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

A. 510(k) Number:

k051058

B. Purpose for Submission:

Clearance of new device

C. Measurand:

Methadone

D. Type of Test:

Qualitative Enzyme Immunoassay

E. Applicant:

Lin-Zhi International, Inc

F. Proprietary and Established Names:

LZI Oral Fluid Methadone Metabolite Enzyme Immunoassay
LZI Oral Fluid Methadone Metabolite Calibrators
LZI Oral Fluid Methadone Metabolite Controls

G. Regulatory Information:

1. Regulation section:

   21 CFR§862.3620, Methadone test system
   21 CFR§862.3200, Clinical toxicology calibrators
   21 CFR§862.3280, Clinical toxicology control material

2. Classification:

   Class II

3. Product code:

   DJR, DLJ and LAS respectively

4. Panel:

   Toxicology (91)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Methadone Enzyme Immunoassays for Drugs of Abuse in Oral Fluid is a homogeneous enzyme immunoassay system to detect methadone in human saliva with a cutoff of 30 ng/mL when testing oral fluid specimen collected with Salivette collector (manufactured by Sarstedt) and diluted with 1 mL of buffer. The calibrators and controls of the analyte (Methadone) are prepared with oral fluid buffer so that it can be used to verify and validate the assay. The assay is intended for use in the qualitative determination of methadone drugs. The assay is designed for professional use with a number of automated clinical analyzers.

   The Methadone Oral Fluid Enzyme Immunoassay is a homogeneous enzyme immunoassay system provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Gas Chromatography/Mass Spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

3. Special conditions for use statement(s):

   For prescription, professional use only in clinical chemistry laboratories.

   The assay is not designated for use in point-of-care settings.

4. Special instrument requirements:

   The device is designed for use on automated clinical chemistry analyzers. Performance data submitted was obtained using the Hitachi 717 analyzer.

I. Device Description:

The assay consists of a ready-to-use liquid reagents. Reagent 1 contains mouse monoclonal antibody to methadone, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide (NAD) and stabilizers. Reagent 2 contains methadone labeled glucose-6-phosphate dehydrogenase (G6PDH) in buffer.

The calibrator standards are sold separately. They are used to construct the standard curve used to calculate the concentration of the unknown samples as well as to qualitatively determine the presences or absences of methadone in the sample. They consist of 3 levels of a buffer matrix spiked with known concentrations of the drug analyte, ranging in concentration from 0-50 μg/mL.

Assayed controls are sold separately and are run with the samples to monitor the performance of the assay. They consist of oral fluid with methadone added.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   OraSure Methadones Intercept Micro-Plate EIA, LZI Methadone EIA and Dade Behring Emit II Plus Methadone Assay

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

   k002010, k023317 and k010962 respectively

3. Comparison with predicate:

   The device and the predicate devices share a similar intended use. The device uses similar reagents and test principle as the LZI urine assay, and the device is intended for the same matrix as the OraSure assay.

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

None referenced.

L. Test Principle:

The assay is based on competition between drug labeled with glucose-6-phosphate dehydrogenase (G6PDH) enzyme and free drug from the saliva sample for a fixed amount of specific antibody. In the absence of free drug from the sample the antibody binds to the drug labeled G6PDH enzyme thus decreasing the enzymatic activity of the G6PDH. The G6PDH activity is measured spectrophotometrically at 340 nm because of conversion of NAD to NADH.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

      Precision studies were performed by using the negative, cutoff, and high calibrators and two levels of controls. Testing was performed in replicates of

6, twice a day for 10 days for all concentrations. The within-run % CV ranged from 0.54 to 0.62% and the total precision %CV ranged from 0.61 to 0.78%.

The recovery study showed that the assay correctly identified spiked samples at approximately 50% above the cutoff as positive and at approximately 50% below the cutoff as negative.

b. *Linearity/assay reportable range:*

Not applicable. This is a qualitative assay.

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

A commercially available 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 have been conducted. Protocols and acceptance criteria were described and found to be acceptable. The manufacturer claims the following expiration date:

When stored at 2-8 ℃ product is good until expiration date which is 18 months.

Stability of methadone in the Salivette collection device was determined by taking a pool of negative oral fluid samples spiked at three different concentrations and split into three hundred and thirty-three samples. On day one 10 samples were run to determine the baseline that subsequent runs were compared to. Of the remaining one hundred samples for each concentration half were stored at 2-8 ℃ and the other half were stored frozen -20 ℃. The study was conducted over 22 days and samples were run on days 1, 2, 5, 8, 14 and 22. The sample is stable for 22 days when stored at refrigerator 2-8 ℃ or frozen -20 ℃.

d. *Detection limit:*

See the Precision/Reproducibility section above for performance around the stated cutoff concentration.

e. *Analytical specificity:*

Various potentially interfering substances were evaluated to determine whether they interfere with assay results. Test compounds were spiked into

the drug-free calibrator to various concentrations and evaluated against the cutoff calibrator. The labeling lists the concentration of each compound that gave a response approximately equal to that of the cutoff calibrator (as positive) or the maximal concentration of compound tested that remained negative.

Cross Reactivity with related compounds

Compounds	Conc. µg/mL	X-reactivity
Methadone	0.02	Positive
EDDP	1.0	Positive
LAAM	0.1	Positive
Methadol	0.1	Positive

f. *Assay cut-off:*

The stated cutoff of this assay, which includes the dilution of the sample with the Salivette collection device, is 30 ng/mL. Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision/reproducibility section above.

2. Comparison studies:

a. *Method comparison with predicate device:*

One hundred and nineteen clinical oral fluid specimens were collected. The oral fluid specimens were tested with LZI Oral Fluid Methadone Enzyme Immunoassay and compared to a Gas Chromatography/ Mass Spectrophotometer (GC/MS).

Results from the study are presented below. The table describes the agreement between the device and the GC/MS.

		GC/MS	
		Positive	Negative
LZI EIA	Positive	60	1*
	Negative	0	58

* Sample was found to be < 2 ng/mL below cutoff when analyzed by GC/MS.

% Agreement = 99.2%

b. *Matrix comparison:*

Not applicable. The assay is intended for only one sample matrix.

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):

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.