September 17, 2020

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

Re: K202007
Trade/Device Name: LZI Oxycodone III Enzyme Immunoassay
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate Test System
Regulatory Class: Class II
Product Code: DJG
Dated: July 17, 2020
Received: July 21, 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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
k202007

Device Name

LZI Oxycodone III Enzyme Immunoassay

Indications for Use *(Describe)*

The LZI Oxycodone III Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of oxycodone in human urine at the cutoff values of 100 ng/mL and 300 ng/mL when calibrated against oxycodone. 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 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 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.

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 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

k202007

Prepared On

September 14, 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 of Operations

Device Name and Classification

Classification Name:	Enzyme Immunoassay, Oxycodone Class II, DJG (91 Toxicology) 21 CFR 862.3650
Common Name:	Oxycodone Enzyme Immunoassay
Proprietary Name:	LZI Oxycodone III Enzyme Immunoassay

Legally Marketed Predicate Device(s)

The LZI Oxycodone III Enzyme Immunoassay (EIA) is substantially equivalent to the LZI Oxycodone Assay (k120763) manufactured by *Lin-Zhi International, Inc.* (LZI). The LZI Oxycodone III 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 Oxycodone III 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 oxycodone standard and referred to as oxycodone-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, oxycodone-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 oxycodone-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 Oxycodone III 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 Oxycodone III Enzyme Immunoassay is traceable to a commercially available oxycodone standard.

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

Intended Use

The LZI Oxycodone III Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of oxycodone in human urine at the cutoff values of 100 ng/mL and 300 ng/mL when calibrated against oxycodone. 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 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 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 Oxycodone III Enzyme Immunoassay is substantially equivalent to the LZI Oxycodone Assay cleared by the FDA under the premarket notification k120763 for its stated intended use.

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

Device Characteristics	**Subject Device** LZI Oxycodone III Enzyme Immunoassay	**Predicate Device (k120763)** LZI Oxycodone Enzyme Immunoassay
Intended Use	The Lin-Zhi International, Inc. (LZI) Oxycodone III Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of oxycodone in human urine at a cutoff value of 100 ng/mL and 300 ng/mL when calibrated against oxycodone. 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 verification by a confirmatory method such as 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 confirmatory method (e.g., gas or liquid chromatography and mass spectrometry) must be used to obtain a confirmed analytical result (1, 2). 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, Inc. (LZI) Oxycodone Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of oxycodone in human urine, at cutoff values of 100 ng/mL and 300 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 analytical chemistry method must be used in order to obtain a confirmed analytical result. Gas or Liquid Chromatography/Mass Spectrometry (GC/MS or LC/MS) are the preferred confirmatory methods. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.**
Target Analyte	oxycodone	oxycodone
Cutoff	100 ng/ and 300 ng/mL	100 and 300 ng/mL
Matrix	Urine	Urine
Calibrator Levels	100 ng/mL Cutoff: 5 Levels 0, 50, 100, 150, and 300 ng/mL 300 ng/mL Cutoff: 5 Levels 0, 150, 300, 500, and 800 ng/mL	0, 50, 100, 300, 500, and 800 ng/mL

Device Characteristics	Subject Device LZI Oxycodone III Enzyme Immunoassay	Predicate Device (k120763) LZI Oxycodone Enzyme Immunoassay
Control Levels	100 ng/mL Cutoff: 2 Levels 75 and 125 ng/mL 300 ng/mL Cutoff: 2 Levels 225 and 375 ng/mL	100 ng/mL Cutoff: 2 Levels 75 and 125 ng/mL 300 ng/mL Cutoff: 2 Levels 225 and 375 ng/mL
Storage	2-8 ºC until expiration date	2-8 ºC until expiration date

Performance Characteristics Summary:

All validation studies below were conducted on the Beckman Coulter® AU480 Analyzer

Precision: 100 ng/mL Cutoff

The assay was tested in qualitative and semi-quantitative mode by spiking oxycodone into pooled negative 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 for 22 days on one Beckman Coulter AU480 automatic clinical analyzer for a total of 88 runs.

Semi-Quantitative Positive/Negative Results:

100 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Oxycodone Concentration	**% of Cutoff**	**Number of Determinations**	**Immunoassay Result**	**Number of Determinations**	**Immunoassay Result**
0 ng/mL	0 %	22	22 Negative	88	88 Negative
25 ng/mL	25 %	22	22 Negative	88	88 Negative
50 ng/mL	50 %	22	22 Negative	88	88 Negative
75 ng/mL	75 %	22	22 Negative	88	88 Negative
100 ng/mL	100 %	22	5 Neg / 17 Pos	88	26 Neg / 62 Pos
125 ng/mL	125 %	22	22 Positive	88	88 Positive
150 ng/mL	150 %	22	22 Positive	88	88 Positive
175 ng/mL	175 %	22	22 Positive	88	88 Positive
200 ng/mL	200 %	22	22 Positive	88	88 Positive

Qualitative Positive/Negative Results:

100 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Oxycodone Concentration	**% of Cutoff**	**Number of Determinations**	**Immunoassay Result**	**Number of Determinations**	**Immunoassay Result**
0 ng/mL	0 %	22	22 Negative	88	88 Negative
25 ng/mL	25 %	22	22 Negative	88	88 Negative
50 ng/mL	50 %	22	22 Negative	88	88 Negative
75 ng/mL	75 %	22	22 Negative	88	88 Negative
100 ng/mL	100 %	22	9 Neg / 13 Pos	88	33 Neg / 55 Pos
125 ng/mL	125 %	22	22 Positive	88	88 Positive
150 ng/mL	150 %	22	22 Positive	88	88 Positive
175 ng/mL	175 %	22	22 Positive	88	88 Positive
200 ng/mL	200 %	22	22 Positive	88	88 Positive

Analytical Recovery: 100 ng/mL Cutoff

To demonstrate recovery of the entire assay range, a drug free-urine pool spiked with oxycodone at 300 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. Results are summarized below:

Target Concentration (ng/mL)	**Determined Concentration Range (ng/mL)**	**Determined Concentration Average (ng/mL)**	**Average % Recovery**
300	299.7 - 304.7	302.1	100.7 %
270	277.5 - 287.4	282.7	104.7 %
240	253.3 - 264.3	260.4	108.5 %
210	219.8 - 241.2	231.0	110.0 %
180	193.3 - 201.8	197.0	109.5 %
150	149.1 - 158.7	153.6	102.4 %
120	118.6 - 124.2	121.4	101.2 %
90	86.3 - 90.7	88.8	98.6 %
60	54.5 - 59.4	56.9	94.8 %
30	25.7 - 29.5	27.1	90.3 %
0	-0.7 - 1.7	0.7	N/A

Method Comparison - Clinical Samples: 100 ng/mL Cutoff

A total of eighty-two (82) unaltered clinical samples were tested with the LZI Oxycodone III Enzyme Immunoassay on the Beckman Coulter AU480 automated clinical analyzer. All samples were tested in singlet.

Semi-Quantitative Results:

Oxycodone Results 100 ng/mL Cutoff	**Negative**	**< 50 % of the cutoff** concentration by LC/MS analysis	**Near Cutoff Negative** (Between 50 % below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50 % above the cutoff concentration)	**High Positive** (Greater than 50 % above the cutoff concentration)	**% Agreement**
Positive	0	0	2*	12	25	90.2 %
Negative	20	9	10	4**	0	95.1 %

Discordant samples determined when comparing LC/MS oxycodone and oxymorphone results with EIA results on the Beckman Coulter AU480 automated clinical analyser are shown in the table below.

Sample #	**LC/MS Oxycodone (ng/mL)**	**LC/MS Oxymorphone (ng/mL)**		**Total Oxycodone + Oxymorphone LC/MS (ng/mL)**
37*	35.5	54.4		89.9
38*	46.4	44.6		91.0
42**	0.0	102.7		102.7
43**	2.2	104.8		107.0

Sample #	LC/MS Oxycodone (ng/mL)	LC/MS Oxymorphone (ng/mL)		Total Oxycodone + Oxymorphone LC/MS (ng/mL)
50**	12.6	118.5		131.1
52**	36.9	101.8		138.7

* Discordant between 50 % below cutoff and cutoff concentration (50 – 99.9 ng/mL)
** Discordant between cutoff and 50 % above cutoff concentration (100 – 149.9 ng/mL)

Qualitative Accuracy Study:

Oxycodone Results 100 ng/mL Cutoff	**Negative**	**< 50 % of the cutoff** concentration by LC/MS analysis	**Near Cutoff Negative** (Between 50 % below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50 % above the cutoff concentration)	**High Positive** (Greater than 50 % above the cutoff concentration)	**% Agreement**
Positive	0	0	2*	12	25	90.2 %
Negative	20	9	10	4**	0	95.1 %

Discordant samples determined when comparing LC/MS oxycodone and oxymorphone results with EIA results on the Beckman Coulter AU480 automated clinical analyser are shown in the table below.

Sample #	LC/MS Oxycodone (ng/mL)	LC/MS Oxymorphone (ng/mL)		Total Oxycodone + Oxymorphone LC/MS (ng/mL)
37*	35.5	54.4		89.9
38*	46.4	44.6		91.0
42*	0.0	102.7		102.7
43*	2.2	104.8		107.0
50*	12.6	118.5		131.1
52*	36.9	101.8		138.7

* Discordant between 50% below cutoff and cutoff concentration (50 – 99.9 ng/mL)
** Discordant between cutoff and 50% above cutoff concentration (100 – 149.9 ng/mL)

Cross-reactivity: 100 ng/mL 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 both qualitative and semi-quantitative modes. 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). Compounds tested below the high concentration (100,000 ng/mL) that gave a result below the cutoff value were given a "< %" value.

Oxycodone and Major Metabolites:

Compound	Test Concentration (ng/mL)	% Cross-reactivity
Oxycodone	100	100.00 %
Oxymorphone	100	100.00 %
Noroxycodone	25,000	0.40 %
Noroxymorphone	60,000	0.17 %

Structurally Related Compounds:

Compound	Test Concentration (ng/mL)	% Cross-reactivity
6-Acetylmorphine	100,000	ND
Buprenorphine	100,000	ND
Codeine	100,000	ND
Codeine-6β-D-Glucuronide	100,000	ND
Dextromethorphan	100,000	ND
Dihydrocodeine	100,000	ND
Hydrocodone	25,000	0.40 %
Hydromorphone	25,000	0.40 %
Levorphanol	100,000	ND
Morphine	100,000	ND
Morphine-3β-D-Glucuronide	100,000	ND
Morphine-6β-D-Glucuronide	100,000	ND
Naloxone	100,000	ND
Naloxone-3β-D-Glucuronide	100,000	ND
Norbuprenorphine	100,000	ND
Norcodeine	100,000	ND
Norhydrocodone	100,000	ND
Oxymorphone-3β-D-Glucuronide	230	43.48 %

Structurally unrelated compounds were additionally spiked into pooled negative human urine to desired concentrations (as described below). These solutions were then split into three portions; one without oxycodone, and the remaining two that were further spiked with oxycodone standards to a final oxycodone concentration of 75 ng/mL or 125 ng/mL (as negative or positive controls, ±25 % of the cutoff concentration, respectively). Samples were then evaluated against the cutoff calibrator in qualitative mode or the assay's calibration curve in semi-quantitative 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). Compounds tested below the high concentration (100,000 ng/mL) that gave a result below the cutoff value were given a "< %" value.

Structurally Unrelated Pharmacological Compounds: 100 ng/mL Cutoff

Compound	Test Concentration (ng/mL)	-25 % Oxycodone Cutoff (75 ng/mL)	+25 % Oxycodone Cutoff (125 ng/mL)
		Result	Result
Acetaminophen	100,000	Neg	Pos
Acetylsalicylic Acid	100,000	Neg	Pos
Amitriptyline	100,000	Neg	Pos
Amlodipine Besylate	100,000	Neg	Pos
Amoxicillin	100,000	Neg	Pos
d-Amphetamine	100,000	Neg	Pos
Atorvastatin	20,000	Neg	Pos
Benzoylecgonine	100,000	Neg	Pos
Bupropion	100,000	Neg	Pos
Caffeine	100,000	Neg	Pos
Carbamazepine	100,000	Neg	Pos
Cetirizine	100,000	Neg	Pos
Chlorpheniramine	100,000	Neg	Pos
Chlorpromazine	100,000	Neg	Pos
Clomipramine	100,000	Neg	Pos
Desipramine	100,000	Neg	Pos
Diphenhydramine	100,000	Neg	Pos
Duloxetine	100,000	Neg	Pos
Fentanyl	100,000	Neg	Pos
Fluoxetine	100,000	Neg	Pos
Fluphenazine	100,000	Neg	Pos
Gabapentin	100,000	Neg	Pos
Ibuprofen	100,000	Neg	Pos
Imipramine	100,000	Neg	Pos
Lisinopril	100,000	Neg	Pos
Losartan	10,000	Neg	Pos
Loratadine	100,000	Neg	Pos
MDA (3,4-methylenedioxyamphetamine)	100,000	Neg	Pos
MDEA	100,000	Neg	Pos
MDMA (3,4-methylenedioxymethamphetamine)	100,000	Neg	Pos
Meperidine	100,000	Neg	Pos
Metformin	100,000	Neg	Pos
Metoprolol	100,000	Neg	Pos
Methadone	100,000	Neg	Pos
d-Methamphetamine	100,000	Neg	Pos
Nicotine	100,000	Neg	Pos
Nortriptyline	100,000	Neg	Pos
Omeprazole	100,000	Neg	Pos
Oxazepam	100,000	Neg	Pos
Phenobarbital	100,000	Neg	Pos
(1S,2S)-(+)Pseudoephedrine	100,000	Neg	Pos
Quetiapine	100,000	Neg	Pos

Compound	Test Concentration (ng/mL)	-25 % Oxycodone Cutoff (75 ng/mL)	+25 % Oxycodone Cutoff (125 ng/mL)
		Result	Result
Ranitidine	100,000	Neg	Pos
Salbutamol (Albuterol)	100,000	Neg	Pos
Sertraline	100,000	Neg	Pos
THC-COOH (11-Nor-Delta-9-THC-9-carboxylic acid)	1000	Neg	Pos
l-Thyroxine	10,000	Neg	Pos
Tramadol	100,000	Neg	Pos
Zolpidem	10,000	Neg	Pos

Endogenous and Preservative Compound Interference: 100 ng/mL 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 oxycodone, and the remaining two that were further spiked with oxycodone standards to a final oxycodone concentration of 75 ng/mL or 125 ng/mL (as negative or positive controls, ±25 % of the cutoff concentration, respectively). Samples were then evaluated against the cutoff calibrator in qualitative mode and the assay's calibration curve in semi-quantitative mode. All samples were tested in duplicates.

Interfering Substance	Concentration of Compound (mg/dL)	-25 % Oxycodone Cutoff (75 ng/mL)	+25 % Oxycodone Cutoff (125 ng/mL)
Acetone	1000	Neg	Pos
Ascorbic Acid	1500	Neg	Pos
Bilirubin	2	Neg	Pos
Boric Acid	1000	Neg	Neg
Calcium Chloride ($CaCl_2$)	300	Neg	Pos
Citric Acid (pH 3)	800	Neg	Pos
Creatinine	500	Neg	Pos
Ethanol	1000	Neg	Pos
Galactose	10	Neg	Pos
γ-Globulin	500	Neg	Pos
Glucose	3000	Neg	Pos
Hemoglobin	300	Neg	Pos
β-hydroxybutyric Acid	100	Neg	Pos
Human Serum Albumin	500	Neg	Pos
Oxalic Acid	100	Neg	Pos
Potassium Chloride	6000	Neg	Pos
Riboflavin	7.5	Neg	Pos
Urea	6000	Neg	Pos
Uric Acid	10	Neg	Pos
Sodium Azide	1000	Neg	Pos
Sodium Chloride	6000	Neg	Pos
Sodium Fluoride	1000	Neg	Pos
Sodium Phosphate	300	Neg	Pos

The following endogenous and preservative compounds which showed interference at ±25 % of the cutoff concentration were then spiked into negative urine and at ±50 % of the cutoff concentration (50 ng/mL and 150 ng/mL) for the assay.

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

Interfering Substance	Concentration of Compound (mg/dL)	-50 % Oxycodone Cutoff (50 ng/mL)	+50 % Oxycodone Cutoff (150 ng/mL)
Boric Acid	1000	Neg	Neg

Specific Gravity Interference: 100 ng/mL Cutoff

Samples ranging in specific gravity from 1.000 to 1.030 were spiked to a final oxycodone concentration of either 75 ng/mL or 125 ng/mL (as negative or positive controls, ±25 % of the cutoff concentration, respectively). These samples were then evaluated in both semi-quantitative and qualitative modes. There were no deviations from the expected positive or negative results.

pH Interference: 100 ng/mL Cutoff

Negative urine and urine spiked with oxycodone to a final oxycodone concentration of either 75 ng/mL or 125 ng/mL (as negative or positive controls, ±25 % of the cutoff concentration, respectively) were adjusted to pH levels from 3 to 11 and tested by the assay. The pH adjusted solutions were evaluated in both qualitative and semi-quantitative modes and there were no deviations from the expected results.

Precision: 300 ng/mL Cutoff

The assay was tested in qualitative and semi-quantitative mode by spiking oxycodone into pooled negative 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 for 22 days on one Beckman Coulter AU480 automatic clinical analyzer for a total of 88 runs.

Semi-Quantitative Positive/Negative Results:

300 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Oxycodone Concentration	% of Cutoff	Number of Determination	Immunoassay Result	Number of Determination	Immunoassay Result
0 ng/mL	0 %	22	22 Negative	88	88 Negative
75 ng/mL	25 %	22	22 Negative	88	88 Negative
150 ng/mL	50 %	22	22 Negative	88	88 Negative
225 ng/mL	75 %	22	22 Negative	88	88 Negative
300 ng/mL	100 %	22	6 Neg/16 Pos	88	27 Neg/61 Pos
375 ng/mL	125 %	22	22 Positive	88	88 Positive
450 ng/mL	150 %	22	22 Positive	88	88 Positive
525 ng/mL	175 %	22	22 Positive	88	88 Positive
600 ng/mL	200 %	22	22 Positive	88	88 Positive

Qualitative Positive/Negative Results:

300 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Oxycodone Concentration	**% of Cutoff**	**Number of Determinations**	**Immunoassay Result**	**Number of Determinations**	**Immunoassay Result**
0 ng/mL	0 %	22	22 Negative	88	88 Negative
75 ng/mL	25 %	22	22 Negative	88	88 Negative
150 ng/mL	50 %	22	22 Negative	88	88 Negative
225 ng/mL	75 %	22	22 Negative	88	88 Negative
300 ng/mL	100 %	22	10 Neg / 12 Pos	88	40 Neg / 48 Pos
375 ng/mL	125 %	22	22 Positive	88	88 Positive
450 ng/mL	150 %	22	22 Positive	88	88 Positive
525 ng/mL	175 %	22	22 Positive	88	88 Positive
600 ng/mL	200 %	22	22 Positive	88	88 Positive

Analytical Recovery: 300 ng/mL Cutoff

To demonstrate recovery of the entire assay range, a drug free-urine pool spiked with oxycodone at 800 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. Results are summarized below.

Target Concentration (ng/mL)	Determined Concentration Range (ng/mL)	Determined Concentration Average (ng/mL)	Average % Recovery
800	829.6 – 859.3	843.5	105.4 %
720	769.7 – 794.1	784.2	108.9 %
640	689.6 – 731.2	712.8	111.4 %
560	603.8 – 640.0	624.3	111.5 %
480	497.8 – 525.2	514.2	107.1 %
400	427.2 – 451.5	436.8	109.2 %
320	327.6 – 359.1	345.0	107.8 %
240	242.9 – 260.8	250.8	104.5 %
160	168.3 – 183.4	173.9	108.7 %
80	82.9 – 95.0	89.0	111.2 %
0	-5.2 – 5.9	0.3	N/A

Method Comparison - Clinical Samples: 300 ng/mL Cutoff

A total of ninety (90) unaltered clinical samples were tested with the LZI Oxycodone III Enzyme Immunoassay on the Beckman Coulter AU480 automated clinical analyzer. All samples were tested in singlet.

All samples were confirmed with LC/MS for oxycodone and oxymorphone concentrations.

Semi-Quantitative Results:

Oxycodone Results 300 ng/mL Cutoff	**Negative**	**< 50 % of the cutoff** concentration by LC/MS analysis	**Near Cutoff Negative** (Between 50 % below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50 % above the cutoff concentration)	**High Positive** (Greater than 50 % above the cutoff concentration)	**% Agreement**
Positive	0	0	2*	11	33	97.8 %
Negative	20	6	17	1**	0	95.6 %

Discordant samples determined when comparing LC/MS oxycodone and oxymorphone results with EIA results on the Beckman Coulter AU480 automated clinical analyser are shown in the table below.

Sample #	**LC/MS Oxycodone (ng/mL)**	**LC/MS Oxymorphone (ng/mL)**		**Total Oxycodone + Oxymorphone LC/MS (ng/mL)**
42*	200.2	49.5		249.7
43*	53.0	203.5		256.5
55**	46.7	367.3		414.0

* Discordant between 50 % below cutoff and cutoff concentration (150 – 299.9 ng/mL)
** Discordant between cutoff and 50 % above cutoff concentration (300 – 449.9 ng/mL)

Qualitative Accuracy Study:

Oxycodone Results 300 ng/mL Cutoff	**Negative**	**< 50 % of the cutoff** concentration by LC/MS analysis	**Near Cutoff Negative** (Between 50 % below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50 % above the cutoff concentration)	**High Positive** (Greater than 50 % above the cutoff concentration)	**% Agreement**
Positive	0	0	2*	10	33	95.6 %
Negative	20	6	17	2**	0	95.6 %

Discordant samples determined when comparing LC/MS oxycodone and oxymorphone results with EIA results on the Beckman Coulter AU480 automated clinical analyser are shown in the table below.

Sample #	**LC/MS Oxycodone (ng/mL)**	**LC/MS Oxymorphone (ng/mL)**		**Total Oxycodone + Oxymorphone LC/MS (ng/mL)**
42*	200.2	49.5		249.7
43*	53.0	203.5		256.5
50**	177.2	212.1		389.3
55**	46.7	367.3		414.0

* Discordant between 50% below cutoff and cutoff concentration (150 – 299.9 ng/mL)
** Discordant between cutoff and 50% above cutoff concentration (300 – 449.9 ng/mL)

Cross-reactivity: 300 ng/mL 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 both qualitative and semi-quantitative modes. 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). Compounds tested below the high concentration (100,000 ng/mL) that gave a result below the cutoff value were given a "< %" value.

Oxycodone and Major Metabolites:

Compound	Test Concentration (ng/mL)	% Cross-reactivity
Oxycodone	300	100.00 %
Oxymorphone	300	100.00 %
Noroxycodone	75,000	0.40 %
Noroxymorphone	100,000	ND

Structurally Related Compounds:

Compound	Test Concentration (ng/mL)	% Cross-reactivity
6-Acetylmorphine	100,000	ND
Buprenorphine	100,000	ND
Codeine	100,000	ND
Codeine-6β-D-Glucuronide	100,000	ND
Dextromethorphan	100,000	ND
Dihydrocodeine	100,000	ND
Hydrocodone	75,000	0.40 %
Hydromorphone	75,000	0.40 %
Levorphanol	100,000	ND
Morphine	100,000	ND
Morphine-3β-D-Glucuronide	100,000	ND
Morphine-6β-D-Glucuronide	100,000	ND
Naloxone	100,000	ND
Naloxone-3β-D-Glucuronide	100,000	ND
Norbuprenorphine	100,000	ND
Norcodeine	100,000	ND
Norhydrocodone	100,000	ND
Oxymorphone-3β-D-Glucuronide	700	42.86 %

Structurally unrelated compounds were additionally spiked into pooled negative human urine to desired concentrations (as described below). These solutions were then split into three portions; one without oxycodone, and the remaining two that were further spiked with oxycodone standards to a final oxycodone concentration of 225 ng/mL or 375 ng/mL (as negative or positive controls, ±25 % of the cutoff concentration, respectively). Samples were then evaluated against the cutoff calibrator in qualitative mode and against the assay's calibration curve in semi-quantitative 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). Compounds tested below the high concentration (100,000 ng/mL) that gave a result below the cutoff value were given a "< %" value.

Structurally Unrelated Pharmacological Compounds: 300 ng/mL Cutoff

Compound	Test Concentration (ng/mL)	-25 % Oxycodone Cutoff (225 ng/mL)	+25 % Oxycodone Cutoff (375 ng/mL)
		Result	Result
Acetaminophen	100,000	Neg	Pos
Acetylsalicylic Acid	100,000	Neg	Pos
Amitriptyline	100,000	Neg	Pos
Amlodipine Besylate	100,000	Neg	Pos
Amoxicillin	100,000	Neg	Pos
d-Amphetamine	100,000	Neg	Pos
Atorvastatin	20,000	Neg	Pos
Benzoylecgonine	100,000	Neg	Pos
Bupropion	100,000	Neg	Pos
Caffeine	100,000	Neg	Pos
Carbamazepine	100,000	Neg	Pos
Cetirizine	100,000	Neg	Pos
Chlorpheniramine	100,000	Neg	Pos
Chlorpromazine	100,000	Neg	Pos
Clomipramine	100,000	Neg	Pos
Desipramine	100,000	Neg	Pos
Diphenhydramine	100,000	Neg	Pos
Duloxetine	100,000	Neg	Pos
Fentanyl	100,000	Neg	Pos
Fluoxetine	100,000	Neg	Pos
Fluphenazine	100,000	Neg	Pos
Gabapentin	100,000	Neg	Pos
Ibuprofen	100,000	Neg	Pos
Imipramine	100,000	Neg	Pos
Lisinopril	100,000	Neg	Pos
Losartan	10,000	Neg	Pos
Loratadine	100,000	Neg	Pos
MDA (3,4-methylenedioxyamphetamine)	100,000	Neg	Pos
MDEA	100,000	Neg	Pos
MDMA (3,4-methylenedioxymethamphetamine)	100,000	Neg	Pos
Meperidine	100,000	Neg	Pos

Compound	Test Concentration (ng/mL)	-25 % Oxycodone Cutoff (225 ng/mL)	+25 % Oxycodone Cutoff (375 ng/mL)
		Result	Result
Metformin	100,000	Neg	Pos
Metoprolol	100,000	Neg	Pos
Methadone	100,000	Neg	Pos
d-Methamphetamine	100,000	Neg	Pos
Nicotine	100,000	Neg	Pos
Nortriptyline	100,000	Neg	Pos
Omeprazole	100,000	Neg	Pos
Oxazepam	100,000	Neg	Pos
Phenobarbital	100,000	Neg	Pos
(1S,2S)-(+)Pseudoephedrine	100,000	Neg	Pos
Quetiapine	100,000	Neg	Pos
Ranitidine	100,000	Neg	Pos
Salbutamol (Albuterol)	100,000	Neg	Pos
Sertraline	100,000	Neg	Pos
THC-COOH (11-Nor-Delta-9-THC-9-carboxylic acid)	1000	Neg	Pos
l-Thyroxine	10,000	Neg	Pos
Tramadol	100,000	Neg	Pos
Zolpidem	10,000	Neg	Pos

Endogenous and Preservative Compound Interference: 300 ng/mL 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 oxycodone, and the remaining two that were further spiked with oxycodone standards to a final oxycodone concentration of 225 ng/mL or 375 ng/mL (as negative or positive controls, ±25 % of the cutoff concentration, respectively). Samples were then evaluated against the cutoff calibration in qualitative mode and against the assay's calibration curve in semi-quantitative mode. All samples were tested in duplicates.

Interfering Substance	Concentration of Compound (mg/dL)	-25 % Oxycodone Cutoff (225 ng/mL)	+25 % Oxycodone Cutoff (375 ng/mL)
Acetone	1000	Neg	Pos
Ascorbic Acid	1500	Neg	Pos
Bilirubin	2	Neg	Pos
Boric Acid	1000	Neg	Neg
Calcium Chloride ($CaCl_2$)	300	Neg	Pos
Citric Acid (pH 3)	800	Neg	Pos
Creatinine	500	Neg	Pos
Ethanol	1000	Neg	Pos
Galactose	10	Neg	Pos
γ-Globulin	500	Neg	Pos
Glucose	3000	Neg	Pos
Hemoglobin	300	Neg	Pos
β-hydroxybutyric Acid	100	Neg	Pos

Interfering Substance	Concentration of Compound (mg/dL)	-25 % Oxycodone Cutoff (225 ng/mL)	+25 % Oxycodone Cutoff (375 ng/mL)
Human Serum Albumin	500	Neg	Pos
Oxalic Acid	100	Neg	Pos
Potassium Chloride	6000	Neg	Pos
Riboflavin	7.5	Neg	Pos
Urea	6000	Neg	Pos
Uric Acid	10	Neg	Pos
Sodium Azide	1000	Neg	Pos
Sodium Chloride	6000	Neg	Pos
Sodium Fluoride	1000	Neg	Pos
Sodium Phosphate	300	Neg	Pos

The following endogenous and preservative compounds which showed interference at ±25 % of the cutoff concentrations were then spiked into negative urine and at ±50 % of the cutoff concentration (150 ng/mL and 450 ng/mL) for the assay.

No other significant undesired cross-reactants or endogenous/preservative substance interference were observed.

Interfering Substance	Concentration of Compound (mg/dL)	-50 % Oxycodone Cutoff (150 ng/mL)	+50 % Oxycodone Cutoff (450 ng/mL)
Boric Acid	1000	Neg	Pos

Specific Gravity Interference: 300 ng/mL Cutoff

Samples ranging in specific gravity from 1.000 to 1.030 were spiked to a final oxycodone concentration of either 225 ng/mL or 375 ng/mL (as negative or positive controls, ±25 % of the cutoff concentration, respectively). These samples were then evaluated in both semi-quantitative and qualitative modes. There were no deviations from the expected positive or negative results.

pH Interference: 300 ng/mL Cutoff

Negative urine and urine spiked with oxycodone to a final oxycodone concentration of either 225 ng/mL or 375 ng/mL (as negative or positive controls, ±25 % of the cutoff concentration, respectively) were adjusted to pH levels from 3 to 11 levels and tested by the assay. The pH adjusted solutions were evaluated in both qualitative and semi-quantitative modes and there were no deviations from the expected results.

Conclusions:

The information provided in this pre-market notification demonstrates that the LZI Oxycodone III Enzyme Immunoassay is substantially equivalent to the legally marketed predicate device for its intended use, as demonstrated through comparison of intended use and performance characteristics.