

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

A. 510(k) Number:

k050988

B. Purpose for Submission:

Clearance of new device

C. Measurand:

Opiates (Morphine)

D. Type of Test:

Qualitative Immunoassay

E. Applicant:

Lin-Zhi International Inc.

F. Proprietary and Established Names:

Opiate Oral Fluid Enzyme Immunoassay, Calibrators, and Controls

G. Regulatory Information:

1. Regulation section:

21 CFR §862.3650, Opiate test system

21 CFR §862.3200, Clinical toxicology calibrator

21 CFR §862.3280, Clinical toxicology control material

2. Classification:

Class II

3. Product code:

DJG, enzyme immunoassay, opiates

DLJ, calibrators, drug specific

LAS, drug specific control materials

4. Panel:

Toxicology (91)

H. Intended Use:

1. Intended use(s):

See Indications for Use

2. Indication(s) for use:

“The Opiate Enzyme Immunoassay is a homogeneous enzyme immunoassay system to detect opiates 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 Morphine 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 Opiate 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:

Roche Hitachi 717 Clinical Chemistry Analyzer

I. Device Description:

The device consists of two liquid reagents; an antibody/substrate reagent and an enzyme/drug conjugate. The antibody/substrate reagent contains mouse monoclonal anti-morphine antibody, glucose-6-phosphate (G6P), NAD, stabilizers, and preservative. The enzyme/drug conjugate contains morphine-labeled glucose-6-phosphate dehydrogenase (G6PDH) in buffer with preservatives. Calibrators (3 levels) and controls (2 levels) are based on oral fluid buffer with preservatives and contain varying levels of morphine.

J. Substantial Equivalence Information:

1. Predicate device name(s):

LZI Opiate EIA

OraSure Opiates Intercept Micro-Plate EIA

Dade Behring Emit II Plus Opiate Assay

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

k020368

k981341

k011289

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. The cutoff differs between the assays.

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

None referenced by the sponsor.

L. Test Principle:

Enzyme-labeled drug and drug present in the sample compete for limited monoclonal mouse anti-morphine antibody binding sites. Binding of the enzyme-labeled drug inhibits its reaction with the substrate, thereby influencing the rate of absorbance change measured by the instrument. The rate of absorbance change is proportional to the concentration of drug in the sample. Concentrations of controls and unknowns are calculated from the standard curve. Results are read at 340 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The negative, cutoff, and high calibrators and two levels of controls were assayed with the Hitachi 717 analyzer in replicates of 6, twice a day for 10 days. The within-run % CV ranged from 0.54 to 0.70% and the total precision %CV ranged from 0.73 to 0.87%.

A recovery study showed that the assay correctly identified six spiked samples at approximately 50% above the cutoff as positive and six spiked samples 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):*

Traceability:

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 meet the manufacture's acceptance criteria and support a claim of 18 months when the product is stored at 2-8 °C

Stability of morphine 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 for comparison to subsequent runs. Of the remaining one hundred samples for each concentration half were stored at 2-8 °C and the other half were stored frozen at -20 °C. The study was conducted over 22 days; samples were run on days 1, 2, 5, 8, 14 and 22. The results support the manufacturer's claim that the sample is stable for 22 days when stored at refrigerator 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 morphine-related and -unrelated compounds were tested for cross-reactivity with the assay. Test compounds were spiked into drug-free negative oral fluid calibrator matrix and evaluated against the cutoff calibrator. The following table lists the lowest concentration that gave a response equivalent to that of the cutoff calibrator. Cross-reactivity was calculated by dividing the concentration at which the compound yielded a positive result by the designated cut-off concentration.

Opiate Oral Fluid Assay: Cross-reactivity of Related Compounds

Compound	Conc (ng/mL)
Morphine	20
Codeine	10
Oxycodone	100
Hydroxycodone	100
Meperidine	2000

Potential interference caused by other substances or drugs was evaluated by adding various concentrations of each drug to oral fluid calibrator matrix and testing with the Opiate Oral Fluid Assay: all compounds below gave a response less than the cutoff calibrator at the concentration specified.

Compounds that Do Not Cross React with the Opiate Oral Fluid Assay

Compound Tested	Conc (ug/mL)	Compound Tested	Conc (ug/mL)
Acetaminophen	100	d-Methamphetamine	25
Acetylsalicylic acid	250	p-Methoxymethamphetamine	25
Amobarbital	100	p-Methoxyamphetamine	100
d-Amphetamine	5	Oxazepam	100
l-Amphetamine	20	Phencyclidine	25
Benzoyllecgonine	100	Phenethylamine	5
Benzphetamine	200	Phenmetrazine	15
Bromopheniramine	25	Phenobarbital	200
Bupropion	250	Phentermine	5

Compound Tested	Conc (ug/mL)	Compound Tested	Conc (ug/mL)
Buspirone	250	d-Phenylpropanolamine	250
Caffeine	300	d,l-Phenylpropanolamine	25
Chlorpheniramine	12.5	l-Phenylpropanolamine	12.5
Chlorpromazine	35	Procainamide	125
Dextromethorphan	2	Promethazone	50
Doxepine	200	Propoxyphene	10
Ecgonine Methyl Ester	5	Propanol	150
d-Ephedrine	300	d-Pseudoephedrine	25
d,l-Ephedrine	40	l-Pseudoephedrine	100
l-Ephedrine	15	Rantidine	2
3-OH Tryamine	250	Secobarbital	200
Isoxsuprine	250	Trazodone	250
Mephentermine	25	Trifluoperazine	250
Methadone	100	Tyramine	50
l-Methamphetamine	100	Valproic acid	300

f. Assay cut-off:

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

2. Comparison studies:

a. Method comparison with predicate device:

Ninety-seven (97) clinical oral fluid specimens were collected. The oral fluid specimens were tested with LZI Oral Fluid Opiate 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	41	5*
	Negative	0	51

*Five samples contain less than 30 ng/mL morphine, but all contain codeine at a concentration that produces a result higher than the cutoff calibrator.

% Agreement = 94.8%

b. Matrix comparison:

Not applicable. This device is intended for use with only saliva.

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.