

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

A. 510(k) Number:

k062242

B. Purpose for Submission:

New device

C. Measurand:

Methamphetamine

D. Type of Test:

Qualitative Enzyme Immunoassay

E. Applicant:

Lin-Zhi International, Inc.

F. Proprietary and Established Names:

LZI Oral Fluid Methamphetamine Enzyme Immunoassay
LZI Oral Fluid Methamphetamine Calibrators
LZI Oral Fluid Methamphetamine Controls

G. Regulatory Information:

1. Regulation section:
 - 21 CFR § 862.3610, Methamphetamine test system
 - 21 CFR § 862.3200, Clinical toxicology calibrator
 - 21 CFR § 862.3280, Clinical toxicology control material
2. Classification:
 - Class II
3. Product code:
 - LAF
 - DLJ
 - LAS

4. Panel:
Toxicology (91)

H. Intended Use:

1. Intended use(s):
Refer to Indications for Use
2. Indication(s) for use:
The Methamphetamine Enzyme Immunoassays for Drugs of Abuse in Oral Fluid is a homogeneous enzyme immunoassay system to detect methamphetamine in human saliva with a cutoff of 45 ng/mL when testing oral fluid specimens collected with a Salivette collector (manufactured by Sarstedt) and diluted with 1 mL of buffer. The calibrators and controls of the analyte (d-methamphetamine) 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 for methamphetamine. The assay is designed for professional use with a number of automated clinical chemistry analyzers.

The Oral Fluid Methamphetamine 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 for this submission was collected using a Hitachi 717 analyzer.

I. Device Description:

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

Calibrators for this assay are sold separately and consist of a negative, cutoff, and high calibrator in an oral fluid buffer, ranging in concentration from 0 to 90 ng/mL.

Assayed negative and positive controls are sold separately and are run with unknown

samples to monitor the performance of the assay. They consist of oral fluid to which methamphetamine has been added.

J. Substantial Equivalence Information:

1. Predicate device name(s):
OraSure Methamphetamine Intercept® Micro-plate EIA
LZI Oral Fluid Cocaine Enzyme Immunoassay
LZI Oral Fluid Opiate Enzyme Immunoassay
LZI Oral Fluid Methadone Enzyme Immunoassay
2. Predicate 510(k) number(s):
k993208
k050945
k050988
k051058
3. Comparison with predicates:

Similarities		
Item	Device	OraSure Methamphetamine Intercept® Micro-plate EIA
Intended Use	Qualitative detection of methamphetamine	Same
Assay Type	Enzyme immunoassay	Same
Matrix	Oral Fluid	Same
Controls	2 levels	Same

Differences		
Item	Device	Predicate
Cutoff	45 ng/mL	40 ng/mL
Calibrators	3 levels	2 levels

The LZI predicate devices are similar to the new device in terms of matrix, calibrators, controls, and assay type. They differ in that they measure different analytes than the new device.

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

CLSI EP5-A, Evaluation of Precision Performance of Clinical Chemistry
CLSI EP7-A, Interference Testing in Clinical Chemistry
CLSI EP9-A, Method Comparison and Bias Estimation Using Patient Samples
CLSI ILA21-A, Clinical Evaluation of Immunoassays

L. Test Principle:

The assay is based on competition for anti-methamphetamine antibody binding sites between methamphetamine in the sample and methamphetamine conjugated to glucose-6-phosphate dehydrogenase (G6PDH). In the absence of free drug in the sample, the antibody binds the conjugated methamphetamine thus decreasing the enzymatic activity of the G6PDH. The G6PDH activity is measured spectrophotometrically at 340 nm due to conversion of NAD to NADH.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

Performance data for this submission was collected using a Hitachi 717 analyzer.

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 0.39 to 0.64 % and the Total precision %CV ranged from 0.58 to 0.80%.

The recovery study showed that the assay correctly identified spiked samples above the cutoff as positive and 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 °C product is good until expiration date which is 18 months.

The stability of methamphetamine 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 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 °C and the other half were stored frozen

-20 °C. The study was conducted over 22 days and samples were run on days 1, 2, 8, 12, 15 and 22. The sample is stable for 22 days when stored refrigerated at 2-8 °C or frozen at -20 °C.

d. Detection limit:

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

e. Analytical specificity:

Various potentially cross-reacting or 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. Results were as follows:

Potential Cross-reactant	Conc. (ng/mL)	X-reactivity
<i>d</i> -Methamphetamine	30	Positive
<i>l</i> -Methamphetamine	500	Negative
<i>d</i> -Amphetamine	1000	Negative
<i>l</i> -Amphetamine	10000	Negative

Potential Interferent	Conc. (µg/mL)	X-reactivity
Acetaminophen	100	Negative
Acetylsalicylic acid	250	Negative
Amobarbital	100	Negative
Benzoylcegonine	100	Negative
Benzphetamine	50	Negative
Brompheniramine	200	Negative
Bupropion	250	Negative
Buspirone	250	Negative
Caffeine	300	Negative
Chlorpheniramine	250	Negative
Chlorpromazine	300	Negative
Codeine	250	Negative
Dextromethorphan	300	Negative
Doxepine	50	Negative
d-Ephedrine	100	Negative
d,l-Ephedrine	45	Negative
l-Ephedrine	7	Negative
Fenfluramine	1	Negative
3-OH Tyramine	125	Negative
Isoxsuprine	250	Negative
Meperidine	200	Negative

Potential Interferent	Conc. (µg/mL)	X-reactivity
Mephentermine	3	Negative
Methadone	200	Negative
Morphine	200	Negative
Oxazepam	200	Negative
Phencyclidine	25	Negative
Phenethylamine	5	Negative
Phenmetrazine	15	Negative
Phenobarbital	200	Negative
Phentermine	5	Negative
d-Phenylpropanolamine	50	Negative
d,l-Phenylpropanolamine	12.5	Negative
l-Phenylpropanolamine	6.25	Negative
Procainamide	125	Negative
Promethazine	300	Negative
Propoxyphene	200	Negative
Propranolol	300	Negative
d-Pseudoephedrine	5	Negative
l-Pseudoephedrine	100	Negative
Ranitidine	10	Negative
Secobarbital	200	Negative
Sertraline	125	Negative
Trazodone	100	Negative
Trifluoperazine	250	Negative
Tyramine	50	Negative
Valproic Acid	300	Negative

f. Assay cut-off:

The stated cutoff of this assay, which includes the dilution of the sample with the Salivette collection device, is 45 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 twelve clinical oral fluid specimens were collected. The oral fluid specimens were tested with LZI Oral Fluid Methamphetamine 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	71	2*
	Negative	0	39

*The two discrepant samples contained 41 and 44 ng/mL methamphetamine

% Agreement = 98.2%

b. Matrix comparison:

Not applicable. This device is intended for use with oral fluid 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.