510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K243462

B Applicant

Diazyme Laboratories, Inc.

C Proprietary and Established Names

Diazyme Colorimetric Lithium Assay

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NDW	Class II	21 CFR 862.3560 - Lithium Test System	TX - Clinical Toxicology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Lithium

C Type of Test:

Quantitative colorimetry

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
Diazyme Colorimetric Lithium Assay kit is for quantitative in vitro determination of lithium in human serum or EDTA plasma. Measurements of lithium are carried out to ensure that proper drug dosage is administered in the treatment of patient suffering from bipolar disorder and to avoid toxicity.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

The assay has been validated on the Roche cobas c701 chemistry analyzer.

IV Device/System Characteristics:

A Device Description:

Diazyme Colorimetric Lithium Assay kit is for quantitative in vitro determination of lithium in human serum or EDTA plasma.

The Diazyme Colorimetric Lithium Assay is a ready to use reagent consisting of >40 mg/L porphyrin derivative, NaOH, water, detergent, and preservative. The reagent is light sensitive.

B Principle of Operation:

Lithium is determined spectrophotometrically through the formation of a lithium/chromogen complex. When a sample containing lithium ion is mixed with the reagent containing porphyrin derivative at an alkaline pH, the lithium/chromogen complex is formed, resulting in a change in absorbance which is directly proportional to the concentration of lithium in the sample.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Lithium Regent Model Tr66056 / Lithium Standard Tr66901

B Predicate 510(k) Number(s):
K003583

C Comparison with Predicate(s):

Device & Predicate Device(s):	K243462	K003583
Device Trade Name	Diazyme Colorimetric Lithium Assay	TRACE Lithium Test System
General Device Characteristic Similarities		
Intended Use/Indications For Use	Lithium Assay is intended for the quantitative determination of lithium.	Same
Sample Matrix	Human serum or EDTA plasma	Same
Methodology	Spectrophotometric method	Same
Test Type	Quantitative	Same
Intended Use	For prescription use	Same
General Device Characteristic Differences		
Reagent Components	One (1) reagent system: Porphyrin derivative, sodium hydroxide, water, detergent, and preservative	One (1) reagent system: Sodium hydroxide, EDTA, and substituted porphyrin

VI Standards/Guidance Documents Referenced:

- CLSI Guideline EP05-A3 – *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline*
- CLSI Guideline EP17-A2 – *Evaluation of Detection capability for Clinical Laboratory Measurement Procedures*
- CLSI Guideline EP6-Ed2 – *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach*
- CLSI Guideline EP7-Ed3 – *Interference Testing in Clinical Chemistry*

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
Precision testing for the Diazyme Colorimetric Lithium Assay was performed according to the CLSI EP05-A3 guideline. The test samples consisted of two levels of serum-based controls containing 1.3 mmol/L and 2.7 mmol/L of lithium and five serum samples containing between 0.5 mmol/L and 2.5 mmol/L of lithium. Testing was performed over 21 days with two runs per day in duplicate using three lots of reagent. A summary of the three reagent lots are shown below.

Sample	Mean (mmol/L)	Within-Run		Between-Run		Between-Day		Total	
	(N=252)	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Control 1	1.38	0.016	1.2%	0.016	1.2%	0.042	3.1%	0.045	3.3%
Control 2	2.79	0.026	0.9%	0.041	1.5%	0.098	3.5%	0.103	3.7%
Sample 1	0.49	0.019	3.9%	0.041	8.4%	0.023	4.7%	0.039	8.1%
Sample 2	0.94	0.016	1.7%	0.030	3.2%	0.047	5.0%	0.053	5.7%
Sample 3	1.37	0.013	0.9%	0.032	2.3%	0.071	5.1%	0.075	5.4 %
Sample 4	1.84	0.021	1.2%	0.035	1.9%	0.081	4.4%	0.086	4.7%
Sample 5	2.26	0.022	1.0%	0.038	1.7%	0.090	4.0%	0.096	4.2%

2. Linearity:
Linearity study was performed based upon guidance in CLSI EP06 2nd Edition. A dilution series was prepared from a specimen containing 3.0 mmol/L of lithium chloride and serum. A total of 11 dilutions were measured in triplicate using one lot of reagent on a Roche cobas c701 chemistry analyzer. The data was analyzed using a linear regression model.

   The results support linearity across the claimed measuring interval of 0.10 – 3.00 mmol/L.

3. Analytical Specificity/Interference:
Interference testing was performed according to CLSI Guideline EP07-3 to determine the effect of various endogenous and exogenous substances on the Diazyme Colorimetric Lithium Assay.

   Endogenous Substances
   To evaluate potential interference from certain endogenous substances, serum samples with 0.9 mmol/L, 1.2 mmol/L, and 2.5 mmol/L lithium were spiked with potentially interfering substances. Five concentrations of each potentially interfering substances was assessed. Each sample spiked with interference substances was tested in triplicate. The highest concentration of interferent tested that produced less than 10% deviation is summarized in the table below.

Interferent	Concentration
Ascorbic Acid	5.0 mM
Bilirubin	40.8 mg/dL
Bilirubin Conjugated	49.8 mg/dL
Biotin	3500 ng/mL
Triglyceride	2000 mg/dL
Hemoglobin	500 mg/dL
Na^+	200 mmol/L
NH_4^+	0.5 mmol/L
Ca^{2+}	4.0 mmol/L
$MgCl_2$	2.0 mmol/L
Fe^{3+}	0.25 mmol/L
Cu^{2+}	1.20 mmol/L
$Zn2^+$	0.25 mmol/L
K^+	10 mmol/L

Exogenous Substances:
To evaluate potential interference from certain exogenous substances, serum samples with 0.9 mmol/L, 1.2 mmol/L, and 2.5 mmol/L lithium were spiked with of potentially interfering substances at the concentrations listed below. Each sample spiked with interference substances was tested in triplicate. No significant interference (< 10%) was observed at the concentrations shown in the table below:

Exogenous Interferent	Test Concentration (mg/dL)
Acetaminophen	200
Acetylcysteine	150
Acetylsalicylic acid	1000
Ampicillin	1000
Ca-dobesilate	200
Cefoxitin	2500
Cyclosporine	5
Doxycycline	50
Ibuprofen	500
Intralipid	2000
Levodopa	20
Methyldopa	20
Metronidazole	200
Phenylbutazone	400
Rifampicin	60
Theophylline	100

4. Assay Reportable Range:

   The manufacturer's claimed assay reportable range is from 0.10 to 3.00 mmol/L.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Diazyme Colorimetric Lithium Assay is traceable to a commercially available material.

6. Detection Limit:
   The sponsor followed recommendations outlined in CLSI Guideline EP 17-A2 to determine the Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ).

   LoB:
   Four blank native serum samples were tested with two reagent lots, on one instrument, with 60 replicates in total per lot of reagent. LoB was determined to be 0.01 mmol/L.

   LoD:
   Four low serum samples prepared from blank native serum samples spiked with a stock solution containing lithium were tested with two reagent lots, on one instrument, with 30 replicates in total per lot of reagent. LoB was determined to be 0.041 mmol/L.

   LoQ:
   Five different serum samples from concentrations 0.05 mmol/L, 0.10 mmol/L, 0.15 mmol/L, 0.20 mmol/L, and 0.25 mmol/L were prepared by spiking normal blank serum samples with a stock solution containing lithium. The samples were tested with two reagent lots, on one instrument, with 75 replicates in total per lot of reagent. LoQ was determined to be 0.10 mmol/L.

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   Method comparison studies were performed to evaluate the performance of the Diazyme Colorimetric Lithium Assay. The study included 67 unaltered individual serum samples and 11 altered serum samples for a total of 78 distinct samples spanning the range of 0.10 to 2.98 mmol/L of lithium. Testing was performed using three reagent lots by two operators at one site. Measurements obtained with the Diazyme Colorimetric Lithium Assay were made on the Roche cobas c701 chemistry analyzer and compared to the predicate assay. The least square regression analysis for the study is shown below.

	Diazyme Colorimetric Lithium vs Diazyme Enzymatic Lithium
N	78
r^2	0.9937
Slope	1.012

Y intercept	0.0439

2. Matrix Comparison:

The matrix comparison study included 20 native matched serum, K2 EDTA plasma, and Na heparin plasma samples and 51 altered matched sets for a total of 71 distinct samples spanning the range of 0 to 3 mmol/L of lithium. The samples were tested on the Roche cobas c701 chemistry analyzer with the Diazyme Colorimetric Lithium Assay using one reagent lot. Results of the serum samples compared to K2 EDTA plasma and Na heparin plasma samples using Passing- Bablok regression analysis are shown below.

Serum compared to Na heparin plasma
Slope: 1.0009 95% CI: 0.9922 to 1.0192
Intercept: -0.0010 95% CI: -0.0156 to 0.0037
N: 71
r^2: 0.9959 (provided by least squares regression)

Serum compared to K2 EDTA plasma
Slope: 1.0137 95% CI: 1.0000 to 1.0294
Intercept: -0.0036 95% CI: -0.0150 to 0.0050
N: 71
r^2: 0.991 (provided by least squares regression)

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

The following is included in the package insert:

A trough concentration for 12-hour post dose is expected to be 1.0- 1.2 mM. Levels higher than 1.5 mM, 12 hours after a dose, indicate a significant risk of intoxication. Values indicated should

be used only as a guide. It is recommended that each laboratory establishes or derives a reference interval for the population it serves.

VIII Proposed Labeling:

The labeling does support the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.