Buprenorphine is a schedule III drug. The Food and Drug Administration (FDA) has approved the use of Suboxone®, which contains buprenorphine for treatment of opiate dependency in the US. Under the US Drug Abuse Treatment Act of 2000 (DATA) buprenorphine can be prescribed in a physician's office for treatment of opiate dependency.

It has been shown that buprenorphine has abuse potential and may itself cause dependency. It produces typical opioid effects and side effects such as euphoria and respiratory depression.

Buprenorphine is metabolized in the human liver primarily by N-dealkylation to pharmacologically active norbuprenorphine, which along with the parent compound is conjugated to form buprenorphine glucuronide and norbuprenorphine glucuronide.[4]

The Emit® II Plus Buprenorphine Assay detects buprenorphine and norbuprenorphine in human urine and gives a positive result if these drugs are present at concentrations equal to or greater than the cutoff. Positive results for specimens containing structurally related opioid compounds have not been observed.

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

3 Principle

The Emit® II Plus Buprenorphine Assay is a homogeneous enzyme immunoassay technique used for the analysis of specific compounds in human urine. The assay is based on competition between drug in the specimen and drug labeled with the recombinant glucose-6-phosphate dehydrogenase (rG6PDH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the specimen can be measured in terms of enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH in the presence of glucose-6-phosphate (G6P), 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
9S039UL 9S029UL 9S129UL	**Emit® II Plus Buprenorphine Assay**	
	Antibody/Substrate Reagent 1	
	Mouse monoclonal antibodies to buprenorphine (0.53 µg/mL)*, NAD (6.9 mM), G6P (10.9 mM), bovine serum albumin, preservatives, and stabilizers	28 mL 115 mL 1000 mL
	Enzyme Reagent 2	
	Norbuprenorphine labeled with bacterial rG6PDH (0.50 µg/mL)*, HEPES buffer, bovine serum albumin, preservatives, and stabilizers	14 mL 50 mL 500 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.

Risk and Safety

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

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For *in vitro* diagnostic use.

Preparation of Assay Components

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

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

Storage

When not in use, reagents must be stored 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 application sheet for instrument stability information. Do not freeze reagents. Avoid prolonged exposure to temperatures above 32°C. **Improper storage of reagents can affect assay performance.**

The purpose of specimen handling and storage information is to provide guidance to users; however, users may validate their own procedures for handling and storing patient samples.

5 Specimen Collection and Preparation

- Urine specimens may be collected in plastic (i.e., polypropylene, polycarbonate, polyethylene) or glass containers. Some plastics can adsorb certain drugs.
- If not analyzed immediately, specimens may be stored refrigerated or unrefrigerated for up to 5 days. After 5 days specimens should be stored frozen at -20°C.[5,6]
- Frozen specimens must be thawed and mixed thoroughly prior to analysis.
- Specimens with high turbidity should be centrifuged before analysis.
- Urine specimens should be within the pH range of 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.
- Repeat freeze/thaw cycles should be avoided.

6 Procedure

Materials Provided

Emit® II Plus Buprenorphine Assay
- Reagent 1
- Reagent 2

Materials Required But Not Provided

Emit® Calibrator/Control
- 9A509UL Level 0 (0 ng/mL)

Emit® II Plus Specialty Drug Calibrators/Controls
- 9S529UL Level 1 (2.5 ng/mL)
- 9S549UL Level 2 (5 ng/mL)
- 9S569UL Level 3 (15 ng/mL)
- 9S589UL Level 4 (25 ng/mL)

Emit® II Plus Specialty Drug Controls
- 9S609UL Negative (3 ng/mL)
- 9S619UL Positive (7 ng/mL)

Instruments

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

Analyzers must be capable of maintaining a constant reaction temperature, pipette specimens/reagents, mix thoroughly, measure enzyme rates precisely and time the reaction accurately.

Daily Maintenance

Refer to the instrument Operator's Guide for maintenance instructions.

Assay Sequence

To run the assay, see the instrument Operator's Guide and the application sheets available from Siemens.

Calibration

Calibrate the assay using the calibrators listed in Table 1.

Note: These reagents are qualified for use with these calibrators only.

Table 1 — Emit® II Plus Specialty Drug Calibrators/Controls for use in Qualitative or Semiquantitative Analysis

Cutoff Level (ng/mL)	Required Calibrator/Control for Qualitative Analysis (ng/mL)	Required Calibrators/Controls for Semiquantitative Analysis (ng/mL)
5	Emit® II Plus Specialty Drug Calibrator/Control Level 2 (5)	Emit® Calibrator/Control Level 0 (0) Emit® II Plus Specialty Drug Calibrators/Controls Level 1 (2.5) Level 2 (5) Level 3 (15) Level 4 (25)

Qualitative Analysis

Calibrate by running the Emit® II Plus Specialty Drug Calibrator/Control Level 2 in duplicate. Validate the calibration by running controls (see Quality Control). Refer to the Emit® II Plus Specialty Drug Calibrators/Controls Instructions for Use and the specific application sheet for additional information. Recalibrate as indicated by control results.

Semiquantitative Analysis

Prepare a calibration curve by running the appropriate Emit® II Plus Specialty Drug Calibrators/Controls listed in Table 1 in duplicate. Validate the calibration by running controls (see Quality Control). Refer to the Emit® II Plus Specialty Drug Calibrators/Controls Instructions for Use and specific application sheet for additional information. Recalibrate as indicated by control results.

Quality Control

Validate the calibration by assaying the controls listed in table 2. Other material may be used for quality control purposes.

Table 2 — Controls for use in Qualitative or Semiquantitative Analysis

Cutoff Level	Recommended Controls for Qualitative Analysis	Controls to be used for Semiquantitative Analysis
5 ng/mL	Emit® Calibrator/Control Level 0 (Negative) Emit® II Plus Specialty Drug Calibrator/Control Level 4 (Positive) or Emit® II Plus Specialty Drug Controls may be used	Emit® II Plus Specialty Drug Control Negative Control Positive

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 buprenorphine concentrations. Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.

Refer to the instrument Operator's Guide for appropriate instrument checks.

Qualitative Analysis

Validate the calibration by assaying controls. Ensure that the control results relates appropriately to the cutoff calibrator result. That is,

- If the Emit® Calibrator/Control Level 0 (0 ng/mL) or the Emit® II Plus Specialty Drug Control Negative was run; ensure that the result is negative relative to the cutoff calibrator level.
- If the Emit® II Plus Specialty Drug Calibrator/Control Level 4 (25 ng/mL) or Emit® II Plus Specialty Drug Control Positive was run; ensure that the result is positive relative to the cutoff calibrator level.

Once the calibration is validated, run urine specimens.

Semiquantitative Analysis

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.

7 Results

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.

Qualitative Analysis

The Emit® II Plus Specialty Drug Calibrator/Control level 2 (cutoff), which contains a concentration of 5 ng/mL buprenorphine, is used as a reference for distinguishing "positive" from "negative" specimens.

Positive Results A specimen that gives a change in rate value greater than or equal to the Emit® II Plus Specialty Drug Calibrator/Control cutoff rate value is interpreted as positive. The specimen is presumptive positive buprenorphine.

Negative Results A specimen that gives a change in rate value less than the Emit® II Plus Specialty Drug Calibrator/Control cutoff rate value is interpreted as negative; either the specimen does not contain buprenorphine or buprenorphine is 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 or LC/MS. Semiquantitation also permits the laboratory to establish quality control procedures and assess control performance. Refer to the Recovery section for the semiquantitative range.

Using the Emit® II Plus Buprenorphine Assay, it is possible to make semiquantitative determinations of buprenorphine. An estimate of relative total drug concentrations may be obtained by running the Emit® Calibrator/Control Level 0 (0 ng/mL) and the appropriate Emit® II Plus Specialty Drug Calibrators/Controls Levels 1 (2.5 ng/mL), 2 (5 ng/mL), 3 (15 ng/mL), 4 (25 ng/mL).

8 Limitations

- The assay is designed for use with human urine only.
- A positive result from the assay indicates the presence of buprenorphine but does not indicate or measure intoxication.
- Boric acid is not recommended as a preservative for urine.
- There is a possibility that substances and/or factors not listed (e.g., 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 Buprenorphine 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 buprenorphine.

When used semiquantitatively, the assay yields approximate, cumulative concentrations of buprenorphine and the metabolites detected by the assay (see Specificity in Section 10).

10 Specific Performance Characteristics

The data that appear in this section were collected from the Viva-E® using the Emit® II Plus Buprenorphine Assay.

Method Comparison

Qualitative and Semiquantitative Results

A total of one-hundred twenty seven (127) unaltered buprenorphine samples were analyzed using the Emit® II Plus Buprenorphine Assay and the reference method Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS). Both methods used a 5 ng/mL cutoff. Thirty-three (33) samples were within +/- 50% of the cutoff by LC/MS/MS.

Sixty-five (65) samples showed positive results by both methods, while fifty-four (54) samples showed negative results by both methods. Seven specimens showed negative results by LC/MS/MS but positive by Emit® II Plus Buprenorphine Assay and one positive results by LC/MS/MS was negative by Emit® II Plus Buprenorphine Assay method. All the discordant samples were within +/- 25% of the cutoff by both the Emit® II Plus Buprenorphine Assay and LC/MS/MS. Data are summarized in Tables 3 and 4.

Table 3 — Qualitative and Semiquantitative Accuracy Summary

		LC/MS/MS				
		LOW NEG <50% below the cutoff (<2.5 ng/mL)	NEG Within 50% below the cutoff (2.5 – 4.9 ng/mL)	POS Within 50% above the cutoff (5.0 – 7.5 ng/mL)	HIGH POS >50% above the cutoff (>7.5 ng/mL)	% Agreement
Qualitative Summary						
Emit®	POS	0	7	16	49	90%
	NEG	45	9	1	0	98%
Semiquantitative Summary						
Emit®	POS	0	7	16	49	90%
	NEG	45	9	1	0	98%

Table 4 — Discordant Result Summary

Sample #	Emit® II Plus Buprenorphine (ng/mL)	LC/MS/MS			Emit® vs LC/MS/MS (Pos/Neg)
		Buprenorphine (ng/mL)	Norbuprenorphine (ng/mL)	Buprenorphine + Norbuprenorphine (ng/mL)	
77	5.5	0	4.60	4.60	+/-
190	5.6	0	3.92	3.92	+/-
193	6.1	0	4.97	4.97	+/-
195	5.4	0	4.06	4.06	+/-
226	5.8	0	4.21	4.21	+/-
250	5.1	0	4.13	4.13	+/-
316	5.7	0	3.86	3.86	+/-
338	4.3	5.12	0	5.12	-/+

Precision

Repeatability and within lab precision was determined by assaying urine pools spiked with buprenorphine at nine different levels. The testing sequence for each level consisted of two replicates, twice a day, for twenty days (n = 80). Precision data were calculated according to the Clinical and Laboratory Standards Institute (CLSI) Guideline EP5-A2.[7] Results are summarized in Tables 5 and 6.

Table 5 — Precision: Qualitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Results	Repeatability Results	Within-Laboratory Results
0	-100%	80	80 Negative	80 Negative
2.50	-50%	80	80 Negative	80 Negative
3	-40%	80	80 Negative	80 Negative
3.75	-25%	80	80 Negative	80 Negative
5	cutoff	80	25 Negative/ 55 Positive	25 Negative/ 55 Positive
6.25	+25%	80	80 Positive	80 Positive
7	+40%	80	80 Positive	80 Positive
7.50	+50%	80	80 Positive	80 Positive
10	100%	80	80 Positive	80 Positive

Table 6 — Precision: Semiquantitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Results	Repeatability Results	Within-Laboratory Results
0	-100%	80	80 Negative	80 Negative
2.50	-50%	80	80 Negative	80 Negative
3	-40%	80	80 Negative	80 Negative
3.75	-25%	80	80 Negative	80 Negative
5	cutoff	80	25 Negative/ 55 Positive	25 Negative/ 55 Positive
6.25	+25%	80	80 Positive	80 Positive
7	+40%	80	80 Positive	80 Positive
7.50	+50%	80	80 Positive	80 Positive
10	100%	80	80 Positive	80 Positive

An additional precision study was performed using urine pools prepared by spiking Buprenorphine into drug-free human urine at one concentration level relative to the 5 ng/mL cutoff: -75% below the cutoff and +75% above the cutoff. The studies were performed on the Viva-E® analyzer. The samples were analyzed in duplicate, 40 times for a total of 80 replicates over one day.

Table 7 — Precision: Qualitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Results	Repeatability Results	Within-Laboratory Results
1.25	-75%	80	80 Negative	80 Negative
8.75	+75%	80	80 Positive	80 Positive

Table 8 — Precision: Semi-Quantitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Results	Repeatability Results	Within-Laboratory Results
1.25	-75%	80	80 Negative	80 Negative
8.75	+75%	80	80 Positive	80 Positive

Recovery

Recovery of buprenorphine samples were prepared by spiking known levels of buprenorphine into negative urine pools. Each spiked sample was analyzed in replicates of five using the Emit® II Plus Buprenorphine Assay. Results are shown in Table 9.

Table 9 — Results of Recovery

Expected Concentration (ng/mL)	Mean Buprenorphine Concentration by Emit® II Plus Buprenorphine Assay (ng/mL)	% Recovery
2	2.1	105.0
3	3.1	103.3
4	3.9	97.5
5	5.0	100.0
8	7.7	96.3
12	11.1	92.5
18	17.7	98.3
22	21.0	95.5
25	23.9	95.6

Specificity

Buprenorphine Metabolites

The buprenorphine metabolites norbuprenorphine, buprenorphine glucuronide and norbuprenorphine glucuronide were spiked into a negative urine pool at the levels shown in Table 10 and run at n=5 replicates. The samples were assayed and the mean recovery results were determined.

Table 10 — Buprenorphine Metabolite Recovery

Compound	Concentration Tested (ng/mL)	Mean Recovery (ng/mL)	% Cross-reactivity
Norbuprenorphine	5	4.6	92.6
Buprenorphine Glucuronide	1000	0.9	0.1
Norbuprenorphine Glucuronide	1000	1.2	0.1

Structurally Related Compounds

The cross-reactivity of the Emit® II Plus Buprenorphine assay was evaluated against structurally related drugs. The structurally related drugs listed below were spiked into negative urine pools and % cross-reactivity was calculated. The compounds at stated concentrations produced a negative response relative to a 5 ng/mL cutoff.

Table 11 — Structurally Related Compounds

Compound	Concentration Tested (ng/mL)	% Cross-Reactivity
6-Acetylcodeine	100,000	<0.01
6-Acetylmorphine	100,000	<0.01
Codeine	100,000	<0.01
Dextromethorphan	100,000	<0.01
Dihydrocodeine	100,000	<0.01
Ethyl Morphine	100,000	<0.01
Heroin	100,000	<0.01
Hydrocodone	100,000	<0.01
Hydromorphone	100,000	<0.01
Levorphanol	100,000	<0.01
Morphine	100,000	<0.01
Morphine 3-glucuronide	100,000	<0.01
Morphine 6-glucuronide	100,000	<0.01
Nalorphine	100,000	<0.01
Naloxone	100,000	<0.01
Naltrexone	100,000	<0.01
Norcodeine	100,000	<0.01
Normorphine	100,000	<0.01
Noroxycodone	100,000	<0.01
Noroxymorphone	100,000	<0.01
Oxycodone	100,000	<0.01
Oxymorphone	100,000	<0.01

Structurally Unrelated Compounds

The interference of structurally unrelated compounds and common over the counter drugs was evaluated qualitatively and semiquantitatively at the concentration listed below. The compounds were spiked into two levels of controls at +/- 40% (3 ng/mL and 7 ng/mL) of the cutoff concentration. The protocol used follows the CLSI Guideline, EP7-A2.[8]

At the stated concentration, the sample did not give a false response relative to the 5 ng/mL cutoff.

Table 12 — Structurally Unrelated Compounds

Compound	Concentration Tested (µg/mL)	-40% of Cutoff (3 ng/mL)	+40% of Cutoff (7 ng/mL)
10, 11-Dihydrocarbamazepine	85	Negative	Positive
Acetaminophen	1000	Negative	Positive
Acetylsalicylic Acid	1500	Negative	Positive
Amitriptyline	100	Negative	Positive
Amoxicillin	500	Negative	Positive
AZT (Zidovudine)	2000	Negative	Positive
Benzoylecgonine	1000	Negative	Positive
Brompheniramine	75	Negative	Positive
Caffeine	1000	Negative	Positive
Captopril	500	Negative	Positive
Chlordiazepoxide	100	Negative	Positive
Chlorpromazine	10	Negative	Positive
Cimetidine	1000	Negative	Positive
Clomipramine	2.5	Negative	Positive
Clonidine	1000	Negative	Positive
Cyclobenzaprine	125	Negative	Positive
d-Amphetamine	700	Negative	Positive
Desipramine	800	Negative	Positive
Diazepam	100	Negative	Positive
Digoxin	0.01	Negative	Positive
Diphenhydramine	1000	Negative	Positive
d-Methamphetamine	500	Negative	Positive
Doxepine	100	Negative	Positive
EDDP	1000	Negative	Positive
EMDP	100	Negative	Positive
Enalapril	500	Negative	Positive
Fluoxetine	500	Negative	Positive
Glutethimide	500	Negative	Positive
Haloperidol	100	Negative	Positive
Hydroxyzine	500	Negative	Positive
Ibuprophen	1000	Negative	Positive
Imipramine	200	Negative	Positive
Ketamine	100	Negative	Positive
Ketorolac Tromethamine	400	Negative	Positive
LAAM (L-a-Acetlymethadol)	25	Negative	Positive
L-Cotinine	100	Negative	Positive
Levofloxacin	100	Negative	Positive
Levothyroxine (L-Thyroxine)	50	Negative	Positive
Lidocaine	1000	Negative	Positive
Lormetazepam	1.0	Negative	Positive
LSD	10	Negative	Positive
MDMA (Ecstasy)	1000	Negative	Positive
Meperidine	800	Negative	Positive
Methadone	500	Negative	Positive
Methaqualone	600	Negative	Positive
NAPA	400	Negative	Positive
Naproxen	1000	Negative	Positive
Nicotinic Acid	500	Negative	Positive
Nifedipine	500	Negative	Positive
Nordiazepam	100	Negative	Positive
Nortryptiline	250	Negative	Positive
Oxazepam	300	Negative	Positive
Perphenazine	150	Negative	Positive
Phencyclidine	900	Negative	Positive
Phenobarbital	500	Negative	Positive
Phenelzine	100	Negative	Positive
Phenytoin	1000	Negative	Positive
Procainamide	1000	Negative	Positive
Procyclidine	800	Negative	Positive
Promethazine	100	Negative	Positive
Propoxyphene	1000	Negative	Positive
Protriptyline	200	Negative	Positive
Pseudoephedrine	1000	Negative	Positive
Quinacrine	900	Negative	Positive
Ranitidine	1000	Negative	Positive
Ritalin	1000	Negative	Positive
Salicylic Acid	500	Negative	Positive
Scopolamine	500	Negative	Positive
Secobarbital	1000	Negative	Positive
Tapentadol	100	Negative	Positive
THC	100	Negative	Positive
Thioridazine	100	Negative	Positive
Tramadol	1000	Negative	Positive
Trazodone	5	Negative	Positive
Trimethoprim	1000	Negative	Positive
Triprolidine (zymine)	50	Negative	Positive
Tyramine	100	Negative	Positive
Verapamil	500	Negative	Positive
Zolpidem	100	Negative	Positive

Endogenous Substances

The endogenous substances were evaluated qualitatively and semiquantitatively at the concentrations listed below. The compounds were spiked into two levels of controls at +/- 40% (3 ng/mL and 7 ng/mL) of the cutoff concentration. The protocol used follows the CLSI Guideline, EP7-A2.[8]

At the stated concentration, the sample did not give a false response relative to the 5 ng/mL cutoff.

Table 13 — Endogenous Substances: Semiquantitative Results

Substance	Concentration Tested	–40% of Cutoff (3 ng/mL)	+40% of Cutoff (7 ng/mL)
Acetone	1.0 g/dL	Negative	Positive
Ascorbic Acid	1.5 g/dL	Negative	Positive
Conjugated Bilirubin	2.0 mg/dL	Negative	Positive
Unconjugated Bilirubin	2.0 mg/dL	Negative	Positive
Creatinine	0.5 g/dL	Negative	Positive
Ethanol	1.0 g/dL	Negative	Positive
IgG	0.5 g/dL	Negative	Positive
Glucose	2.0 g/dL	Negative	Positive
Hemoglobin	115 mg/dL	Negative	Positive
Human Serum Albumin	0.5 g/dL	Negative	Positive
Oxalic Acid	0.1 g/dL	Negative	Positive
Riboflavin	7.5 mg/dL	Negative	Positive
Sodium Chloride	6.0 g/dL	Negative	Positive
Urea	6.0 g/dL	Negative	Positive
Sodium Azide	1%	Negative	Positive
Sodium fluoride	1%	Negative	Positive
Galactose	1.0 g/dL	Negative	Positive

Specific Gravity and pH

Negative urine pools with specific gravity values ranging from 1.002–1.035 and pH values ranging from 3.0–11.0 were tested in the presence of two levels of controls at +/- 40% (3 ng/mL and 7 ng/mL) of the cutoff concentration and no interference was observed.

12 Bibliography

1. Kronstrand R, Selden TG, and Josefsson M. Analysis of Buprenorphine, Norbuprenorphine and Their Glucuronides in Urine by Liquid Chromatography-Mass Spectrometry, *JAT*. 2003:27:464-470.
2. Fuller DC. A Simple Gas Chromatography-Mass Spectrometry Procedure for the Simultaneous Determination of Buprenorphine and Norbuprenorphine in Human Urine, *JAT*. 2008:32:626-630.
3. Baselt RC. *Disposition of Toxic Drugs and Chemicals in Man*, Biomedical Publications, 8th Ed. 2008:730-35.
4. Cone EJ. et al, The Metabolism and Excretion of Buprenorphine in Humans, Drug Metabolism and Disposition. 1984:12:577:581.
5. ARUP Consult Physicians Guide http://ltd.aruplab.com/Tests/Pub/2010092
6. Huang W, Moody DE, McCance-Katz EF. The In Vivo Glucuronidation of Buprenorphine and Norbuprenorphine Determined by Liquid Chromatography-Electrospray Ionization-Tandem Mass Spectrometry, *Therapeutic Drug Monitoring*. 2006:28(2):245-251.
7. Clinical and Laboratory Standards Institute/NCCLS. Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition. CLSI/NCCLS document EP5-A2 [ISBN 1-56238-542-9]. CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2004.
8. Clinical and Laboratory Standards Institute/NCCLS. Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition. CLSI document EP7-A2 [ISBN 1-56238-584-4]. CLSI, Wayne, PA USA, 2005.

13 Symbols Key

	Do not reuse / Nicht zur Wiederverwendung / Ne pas réutiliser / Non riutilizzare / No reutilizar
	Use By / Verwendbar bis / Utiliser jusque / Utilizzare entro / Fecha de caducidad
LOT	Batch Code / Chargenbezeichnung / Code du lot / Codice del lotto / Código de lote
REF	Catalogue Number / Bestellnummer / Référence du catalogue / Numero di catalogo / Número de catálogo
	Caution, consult accompanying documents / Achtung, Begleitdokumente beachten / Attention voir notice d'instructions / Attenzione, vedere le istruzioni per l'uso / Atención, ver instrucciones de uso
	Manufacturer / Hersteller / Fabricant / Fabbricante / Fabricante
EC REP	Authorized Representative in the European Community / Bevollmächtigter in der Europäischen Gemeinschaft / Mandataire dans la Communauté européenne / Mandatario nella Comunità Europea / Representante autorizado en la Comunidad Europea
Σ	Contains sufficient for <n> tests / Inhalt ausreichend für <n> Tests / Contenu suffisant pour "n" tests / Contenuto sufficiente per "n" saggi / Contenido suficiente para <n> ensayos
IVD	*In Vitro* Diagnostic Medical Device / *In-Vitro*-Diagnostikum / Dispositif médical de diagnostic *in vitro* / Dispositivo medico-diagnostico *in vitro* / Producto sanitario para diagnóstico *in vitro*
	Temperature Limitation / Temperaturbegrenzung / Limites de température / Limiti di temperatura / Límite de temperatura
	Consult Instructions for Use / Gebrauchsanweisung beachten / Consulter les instructions d'utilisation / Consultare le istruzioni per l'uso / Consulte las instrucciones de uso
NON STERILE	Non-sterile / Nicht steril / Non stérile / Non sterile / No estéril
CE	CE Mark / CE Zeichen / Marquage CE / Marchio CE / Marca CE
CONTENTS	Contents / Inhalt / Contenu / Contenuto / Contenido
	Reconstitution Volume / Rekonstitutionsvolumen / Volume de reconstitution / Volume di ricostituzione / Volumen de reconstitución
LEVEL	Level / Konzentration / Niveau / Livello / Nivel
RxOnly	Prescription Device (US Only) / Verschreibungspflichtiges Medizinprodukt (nur USA) / Dispositif soumis à prescription (États-Unis uniquement) / Dispositivo su prescrizione (solo USA) / Dispositivo de prescripción médica (solo EE. UU.)

2015-10_EFIGS

For technical assistance, call Siemens Healthcare Diagnostics:
1-800-227-8994 in the USA
1-800-264-0083 in Canada
Outside the USA and Canada, call your local Siemens representative.

Notice: Adulteration of reagents, use of instruments without appropriate capabilities, or other failure to follow instructions as set forth in this labeling can affect performance characteristics and stated or implied label claims.

U.S. Patent Numbers 7,220,842 B2 and 7,863,427 B2

Syva®, Syva® and Emit® are trademarks of Siemens Healthcare Diagnostics.

Siemens Healthcare Diagnostics Inc.
500 GBC Drive
Newark, DE 19714 USA

Global Siemens Headquarters
Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

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

Global Division
Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens.com/healthcare

CE

Printed in USA
2019-05
10872256_B