

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k120763

B. Purpose for Submission:

Modification to a previously cleared device (k050733) using a new mouse monoclonal anti-Oxycodone antibody

C. Measurand:

Oxycodone

D. Type of Test:

Qualitative or semi-quantitative enzyme immunoassay

E. Applicant:

Lin-Zhi International, Inc.

F. Proprietary and Established Names:

LZI Oxycodone Enzyme Immunoassay
LZI Oxycodone Drug of Abuse Calibrators
LZI Oxycodone Drug of Abuse Controls

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DJG – enzyme immunoassay, opiates	II	862.3650	91-Toxicology
DLJ -Clinical toxicology calibrator	II	862.3200	91- Toxicology
LAS -Clinical toxicology control material	I, reserved	862.3280	91- Toxicology

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

The LZI Oxycodone Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of oxycodone in human urine at the cutoff values of 100 and 300 ng/mL. The assay is designed for professional 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 GCMS and LCMS or (2) permitting laboratories to establish quality control procedures.

The LZI Oxycodone Drug of Abuse (DAU) Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the LZI Oxycodone Enzyme Immunoassay.

The LZI Oxycodone Drug of Abuse (DAU) Controls are for use as assayed quality control materials to monitor the precision of the LZI Oxycodone Enzyme Immunoassay.

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.

3. Special conditions for use statement(s):

For prescription use only.

Positive results should be confirmed by other affirmative, analytical methods (e.g., chromatography), and preferably GC/MS or LC/MS.

The test is designed for use with human urine only.

4. Special instrument requirements:

Performance characteristics have been validated on the Hitachi 717.

I. Device Description:

The assay consists of ready-to-use liquid reagents. Reagent 1 contains a mouse monoclonal anti-oxycodone antibody, glucose-6-phosphate (G6P), nicotinamide

adenine dinucleotide (NAD), stabilizers and sodium azide (0.09%) as a preservative. Reagent 2 contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with oxycodone in buffer with sodium azide (0.09%) as preservative.

The calibrators and controls are sold separately. The calibrator has 6 levels and the control has 4 levels. They consist of human urine samples containing oxycodone with sodium azide (0.09%) as preservative.

J. Substantial Equivalence Information:

1. Predicate device name (s):

LZI Oxycodone Enzyme Immunoassay

2. Predicate 510(k) number(s):

k050733

3. Comparison with predicate:

Items	LZI Oxycodone Enzyme Immunoassay (Candidate Device)	LZI Oxycodone Enzyme Immunoassay (Predicate Device)
Similarity		
Intended use /Indication for use	Same	Qualitative and semi-quantitative determination of Oxycodone in human urine.
Sample type	Same	Urine
Calibrated against	Same	Oxycodone
Test Principle	Same	Competitive enzyme immunoassay
Cutoff	Same	100 or 300 ng/mL
Control Levels	Same	100 ng/mL cutoff: 75, 125 ng/mL 300 ng/mL cutoff: 225, 375ng/mL
Difference		
Antibody	Different mouse monoclonal anti-Oxycodone antibody	mouse monoclonal anti-Oxycodone antibody
Calibrator Levels	0, 50, 100, 300, 500, 800 ng/mL	100 ng/mL cutoff: 0, 75, 100, 225, 300 ng/mL 300 ng/mL cutoff: 0, 100, 300, 500, 800 ng/mL

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A, Evaluation of precision performance of clinical chemistry devices.

L. Test Principle:

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. 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 drug is present in the sample, antibody binds to the 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision of the qualitative and semi-quantitative assays was evaluated by assaying calibrator and control material in replicates of 2, two runs a day for 22 days on one Hitachi 717 analyzer (n =88 per sample). Results are summarized below for each cutoff for qualitative and semi-quantitative protocols.

Semi-Quantitative

100 ng/mL Cutoff Result:		Within Run		Total Precision	
Sample Concentration	% of Cutoff	Number of Determination	Immunoassay Result	Number of Determination	Immunoassay Result
0 ng/mL	-100.0%	22	22 Negative	88	88 Negative
25 ng/mL	-75.0%	22	22 Negative	88	88 Negative
50 ng/mL	-50.0%	22	22 Negative	88	88 Negative
75 ng/mL	-25.0%	22	22 Negative	88	88 Negative
100 ng/mL	100.0%	22	9 Pos/13 Neg	88	39 Pos/49 Neg
125 ng/mL	+25.0%	22	22 Positive	88	88 Positive
150 ng/mL	+50.0%	22	22 Positive	88	88 Positive
175 ng/mL	+75.0%	22	22 Positive	88	88 Positive
200 ng/mL	+100.0%	22	22 Positive	88	88 Positive

300 ng/mL Cutoff Result:		Within Run		Total Precision	
Sample Concentration	% of Cutoff	Number of Determination	Immunoassay Result	Number of Determination	Immunoassay Result

0 ng/mL	-100.0%	22	22 Negative	88	88 Negative
75 ng/mL	-75.0%	22	22 Negative	88	88 Negative
150 ng/mL	-50.0%	22	22 Negative	88	88 Negative
225 ng/mL	-25.0%	22	22 Negative	88	88 Negative
300 ng/mL	100.0%	22	3 Pos/ 19 Neg	88	26 Pos/ 62 Neg
375 ng/mL	+25.0%	22	22 Positive	88	88 Positive
450 ng/mL	+50.0%	22	22 Positive	88	88 Positive
525 ng/mL	+75.0%	22	22 Positive	88	88 Positive
600 ng/mL	+100.0%	22	22 Positive	88	88 Positive

Qualitative

100 ng/mL Cutoff Result:		Within Run		Total Precision	
Sample Concentration	% of Cutoff	Number of Determination	Immunoassay Result	Number of Determination	Immunoassay Result
0 ng/mL	-100.0%	22	22 Negative	88	88 Negative
25 ng/mL	-75.0%	22	22 Negative	88	88 Negative
50 ng/mL	-50.0%	22	22 Negative	88	88 Negative
75 ng/mL	-25.0%	22	22 Negative	88	88 Negative
100 ng/mL	100.0%	22	6 Pos/ 16 Neg	88	25 Pos/63 Neg
125 ng/mL	+25.0%	22	22 Positive	88	88 Positive
150 ng/mL	+50.0%	22	22 Positive	88	88 Positive
175 ng/mL	+75.0%	22	22 Positive	88	88 Positive
200 ng/mL	+100.0%	22	22 Positive	88	88 Positive

300 ng/mL Cutoff Result:		Within Run		Total Precision	
Sample Concentration	% of Cutoff	Number of Determination	Immunoassay Result	Number of Determination	Immunoassay Result
0 ng/mL	-100.0%	22	22 Negative	88	88 Negative
75 ng/mL	-75.0%	22	22 Negative	88	88 Negative
150 ng/mL	-50.0%	22	22 Negative	88	88 Negative
225 ng/mL	-25.0%	22	22 Negative	88	88 Negative
300 ng/mL	100.0%	22	1 Pos/21 Neg	88	23 Pos/65 Neg
375 ng/mL	+25.0%	22	22 Positive	88	88 Positive
450 ng/mL	+50.0%	22	22 Positive	88	88 Positive
525 ng/mL	+75.0%	22	22 Positive	88	88 Positive
600 ng/mL	+100.0%	22	22 Positive	88	88 Positive

Conclusion:

All samples spiked at levels below the cutoff detected as negative and all samples spiked at levels above the cutoff detected as positive.

b. *Linearity/assay reportable range:*

Linearity across the range was tested by spiking negative urine samples to increasing concentrations within the calibration ranges listed in the table below. Each sample was assayed in replicates of 10 in the semi-quantitative mode using all 6 calibrators for 100 ng/mL and 300 ng/mL cutoffs (0, 50, 100, 300, 500, 800 ng/mL). The results were averaged and compared to the expected result and the percent recovery was calculated.

Target Concentration (ng/mL)	Determined Concentration (ng/mL)	% Recovery
800	801.4	100.2
700	657.1	93.9
600	585.3	97.6
500	494.4	98.9
400	383.9	96.0
300	302.9	101.0
200	190.5	95.2
100	102.2	102.2
50	50.4	100.8
0	1.6	N/A

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability

The controls and calibrators are prepared using commercially available Oxycodone standard the accuracy of which is ensured by purity determinations and gravimetric preparation using balances calibrated with NIST traceable weight. Concentration of drug in the controls and calibrators are confirmed by GC/MS analysis.

Stability

Real time testing is on going. Protocol and acceptance criterion were described and found to be acceptable. Data obtained so far support 41 weeks of product stability at 2-8°C for the calibrators and controls.

d. *Detection limit:*

Not applicable

e. *Analytical specificity:*

Cross-reactivity:

The parent drug, metabolites, and drugs commonly found in samples were

tested for cross-reactivity with the assay. Test compounds were spiked into GC/MS verified negative urine and each sample was evaluated against the cut-off calibrators. The percent cross-reactivity of those compounds are presented below:

Structurally Related Oxycodone Compounds: 100 ng/mL Cutoff

Compound	Equivalent Conc. to 100 ng/mL	Dose	% Cross Reactivity
	ng/mL	ng/mL	
Oxycodone	100	110.4	110.40%
Hydrocodone	22,300	129.6	0.58%
Hydromorphone	14,100	95.6	0.68%
Oxymorphone	200	117.3	58.65%
Noroxycodone	1,100	106.7	9.70%
Noroxymorphone	1,000	119.6	11.96%
Codeine	60,000	95.3	0.16%
Dextromethorphan	1,000,000	113.4	0.01%
Dihydrocodeine	250,000	90.9	0.04%
Levorphanol	60,000	100.1	0.17%
Naloxone	9,000	84.1	0.93%
Norcodeine	1,000,000	210.0	0.02%
Morphine	50,000	111.3	0.22%
Oxymorphone-Glucuronide	85	115.5	135.88%
Codeine-6-b-Glucuronide	5,000	2.8	0.06%
Morphine-3-Glucuronide	250,000	19.4	0.01%
6-AM	62,100	4.8	0.01%
NorBuprenorphine	100,000	3.6	0.00%

Structurally Unrelated Compounds: 100 ng/mL Cutoff

Compound	(ng/mL)	Oxycodone Concentration		
		0 ng/mL	75 ng/mL Control	125 ng/mL Control
Acetaminophen	500,000	Neg	Neg	Pos
Acetylsalicylic acid	500,000	Neg	Neg	Pos
Amobarbital	500,000	Neg	Neg	Pos
Benzoyllecgonine	500,000	Neg	Neg	Pos
Brompheniramine	100,000	Neg	Neg	Pos
Bupropion	500,000	Neg	Neg	Pos
Caffeine	500,000	Neg	Neg	Pos
Chlorpheniramine	500,000	Neg	Neg	Pos
Chlorpromazine	500,000	Neg	Neg	Pos
d-l Phenylpropanolamine (Phenethylamine)	250,000	Neg	Neg	Pos
d-Ephedrine	500,000	Neg	Neg	Pos
l-Ephedrine	300,000	Neg	Neg	Pos
d-	250,000	Neg	Neg	Pos

Methamphetamine				
Ecgonine (Ecgonine Methyl- ester)	500,000	Neg	Neg	Pos
Meperidine	500,000	Neg	Neg	Pos
Methadone	500,000	Neg	Neg	Pos
Nicotine	500,000	Neg	Neg	Pos
Norpropoxyphene	100,000	Neg	Neg	Pos
Phencyclidine	250,000	Neg	Neg	Pos
Promethiazine	500,000	Neg	Neg	Pos
Propranolol	100,000	Neg	Neg	Pos
Secobarbital	500,000	Neg	Neg	Pos
Trazodone	500,000	Neg	Neg	Pos
Tyramine	500,000	Neg	Neg	Pos
Valproic acid	500,000	Neg	Neg	Pos

Structurally Related Oxycodone Compounds: 300 ng/mL Cutoff

Compound	Equivalent Conc. to 300 ng/mL	Dose	% Cross Reactivity
	ng/mL	ng/mL	
Oxycodone	300	306.2	102.07%
Hydrocodone	66,000	302.1	0.46%
Hydromorphone	41,800	227.7	0.54%
Oxymorphone	650	372.2	57.26%
Noroxycodone	3,100	225.3	7.27%
Noroxymorphone	4,700	309.7	6.59%
Codeine	250,000	268.0	0.11%
Dextromethorphan	4,500,000	304.2	0.01%
Dihydrocodeine	1,100,000	285.7	0.03%
Levorphanol	300,000	367.6	0.12%
Naloxone	20,000	319.4	1.60%
Norcodeine	2,500,000	352.6	0.01%
Morphine	125,000	313.8	0.25%
Oxymorphone-Glucuronide	200	306.3	153.15%
Codeine-6-b-Glucuronide	10,000	2.45	0.02%
Morphine-3-Glucuronide	183,600	17.3	0.01%
6-AM	100,000	3.1	0.00%
NorBuprenorphine	500,000	35.8	0.01%
Morphine-3-Glucose	300	306.2	102.07%

Structurally Unrelated Compounds: 300 ng/mL Cutoff

Compound	(ng/mL)	Oxycodone Concentration		
		0 ng/mL	225 ng/mL Control	375 ng/mL Control
Acetaminophen	500,000	Neg	Neg	Pos
Acetylsalicylic acid	500,000	Neg	Neg	Pos
Amobarbital	500,000	Neg	Neg	Pos

Benzoyllecgonine	500,000	Neg	Neg	Pos
Brompheniramine	100,000	Neg	Neg	Pos
Bupropion	500,000	Neg	Neg	Pos
Caffeine	500,000	Neg	Neg	Pos
Chlorpheniramine	500,000	Neg	Neg	Pos
Chlorpromazine	500,000	Neg	Neg	Pos
d-l Phenylpropanolamine (Phenethylamine)	250,000	Neg	Neg	Pos
d-Ephedrine	500,000	Neg	Neg	Pos
l-Ephedrine	300,000	Neg	Neg	Pos
d-Methamphetamine	250,000	Neg	Neg	Pos
Ecgonine (Ecgonine Methyl-ester)	500,000	Neg	Neg	Pos
Meperidine	500,000	Neg	Neg	Pos
Methadone	500,000	Neg	Neg	Pos
Nicotine	500,000	Neg	Neg	Pos
Norpropoxyphene	100,000	Neg	Neg	Pos
Phencyclidine	250,000	Neg	Neg	Pos
Promethiazine	500,000	Neg	Neg	Pos
Propranolol	100,000	Neg	Neg	Pos
Secobarbital	500,000	Neg	Neg	Pos
Trazodone	500,000	Neg	Neg	Pos
Tyramine	500,000	Neg	Neg	Pos
Valproic acid	500,000	Neg	Neg	Pos

Interference

The potential effect of endogenous compounds and pH on the recovery of Oxycodone was assessed by spiking known amounts of potentially interfering substances into GC/MS verified negative urine and urine samples with Oxycodone concentrations +/- 25% of the assay cut-off. Substances were determined not to interfere with the assay if the recovery of the negative sample was below the assay cut-off and if the +/-25% samples recovered within 10% of a sample containing no interferent.

100 ng/mL cutoff

Interfering Substances	Spiked Conc. mg/dL	0 ng/mL	75 ng/mL Control	125 ng/mL Control
Acetone	1000	Neg	Neg	Pos
Ascorbic Acid	400	Neg	Neg	Pos
Creatinine	500	Neg	Neg	Pos
Ethanol	1000	Neg	Neg	Pos
Galactose	10	Neg	Neg	Pos
r-Globulin	500	Neg	Neg	Pos
Glucose	1500	Neg	Neg	Pos

Hemoglobin	300	Neg	Neg	Pos
HSA*	500	Neg	Neg	Pos
Sodium Chloride	3000	Neg	Neg	Pos
Oxalic Acid	100	Neg	Neg	Pos
Urea	2000	Neg	Neg	Pos
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

*Human Serum Albumin

300 ng/mL cutoff

Interfering Substances	Spiked Conc.	0 ng/mL	225 ng/mL Control	375 ng/mL Control
	mg/dL	ng/mL	ng/mL	ng/mL
Acetone	1000	Neg	Neg	Pos
Ascorbic Acid	400	Neg	Neg	Pos
Creatinine	500	Neg	Neg	Pos
Ethanol	1000	Neg	Neg	Pos
Galactose	10	Neg	Neg	Pos
r-Globulin	500	Neg	Neg	Pos
Glucose	1500	Neg	Neg	Pos
Hemoglobin	300	Neg	Neg	Pos
HSA*	500	Neg	Neg	Pos
Sodium Chloride	6000	Neg	Neg	Pos
Oxalic Acid	100	Neg	Neg	Pos
Urea	2000	Neg	Neg	Pos
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

*Human Serum Albumin

Specific gravity: Urine samples with specific gravity value ranging from 1.000 to 1.0275 were tested with the assay in the presence of 0, 75, 225, and 375 ng/mL of Oxycodone and no interference was observed.

Note: All endogenous substances listed above, including specific gravity, were also tested in “qualitative-mode”. No interference is observed. The results are identical to the “semi-quantitative” mode as all samples gave correct positive/negative result corresponding to the cutoff values of 100 or 300 ng/mL.

f. Assay cut-off:

100ng/mL or 300 ng/mL

2. Comparison studies:

a. *Method comparison with predicate device:*

100 ng/mL cutoff

Eighty-nine (89) unaltered clinical urine specimens were tested with the LZI Oxycodone Enzyme Immunoassay and confirmed with GC/MS or LC/MS. Specimens having an Oxycodone concentration greater than 100 ng/mL by GC/MS or LC/MS are defined as positive, and specimens with lower concentrations by GC/MS or LC/MS are defined as negative in the table below. The correlation results are summarized as follows: (near cutoff samples are defined as $\pm 50\%$ of the cutoff value)

Qualitative Accuracy Study:

100 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg.	Near Cutoff Pos.	High Pos.	% Agreement
Positive	0	0	0	7	38	93.75 %
Negative	20	9	12	3*	0	100.0 %

Discordant samples:

Cutoff Value (100 ng/mL)	Assay Result	Sample Testing Method
	LZI EIA	GC/MS or LC/MS (ng/mL)
Sample #42*	-	108
Sample #43*	-	110
Sample #48*	-	135

Semi-Quantitative Accuracy Study:

100 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg.	Near Cutoff Pos.	High Pos.	% Agreement
Positive	0	0	0	7	38	93.75 %
Negative	20	9	12	3*	0	100.0 %

Discordant samples:

Cutoff Value (100 ng/mL)	Assay Result	Sample Testing Method
	LZI EIA	GC/MS or LC/MS (ng/mL)
Sample #42*	-	108
Sample #43*	-	110
Sample #48*	-	135

300 ng/mL cutoff:

One-hundred-one (101) unaltered clinical urine specimens were tested with the LZI Oxycodone Enzyme Immunoassay and confirmed with GC/MS or LC/MS. Specimens having an Oxycodone concentration greater than 300 ng/mL by GC/MS or LC/MS are defined as positive, and specimens with lower concentrations by GC/MS or LC/MS are defined as negative in the table below. The correlation results are summarized as follows: (near cutoff samples are defined as $\pm 50\%$ of the cutoff value)

Qualitative Accuracy Study

300 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg.	Near Cutoff Pos.	High Pos.	% Agreement
Positive	0	0	1*	11	43	96.1 %
Negative	20	18	11	2**	0	98.0 %

Discordant samples:

Cutoff Value (300 ng/mL)	Assay Result:	Sample Testing Method
	LZI EIA	GC/MS or LC/MS (ng/mL)
Sample #49*	+	288
Sample #52**	-	309
Sample #54**	-	336

Semi-Quantitative Accuracy Study

300 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg.	Near Cutoff Pos.	High Pos.	% Agreement
Positive	0	0	1*	11	43	96.1 %
Negative	20	18	11	2**	0	98.0 %

Discordant samples:

Cutoff Value (300 ng/mL)	Assay Result:	Sample Testing Method
	LZI EIA	GC/MS or LC/MS (ng/mL)
Sample #49*	+	288
Sample #52**	-	309
Sample #54**	-	336

b. Matrix comparison:

Not applicable. The assay is intended for urine samples only.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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