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

A. 510(k) Number:

k113139

B. Purpose for Submission:

New device

C. Measurand:

Cocaine

D. Type of Test:

Qualitative and semi-quantitative enzyme immunoassay

E. Applicant:

Lin-Zhi International, Inc.

F. Proprietary and Established Names:

Cocaine Metabolite Enzyme Immunoassay
Cocaine Metabolite Drugs of Abuse (DAU) Calibrators
Cocaine Metabolite Drugs of Abuse (DAU) Controls

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DIO – Cocaine and cocaine metabolite test system	II	862.3250	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 Cocaine Metabolite Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of benzoylecgonine in human urine, at a cutoff value of 150 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 or (2) permitting laboratories to establish quality control procedures.

   This assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or Liquid Chromatograph/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 result is positive.

   The Cocaine Metabolite Drugs of Abuse (DAU) Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the Cocaine Metabolite Enzyme Immunoassay at a cutoff value of 150 ng/mL.

   The Cocaine Metabolite Drugs of Abuse (DAU) Controls are for use as assayed quality control materials to monitor the precision of the Cocaine Metabolite Enzyme Immunoassay at a cutoff value of 150 ng/mL.

3. Special conditions for use statement(s):

   For professional use only

4. Special instrument requirements:

   Clinical chemistry analyzers capable of maintaining a constant temperature, pipetting sample, mixing reagent, measuring enzymatic rates at 340 nm and timing the reaction accurately can be used to perform this homogeneous immunoassay.

   Performance testing was conducted on the Roche Diagnostics Hitachi 717 analyzer.

I. Device Description:

The assay consists of ready-to-use liquid reagents. Reagent 1 contains a mouse monoclonal anti-benzoylecgonine 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 benzoylecgonine in buffer with sodium azide (0.09%) as a preservative.

The calibrators and controls are sold separately. The calibrator has 5 levels and the control has 2 levels. They consist of human urine samples containing benzoylecgonine with sodium azide (0.09%) as a preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Lin-Zhi International Inc., Cocaine Metabolite Enzyme Immunoassay
   Lin-Zhi International Inc., Cocaine Metabolite calibrators and controls

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

   k020763 and k020769, respectively

3. Comparison with predicate:

Similarities/Differences		
Item	Device	Predicates
Intended Use	Intended for the qualitative and semi-quantitative determination of benzoylecgonine in human urine. The Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the Cocaine Metabolite Enzyme Immunoassay. The Controls are for use as assayed quality control materials to monitor the precision of the Cocaine Metabolite Enzyme Immunoassay.	Same
Analyte	Benzoylecgonine	Same
Cutoff	150 ng/mL	300 ng/mL
Matrix	Urine	Same
Calibrators	5 levels	5 levels

Similarities/Differences		
Item	Device	Predicates
	(0, 75, 150, 300, 1000 ng/mL)	(0, 150,300,1000, 3000 ng/mL)
Controls	2 levels (112.5 ng/mL, 187.5 ng/mL)	2 levels (225 ng/mL, 375 ng/mL)
Storage	2-8 ºC until expiration date	2-8 ºC until expiration date

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

CLSI EP5-A, Evaluation of Precision Performance of Clinical Chemistry Devices

L. Test Principle:

The Cocaine Metabolite assay is a homogenous enzyme immunoassay with ready-to-use liquid reagent. The assay is based on competition between drug in the sample and dug labeled with enzyme glucose-6-phodphate 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, benzoylecgonine-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 benzoylecgonine-labeled G6PDH then exhibits its maximal enzyme activity. Active enzyme converts nictinamide 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 was determined by spiking benzoylecgonine into drug free urine at various concentrations (zero, -75%, -50%, -25%, at the cutoff, 125%, 150%, 175% and 200% of the cutoff). Concentrations were confirmed by GC/MS. Testing for both the with-in run and between-run studies were performed by testing each sample in replicate, with two runs per day, for 22 days. The qualitative and semi-quantitative results are presented below:

Qualitative:

		Within Run		Between Run
Sample concentration (ng/mL)	No. Observations	# Neg/#Pos	No. Observations	# Neg/#Pos
0 (negative)	22	22/0	88	88/0
37.5 (-75% c/o)	22	22/0	88	88/0
75 (-50% c/o)	22	22/0	88	88/0
112.5 (-25% c/o)	22	22/0	88	88/0
150 (cutoff)	22	19/3	88	73/15
187.5 (+25% c/o)	22	0/22	88	0/88
225 (+50% c/o)	22	0/22	88	0/88
267.5 (+50% c/o)	22	0/22	88	0/88
300 (+100% c/o)	22	0/22	88	0/88

Semi-Quantitative:

		Within Run		Between Run
Sample concentration (ng/mL)	No. Observations	# Neg/#Pos	No. Observations	# Neg/#Pos
0 (negative)	22	22/0	88	88/0
37.5 (-75% c/o)	22	22/0	88	88/0
75 (-50% c/o)	22	22/0	88	88/0
112.5 (-25% c/o)	22	22/0	88	88/0
150 (cutoff)	22	18/4	88	59/29
187.5 (+25% c/o)	22	0/22	88	0/88
225 (+50% c/o)	22	0/22	88	0/88
267.5 (+50% c/o)	22	0/22	88	0/88
300 (+100% c/o)	22	0/22	88	0/88

b. Linearity/assay reportable range:

Linearity across the range was confirmed by serially diluting a spiked urine pool containing 1000 ng/mL of benzoylecgonine in to concentration levels listed in the table below. Each sample was assayed in the semi-quantitative mode. The results were averaged and compared to the expected result and the percent recovery was calculated. Results are presented in the table below:

Expected Concentration (ng/mL)	Mean Observed Concentration (ng/mL)	Recovery (%)
Negative	4.0	not applicable
48.1	58.1	120.8
96.2	96.6	100.4
144.3	151.4	104.9
192.4	200.5	104.2
288.6	312.1	108.1
384.8	403.1	104.8
481	488.3	101.5
577.2	588.2	101.9
673.4	694.8	103.2
769.6	812	105.5
865.8	917.5	106
962	1017.8	105.8

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

Five levels of calibrators (0, 75, 150, 300, 1000 ng/mL) and two levels of control material (112.5 ng/mL, 187.5 ng/mL) are available for use with the Cocaine Metabolite Enzyme Immunoassay. A commercially available benzoylecgonine standard solution from Cerilliant Analytical Reference Standards is used and traceable to NIST standard. This standard solution is made into a secondary (lower concentration) stock solution. The secondary stock solution is then spiked into the calibrators and controls to the desired concentration. The concentrations are confirmed by GC/MS.

Stability Studies:

Real time and accelerated studies for both controls and calibrators have been conducted. Protocols and acceptance criteria were described and found to be acceptable. The manufacturer claims the following expiration date for both controls and calibrators:

When stored at 2-8 ºC unopened product is stable until expiration date which is 18 months.

On board stability is good for 14 days when stored at 2-8 ºC.

d. *Detection limit:*

Performance at low drug concentrations in the semi-quantitative assay was

characterized by determination of recovery (see section b above).

e. Analytical specificity:

Cross-reactivity was established by spiking various concentrations of structurally related into drug-free urine. Results are expressed as a minimum concentration of metabolite or compound required to produce a response approximately equivalent to the cutoff concentration of the assay. The percent cross-reactivity of those compounds are presented below:

Structurally related

Compound	Equivalent to 150 ng/mL	% Cross reactivity
Benzoylecgonine	150	96.03%
Cocaethylene	4,000	4.58%
Cocaine	25,000	0.62%
Ecgonine	400,000	0.03%
Ecgonine, Methyl Ester	500,000	0%
Norcocaine	30,000	0.68%
Atropine	500,000	0%

Structurally unrelated

Compound	Tested concentrations ng/mL	-25% Benzoylecgonine	+25% Benzoylecgonine
Acetaminophen	500,000	Negative	Positive
Acetylsalicylic Acid	500,000	Negative	Positive
Amobarbital	500,000	Negative	Positive
Amoxicillin	500,000	Negative	Positive
Amphetamine	500,000	Negative	Positive
Bupropion	500,000	Negative	Positive
Cat\ptopril	500,000	Negative	Positive
Caffeine	500,000	Negative	Positive
Chlordiazepoxide	500,000	Negative	Positive
Chlorpheniramine	500,000	Negative	Positive
Chlorpomazine	500,000	Negative	Positive
Codeine	500,000	Negative	Positive
Dextromethorphan	500,000	Negative	Positive
Diazepam	500,000	Negative	Positive
Digoxin	500,000	Negative	Positive
Enalapril	500,000	Negative	Positive
Fluoxetine	100,000	Negative	Positive
Glyburide	500,000	Negative	Positive
Ibuprofen	500,000	Negative	Positive
Lidocaine	500,000	Negative	Positive

Compound	Tested concentrations ng/mL	-25% Benzoylecgonine	+25% Benzoylecgonine
Meperidine	500,000	Negative	Positive
Methadone	100,000	Negative	Positive
Methamphetamine	500,000	Negative	Positive
Methaqualone	500,000	Negative	Positive
Morphine	500,000	Negative	Positive
Nicodine	500,000	Negative	Positive
Nifedipine	100,000	Negative	Positive
Oxazepam	100,000	Negative	Positive
Phencyclidine	500,000	Negative	Positive
Phenobarbital	500,000	Negative	Positive
Propoxyphene	100,000	Negative	Positive
Ranitidine	500,000	Negative	Positive
Salicyluric acid	500,000	Negative	Positive
Secobarbital	500,000	Negative	Positive
11-nor-THC-COOH	500,000	Negative	Positive
Valproic Acid	500,000	Negative	Positive
Verapamil	500,000	Negative	Positive

Endogenous Compounds

The following endogenous compounds were added into drug-free urine, urine sample spiked to -25% of benzoylecgonine and one urine spiked to +25% of benzoylecgonine at various concentrations. The substances listed in the table below were determined not to interfere at the concentration shown:

Interfering Substance	Concentration Tested mg/dL	-25% Benzoylecgonine	+25% Benzoylecgonine
Acetone	1000	Negative	Positive
Ascorbic Acid	400	Negative	Positive
Creatinine	500	Negative	Positive
Ethanol	1000	Negative	Positive
Galactose	10	Negative	Positive
r-Globulin	500	Negative	Positive
Glucose	1500	Negative	Positive
Hemoglobin	300	Negative	Positive
Human Serum Albumin	500	Negative	Positive
Oxalic Acid	100	Negative	Positive
Sodium Chloride	3000	Negative	Positive
Urea	2000	Negative	Positive

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

pH and Specific Gravity

To test for possible positive and/or negative interference from pH urine samples having pH from 3, 4, 5, 7, 8, 9, 10 and 11 were used. Each of these samples were divided into two aliquots for each drug and spiked to -25% of the cutoff and +25% of the cutoff. No positive or negative interference due to pH was observed.

To test for possible positive and/or negative interference from specific gravity urine samples having specific gravity from 1.000, 1.002, 1.005, 1.007, 1.010, 1.015, 1.017, 1.025 and 1.030 were used. Each of these samples were divided into two aliquots for each drug and spiked to -25% of the cutoff and 125% of the cutoff. No positive or negative interference due to specific gravity was observed.

f. Assay cut-off:

Analytical performance of the device around the claimed cutoff is described in precision section (1 a.) above

2. Comparison studies:

a. Method comparison with predicate device:

Eighty unaltered clinical urine samples (40 negative and 40 positive) were evaluated by the Lin-Zhi Cocaine Metabolite Enzyme Immunoassay and compared to LC/MS. Results from the study are presented below:

Qualitative

Candidate Device Results	Negative	Less than half the cutoff concentration by GC/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)
Positive	0	0	2	5	31
Negative	20	4	14	4	0

% Agreement among positives is 90% (36/40)
% Agreement among negatives is 95% (38/40)

Discordant

Cutoff Value (ng/mL)	LZI Cocaine Assay (POS/NEG)	Drug/Metabolite LC/MS value (ng/mL)
150	Positive	141
150	Positive	147
150	Negative	150
150	Negative	152
150	Negative	167
150	Negative	176

Semi-quantitative

Candidate Device Results	Negative	Less than half the cutoff concentration by GC/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)
Positive	0	0	1	5	31
Negative	20	4	15	4	0

% Agreement among positives is 90% (36/40)
% Agreement among negatives is 98% (39/40)

Discordant

Cutoff Value (ng/mL)	LZI 6-Acetylmorphine Assay (POS/NEG)	Drug/Metabolite LC/MS value (ng/mL)
150	Positive	141
150	Negative	150
150	Negative	167
150	Negative	167
150	Negative	176

b. Matrix comparison:

Test is for urine samples only

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

*b. Clinical specificity**:***

Not applicable

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.