DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

April 6, 2017

MICROGENICS CORPORATION
MINOTI PATEL
SR. REGULATORY AFFAIRS SPECIALIST
46500 KATO ROAD
FREMONT CA 94538

Re: k163101
Trade/Device Name: CEDIA Buprenorphine II Assay
CEDIA Buprenorphine II Calibrators and
CEDIA Negative Calibrator II
CEDIA Buprenorphine II Control Set
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate test system
Regulatory Class: II
Product Code: DJG, DLJ, LAS
Dated: March 17, 2017
Received: March 20, 2017

Dear Minoti Patel:

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k163101

Device Name
CEDIA Buprenorphine II Assay
CEDIA Buprenorphine II Calibrators and CEDIA Negative Calibrator II
CEDIA Buprenorphine II Control Set

Indications for Use *(Describe)*

CEDIA Buprenorphine II Assay:
The CEDIA Buprenorphine II Assay is a homogeneous enzyme immunoassay for the qualitative and/or semiquantitative determination for the presence of buprenorphine and its metabolites in human urine at a cut-off concentration of 10 ng/mL. The assay is intended to be used in laboratories and provides a simple and rapid analytical screening procedure to detect buprenorphine and its metabolites in human urine. The assay is designed for use with a number of clinical 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 Liquid chromatography/tandem mass spectrometry (LC-MS/MS) or permitting laboratories to establish quality control procedures.

The 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) or Liquid chromatography/tandem mass spectrometry (LC-MS/MS) is the preferred confirmatory method.
Clinical and professional judgment should be applied to any drug of abuse test result, particularly when preliminary results are used. For In Vitro Diagnostic Use Only.

CEDIA Buprenorphine II Calibrators:
The CEDIA Buprenorphine II calibrators and CEDIA Negative Calibrator II are intended for the calibration of the CEDIA Buprenorphine II Assay in human urine. For In Vitro Diagnostic Use Only.

CEDIA Buprenorphine II Control Set:
The CEDIA Buprenorphine II controls are used to validate the CEDIA Buprenorphine II Assay calibration in human urine. For In Vitro Diagnostic Use Only.

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

A. Device Information

Category	Comments
Sponsor:	Microgenics Corporation Thermo Fisher Scientific 46500 Kato Road Fremont, CA 94538 Phone: 510-979-5000 FAX: 510-979-5002
Correspondent Contact Information:	Minoti Patel, RAC Sr. Regulatory Affairs Specialist Email: Minoti.patel@thermofisher.com Phone: 510-749-5000 FAX: 510-749-5002
Device Common Name:	Buprenorphine Immunoassay Test System
Trade or Proprietary Name	CEDIA® Buprenorphine II Assay CEDIA® Buprenorphine II Calibrators CEDIA® Negative Calibrator II CEDIA® Buprenorphine II Control Set
Predicate Device Product Code, Classification, Classification Name & Panel	DJG, Class II, 21 CFR 862.3650 – Opiate test system, 91 – Toxicology DLJ, Class II, 21 CFR 862.3200 – Clinical toxicology control material, 91 – Toxicology LAS, Class I, reserved; 21 CFR 862.3280 – Clinical toxicology control material, 91 – Toxicology

Predicate Device Information:

Predicate Device:	CEDIA® Buprenorphine Assay CEDIA® Negative Calibrator II CEDIA® Buprenorphine Calibrators CEDIA® Buprenorphine Control Set
Predicate Device Manufacturer:	Microgenics Corporation
Predicate Device Common Name:	Buprenorphine Immunoassay Test System
Predicate Device Premarket Notification #:	K040316
Predicate Device Product Code, Classification, Classification Name & Panel	DJG, Class II, 21 CFR 862.3650 – Opiate test system, 91 – Toxicology DLJ, Class II, 21 CFR 862.3200 – Clinical toxicology control material, 91 – Toxicology LAS, Class I, reserved; 21 CFR 862.3280 – Clinical toxicology control material, 91 – Toxicology

B. Date Summary Revised

April 04, 2017

C. Description of Device

The assay consists of buffers (1 and 2) and lyophilized reagents (1a and 2a). The components include mouse monoclonal anti-buprenorphine antibody, recombinant microbial "enzyme donor" – buprenorphine conjugate, "enzyme acceptor", chlorophenol red β-D-galactopyranoside, stabilizers and preservatives. Calibrators and controls are sold separately.

D. Intended Use

Intended Use:

CEDIA® Buprenorphine II Assay:

The CEDIA® Buprenorphine II Assay is a homogeneous enzyme immunoassay for the qualitative and/or semiquantitative determination for the presence of buprenorphine and its metabolites in human urine at a cut-off concentration of 10 ng/mL. The assay is intended to be used in laboratories and provides a simple and rapid analytical screening procedure to detect buprenorphine and its metabolites in human urine. The assay is designed for use with a number of clinical 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 Liquid chromatography/tandem mass spectrometry (LC-MS/MS) or permitting laboratories to establish quality control procedures.

The 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) or Liquid chromatography/tandem mass spectrometry (LC-MS/MS) is the preferred confirmatory method.

Clinical and professional judgment should be applied to any drug of abuse test result, particularly when preliminary results are used. For In Vitro Diagnostic Use Only.

CEDIA® Buprenorphine II Calibrators:

The CEDIA® Buprenorphine II calibrators and CEDIA® Negative Calibrator II are intended for the calibration of the CEDIA® Buprenorphine II Assay in human urine. For *In Vitro* Diagnostic Use Only.

CEDIA® Buprenorphine II Control Set:

The CEDIA® Buprenorphine II controls are used to validate the CEDIA® Buprenorphine II Assay calibration in human urine. For *In Vitro* Diagnostic Use Only.

E. Comparison to Predicate Device

Both devices use similar reagent and instrument systems. Both devices detect buprenorphine. The predicate device's specific antibody detects buprenorphine and buprenorphine glucuronide at cutoff concentration of 5 ng/mL. The CEDIA device's specific antibody detects buprenorphine, buprenorphine glucuronide, norbuprenorphine and norbuprenorphine

glucuronide at a buprenorphine cutoff concentration of 10 ng/ml. Other differences and similarities are presented below.

Similarities - Assay		
Item	Device	k040316 – Microgenics CEDIA Buprenorphine Assay
Intended Use	Same	Detection of buprenorphine in human urine
Methodology	Same	CEDIA (Cloned Enzyme Donor Immunoassay)
Intended Users	Same	Prescription users only
Reagents Form	Same	Lyophilized (requiring reconstitution) and liquid ready to use
Antibody	Same	Mouse monoclonal
Storage	Same	2 – 8^{o} C until expiration date
Target Analyte	Same	Buprenorphine

Differences - Assay		
Item	Device	Predicate
Cutoff	10 ng/mL	5 ng/mL

Similarities – Calibrators		
Item	Device	Predicate
Form	Same	Liquid – ready to use
Storage	Same	2 – 8^{o} C until expiration date

Differences - Calibrators		
Item	Device	Predicate
Calibrator Name	CEDIA® Buprenorphine II calibrators and controls	CEDIA® Buprenorphine calibrators and controls
Calibrator Levels	0, 10, 20, 50, 100 ng/mL	0, 5, 20, 50, 75 ng/mL

Similarities – Controls		
Item	Device	Predicate
Form	Same	Liquid – ready to use
Storage	Same	2 – 8° C until expiration date

Differences - Controls		
Item	Device	Predicate
Control Names	CEDIA® Buprenorphine II controls	CEDIA® Buprenorphine controls
Control Levels	7.5 and 12.5 ng/mL	3 and 7 ng/mL
Form	Same	Liquid – ready to use
Storage	Same	2 – 8° C until expiration date

F. Test Principle

The assay is based on bacterial enzyme β-galactosidase genetically engineered to two inactive fragments, one of which is conjugated to buprenorphine. Buprenorphine in the sample competes with the enzyme fragment-conjugated buprenorphine for binding to anti-buprenorphine antibody. In the absence of buprenorphine in the sample, the fragment binds antibody and does not re-associate to form active enzyme. If buprenorphine is present in the sample it binds to the antibody, allowing the enzyme fragments to re-associate. The re-associated enzyme cleaves the substrate, generating a color change that can be measured spectrophotometrically (570/660 nm). The amount of active enzyme is proportional to the analyte present.

G. Summary of Supporting Data

1. Analytical Performance:

Performance is evaluated at the manufacturer's site on Beckman Coulter AU 680 Analyzer.

a) **Precision –** Study is performed for two runs per day, twice a day, for 20 days (total n=80). Samples are prepared by spiking Buprenorphine into drug free urine at the cutoff, 25%, 50%, 75% & 100% above and below the cutoff and tested in both qualitative and semi-quantitative modes. Representative data is presented below.

Qualitative Results:

% of Cutoff	Spiked Conc. (ng/mL)	LC-MS/MS (ng/mL)	Within Run (n=80)	
			Number of determinants	Immunoassay Results
-100%	0	0	80	80 Neg
-75%	2.5	2.99	80	80 Neg
-50%	5	5.31	80	80 Neg
-25%	7.5	7.63	80	80 Neg
100%	10	10.99	80	27 Neg/53 Pos
+25%	12.5	12.97	80	80 Pos

% of Cutoff	Spiked Conc. (ng/mL)	LC-MS/MS (ng/mL)	Within Run (n=80)	
			Number of determinants	Immunoassay Results
+50%	15	15.05	80	80 Pos
+75%	17.5	18.92	80	80 Pos
+100%	20	20.38	80	80 Pos

Semi-Quantitative Results:

% of Cutoff	Spiked Conc. (ng/mL)	LC-MS/MS (ng/mL)	Within Run (n=80)	
			Number of determinants	Immunoassay Results
-100%	0	0	80	80 Neg
-75%	2.5	2.99	80	80 Neg
-50%	5	5.31	80	80 Neg
-25%	7.5	7.63	80	80 Neg
100%	10	10.99	80	35 Neg/45 Pos
+25%	12.5	12.97	80	80 Pos
+50%	15	15.05	80	80 Pos
+75%	17.5	18.92	80	80 Pos
+100%	20	20.38	80	80 Pos

b) **Spike Recovery** - All 20 replicates of spiked 7.5 ng/mL and 12.5 ng/mL sample detect as Negative and Positive, respectively, when compared to 10 ng/mL spiked sample.

In semi-quantitative mode, the spiked samples recover within 80–120% of the nominal values.

c) **Analytical Recovery and Dilution Linearity** - To demonstrate the dilution linearity for purpose of sample dilution and quality control of the entire assay range, drug free urine is spiked to the high calibrator level of Buprenorphine (100 ng/mL) and diluted with drug free urine to generate 10 intermediate levels.

Each sample is run in replicates of five in semi-quantitative mode and the average is used to determine percent recovery compared to the expected target value. Representative data is presented below.

Level	**Target Concentration (ng/mL)**	**Observed Concentration (ng/mL)**	**Recovery (%)**
1	0	-0.09	n/a
2	5	5.99	119.8
3	10	10.97	109.7
4	20	19.66	98.3
5	30	33.03	110.1
6	40	43.83	109.6

Level	Target Concentration (ng/mL)	Observed Concentration (ng/mL)	Recovery (%)
7	50	52.98	106.0
8	60	67.28	112.1
9	70	77.54	110.8
10	80	85.14	106.4
11	90	95.38	106.0
12	100	104.70	104.7

d) **Method Comparison and Accuracy** - One hundred and fifty three urine patient samples are analyzed by the CEDIA® Buprenorphine II Assay in both qualitative and semi-quantitative modes and the results are compared to LC-MS/MS.

Qualitative mode using stratified Buprenorphine values by LC-MS/MS

Candidate Device Results	Negative	<50% of Cutoff concentration by LC-MS/MS (<5ng/mL)	Near Cutoff Negative (Between 50% below the cutoff concentration as determined by LC-MS/MS) (5-9.9ng/mL)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration as determined by LC-MS/MS) (10-15ng/mL)	High Positives (Greater than 50% above cutoff concentration) (>15ng/mL)
Positive	31*	11*	4*	5	45
Negative	49	2	6	0	0

* Discordant samples summarized in table 5 below.

Semi-Quantitative mode using stratified Buprenorphine values by LC-MS/MS

Candidate Device Results	Negative	<50% of Cutoff concentration by LC-MS/MS (<5ng/mL)	Near Cutoff Negative (Between 50% below the cutoff concentration as determined by LC-MS/MS) (5-9.9ng/mL)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration as determined by LC-MS/MS) (10-15ng/mL)	High Positives (Greater than 50% above cutoff concentration) (>15ng/mL)
Positive	32* ǂ	11*	4*	5	45
Negative	48	2	6	0	0

* Discordant samples summarized in table 5 below.

ǂ Additional discordant sample (ID #53) in Lot #3 Semi-quantitative mode shown in table 5 below.

***Table for Discordant Samples**

Accuracy samples were categorized based upon the LC-MS/MS concentration for Buprenorphine only. The table below identifies those samples with Buprenorphine concentration below the cutoff, in which the observed CEDIA Buprenorphine II assay result was positive.

	EIA		LC-MS/MS Concentration (ng/mL)				
Sample ID	Qual mode	SQ (ng/mL)	Bup***	NorBup[#]	Bup-Glu[†]	NorBup-Glu[‡]	Total by LC-MS/MS
51	Pos	10.08	<LLOQ **	2.27	1.96	6.18	10.41
52	Pos	10.02	<LLOQ	0.69	3.15	6.84	10.68
53[╫]	Neg	10.42	<LLOQ	1.08	7.89	1.82	10.79
54	Pos	11.59	<LLOQ	1.09	5.67	5.54	12.30
55	Pos	10.40	<LLOQ	3.27	2.54	7.92	13.73
56	Pos	16.36	<LLOQ	4.02	7.46	3.73	15.21
57	Pos	17.31	<LLOQ	3.28	10.67	3.09	17.04
58	Pos	19.82	<LLOQ	5.03	10.91	2.05	17.99
59	Pos	18.73	<LLOQ	3.10	9.09	6.59	18.78
60	Pos	22.63	<LLOQ	4.18	8.30	7.34	19.82
61	Pos	18.95	<LLOQ	1.96	9.90	9.90	21.76
62	Pos	26.11	<LLOQ	4.36	10.87	6.92	22.15
63	Pos	24.99	<LLOQ	5.26	8.41	9.01	22.68
64	Pos	24.91	<LLOQ	3.86	23.19	<LLOQ	27.05
65	Pos	20.87	<LLOQ	1.44	14.06	14.06	29.56
66	Pos	23.21	<LLOQ	2.23	25.24	2.50	29.97
67	Pos	30.27	<LLOQ	4.42	8.82	16.84	30.08
68	Pos	31.35	<LLOQ	16.52	9.41	5.47	31.40
69	Pos	35.38	<LLOQ	7.13	5.30	22.38	34.81
70	Pos	40.38	<LLOQ	12.21	18.65	9.11	39.97
71	Pos	38.44	<LLOQ	2.93	12.40	28.84	44.17
72	Pos	48.60	<LLOQ	23.41	15.34	5.44	44.19
73	Pos	62.31	<LLOQ	5.47	36.52	25.00	66.99
74	Pos	81.31	<LLOQ	33.59	23.42	12.72	69.73
75	Pos	88.67	<LLOQ	26.22	32.43	23.10	81.75
76	Pos	79.26	<LLOQ	6.34	80.00	2.77	89.11
77	Pos	>100.01	<LLOQ	8.63	56.89	46.95	112.47
78	Pos	>100.01	<LLOQ	101.98	10.40	9.90	122.28
79	Pos	>100.01	<LLOQ	7.91	26.43	144.00	178.34
80	Pos	>100.01	<LLOQ	49.66	97.61	121.12	268.39
81	Pos	>100.01	<LLOQ	<LLOQ	145.72	394.81	540.53
82	Pos	>100.01	<LLOQ	129.95	105.07	664.47	899.49

	EIA		LC-MS/MS Concentration (ng/mL)				
Sample ID	Qual mode	SQ (ng/mL)	Bup***	NorBup[#]	Bup-Glu[†]	NorBup-Glu[‡]	Total by LC-MS/MS
83	Pos	>100.01	0.81	32.14	39.52	59.14	131.61
84	Pos	63.54	0.86	7.41	29.46	31.38	69.11
85	Pos	20.48	0.90	5.42	11.54	<LLOQ	17.86
86	Pos	>100.01	0.91	54.00	18.10	10.52	83.53
87	Pos	46.32	2.00	12.03	13.58	16.24	43.85
88	Pos	>100.01	2.00	6.83	193.42	131.65	333.90
89	Pos	>100.01	2.02	75.75	174.74	442.98	695.49
90	Pos	66.32	2.48	6.53	57.67	1.52	68.20
91	Pos	>100.01	3.63	80.26	733.7	624.02	1441.61
92	Pos	>100.01	4.38	69.28	146.16	349.33	569.15
93	Pos	>100.01	4.45	59.03	55.01	17.31	135.80
100	Pos	>100.01	8.64	36.91	>ULOQ**	224.42	>1000
101	Pos	>100.01	8.94	51.32	497.32	55.06	612.64
102	Pos	>100.01	5.22	35.13	85.99	22.24	148.58
103	Pos	77.36	6.60	147.58	195.67	40.28	390.13

** <LLOQ: Lower Limit of Quantitation (0.65 ng/mL), >ULOQ: Upper Limit of Quantitation (1000ng/mL);
*** Bup: Buprenorphine;
[#] NorBup: Norbuprenorphine;
† Bup-Glu: Buprenorphine-β-D-glucuronide;
‡ NorBup-Glu: Norbuprenorphine-β-D-glucuronide;
ǂ Additional discordant sample for Lot #3 Semi-Quantitative mode

e) **Specificity** - The cross-reactivity of Buprenorphine and its metabolites is evaluated by adding known amounts of each analyte to drug-free negative urine. As indicated by the results in the table below, Buprenorphine, Norbuprenorphine and Norbuprenorphine-β-D-glucuronide exhibit ≥ 100% cross-reactivity. Buprenorphine-β-D-glucuronide showed 76.9% cross-reactivity.

Buprenorphine and its metabolites	Tested Concentration (ng/mL)	Positive/ Negative	Cross-reactivity (%)
Buprenorphine	10	Positive	100
Norbuprenorphine	8	Positive	125
Buprenorphine-β-D-glucuronide	13	Positive	76.9
Norbuprenorphine-β-D-glucuronide	10	Positive	100

Cross Reactivity of Structurally Related or Unrelated Opiate Compounds

Structurally Related Compounds and Other Opiates	Tested Concentration (ng/mL)	Positive/ Negative	Cross-reactivity (%)
6-Acetyl morphine	100,000	Negative	< 0.01
Diacetylmorphine (Heroin)	100,000	Negative	< 0.01
Codeine	100,000	Negative	< 0.01
Dextromethorphan	100,000	Negative	< 0.01
Dihydrocodeine	100,000	Negative	< 0.01
EDDP (2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine)	100,000	Negative	< 0.01
EMDP (2-Ethyl-5-methyl-3,3-diphenylpyrroline)	100,000	Negative	< 0.01
Fentanyl	100,000	Negative	< 0.01
Hydrocodone	100,000	Negative	< 0.01
Hydromorphone	100,000	Negative	< 0.01
Hydromorphone-β-D-glucuronide	10,000	Negative	< 0.1
LAAM (Levo-alpha-acetylmethadol)	100,000	Negative	< 0.01
Levorphanol	100,000	Negative	< 0.01
Methadone	100,000	Negative	< 0.01
Meperidine	100,000	Negative	< 0.01
Morphine	100,000	Negative	< 0.01
Morphine-3β-D-glucuronide	100,000	Negative	< 0.01
Morphine-6β-D-glucuronide	100,000	Negative	< 0.01
Nalorphine	100,000	Negative	< 0.01
Naloxone	100,000	Negative	< 0.01
Naltrexone	100,000	Negative	< 0.01
Norcodeine	100,000	Negative	< 0.01
Norhydrocodone	100,000	Negative	< 0.01
Norpropoxyphene	100,000	Negative	< 0.01
Noroxycodone	100,000	Negative	< 0.01
Noroxymorphone	100,000	Negative	< 0.01
Oxymorphone-β-D-glucuronide	10,000	Negative	< 0.1
Oxycodone	100,000	Negative	< 0.01
Oxymorphone	100,000	Negative	< 0.01
Tapentadol	100,000	Negative	< 0.01
Tramadol	100,000	Negative	< 0.01

The potential cross-reactivity posed by drugs commonly co-administered with Buprenorphine is evaluated by adding each substance to Buprenorphine spiked at Low Control (7.5 ng/mL) and High Control (12.5 ng/mL) levels at the concentrations indicated. A drug is considered to cross-react if the observed Buprenorphine concentrations result exceed 10 ng/mL. As shown in the table below, all the pharmacologic compounds evaluated exhibited negligible cross reactivity at the concentrations tested.

Structurally Unrelated Compounds Spiked at the Concentration Listed Below into Low Control and High Control

Compound	Tested Concentration (ng/mL)	Spiked Buprenorphine Level	
		Low Control	High Control
Negative Urine	0	Negative	Positive
Acetaminophen	500,000	Negative	Positive
Acetylsalicylic acid	500,000	Negative	Positive
Amitryptyline	50,000	Negative	Positive
Amoxicillin	100,000	Negative	Positive
Amphetamine	1,000,000	Negative	Positive
Amisulpride	100,000	Negative	Positive
Benzoylecgonine	1,000,000	Negative	Positive
Caffeine	100,000	Negative	Positive
Carbamazepine	100,000	Negative	Positive
Chlorpromazine	100,000	Negative	Positive
Clomipramine	25,000	Negative	Positive
Chloroquine	100,000	Negative	Positive
Cimetidine	500,000	Negative	Positive
Desipramine	10,000	Negative	Positive
Doxepine	25,000	Negative	Positive
Diphenylhydramine	100,000	Negative	Positive
Ephedrine	100,000	Negative	Positive
Fluoxethine	100,000	Negative	Positive
Fluphenazine	100,000	Negative	Positive
Hydroxychloroquine	100,000	Negative	Positive
Ibuprofen	100,000	Negative	Positive
Imipramine	25,000	Negative	Positive
Maprotiline	100,000	Negative	Positive
Mitragynine	100,000	Negative	Positive
7-OH Mitragynine	10,000	Negative	Positive
Nalbuphine	100,000	Negative	Positive
Nortryptiline	50,000	Negative	Positive
Oxazepam	100,000	Negative	Positive
Phencyclidine	100,000	Negative	Positive
Phenobarbital	100,000	Negative	Positive
Ranitidine	500,000	Negative	Positive
Secobarbital	100,000	Negative	Positive
Sulpiride	100,000	Negative	Positive
Thioridazine	100,000	Negative	Positive
Trimipramine	25,000	Negative	Positive

f) **Interference** - The potential interference of pH and endogenous physiologic substances on recovery of Buprenorphine using CEDIA® Buprenorphine II Assay is assessed by spiking known compounds of potentially interfering substances into the Low Control (7.5 ng/mL) and High Control (12.5 ng/mL). In the presence of the compounds listed below, the controls are detected accurately, indicating that these compounds did not show interference in the assay.

Compound	Tested Concentration (mg/dL)	Spiked Buprenorphine Level	
		Low Control	High Control
Negative Urine	0	Negative	Positive
Acetaminophen	10	Negative	Positive
Acetone	500	Negative	Positive
Acetyl Salicylic Acid	10	Negative	Positive
Ascorbic Acid	150	Negative	Positive
Caffeine	10	Negative	Positive
Creatinine	400	Negative	Positive
Ethanol	10	Negative	Positive
Galactose	5	Negative	Positive
Glucose	1000	Negative	Positive
Hemoglobin	150	Negative	Positive
Human Serum Albumin	200	Negative	Positive
Ibuprophen	10	Negative	Positive
Oxalic acid	50	Negative	Positive
Riboflavin	3	Negative	Positive
Sodium Chloride	1000	Negative	Positive
Urea	1000	Negative	Positive
pH			
pH	3	Negative	Positive
pH	4	Negative	Positive
pH	5	Negative	Positive
pH	6	Negative	Positive
pH	7	Negative	Positive
pH	8	Negative	Positive
pH	9	Negative	Positive
pH	10	Negative	Positive
pH	11	Negative	Positive

Specific Gravity - Drug free urine samples with specific gravity ranging in value within 1.000 to 1.030 are split and spiked to a final concentration of either 7.5 ng/mL or 12.5 ng/mL (the Low Control and High Control concentrations, respectively). These samples are then evaluated in both qualitative and semi-quantitative modes. No interference is observed.

	Spiked Buprenorphine Concentration	
Specific Gravity	Low Control	High Control
1.002	Negative	Positive
1.004	Negative	Positive
1.008	Negative	Positive
1.013	Negative	Positive
1.016	Negative	Positive
1.018	Negative	Positive

	Spiked Buprenorphine Concentration	
Specific Gravity	Low Control	High Control
1.022	Negative	Positive
1.023	Negative	Positive
1.025	Negative	Positive
1.030	Negative	Positive

g) **Stability**

Open Vial Stability:

Open Vial stability studies for two lots stored at 2–8°C supports the claim of 60 days for qualitative and semi-quantitative modes.

Reagent On-Board Stability:

Reagent On-Board stability studies for two lots stored on-board clinical analyzer supports the claim of 60 days for qualitative and semi-quantitative modes.

Reconstituted Reagent Stability:

Reconstituted Reagent stability studies for two lots stored at 2–8°C supports the claim of 60 days for qualitative and semi-quantitative modes.

Real Time Stability for Reagent, Calibrators and Controls

Real time stability studies for three lots of reagents, calibrators and controls stored at 2–8°C are ongoing and have been carried out for up to six months.

Accelerated Stability Results for Reagents, Calibrators and Controls

Accelerated stability testing results show that the Low Control is detected as negative and the High Control is detected as positive for each time point for a period of six months at 23°±2°C. This is equivalent to 19 months of stability based on Q10 math model. The recoveries of the Low Control and High Control are within 80–120%. The data for six month accelerated stability confirms that the Low Control and the High Control are detected as negative and positive, respectively.

H. Conclusion

Comparison of CEDIA® Buprenorphine II Assay, Calibrators, Controls and CEDIA® Negative Calibrator II and predicate devices demonstrated that the technological characteristics and intended use are substantially equivalent to the currently marketed predicate devices, CEDIA® Buprenorphine Assay, (K040316)