

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

A. 510(k) Number:

K032764

B. Analyte:

Barbiturates

C. Type of Test:

Homogeneous Enzyme Immunoassay for the qualitative and semi-quantitative measurement of barbiturates

D. Applicant:

Lin-Zhi International, Inc.

E. Proprietary and Established Names:

Barbiturate Enzyme Immunoassay

Barbiturate Drugs of Abuse Calibrators and Controls

F. Regulatory Information:

1. Regulation section:

CFR 862.3150, Barbiturate test system

862.3200, Clinical toxicology calibrator

862.3280, Clinical toxicology control material

2. Classification:

Class II (reagents and calibrators)

Class I (controls)

3. Product Code:

DIS, DLJ, LAS

4. Panel:

Clinical Toxicology

G. Intended Use:

1. Indication(s) for use:

The Barbiturate Enzyme Immunoassay is a homogeneous enzyme immunoassay with a 200 ng/mL and/or 300 ng/mL cutoffs. The assay is intended for use in the qualitative and semi-quantitative analyses of barbiturates in human urine. The assay is designed for professional use with a number of automated clinical chemistry analyzers.

Measurements obtained by this device are used in the diagnosis and treatment of barbiturate use or overdose and in monitoring levels of barbiturate to ensure appropriate therapy.

2. Special condition for use statement(s):

Prescription use only.

The Barbiturate Enzyme Immunoassay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method. Other chemical confirmation methods are available. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when the preliminary test result is positive.

Semi-quantitative analysis is helpful in estimating the concentrations of drugs in the samples. This can aid users in preparing dilutions of the samples for further analysis.

3. Special instrument Requirements:

Analyzers using this device must be able to maintain a constant temperature, pipette samples, mix reagents, measure enzyme rates at 340 nm, and time the reaction accurately.

H. Device Description:

The Barbiturate Enzyme Immunoassay calibrators have secobarbital concentrations of 0 (negative), 100, 200, 300, and 1000 ng/mL in human urine with sodium azide added as a preservative. The Assay controls have concentrations of 100, 200, 300, and 400 ng/mL

The Buffer Reagent (R1) contains tris-based buffer (50nM) with sodium azide. The Enzyme Reagent (R2) contains alcohol dehydrogenase (ADH), nicotinamide adenine dinucleotide (NAD, 10 nM), stabilizers, and sodium azide.

I. Substantial Equivalence Information:

1. Predicate device name(s):

Emit ® II Plus Barbiturate Assay (Syva-Dade Behring)

2. Predicate K number(s):

K010934

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Same	Qualitative and semi-quantitative determination of barbiturates in urine
Cutoff	Same	200 and 300 ng/mL
Semi-quant Calibration	Same	5 levels
Calibrators and Controls	Same	Secobarbital
Differences		
Item	Device	Predicate
Specific Calibrator Concentrations (ng/mL)	0, 100, 200, 300, 1000	0, 100, 200, 300, 800
Specific Control Concentrations (ng/mL)	100, 200, 300, 400	150, 225, 250, 375
Sensitivity (ng/mL)	25	20
Antibodies	Monoclonal to Secobarbital Polyclonal to Phenobarbital	Polyclonal to secobarbital

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

None Referenced

K. Test Principle:

The barbiturate assay is a well-established homogeneous enzyme immunoassay with ready-to-use liquid reagent. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate 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, barbiturate-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. Alternately, when drug is present in the sample, antibody binds to the free drug and the unbound barbiturate-labeled G6PDH exhibits its maximal enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that can be measured spectrophotometrically at 340 nm.

L. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

With-in run precision in the qualitative mode was assessed by measuring mA/min at 0, 100, 200, 300, 400, and 1000 ng/mL, where n=21 for all concentrations. The Coefficients of Variation (CV)

ranged from 0.60 to 1.05. Between-run precision in the qualitative mode was assessed by measuring the same concentrations in 12 runs over a three week period. For n=12, the CVs ranged from 0.35 to 0.83.

The precision and accuracy of the qualitative mode was also assessed by analyzing samples at concentrations of 40, 80, 150, 250, 375, 500, 700, and 900 ng/mL. All samples were correctly identified as positive or negative using both the 200 and 300 ng/mL cutoffs.

With-in run precision in the semi-quantitative mode was assessed by assaying the 100, 200, 300, and 400 ng/mL controls, where n=21 for all concentrations. The Coefficients of Variation (CV) ranged from 2.83 to 4.79. Between-run precision in the semi-quantitative mode was assessed by measuring the same concentrations in 12 runs over a three week period. For n=12, the CVs ranged from 3.08 to 4.85.

b. Linearity/assay reportable range:

Linearity was assessed by spiking secobarbital into negative urine samples and measuring the recovery. The equation of the line of target vs. measured was $y = 1.0005x + 6.47$ with $R^2 = 0.996$

Results were as follows:

Target (ng/mL)	Measured (ng/mL)	% Recovery
40	45.2	113
80	86.7	108
150	151.2	101
250	257.2	103
375	396.8	106
500	516.2	103
700	697.3	100
900	887.6	99

c. Traceability (controls, calibrators, or method):

Traceable to USP reference standard

d. Detection limit:

The functional sensitivity was determined to be 25 ng/mL

e. Analytical specificity:

Potential cross-reactivity was tested with various barbiturate-related compounds and with compounds structurally unrelated to barbiturates. Results were as follows:

Barbiturate Compound	Conc. Equiv. to 200 ng/mL cutoff	% Cross-reactivity	Conc. Equiv. to 300 ng/mL cutoff	% Cross-reactivity
Secobarbital	200	100	300	100
Allobarbital	1000	20	1700	18
Amobarbital	2000	10	5000	6
Aprobarbital	450	44	700	43
Barbital	7000	3	13000	2.3
Butabarbital	800	25	1200	25
Butalbital	470	43	1000	33
Cyclopentobarbital	250	80	600	50
Pentobarbital	650	31	1000	33
Phenobarbital	400	50	1100	27
Thiopental	1300	1.5	25000	1.2

The following compounds were tested for cross-reactivity at a concentration of 1000µg/mL. All tested negative at the 200 and 300 ng/mL cutoff:

Acetaminophen, ASA, Amitriptyline, Amphetamine, Benzoyllecgonine, Caffeine, Chlorpromazine, Cocaine, Codeine, Dextromethorphan, Ephedrine, Imipramine, Meperidine, Methadone, Methamphetamine, Methaqualone, Morphine, Nortriptyline, Promethazine, Propoxyphene, Valproic Acid, Lidocaine, Chloramphenamine, Ecgonine, Bupropion, Ranitidine.

f. Assay cut-off:

The user may choose a 200 or 300 ng/mL cutoff

2. Comparison studies:

a. Method comparison with predicate device:

The device was compared to the predicate in the qualitative mode.

Results were as follows:

200 ng/mL Cutoff	Predicate (Syva)		
LZI Barbiturate		Positive	Negative
	Positive	41	4*
	Negative	0	60

300 ng/mL Cutoff	Predicate (Syva)		
LZI Barbiturate		Positive	Negative
	Positive	39	4*
	Negative	0	62

* These samples were further tested by HPLC or GC/MS and were confirmed to contain only Phenobarbital. The reagents in the predicate device do not contain antibodies to Phenobarbital.

The device was also compared to the GC-MS in the qualitative mode. Results were as follows:

200 ng/mL Cutoff	GC-MS		
LZI Barbiturate		Positive	Negative
	Positive	42	3*
	Negative	1**	59

* measured by GC-MS, butalbital concentrations ranged from 178 to 383 ng/mL

** measured by GC-MS, Phenobarbital concentration was 422 ng/mL

300 ng/mL Cutoff	GC-MS		
LZI Barbiturate		Positive	Negative
	Positive	38	4*
	Negative	0	63

* measured by GC-MS, butalbital concentrations ranged from 178 to 621 ng/mL

b. Matrix comparison:

N/A

3. Clinical studies:

a. Clinical sensitivity:

N/A

b. Clinical specificity:

N/A

c. Other clinical supportive data (when a and b are not applicable):

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

A positive result indicates barbiturate use. This assay cannot distinguish between licit and illicit use of barbiturates.

M. Conclusion:

Based upon the information provided for the file, I recommend that the LZI Barbiturate Enzyme Immunoassay is substantially equivalent to the predicate device