510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K200865

B Applicant

Abaxis, Inc.

C Proprietary and Established Names

Piccolo® Potassium Test System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MZV	Class II	21 CFR 862.1600 - Potassium Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

This submission is a Dual 510(k) and CLIA Waiver by Application (Dual Submission) tracked as k200865 and CW200007. This 510(k) is for a modification to the calibration of the Piccolo® Potassium Test (previously cleared device) run on the Piccolo Xpress® chemistry analyzer.

B Measurand:

Potassium

C Type of Test:

Quantitative, enzymatic colorimetric assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Piccolo® Potassium Test, used with the Piccolo® blood chemistry analyzer or the Piccolo Xpress® chemistry analyzer, is intended to be used for the in vitro quantitative determination of potassium, in heparinized whole blood, heparinized plasma, or serum in a clinical laboratory setting or point-of-care location.

The potassium assay is used for the quantitation of potassium in human heparinized whole blood, heparinized plasma, or serum. Potassium measurements are used in the diagnosis and treatment of renal glomerular or tubular disease, adrenocortical insufficiency, diabetic ketoacidosis, excessive intravenous potassium therapy, sepsis, panhypopituitarism, in vitro hemolysis, hyperaldosteronism, malnutrition, hyperinsulinism, metabolic alkalosis and gastrointestinal loss.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only
For clinical laboratory or point-of-care settings.

D Special Instrument Requirements:

Piccolo Xpress® chemistry analyzer

IV Device/System Characteristics:

A Device Description:

The Piccolo® Potassium Test System is a single-use, disposable system used with the Piccolo Xpress® chemistry analyzer for the in vitro quantitative determination of potassium in lithium heparinized whole blood, lithium heparinized plasma, or serum in a clinical laboratory setting or point-of-care location. The Piccolo® Potassium Test System consists of the Piccolo Xpress® chemistry analyzer and the dry reagent for the detection of potassium which is contained in a single-use disposable reagent discs designed to separate a lithium heparinized whole blood sample into plasma and blood cells. The disc meters the required quantity of plasma and diluent, mixes the plasma with diluent, and delivers the mixture to the reaction cuvettes along the disc perimeter. The diluted plasma mixes with the lyophilized microsphere reagent beads contained in the cuvettes, initiating the chemical reactions that are then monitored by the analyzer. Alternatively, the disc may also be used with serum. The Piccolo® Potassium Test System dry reagent contains pyruvate kinase (0.01 U), lactate dehydrogenase (0.27 U), adenosine diphosphate (36 µg), phosphoenolpyruvate (57 µg) and nicotinamide adenine dinucleotide (48 µg).

All performance studies for the Piccolo® Potassium Test System in this submission were conducted on the Piccolo Xpress® Chemistry Analyzer using the Piccolo® Comprehensive Metabolic Panel (CMP) disc. The potassium test included in the Piccolo® CMP disc is representative for the potassium assay found in all currently marketed Piccolo reagent discs that include the potassium assay.

B Principle of Operation:

The principle of operation of the Piccolo® Potassium Test is based on an enzymatic method with photometric detection. In the coupled-enzyme reaction, pyruvate kinase (PK) dephosphorylates phosphoenolpyruvate (PEP) to form pyruvate. Lactate dehydrogenase (LDH) catalyzes conversion of pyruvate to lactate. Concomitantly, NADH is oxidized to NAD+. The rate of change in absorbance difference between 340 nm and 405 nm is due to the conversion of NADH to NAD+ and is directly proportional to the amount of potassium in the sample.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Piccolo® Metlyte 7 Reagent Disc - Potassium Test System

B Predicate 510(k) Number(s):

K992140

C Comparison with Predicate(s):

Device & Predicate Device(s):	K200865	K992140
Device Trade Name	Piccolo® Potassium Test System	Piccolo® Metlyte 7 Reagent Disc - Potassium Test System
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the in vitro quantitative determination of potassium	Same
Principle of Operation/Methodology	Enzymatic colorimetric assay	Same
Sample Type	Lithium heparinized venous whole blood, lithium heparinized plasma, and serum	Same
Measuring Range	1.5 – 8.5 mmol/L	Same
Sample Volume	Approximately 100 µL	Same

Device & Predicate Device(s):	K200865	K992140
Device Trade Name	Piccolo® Potassium Test System	Piccolo® Metlyte 7 Reagent Disc - Potassium Test System
General Device Characteristic Differences		
Calibration	Bar code with factory calibrated lot specific data – modified calibration	Bar code with factory calibrated lot specific data – original calibration

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures- Second Edition

CLSI EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory-Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision
Precision was evaluated at a point-of-care (POC) site using two levels of control (target values of 3.1 and 6.1 mmol/L) and two pooled plasma samples (approximate values of 3.2 and 5.4 mmol/L). The operators each tested these samples in five replicates on three Piccolo Xpress® chemistry analyzers over five days. One lot of CMP reagent discs was used. The total number of replicates was 75 per sample. The results are shown below:

Sample	Mean mmol/L	Within Run		Total	
		SD	%CV	SD	%CV
Control 1	3.2	0.09	2.79	0.11	3.28
Control 2	6.2	0.32	5.26	0.33	5.34
Plasma Pool 1	3.2	0.07	2.31	0.09	2.89
Plasma Pool 2	5.4	0.09	1.58	0.10	1.89

Whole Blood Precision
Whole blood precision was tested at a POC site by two operators with one lot of CMP reagent discs using four fresh, lithium heparin venous whole blood samples on four Piccolo Xpress® chemistry analyzers with 16 replicates per sample. The study design for this precision study included repeatability, between-analyzer, and between-operator components. The design considered the one-hour limit for testing of potassium in whole blood samples on this device. The results are shown below:

Sample	Mean mmol/L	Within Run		Between Operator		Between Analyzer		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Whole Blood 1	3.9	0.06	1.6	0.02	0.4	0.09	2.2	0.11	2.8
Whole Blood 2	4	0.11	2.9	0.00	0.0	0.07	1.9	0.14	3.4
Whole Blood 3	4	0.11	2.8	0.03	0.9	0.10	2.5	0.15	3.9
Whole Blood 4	4	0.11	2.7	0.02	0.6	0.08	1.9	0.13	3.4

2. Linearity:

Whole Blood
A linearity study was performed on three Piccolo Xpress® Chemistry Analyzers using one CMP reagent disc lot. To provide elevated concentrations of potassium in whole blood, individual lithium heparinized whole blood samples were enriched by the addition of a concentrated plasma with a concentration of 48.9 mmol/L potassium. A human, potassium free plasma pool was prepared by exhaustive dialysis against physiological saline containing lithium heparin. To provide low concentrations of potassium in whole blood, individual lithium heparinized whole blood samples were diluted with this potassium free plasma. Nineteen levels of potassium were prepared resulting in a panel with concentrations targeted at 1.2, 1.4, 1.9, 2.3, 3.0, 3.4, 3.9, 4.9, 5.6, 6.1, 6.9, 7.6, 7.8, 8.3, 8.4, 8.5, 9.1 and 9.5 mmol/L. Each sample was assayed in singlicate on three (3) Piccolo Xpress® chemistry analyzers to ensure that the recoveries were not instrument-specific (i.e., each sample was tested in triplicate). Samples were then processed to plasma and measured in triplicate by the Siemens VISTA integrated system (VISTA ISE) K+ method (k051087) at a central reference laboratory. Expected values were calculated and then predicted values were calculated using a weighted least squares linear regression analysis and the average of the triplicate measurements. The deviation from linearity was within ±0.5mmol/L. In addition, an assessment of the systematic difference between the candidate device whole blood values and

the Siemens VISTA ISE plasma values by Deming regression was performed. Results of the regression analysis are presented below:

Reportable Range mmol/L	Range Tested mmol/L	Slope	Intercept	R^2
1.5 – 8.5	1.2 to 8.5	0.985 (0.952 to 1.018)	0.075 (-0.113 to 0.262)	0.987

Plasma

Immediately after the venous whole blood was tested as described above, it was centrifuged to obtain plasma. Each plasma sample was assayed in singlicate on three Piccolo Xpress® chemistry analyzers to ensure that the recoveries were not instrument-specific (i.e., each sample was tested in triplicate). The target concentrations of the samples were the same as in the whole blood linearity study. The plasma samples were also measured at a central reference laboratory by the Siemens VISTA integrated system (VISTA ISE) K+ method in triplicate. Expected values were calculated and then predicted values were calculated using a weighted least squares linear regression analysis and the average of the triplicate measurements. The deviation from linearity was within 0.5mmol/L. In addition, an assessment of the systematic difference between the candidate device plasma values and the Siemens VISTA ISE plasma values by Deming regression was performed. Results of the regression analysis are presented below:

Reportable Range mmol/L	Range Tested mmol/L	Slope	Intercept	R^2
1.5 – 8.5	1.2 to 8.5	0.972 (0.952 to 0.992)	0.032 (-0.081 to 0.146)	0.995

Serum

A serum linearity study was performed using samples prepared by exhaustive dialysis against physiological saline. A serum concentrate was prepared by addition of KCl to a serum pool to provide a final concentration of 51.0 mmol/L. The potassium free serum pool was supplemented with this potassium concentrate to provide a high pool with a target value of 9.5 mmol/L. A low potassium pool was prepared in a similar manner to provide a pool with a target value of 1.2 mmol/L. Admixtures of this high potassium pool were made into the low pool to provide the following 14 levels of potassium, 1.2, 1.8, 2.4, 3.1, 3.6, 4.3, 4.9, 5.6, 6.3, 6.9, 7.6, 8.2, 8.8 and 9.5 mmol/L as determined at a central reference lab by the Siemens VISTA integrated system (VISTA ISE) K+ method, results run in triplicate. Each serum sample was assayed in singlicate on three (3) Piccolo Xpress® chemistry analyzers to ensure that the recoveries were not instrument-specific (i.e., each sample was tested in triplicate). Expected values were calculated and then predicted values were calculated using a weighted least squares linear regression analysis and the average of the triplicate measurements. The deviation from linearity was within 0.5mmol/L. In addition, an assessment of the systematic difference between the candidate device serum values and the Siemens VISTA ISE serum values by Deming regression was performed. Results of the regression analysis are presented below:

Reportable Range mmol/L	Range Tested mmol/L	Slope	Intercept	R^2
1.5 – 8.5	1.0 to 9.5	1.002 (0.914 to 1.091)	-0.128 (-0.577 to 0.321)	0.995

3. Analytical Specificity/Interference:

   The Analytical Specificity/Interference was established in K992140.

4. Assay Reportable Range:

   1.5 – 8.5 mmol/L

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

   Traceability
   Every Potassium reagent bead set is calibrated against plasma samples with assigned values by the Siemens VISTA ISE K+ method and all three (3) levels of NIST SRM 956d. Secondary standards and controls are tested on every lot of reagent discs during processing and final testing.

   Sample Stability
   Whole blood venipuncture sample stability was established in K992140. Whole blood venipuncture samples should be run within 60 minutes of collection.

6. Detection Limit:

   The limit of quantitation (LoQ) of the Piccolo® Potassium Test System was evaluated on the Piccolo Xpress® chemistry analyzer using venous whole blood, plasma and serum prepared by taking a native blood sample of known potassium concentration and diluting it to four target concentrations using dialyzed (potassium free) serum/plasma as the diluent. The sponsor defines LoQ as the lowest measurable concentration (in mmol/L) that can be measured with respect to the predefined accuracy goal, in this case total error of +0.5 mmol/L. Each sample level was tested in replicates of five using two CMP reagent disc lots. Ten analyzers were used for whole blood testing, five per disc lot. Four analyzers were used for serum and plasma testing. Sixty low level sample replicates per lot were generated. The LoQ for whole blood, plasma, and serum on the Piccolo® Potassium Test System was determined to be 1.5 mmol/L.

7. Assay Cut-Off:

   Not Applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Method comparison studies were conducted at two point-of-care sites.

At the first site, one hundred and seventy-eight (178) venous whole blood samples were drawn into lithium heparinized tubes and immediately tested for potassium with the candidate device. Immediately after testing, the same tube was centrifuged to plasma by standard laboratory techniques and tested. A separate serum tube (SST) was also drawn, allowed to coagulate, and processed to serum then tested. Testing was performed by three intended operators using seven Piccolo Xpress® chemistry analyzers and one reagent lot of the Comprehensive Metabolic Panel (CMP) reagent disc. A total of 16 samples (9%) in the extreme high and low ranges were contrived to cover the entire measuring range. After testing with the candidate device, the plasma samples and serum samples were aliquoted, frozen, and shipped to a central reference laboratory for comparator testing by the Siemens VISTA integrated system (VISTA ISE) K+ method cleared by FDA in k051087. Data was analyzed using Deming regression. The average of the Siemens VISTA ISE potassium values was used as the x-axis and the individual candidate device values were used as the y-axis in the regression analysis.

Sample type Candidate Method	Sample type Comparator Method	N	Slope	Intercept	R^2
Heparinized venous whole blood	Heparinized plasma	178	0.98 (0.921 to 1.047)	0.12	0.969
Heparinized plasma	Heparinized plasma	178	0.98 (0.917 to 1.033)	0.03	0.979
Serum	Serum	178	0.98 (0.923 to 1.036)	0.06	0.979

The second site tested one hundred and thirty (130) venous whole blood samples drawn into lithium heparinized tubes and immediately tested for potassium using six Piccolo Xpress® chemistry analyzers and one reagent lot of the CMP reagent disc. Testing was performed by three intended use operators. A total of 13 samples (10%) in the extreme high and low range were contrived to cover the entire measuring range. After the initial testing, the whole blood was processed to plasma, frozen, and shipped to a central reference laboratory for duplicate testing by the Siemens VISTA integrated system (VISTA ISE) K+ method cleared by FDA in k051087. Data was analyzed using Deming regression. The average of the Siemens VISTA ISE potassium values was used as the x-axis and the individual candidate device values were used as the y-axis in the regression analysis.

Sample type Waived Method	Sample type Comparator Method	N	Slope	Intercept	R^2
Heparinized venous whole blood	Heparinized plasma	130	0.99 (0.931 to 1.043)	0.13	0.969

2. Matrix Comparison:

Not applicable. The sponsor provided performance data (refer to Sections VII A and B above) to support that the assay is suitable for use with lithium heparin whole blood, lithium heparin plasma and serum.

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:

A study was performed to validate the current reference interval, 3.6 – 5.1 mmol/L, using 126 results from subjects who self- reported as healthy between the ages of 18 and 70 years old and approximately 50% male and female. Venous whole blood samples were drawn into lithium heparinized tubes and immediately tested for potassium using one lot of the CMP reagent disc on eight Piccolo Xpress® chemistry analyzers. Immediately after testing, the same tube was centrifuged to plasma by standard laboratory techniques and tested on eight Piccolo Xpress® chemistry analyzers and one CMP reagent disc lot. A separate serum tube (SST) was also drawn, allowed to coagulate, and processed to serum then tested on eight Piccolo Xpress® chemistry analyzers and one CMP reagent disc lot. All testing was done in singlicate.

The reference range study data supports the labeled reference interval of 3.6 – 5.1 mmol/L for venous whole blood and serum. The reference interval for plasma was determined to be 3.3 – 4.6 mmol/L.

VIII Proposed Labeling:

The labeling supports 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.