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

A. 510(k) Number:
k130113

B. Purpose for Submission:
Addition of lactate analyte to Piccolo® MetLac 12 Panel Reagent Disc which contains eleven other previously cleared analytes

C. Measurand:
Lactate

D. Type of Test:
Quantitative, enzymatic colorimetric

E. Applicant:
Abaxis Inc.

F. Proprietary and Established Names:
Piccolo® Lactate Test System

G. Regulatory Information:

1. Regulation section:
   21 CFR § 862.1450; Lactic acid test system

2. Classification:
   Class I, meets limitations of exemptions per 21 CFR § 862.9 (c)(9)

3. Product code:
   KHP; Lactic Acid, Enzymatic Method

4. Panel:
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):
   The Piccolo® Lactate Test System (presently contained on the MetLac 12 Panel Reagent Disc) used with the Piccolo® xpress™ Chemistry Analyzer is intended to be used for the in vitro quantitative determination of lactate concentration in heparinized whole blood or heparinized plasma in a clinical laboratory setting or point-of-care location.

2. Indication(s) for use:
   Lactate measurements are used in the diagnosis and treatment of lactic acidosis, monitoring tissue hypoxia, and diagnosis of hyperlactatemia.

3. Special conditions for use statement(s):
   For prescription use only

4. Special instrument requirements:
   Piccolo® xpress™ Chemistry Analyzer

I. Device Description:

The Piccolo® MetLac 12 Panel Reagent Disc (which contains the Piccolo® Lactate Test System) is designed for lithium heparinized whole blood and lithium heparinized plasma. The disc is an 8 cm diameter single-use device that contains chambers for reagents along the outer edge of the disc, chambers for the sample and diluent (sealed in diluent container in the center of the disc), and chambers for dilution of sample. Through capillary action and centrifugal force, the required quantity of sample and diluent are mixed, and the mixture is delivered to the reaction cuvettes along the disc perimeter. The diluted sample mixes with the reagent beads in the reaction chambers, initiating the chemical reactions that are colorimetrically monitored by the analyzer.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Abbott i-STAT Lactate/LAC

2. Predicate k number(s):
   k982071

3. Comparison with predicate:

Similarities		
Item	Candidate device	Predicate device
Intended use	For in vitro quantitative determination of lactic acid/lactate concentration	same
Methodology	Enzymatic	same
Temperature of reaction	37ºC	same
Testing environment	Point-of-care and clinical laboratories	same

Differences		
Item	Candidate device	Predicate device
Test principle	Colorimetric	Amperometric
Specimen type	Heparinized venous whole blood and heparinized plasma	Arterial, venous, or capillary whole blood (with or without heparin)
Reportable range	0.30 to 9.99 mmol/L	0.30 to 20.00 mmol/L
Calibration	Each disc is bar coded with factory-calibrated lot-specific data	Automatically calibrated during each analysis using on-board reagent
Reagents	Dry test-specific reagent beads and liquid diluent; reconstitution performed by analyzer.	Immobilized enzyme on a biosensor and liquid reagents.
Sample Size	Approximately 100 µL	95 µL

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

- CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline- Second Edition
- CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.
- CLSI EP7-A2: Interference Testing in Clinical Chemistry: Approved Guideline- Second Edition
- CLSI EP17-A: Protocol for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.
- CLSI EP9-A2-IR: Method of Comparison and Bias Estimation Using Patient Samples: Approved Guideline- Second Edition (Interim Revision)
- CLSI C28-A3c: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline- Third Edition (corrected)

L. Test Principle:

Lactate is oxidized by lactate oxidase (LOX) to pyruvate and hydrogen peroxide (H_2O_2). Peroxidase (horseradish) catalyzes the reaction of H_2O_2, 4-amoniantipyrine (4-AAP), and 3,5-dichloro-2-hydroxybenzenesulfonic acid (DHBSA) into a red dye. The rate of formation of the dye is proportional to the lactate concentration in the sample. The reaction is measured bichromatically at 515 nm and 600 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

   Precision was evaluated per CLSI EP5-A2 using three commercially available human serum-based controls. Samples were run in duplicate on two instruments

twice per day for five days at each of two sites. Data from both sites were combined to yield N = 80 per control level. The results are summarized below (units = mmol/L):

N=80	Within Run			Total		
	Mean	SD	%CV	Mean	SD	%CV
Control 1	1.62	0.03	1.8%	1.62	0.04	2.2%
Control 2	3.63	0.05	1.5%	3.63	0.08	2.3%
Control 3	6.99	0.18	2.6%	6.99	0.36	5.2%

The sponsor evaluated precision performance of two levels of heparinized plasma samples in house. The samples were run in duplicate on two instruments twice per day for five days. The results are summarized below (units = mmol/L):

N=40	Within Run			Total		
	Mean	SD	%CV	Mean	SD	%CV
Plasma 1	0.86	0.02	1.9%	0.86	0.02	1.9%
Plasma 2	6.22	0.20	3.2%	6.22	0.20	3.2%

The sponsor also identified three point-of-care (POC) sites and tested four whole blood samples at each POC site. The four whole blood samples contain two samples with normal lactate values and two samples with elevated lactate values. At each POC site, two operators tested every whole blood sample in ten replicates simultaneously on twenty analyzers. Data from both operators were combined to yield N = 20 per sample per site. The results are summarized below (units = mmol/L):

N=20	Site 1			Site 2			Site 3		
	Mean	SD	%CV	Mean	SD	%CV	Mean	SD	%CV
Normal lactate sample	0.71	0.02	2.7%	1.01	0.03	2.5%	0.88	0.03	3.8%
Normal lactate sample	1.51	0.03	2.0%	1.10	0.03	2.7%	1.08	0.03	3.2%
Elevated lactate sample	4.15	0.15	3.5%	5.89	0.25	4.2%	5.89	0.20	3.3%
Elevated lactate sample	4.63	0.15	3.1%	6.28	0.24	3.9%	7.76	0.27	3.5%

b. *Linearity/assay reportable range:*
A human plasma pool spiked with lactate was diluted to produce eleven lactate levels of samples ranging from 0.19 to 10.55 mmol/L. Each sample was assayed in quadruplicate on four different analyzers. Results are summarized below using the first replicate of the data from one analyzer.

Slope	1.016
Intercept	-0.023
R^2	0.999

The reportable range of this device for lactate measurements is 0.3 to 9.99 mmol/L.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The reagent discs are calibrated at the manufacturer using 6-8 human lactate pools that are spiked with lactate covering the reportable range of the assay. The calibrator lactate values are assigned by a commercially available method, whose calibration was traceable to a commercially available standard sodium L-lactate. The pools are then analyzed on the Piccolo® xpress™ analyzer to determine the enzymatic rate at each level, and a linear regression calibration line is calculated with the slope and intercept serving as the calibration factors. The calibration information is bar-encoded on each reagent disc. No user calibration is required.

Quality control beads are included on each reagent disk and automatically run with each assay. The information from this quality control analysis is stored with the test results and can be printed by the user. This is the internal build-in control to check fluidics, spectrophotometer, temperature, and sufficient sample delivery. In addition, sponsor recommends user to test quality controls according the federal, state, and local regulations in the labeling.

The shelf life of the lactate assay is 12 months when stored at 2-8^{o}C. Stability protocols and acceptance criteria for real time stability study for lactate system were reviewed and considered acceptable.

d. *Detection limit:*
Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Detection (LoQ) were determined based on CLSI guideline EP17-A as described below:

Limit of Blank (LoB):
A saline blank sample was assayed sixty times on one day (three times on each of twenty analyzers). The results were ordered according to their values and the 95th percentile of the zero-level samples concentration level was deemed as LoB level. The sponsor claimed the LoB = 0.02 mmol/L.

Limit of Detection (LoD):

Six low level samples, including 5 samples prepared by diluting a normal human plasma pool (lowest non-zero lactate calibrator) with saline, and one normal human plasma pool, were assayed sixty times each on one day (three times on each of twenty analyzers per sample). The low level samples were examined to see where 5% or fewer of the observed measurements were below LoB. The sponsor claimed the LoD = 0.07 mmol/L.

Limit of Detection (LoQ):
The LoQ was determined as the concentration that displayed a total error (TE) of 20% (TE = %bias + 2*%CV). The sponsor claimed the LoQ = 0.11 mmol/L. The LoQ value supports the sponsor's claimed measuring range of 0.3 – 9.99 mmol/L.

e. Analytical specificity:

To evaluate potential endogenous interference, two levels of lactate plasma pools were spiked to prepare at least four test pools containing different levels of the potential endogenous interferents. Four replicates of each pool were assayed on four different analyzers and compared to the control pool. The sponsor defined non significant interference if the bias between control pool and test pool was within ± 10%. Below are the levels of the endogenous substances that exhibit ≤10% interference.

endogenous substance	Level with ≤10% interference (mg/dL)
Hemoglobin	500*
Bilirubin	15*
Triglycerides	3000*
Glucose	700
Uric Acid	30

*Samples with values above these levels will be reported as "HEM", "LIP", or "ICT" on the result card, respectively.

To evaluate potential exogenous interference, 41 drugs were spiked into two levels of lactate plasma pools. The un-spiked plasma pool served as the control pool. The control pool and each interferent pool were tested in quadruplicate on four analyzers. The sponsor defined non significant interference if the bias between control pool and test pool was within ± 10%.

The following table summarized the 39 substances that showed non significant interference at the highest concentration tested:

Substance	Highest Concentration Tested (mg/dL)
Acetaminophen	100
Acetoacetate	102
Acetylsalicylic acid	50
Ampicillin	30
Ascorbic Acid	3

Bromide	30
Caffeine	10
Cephalothin (Keflin)	400
Chloramphenicol	100
Cimetidine	16
Digoxin	5
D-lactate	45
Epinephrine	1
Erythromycin	10
Glutathione	30
Glycolic acid	7.6
Hydrochlorothiazide	7.5
Hydroxyurea	0.7
Ibuprofen	50
Isoniazide	4
Ketoprofen	50
Lidocaine	1
Metformin	500
Methicillin	100
Methotrexate	0.5
Metronidazole	5
Nafcillin	1
Nitrofurantoin	20
Oxacillin	1
Oxaloacetate	132
Penicillin G	100
Phenytoin (5 ,5-Diphenylhydantion)	3
Proline	4
Pyruvate	44
Rifampin	0.5
Salicylic Acid	50
Sulfadiazine	150
Sulfanilamide	50
Theophylline	20

The sponsor states that dopamine and L-dopa demonstrate interference, and includes the following information in the device's labeling:

Substance	Concentration (mg/dL)	% interference
Dopamine	13	85% decrease
	0.52	<10% decrease
L-dopa	5	49% decrease
	0.5	<10% decrease

f. Assay cut-off:
Not applicable

2. Comparison studies:

   a. *Method comparison with predicate device:*

   The sponsor performed method comparison study at a POC site using 126 unaltered heparinized whole blood patient samples. In order to obtain samples with high lactate results, seven samples were allowed to sit at room temperature for glycolysis process to occur to raise lactate levels. A total of four Piccolo xpress analyzers were used for the study. Each sample was tested on the predicate and on one of the four Piccolo® xpress™ analyzers. Both linear and Deming regression analysis was performed for comparison. Summary data is as follows (Piccolo® range = 0.30 – 9.88 mmol/L, Predicate range = 0.42 – 9.85 mmol/L).

N=126	Linear Regression	Deming Regression
Slope (95% CI)	1.02 (1.01 to 1.04)	1.03 (0.99 to 1.06)
Intercept (95% CI)	0.13 (0.07 to 0.19)	0.06 (-0.01 to 0.14)
Correlation coefficient	0.996	0.996

   b. *Matrix comparison:*

   Lithium heparin is the only acceptable anti-coagulant for the lactate assay. Either whole blood or plasma sample may be used for the test.

   Lithium heparinized whole blood and plasma (processed from the whole blood samples) were collected from 10 individuals and tested in replicates of four on eight Piccolo® xpress™ analyzers. Samples range tested from 0.68 to 9.81 mmol/L. Deming regression analysis was performed and regression yielded: Y= 1.01X + 0.071, R^2= 0.997.

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):*
   Not applicable.

4. Clinical cut-off:
   Not applicable.

5. Expected values/Reference range:
   The sponsor established the reference range for the Piccolo® Lactate system using venous lithium heparin whole blood samples collected from 130 apparently healthy individuals (47% male; 53% female). The reference range was defined by the limits of the central 95% of values tested.

Reference range: 0.53 – 2.10 mmol/L

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.