August 7, 2020

Lin-Zhi International, Inc.
Bernice Lin
VP Operations
2945 Oakmead Village Court
Santa Clara, CA 95051

Re: K201938
Trade/Device Name: LZI Fentanyl II Enzyme Immunoassay
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate test system
Regulatory Class: Class II
Product Code: DJG
Dated: July 8, 2020
Received: July 13, 2020

Dear Bernice Lin:

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. 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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 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 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 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,

Marianela Perez-Torres, Ph.D.
Acting Deputy Director
Division of Chemistry and Toxicology Devices
OHT7: Office of In Vitro Diagnostics and Radiological Health
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
k201938

Device Name
LZI Fentanyl II Enzyme Immunoassay

Indications for Use *(Describe)*
The LZI Fentanyl II Enzyme Immunoassay is intended for the qualitative determination of norfentanyl in human urine at the cutoff value of 5 ng/mL. 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. 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.

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510(k) Summary of Safety and Effectiveness

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

510(k) Number

k201938

Prepared On

July 2, 2020

Introduction

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter Name, Address, and Contact:

Lin-Zhi International, Inc.
2945 Oakmead Village Court
Santa Clara, CA 95051
Phone: (408) 970-8811
Fax: (408) 970-9030
e-mail: bclin@lin-zhi.com

Contact: Bernice Lin, Ph.D.
VP Operations

Device Name and Classification

Classification Name:	Enzyme Immunoassay, Opiates Class II, DJG (91 Toxicology), 21 CFR 862.3650
Common Name:	Homogeneous Fentanyl Enzyme Immunoassay
Proprietary Name:	LZI Fentanyl II Enzyme Immunoassay

Legally Marketed Predicate Device(s)

The LZI Fentanyl II Enzyme Immunoassay is substantially equivalent to the LZI Fentanyl Enzyme Immunoassay (k181159) manufactured by Lin-Zhi International, Inc. The LZI Fentanyl II Enzyme Immunoassay is identical or similar to its predicate in terms of intended use, method principle, device components, and clinical performance.

Device Description

The LZI Fentanyl II Enzyme Immunoassay is a homogeneous enzyme immunoassay with ready-to-use liquid reagents. 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. The drug-labeled G6PDH conjugate is traceable to a commercially available fentanyl standard and referred to as fentanyl-labeled G6PDH conjugate. 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, fentanyl-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when free drug is present in the sample, antibody would bind to free drug; the unbound fentanyl-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 Fentanyl II Enzyme Immunoassay is a kit comprised of two reagents, an R_1 and R_2, which are bottled separately but sold together within the kit. The LZI Fentanyl II Enzyme Immunoassay is traceable to a commercially available fentanyl standard.

The R_1 solution contains mouse monoclonal anti-fentanyl 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 fentanyl in buffer with sodium azide (0.09 %) as a preservative.

Intended Use

The LZI Fentanyl II Enzyme Immunoassay is intended for the qualitative determination of norfentanyl in human urine at the cutoff value of 5 ng/mL. 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 chromatograpy 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.

Comparison to Predicate Device

The LZI Fentanyl II Enzyme Immunoassay is substantially equivalent to the LZI Fentanyl Enzyme Immunoassay which was cleared by the FDA under the premarket notification k181159 for its stated intended use.

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

Device Characteristics	**Subject Device** LZI Fentanyl II Enzyme Immunoassay	**Predicate Device (k181159)** LZI Fentanyl Enzyme Immunoassay
Intended Use	The LZI Fentanyl II Enzyme Immunoassay is intended for the qualitative determination of norfentanyl in human urine at the cutoff value of 5 ng/mL when calibrated against norfentanyl. The assay is designed for professional use with a number of automated clinical chemistry analyzers. ***This assay provides a rapid screening procedure for determining the presence of norfentanyl in urine. The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.***	The LZI Fentanyl Enzyme Immunoassay is intended for the qualitative determination of norfentanyl in human urine at the cutoff value of 5 ng/mL when calibrated against norfentanyl. The assay is designed for professional use with a number of automated clinical chemistry analyzers. ***This assay provides a rapid screening procedure for determining the presence of norfentanyl in urine. The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.***
Analyte	norfentanyl	norfentanyl
Cutoff	5 ng/mL	5 ng/mL
Matrix	Urine	Urine
Calibrator Level	5 ng/mL	5 ng/mL
Controls Level	3.75 ng/mL and 6.25 ng/mL	3.75 ng/mL and 6.25 ng/mL
Storage	2-8 ºC until expiration date	2-8 ºC until expiration date
Instrument used for performance Validation	Beckman Coulter® AU480 automated clinical analyzer	Beckman Coulter® AU680 automated clinical analyzer

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. Norfentanyl sample concentrations were prepared by spiking a norfentanyl standard into a pool of negative human urine at concentrations ±25 %, ±50 %, ±75 %, and ±100 % of the cutoff concentration.

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

Precision: 5 ng/mL Cutoff

Precision: Qualitative, results in ΔOD (mAU)

Norfentanyl Concentration	Within Run (N=22)			Total Precision (N=88)		
	Mean	SD	% CV	Mean	SD	% CV
0 ng/mL	0.0	0.0	N/A	0.0	0.2	N/A
1.25 ng/mL	15.5	3.0	20.2 %	15.5	4.1	26.6 %
2.5 ng/mL	35.1	2.9	8.4 %	35.1	3.5	10.0 %
3.75 ng/mL	58.8	3.0	5.1 %	58.8	3.8	6.5 %
5 ng/mL	81.0	3.3	4.1 %	81.0	3.7	4.6 %
6.25 ng/mL	105.5	2.7	2.5 %	105.5	3.9	3.7 %
7.5 ng/mL	128.0	2.9	2.3 %	128.0	3.5	2.8 %
8.75 ng/mL	150.1	3.2	2.2 %	150.1	4.2	2.8 %
10 ng/mL	171.3	4.3	2.5 %	171.3	5.2	3.0 %

Qualitative Positive/Negative Results:

5 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Norfentanyl Concentration	% of Cutoff	Number of Determination	Immunoassay Result	Number of Determination	Immunoassay Result
0 ng/mL	0.0 %	22	22 Negative	88	88 Negative
1.25 ng/mL	25.0 %	22	22 Negative	88	88 Negative
2.5 ng/mL	50.0 %	22	22 Negative	88	88 Negative
3.75 ng/mL	75.0 %	22	22 Negative	88	88 Negative
5 ng/mL	100.0 %	22	13 Neg/9 Pos	88	59 Neg/29 Pos
6.25 ng/mL	125.0 %	22	22 Positive	88	88 Positive
7.5 ng/mL	150.0 %	22	22 Positive	88	88 Positive
8.75 ng/mL	175.0 %	22	22 Positive	88	88 Positive
10 ng/mL	200.0 %	22	22 Positive	88	88 Positive

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

Method Comparison - Clinical Samples:
A total of one hundred (100) unaltered clinical samples were tested with the LZI Fentanyl II Enzyme Immunoassay on the Beckman Coulter® AU480 automated clinical analyzer. Samples were evaluated against the cutoff calibrator in qualitative mode. All samples were tested in singlet.

All samples were confirmed with LC/MS for norfentanyl concentrations. Samples were collected by Lin-Zhi International, Inc. and from various clinical labs including University of California, San Francisco (UCSF) (San Francisco, CA), Northwest Physicians Labs (NWPL) (Bellevue, Washington), Soloniuk Pain Clinic (Redding, CA), and Calgary Labs (Calgary, Canada).

Qualitative Accuracy Study:

NFEN 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 LC/MS analysis)	**High Positive** (Greater than 50 % above the cutoff concentration by LC/MS analysis)
Positive (at or above the cutoff by EIA analysis)	0	1*	8*	10	40
Negative (below the cutoff by EIA analysis)	20	19	2	0	0

Discrepant samples determined when comparing LC/MS norfentanyl results with the LZI Fentanyl II EIA results on the Beckman Coulter® AU480 automated clinical analyzer.

Sample #	**LC/MS Norfentanyl (ng/mL)**	**Pos/ Neg Result**		**AU480 EIA Qualitative Result (mAU)**	**Pos/ Neg Result**	**Qualitative Cutoff Rate (mAU)**
37*	1.5	-		85.9	+	83.0
41*	2.7	-		111.3	+	83.0
43*	3.0	-		207.9	+	83.0
44*	3.0	-		107.7	+	83.0
45*	3.3	-		124.7	+	83.0
46*	3.5	-		169.6	+	83.0
47*	3.8	-		204.6	+	83.0
48*	3.9	-		113.6	+	83.0
49*	4.2	-		263.1	+	83.0

* Values are discrepant below the cutoff concentration (0 ng/mL – 4.9 ng/mL)

These samples contained levels of fentanyl that contributed to the false positive result.

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

Cross-reactivity
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. Percent cross-reactivity was calculated by dividing the cutoff concentration by the lowest concentration of the compound where the assay response was near cutoff positive x 100.

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).

Fentanyl and Metabolites:

Compound	Test Concentration (ng/mL)	Qualitative Result (mAU)	Qualitative Cutoff Rate (mAU)	% Cross-reactivity
Fentanyl	3.8	107.8	84.6	131.58 %
Norfentanyl	5	88.9	84.6	100.00 %

Structurally Related Compounds:

Compound	Test Concentration (ng/mL)	Qualitative Result (mAU)	Qualitative Cutoff Rate (mAU)	% Cross-reactivity
4-Fluoro-Isobutyryl Fentanyl	20	84.5	83.3	25.00 %
9-Hydroxy Risperidone	100,000	1.8	84.6	ND
Acetyl Fentanyl	7	103.7	88.3	71.43 %
Acetyl Norfentanyl	100	97.3	83.3	5.00 %
Acryl Fentanyl	4	112.2	88.3	125.00 %
Alfentanil	100,000	0.4	84.6	ND
Butyryl Fentanyl	6	99.7	88.3	83.33 %
Butyryl Norfentanyl	40	96.4	83.3	12.50 %
Carfentanil Oxalate	100,000	22.9	84.6	ND
Cis- d,I 3-Methyl Fentanyl	8	97.8	83.3	62.50 %
Cyclopropyl Fentanyl	3.2	94.8	79.7	156.25 %
Cyclopropyl Norfentanyl	25	89.7	83.9	20.00 %
Despropionyl Fentanyl (4-ANPP)	100,000	0.0	88.3	ND
Furanyl Fentanyl	5.5	93.6	83.9	90.91 %
Furanyl Norfentanyl	180	98.3	83.9	2.78 %
(±) β-Hydroxy ThioFentanyl	5	105.3	87.0	100.00 %
Isobutyryl Fentanyl	15	87.5	83.9	33.33 %
Isobutyryl Norfentanyl	500	81.3	79.5	1.00 %
Labetalol Hydrochloride	100,000	0.0	84.6	ND
Methoxyacetyl Fentanyl	3.5	90.3	79.5	142.86 %
MT-45	100,000	0.0	84.6	ND

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

Cross-reactivity, continued
Structurally Related Compounds, continued:

Compound	Test Concentration (ng/mL)	Qualitative Result (mAU)	Qualitative Cutoff Rate (mAU)	% Cross-reactivity
N-benzyl Furanyl Norfentanyl	11	82.1	79.5	45.45 %
N-benzyl Para-fluoro Norfentanyl	4	89.1	79.5	125.00 %
Norcarfentanil Oxalate	100,000	17.4	84.6	ND
Ocfentanil	3.8	116.7	79.5	131.58 %
Para-fluoro Butyryl Fentanyl (p-FBF)	4.5	105.5	79.5	111.11 %
Para-fluoro Fentanyl	3.2	122.1	79.5	156.25 %
Remifentanil	100,000	0.2	84.6	ND
Risperidone	100,000	0.5	84.6	ND
Sufentanil	100,000	77.1	84.6	ND
Thienyl Fentanyl	4	89.7	79.5	125.00 %
Thiofentanyl	3.2	92.6	79.7	156.25 %
Trans- d,I 3-Methyl Fentanyl	6	96.3	79.7	83.33 %
Trazodone	100,000	0.0	84.6	ND
U-47700	100,000	0.0	84.6	ND
Valeryl Fentanyl	70	101.1	88.3	7.14 %
ω-1-Hydroxy Fentanyl	300	94.8	79.7	1.67 %

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

Cross-reactivity, 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 norfentanyl, and the remaining two that were further spiked with norfentanyl standards to a final norfentanyl 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. Compounds tested at high concentration (100,000 ng/mL) with results below the cutoff value were listed as Not Detected (ND).

Interference was observed with Dextromethorphan at 40,000 ng/mL. No other significant cross-reactivity was observed.

Structurally Unrelated Pharmacological Compounds:

Compound	Test Concentration (ng/mL)	0 ng/mL Norfentanyl % Cross	-25 % Norfentanyl Cutoff (3.75 ng/mL) Result	+25 % Norfentanyl Cutoff (6.25 ng/mL) Result
Acetaminophen	100,000	ND	Neg	Pos
6-Acetylmorphine	100,000	ND	Neg	Pos
Acetylsalicylic Acid	100,000	ND	Neg	Pos
Amitriptyline	100,000	ND	Neg	Pos
Amlodipine Besylate	100,000	ND	Neg	Pos
Amoxicillin	100,000	ND	Neg	Pos
d-Amphetamine	100,000	ND	Neg	Pos
Atorvastatin	100,000	ND	Neg	Pos
Benzoylecgonine	100,000	ND	Neg	Pos
Buprenorphine	100,000	ND	Neg	Pos
Bupropion	100,000	ND	Neg	Pos
Caffeine	100,000	ND	Neg	Pos
Carbamazepine	100,000	ND	Neg	Pos
Cetirizine	100,000	ND	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 Norfentanyl % Cross	-25 % Norfentanyl Cutoff (3.75 ng/mL) Result	+25 % Norfentanyl Cutoff (6.25 ng/mL) Result
Chlorpheniramine	100,000	ND	Neg	Pos
Chlorpromazine	100,000	ND	Neg	Pos
Clomipramine	100,000	ND	Neg	Pos
Codeine	100,000	ND	Neg	Pos
Desipramine	100,000	ND	Neg	Pos
Dextromethorphan	40,000	0.01 %	Pos	Pos
Diphenhydramine	100,000	ND	Neg	Pos
Duloxetine	100,000	ND	Neg	Pos
Fluoxetine	100,000	ND	Neg	Pos
Fluphenazine	100,000	ND	Neg	Pos
Gabapentin	100,000	ND	Neg	Pos
Hydrocodone	100,000	ND	Neg	Pos
Hydromorphone	100,000	ND	Neg	Pos
Ibuprofen	100,000	ND	Neg	Pos
Imipramine	100,000	ND	Neg	Pos
Lisinopril	100,000	ND	Neg	Pos
Losartan	100,000	ND	Neg	Pos
Loratidine	100,000	ND	Neg	Pos
MDA (3,4-methylene-dioxyamphetamine)	100,000	ND	Neg	Pos
MDEA	100,000	ND	Neg	Pos
MDMA (3,4-methylene-dioxymethamphetamine)	100,000	ND	Neg	Pos
Meperidine	100,000	ND	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 Norfentanyl	-25 % Norfentanyl Cutoff (3.75 ng/mL)	+25 % Norfentanyl Cutoff (6.25 ng/mL)
		% Cross	Result	Result
Metformin	100,000	ND	Neg	Pos
Metoprolol	100,000	ND	Neg	Pos
Methadone	100,000	ND	Neg	Pos
d-Methamphetamine	100,000	ND	Neg	Pos
Morphine	100,000	ND	Neg	Pos
Nalmefene	100,000	ND	Neg	Pos
Nicotine	100,000	ND	Neg	Pos
Nortriptyline	100,000	ND	Neg	Pos
Omeprazole	100,000	ND	Neg	Pos
Oxazepam	100,000	ND	Neg	Pos
Oxycodone	100,000	ND	Neg	Pos
Oxymorphone	100,000	ND	Neg	Pos
Phencyclidine	100,000	ND	Neg	Pos
Phenobarbital	100,000	ND	Neg	Pos
(1S,2S)-(+)Pseudoephedrine	100,000	ND	Neg	Pos
Quetiapine	100,000	ND	Neg	Pos
Ranitidine	100,000	ND	Neg	Pos
Salbutamol (Albuterol)	100,000	ND	Neg	Pos
Sertraline	100,000	ND	Neg	Pos
THC-COOH (11-Nor-Delta-9-THC-9-carboxylic acid)	100,000	ND	Neg	Pos
l-Thyroxine	100,000	ND	Neg	Pos
Tramadol	100,000	ND	Neg	Pos
Zolpidem	100,000	ND	Neg	Pos

It is possible that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Endogenous and Preservative Compound Interference:

Endogenous and Preservative compounds were spiked into pooled negative human urine to desired concentrations. These solutions were then split into three portions; one without norfentanyl, and the remaining two that were further spiked with norfentanyl standards to a final norfentanyl 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.

Interfering Substance	Concentration of Compound (mg/dL)	0 ng/mL Norfentanyl	-25% Norfentanyl Cutoff (3.75 ng/mL)	+25% Norfentanyl Cutoff (6.25 ng/mL)
Acetone	1000	Neg	Neg	Pos
Ascorbic Acid	500	Neg	Neg	Pos
Bilirubin	2	Neg	Neg	Pos
Biotin	0.5	Neg	Neg	Pos
Boric Acid	1000	Neg	Neg	Neg
Calcium Chloride ($CaCl_2$)	300	Neg	Neg	Pos
Citric Acid (pH 3)	200	Neg	Neg	Pos
Creatinine	500	Neg	Neg	Pos
Ethanol	1000	Neg	Neg	Pos
Galactose	10	Neg	Neg	Pos
γ-Globulin	500	Neg	Neg	Pos
Glucose	3000	Neg	Neg	Pos
Hemoglobin	300	Neg	Neg	Pos
HSA	500	Neg	Neg	Pos
Human Urine (pooled)	N/A	Neg	Neg	Pos
β-hydroxybutyric Acid	100	Neg	Neg	Pos
Oxalic Acid	100	Neg	Neg	Pos
Potassium Chloride	1000	Neg	Neg	Pos
Riboflavin	7.5	Neg	Neg	Pos
Sodium Azide	1000	Neg	Neg	Pos

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

Endogenous and Preservative Compound Interference, continued:

Interfering Substance	Concentration of Compound (mg/dL)	0 ng/mL Norfentanyl	-25 % Norfentanyl Cutoff (3.75 ng/mL)	+25 % Norfentanyl Cutoff (6.25 ng/mL)
Sodium Chloride	1000	Neg	Neg	Pos
Sodium Fluoride	1000	Neg	Neg	Pos
Sodium Phosphate	300	Neg	Neg	Pos
Urea	6000	Neg	Neg	Pos
Uric Acid	10	Neg	Neg	Pos
LZI Urine-base Calibrator Buffer	N/A	Neg	Neg	Pos

The following endogenous and preservative compounds which showed interference at ±25 % of cutoff concentrations were then spiked into negative urine and at ±50 % of the cutoff concentration (2.5 ng/mL and 7.5 ng/mL) for the assay.

Interfering Substance	Concentration of Compound (mg/dL)	0 ng/mL Norfentanyl	-50 % Norfentanyl Cutoff (2.5 ng/mL)	+50 % Norfentanyl Cutoff (7.5 ng/mL)
Boric Acid	1000	Neg	Neg	Neg

Interference was observed with Boric Acid at 1 % w/v. No other significant cross-reactants or endogenous/preservative substance interference was observed.

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

Specific Gravity Interference:
Samples ranging in specific gravity from 1.000 to 1.027 were split into three portions each and either left un-spiked or further spiked to a final norfentanyl 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 mode. No interference was observed.

Specific Gravity Value	0 ng/mL Norfentanyl	-25 % Norfentanyl Cutoff (3.75 ng/mL)	+25 % Norfentanyl Cutoff (6.25 ng/mL)
1.000	Neg	Neg	Pos
1.003	Neg	Neg	Pos
1.005	Neg	Neg	Pos
1.008	Neg	Neg	Pos
1.010	Neg	Neg	Pos
1.012	Neg	Neg	Pos
1.015	Neg	Neg	Pos
1.018	Neg	Neg	Pos
1.020	Neg	Neg	Pos
1.022	Neg	Neg	Pos
1.025	Neg	Neg	Pos
1.027	Neg	Neg	Pos

Performance Characteristics Summary, continued:
Beckman Coulter® AU480 Analyzer

pH Interference:
Negative urine and urine spiked with norfentanyl to the final norfentanyl 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 Norfentanyl	-25 % Norfentanyl Cutoff (3.75 ng/mL)	+25 % Norfentanyl 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

Summary:
The information provided in this pre-market notification demonstrates that the LZI Fentanyl 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 (GC/MS or LC/MS), an independent analytical method. The information supplied in this pre-market notification provides reasonable assurance that the LZI Fentanyl II Enzyme Immunoassay is safe and effective for its stated intended use.