

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

A. 510(k) Number:

k051108

B. Purpose for Submission:

New Device

C. Analyte:

Lactate Dehydrogenase

D. Type of Test:

Quantitative

E. Applicant:

Abaxis, Inc.

F. Proprietary and Established Names:

Piccolo® Lactate Dehydrogenase Test System

G. Regulatory Information:

1. Regulation section:
21 CFR 862.1440
2. Classification:
Class II
3. Product Code:
CFJ
4. Panel:
75 (Chemistry)

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

The Piccolo Lactate Dehydrogenase Test System (presently contained on the Chemotherapy Evaluation Panel Reagent Disc) used with the Piccolo Point-of-Care Chemistry Analyzer is intended to be used for the *in vitro* quantitative determination of lactate dehydrogenase activity in heparinized plasma or serum in a clinical laboratory setting or point-of-care location.

Lactate dehydrogenase measurements are used in the diagnosis and treatment of liver diseases such as acute viral hepatitis and cirrhosis; cardiac diseases such as myocardial infarction; and tissue alterations of the heart, kidney, liver, and muscle.

3. Special condition for use statement(s):

For prescription use only

4. Special instrument Requirements:

Piccolo Point-of-Care Chemistry Analyzer

I. Device Description:

According to the sponsor the Piccolo Chemotherapy Evaluation Panel Reagent Disc which contains the Piccolo Lactate Dehydrogenase Test System is designed for heparinized plasma and serum use only. The disc meters the required quantity of sample and diluent, mixes the sample with the diluent, and delivers the mixture to the reaction cuvettes along the disc perimeter. The diluted sample then mixes with the reagent beads, initiating the chemical reactions that are then monitored by the analyzer. The disc is an 8 cm. diameter single-use device. Upon completion of the analysis, the disc, containing the diluted heparinized plasma or serum, is discarded.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Lactate Dehydrogenase Synchron LX20

2. Predicate K number(s):

k011213

3. Comparison with predicate:

Similarities		
Item	Piccolo Point-of-Care Chemistry Analyzer	Synchron LX20 Chemistry System
Intended Use	Quantitative analysis of Lactate Dehydrogenase	Quantitative analysis of Lactate Dehydrogenase
Methodology	Enzymatic	Enzymatic
Sample Type	Heparinized Plasma and Serum	Heparinized Plasma and Serum
Sensitivity	50 U/L	5 U/L
Reagents	Dry test-specific reagent beads and liquid diluent; reconstitution performed by analyzer Active ingredients: Lactate Nicotinamide adenine dinucleotide (NAD+) Diaphorase p-Iod Nitrotetrazolium Violet (INT)	Liquid reagents Active ingredients: Lactate Nicotinamide adenine dinucleotide (NAD+)
Temperature of Reaction	37°C	37°C
Calibration	Bar code with factory calibrated lot specific data	Calibration not required
Assay Range	50-1,000 U/L	5-750 U/L (600-2,700 U/L ORDAC*)
Testing Environment	Professional Use	Professional Use
Sample Size	~ Approximately 100 mL	13 mL

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

In Vitro Diagnostic Devices: Guidance for the Preparation of 510 (k) Submissions. HHS Publication FDA 97-4224, January, 1997.

Method comparison and bias estimation using patient samples. 2nd ed. NCCLS Document EP9-A2, 2002.

Evaluation of precision performance of clinical chemistry devices. 2nd ed. NCCLS Document EP5-A2, 2004.

Quality Management for unit-use testing. NCCLS Document EP18-A, 2002.

Evaluation of the linearity of quantitative analytical methods. NCCLS Document EP6-A, 2003.

Interference testing in clinical chemistry. NCCLS Document EP7-A, 2002.

How to define and determine reference intervals in the clinical laboratory. 2nd ed. NCCLS Document C28-A2, 2000.

L. Test Principle:

Reagents are formed into lyophilized microspheres and placed in reaction cuvettes along the periphery of the reagent disc. In the first step, L-Lactate and Nicotinamide adenine dinucleotide (NAD⁺) is oxidized to pyruvate and nicotinamide adenine dinucleotide (NADH) by lactate dehydrogenase. The resulting NADH is then used to reduce p-Iodo Nitrotetrazolium Violet (INT) to formazan through the catalysis of diaphorase. The highly colored formazan is measured at 500 nm and 630 nm bi chromatically and is directly proportional to the lactate dehydrogenase activity of the sample.

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

According to the sponsor, precision studies were conducted using 2 levels of a commercially available human serum-based control. The controls were run in duplicate on the Chemotherapy Evaluation Reagent Disc containing Lactate Dehydrogenase. The sponsor used a total of 4 separate Piccolo Point-of-Care Chemistry Analyzers, 2 at the clinical trial site and 2 at Abaxis. Each level of control was assayed twice a day, once in the morning and once in the afternoon for 5 days for a total of 80 data points. A summary of the within-run and total precision of Lactate Dehydrogenase (LD) assayed on the Piccolo Point-of-care Chemistry Analyzer is shown in the table below.

Lactate Dehydrogenase (U/L)	Within-Run Precision (n=80)	Total Precision (n=80)
Control Level 1		
Mean	87.2	87.2
SD	3.0	4.4
%CV	3.4	5.0
Control Level 2		
Mean	350.0	350.0
SD	3.8	7.0
%CV	1.1	2.0

b. *Linearity/assay reportable range:*

According to the sponsor a human serum pool containing a low concentration of LD (48 U/L) was spiked with LD to a concentration of 1,143 U/L. Dilutions of this high LD sample were made into the low LD serum pool according to NCCLS EP6-A.

Pools containing the 5 levels of LD were assayed in replicates of 4 on 4 Piccolo Point-of-Care Chemistry Analyzers. Four analyzers were used to ensure that recoveries were not instrument-specific. The results for Lactate Dehydrogenase were plotted and the graphic representation is summarized in the table below.

Pool	Linearity Equation	R²
1	$y=0.972x + 0.942$	0.998
2	$y=1.053x - 6.766$	0.999
3	$y=0.983x + 6.031$	0.998
4	$y=1.040x + 1.447$	0.998
Averaged	$y=1.012x + 0.253$	0.995

Summary of Linearity Results

Slope	1.012
Intercept	+0.253
Corr. Coefficient	0.998

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

The sponsor calibrated the LD assay to match the LD assay with an internationally used commercial assay.

Stability was determined by real-time stability at 0, 1, 3, 6, 9, 12, 15, 18 and 21 months at 2-8° C. Accelerated stability testing at 25° C at 0, 14, 21 and 28 days and at 35° C at 0, 3 and 10 days. The sponsor recommends storage for the Lactate Dehydrogenase assay at 2-8° C for 6 months after manufactured disc date.

d. Detection limit:

According to the sponsor the concentration of Lactate Dehydrogenase that could be differentiated above 0 mg/dL by the Piccolo Lactate Dehydrogenase Test system with 95% confidence (twice the standard deviation was 8 U/L) Abaxis decided to take a conservative approach and use 50 U/L as the lowest reportable LD value.

Abaxis piccolo LD Sensitivity Data

Assigned value	LD-free 7% Human Alb (diluent) 0.0 U/L	LD-Diluted NHS 9.9 U/L	LD Diluted NHS 12.5 U/L	LD Normal Human Serum NHS 54 U/L
1	1.2	3.5	9.2	51.2
2	5.3	4.5	13.8	54.8
3	7.8	8.6	6.5	57.1
4	1.7	14.7	27.41	54.7
5	-4.8	0.8	8.55	58.5
6	-0.7	6.9	13.5	58.0
7	0.7	3.6	5.1	55.8
8	-5.2	6.9	9.4	55.9
9	4.1	10.3	8.5	52.5
10	4.7	13.8	17.6	56.4
11	1.6	7.3	9.8	65.7
12	3.3	10.3	10.9	56.1
13	-3.6	7.0	11.0	57.2
14	0.7	8.9	18.0	67.7
15	-7.2	1.2	10.0	52.9
16	-3.0	3.7	15.5	53.1
17	6.1	9.4	12.1	66.6
18	-0.3	16.7	14.5	56.76
19	1.8	6.3	10.9	62.5
20	-1.6	8.2	18.0	56.3
Average	0.6	7.6	12.5	57.5
SD	4.02	4.23	5.082	4.66
N	20	20	20	20

Dynamic Range

Calibration of the Piccolo Lactate Dehydrogenase Test System makes use of a calibrator above 1000 U/L (the current calibrator is 1,203 U/L). The lowest calibrator has a value of 54 U/L). Based on the above sensitivity studies the sponsor used 50 U/L as the lowest reportable LD value. The dynamic range is indicated in below.

Dynamic Range

Analyte	Low	High	Unit
Lactate Dehydrogenase	50	1,000	U/L

e. Analytical specificity:

Analytical specificity was conducted according to NCCLS EP7-A, using supplemented human serum pools. Test pools with different

levels of potential interferents (endogenous and exogenous substances), and a control pool containing LD were tested by running 4 replicates on different Piccolo Point-of-Care Chemistry analyzers. The difference in mean LD concentrations between each test pool and the control pools was determined. The below chart indicates how values are displayed when elevated hemoglobin values are detected.

Hemoglobin values	Displayed
50-100 mg/dL	The LD value followed by an “H”
100-150 mg/dL	“<H” followed by the LD value
Greater than 150 mg/dL	No LD value and “HEM” will be displayed.

The “H” indicates influence from hemolysis. The sponsor used this annotation to help the operator interpret LD activity in the presence of small amounts of hemolysis. The endogenous interference limits are noted in the below chart.

Hemolysis (Hemoglobin, mg/dL)	Icterus (Bilirubin, mg/dL)	Lipemia (Triglycerides, mg/dL)
50	64	1,720

Thirteen drugs were selected as potential interferents with the Lactate Dehydrogenase method based on literature recommendations and are presented in the below table.

	Physiological or Therapeutic Range (mg/dL)	Concentration with No Significant Interference (mg/dL)
Acetaminophen	2-10	20
Acetoacetate	0.05-3.6	102
Acetylsalicylic acid	1-2	50
Ascorbic acid	--	3
Caffeine	--	10
Ibuprofen	0.5-4.2	40
Lactic Acid	4.5-19.8	60
Lidocaine	0.5-0.6	6
Lithium Citrate	0.4-0.8	3.5
Methotrexate	0.1	450
Oxaloacetate	--	66
Phenytoin (5,5- Diphenylhydantion)	1-2	10
Pyruvate	0.3-0.9	44

f. Assay cut-off:

See Detection Limit section above.

2. Comparison studies:

a. Method comparison with predicate device:

The sponsor conducted a method comparison study to assess the accuracy of the Abaxis Lactate Dehydrogenase method to the results obtained from the predicate Beckman Synchron LX20 Chemistry System. Paired samples were run on each analyzer for comparison. See the Method Comparison Data for Lactate Dehydrogenase Assayed on the Synchron LX20 Chemistry System and Piccolo Point-of-Care Analyzer below.

Parameters	Statistics
Piccolo Lactate Dehydrogenase Test System: 60 specimens in singlicate	60
Synchron LX20: 60 specimens in singlicate	60
Piccolo Lactate Dehydrogenase Test System Mean	306.2 U/L
Synchron LX20 Mean	307.9 U/L
Piccolo Lactate Dehydrogenase Test System Std. Dev	234.0
Synchron LX20 Std. Dev	236.7
Piccolo Lactate Dehydrogenase Test System range of samples	38-1126 U/L
Synchron LX20 range of samples	44-1172 U/L

	Linear Regression	Deming Regression
N	60	60
Slope	0.983	0.989
Intercept	3.8	1.9
Correlation coefficient	0.994	0.994
Std. Error of Estimate	26.3	N/A

b. Matrix comparison:

Matrix comparison studies were performed by the sponsor to compare heparinized plasma and serum on the Piccolo Point-of-Care Analyzer. Heparinized plasma and serum samples were collected from 10 subjects and run in replicates of 4 within 30 minutes. Serum values were found to be slightly higher than plasma, demonstrating

an average positive bias of 6 U/L. The average LD in serum and plasma was 130.0 and 124.5 U/L, respectively.

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):*

N/A

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

The reference interval for the Piccolo Lactate Dehydrogenase Test System was determined in accordance with NCCLS C28-A2. The Sponsor used the data from the method comparison with the Synchron LX20. The plasma samples tested resulted in the Deming regression equation of

$$Y (\text{Piccolo LD}) = 0.989X (\text{Synchron LX20 LD}) + 1.9$$

Synchron LX20 LD has a reference interval published for plasma or serum of 98-192. The calculated reference interval for the LD assay was determined to be 99-192 mg/dL.

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.