



Food and Drug Administration
10903 New Hampshire Avenue
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SIEMENS HEALTHCARE DIAGNOSTICS, INC.
FRANCES DILLON
SR. MANAGER, REGULATORY AFFAIRS
P.O. BOX 6101, M/S 514
NEWARK DE 19714-6101

October 23, 2015

Re: K150606

Trade/Device Name: Emit II Plus Buprenorphine Assay,
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,
Emit II Plus Specialty Drug Control Negative,
Emit II Plus Specialty Drug Control Positive

Regulation Number: 21 CFR 862.3650

Regulation Name: Opiate test system

Regulatory Class: II

Product Code: DJG, DLJ, LAS

Dated: September 4, 2015

Received: September 8, 2015

Dear Ms. Dillon:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,


Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)
K150606

Device Name

Emit® II Plus Buprenorphine Assay, 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, Emit® II Plus Specialty Drug Control Negative, Emit® II Plus Specialty Drug Control Positive.

Indications for Use (Describe)

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 semiquantitative 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. Gas Chromatography/Mass Spectrometry (GC/MS) or 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 Control Negative and Emit® II Plus Specialty Drug Control Positive

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

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) Summary

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of the Safe Medical Device Act of 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K150606

1. Submitter

Siemens Healthcare Diagnostics Inc.
P.O. Box 6101
Newark, DE 19714

Tel: 302-631-6951
FAX: 3023-631-6299

Contact Person: Frances Dillon
Date of Preparation: October 20, 2015

2. Device Information

Trade Name: Emit[®] II Plus Buprenorphine Assay
Common Name: Buprenorphine Assay
Classification Name: Opiates test system - 21CFR 862.3650
Regulatory Class: II
Product Code: DJG – Enzyme Immunoassay, Opiates
Panel: Clinical Toxicology (91)

Trade Name: 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
Common Name: Buprenorphine Calibrator/Control
Classification Name: Clinical Toxicology Calibrator - 21CFR 862.3200
Clinical Toxicology Control Material - 21CFR 862.3280
Regulatory Class: II (Calibrator)
I (Control)
Product Code: DLJ - Calibrators, Drug Specific
LAS – Drug Specific Control Materials
Panel: Clinical Toxicology (91)

Trade Name: Emit[®] II Plus Specialty Drug Control Negative
Emit[®] II Plus Specialty Drug Control Positive
Common Name: Buprenorphine Negative Control and Buprenorphine
Positive Control
Classification Name: Clinical Toxicology Control material - 21CFR 862.3280
Regulatory Class: I
Product Code: LAS – Drug Specific Control Materials
Panel: Clinical Toxicology (91)

3. Predicate Device

Assay: Microgenics CEDIA® Buprenorphine Assay, K040316.
Calibrator: Microgenics CEDIA® Buprenorphine Calibrators, K040316
Control: Microgenics CEDIA® Buprenorphine Controls, K040316

4. Device Description

Assay

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 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 / Controls

Emit® II Plus Specialty Drug Calibrators / Controls are in-vitro diagnostic products 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. The matrix is pooled, drug-free, human urine based product containing buprenorphine, preservatives and surfactants. Each level of calibrator is packaged and sold separately, 1 plastic bottle per box, 10 mL in a 15 mL bottle. Values are nominal and are verified with urine based buprenorphine anchor pool and adjusted if needed. The anchor pool levels are verified by LC/MS/MS and are within 10% of nominal drug concentration for levels 2.5 and 5.0 ng/mL and within 5 % of nominal concentrations for levels 15 and 25 ng/mL.

Emit® II Plus Specialty Drug Calibrator/Control levels are as follows:

Specialty Drug Calibrator/Control	Targeted Buprenorphine Concentration (ng/mL)
Level 1	2.5
Level 2	5
Level 3	15
Level 4	25

The Emit[®] Calibrator/Control Level 0, which contains no drug and was cleared under K993755 is used with the Emit[®] II Plus Buprenorphine Assay. There are no changes to the Calibrator Level 0 product.

Controls

Emit[®] II Plus Specialty Drug Control Negative and Emit[®] II Plus Specialty Drug Control Positive are in-vitro diagnostic products are for use with the Emit[®] II Plus Buprenorphine assay. The matrix is pooled, drug-free, human urine based product containing buprenorphine, preservatives and surfactants. The Control Negative and Control Positive are packaged separately in 15 mL plastic vials with a 10 mL fill per vial. Values are nominal and are verified with urine based buprenorphine anchor pool and adjusted if needed. Anchor pool levels are verified by LC/MS/MS.

Emit[®] II Plus Specialty Drug Control Negative and Control Positive levels are as follows:

Specialty Drug Control	Targeted Buprenorphine Concentration (ng/mL)
Negative	3
Positive	7

5. Indications 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 semiquantitative 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, Level 2, Level 3, and 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 Control Negative and Emit[®] II Plus Specialty Drug Control Positive

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

6. Comparison of Technological Characteristics with the Predicate Device

Attributes	<u>Predicate Device</u> CEDIA[®] Buprenorphine Assay (K040316)	<u>Proposed Device</u> Emit[®] II Plus Buprenorphine Assay
Similarities		
Intended Use	A homogeneous enzyme immunoassay for qualitative or semi-quantitative determination of the presence of buprenorphine in human urine at a cutoff concentration of 5 ng/mL. Preliminary analytical test result.	Same
Analyte	Buprenorphine	Same
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 Level	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 Levels	High Control 7 ng/mL Low Control 3 ng/mL	Same
Differences		
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

**Comparison of Calibrator/Control
Similarities and Differences**

Attributes	<u>Predicate Device</u> CEDIA® Buprenorphine Calibrator (K040316)	<u>Proposed Device</u> Emit® II Plus Specialty Drug Calibrator / Control
Similarities		
Intended Use	The CEDIA® Buprenorphine calibrators are used to calibrate the CEDIA® Buprenorphine Assay in human urine.	Same
Matrix	Human urine	Same
Analyte	Buprenorphine	Same
Preparation	Liquid - Ready to use	Same
Storage	2 – 8°C	Same
Differences		
Target Concentrations for Buprenorphine	0, 5, 20, 50, and 75 ng/mL	2.5, 5, 15, and 25 ng/mL (0 ng/mL calibrator is Emit® Calibrator/Control Level 0)

**Comparison of Control
Similarities**

Attributes	<u>Predicate Device</u> CEDIA® Buprenorphine Negative Control and Positive Control (K040316)	<u>Proposed Device</u> Emit® II Plus Specialty Drug Control Negative and Control Positive
Similarities		
Intended Use	The CEDIA® Buprenorphine controls are used to qualify the CEDIA® Buprenorphine Assay in human urine.	Same
Matrix	Human urine	Same
Analyte	Buprenorphine	Same
Target Concentrations for Buprenorphine	High Control 7 ng/mL Low Control 3 ng/mL	Same
Preparation	Liquid, ready to use	Same
Storage	2 – 8°C	Same

7. Performance Data

Performance of the Emit® II Plus Buprenorphine Assay was evaluated at Siemens Healthcare Diagnostics Inc. on a Viva-E® Analyzer.

a. Precision / Cutoff Characterization

Studies were conducted using urine pools prepared by spiking Buprenorphine into drug-free human urine at 8 concentrations (levels). The concentrations tested represent the following levels relative to the 5 ng/mL cutoff: 100, -50%,

-40%, and -25% below the cutoff, at the cutoff, and +25%, +40%, +50%, and +100% of the cutoff. The drug-free human urine pool was also tested as the 0 ng/mL buprenorphine level. The studies were performed on Viva-E® analyzer. For each level, samples were analyzed in duplicate twice a day, for 20 days (N=80).

Precision: Qualitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Results	Repeatability Results	Within-Laboratory Results
0	-100%	80	80 Negative	80 Negative
2.5	-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
7.5	+50%	80	80 Positive	80 Positive
10	+100%	80	80 Positive	80 Positive

Precision: Semi-quantitative Analysis

Urine Pool (ng/mL)	% of Cutoff	# of Results	Repeatability Results	Within-Laboratory Results
0	-100%	80	80 Negative	80 Negative
2.5	-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
7.5	+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 Viva-E[®] analyzer. The samples were analyzed in duplicate, 40 times for a total of 80 replicates over one day.

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

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

b. Specificity and Cross-reactivity

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	Concentration Tested (ng/mL)	Semi-quantitative Results	
		Recovery (ng/mL)	% Cross-reactivity
Buprenorphine	5	5.2	103.2
Norbuprenorphine	5	4.6	92.6
Buprenorphine Glucuronide	1000	0.9	0.1
Norbuprenorphine Glucuronide	1000	1.2	0.1

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.

For qualitative analysis, cross-reactivity is reported as the level of cross-reactant that produces a rate response \geq the cutoff. For semi-quantitative analysis the percent cross-reactivity was calculated.

Cross-reactivity with the Structurally Related Compound

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

c. Interference

Structurally Unrelated Compounds - Interference from the structurally unrelated compounds was evaluated by spiking each compound into a 3 ng/mL and 7 ng/mL spiked urine pool. A control (blank) was also prepared without the interferent compound. Samples were evaluated on the Viva-E[®] analyzer. The blank sample was run, followed by the sample containing the interfering compound. All samples were tested in replicates of N=5. The mean rate and concentration were calculated for qualitative and semi-quantitative analysis, respectively. The sample containing the drug was compared to the control, which contained only buprenorphine (3 or 7 ng/mL) to determine if there was a false response relative to the assay cutoff (5 ng/mL). At the stated concentration, the samples did not give a false response relative to the 5 ng/mL cutoff.

Interference of Structurally Unrelated Compounds

Interference (Structurally Unrelated Compounds)	Conc. Tested (µg/mL)	- 40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
		Qualitative Result	Semi- quantitative Result	Qualitative Result	Semi- quantitative Result
10, 11- dihydrocarbamazepine	85	Negative	Negative	Positive	Positive
Acetaminophen	1000	Negative	Negative	Positive	Positive
Acetylsalicylic Acid	1500	Negative	Negative	Positive	Positive
Amitriptyline	100	Negative	Negative	Positive	Positive
Amoxicillin	500	Negative	Negative	Positive	Positive
ZT (Zidovudine)	2000	Negative	Negative	Positive	Positive
Benzoylcegonine	1000	Negative	Negative	Positive	Positive
Brompheniramine	75	Negative	Negative	Positive	Positive
Caffeine	1000	Negative	Negative	Positive	Positive
Captopril	500	Negative	Negative	Positive	Positive
Chlordiazepoxide	100	Negative	Negative	Positive	Positive
Chlorpromazine	10	Negative	Negative	Positive	Positive
Cimetidine	1000	Negative	Negative	Positive	Positive
Clomipramine	2.5	Negative	Negative	Positive	Positive
Clonidine	1000	Negative	Negative	Positive	Positive
Cyclobenzaprine	125	Negative	Negative	Positive	Positive
d-amphetamine	700	Negative	Negative	Positive	Positive
Desipramine	800	Negative	Negative	Positive	Positive
Diazepam	100	Negative	Negative	Positive	Positive
Digoxin	0.01	Negative	Negative	Positive	Positive
Diphenhydramine	1000	Negative	Negative	Positive	Positive
d-methamphetamine	500	Negative	Negative	Positive	Positive
Doxepine	100	Negative	Negative	Positive	Positive

EDDP	1000	Negative	Negative	Positive	Positive
EMDP	100	Negative	Negative	Positive	Positive
Enalapril	500	Negative	Negative	Positive	Positive
Fluoxetine	500	Negative	Negative	Positive	Positive
Glutethimide	500	Negative	Negative	Positive	Positive
Haloperidol	100	Negative	Negative	Positive	Positive
Hydroxyzine	500	Negative	Negative	Positive	Positive
Ibuprophen	1000	Negative	Negative	Positive	Positive
Imipramine	200	Negative	Negative	Positive	Positive
Ketamine	100	Negative	Negative	Positive	Positive
Ketorolac Tromethamine	400	Negative	Negative	Positive	Positive
LAAM (L-a- acetylmethadol)	25	Negative	Negative	Positive	Positive
L-Cotinine	100	Negative	Negative	Positive	Positive
Levofloxacin	100	Negative	Negative	Positive	Positive
Levothyroxine (L- Thyroxine)	50	Negative	Negative	Positive	Positive
Lidocaine	1000	Negative	Negative	Positive	Positive
Lormetazepam	1	Negative	Negative	Positive	Positive
LSD	10	Negative	Negative	Positive	Positive
MDMA (Ecstasy)	1000	Negative	Negative	Positive	Positive
Meperidine	800	Negative	Negative	Positive	Positive
Methadone	500	Negative	Negative	Positive	Positive
Methaqualone	600	Negative	Negative	Positive	Positive
NAPA	400	Negative	Negative	Positive	Positive
Naproxen	1000	Negative	Negative	Positive	Positive
Nicotinic Acid	500	Negative	Negative	Positive	Positive
Nifedipine	500	Negative	Negative	Positive	Positive
Nordiazepam	100	Negative	Negative	Positive	Positive
Nortryptiline	250	Negative	Negative	Positive	Positive
Oxazepam	300	Negative	Negative	Positive	Positive
Perphenazine	150	Negative	Negative	Positive	Positive
Phencyclidine	900	Negative	Negative	Positive	Positive
Phenobarbital	500	Negative	Negative	Positive	Positive
Phenelzine	100	Negative	Negative	Positive	Positive
Phenytoin	1000	Negative	Negative	Positive	Positive
Procainamide	1000	Negative	Negative	Positive	Positive
Procyclidine	800	Negative	Negative	Positive	Positive
Promethazine	100	Negative	Negative	Positive	Positive
Propoxyphene	1000	Negative	Negative	Positive	Positive
Protriptyline	200	Negative	Negative	Positive	Positive
Pseudoephedrine	1000	Negative	Negative	Positive	Positive
Quinacrine	900	Negative	Negative	Positive	Positive
Ranitidine	1000	Negative	Negative	Positive	Positive

Ritalin	1000	Negative	Negative	Positive	Positive
Salicylic Acid	500	Negative	Negative	Positive	Positive
Scopolamine	500	Negative	Negative	Positive	Positive
Secobarbital	1000	Negative	Negative	Positive	Positive
Tapentadol	100	Negative	Negative	Positive	Positive
THC	100	Negative	Negative	Positive	Positive
Thioridazine	100	Negative	Negative	Positive	Positive
Tramadol	1000	Negative	Negative	Positive	Positive
Trazodone	5	Negative	Negative	Positive	Positive
Trimethoprim	1000	Negative	Negative	Positive	Positive
Tripolidine (zymine)	50	Negative	Negative	Positive	Positive
Tyramine	100	Negative	Negative	Positive	Positive
Verapamil	500	Negative	Negative	Positive	Positive
Zolpidem	100	Negative	Negative	Positive	Positive

Endogenous Substances Interference - Each compound was spiked into a -40% cutoff and a +40% cutoff which was prepared by spiking buprenorphine to aliquots of drug-free human urine. The results show that the endogenous substances, pH and sG caused no interference relative to the 5 ng/mL cutoff. Qualitative and semi-quantitative results are provided.

Interferences (Endogenous Substances)	Conc. Tested	-40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
		Qualitative Result	Semi- Quantitative Result	Qualitative Result	Semi- Quantitative Result
Acetone	1.0 g/dL	Negative	Negative	Positive	Positive
Ascorbic Acid	1.5 g/dL	Negative	Negative	Positive	Positive
Conjugated Bilirubin	2.0 mg/dL	Negative	Negative	Positive	Positive
Unconjugated Bilirubin	2.0 mg/dL	Negative	Negative	Positive	Positive
Creatinine	0.5 g/dL	Negative	Negative	Positive	Positive
Ethanol	1.0 g/dL	Negative	Negative	Positive	Positive
Immuno Gamma Globulin (IgG)	0.5 g/dL	Negative	Negative	Positive	Positive
Glucose	2.0 g/dL	Negative	Negative	Positive	Positive
Galactose	1.0 g/dL	Negative	Negative	Positive	Positive
Hemoglobin	115 mg/dL	Negative	Negative	Positive	Positive
Human Serum Albumin	0.5 g/dL	Negative	Negative	Positive	Positive
Oxalic Acid	0.1 g/dL	Negative	Negative	Positive	Positive
Riboflavin	7.5 mg/dL	Negative	Negative	Positive	Positive
Sodium Chloride	6.0 g/dL	Negative	Negative	Positive	Positive
Urea	6.0 g/dL	Negative	Negative	Positive	Positive
Sodium Azide	1% w/v	Negative	Negative	Positive	Positive
Sodium Fluoride	1% w/v	Negative	Negative	Positive	Positive

Potential Interference (pH)	-40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
	Qualitative Result	Semi-Quantitative Result	Qualitative Result	Semi-Quantitative Result
pH 3	Negative	Negative	Positive	Positive
pH 4	Negative	Negative	Positive	Positive
pH 5	Negative	Negative	Positive	Positive
pH 6	Negative	Negative	Positive	Positive
pH 7	Negative	Negative	Positive	Positive
pH 8	Negative	Negative	Positive	Positive
pH 9	Negative	Negative	Positive	Positive
pH 11	Negative	Negative	Positive	Positive
Potential Interference (Specific Gravity)	-40% Cutoff (3 ng/mL)		+40% Cutoff (7 ng/mL)	
	Qualitative Result	Semi-Quantitative Result	Qualitative Result	Semi-Quantitative Result
sG 1.002	Negative	Negative	Positive	Positive
sG 1.005	Negative	Negative	Positive	Positive
sG 1.010	Negative	Negative	Positive	Positive
sG 1.015	Negative	Negative	Positive	Positive
sG 1.020	Negative	Negative	Positive	Positive
sG 1.025	Negative	Negative	Positive	Positive
sG 1.030	Negative	Negative	Positive	Positive
sG 1.035	Negative	Negative	Positive	Positive

d. Recovery/Linearity

Drug free urine pools were spiked with nine concentrations of buprenorphine at levels 2-25 ng/mL and analyzed semi-quantitatively in replicates of N= 5 on a Viva-E[®] analyzer. The mean observed Buprenorphine concentration was compared to the expected Buprenorphine concentration and percent recovery calculated.

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

e. Method Comparison

Split sample method comparison was conducted with one-hundred twenty seven (127) unaltered human urine samples, which were analyzed by the Emit[®] II Plus Buprenorphine Assay on a Viva-E[®] Analyzer vs. LC/MS/MS. The results are presented below:

Emit[®] II Plus Buprenorphine Assay vs. LC/MS/MS

	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%

Comparison Table for Qualitative and Semi-quantitative Assay Performance

Emit [®] II Plus Buprenorphine		LC/MS/MS	
		+	-
		+	65
-	1	54	

Discordant Result Summary

Sample ID	Emit [®] II Plus Buprenorphine (ng/mL)	LC/MS/MS			Emit +/-	LC/MS/MS +/-
		Bup (ng/mL)	NorBup (ng/mL)	Bup+NorBup (ng/mL)		
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	+	-
77	5.5	0	4.60	4.60	+	-
316	5.7	0	3.86	3.86	+	-
338	4.3	5.12	0	5.12	-	+

Bup = Buprenorphine; NorBup = Norbuprenorphine

f. Calibrator/Control and Cutoff Control Traceability

The Emit[®] II Plus Specialty Drug Calibrator/Control and Emit[®] II Plus Specialty Drug Control Negative and Control Positive are traceable to Cerilliant Buprenorphine Cat. No. B-902. When stored refrigerated at 2–8°C the calibrators/controls are stable opened or unopened until the expiration date printed on the vial label.

8. Conclusion

The information provided in this premarket notification demonstrates the Emit[®] II Plus Buprenorphine Assay, Emit[®] II Plus Specialty Drug Calibrator / Control, Emit[®] II Plus Specialty Drug Control Negative and Control Positive are substantially equivalent to the legally marketed predicate devices for their general intended use. Substantial equivalence was demonstrated through comparison of intended use and technological features to the commercially available predicate devices and confirmed by liquid chromatography/ tandem mass spectrometry (LC/MS/MS), a reference analytical method. The information in this pre-market notification provides reasonable assurance that the Emit[®] II Plus Buprenorphine Assay, Emit[®] II Plus Specialty Drug Calibrator / Control, Emit[®] II Plus Specialty Drug Control Negative and Control Positive demonstrate safety and effectiveness similar to the predicate devices - Microgenics CEDIA[®] Buprenorphine Assay, CEDIA[®] Buprenorphine Calibrators, and CEDIA[®] Buprenorphine Controls (cleared under K040316).