

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k150606

B. Purpose for Submission:

New device

C. Measurand:

Buprenorphine

D. Type of Test:

Qualitative and semi-quantitative immunoassay

E. Applicant:

Siemens Healthcare Diagnostics Inc.

F. Proprietary and Established Names:

Emit® II Plus Buprenorphine Assay
Emit® II Plus Specialty Drug Calibrator/Control Levels 1-4
Emit® II Plus Specialty Drug Control Negative
Emit® II Plus Specialty Drug Control Positive

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DJG	II	862.3650 - Opiate test system	91 - Toxicology
DLJ	II	862.3200 - Clinical toxicology calibrator	91 - Toxicology
LAS	I, reserved	862.3280 - Clinical toxicology control material	91 - Toxicology

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

Emit® II Plus Buprenorphine Assay.

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 semi-quantitative analyses of buprenorphine in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.

The semi-quantitative mode is for the purpose of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as 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. GC/MS and LC/MS are the preferred confirmatory methods. 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.

Emit® II Plus Specialty Drug Calibrator/Control Level 1, Emit® II Plus Specialty Drug Calibrator/Control Level 2, Emit® II Plus Specialty Drug Calibrator/Control Level 3, Emit® II Plus Specialty Drug Calibrator/Control Level 4

The Emit® II Plus Specialty Drug Calibrators/Controls are used in the calibration of the Emit® II Plus Buprenorphine Assay. These products may also be used as quality control materials based on the Buprenorphine Assay cutoff.

Emit® II Plus Specialty Drug Negative Control and Emit® II Plus Specialty Drug Positive Control

The Emit® II Plus Specialty Drug Negative Control and Emit® II Plus Specialty Drug Positive Control are for use with the Emit® II Plus Buprenorphine Assay.

3. Special conditions for use statement(s):

For prescription use.

4. Special instrument requirements:

Analyzers must be capable of maintaining a constant reaction temperature, pipette specimens/reagents, mix thoroughly, measure enzyme rates precisely and time the reaction accurately. All performance studies were conducted on the Viva-E® analyzer.

I. Device Description:

The Emit® II Plus Buprenorphine assay is a homogeneous enzyme immunoassay with a 5 ng/mL cutoff. The assay, used for the detection of Buprenorphine in human urine, utilizes a

two-reagent system. The Antibody/Substrate Reagent 1 is a liquid ready-to-use product comprised of mouse monoclonal antibodies to buprenorphine, glucose-6-phosphate (G6P), and nicotinamide adenine dinucleotide (NAD) in a diluent containing bovine serum albumin (BSA), preservatives and stabilizers. The Enzyme Reagent 2 is a liquid, ready-to-use product containing norbuprenorphine labeled bacterial recombinant glucose-6 phosphate dehydrogenase (rG6PDH) in a diluent containing bovine serum albumin (BSA), Hepes buffer, preservatives and stabilizers.

The assay kit consists of Reagent 1 and Reagent 2 in plastic containers and is available in three sizes: large kit (1L), small kit (115 mL), and 28 mL kit. Emit II Plus assays are designed for use with a number of chemistry analyzers.

The Emit® II Plus Buprenorphine assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result.

Calibrators and controls are sold separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Microgenics CEDIA® Buprenorphine Assay
 Microgenics CEDIA® Buprenorphine Calibrators
 Microgenics CEDIA® Buprenorphine Controls

2. Predicate 510(k) number(s):

K040316

3. Comparison with predicate:

Similarities - Reagent		
Item	Predicate Device CEDIA® Buprenorphine Assay (K040316)	Proposed Device Emit® II Plus Buprenorphine Assay
Intended Use	A homogeneous enzyme immunoassay for qualitative or semi-quantitative determination of the presence of burprenorphine in human urine at a cutoff concentration of 5ng/mL. Preliminary analytical test result.	Same
Analyte	Buprenorphine	Same

Similarities - Reagent		
Item	Predicate Device CEDIA [®] Buprenorphine Assay (K040316)	Proposed Device Emit [®] II Plus Buprenorphine Assay
Antibody	Mouse monoclonal antibody to buprenorphine	Same
Test System	Homogeneous enzyme immunoassay	Same
Detection	Absorbance change measured spectrophotometrically	Same
Sample type	Human urine	Same
Cutoff	5 ng/mL	Same
Instrument	Automated clinical analyzers capable of maintaining a constant temperature, pipetting, mixing reagents, measuring enzymatic rates, and timing the reaction.	Same
Calibrator levels	0 ng/mL + four (4) levels	Same
Control Positive and Control Negative Levels	High Control: 7 ng/mL Low Control: 3 ng/mL	Same

Differences - Reagent		
Item	Predicate Device CEDIA [®] Buprenorphine Assay (K040316)	Proposed Device Emit [®] II Plus Buprenorphine Assay
Assay methodology	Uses CEDIA [®] technology	Uses EMIT [®] technology
Detection	Absorbance change measured spectrophotometrically at 660 nm.	Absorbance change measured spectrophotometrically at 340 nm.
Reference Methodology	GC/MS	LC/MS
Reagents Form	R1 and R2: Lyophilized (Reconstitution Required)	R1: Liquid – Ready to use R2: Liquid – Ready to use
Calibrator levels	0, 5, 20, 50, and 75 ng/mL	0, 2.5, 5, 15, and 25 ng/mL

Similarities - Calibrators		
Attributes	Predicate Device CEDIA [®] Buprenorphine Calibrator (K040316)	Proposed Device Emit [®] II Plus Specialty Drug Calibrator/Control
Intended Use	The CEDIA [®] Buprenorphine calibrators are used to calibrate the CEDIA [®] Buprenorphine Assay in human urine.	For calibration of the Emit [®] II Plus Buprenorphine Assay. These products may also be used as quality control materials based on the Buprenorphine Assay
Matrix	Human urine	Same
Analyte	Buprenorphine	Same
Target Concentrations for Buprenorphine	0 ng/mL + four (4) levels	Same
Preparation	Liquid - Ready to use	Same
Storage	2 – 8°C	Same

Differences - Calibrators		
Attributes	Predicate Device CEDIA [®] Buprenorphine Calibrator (K040316)	Proposed Device Emit [®] II Plus Specialty Drug Calibrator/Control
Target Concentration for Buprenorphine	0, 5, 20, 50, and 75 ng/mL	0, 2.5, 5, 15, and 25 ng/mL

Similarities and Differences - Controls		
Attributes	Predicate Device CEDIA [®] Buprenorphine Negative Control and Positive Control (K040316)	Proposed Device Emit [®] II Plus Specialty Drug Negative Control and Positive Control
Intended Use	The CEDIA [®] Buprenorphine controls are used to qualify the CEDIA [®] Buprenorphine Assay in human urine.	The Emit [®] II Plus Specialty Drug Control Negative and Control Positive are for use with the Emit [®] II Plus Buprenorphine Assay.
Matrix	Human urine	Same
Analyte	Buprenorphine	Same

Similarities and Differences - Controls		
Attributes	Predicate Device CEDIA [®] Buprenorphine Negative Control and Positive Control (K040316)	Proposed Device Emit [®] II Plus Specialty Drug Negative Control and Positive Control
Target Concentrations for Buprenorphine	High Control: 7 ng/mL Low Control: 3 ng/mL	Positive Control: 7 ng/mL Negative Control: 3 ng/mL
Preparation	Liquid, ready to use	Same
Storage	2 – 8°C	Same

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods
 CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures

CLSI EP7-A2: Interference Testing in Clinical Chemistry

L. Test Principle:

The Emit[®] II Plus Buprenorphine Assay is a homogeneous enzyme immunoassay technique used for the analysis of a specific compound 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were conducted using urine pools spiked with Buprenorphine into drug free human urine at 8 concentrations. For each level, samples were analyzed in duplicate twice a day, for 20 days (N=80). Precision data were calculated according to the Clinical and Laboratory Standards Institute (CLSI) Guidelines EP5-A2. Results are summarized in tables below:

Qualitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Determinations	Results
Repeatability			
0	-100%	80	80 Negative / 0 Positive
2.50	-50%	80	80 Negative / 0 Positive
3.00	-40%	80	80 Negative / 0 Positive
3.75	-25%	80	80 Negative / 0 Positive
5.00	cutoff	80	25 Negative / 55 Positive
6.25	+25%	80	80 Positive / 0 Negative
7.00	+40%	80	80 Positive / 0 Negative
7.50	+50%	80	80 Positive / 0 Negative
10.00	+100%	80	80 Positive / 0 Negative
Within-lab			
0	-100%	80	80 Negative / 0 Positive
2.50	-50%	80	80 Negative / 0 Positive
3.00	-40%	80	80 Negative / 0 Positive
3.75	-25%	80	80 Negative / 0 Positive
5.00	cutoff	80	25 Negative / 55 Positive
6.25	+25%	80	80 Positive / 0 Negative
7.00	+40%	80	80 Positive / 0 Negative
7.50	+50%	80	80 Positive / 0 Negative
10.00	+100%	80	80 Positive / 0 Negative

Semi-quantitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Determinations	Result
Repeatability			
0	-100%	80	80 Negative / 0 Positive
2.50	-50%	80	80 Negative / 0 Positive
3.00	-40%	80	80 Negative / 0 Positive
3.75	-25%	80	80 Negative / 0 Positive
5.00	cutoff	80	25 Negative/55 Positive
6.25	+25%	80	80 Positive / 0 Positive
7.00	+40%	80	80 Positive / 0 Positive
7.50	+50%	80	80 Positive / 0 Positive
10.00	+100%	80	80 Positive / 0 Positive

Urine Pool (ng/mL)	% of Cutoff	# of Determinations	Result
Within- Lab 0	-100%	80	80 Negative / 0 Positive
2.50	-50%	80	80 Negative / 0 Positive
3.00	-40%	80	80 Negative / 0 Positive
3.75	-25%	80	80 Negative / 0 Positive
5.00	cutoff	80	25 Negative / 55 Positive
6.25	+25%	80	80 Positive / 0 Positive
7.00	+40%	80	80 Positive / 0 Positive
7.50	+50%	80	80 Positive / 0 Positive
10.00	+100%	80	80 Positive / 0 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 Viva-E® analyzer. The samples were analyzed in duplicate, 40 times for a total of 80 replicates.

Qualitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Determinations	Results
Repeatability 1.25	-75%	80	80 Negative / 0 Positive
Within-Lab 8.75	-75%	80	80 Negative / 0 Positive

Semi-Quantitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Determinations	Results
Repeatability 1.25	-75%	80	80 Positive / 0 Positive
Within-Lab 8.75	-75%	80	80 Positive / 0 Positive

b. Linearity/assay reportable range:

Drug free urine pools were spiked with eight concentrations of buprenorphine at levels 2-25 ng/mL and analyzed semi-quantitatively in five replicates on a Viva-E® analyzer. The mean observed Buprenorphine concentration was compared to the expected Buprenorphine concentration and percent recovery results shown in the table below:

Expected Buprenorphine 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

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
 Emit® II Plus Specialty Drug Calibrator/Control is traceable to Cerilliant Buprenorphine Cat. No. B-902. This stock solution is used directly to prepare Master pools. The secondary stock solution is then spiked into the calibrators and controls to the desired concentration. The concentrations are confirmed by LC/MS/MS.

Stability Studies:

Real time and on-board stability studies for both controls and calibrators were conducted. Protocols and acceptance criteria were reviewed and found to be acceptable. The manufacturer claims the following expiration date for both controls and calibrators:

Real-time stability studies show that when stored at 2-8 °C, open and unopened product is stable for nine months. Real time stability studies are on-going to support a 12 month shelf life stability claim.

Testing supports on-board storage stability of over 30 days.

- d. *Detection limit:*
 Not applicable

- e. *Analytical specificity:*

Buprenorphine Metabolite Recovery:

Buprenorphine and the buprenorphine metabolites norbuprenorphine, buprenorphine glucuronide and norbuprenorphine glucuronide were spiked into aliquots of drug free urine at the levels shown and run at N=5 replicates. The samples were assayed and the mean recovery results were determined.

Buprenorphine and Buprenorphine Metabolite Recovery

Compound	Conc. Tested (ng/mL)	% Cross-reactivity
Buprenorphine	5	103
Norbuprenorphine	5	92
Buprenorphine Glucuronide	1000	0.09
Norbuprenorphine Glucuronide	1000	0.12

Structurally Related Compounds:

Samples were prepared by spiking drug-free human urine with individual cross-reactants to the targeted level. The samples were evaluated on the Viva-E® analyzer. All samples were tested in replicates of N=5.

Cross-Reactivity with the Structurally Related Drugs

Compound	Conc. Tested (ng/mL)	Qual. Result (Neg/Pos)	Semi-quant. Result (Neg/Pos)	% Cross-reactivity
6-acetylcodeine	100000	Neg	Neg	<0.01
6-acetylmorphine	100000	Neg	Neg	<0.01
Codeine	100000	Neg	Neg	<0.01
Dextromethorphan	100000	Neg	Neg	<0.01
Dihydrocodeine	100000	Neg	Neg	<0.01
Ethyl Morphine	100000	Neg	Neg	<0.01
Heroin	100000	Neg	Neg	<0.01
Hydrocodone	100000	Neg	Neg	<0.01
Hydromorphone	100000	Neg	Neg	<0.01
Levorphanol	100000	Neg	Neg	<0.01
Morphine	100000	Neg	Neg	<0.01
Morphine 3-glucuronide	100000	Neg	Neg	<0.01
Morphine 6-glucuronide	100000	Neg	Neg	<0.01
Nalorphine	100000	Neg	Neg	<0.01
Naloxone	100000	Neg	Neg	<0.01
Naltrexone	100000	Neg	Neg	<0.01
Norcodeine	100000	Neg	Neg	<0.01
Normorphine	100000	Neg	Neg	<0.01
Noroxycodone	100000	Neg	Neg	<0.01
Noroxymorphone	100000	Neg	Neg	<0.01
Oxycodone	100000	Neg	Neg	<0.01
Oxymorphone	100000	Neg	Neg	<0.01

Structurally Unrelated Compounds:

The following structurally unrelated compounds were added into drug-free urine spiked into two levels of controls at $\pm 40\%$ of the cutoff concentration. The substances listed in the table below do not yield a false response relative to the cutoff in both qualitative and semi-quantitative mode.

Interference (Structurally Unrelated Compounds)	Conc. Tested ($\mu\text{g/mL}$)	- 40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
		Qualit. Result Pos/ Neg	Semi-quant. Result Pos/ Neg	Qualit. Result Pos/ Neg	Semi-quant. Result Pos/ Neg
10, 11- dihydrocarbamazepine	85	Neg	Neg	Pos	Pos
Acetaminophen	1000	Neg	Neg	Pos	Pos
Acetylsalicylic Acid	1500	Neg	Neg	Pos	Pos
Amitriptyline	100	Neg	Neg	Pos	Pos
Amoxicillin	500	Neg	Neg	Pos	Pos
ZT (Zidovudine)	2000	Neg	Neg	Pos	Pos
Benzoylcegonine	1000	Neg	Neg	Pos	Pos
Brompheniramine	75	Neg	Neg	Pos	Pos
Caffeine	1000	Neg	Neg	Pos	Pos
Captopril	500	Neg	Neg	Pos	Pos
Chlordiazepoxide	100	Neg	Neg	Pos	Pos
Chlorpromazine	10	Neg	Neg	Pos	Pos
Cimetidine	1000	Neg	Neg	Pos	Pos
Clomipramine	2.5	Neg	Neg	Pos	Pos
Clonidine	1000	Neg	Neg	Pos	Pos
Cyclobenzaprine	125	Neg	Neg	Pos	Pos
d-amphetamine	700	Neg	Neg	Pos	Pos
Desipramine	800	Neg	Neg	Pos	Pos
Diazepam	100	Neg	Neg	Pos	Pos
Digoxin	0.01	Neg	Neg	Pos	Pos
Diphenhydramine	1000	Neg	Neg	Pos	Pos
d-methamphetamine	500	Neg	Neg	Pos	Pos
Doxepine	100	Neg	Neg	Pos	Pos
EDDP	1000	Neg	Neg	Pos	Pos
EMDP	100	Neg	Neg	Pos	Pos
Enalapril	500	Neg	Neg	Pos	Pos
Fluoxetine	500	Neg	Neg	Pos	Pos
Glutethimide	500	Neg	Neg	Pos	Pos
Haloperidol	100	Neg	Neg	Pos	Pos
Hydroxyzine	500	Neg	Neg	Pos	Pos
Ibuprofen	1000	Neg	Neg	Pos	Pos
Imipramine	200	Neg	Neg	Pos	Pos

Interference (Structurally Unrelated Compounds)	Conc. Tested (µg/mL)	- 40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
		Qualit. Result Pos/ Neg	Semi-quant. Result Pos/ Neg	Qualit. Result Pos/ Neg	Semi-quant. Result Pos/ Neg
Ketamine	100	Neg	Neg	Pos	Pos
Ketorolac					
Tromethamine	400	Neg	Neg	Pos	Pos
LAAM (L-a-acetylmethadol)	25	Neg	Neg	Pos	Pos
L-Cotinine	100	Neg	Neg	Pos	Pos
Levofloxacin	100	Neg	Neg	Pos	Pos
Levothyroxine (L-Thyroxine)	50	Neg	Neg	Pos	Pos
Lidocaine	1000	Neg	Neg	Pos	Pos
Lormetazepam	1	Neg	Neg	Pos	Pos
LSD	10	Neg	Neg	Pos	Pos
MDMA (Ecstasy)	1000	Neg	Neg	Pos	Pos
Meperidine	800	Neg	Neg	Pos	Pos
Methadone	500	Neg	Neg	Pos	Pos
Methaqualone	600	Neg	Neg	Pos	Pos
NAPA	400	Neg	Neg	Pos	Pos
Naproxen	1000	Neg	Neg	Pos	Pos
Nicotinic Acid	500	Neg	Neg	Pos	Pos
Nifedipine	500	Neg	Neg	Pos	Pos
Nordiazepam	100	Neg	Neg	Pos	Pos
Nortryptiline	250	Neg	Neg	Pos	Pos
Oxazepam	300	Neg	Neg	Pos	Pos
Perphenazine	150	Neg	Neg	Pos	Pos
Phencyclidine	900	Neg	Neg	Pos	Pos
Phenobarbital	500	Neg	Neg	Pos	Pos
Phenelzine	100	Neg	Neg	Pos	Pos
Phenytoin	1000	Neg	Neg	Pos	Pos
Procainamide	1000	Neg	Neg	Pos	Pos
Procyclidine	800	Neg	Neg	Pos	Pos
Promethazine	100	Neg	Neg	Pos	Pos
Propoxyphene	1000	Neg	Neg	Pos	Pos
Protriptyline	200	Neg	Neg	Pos	Pos
Pseudoephedrine	1000	Neg	Neg	Pos	Pos
Quinacrine	900	Neg	Neg	Pos	Pos
Ranitidine	1000	Neg	Neg	Pos	Pos
Ritalin	1000	Neg	Neg	Pos	Pos
Salicylic Acid	500	Neg	Neg	Pos	Pos
Scopolamine	500	Neg	Neg	Pos	Pos
Secobarbital	1000	Neg	Neg	Pos	Pos

Interference (Structurally Unrelated Compounds)	Conc. Tested (µg/mL)	- 40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
		Qualit. Result Pos/ Neg	Semi-quant. Result Pos/ Neg	Qualit. Result Pos/ Neg	Semi-quant. Result Pos/ Neg
Tapentadol	100	Neg	Neg	Pos	Pos
THC	100	Neg	Neg	Pos	Pos
Thioridazine	100	Neg	Neg	Pos	Pos
Tramadol	1000	Neg	Neg	Pos	Pos
Trazodone	5	Neg	Neg	Pos	Pos
Trimethoprim	1000	Neg	Neg	Pos	Pos
Triprolidine (zymine)	50	Neg	Neg	Pos	Pos
Tyramine	100	Neg	Neg	Pos	Pos
Verapamil	500	Neg	Neg	Pos	Pos
Zolpidem	100	Neg	Neg	Pos	Pos

Endogenous Substances Interference:

Each compound was spiked into a -40% cutoff and a +40% cutoff concentration pool which were prepared by spiking buprenorphine to aliquots of drug-free human urine. The results show that the tested endogenous substances at the levels tested caused no interference relative to the 5 ng/mL cutoff. Qualitative and semi-quantitative results are provided in the table below.

Interferences (Endogenous Substances)	Conc. Tested	-40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
		Qualit. Result (Pos/Neg)	Semi-Quant. Result (Pos/ Neg)	Qualit. Result (Pos/Neg)	Semi-Quant. Result (Pos/Neg)
Acetone	1.0 g/dL	Neg	Neg	Pos	Pos
Ascorbic Acid	1.5 g/dL	Neg	Neg	Pos	Pos
Conjugated Bilirubin	2.0 mg/dL	Neg	Neg	Pos	Pos
Unconjugated Bilirubin	2.0 mg/dL	Neg	Neg	Pos	Pos
Creatinine	0.5 g/dL	Neg	Neg	Pos	Pos
Ethanol	1.0 g/dL	Neg	Neg	Pos	Pos
Immuno Gamma Globulin (IgG)	0.5 g/dL	Neg	Neg	Pos	Pos
Glucose	2.0 g/dL	Neg	Neg	Pos	Pos
Galactose	1.0 g/dL	Neg	Neg	Pos	Pos
Hemoglobin	115 mg/dL	Neg	Neg	Pos	Pos
Human Serum Albumin	0.5 g/dL	Neg	Neg	Pos	Pos
Oxalic Acid	0.1 g/dL	Neg	Neg	Pos	Pos
Riboflavin	7.5 mg/dL	Neg	Neg	Pos	Pos

Interferences (Endogenous Substances)	Conc. Tested	-40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
		Qualit. Result (Pos/Neg)	Semi- Quant.Result (Pos/ Neg)	Qualit. Result (Pos/Neg)	Semi-Quant. Result (Pos/Neg)
Sodium Chloride	6.0 g/dL	Neg	Neg	Pos	Pos
Urea	6.0 g/dL	Neg	Neg	Pos	Pos
Sodium Azide	1% w/v	Neg	Neg	Pos	Pos
Sodium Fluoride	1% w/v	Neg	Neg	Pos	Pos

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 and 7 ng/mL) of the cutoff concentration. All samples were tested in triplicates and no interference was observed.

f. Assay cut-off:

Analytical performance of the device around the claimed cutoff is described in precision section (1 a.) above.

2. Comparison studies:

a. Method comparison with predicate device:

One-hundred twenty seven (127) unaltered human urine samples were qualitatively and semiquantitatively evaluated using the Emit® II Plus Buprenorphine Assay on the Viva-E® analyzer and compared with the results obtained by the reference method – LC/MS/MS. Two replicates were run on each sample on one reagent lot. The results are presented below:

Emit® II Plus Buprenorphine Assay vs. LC/MS/MS
Comparison Table for Qualitative and Semi-quantitative Assay Performance

	LC/MS/MS				% Agreement
	Negative (<2.5 ng/mL)	Negative Within 50% below the cutoff (2.5-4.9 ng/mL)	Positive Within 50% above the cutoff (5.0-7.5 ng/mL)	Positive (>7.5 ng/mL)	
Qualitative					
Emit® Positive	0	7	16	49	90%
Emit® Negative	45	9	1	0	98%
Semi-quantitative					
Emit® Positive	0	7	16	49	90%

Emit® Negative	45	9	1	0	98%
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Discordant Result Summary

Sample ID	LC/MS/MS		Emit +/-
	Bup (ng/mL)	NorBup (ng/mL)	
190	0	3.92	+
193	0	4.97	+
195	0	4.06	+
226	0	4.21	+
250	0	4.13	+
77	0	4.60	+
316	0	3.86	+
338	5.12	0	-

Bup = Buprenorphine; NorBup = Norbuprenorphine

b. *Matrix comparison:*

Test is for urine samples only.

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable.

b. *Clinical specificity:*

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.