DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

June 26, 2017

LIN-ZHI INTERNATIONAL, INC.
BERNICE LIN
VP OPERATIONS
2945 OAKMEAD VILLAGE COURT
SANTA CLARA CA 95051

Re: k170416
Trade/Device Name: LZI Methadone Metabolite (EDDP) Enzyme Immunoassay,
LZI Methadone Metabolite (EDDP) (100 And 300) Calibrators
Regulation Number: 21 CFR 862.3620
Regulation Name: Methadone test system
Regulatory Class: II
Product Code: DJR, DLJ
Dated: May 24, 2017
Received: May 25, 2017

Dear Ms. 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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k170416

Device Name
LZI Methadone Metabolite (EDDP) Enzyme Immunoassay
The LZI Methadone Metabolite (EDDP) (100 and 300) Calibrators

Indications for Use *(Describe)*

The LZI Methadone Metabolite (EDDP) Enzyme Immunoassay is an in vitro diagnostic test intended for the qualitative and semi-quantitative determination of Methadone Metabolite in human urine. The cutoff for both the qualitative and semi-quantitative modes of the assay are 100 ng/mL and 300 ng/mL for methadone metabolite. The assay is designed for prescription use on automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) or (2) permitting laboratories to establish quality control procedures.

The assay provides only a preliminary analytical result. A more specific alternative 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) 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 Methadone Metabolite (EDDP) (100 and 300) Calibrators are for use as calibrators in the qualitative and semiquantitative calibration of the LZI Methadone Metabolite (EDDP) Enzyme Immunoassay at the cutoff values of 100 ng/mL and 300 ng/mL.

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.

Submitted On

February 9, 2017

Last Updated On

June 26, 2017

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, Methadone Metabolite Class II, DJR (91 Toxicology), 21 CFR 862.3620
	Drug Specific Calibrators, Class II, DLJ (91 Toxicology), 21 CFR 862.3200
Common Name:	Homogeneous Methadone Metabolite Enzyme Immunoassay
Proprietary Name:	LZI Methadone Metabolite (EDDP) Enzyme Immunoassay, LZI Methadone Metabolite (EDDP) (100 and 300) Calibrators

Legally Marketed Predicate Device(s)

The LZI Methadone Metabolite (EDDP) Enzyme Immunoassay (EIA) is substantially equivalent to the Lin-Zhi International, Inc. Methadone Metabolite (EDDP) Enzyme Immunoassay (k031797) manufactured by Lin-Zhi International, Inc. The LZI Methadone Metabolite (EDDP) 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 Methadone Metabolite (EDDP) Enzyme Immunoassay is a homogeneous enzyme immunoassay with ready-to-use liquid reagents. The assay is based on competition between EDDP in the sample and EDDP labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the EDDP concentration in the sample is measured in terms of enzyme activity. In the absence of EDDP in the sample, EDDP-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when free EDDP is present in the sample, antibody would bind to free EDDP; the unbound EDDP-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 Methadone Metabolite (EDDP) 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 R_1 solution contains mouse monoclonal anti-methadone metabolite 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 methadone metabolite in buffer with sodium azide (0.09 %) as a preservative.

The LZI Methadone Metabolite (EDDP) Enzyme Immunoassay calibrators and controls designated for use at the 100 ng/mL cutoff contain 0, 50, 75, 100, 125, 250, 500 ng/mL of methadone metabolite (EDDP) in human urine with sodium azide (0.09 %) as a preservative. These five calibrators and two controls are sold as individual bottles.

The LZI Methadone Metabolite (EDDP) Enzyme Immunoassay calibrators and controls designated for use at the 300 ng/mL cutoff contain 0, 150, 225, 300, 375, 600, and 1000 ng/mL of methadone metabolite (EDDP) in human urine with sodium azide (0.09 %) as a preservative. These five calibrators and two controls are sold as individual bottles.

Intended Use

The LZI Methadone Metabolite (EDDP) Enzyme Immunoassay is an in vitro diagnostic test intended for the qualitative and semi-quantitative determination of Methadone Metabolite in human urine. The cutoff for both the qualitative and semi-quantitative modes of the assay are 100 ng/mL and 300 ng/mL for methadone metabolite. The assay is designed for prescription use on automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GCMS or LCMS) or (2) permitting laboratories to establish quality control procedures.

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) 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 Methadone Metabolite (EDDP) (100 and 300) Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the LZI Methadone Metabolite (EDDP) Enzyme Immunoassay at the cutoff values of 100 ng/mL and 300 ng/mL.

Comparison to Predicate Device

The LZI Methadone Metabolite (EDDP) Enzyme Immunoassay is substantially equivalent to the Lin-Zhi International, Inc. Methadone Metabolite Enzyme Immunoassay, Calibrators and Controls cleared by the FDA under the premarket notification k031797 for its stated intended use.

The following table compares LZI's Methadone Metabolite (EDDP) Enzyme Immunoassay with the predicate device.

Device Characteristics	**Subject Device (k170416)** LZI Methadone Metabolite (EDDP) Enzyme Immunoassay and Methadone Metabolite (EDDP) (100 and 300) Calibrators	**Predicate Device (k031797)** LZI Methadone Metabolite (EDDP) Enzyme Immunoassay, Calibrators and Controls
Intended Use	The LZI Methadone Metabolite (EDDP) Enzyme Immunoassay is an in vitro diagnostic test intended for the qualitative and semi-quantitative determination of Methadone Metabolite in human urine. The cutoff for the qualitative and semi-quantitative modes of the assay are 100 ng/mL and 300 ng/mL for methadone metabolite. The assay is designed for prescription use on 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) 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 Lin-Zhi International, Inc. (LZI) Methadone Metabolite (EDDP) Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of methadone metabolite in human urine at a cutoff value of 300 ng/mL. 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 methadone metabolite 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	Methadone Metabolite (EDDP)	Methadone Metabolite (EDDP)
Cutoff	100 and 300 ng/ml	300 ng/mL
Matrix	Urine	Urine
Calibrators Level	100 ng/mL Cutoff: 5 Levels 0, 50, 100, 250, and 500 ng/mL 300 ng/mL Cutoff: 5 Levels 0, 150, 300, 600, and 1000 ng/mL	0, 150, 300, 600, and 1000 ng/mL
Storage	2-8ºC until expiration date	2-8ºC until expiration date

Performance Characteristics Summary:
Beckman Coulter AU480 Analyzer

Precision: 100 ng/mL Cutoff

Semi-Quantitative Precision Analysis Summary: Qualitative Results

Methadone Metabolite (EDDP) Concentration	Within Run (N=22)	Total Precision (N=88)
0 ng/mL	-	-
25 ng/mL	-	-
50 ng/mL	-	-
75 ng/mL	-	-
100 ng/mL	-	-
125 ng/mL	+	+
150 ng/mL	+	+
175 ng/mL	+	+
200 ng/mL	+	+

Semi-Quantitative Positive/Negative Results:

100 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Methadone Metabolite (EDDP) Concentration	**% of Cutoff**	**# of Samples**	**EIA Result**	**# of Samples**	**EIA Result**
0 ng/mL	0.0 %	22	22 Negative	88	88 Negative
25 ng/mL	25.0 %	22	22 Negative	88	88 Negative
50 ng/mL	50.0 %	22	22 Negative	88	88 Negative
75 ng/mL	75.0 %	22	22 Negative	88	88 Negative
100 ng/mL	100.0 %	22	11 Neg/11 Pos	88	40 Pos/48 Neg
125 ng/mL	125.0 %	22	22 Positive	88	88 Positive
150 ng/mL	150.0 %	22	22 Positive	88	88 Positive
175 ng/mL	175.0 %	22	22 Positive	88	88 Positive
200 ng/mL	200.0 %	22	22 Positive	88	88 Positive

Qualitative Positive/Negative Results:

100 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Methadone Metabolite (EDDP) Concentration	**% of Cutoff**	**# of Samples**	**EIA Result**	**# of Samples**	**EIA Result**
0 ng/mL	0.0 %	22	22 Negative	88	88 Negative
25 ng/mL	25.0 %	22	22 Negative	88	88 Negative
50 ng/mL	50.0 %	22	22 Negative	88	88 Negative
75 ng/mL	75.0 %	22	22 Negative	88	88 Negative
100 ng/mL	100.0 %	22	13 Neg/ 9 Pos	88	54 Neg/34 Pos
125 ng/mL	125.0 %	22	22 Positive	88	88 Positive
150 ng/mL	150.0 %	22	22 Positive	88	88 Positive
175 ng/mL	175.0 %	22	22 Positive	88	88 Positive
200 ng/mL	200.0 %	22	22 Positive	88	88 Positive

Performance Characteristics Summary, continued:

Beckman Coulter AU480 Analyzer

Precision: 300 ng/mL Cutoff

Semi-Quantitative Precision Analysis Summary: Qualitative Results

Methadone Metabolite (EDDP) Concentration	Within Run (N=22)	Total Precision (N=88)
0 ng/mL	-	-
75 ng/mL	-	-
150 ng/mL	-	-
225 ng/mL	-	-
300 ng/mL	+	+
375 ng/mL	+	+
450 ng/mL	+	+
525 ng/mL	+	+
600 ng/mL	+	+

Semi-Quantitative Positive/Negative Results:

300 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Methadone Metabolite (EDDP) Concentration	**% of Cutoff**	**# of Samples**	**EIA Result**	**# of Samples**	**EIA Result**
0 ng/mL	0.0 %	22	22 Negative	88	88 Negative
75 ng/mL	25.0 %	22	22 Negative	88	88 Negative
150 ng/mL	50.0 %	22	22 Negative	88	88 Negative
225 ng/mL	75.0 %	22	22 Negative	88	88 Negative
300 ng/mL	100.0 %	22	6 Neg/ 16 Pos	88	36 Neg/ 52 Pos
375 ng/mL	125.0 %	22	22 Positive	88	88 Positive
450 ng/mL	150.0 %	22	22 Positive	88	88 Positive
525 ng/mL	175.0 %	22	22 Positive	88	88 Positive
600 ng/mL	200.0 %	22	22 Positive	88	88 Positive

Qualitative Positive/Negative Results:

300 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Methadone Metabolite (EDDP) Concentration	**% of Cutoff**	**# of Samples**	**EIA Result**	**# of Samples**	**EIA Result**
0 ng/mL	0.0 %	22	22 Negative	88	88 Negative
75 ng/mL	25.0 %	22	22 Negative	88	88 Negative
150 ng/mL	50.0 %	22	22 Negative	88	88 Negative
225 ng/mL	75.0 %	22	22 Negative	88	88 Negative
300 ng/mL	100.0 %	22	7 Neg/15 Pos	88	33 Neg/55 Pos
375 ng/mL	125.0 %	22	22 Positive	88	88 Positive
450 ng/mL	150.0 %	22	22 Positive	88	88 Positive
525 ng/mL	175.0 %	22	22 Positive	88	88 Positive
600 ng/mL	200.0 %	22	22 Positive	88	88 Positive

Performance Characteristics Summary, continued:
Beckman Coulter AU480 Analyzer

Method Comparison - Clinical Samples: 100 ng/mL Cutoff
From a total of eighty-seven (87) clinical unaltered samples,
Semi-Quantitative & Qualitative Data:

Qualitative Accuracy Study:

100 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg	Near Cutoff Pos	High Pos
Positive	**0**	**0**	**0**	**2**	**40**
Negative	**23**	**11**	**9**	**2***	**0**

The following table summarizes the result for the two discordant samples:

100 ng/mL Cutoff	Assay Result:		LC/MS (ng/mL)
	LC/MS	LZI EIA	
Sample #45	+	-	**103.1**
Sample #46	+	-	**126.0**

Concentration for the discrepant samples are based on the absorbance rate from a single point calibration.

Semi-Quantitative Accuracy Study:

100 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg	Near Cutoff Pos	High Pos
Positive	**0**	**0**	**0**	**2**	**40**
Negative	**23**	**11**	**9**	**2***	**0**

The following table summarizes the result for the two discordant samples:

100 ng/mL Cutoff	Assay Result:		LC/MS (ng/mL)
	LC/MS	LZI EIA	
Sample #45	+	-	**103.1**
Sample #46	+	-	**126.0**

Method Comparison - Clinical Samples: 300 ng/mL Cutoff

From a total of eighty-four (84) clinical unaltered samples, Semi-Quantitative & Qualitative

Qualitative Accuracy Study:

300 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg	Near Cutoff Pos	High Pos
Positive	**0**	**0**	**0**	**4**	**38**
Negative	**21**	**15**	**6**	**0**	**0**

Semi-Quantitative Accuracy Study:

300 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg	Near Cutoff Pos	High Pos
Positive	**0**	**0**	**0**	**4**	**38**
Negative	**21**	**15**	**6**	**0**	**0**

Cross-reactivity: 100 ng/mL Cutoff

Methadone Metabolite and Structurally Related Compounds for 100 ng/mL Cutoff:

Cross-reactant	**Spiked [ ] (ng/mL)**	**EIA [ ] (ng/mL)**	**% Cross Reactivity**
EDDP	100	Pos	100 %
EMDP	100,000	Neg	<0.1 %
Methadone	300,000	Neg	<0.1 %
LAAM HCl	500,000	Neg	<0.1 %
(±)-α-Methadol	300,000	Neg	<0.1 %
(-)-Isomethadone HCl	60,000	Neg	<0.2 %
(-)-α-Noracetylmethadol (Nor-LAAM) HCl	300,000	Neg	<0.1 %

Cross-reactivity: 300 ng/mL Cutoff

Methadone Metabolite and Structurally Related Compounds for 100 ng/mL Cutoff:

Cross-reactant	**Spiked [ ] (ng/mL)**	**EIA [ ] (ng/mL)**	**% Cross Reactivity**
EDDP	300	Pos	100 %
EMDP	100,000	Neg	<0.1 %
Methadone	500,000	Neg	<0.1 %
LAAM HCl	500,000	Neg	<0.1 %
(±)-α-Methadol	300,000	Neg	<0.1 %
(-)-Isomethadone HCl	200,000	Neg	<0.1 %
(-)-α-Noracetylmethadol (Nor-LAAM) HCl	300,000	Neg	<0.1 %

Endogenous Compound Interference & Specific Gravity:

No significant undesired cross-reactants or endogenous substance interference was observed.

Performance Characteristics Summary, continued:

Beckman Coulter AU480 Analyzer

Summary:

The information provided in this pre-market notification demonstrates that the LZI Methadone Metabolite (EDDP) Enzyme Immunoassay and LZI Methadone Metabolite (EDDP) (100 and 300) Calibrators are substantially equivalent to the legally marketed predicate device for its general intended use. Substantial equivalence was demonstrated through comparison of intended use and physical properties to the commercially available predicate device as confirmed by chromatography/mass spectrometry (LC/MS), an independent analytical chemistry method. The information supplied in this pre-market notification provides reasonable assurance that the LZI Methadone Metabolite (EDDP) Enzyme Immunoassay and LZI Methadone Metabolite (EDDP) (100 and 300) Calibrators are safe and effective for its stated intended use.