510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number
K253082

B Applicant
Lin-Zhi International, Inc

C Proprietary and Established Names
Proprietary name: LZI Buprenorphine II Enzyme Immunoassay
Common name: Homogeneous Buprenorphine Enzyme Immunoassay

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DJG	II	21 CFR 862.3650	91-Toxicology

II Submission/Device Overview:

A Purpose for Submission:
Modification to previously cleared assay

B Measurand:
Norbuprenorphine (buprenorphine metabolite)

C Type of Test:
Homogeneous enzyme immunoassay – qualitative and semi- quantitative

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
The LZI Buprenorphine II Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of norbuprenorphine in human urine at the cutoff

value of 5 ng/mL when calibrated against norbuprenorphine. The assay is designed for prescription use with a number of automated clinical chemistry analyzers.
The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) or (2) permitting laboratories to establish quality control procedures

The assay provides only a preliminary analytical result. A more specific alternative chemical method (e.g., gas or liquid chromatography and mass spectrometry) must be used in order to obtain a confirmed analytical result. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

C Special Conditions for Use Statement(s):
The assay is for prescription use.

D Special Instrument Requirements:
Automated clinical chemistry analyzers. (Performance in the studies submitted in the 510(k) are based on the Beckman Coulter AU480 Analyzer.

IV Device/System Characteristics:

A Device Description:

The LZI Buprenorphine II Enzyme Immunoassay is a kit comprised of two reagents, R1 and R2, which are bottled separately but sold together within the kit.

The R1 solution contains mouse monoclonal anti-norbuprenorphine antibody, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide (NAD), stabilizers, and sodium azide (0.09%) as a preservative. The R2 solution contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with norbuprenorphine in buffer with sodium azide (0.09%) as a preservative.

B Principle of Operation:

The LZI Buprenorphine II Enzyme Immunoassay is a homogeneous enzyme immunoassay ready-to-use liquid reagent. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the drug concentration in the sample is measured in terms of enzyme activity. In the absence of drug in the sample, norbuprenorphine-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when drug is present in the sample, antibody would bind to free drug; the unbound norbuprenorphine-labeled G6PDH then exhibits its maximal enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that can be measured spectrophotometrically at 340 nm.

V Substantial Equivalence Information:

A Predicate Device Name(s): LZI Buprenorphine Enzyme Immunoassay

B Predicate 510(k) Number(s): k090844

C Comparison with Predicate(s):

Device & Predicate Device(s):	K253082	K090844
Device Trade Name	LZI Buprenorphine II Enzyme Immunoassay	LZI Buprenorphine Enzyme Immunoassay
General Device Characteristic Similarities		
Intended Use	For the qualitative and semi-quantitative determination of norbuprenorphine in human urine at the cutoff value of 5 ng/mL when calibrated against norbuprenorphine. The assay is designed for prescription use with a number of automated clinical chemistry analyzers. ***The assay provides only a preliminary analytical result. A more specific alternative chemical method (e.g., gas or liquid chromatography and mass spectrometry) must be used in order to obtain a confirmed analytical result.***	Same

Analyte	norbuprenorphine	Same
Matrix	Urine	Same
Storage	2-8 ºC until expiration date	Same
Detection	Absorbance change measured spectrophotometrically at 340 nm	Same
User Environment	Clinical laboratories: Prescription use only	Same
Mass Spectrometry Confirmation	Required to confirm preliminary positive analytical results	Same
Platform Required	Automated clinical chemistry analyzer	Same
Reagents Form	Liquid – ready-to-use	Same
General Device Characteristic Differences		
Cutoff	5 ng/mL	5 ng/mL and 10 ng/mL
Instrument for performance validation	Beckman Coulter AU480	Hitachi 717
Calibrator Level	0, 2.5, 5, 10, and 20 ng/mL	0, 5, 10, 20, 40, and 75 ng/mL
Controls Level	5 ng/mL Cutoff: 2 Levels: 3.75 and 6.25 ng/mL 10 ng/mL Cutoff: 2 Levels 7 and 13 ng/mL	5 ng/mL Cutoff: 2 Levels: 3 and 7 ng/mL 10 ng/mL Cutoff: 2 Levels 7 and 13 ng/mL

VI Standards/Guidance Documents Referenced:

No device-specific guidance documents or special controls are applicable to the LZI Buprenorphine II Enzyme Immunoassay under the classification regulation 21 CFR 862.3650 (Product Code: DJG).

VII Performance Characteristics (if/when applicable):

All 510(k) studies below were conducted on the Beckman Coulter AU480 Analyzer

A Analytical Performance:

1. Precision/Reproducibility:

Spiked samples of norbuprenorphine were prepared in a urine matrix at the concentrations shown in the table below, and were measured, 2 runs per day, with 2 replicates per run, for 22 days.
Results are tabulated below:

Precision: 5 ng/mL Cutoff

Semi-Quantitative Positive/Negative Results:

5 ng/mL Cutoff Result:		**Within Run (N=22)**		**Total Precision (N=88)**	
Norbuprenorphine Concentration	**% of Cutoff**	**Number of Determination**	**Immunoassay Result**	**Number of Determination**	**Immunoassay Result**
0 ng/mL	0%	22	22 Negative	88	88 Negative
1.25 ng/mL	25%	22	22 Negative	88	88 Negative
2.5 ng/mL	50%	22	22 Negative	88	88 Negative
3.75 ng/mL	75%	22	22 Negative	88	88 Negative
5 ng/mL	100%	22	22 Positive	88	2 Neg / 86 Pos
6.25 ng/mL	125%	22	22 Positive	88	88 Positive
7.5 ng/mL	150%	22	22 Positive	88	88 Positive
8.75 ng/mL	175%	22	22 Positive	88	88 Positive
10 ng/mL	200%	22	22 Positive	88	88 Positive

Semi-Quantitative Precision Analysis Summary (ng/mL):

Norbuprenorphine concentration	Within Run (N=22)		Total Precision (N=88)	
	SD	%CV	SD	%CV
0 ng/mL	0.15	N/A	0.2	N/A
1.25 ng/mL	0.17	12.0%	0.21	14.6%
2.5 ng/mL	0.17	6.4%	0.24	8.8%
3.75 ng/mL	0.19	4.7%	0.28	6.9%
5 ng/mL	0.19	3.5%	0.24	4.4%
6.25 ng/mL	0.19	2.8%	0.27	4.0%
7.5 ng/mL	0.2	2.5%	0.24	3.0%
8.75 ng/mL	0.21	2.2%	0.26	2.8%
10 ng/mL	0.3	2.8%	0.36	3.4%

Qualitative Positive/Negative Results:

5 ng/mL Cutoff Result:		5 ng/mL Cutoff Result:		Total Precision (N=88)	
Norbuprenorphine Concentration	**% of Cutoff**	**Number of Determination**	**Immunoassay Result**	**Number of Determination**	**Immunoassay Result**
0 ng/mL	0%	22	22 Negative	88	88 Negative
1.25 ng/mL	25%	22	22 Negative	88	88 Negative
2.5 ng/mL	50%	22	22 Negative	88	88 Negative
3.75 ng/mL	75%	22	22 Negative	88	88 Negative
5 ng/mL	100%	22	1 Neg / 21 Pos	88	19 Neg / 69 Pos
6.25 ng/mL	125%	22	22 Positive	88	88 Positive
7.5 ng/mL	150%	22	22 Positive	88	88 Positive
8.75 ng/mL	175%	22	22 Positive	88	88 Positive
10 ng/mL	200%	22	22 Positive	88	88 Positive

2. Linearity/Reportable range:

   To demonstrate linearity in the semiquantitative mode, which is used for purposes of sample dilution and quality control procedures, a drug-free urine pool spiked with norbuprenorphine 20 ng/mL was serially diluted in increments of 10% and results were obtained. The recovery of norbuprenorphine spiked to various concentrations was evaluated and the average recovery from these 10 replicates was used to determine the functional linearity range of the assay. The average recovery across the linear range of the assay was found to range between 99.6% - 106.3%.

3. Analytical Specificity/Interference:
   Various potentially interfering substances were evaluated for positive and negative interference with the assay. Test compounds were spiked into a buprenorphine-free sample, as well as samples containing buprenorphine at 3.75 ng/mL or 6.25 ng/mL, (as negative or positive controls, ±25% of the cutoff concentration, respectively). Samples were then evaluated against the assay's calibration curve in qualitative mode.

   Negative interference was observed with Boric Acid at 1% w/v. at ± 50% of the cutoff concentration. No other significant cross-reactivity was observed. The potential interferents and the concentrations at which they were tested are shown below:

Interfering Substance	**Concentration of Compound (mg/dL)**
Acetone	1,000
Ascorbic acid	500
Bilirubin	2
Biotin	2
Boric acid	1,000
Calcium chloride	300
Citric acid	200
Creatinine	500

Ethanol	1,000
Galactose	10
γ-Globulin	500
Glucose	3,000
Hemoglobin	300
Human urine (pooled)	N/A
Human serum albumin	500
β-Hydroxybutyric acid	100
Oxalic acid	100
Potassium chloride	1,000
Riboflavin	7.5
Sodium azide	1,000
Sodium chloride	1,000
Sodium fluoride	1,000
Sodium phosphate	300
Urea	6,000
Uric acid	10
Urine-based calibrator buffer	N/A

Cross reactivity of various potentially interfering drugs was evaluated by spiking various concentrations of each substance up to 100,000 ng/mL of buprenorphine metabolites into a pool of drug-free human urine. Results for both 5 and 10 cutoffs are shown below:

Cross reactivity: 5 cutoff

Buprenorphine and Major Metabolites:

Compound	**Test Concentration (ng/mL)**	**Semi-Quantitative Result (ng/mL)**	**% Cross-reactivity**
Norbuprenorphine	10	10.5	100.0%
Buprenorphine	10	10.5	100.0%
Buprenorphine Glucuronide	105	12.0	9.5%
Norbuprenorphine Glucuronide	600	10.5	1.7%

The sponsor also tested a list of structurally related and un-related Opiate compounds. Results are shown below:

Structurally related or unrelated Opiate compounds:

Compound	**Test Concentration (ng/mL)**	**Qualitative Result (mAU)**	**Semi-Quantitative Result (ng/mL)**	**% Cross-reactivity**

Codeine	100,000	-17.2	-0.98	ND
Codeine 6ß D-Glucuronide	100,000	0.0	0.18	ND
Dextromethorphan	100,000	14.3	1.43	ND
Dextrorphan Tartrate	100,000	-7.3	-0.15	ND
Dihydrocodeine	100,000	3.5	0.51	ND
Dihydromorphine	100,000	-7.4	-0.23	ND
EDDP	100,000	-6.0	-0.08	ND
EMDP	100,000	12.1	1.28	ND
Ethylmorphine	100,000	-8.0	-0.15	ND
Fentanyl	100,000	-22.4	-0.66	ND
Heroin	100,000	-8.8	-0.09	ND
Hydrocodone	100,000	-18.4	-0.63	ND
Hydromorphone	100,000	-20.8	-0.81	ND
Hydromorphone 3ß D- Glucuronide	10,000	-5.0	-0.02	ND
LAAM	100,000	12.3	1.33	ND
Levorphanol	100,000	-5.8	-0.05	ND
Meperidine	100,000	12.6	1.38	ND
Meperidine	100,000	-15.6	-0.68	ND
Methadone	100,000	-18.7	-0.73	ND
Morphine	100,000	-11.8	-0.73	ND
Morphine 3ß D-Glucuronide	100,000	-6.0	-0.32	ND
Morphine 6 D-Glucuronide	100,000	-3.1	0.24	ND
N-Desmethyl-cis-Tramadol	100,000	-7.5	-0.10	ND
Nalbuphine	100,000	-5.8	-0.21	ND
Nalorphine	100,000	-2.1	0.12	ND
Naloxegol	100,000	36.9	1.86	ND
Naloxone	100,000	1.0	-0.20	ND
Naltrexone	100,000	15.2	1.26	ND
Norcodeine	100,000	-8.9	-0.35	ND
Norhydrocodone	100,000	-7.4	-0.09	ND
Normorphine	100,000	-8.6	-0.27	ND
Noroxycodone	100,000	-4.6	-0.05	ND
Noroxymorphone	100,000	-4.5	0.29	ND
Norpropoxyphene	100,000	12.0	1.40	ND
O-Desmethyl-cis-Tramadol	100,000	-8.5	-0.36	ND
Oxycodone	100,000	-13.5	-0.57	ND
Oxymorphone	100,000	-15.6	-0.80	ND
Oxymorphone 3ß D- Glucuronide	10,000	-3.9	0.14	ND
Pentazocine	100,000	-8.2	-0.32	ND

Tapentadol	100,000	-6.8	-0.38	ND
Thebaine	100,000	11.7	1.37	ND
Tilidine	100,000	-7.0	-0.17	ND
Tramadol	100,000	-5.2	-0.33	ND

Structurally Unrelated Pharmacological Compounds:

Compound	Test Concentration (ng/mL)	0 ng/mL Norbuprenorphine % Cross	-25% Norbuprenorphine Cutoff (3.75 ng/mL) Result	+25% Norbuprenorphine Cutoff (6.25 ng/mL) Result
Acetaminophen	100,000	Neg	Neg	Pos
6-Acetylmorphine	100,000	Neg	Neg	Pos
Acetylsalicylic Acid	100,000	Neg	Neg	Pos
Amitriptyline	100,000	Neg	Neg	Pos
Amlodipine Besylate	100,000	Neg	Neg	Pos
Amoxicillin	100,000	Neg	Neg	Pos
d-Amphetamine	100,000	Neg	Neg	Pos
Atorvastatin	100,000	Neg	Neg	Pos
Benzoylecgonine	100,000	Neg	Neg	Pos
Bupropion	100,000	Neg	Neg	Pos
Caffeine	100,000	Neg	Neg	Pos
Carbamazepine	100,000	Neg	Neg	Pos
Cetirizine	100,000	Neg	Neg	Pos
Chlorpheniramine	100,000	Neg	Neg	Pos
Chlorpromazine	100,000	Neg	Neg	Pos
Clomipramine	100,000	Neg	Neg	Pos
Desipramine	100,000	Neg	Neg	Pos
Diphenhydramine	100,000	Neg	Neg	Pos
Duloxetine	100,000	Neg	Neg	Pos
Fluoxetine	100,000	Neg	Neg	Pos
Fluphenazine	100,000	Neg	Neg	Pos
Gabapentin	100,000	Neg	Neg	Pos
Ibuprofen	100,000	Neg	Neg	Pos
Imipramine	100,000	Neg	Neg	Pos
Lisinopril	100,000	Neg	Neg	Pos
Losartan	100,000	Neg	Neg	Pos
Loratidine	100,000	Neg	Neg	Pos
MDA (3,4-methylenedioxyamphetamine)	100,000	Neg	Neg	Pos
MDEA	100,000	Neg	Neg	Pos
MDMA (3,4-methylenedioxymethamphetamine)	100,000	Neg	Neg	Pos
Metformin	100,000	Neg	Neg	Pos

Metoprolol	100,000	Neg	Neg	Pos
d-Methamphetamine	100,000	Neg	Neg	Pos
Nalmefene	100,000	Neg	Neg	Pos
Nicotine	100,000	Neg	Neg	Pos
Nortriptyline	100,000	Neg	Neg	Pos
Omeprazole	100,000	Neg	Neg	Pos
Oxazepam	100,000	Neg	Neg	Pos
Phenobarbital	100,000	Neg	Neg	Pos
(1S,2S)-(+)Pseudoephedrine	100,000	Neg	Neg	Pos
Quetiapine	100,000	Neg	Neg	Pos
Ranitidine	100,000	Neg	Neg	Pos
Salbutamol (Albuterol)	100,000	Neg	Neg	Pos
Sertraline	100,000	Neg	Neg	Pos
THC-COOH (11-Nor-Delta-9-THC-9-carboxylic acid)	100,000	Neg	Neg	Pos
L-Thyroxine	100,000	Neg	Neg	Pos
Zolpidem	100,000	Neg	Neg	Pos

Structurally related or unrelated Opiate compounds:

Compound	Test Concentration (ng/mL)	Qualitative Result (mAU)	Semi-Quantitative Result (ng/mL)	% Cross-reactivity
Codeine	100,000	-7.6	-1.2	ND
Codeine 6ß D-Glucuronide	100,000	-2.0	0.1	ND
Dextromethorphan	100,000	5.6	1.4	ND
Dextrorphan Tartrate	100,000	-2.9	-0.7	ND
Dihydrocodeine	100,000	2.0	0.6	ND
Dihydromorphine	100,000	0.2	-0.1	ND
EDDP	100,000	-4.2	-0.4	ND
EMDP	100,000	5.1	1.0	ND
Ethylmorphine	100,000	-4.9	-0.4	ND
Fentanyl	100,000	-8.9	-1.7	ND
Heroin	100,000	-4.6	-0.7	ND
Hydrocodone	100,000	-5.7	-1.0	ND
Hydromorphone	100,000	-7.6	-1.3	ND
Hydromorphone 3ß D-Glucuronide	10,000	-2.2	-0.2	ND
LAAM	100,000	5.9	1.4	ND
Levorphanol	100,000	-3.2	-0.4	ND
Meperidine	100,000	4.6	0.9	ND
Meperidine	100,000	-16.3	-1.1	ND
Methadone	100,000	-16.4	-1.3	ND
Morphine	100,000	-14.2	-1.0	ND
Morphine 3ß D-Glucuronide	100,000	-4.8	-0.1	ND

Morphine 6 D-Glucuronide	100,000	-1.9	-0.2	ND
N-Desmethyl-cis-Tramadol	100,000	-4.6	-0.5	ND
Nalbuphine	100,000	-5.7	-0.5	ND
Nalorphine	100,000	-4.7	-0.1	ND
Naloxegol	100,000	14.1	2.1	ND
Naloxone	100,000	1.5	-0.5	ND
Naltrexone	100,000	5.8	1.2	ND
Norcodeine	100,000	-3.9	-0.3	ND
Norhydrocodone	100,000	-4.7	-0.3	ND
Normorphine	100,000	-6.3	-0.3	ND
Noroxycodone	100,000	-4.2	-0.1	ND
Noroxymorphone	100,000	-1.8	0.1	ND
Norpropoxyphene	100,000	6.7	0.9	ND
O-Desmethyl-cis-Tramadol	100,000	-4.1	-0.1	ND
Oxycodone	100,000	-12.3	-0.6	ND
Oxymorphone	100,000	-12.6	-0.7	ND
Oxymorphone 3ß D-Glucuronide	10,000	-1.8	-0.1	ND
Pentazocine	100,000	-7.3	-0.4	ND
Tapentadol	100,000	-3.5	-0.1	ND
Thebaine	100,000	5.9	1.0	ND
Tilidine	100,000	-2.3	-0.4	ND
Tramadol	100,000	-6.8	-0.3	ND

Structurally Unrelated Pharmacological Compounds:

Compound	**Test Concentration (ng/mL)**	**0 ng/mL Norbuprenorphine**	**-25% Norbuprenorphine Cutoff (3.75 ng/mL)**	**+25% Norbuprenorphine Cutoff 6.25 ng/mL)**
		% Cross	**Result**	**Result**
Acetaminophen	100,000	Neg	Neg	Pos
6-Acetylmorphine	100,000	Neg	Neg	Pos
Acetylsalicylic Acid	100,000	Neg	Neg	Pos
Amitriptyline	100,000	Neg	Neg	Pos
Amlodipine Besylate	100,000	Neg	Neg	Pos
Amoxicillin	100,000	Neg	Neg	Pos
d-Amphetamine	100,000	Neg	Neg	Pos
Atorvastatin	100,000	Neg	Neg	Pos
Benzoylecgonine	100,000	Neg	Neg	Pos
Bupropion	100,000	Neg	Neg	Pos
Caffeine	100,000	Neg	Neg	Pos
Carbamazepine	100,000	Neg	Neg	Pos
Cetirizine	100,000	Neg	Neg	Pos
Chlorpheniramine	100,000	Neg	Neg	Pos
Chlorpromazine	100,000	Neg	Neg	Pos
Clomipramine	100,000	Neg	Neg	Pos

Desipramine	100,000	Neg	Neg	Pos
Diphenhydramine	100,000	Neg	Neg	Pos
Duloxetine	100,000	Neg	Neg	Pos
Fluoxetine	100,000	Neg	Neg	Pos
Fluphenazine	100,000	Neg	Neg	Pos
Gabapentin	100,000	Neg	Neg	Pos
Ibuprofen	100,000	Neg	Neg	Pos
Imipramine	100,000	Neg	Neg	Pos
Lisinopril	100,000	Neg	Neg	Pos
Losartan	100,000	Neg	Neg	Pos
Loratidine	100,000	Neg	Neg	Pos
MDA (3,4-methylenedioxyamphetamine)	100,000	Neg	Neg	Pos
MDEA	100,000	Neg	Neg	Pos
MDMA (3,4-methylenedioxymethamphetamine)	100,000	Neg	Neg	Pos
Metformin	100,000	Neg	Neg	Pos
Metoprolol	100,000	Neg	Neg	Pos
d-Methamphetamine	100,000	Neg	Neg	Pos
Nalmefene	100,000	Neg	Neg	Pos
Nicotine	100,000	Neg	Neg	Pos
Nortriptyline	100,000	Neg	Neg	Pos
Omeprazole	100,000	Neg	Neg	Pos
Oxazepam	100,000	Neg	Neg	Pos
Phenobarbital	100,000	Neg	Neg	Pos
(1S,2S)-(+)Pseudoephedrine	100,000	Neg	Neg	Pos
Quetiapine	100,000	Neg	Neg	Pos
Ranitidine	100,000	Neg	Neg	Pos
Salbutamol (Albuterol)	100,000	Neg	Neg	Pos
Sertraline	100,000	Neg	Neg	Pos
THC-COOH (11-Nor-Delta-9-THC-9-carboxylic acid)	100,000	Neg	Neg	Pos
L-Thyroxine	100,000	Neg	Neg	Pos
Zolpidem	100,000	Neg	Neg	Pos

Among all structurally unrelated pharmacological compounds tested, no cross-reactivity was observed with any compound tested at -25% of the norbuprenorphine cutoff concentration with the 5 ng/mL cutoff.

Samples ranging in specific gravity from 1.000 to 1.030 were split into three portions each and either left un-spiked or further spiked to a final buprenorphine concentration of either 3.75 ng/mL or 6.25 ng/mL. Samples were evaluated in both qualitative and semi-quantitative modes. No interference was observed.

Negative urine and urine spiked with norbuprenorphine to the final buprenorphine concentration of either 3.75 ng/mL or 6.25 ng/mL were assessed for interference from pH. No interference was observed between pH of 3 to 11.

4. Detection Limit: The lowest concentration that can be differentiated from the negative urine with 95% confidence is determined as 1.0 ng/mL

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   Traceable to a commercially available standard.

6. Assay Cut-Off:

   See Precision section above.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   A total of ninety-four (94) unaltered clinical samples were tested with the LZI Buprenorphine II Enzyme Immunoassay on the Beckman Coulter AU480 automated clinical analyzer. All samples were tested in singlet. All samples were confirmed with LC/MS for both buprenorphine and norbuprenorphine concentrations.
   Results are shown in the tables below.

Semi-Quantitative Accuracy Study:

BUP II Results 5 ng/mL Cutoff	**Negative** by LC/MS analysis	**< 50% of the cutoff concentration** by LC/MS analysis	**Near Cutoff Negative** between 50% below the cutoff and the cutoff concentration by LC/MS analysis	**Near Cutoff Positive** between the cutoff and 50% above the cutoff concentration by LCMS analysis	**High Positive** greater than 50% above the cutoff concentration by LC/MS analysis
Positive at or above the cutoff by EIA analysis	0	7*	12*	14	33
Negative below the cutoff by EIA analysis	20	6	2	0	0

* These samples were confirmed to contain known cross reactants (buprenorphine glucuronide and norbuprenorphine glucuronide), which significantly contributed to the discrepant results observed.

2. Matrix Comparison:
   Not applicable.

C Clinical Studies:

1. Clinical Sensitivity: Not applicable.

2. Clinical Specificity: Not applicable.

3. Clinical Cut-Off: Not applicable

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable): Not applicable.

D Expected Values/Reference Range:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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