Jan 16, 2026

Lin-Zhi International, , Inc.
Thet Wai
Manager, TDM Immunoassay Development
2945 Oakmead Village Ct.
Santa Clara, California 95051

Re: K253082
Trade/Device Name: LZI Buprenorphine II Enzyme Immunoassay
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate test system
Regulatory Class: Class II
Product Code: DJG
Dated: December 5, 2025
Received: December 8, 2025

Dear Thet Wai:

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 (the 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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

JOSEPH A. KOTAREK -S

Digitally signed by JOSEPH A. KOTAREK -S
Date: 2026.01.16 15:05:50 -05'00'

Joseph Kotarek
Branch Chief
Division of Chemistry and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
k253082

Device Name
LZI Buprenorphine II Enzyme Immunoassay

Indications for Use *(Describe)*
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 norburprenorphine. 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.

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.

510(k) Summary

510(k) Number

k253082

Prepared On

January 14, 2026

Submitter Name and Contact Person:

Thet Wai
Manager, TDM Assay Development
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Introduction

This submission is provided in accordance with 21 CFR 807.92 as a 510(k) for the LZI Buprenorphine II Enzyme Immunoassay. The LZI Buprenorphine II Enzyme Immunoassay is similar to its legally marketed predicate device, LZI Buprenorphine Enzyme Immunoassay (k090844), in terms of intended use, method principle, device components, and clinical performance.

Verification and validation activities were conducted using well-established methods consistent with those performed for the predicate device. These included method comparison with LC/MS, precision studies, cross-reactivity evaluation, and interference testing. Collectively, the data confirm that the modified device supports its intended use, safety, and effectiveness, and performs substantially equivalent to the predicate.

This submission includes a summary of design control activities and performance characteristics, which together provide a complete basis for a determination of substantial equivalence.

Device Name and Classification

Classification Name:	Enzyme Immunoassay, Opiates
Regulation Number:	21 CFR 862.3650
Product Code:	Class II, DJG
Common Name:	Homogeneous Buprenorphine Enzyme Immunoassay
Proprietary Name:	LZI Buprenorphine II Enzyme Immunoassay
Submission Type:	510(k)
510(k) Number:	k253082

Legally Marketed Predicate Device

The subject device is compared to the predicate:

- **Predicate Device:** LZI Buprenorphine Enzyme Immunoassay
- **510(k) Number:** k090844

The LZI Buprenorphine II Enzyme Immunoassay is substantially equivalent to the LZI Buprenorphine Enzyme Immunoassay (k090844) manufactured by LZI in terms of intended use, method principle, device components, and clinical performance.

Device Description

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.

The LZI Buprenorphine II Enzyme Immunoassay is a kit comprised of two reagents, R_1 and R_2, which are bottled separately but sold together within the kit.

The R_1 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 R_2 solution contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with norbuprenorphine in buffer with sodium azide (0.09%) as a preservative.

Intended 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 norburprenorphine. 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.

Substantial Equivalence Comparison to Predicate Device

The LZI Buprenorphine II Enzyme Immunoassay is substantially equivalent to the LZI Buprenorphine Enzyme Immunoassay which was cleared by the FDA under the premarket notification k090844 for its stated intended use.

The following table compares the LZI Buprenorphine II Enzyme Immunoassay with the predicate device.

Device Characteristics	**Subject Device** LZI Buprenorphine II Enzyme Immunoassay	**Predicate Device (k090844)** LZI Buprenorphine Enzyme Immunoassay
Intended 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 norburprenorphine. 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.***	The Lin-Zhi International (LZI) Buprenorphine Enzyme Immunoassay is intended for the qualitative and semiquantitative determination of norbuprenorphine (buprenorphine metabolite) in human urine, at cutoff values of 5 ng/mL and 10 ng/mL. The assay is designed for prescription use with a number of automated clinical chemistry analyzers.
Analyte	norbuprenorphine	norbuprenorphine
Cutoff	5 ng/mL	5 ng/mL and 10 ng/mL
Matrix	Urine	Urine
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	5 ng/mL Cutoff: 2 Levels 3 and 7 ng/mL 10 ng/mL Cutoff: 2 Levels 7 and 13 ng/mL
Storage	2-8 ºC until expiration date	2-8 ºC until expiration date
Detection	Absorbance change measured spectrophotometrically at 340 nm.	same
User Environment	Clinical laboratories; Prescription use only	same
Mass Spectormetry Confirmation	Required to confirm preliminary positive analytical results	same
Platform Requireed	Automated clinical chemistry analyzer	same

Device Characteristics	Subject Device LZI Buprenorphine II Enzyme Immunoassay	Predicate Device (k090844) LZI Buprenorphine Enzyme Immunoassay
Reagents Form	Lqiuid – ready-to-use	same
Reagent Materials	Two (2) reagent system: Antibody/substrate reagent (R_1) and enzyme labeled conjugates (R_2) with sodium azide preservative	same

Performance Characteristics Summary:

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

Precision: 5 ng/mL Cutoff

The assay was tested in qualitative (ΔOD, mAU) mode using a modified NCCLS-EP5 protocol. Norbuprenorphine sample concentrations were prepared by spiking a norbuprenorphine standard into a pool of negative human urine at the cutoff concentration and ±25%, ±50%, ±75%, and ±100% of the cutoff concentration.

Results shown below were obtained by testing all norbuprenorphine samples in replicate of two, two runs a day (one in the morning and one in the afternoon) for 22 days (within-run precision) on one Beckman Coulter AU480 automated clinical analyzer for a total of 88 runs (total precision). One single lot of reagents and calibrators and controls were used and stored at 2-8ºC when not in use.

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

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

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

NBUP Concentration	Within Run (N=22)		Total Precision (N=88)	
	SD	% CV	SD	% CV
0 ng/mL	0.15	N/A	0.20	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	0.20	2.5%	0.24	3.0%
8.75 ng/mL	0.21	2.2%	0.26	2.8%
10 ng/mL	0.30	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

Limit of Detection: 5 ng/mL Cutoff

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

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

Linearity: 5 ng/mL Cutoff

To demonstrate recovery of the entire assay range, a drug-free urine pool spiked with norbuprenorphine at 20 ng/mL was serially diluted. Each sample was run in 10 replicates and the average was used to determine percent recovery compared to the expected target value.

Determined concentration averages were obtained and all averages were ±15 % of the target concentrations. The determined average percent recovery (Determined Concentration Average divided by the Target Concentration) was considered acceptable between 85 – 115 %.

The recovery of norbuprenorphine spiked to various concentrations was evaluated and the average recovery for the linear range of the assay was found to range between 99.6% - 106.3%.

Target Concentration (ng/mL)	Determined Concentration Range (ng/mL)	Determined Concentration Average (ng/mL)	Average % Recovery
20	18.73 - 20.41	19.91	99.6%
18	18.06 – 18.96	18.54	103.0%
16	16.37 – 16.95	16.66	104.1%
14	13.51 - 15.14	14.18	101.3%
12	12.17 – 13.23	12.75	106.3%
10	9.74 - 10.68	10.24	102.4%
8	7.92 – 8.56	8.21	102.6%
6	6.08 – 6.59	6.29	104.8%
4	3.70 – 4.29	4.07	101.9%
2	1.70 – 2.09	1.90	94.8%
1	0.60 – 1.36	0.94	94.2%
0	-0.22 – 0.29	0.05	N/A

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

Method Comparison - Clinical Samples: 5 cutoff

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. Samples were collected by:

- Lin-Zhi International, Inc. (LZI) at Santa Clara, CA, USA
- University of California, San Francisco (UCSF) at San Francisco, CA, USA
- Millenium Health (Millenium) at San Diego, CA, USA
- Boca Biolistics at Pompano Beach, FL, USA
- University of Leeds at Leeds, UK
- BirdRock Laboratories (BirdRock) at San Diego, CA, USA
- APC Health at Pearland, TX),
- Altius Diagnostics (Altius) at Bellevue, WA, USA
- Tricore Research Institute (Tricore) at Albuquerque, NM, USA
- Cozart at Oxfordshire, UK

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

** Discrepant <50% of the cutoff concentration (0.1 – 2.49 ng/mL)*
*** Discrepant between 50% of the cutoff to the cutoff concentration (2.5 – 4.99 ng/mL)*

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Method Comparison 5 cutoff, continued:

Discrepant samples determined when comparing total buprenorphine and norbuprenorphine LC/MS results with EIA results on the Beckman Coulter AU480 automated clinical analyzer are shown in the table below.

Sample #	BUP LC/MS (ng/mL)	NBUP LC/MS (ng/mL)	Total LC/MS (ng/mL)	Pos/ Neg Result	AU480 EIA Semi-Quantitative Result (ng/mL)	Pos/ Neg Result
21*	0.75	0.27	1.02	-	21.59	+
22*	0.00	1.09	1.09	-	5.20	+
24*	1.04	0.07	1.11	-	21.96	+
26*	0.57	0.68	1.25	-	9.79	+
28*	1.23	0.06	1.29	-	16.74	+
31*	1.24	0.16	1.40	-	20.56	+
32*	0.62	0.83	1.45	-	8.98	+
35**	0.24	2.38	2.62	-	9.59	+
36**	0.20	2.48	2.68	-	12.35	+
37**	2.05	0.67	2.72	-	24.57	+
38**	0.11	2.64	2.75	-	7.87	+
39**	0.94	1.83	2.77	-	5.89	+
40**	0.23	2.55	2.78	-	15.47	+
41**	1.69	1.29	2.98	-	23.60	+
42**	1.04	1.97	3.01	-	5.62	+
43**	2.54	0.52	3.06	-	22.99	+
44**	0.19	2.99	3.18	-	8.02	+
45**	0.00	3.19	3.19	-	5.78	+
47**	1.61	1.66	3.27	-	24.45	+

** Discrepant <50% of the cutoff concentration (0.1 – 2.49 ng/mL)*

*** Discrepant between 50% of the cutoff to the cutoff concentration (2.5 – 4.99 ng/mL)*

** These discrepancies are due to known causes. LZI Buprenorphine II Enzyme Immunoassay cross-reacts with both buprenorphine glucuronide and norbuprenorphine glucuronide, which explains the elevated EIA values and false positives observed in discrepant samples #21, #22, #24, #26, #28, #31 and #32.*

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Qualitative 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

** Discrepant <50% of the cutoff concentration (0.1 – 2.49 ng/mL)*

*** Discrepant between 50% of the cutoff to the cutoff concentration (2.5 – 4.99 ng/mL)*

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Discrepant samples determined when comparing total buprenorphine and norbuprenorphine LC/MS results with EIA results on the Beckman Coulter AU480 automated clinical analyzer are shown in the table below.

Sample #	BUP LC/MS (ng/mL)	NBUP LC/MS (ng/mL)	Total LC/MS (ng/mL)	Pos/ Neg Result	AU480 EIA Qualitative Result (mAU)	Qualitative Cutoff Rate (mAU)	Pos/ Neg Result
21*	0.75	0.27	1.02	-	359.3	88.6	+
22*	0.00	1.09	1.09	-	99.8	87.8	+
24*	1.04	0.07	1.11	-	372.5	88.6	+
26*	0.57	0.68	1.25	-	185.0	88.6	+
28*	1.23	0.06	1.29	-	296.1	88.6	+
31*	1.24	0.16	1.40	-	358.2	88.6	+
32*	0.62	0.83	1.45	-	171.6	88.6	+
35**	0.24	2.38	2.62	-	181.9	88.6	+
36**	0.20	2.48	2.68	-	233.1	88.6	+
37**	2.05	0.67	2.72	-	410.0	88.6	+
38**	0.11	2.64	2.75	-	155.9	88.6	+
39**	0.94	1.83	2.77	-	105.7	88.6	+
40**	0.23	2.55	2.78	-	275.8	88.6	+
41**	1.69	1.29	2.98	-	404.6	88.6	+
42**	1.04	1.97	3.01	-	107.2	88.6	+
43**	2.54	0.52	3.06	-	389.8	88.6	+
44**	0.19	2.99	3.18	-	153.0	88.6	+
45**	0.00	3.19	3.19	-	105.6	88.6	+
47**	1.61	1.66	3.27	-	412.3	88.6	+

** Discrepant <50% of the cutoff concentration (0.1 – 2.49 ng/mL)*
*** Discrepant between 50% of the cutoff to the cutoff concentration (2.5 – 4.99 ng/mL)*

** These discrepancies are due to known causes. LZI Buprenorphine II Enzyme Immunoassay cross-reacts with both buprenorphine glucuronide and norbuprenorphine glucuronide, which explains the elevated EIA values and false positives observed in discrepant samples #21, #22, #24, #26, #28, #31 and #32.*

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Cross-reactivity: 5 cutoff

The cross-reactivity of various potentially interfering drugs were tested by spiking various concentrations of each substance into a pool of negative human urine and then evaluated against the assay's calibration curve in qualitative mode. All samples were tested in duplicates.

The table below lists the concentration of each test compound that gave a response approximately equivalent to that of the cutoff calibrator (as positive) or the maximal concentration of the compound tested that gave a response below the response of the cutoff calibrator (as negative). Compounds tested at high concentration (100,000 ng/mL) with results below the cutoff value were listed as Not Detected (ND).

Buprenorphine and Major Metabolites:

Compound	Test Concentration (ng/mL)	Qualitative Result (mAU)	Semi-Quantitative Result (ng/mL)	% Cross-reactivity
Norbuprenorphine	5.0	66.9	5.3	100.0%
Buprenorphine	5.0	71.0	5.6	100.0%
Buprenorphine Glucuronide	32.0	83.4	6.1	15.6%
Norbuprenorphine Glucuronide	210.0	66.4	5.0	2.4%

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

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Cross-reactivity: 5 cutoff, continued

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

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Cross-reactivity: 5 cutoff, continued

Structurally unrelated compounds were additionally spiked into pooled negative human urine to desired concentrations (as described above). These solutions were then split into three portions; one without norbuprenorphine, and the remaining two that were further spiked with norbuprenorphine standards to a final norbuprenorphine concentration of 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. All samples were tested in duplicates. If discrepant results were observed, the lowest tested concentration at which discrepancies occurred is presented in the following table.

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

Performance Characteristics Summary, continued:
Beckman Coulter AU480 Analyzer

Cross-reactivity, continued:
Structurally Unrelated Pharmacological Compounds, continued:

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
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

Performance Characteristics Summary, continued:
Beckman Coulter AU480 Analyzer

Endogenous and Preservative Compound Interference 5 cutoff:
Endogenous and Preservative compounds were spiked into pooled negative human urine to desired concentrations. These solutions were then split into three portions; one without norbuprenorphine, and the remaining two that were further spiked with norbuprenorphine standards to a final norbuprenorphine concentration of 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. All samples were tested in duplicates.

Interference was observed with Boric Acid at 1% w/v. No other significant cross-reactivity was observed.

Interfering Substance	Concentration of Compound (mg/dL)	0 ng/mL Norbuprenorphine	-25% Norbuprenorphine Cutoff (3.75 ng/mL)	+25% Norbuprenorphine Cutoff (6.25 ng/mL)
Acetone	1,000	Neg	Neg	Pos
Ascorbic acid	500	Neg	Neg	Pos
Bilirubin	2	Neg	Neg	Pos
Biotin	2	Neg	Neg	Pos
Boric acid	1,000	Neg	Neg	Neg
Calcium chloride	300	Neg	Neg	Pos
Citric acid	200	Neg	Neg	Pos
Creatinine	500	Neg	Neg	Pos
Ethanol	1,000	Neg	Neg	Pos
Galactose	10	Neg	Neg	Pos
γ-Globulin	500	Neg	Neg	Pos
Glucose	3,000	Neg	Neg	Pos
Hemoglobin	300	Neg	Neg	Pos
Human urine (pooled)	N/A	Neg	Neg	Pos
Human serum albumin	500	Neg	Neg	Pos
β-Hydroxybutyric acid	100	Neg	Neg	Pos
Oxalic acid	100	Neg	Neg	Pos
Potassium chloride	1,000	Neg	Neg	Pos
Riboflavin	7.5	Neg	Neg	Pos
Sodium azide	1,000	Neg	Neg	Pos
Sodium chloride	1,000	Neg	Neg	Pos
Sodium fluoride	1,000	Neg	Neg	Pos
Sodium phosphate	300	Neg	Neg	Pos
Urea	6,000	Neg	Neg	Pos
Uric acid	10	Neg	Neg	Pos
Urine-based calibrator buffer	N/A	Neg	Neg	Pos

Performance Characteristics Summary, continued:

Beckman Coulter AU480 Analyzer

Specific Gravity Interference 5 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 norbuprenorphine concentration of either 3.75 ng/mL or 6.25 ng/mL (as negative or positive controls, ±25% of the cutoff concentration, respectively). These samples were then evaluated in qualitative and semi-quantitative modes. No interference was observed.

Specific Gravity Value	0 ng/mL Norbuprenorphine	-25% Norbuprenorphine Cutoff (3.75 ng/mL)	+25% Norbuprenorphine Cutoff (6.25 ng/mL)
1.000	Neg	Neg	Pos
1.005	Neg	Neg	Pos
1.007	Neg	Neg	Pos
1.010	Neg	Neg	Pos
1.013	Neg	Neg	Pos
1.015	Neg	Neg	Pos
1.017	Neg	Neg	Pos
1.020	Neg	Neg	Pos
1.030	Neg	Neg	Pos

Performance Characteristics Summary, continued:

Beckman Coulter AU480 Analyzer

pH Interference 5 cutoff:

Negative urine and urine spiked with norbuprenorphine to the final norbuprenorphine concentration of either 3.75 ng/mL or 6.25 ng/mL (as negative or positive controls, ±25% of the cutoff concentration, respectively) were adjusted to the following pH levels and tested by the assay. The pH adjusted solutions were evaluated in qualitative mode.

No major interference was observed between pH 3 to pH 11. Results are summarized in the following table:

Interfering Substance	0 ng/mL Norbuprenorphine	-25% Norbuprenorphine Cutoff (3.75 ng/mL)	+25% Norbuprenorphine Cutoff (6.25 ng/mL)
pH 3	Neg	Neg	Pos
pH 4	Neg	Neg	Pos
pH 5	Neg	Neg	Pos
pH 6	Neg	Neg	Pos
pH 7	Neg	Neg	Pos
pH 8	Neg	Neg	Pos
pH 9	Neg	Neg	Pos
pH 10	Neg	Neg	Pos
pH 11	Neg	Neg	Pos

Conclusion:

The information provided in this pre-market notification demonstrates that the LZI Buprenorphine II Enzyme Immunoassay is substantially equivalent to the legally marketed predicate device for its general intended use. Substantial equivalence was demonstrated through comparison of intended use and physical properties to the commercially available predicate device as confirmed by chromatography/mass spectrometry (LC/MS), an independent analytical method. The information supplied in this pre-market notification provides reasonable assurance that the LZI Buprenorphine II Enzyme Immunoassay is safe and effective for its stated intended use.