510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K202007

B Applicant

Lin-Zhi International, Inc.

C Proprietary and Established Names

LZI Oxycodone III Enzyme Immunoassay

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DJG	Class II	21 CFR 862.3650 - Opiate Test System	TX - Clinical Toxicology

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Oxycodone

C Type of Test:

Qualitative and semi-quantitative enzyme immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for 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 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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Performance characteristics have been validated on the Beckman Coulter® AU480 clinical analyzer.

IV Device/System Characteristics:

A Device Description:

The LZI Oxycodone III Enzyme Immunoassay is a kit comprised of two reagents, an R1 and R2 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 R1 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 R2 solution contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with oxycodone in buffer with sodium azide (0.09 %) as a preservative.

B Principle of Operation:

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. If free drug is present in the sample, the 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.

V Substantial Equivalence Information:

A Predicate Device Name(s):

LZI Oxycodone Homogeneous Enzyme Immunoassay, LZI Oxycondone Calibrators, LZI Oxycodone Controls

B Predicate 510(k) Number(s):

K120763

C Comparison with Predicate(s):

Device & Predicate Device(s):	K202007	K120763
Device Trade Name	LZI Oxycodone III Enzyme Immunoassay	LZI Oxycodone Enzyme Immunoassay
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the qualitative and semiquantitative determination of oxycodone in human urine, at cutoff values of 100 ng/mL and 300 ng/mL.	Same
Cutoffs	100 and 300 ng/mL	Same
Matrix	Urine	Same
General Device Characteristic Differences		
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

VI Standards/Guidance Documents Referenced:

None referenced.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The precision performance of the assay was evaluated in qualitative and semi-quantitative mode.

All samples were run in replicates of two, with two runs a day for 22 days on one Beckman Coulter® AU480 automated clinical analyzer for a total of 88 results per concentration.

The oxycodone sample concentrations were prepared by spiking oxycodone into negative urine samples, and all concentrations for the precision studies were confirmed by LC/MS testing. Results are summarized below:

100 ng/mL cutoff semi-quantitative mode:

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

100 ng/mL cutoff qualitative mode:

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

300 ng/mL cutoff semi-quantitative mode:

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

300 ng/mL cutoff qualitative mode:

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

2. Linearity:

Linearity and recovery were evaluated in the semi-quantitative mode by analyzing serial dilutions of a sample with an oxycodone concentration of 300 ng/mL (for the 100 ng/mL cutoff) and an 800 ng/mL concentration sample (for the 300 ng/mL cutoff). Results are summarized below:

100 ng/mL cutoff

Target Concentration (ng/mL)	Mean Concentration (ng/mL)	Mean % Recovery
300	302.1	100.7 %
270	282.7	104.7 %
240	260.4	108.5 %
210	231.0	110.0 %
180	197.0	109.5 %
150	153.6	102.4 %
120	121.4	101.2 %
90	88.8	98.6 %
60	56.9	94.8 %
30	27.1	90.3 %
0	0.7	N/A

300 ng/mL cutoff

Target Concentration (ng/mL)	Mean Concentration (ng/mL)	Mean % Recovery
800	843.5	105.4 %
720	784.2	108.9 %
640	712.8	111.4 %
560	624.3	111.5 %
480	514.2	107.1 %
400	436.8	109.2 %
320	345.0	107.8 %
240	250.8	104.5 %
160	173.9	108.7 %
80	89.0	111.2 %
0	0.3	N/A

3. Analytical Specificity/Interference:

Cross-reactivity

The cross-reactivity of structurally related compounds was tested by spiking each potential cross-reactant into pooled negative human urine and then evaluating the sample with the candidate assay. Results are summarized below using the 100 ng/mL cutoff. Results obtained using the 300 ng/mL cutoff were nearly identical.

Potential Cross-Reacting 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 %
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

Potential Cross-Reacting Compound	Test Concentration (ng/mL)	% Cross-reactivity
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 %

Interference Testing - Drugs

Potential interference from structurally unrelated compounds was evaluated by spiking a high concentration (as noted in the table below) of the potential interferent into two sample aliquots with oxycodone concentrations at -25% and +25% of the cutoff concentration. Samples were then evaluated with the candidate assay and the results are summarized below.

There were no deviations from the expected positive or negative results.

Compound	Test Concentration (ng/mL)	-25 % Oxycodone Cutoff (75 ng/mL)	+25 % Oxycodone Cutoff (125 ng/mL)
		Result	Result
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

Compound	Test Concentration (ng/mL)	-25 % Oxycodone Cutoff (75 ng/mL)	+25 % Oxycodone Cutoff (125 ng/mL)
		Result	Result
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
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

Potential interference from endogenous compounds and urine preservatives was also evaluated in a separate study. Results indicated that there is interference from boric acid at 1000 mg/dL. No other compounds showed interference concentrations at the concentrations tested. Results are summarized below:

Interference Testing – Endogenous

Potential Interfering Endogenous Substance	Concentration of Compound (mg/dL)	-25 % Oxycodone Cutoff (75 ng/mL)	+25 % Oxycodone Cutoff (125 ng/mL)
		Result	Result
Acetone	1000	Neg	Pos
Ascorbic Acid	1500	Neg	Pos
Bilirubin	2	Neg	Pos
Calcium Chloride (CaCl2)	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

Boric acid at 1000 mg/dL was found to cause false negative results at +25 and +50% of the cutoff. The following limitation is included in the device labeling: *Boric Acid at 1% w/v may cause false negative results. Boric Acid is not recommended as a preservative for urine.*

Effect of pH

The sponsor evaluated the effect of pH on the results by preparing aliquots with oxycodone concentrations at -25% and +25% of the cutoff and adjusting the pH from 3 to 11 in increments of one pH unit. There were no deviations from the expected positive or negative results.

Effect of specific gravity

The sponsor evaluated the effect of specific gravity on the results by preparing aliquots with oxycodone concentrations at -25% and +25% of the cutoff and adjusting the specific gravity

from 1.000 to 1.030. There were no deviations from the expected positive or negative results.

4. Assay Reportable Range:

   Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The LZI Oxycodone III Enzyme Immunoassay is traceable to a commercially available oxycodone standard.

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   The performance of the assay around the claimed cutoffs is presented in sections VII.A.1 and VII.A.2 above.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   For the *100 ng/mL cutoff*, the sponsor conducted a method comparison study using 82 unaltered clinical urine samples comparing results on the candidate device to those using a validated LC-MS/MS method. Since the assay demonstrated 100% cross-reactivity with oxymorphone, samples were binned according to the sum of the oxycodone and oxymorphone concentrations, which ranged from 0 to 400.0 ng/mL. The results were identical between the qualitative and semi-quantitative modes and are summarized in the tables below:

Candidate device results	< 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	0	2*	12	25
Negative	29	10	4**	0

*concentrations of the discordant samples were 89.9 and 91.0 ng/mL.
**concentrations of the discordant samples were 102.7, 107.0, 131.1, and 138.7 ng/mL.

For the *300 ng/mL cutoff*, the sponsor conducted a method comparison study using 90 unaltered clinical urine samples comparing results on the candidate device to those using a validated LC-MS/MS method. Since the assay demonstrated 100% cross-reactivity with oxymorphone, samples were binned according to the sum of the oxycodone and oxymorphone concentrations, which ranged from 0 to 1302.5 ng/mL. There were slight differences between the qualitative and semi-quantitative modes and results for both modes are summarized in the tables below:

Semi-quantitative mode

Candidate device results	< 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	0	2*	11	33
Negative	26	17	1**	0

*concentrations of the discordant samples were 249.7 and 256.5 ng/mL.
**concentration of the discordant sample was 414.0 ng/mL.

Qualitative mode

Candidate device results	< 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	0	2*	10	33
Negative	26	17	2**	0

*concentrations of the discordant samples were 249.7 and 256.5 ng/mL.
**concentrations of the discordant samples were 389.3 and 414.0 ng/mL.

2. Matrix Comparison:

Not applicable. The assay is for use with urine samples only.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.