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

A. 510(k) Number:

k093297

B. Purpose for Submission:

The lactate test is an addition to the previously cleared epoc Blood Analysis System. All other system features are the same as previously cleared in k061597 and k090109.

C. Measurand:

Lactate

D. Type of Test:

Quantitative, amperometry

E. Applicant:

Epocal, Inc.

F. Proprietary and Established Names:

epoc Lactate test

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
KHP	Class I, meets limitations of exemptions per 21 CFR 862.9 (c)(9)	21 CFR§ 862.1450	75

H. Intended Use:

1. Intended use(s):

   See Indications for Use below

2. Indication(s) for use:

The Lactate test, as part of the epoc Blood Analysis System, is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical institutions.

Lactate measurements from the epoc Blood Analysis System are used to evaluate the acid-base status and are used in the diagnosis and treatment of lactic acidosis (abnormally high acidity of the blood.)

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   epoc Blood Analysis System

I. Device Description:

Each card box includes 50 pouched unit use test cards. Each test card incorporating a Lactate test contains a sensing electrode with a redox mediated enzymatic membrane covered with an oxygen permeable diffusion layer, a reference electrode, a counter electrode and a calibrator fluid containing a known concentration of lactate.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   I-STAT™ Lactate test

2. Predicate 510(k) number(s):

   k001387

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use/Indications for use	For the quantitative testing of venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical institutions. Lactate measurements are used to evaluate the acid-base status and are used in the diagnosis and treatment of lactic acidosis	Same

Sample type	Venous, arterial and capillary whole blood	same
Measuring range	0.3 – 20 mmol/L	same
Analytes	Lactate	A variety of clinical chemistry analytes including lactate

Differences		
Item	Device	Predicate
Instrument	epoc Blood Analysis System	i-STAT Analyzer
Test format	Unit-use card with on-board calibrator in sealed reservoir, an electrochemical multi-sensor array, port for sample introduction and fluid waste chamber	Unit-use cartridge with on-board calibrator in sealed reservoir, an electrochemical multi-sensor array, port for sample introduction and fluid waste chamber

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition (2004)
CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures, A Statistical Approach: Approved Guideline (2003)
CLSI EP7-A: Interference Testing in Clinical Chemistry; Approved Guideline (2002)
CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (2004)
CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (2002)

L. Test Principle:

Lactate is measured by amperometry. The sensor comprises an immobilized enzyme first layer coated onto a gold electrode of the electrode module, with a diffusion barrier second layer. The lactate oxidase enzyme is employed to convert lactate to hydrogen peroxide. An amperometric sensor is used to detect the enzymatically produced hydrogen peroxide. Peroxide detection is by redox mediated (ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt), horseradish peroxidase (HRP) catalyzed, reduction on a gold electrode. The reduction current is proportional to the concentration of lactate in the test fluid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*
   This study followed the CLSI guideline (CLSI EP5-A2 "Evaluation of Precision Performance of Clinical Chemistry Devices") for a 20 day in-house precision study with 2 runs per day for 4 different card lots and 40 different epoc Readers. Duplicates from each lot for 2 levels of control material were tested 2 times a day over a 20 day span. The results are shown in the following table:

Lactate (mmol/L)	All	
	Level 1	Level 3
N	320	320
Mean	7.99	0.94
SWD	0.39	0.03
SDD	0.32	0.03
ST	0.51	0.04
Total CV %	6.3%	4.7%

An aqueous precision study was performed at 2 point of care sites to demonstrate precision in the hands of the end users 14-15 replicates of commercial aqueous blood gas, electrolytes and metabolites controls were tested by potential end users of the epoc system. Each study used at least 5 different epoc Readers with 3 epoc card lots. The following results were obtained:

Aqueous Precision				Lactate, mmol/L		
Site	User	QC level	N	Mean	SD	% CV
1	Operator 1	L3	15	0.95	0.031	3.3
1	Operator 2	L3	15	0.94	0.027	2.9
1	Operator 3	L2	14	2.88	0.05	1.8
1	Operator 4	L2	15	2.91	0.08	2.8
2	Operator 1	L1	15	7.34	0.57	7.8
2	Operator 2	L1	15	7.45	0.42	5.6

A whole blood precision study was performed at 2 point of care sites to demonstrate precision in the hands of the end users. 15 replicates of venous whole blood were tested by potential end users of the epoc system. Each study used at least 5 different epoc Readers with 4 epoc card lots. The following results were obtained:

Whole blood Precision				Lactate, mmol/L		
Site	User	Level	N	Mean	SD	% CV
1	Operator 1	WBL1	15	10.24	0.62	6.0
1	Operator 2	WBL1	15	10.27	0.34	3.3
2	Operator 1	WBL2	14	2.77	0.07	2.7
2	Operator 2	WBL2	15	2.67	0.12	4.7

b. *Linearity/assay reportable range:*

The reportable range is 0.3 to 20.0 mmol/L.
A linearity study was conducted based on CLSI EP6-A using whole blood samples collected from a fasting donor. Two (2) tubes were pooled and dialyzed in Ringer's buffer containing no lactate or glucose to produce low lactate ($\leq$0.3 mM) blood. This sample was then spiked to 0.3 mM lactate using 1 M sodium lactate stock solution. The remaining two (2) tubes were pooled and spiked with 1 M sodium lactate stock solution to a level over 20 mM. The concentration of lactate in the two pools of blood was confirmed using an ABL instrument.

Seven (7) samples of blood were prepared by mixing known volumes of low lactate specimen with high lactate with values ranging from 0.3 to 24 mM. Seven (7) lots of epoc cards were included in the study. Regression analysis was performed as per CLSI EP6-A recommendations. Linear regression of first, second and third order was carried out. The non-linear terms were statistically insignificant over the range 0.3 to 20 mmol/L. Regression analysis for the sponsor's claimed range is $y = 1.0014x + 0.2705$. The studies supported the sponsor's claimed range of 0.3 to 20 mmol/L.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The epoc System is calibrated is against methods traceable to NIST standards. The epoc System's test card comprises an on-board calibration material, prepared gravimetrically and assayed on reference systems calibrated with traceability to NIST standards.

d. *Detection limit:*
The low end of the reportable range for the EPOC lactate test is 0.3 mmol/L. The determination of Limit of Blank (LOB) and the verification of the claimed low end range using Limit of Detection confirmation (LoD) studies were performed according to CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantification.

The LoB determination was performed on an aqueous sample with known zero lactate. Sixty (60) cards from 3 lots were tested. The LoB was determined to be 0.084 mmol/L. For the LoD study, two matrices were compared, an aqueous buffer and a whole blood sample adjusted to 0.3 mmol/L. The concentration of the sample was confirmed using an ABL instrument. The aqueous sample was tested on a single occasion on 3 test card lots. Three whole blood samples were tested on 3 occasions using 6 test card lots. The LoD was verified as 0.3 mmol/L, which also is supported by the linearity studies in which the lowest level sample tested was 0.3 mmol/L. The % CV at 0.3 mmol/L lactate measured in whole blood is approximately 20 %.

e. *Analytical specificity:*

Interference testing was performed in-house using samples at two levels of lactate, 0.7 and 2.6 mmol/L as recommended by CLSI guideline EP7-A2. Samples were prepared in freshly drawn heparinized whole blood and plasma was added or removed from the samples to decrease or increase the hematocrit for the hematocrit studies.

Clinically significant interfering substances are listed below and in the labeling:

- Acetaminophen will have no significant effect (defined as less than or equal to 5% bias between control and test samples) up to 0.81 mM after which it will increase the lactate reading up to 306 µM/mM Tylenol.
- Iodide will decrease the lactate reading up to -1.2mM/mM of Iodide up to an Iodide concentration of 0.67 mM.
- Bromide will have no significant effect up to 25.4 mM after which it will decrease the lactate reading up to 14.6 µM/mM Bromide.
- Thiocyanate will have no significant effect up to 2.7 mM after which it will decrease the lactate reading by up to 96.6 µM/mM thiocyanate.
- N-Acetylcysteine will have no significant effect up to 3.7 mM after which it will decrease the lactate reading by up to 96.3 µM/mM N-Acetylcysteine.
- Ethylene glycol ingestion and metabolism has been shown to produce falsely elevated lactate measurements. Ethylene glycol plus three metabolism products - Glycolic Acid, Glyoxylic Acid and Oxalic Acid - were tested for interference. Ethylene Glycol and Oxalic Acid do not interfere significantly.
- Glycolic Acid will have no significant effect up to 0.87 mM after which it will increase the lactate reading up to 142 µM/mM glycolic acid.
- Glyoxylic Acid will have no significant effect up to 0.85 mM after which it will increase the lactate reading up to 373 µM/mM glyoxylic acid.

The following levels of endogenous interferences were tested and showed no significant interference defined as less than or equal to 5% bias between

control and test samples: 20.1 mg/dL unconjugated bilirubin, 29.0 mg/dL conjugated bilirubin, 503 mg/dL cholesterol and 1430 mg/dL triglycerides. Hematocrit did not interfere down to a level of 21% and up to a level of 61 % hematocrit.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Consolidated results from seven (7) studies – two (2) with venous samples, two (2) with arterial samples and three (3) with capillary samples are shown below against the predicate device (i-STAT System using CG4+ cartridges). All studies used heparinized whole blood. Testing was performed at 3 point of care hospital sites by phlebotomists or similar point of care operators. Venous samples were tested at Sites 1 and 3; arterial samples were tested at Sites 2 and 3; capillary samples were tested at Sites 2 and 3 and in-house.

The table below demonstrates the overall performance of the device at all sites.

	epoc Lactate vs. i-STAT			
	venous	**arterial**	**capillary**	**all**
N	126	73	174	373
Sxx	0.113	0.116	0.290	0.215
Syy	0.586	0.455	0.517	0.530
intercept	0.211	-0.165	0.257	0.132
slope	0.937	1.032	0.955	0.967
Syx	0.750	0.831	1.062	0.948
X min	0.66	0.57	0.48	0.48
X max	19.88	19.95	19.57	19.95
R^2	0.9769	0.9829	0.9653	0.9711

b. Matrix comparison:

Results are shown below as lactate results obtained from heparinized samples versus lactate results obtained on un-anticoagulated samples with values ranging from 0.52 to 11.21 mmol/L. The studies were performed at a point of care hospital site and in-house. During the course of this study there were four (4) epoc Readers in use and three (3) different manufacturing lots.

epoc Lactate No heparin vs. Heparinized	
N	60
Sxx	0.091
Syy	0.160
intercept	-0.045
slope	1.036
Syx	0.232
X min	0.52
X max	11.21
R^2	0.9916

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 normal venous range for lactate is 0.56 to 1.39 mmol/L based on literature from Tietz 2006.

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.