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

A. 510(k) Number: K031797

B. Analyte: methadone

C. Type of Test: qualitative and semi-quantitative homogeneous enzyme immunoassay

D. Applicant: Lin-Zhi International Inc

E. Proprietary and Established Names: Methadone Metabolite Enzyme Immunoassay

F. Regulatory Information:
1. Regulation section: 21CFR862.3620, Methadone Test System.

2. Classification: Class II

3. Product Code: DJR

4. Panel: Toxicology (91)

G. Intended Use:
1. Indication(s) for use: The Methadone Metabolite Enzyme Immunoassay is a homogeneous enzyme immunoassay with a 300 ng/ml cutoff.   The assay is intended for use in the qualitative and semi-quantitative analyses of methadone metabolite in human urine. The assay is designed for professional use with automated clinical chemistry analyzers.

2. Special condition for use statement(s): The assay 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 is the preferred confirmatory method. Other chemical confirmation methods are available. Clinical consideration and professional judgement should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

For prescription use.

3. Special instrument Requirements: The device is designed for use on automated clinical chemistry analyzers.

H. Device Description:
The device consists of an antibody/substrate reagent and an enzyme-drug conjugate reagent containing all components of the immunoassay.

I. Substantial Equivalence Information:

1. Predicate device name(s): DRI Microgenics Methadone Metabolite Enzyme Immunoassay.

2. Predicate K number(s): K931780

3. Comparison with predicate: Operating principle and reagent composition are similar to the predicate device. The cutoff concentration for this device (300 ng/ml) is lower than that of the predicate device (1000 ng/ml).

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

K. Test Principle: The test is a homogeneous enzyme immunoassay for use on automated clinical chemistry analyzers.

L. Performance Characteristics (if/when applicable):
Performance was evaluated on the Hitachi 717 analyzer.

1. Analytical performance:
   a. *Precision/Reproducibility:* Qualitative assay:
   Precision within one run was evaluated by assaying 21 replicates each of calibrators and control material at the concentrations indicated below, during one run. The mean and standard deviation of the 21 replicates are shown below:

concentrations (ng/ml)	225	300	375	1000
average reading (mA/min)		354.0	374.9	390.9	449.4
standard deviation (mA/min)	2.4	2.7	3.0	3.4
%cv		0.7	0.7	0.8	0.8

Precision was evaluated using calibrator and control material for 12 runs over a 3 week period. The mean and standard deviations over all readings are shown below:

concentrations (ng/ml)	225	300	375	1000
average reading (mA/min)		357.3	377.2	390.6	452.5
standard deviation (mA/min)	2.9	1.8	2.5	4.2
%cv		0.8	0.5	0.6	0.9

Semi-Quantitative Assay:
Using 5 calibrators as reference, precision within one run was determined by assaying 21 replicates each of calibrators and control material at the concentrations indicated below, during one run. The mean and standard deviation of the 21 replicates are shown below:

concentrations (ng/ml)	225	300	375
average reading (ng/ml)	227.9	304.9	382.8
standard deviation (ng/ml)		8.8	13.7	13.0
%cv		3.9	4.5	3.4

Using 5 calibrators as reference, precision was evaluated for 12 runs over a 3 week period. The mean and standard deviations over all readings are shown below:

concentrations (ng/ml)	225	300	375
average reading (ng/ml)	227.2	298.4	371.1
standard deviation (ng/ml)	8.2	10.8	11.8
%cv	3.6	3.6	3.2

b. *Linearity/assay reportable range*
Semiquantitation of positive results enables the laboratory to determine an appropriate dilution of the specimen for confirmation by GC/MS. The semiquantitative mode also permits the laboratory to establish quality control procedures and assess control performance.

Percent recovery was evaluated using spiked negative urine samples (5 replicates per level) between the range of 30-900. Average % recoveries for each level and standard deviations are shown below:

Target concentration	Measured concentration	% recovery	STDEV	%CV
30	33	109	3.0	9.2
60	61	102	5.7	9.3
120	124	104	6.7	5.4
180	172	95	15.5	9.1
225	214	95	16.1	7.5
375	395	105	12.7	3.2
400	477	95	6.2	1.3
600	569	95	15.1	3.7
750	699	93	38.8	5.5
900	863	96	35.0	4.3

c. *Traceability (controls, calibrators, or method):* Calibrators are prepared as spiked methadone metabolite in a processed drug-free human urine matrix. Value assignments for calibrator and control lots are based on dilutions of known stock solutions and are confirmed by GCMS (to target concentrations of 0, 150, 300, 600 and 1000 ng/ml). Observed recoveries ranged from 96-103%. The material used to prepare the solutions is a commercial material, reported to be traceable to NIST standards.

Calibrators stability was evaluated at room temperature and 2-8 degrees C over 10 months. The recoveries in terms of absolute reading (mA/min) were greater than 97% over this time. The ratios of recoveries for the room temperature calibrators relative to the cold calibrators were greater than 99% over this time.

d. *Detection limit:* Sensitivity was determined by evaluating ten replicates of zero calibrators and serial dilutions of calibrators of low concentration. A concentration of 15 ng/ml can be differentiated from negative urine with 95% confidence.

e. *Analytical specificity:* Test compounds were spiked into the drug-free urine calibrator matrix to various concentrations and evaluated against the cutoff calibrator. The following results were obtained for potential cross-reacting compounds. Values represent concentration of each test compound giving a response approximately equal to the cutoff calibrator (for positives) or the highest concentration tested (for negatives).

EDDP	positive at 300 ng/ml
Methadone	positive at 200 ug/ml
EMDP	positive at 550 ug/ml
(-) alpha-Methadol	positive at 60 ug/ml
LAAM	negative at 100 ug/ml
nor-LAAM	negative at 10 ug/ml

A variety of over-the-counter and prescription drugs were tested for interference by spiking into negative urine. The drugs and levels in the samples tested are listed in the package insert. These compounds are listed in the package insert. No unusual interference was observed.

f. *Assay cut-off:* The assay cutoff is 300 ng/ml

2. Comparison studies:
   a. *Method comparison with predicate device:*
   Comparison to GCMS was evaluated at the manufacturer's site for 139 randomly selected banked clinical urine specimens, previously analyzed by GCMS. Sample concentrations ranged up to 22,000 ng/ml included two positive near-cutoff samples). Reported results were similar for the qualitative and semi-quantitative modes. Results are shown below:

Method Comparison Tables
300 ng/ml cutoff, qualitative

	GCMS +	GCMS -
Lin-Zhi Methadone metabolite +	48	0
Lin-Zhi Methadone metabolite -	0	91

To evaluate accuracy around the cutoff concentration, 20 positive clinical specimens that were diluted to near cutoff concentrations were tested by

GCMS and the Lin-Zhi Methadone Metabolite Assay. Sample concentrations ranged between 125-1360 g/ml and included 11 samples within +/- 25% of the cutoff). Results, which were similar for the qualitative and semi-quantitative mode are shown below.

300 ng/ml cutoff, qualitative mode, near cutoff samples:

	GCMS +	GCMS -
+ Lin-Zhi Methadone metabolite	12	0
-	1	7

   b. *Matrix comparison:* Not applicable. The device is indicated only for urine specimens.

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):*

4. Clinical cut-off: Not applicable

5. Expected values/Reference range: Not applicable

M. Conclusion:

I recommend that the Lin-Zhi Methadone Metabolite Enzyme Immunoassay is substantially equivalent to the predicate device.