June 18, 2025

Lin-Zhi International, Inc.
Chris Wang
Senior Manager, DAU Assay Development
2945 Oakmead Village Court
Santa Clara, California 95051

Re: K251634
Trade/Device Name: LZI Fentanyl III Enzyme Immunoassay
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate Test System
Regulatory Class: Class II
Product Code: DJG
Dated: May 28, 2025
Received: May 29, 2025

Dear Chris Wang:

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.

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: 2025.06.18 14:21:24 -04'00'

Joseph Kotarek
Branch Chief for Toxicology
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)*
k251634

Device Name
LZI Fentanyl III Enzyme Immunoassay

Indications for Use *(Describe)*
The LZI Fentanyl III Enzyme Immunoassay is intended for the qualitative determination of fentanyl in human urine at the cutoff value of 1 ng/mL when calibrated against fentanyl. 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

510(k) Number

k251634

Prepared On

June 17, 2025

Submitter Name and Contact Person:

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Introduction

This submission is provided in accordance with 21 CFR 807.92 as a Special 510(k) for the LZI Fentanyl III Enzyme Immunoassay. The purpose of this application is to support modifications made to LZI's legally marketed predicate device, the LZI Fentanyl II Enzyme Immunoassay (k201938). These modifications include a change in target analyte from norfentanyl to fentanyl, an updated cutoff concentration, and changes to assay application parameters.

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 (91 Toxicology)
Common Name:	Homogeneous Fentanyl Enzyme Immunoassay
Proprietary Name:	LZI Fentanyl III Enzyme Immunoassay
Submission Type:	Special 510(k)
510(k) Number:	k251634

Legally Marketed Predicate Device

The subject device is compared to the predicate:

- **Predicate Device:** LZI Fentanyl II Enzyme Immunoassay
- **510(k) Number:** k201938

The LZI Fentanyl III Enzyme Immunoassay is substantially equivalent to the LZI Fentanyl II Enzyme Immunoassay (k201938) manufactured by LZI in terms of intended use, method principle, device components, and clinical performance.

Device Description

The LZI Fentanyl III Enzyme Immunoassay is a homogeneous enzyme immunoassay with ready-to-use liquid reagents. The assay is based on competition between the drug in the sample and the 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 a drug in the sample, fentanyl-labeled G6PDH conjugate is bound to the antibody, and the enzyme activity is inhibited. On the other hand, when the free drug is present in the sample, the antibody would bind to the 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 III 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-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 III Enzyme Immunoassay is intended for the qualitative determination of fentanyl in human urine at the cutoff value of 1 ng/mL when calibrated against fentanyl. 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.

Substantial Equivalence Comparison to Predicate Device

The LZI Fentanyl III Enzyme Immunoassay is substantially equivalent to the LZI Fentanyl II Enzyme Immunoassay which was cleared by the FDA under the premarket notification k201938 for its stated intended use.

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

Device Characteristics	**Subject Device** LZI Fentanyl III Enzyme Immunoassay	**Predicate Device (k201938)** LZI Fentanyl II Enzyme Immunoassay
Intended Use	The LZI Fentanyl III Enzyme Immunoassay is intended for the qualitative determination of fentanyl in human urine at the cutoff value of 1 ng/mL when calibrated against fentanyl. 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.***	The LZI Fentanyl II Enzyme Immunoassay is intended for the qualitative detection 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.***
Analyte	Fentanyl	Norfentanyl
Cutoff	1 ng/mL	5 ng/mL
Matrix	Urine	same
Calibrator Level	1 ng/mL	5 ng/mL
Controls Level	0.5 ng/mL and 1.5 ng/mL	3.75 ng/mL and 6.25 ng/mL
Storage	2-8 ºC until expiration date	same
Application Volume	R1: 65 µL; R2: 25 µL; Sample: 15 µL	R1: 120 µL; R2: 45 µL; Sample: 15 µL
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
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 AU5800 Analyzer

Precision: 1 ng/mL Cutoff

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

The results shown below were obtained by testing all samples in replicates of two, two runs a day (one in the morning and one in the afternoon) for 22 days on one Beckman Coulter AU5800 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 was used and stored at 2-8ºC when not in use.

Precision: 1 ng/mL Cutoff

Qualitative Positive/Negative Results:

1 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Fentanyl Concentration	**% of Cutoff**	**Number of Determination**	**Immunoassay Result**	**Number of Determination**	**Immunoassay Result**
0 ng/mL	0%	22	22 Negative	88	88 Negative
0.25 ng/mL	25%	22	22 Negative	88	88 Negative
0.5 ng/mL	50%	22	22 Negative	88	88 Negative
0.75 ng/mL	75%	22	22 Negative	88	88 Negative
1 ng/mL	100%	22	22 Positive	88	4 Neg/84 Pos
1.25 ng/mL	125%	22	22 Positive	88	88 Positive
1.5 ng/mL	150%	22	22 Positive	88	88 Positive
1.75 ng/mL	175%	22	22 Positive	88	88 Positive
2 ng/mL	200%	22	22 Positive	88	88 Positive

Performance Characteristics Summary, continued:
Beckman Coulter® AU5800 Analyzer

Method Comparison - Clinical Samples:
A total of one hundred and fifty (150) unaltered clinical samples were tested with the LZI Fentanyl III Enzyme Immunoassay on the Beckman Coulter AU5800 automated clinical analyzer. Samples were evaluated against the cutoff calibrator in qualitative mode. All samples were tested in singlet.

All samples were confirmed by LC/MS for fentanyl concentrations. Samples were obtained by LZI and through collaboration with various clinical laboratories across the United States and Canada, including:

- APC Health (Tampa, Florida)
- Calgary Labs (Calgary, Canada)
- Carolina Liquid Chemistries Corporation (Greensboro, North Carolina)
- DTPM (Fort Payne, Alabama)
- Northwest Physicians Laboratories (Bellevue, Washington)
- Soloniuk Pain Clinic (Redding, California)
- Sterling Labs (Chicago, Illinois)
- TriCore Reference Laboratories (Santa Clara, California)
- University of California, San Francisco (San Francisco, California)

Qualitative Accuracy Study:

FEN Results 1 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	20*	12**	22	61
Negative below the cutoff by EIA analysis	35	0	0	0	0

Performance Characteristics Summary, continued:
Beckman Coulter® AU5800 Analyzer

Method Comparison, continued:

Discrepant samples determined when comparing LC/MS fentanyl results with the LZI Fentanyl III EIA results on the Beckman Coulter AU5800 automated clinical analyzer.

Sample #	LC/MS Fentanyl (ng/mL)	LC/MS Norfentanyl (ng/mL)	Pos/ Neg Result		AU5800 EIA Qualitative Result (mAU)	Pos/ Neg Result	Qualitative Cutoff Rate (mAU)
36*	0.0	1.5	-		83.7	+	19.3
37*	0.0	4.1	-		172.3	+	19.3
38*	0.1	1.1	-		57.3	+	19.3
39*	0.1	6.7	-		203.9	+	19.3
40*	0.1	4.1	-		234.2	+	19.3
41*	0.1	4.4	-		192.7	+	19.3
42*	0.1	6.1	-		134.5	+	19.3
43*	0.1	5.3	-		150.6	+	19.3
44*	0.1	4.4	-		104.9	+	19.3
45*	0.2	4.8	-		206.2	+	19.3
46*	0.2	1.9	-		214.7	+	19.3
47*	0.2	2.0	-		151.3	+	19.3
48*	0.2	5.1	-		101.1	+	19.3
49*	0.2	5.0	-		206.2	+	19.3
50*	0.2	39.9	-		213.6	+	22.1
51*	0.2	10.0	-		155.3	+	19.3
52*	0.3	2.4	-		171.4	+	19.3
53*	0.3	9.7	-		253.1	+	19.3
54*	0.3	4.2	-		166.2	+	19.3
55*	0.3	5.4	-		162.5	+	19.3
56**	0.6	2.2	-		185.6	+	19.3
57**	0.6	362.5	-		225.1	+	19.3
58**	0.7	15.9	-		228.2	+	22.1
59**	0.7	101.7	-		246.8	+	22.1
60**	0.7	167.1	-		260.2	+	19.3
61**	0.8	30.2	-		314.7	+	19.3
62**	0.8	2.8	-		45.0	+	22.1
63**	0.8	0.5	-		108.2	+	19.3
64**	0.8	2.8	-		134.8	+	19.3
65**	0.9	15.8	-		224.3	+	19.3
66**	0.9	106.7	-		318.7	+	22.1
67**	0.9	12.0	-		258.4	+	19.3

* Values are discrepant below 50% of the cutoff concentration (0 ng/mL – 0.5 ng/mL fentanyl)
** Values are discrepant between 50% of the cutoff to the cutoff concentration (0.5 ng/mL – 1.0 ng/mL fentanyl)

All discrepant samples contained norfentanyl concentrations that contributed to the positive results.

Performance Characteristics Summary, continued:
Beckman Coulter® AU5800 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.

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	1.0	26.1	17.9	100.00 %
Norfentanyl	2.5	24.4	17.9	40.00 %

Structurally Related Compounds:

Compound	Test Concentration (ng/mL)	Qualitative Result (mAU)	Qualitative Cutoff Rate (mAU)	% Cross-reactivity
4-Fluoro-isobutyryl fentanyl	25	22.1	20.2	4.00%
9-Hydroxy risperidone	100,000	-19.8	20.2	ND
Acetyl fentanyl	4	22.8	20.2	25.00%
Acetyl norfentanyl	100	22.1	20.2	1.00%
Acryl fentanyl	1	36.1	21.1	100.00%
Alfentanil	100,000	-18.5	20.2	ND
Benzyl fentanyl	2	20.7	20.2	50.00%
Butyryl fentanyl	1	24.5	21.1	100.00%
Butyryl norfentanyl	40	26.1	17.9	2.50%
Carfentanil oxalate	100,000	2.7	20.2	ND
(±)cis-3-methyl fentanyl	4.5	34.8	20.2	22.22%
Cyclopropyl norfentanyl	15	21.3	17.9	6.67%
Despropionyl fentanyl (4-ANPP)	100,000	-2.1	20.2	ND
Furanyl fentanyl	2.5	25.5	21.1	40.00%
Furanyl norfentanyl	150	22.4	17.9	0.67%
β-Hydroxyfentanyl	1.1	30.4	17.9	90.91%
(±)-β-hydroxythiofentanyl	1	25.6	21.1	100.00%
Isobutyryl fentanyl	12.5	21.9	17.9	8.00%
Isobutyryl norfentanyl	390	24.5	17.9	0.26%
Methoxyacetyl fentanyl	1	30.1	21.1	100.00%

Performance Characteristics Summary, continued:
Beckman Coulter AU5800 Analyzer

Cross-reactivity, continued:
Structurally Related Compounds, continued:

Compound	Test Concentration (ng/mL)	Qualitative Result (mAU)	Qualitative Cutoff Rate (mAU)	% Cross-reactivity
MT-45	100,000	-22.3	20.2	ND
N-benzyl furanyl norfentanyl	0.75	20.4	20.2	133.33%
N-benzyl para-fluoro norfentanyl	1	32.2	20.2	100.00%
Norcarfentanil oxalate	100,000	-6.5	20.2	ND
Ocfentanil	1	27.4	21.1	100.00%
Para-fluorobutyryl fentanyl	1.2	19.4	17.9	83.33%
Para-fluoro fentanyl	1	32.3	21.1	100.00%
Para-methoxy-butyryl fentanyl	1	24.6	17.9	100.00%
Remifentanil	100,000	-5.5	28.3	ND
Risperidone	100,000	-40.5	20.2	ND
Sufentanil	1,000	23.2	20.2	0.10%
Thienyl fentanyl	0.75	24.9	17.9	133.33%
Thiofentanyl	0.50	21.6	20.2	200.00%
Trans-3-methyl fentanyl	2	18.9	17.9	50.00%
Trazodone	100,000	-7.0	20.2	ND
U-47700	100,000	-22.6	20.2	ND
Valeryl fentanyl	50	21.3	20.2	2.00%
Ortho-methyl fentanyl	3.5	27.5	20.2	28.57%

Performance Characteristics Summary, continued:
Beckman Coulter AU5800 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 fentanyl, and the remaining two that were further spiked with fentanyl standards to a final fentanyl concentration of 0.5 ng/mL or 1.5 ng/mL (as negative or positive controls, ±50% 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.

Interference was observed with Dextromethorphan at 20,000 ng/mL. No other significant cross-reactivity was observed.

Structurally Unrelated Pharmacological Compounds:

Compound	Test Concentration (ng/mL)	0 ng/mL Fentanyl	-50% Fentanyl Cutoff (0.5 ng/mL)	+50% Fentanyl Cutoff (1.5 ng/mL)
		% Cross	Result	Result
(1S,2S)-(+)Pseudoephedrine	100,000	Neg	Neg	Pos
6-Acetylmorphine	100,000	Neg	Neg	Pos
7-Hydroxymitragynine	100,000	Neg	Neg	Pos
Acetaminophen	100,000	Neg	Neg	Pos
Acetylsalicylic acid	100,000	Neg	Neg	Pos
AH 7921	100,000	Neg	Neg	Pos
Alprazolam	100,000	Neg	Neg	Pos
Amitriptyline	100,000	Neg	Neg	Pos
Amlodine besylate	100,000	Neg	Neg	Pos
Amobarbital	100,000	Neg	Neg	Pos
Amoxicillin	100,000	Neg	Neg	Pos
d-Amphetamine	100,000	Neg	Neg	Pos
Aripiprazole	100,000	Neg	Neg	Pos
Atorvastatin	100,000	Neg	Neg	Pos
Benzoylecgonine	100,000	Neg	Neg	Pos
Bisoprolol	100,000	Neg	Neg	Pos
Bromazepam	100,000	Neg	Neg	Pos
Buprenorphine	100,000	Neg	Neg	Pos
Buprenorphine glucuronide	100,000	Neg	Neg	Pos
Bupropion	100,000	Neg	Neg	Pos
Butalbital	100,000	Neg	Neg	Pos
Caffeine	100,000	Neg	Neg	Pos
Cannabidiol	100,000	Neg	Neg	Pos

Performance Characteristics Summary, continued:
Beckman Coulter AU5800 Analyzer

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

Compound	Test Concentration (ng/mL)	0 ng/mL Fentanyl	-50% Fentanyl Cutoff (0.5 ng/mL)	+50% Fentanyl Cutoff (1.5 ng/mL)
		% Cross	Result	Result
Carbamazepine	100,000	Neg	Neg	Pos
Carisoprodol	100,000	Neg	Neg	Pos
Cetirizine	100,000	Neg	Neg	Pos
Chlordiazepoxide	100,000	Neg	Neg	Pos
Chlorpheniramine	100,000	Neg	Neg	Pos
Chlorpromazine	100,000	Neg	Neg	Pos
Clobazam	100,000	Neg	Neg	Pos
Clomipramine	100,000	Neg	Neg	Pos
Clonazepam	100,000	Neg	Neg	Pos
Cocaine	100,000	Neg	Neg	Pos
Codeine	100,000	Neg	Neg	Pos
Cotinine	100,000	Neg	Neg	Pos
Cyclobenzaprine	100,000	Neg	Neg	Pos
Desipramine	100,000	Neg	Neg	Pos
Dextromethorphan	20,000	Neg	Pos	Pos
Diazepam	100,000	Neg	Neg	Pos
Diphenhydramine	100,000	Neg	Neg	Pos
Doxepin	100,000	Neg	Neg	Pos
Doxylamine	100,000	Neg	Neg	Pos
Duloxetine	100,000	Neg	Neg	Pos
EDDP	100,000	Neg	Neg	Pos
Ecgonine	100,000	Neg	Neg	Pos
Ecgonine methyl ester	100,000	Neg	Neg	Pos
EMDP	100,000	Neg	Neg	Pos
Ephedrine	100,000	Neg	Neg	Pos
Fexofenadine	100,000	Neg	Neg	Pos
Flunitrazepam	5000	Neg	Neg	Pos
Fluoxetine	100,000	Neg	Neg	Pos
Fluphenazine	100,000	Neg	Neg	Pos
Flurazepam	100,000	Neg	Neg	Pos
Furosemide	100,000	Neg	Neg	Pos
Gabapentin	100,000	Neg	Neg	Pos
Haloperidol	100,000	Neg	Neg	Pos
Heroin	100,000	Neg	Neg	Pos
Hexobarbital	100,000	Neg	Neg	Pos
Hydrochlorothiazide	100,000	Neg	Neg	Pos
Hydrocodone	100,000	Neg	Neg	Pos
Hydromorphone	100,000	Neg	Neg	Pos

Performance Characteristics Summary, continued:
Beckman Coulter AU5800 Analyzer

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

Compound	Test Concentration (ng/mL)	0 ng/mL Fentanyl	-50% Fentanyl Cutoff (0.5 ng/mL)	+50% Fentanyl Cutoff (1.5 ng/mL)
		% Cross	Result	Result
Ibuprofen	100,000	Neg	Neg	Pos
Imipramine	100,000	Neg	Neg	Pos
Ketamine	100,000	Neg	Neg	Pos
Labetalol	100,000	Neg	Neg	Pos
Lamotrigine	100,000	Neg	Neg	Pos
Levorphanol	100,000	Neg	Neg	Pos
Lidocaine	100,000	Neg	Neg	Pos
Lisinopril	100,000	Neg	Neg	Pos
Loratadine	100,000	Neg	Neg	Pos
Lormetazepam	100,000	Neg	Neg	Pos
Losartan	100,000	Neg	Neg	Pos
LSD	100,000	Neg	Neg	Pos
Maprotiline	100,000	Neg	Neg	Pos
mCPP	100,000	Neg	Neg	Pos
MDA	100,000	Neg	Neg	Pos
MDEA	100,000	Neg	Neg	Pos
MDMA	100,000	Neg	Neg	Pos
Meperidine	100,000	Neg	Neg	Pos
Mephobarbital	100,000	Neg	Neg	Pos
Meprobamate	100,000	Neg	Neg	Pos
Metformin	100,000	Neg	Neg	Pos
Methadone	100,000	Neg	Neg	Pos
d-Methamphetamine	100,000	Neg	Neg	Pos
Methapyrilene	100,000	Neg	Neg	Pos
Methaqualone	100,000	Neg	Neg	Pos
Methylphenidate	100,000	Neg	Neg	Pos
Metoprolol	100,000	Neg	Neg	Pos
Metronidazole	100,000	Neg	Neg	Pos
Minocycline	100,000	Neg	Neg	Pos
Mirtazapine	100,000	Neg	Neg	Pos
Morphine	100,000	Neg	Neg	Pos
Morphine-3-glucuronide	100,000	Neg	Neg	Pos
Nalmefene	100,000	Neg	Neg	Pos
Naloxone	100,000	Neg	Neg	Pos
Naltrexone	100,000	Neg	Neg	Pos
Naproxen	100,000	Neg	Neg	Pos
Nicotine	100,000	Neg	Neg	Pos

Performance Characteristics Summary, continued:
Beckman Coulter AU5800 Analyzer

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

Compound	Test Concentration (ng/mL)	0 ng/mL Fentanyl	-50% Fentanyl Cutoff (0.5 ng/mL)	+50% Fentanyl Cutoff (1.5 ng/mL)
		% Cross	Result	Result
Nitrazepam	100,000	Neg	Neg	Pos
Norbuprenorphine	100,000	Neg	Neg	Pos
Norcodeine	100,000	Neg	Neg	Pos
Norketamine	100,000	Neg	Neg	Pos
Normeperidine	100,000	Neg	Neg	Pos
Normorphine	100,000	Neg	Neg	Pos
Norquetiapine	100,000	Neg	Neg	Pos
Nortriptyline	100,000	Neg	Neg	Pos
Olanzapine	100,000	Neg	Neg	Pos
Omeprazole	100,000	Neg	Neg	Pos
Oxazepam	100,000	Neg	Neg	Pos
Oxycodone	100,000	Neg	Neg	Pos
Oxymorphone	100,000	Neg	Neg	Pos
Paroxetine	100,000	Neg	Neg	Pos
Pentazocine	100,000	Neg	Neg	Pos
Pentobarbital	100,000	Neg	Neg	Pos
Perphenazine	100,000	Neg	Neg	Pos
Phencyclidine	100,000	Neg	Neg	Pos
Phenobarbital	100,000	Neg	Neg	Pos
Phentermine	100,000	Neg	Neg	Pos
Propoxyphene	100,000	Neg	Neg	Pos
Quetiapine	100,000	Neg	Neg	Pos
Quinidine	100,000	Neg	Neg	Pos
Ranitidine	100,000	Neg	Neg	Pos
Ritalinic acid	100,000	Neg	Neg	Pos
Phenytoin	100,000	Neg	Neg	Pos
Salbutamol	100,000	Neg	Neg	Pos
Salicylic acid	100,000	Neg	Neg	Pos
Secobarbital	100,000	Neg	Neg	Pos
Sertraline	100,000	Neg	Neg	Pos
Sildenafil	100,000	Neg	Neg	Pos
Tapentadol	100,000	Neg	Neg	Pos
Temazepam	100,000	Neg	Neg	Pos
THC	100,000	Neg	Neg	Pos
Thebaine	100,000	Neg	Neg	Pos
Theophylline	100,000	Neg	Neg	Pos
Thioridazine	100,000	Neg	Neg	Pos
l-Thyroxine	100,000	Neg	Neg	Pos

Performance Characteristics Summary, continued:
Beckman Coulter AU5800 Analyzer

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

Compound	Test Concentration (ng/mL)	0 ng/mL Fentanyl	-50% Fentanyl Cutoff (0.5 ng/mL)	+50% Fentanyl Cutoff (1.5 ng/mL)
		% Cross	Result	Result
Tilidine	100,000	Neg	Neg	Pos
Tramadol	100,000	Neg	Neg	Pos
Trazadone	100,000	Neg	Neg	Pos
Triazolam	100,000	Neg	Neg	Pos
Trimipramine	100,000	Neg	Neg	Pos
Valproic Acid	100,000	Neg	Neg	Pos
Verapamil	100,000	Neg	Neg	Pos
Venlafaxine	100,000	Neg	Neg	Pos
Ziprasidone	100,000	Neg	Neg	Pos
Zolpidem	100,000	Neg	Neg	Pos
Zopiclone	100,000	Neg	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

The following structurally unrelated compound which showed interference at ±50% of the cutoff concentration was then tested at the highest concentration that did not cause a discrepant result. The result is summarized in the following table:

Compound	Spiked [ ] (ng/mL)	Spiked Fentanyl Concentration		
		0 ng/mL (ng/mL)	0.5 ng/mL Control (ng/mL)	1.5 ng/mL Control (ng/mL)
Dextromethorphan	15,000	Neg	Neg	Pos

Performance Characteristics Summary, continued:
Beckman Coulter AU5800 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 fentanyl, and the remaining two that were further spiked with fentanyl standards to a final fentanyl concentration of 0.5 ng/mL or 1.5 ng/mL (as negative or positive controls, ±50% 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 Fentanyl	-50% Fentanyl Cutoff (0.5 ng/mL)	+50% Fentanyl Cutoff (1.5 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 AU5800 Analyzer

Specific Gravity Interference:
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 fentanyl concentration of either 0.5 ng/mL or 1.5 ng/mL (as negative or positive controls, ±50% of the cutoff concentration, respectively). These samples were then evaluated in qualitative mode. No interference was observed.

Specific Gravity Value	0 ng/mL Fentanyl	-50% Fentanyl Cutoff (0.5 ng/mL)	+50% Fentanyl Cutoff (1.5 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
1.011	Neg	Neg	Pos
1.013	Neg	Neg	Pos
1.015	Neg	Neg	Pos
1.018	Neg	Neg	Pos
1.020	Neg	Neg	Pos
1.022	Neg	Neg	Pos
1.023	Neg	Neg	Pos
1.025	Neg	Neg	Pos
1.030	Neg	Neg	Pos

Performance Characteristics Summary, continued:
Beckman Coulter AU5800 Analyzer

pH Interference:
Negative urine and urine spiked with fentanyl to the final fentanyl concentration of either 0.5 ng/mL or 1.5 ng/mL (as negative or positive controls, ±50% 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 Fentanyl	-50% Fentanyl Cutoff (0.5 ng/mL)	+50% Fentanyl Cutoff (1.5 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 Fentanyl III 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 III Enzyme Immunoassay is safe and effective for its stated intended use.