CLIA Waiver Determination Decision Summary

A. **Document Number:**

k992140/A002

B. Purpose for Submission:

Request for Waiver

C. Measurand (Analyte):

Potassium

D. Type of Test:

Quantitative

E. Applicant:

Abaxis, Inc.

F. Test System Name:

Piccolo and Piccolo xpress Comprehensive Metabolic Panel, Basic Metabolic Panel and Electrolyte Panel

G. Special Instrument Requirements:

Piccolo and Piccolo xpress

H. Test System Description:

The Piccolo Potassium assay is contained within the Comprehensive Metabolic, Basic Metabolic and Electrolyte Reagent Discs. The discs are designed to separate a heparinized whole blood sample into plasma and blood cells. The meter samples the required quantity of patient's sample and diluent. Then it mixes the plasma sample with the diluent and delivers the mixture to the reaction cuvette contained in the disc perimeter. The diluted sample mixes with the reagent beads initiating the chemical reactions that are then monitored by the analyzer. The discs are 8 cms in diameter and are single-use devices.

I. Demonstrating "Simple":

Test system is: (if NO or N/A provide explanation)

1. Fully automated instrument __X__
   Unitized ____
   Self contained ____

2. Uses direct unprocessed specimens
   _X_ Yes ___No

3. Sample type
   Fingerstick ____
   Venous whole blood _X_
   Urine ____
   Oral Fluid ____
   Nasal Swabs ____
   Throat Swabs _____
   Other ____

4. Requires only basic, non-technique-dependent specimen manipulation
   _X_ Yes ___No

5. Requires only basic, non-technique-dependent reagent manipulation
   _X_ Yes ___No ___N/A

6. Has no operator intervention during the analysis
   _X_ Yes ___No

7. Requires no technical or specialized training with respect to troubleshooting (interpreting error codes does not constitute troubleshooting)
   _X_ Yes ___No

8. Requires no electronic or mechanical maintenance
   _X_ Yes ___No

9. Provides direct readout of results, i.e. requires no calculation or conversions
   _X_ Yes ___No

J. Demonstrating "Insignificant Risk of an Erroneous Result- Failure Alerts and Fail-safe Mechanisms:

A. Risk Assessment

A report describing the risk assessment is present and the following were tested: improper disc storage, endogenous substances (hemolyzed, lipemic and itcteric samples), interference from exogenous substances (drugs and metabolites), sample type and stability, disc stability and operator errors such as; use of expired disc, used disc, abused disc, incorrect disc or use of inadequate sample applied to the disc. The instrument performs a self check to detect hardware problems such as drawer motor failed and software such as checking the software card and memory. Information such as test name, lot number and expiration date are incorporated into the barcode. See the mitigations for the risks below.

B. Fail-safe and Failure Alert Mechanisms.

1. General Recommendations.

    a. Lockout features – instrument will not operate if discs are stored improperly (too cold or too hot), if the operator uses an expired disc, used disc or insufficient sample is applied. The sample is rated for hemolysis, lipemia and icterus on the following scale 0 clear, 1+ slight, 2+ moderate and 3+ gross. Patient results will not report if there is interference from hemolysis, lipemia or icterus more than 10%. The codes HEM, LIP and ICT report instead of a quantitative value.

    b. Monitors of environmental conditions - an error code insufficient sample will display for disc stored at <2°C. A temperature sensitive bead in each disc is used to detected discs stored at >8°C an error code of bead deterioration will be displayed.

    c. Internal procedure controls – operator is locked out if the internal control fails. This testing indicates that all instrument, disc and chemistry parameters meet specifications.

    d. Electronic Controls - none

    e. Calibration – Is factory set. The barcode printed on each disc provides the analyzer with specific calibration data.

    f. Specimen Identification – can be entered into the system through the touch screen on the xpress analyzer and integrated keyboard On the Piccolo analyzer.

2. External Control Materials.
    a. External liquid Control material recommended - Yes
    b. Frequency recommendation – whenever laboratory conditions have changed significantly, each new lot, training or retraining users, at least every 30 days
    c. Directions for use – to assay a control sample just like assaying a patient's sample
    d. Storage and stability – to follow manufacturer's recommendations in the control package insert.
    e. Number of levels - 2
    f. Manufacturer – The sponsor states to contact them for quality control material recommendations.

3. Validation/Verification Studies for Fail-safe and Failure Alert Mechanisms.
    a. Stress studies – list the types of testing that was performed.
        Field studies were performed at three non-laboratory sites with a total of 62 untrained subjects with no reported laboratory experience. Subjects were asked to perform testing on three blinded samples solely by following the provided written instructions. The short sample/under-fill error code was obtained only once at one site. This occurred during the first attempts to use the system at that site. The Piccolo xpress identified the problem and correctly cancelled the run. The operator easily became aware of the error and successfully ran the Piccolo xpress for subsequent testing.

    b. Contains fail-safe mechanisms that render no result when the test system malfunctions and rendering no test result when results are outside the reportable range.
        The system will display an error code if the instrument hardware and software problems, reagent instability, procedural errors and if there is a sample problem. If the value is above or below the reportable range the instrument will display < lowest reportable range value or > with highest reportable range value. Results will be suppressed which are affected by >10% interference from hemolysis, lipemia and icterus HEM, LIP or ICT will print in place of the patient's result.

K. Demonstrating "Insignificant Risk of an Erroneous Results" (Accuracy)

A. Testing Sites, Participants and Testing Duration.

Field studies were conducted at three non-laboratory sites. A total of 62 untrained operator with varying demographics were enrolled in the study. Each participant assayed three panels using masked samples following only the written instructions provided. The samples contained concentrations of the test constituents in the low, medium and high ranges. The protocol followed was according to the Sept 13, 1995, CDC proposed rule for CLIA waiver found at: http://www.fda.gov/cdrh/clia/fr/hsq225p.pdf

B. Quantative Tests:

1. Comparative Method (CM), Type.

   Flame Photometry for Potassium, Type A

2. Descriptive Statistical Analysis.

   Precision Study- The data collected at each site was analyzed and compared by performing the following:

   a.) Does the data demonstrate that the total amount of imprecision is less than one-fourth of the reference range for the analyte divided by the mean of the reference interval? All the results are within the allowable range for each sample tested at each site. The data are presented in the table below:

Potassium

	Level 1	Level 2	Level 3
Number	62	62	62
Target Concentration	3.4	5.6	7.2
Mean value By Piccolo	3.42	5.66	7.19
SD	0.11	0.14	0.14
%CV	3.3	2.5	1.9
Observed Range	3.2 – 3.7	5.2 – 5.9	6.7 – 7.5
Allowable Range Mean ± 8.6% of mean	3.1 – 3.7	5.2 – 6.1	6.6 – 7.8
% values in allowable range	100% (62/62)	100% (62/62)	100% (62/62)
95% CI:	(94%; 100%)	(94%; 100%)	(94%; 100%)

b.) Evaluate among-site imprecision at an adequate number of sites to produce measures of performance that are statistically valid and defensible.

For every level of the analyte, ANOVA test was performed to determine whether there are statistically significant differences among the sites. None of the sites showed a statistical significant p-value indicating that there were no among-site imprecision difference. Results are in the tables below:

Potassium

	Level 1	Level 2	Level 3
Site 1 (n=20)	3.43	5.68	7.19
Site 2 (n=21)	3.37	5.61	7.18
Site 3 (n=21)	3.45	5.69	7.21
Combined	3.42	5.66	7.19
p-value	0.06	0.17	0.66

3. Accuracy

Does the method accuracy studies demonstrating that the test system is not affected by systematic error when using patient samples instead of reference materials, proving that there is no statistically significant difference between test results obtained on patient and reference materials due to the effects of the sample matrix?

a. Regression analysis:

Analyte	n	Range	Intercept (β_0)	95% CI (β_0)	Slope (β)	95% CI (β)
Reference K^+ (x) vs. Piccolo K^+ replicate 1 (y)	40	2.4-8.6	0.3755	(0.23; 0.52)	0.9161	(0.86; 0.95)
Reference K^+ (x) vs. Piccolo K^+ replicate 2 (y)	40	2.4-8.6	0.5133	(0.39; 0.63)	0.8822	(0.86; 0.91)

b. Bias analysis:

Test	Medical Decision Point (mmol/L)	Bias (replicate 1)	Bias (replicate 2)	CLIA limits for Target Value
Potassium	3	0.1238	0.1599	± 0.5
	6	-0.1279	-0.1935	± 0.5

C. Qualitaive Tests:

Not applicable

1. Comparative Method (CM), Type.

   Not applicable

2. Statistical Analysis.

   a. Method comparison

      Not applicable

   b. Device performance with analyte concentration near the cutoff.

      Not applicable

   c. Test performance with analyte concentration overall.

      Not applicable

M. Proposed Labeling:

1. The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10 and the test procedures steps are at no higher than a 7th grade reading level and provides pictures and diagrams.
2. The Quick Reference Instructions are easy to read.
3. Instrument Manual is easy to read and contains the required instruction information.

N. Type of Education Material Provided:

None

O. Conclusion:

The Submitted Information in this CLIA Waiver is complete and Supports a Waiver decision.

1. Review documentation:

   Accuracy:
   The data submitted for Potassium had all values at the three sites fall within the Tonks limit of 8.6% which is based on the range of 3.6-5.1 mmol/L.

   Among Site Variation:
   There was no statistically significant difference among the sites for the Potassium assay.

2. Waiver Performance for Labeling:

   The following labeling information is what the sponsor included.

   An "untrained user" study was conducted in which participants were given only the test instructions and asked to perform testing of 3 discs with blinded randomized samples. The samples consisted of serum pools prepared at three levels for the potassium analyte. The participants were not given any training on the use of the test. A total of 62 participants were enrolled from 3 sites, representing a diverse demographic (educational, age, gender, etc.) population.

   Tables below present the summary of the performance for each analyte.

Potassium (K+)

	Level 1	Level 2	Level 3
N	62	62	62
Mean	3.4	5.7	7.2
%CV	3.3	2.5	2.0
Observed Range	3.2-3.7	5.2-5.9	6.7-7.5
Percent of Results In the Range ± 8.6%	100% 62/62 95%CI: 94.2 to100%	100% 62/62 95%CI: 94.2% to 100%	100% 62/62 95%CI: 94.2 to 100%