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

A. 510(k) Number:

k163271

B. Purpose for Submission:

Adding previously cleared glucose assay to the i-STAT Alinity System

C. Measurand:

Glucose

D. Type of Test:

Quantitative amperometric assay, glucose oxidase

E. Applicant:

Abbott Point of Care, Inc.

F. Proprietary and Established Names:

i-STAT Alinity System with the i-STAT Glucose test

G. Regulatory Information:

Product Code	Regulation	Classification	Panel
CGA	21 CFR §862.1345, Glucose test system	Class II	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   The i-STAT Alinity System with i-STAT Glucose test is intended for use in point of care or clinical laboratory settings. The i-STAT Alinity System with Glucose test is intended for the quantitative measurement of glucose in arterial and venous whole blood.

   Glucose measurements are used in the diagnosis, monitoring, and treatment of carbohydrate metabolism disorders including, but not limited to, diabetes mellitus, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.

   The i-STAT Glucose test with the i-STAT Alinity System has not been evaluated in neonates.

   For in vitro diagnostic use.

3. Special conditions for use statement(s):

   For prescription use only

   For point-of-care or clinical laboratory setting

4. Special instrument requirements:

   i-STAT Alinity Instrument

I. Device Description:

The i-STAT test cartridge contains test reagents which are located on the sensors. The instrument interacts with the cartridge to move fluid across the sensors and generate a quantitative result. Cartridges require two to three drops of whole blood which are typically applied to the cartridge using a syringe.

For cartridges that contain a sensor for the measurement of glucose, a list of reactive ingredients is indicated below:

Reactive Ingredient	Biological Source	Minimum Quantity
Glucose	N/A	7 mmol/L
Glucose Oxidase	*Aspergillus Niger*	0.002 IU

The i-STAT Glucose test was most recently cleared under k103195. The i-STAT glucose test is included in previously cleared i-STAT test cartridges (E3+, EC4+, EC8+, CG8+, CHEM8+, and 6+).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   i-STAT 1 Wireless Analyzer

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

   k103195

3. Comparison with predicate:

Similarities		
Item	**Candidate Device (k163271)**	**Predicate Device (k103195)**
Intended Use	The test for glucose is intended for use in the in vitro quantification of glucose in whole blood.	Same
Calibration	1-point on-board (contained within the cartridge)	Same
Reportable Range	20 – 700 mg/dL	Same
Sample Volume	65 – 95 µL	Same
Traceability	NIST SRM965	Same
Principle of Measurement	Glucose is measured amperometrically. Oxidation of glucose, catalyzed by the enzyme glucose oxidase, produces hydrogen peroxide (H2O2).	Same
Test Format	Cartridge	Same
Test Storage	Storage: 2°C to 8°C (35-46°F)	Same
Quality Checks	A series of quality checks are automatically run each test cycle prior to the system generating a result. Quality checks verify the analyzer motor, electrical, pressure and temperature systems and cartridge elements.	Same
Time to test	~2 minutes	Same

Differences		
Item	**Candidate Device (k163271)**	**Predicate Device (k103195)**
Sample type	Fresh arterial or venous whole blood.	Fresh arterial, venous or capillary whole blood

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

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline

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

CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition

CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline

CLSI EP 17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline

L. Test Principle:

The i-STAT Glucose test is measured amperometrically. In amperometric measurements, a potential is applied to the measuring electrode while current generated by the resulting oxidation or reduction reactions in the test system is measured. The current generated is directly proportional to the concentration of the analyte. Oxidation of glucose, catalyzed by the enzyme glucose oxidase, produces hydrogen peroxide (H_2O_2). The liberated hydrogen peroxide is oxidized at the electrode to produce an electrical current that is proportional to the sample glucose concentration.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   All performance studies for the i-STAT Glucose test were conducted using the i-STAT EC4+ cartridge. The glucose test included in the EC4+ cartridge is identical to the assay cleared in k103195 and is representative for the glucose assay found in all i-STAT cartridges that include the glucose assay.

a. Precision/Reproducibility:

i.) 20 day Precision study at internal site

The precision of the i-STAT Glucose Test on the i-STAT Alinity System was evaluated using one lot of 5 levels of i-STAT Calibration Verification material. The study was conducted by two operators using 10 instruments and one EC4+ cartridge lot over 20 days at one site. The results are shown below:

Level	N	Mean (mg/dL)	Within-run		Between Run		Total	
			SD	%CV	SD	%CV	SD	%CV
CV L1	80	26.9	0.22	0.82	0.34	1.26	0.42	1.56
CV L2	80	41.0	0.20	0.49	0.18	0.44	0.34	0.83
CV L3	80	125.0	0.21	0.17	0.23	0.18	0.32	0.26
CV L4	80	286.7	0.53	0.18	0.52	0.18	0.77	0.27
CV L5	80	600.6	2.42	0.40	2.26	0.38	3.47	0.58

ii.) Multi-day Precision Study at 3 POC sites (using aqueous materials)

Multi-day precision was evaluated by testing one lot of 5 levels of i-STAT TriControl Calibration Verification material at each of 3 sites for five days. One lot of EC4+ cartridges was included in the testing. The same 5 instruments were used at each site for all 5 days of testing at sites 1, 2, and 4. The results are shown below:

Level	Site	N	Mean (mg/dL)	Within-Run		Within-Site (Total)	
				SD	CV (%)	SD	CV (%)
CV L1	1	25	580.8	3.28	0.57	4.74	0.82
	2	25	589.1	2.94	0.50	4.27	0.72
	4	25	580.8	4.24	0.73	4.76	0.82
	Combined	75	583.5	3.53	0.61	4.59	0.79
CV L2	1	25	270.0	0.73	0.27	1.02	0.38
	2	25	272.3	1.03	0.38	1.36	0.50
	4	25	270.3	0.68	0.25	1.09	0.40
	Combined	75	270.9	0.83	0.31	1.17	0.43
CV L3	1	25	129.4	0.35	0.27	0.62	0.48
	2	25	130.1	0.49	0.38	0.83	0.64
	4	25	130.0	0.68	0.52	0.68	0.52
	Combined	75	129.8	0.53	0.41	0.71	0.55

Level	Site	N	Mean (mg/dL)	Within-Run		Within-Site (Total)	
				SD	CV (%)	SD	CV (%)
CV L4	1	25	42.3	0.47	1.11	0.48	1.13
	2	25	42.7	0.47	1.10	0.57	1.34
	4	25	43.0	0.51	1.19	0.63	1.46
	Combined	75	42.7	0.48	1.13	0.56	1.32
CV L5	1	25	30.5	0.45	1.47	0.61	2.00
	2	25	30.5	0.37	1.23	0.53	1.75
	4	25	30.9	0.42	1.37	0.44	1.43
	Combined	75	30.6	0.42	1.36	0.53	1.74

iii.) Precision study at 3 POC sites (using whole blood (WB))

The precision of the i-STAT Glucose Test on the i-STAT Alinity System was evaluated using venous whole blood (native and altered) samples targeted to six different glucose levels (30 – 50 mg/dL, 51 - 110 mg/dL, 111 – 150 mg/dL, 151 – 250 mg/dL, 251 – 400 mg/dL, and 401 – 700 mg/dL) within the i-STAT Glucose test reportable range. One EC4+ test cartridge lot was used across 3 point of care sites. At each site, each sample was tested 3 times on each of 7 i-STAT Alinity instruments (total of 21 test results per sample). The results are shown below:

Concentration Level mg/dL	Site	N	Mean (mg/dL)	Within-Instrument		Total	
				SD	%CV	SD	%CV
30-50	1	21	37.1	0.36	0.97	0.36	0.97
	2	21	35.3	0.56	1.59	0.56	1.59
	4	21	43.6	0.51	1.16	0.51	1.16
51-110	1	21	104.0	0.22	0.21	0.22	0.21
	2	21	84.5	0.51	0.61	0.51	0.61
	4	21	92.7	0.46	0.50	0.46	0.50
111-150	1	21	134.6	0.49	0.36	0.51	0.38
	2	21	120.3	0.64	0.54	0.64	0.54
	4	21	115.3	0.48	0.42	0.48	0.42
151-250	1	21	182.9	0.70	0.38	0.70	0.38
	2	21	194.0	0.63	0.33	0.63	0.33
	4	21	217.2	0.49	0.22	0.54	0.25
251-400	1	21	347.3	1.71	0.49	1.71	0.49
	2	21	352.0	1.43	0.41	1.43	0.41
	4	21	348.7	2.53	0.73	2.53	0.73

Concentration Level mg/dL	Site	N	Mean (mg/dL)	Within-Instrument		Total	
				SD	%CV	SD	%CV
401-700	1	21	548.9	7.46	1.36	7.46	1.36
	2	21	575.8	2.60	0.45	2.81	0.49
	4	21	526.5	3.56	0.68	3.56	0.68

b. Linearity/assay reportable range:

The study was designed based on CLSI EP06-A guideline. The linearity of the i-STAT Glucose test on the i-STAT Alinity System was evaluated by preparing a series of glucose concentration levels in whole blood that spanned the reportable range of the test. Whole blood was obtained from a healthy subject and altered to produce a high sample pool and a low sample pool. Intermediate test samples were created from the high and low pool. The test sample expected values are found in the table below. An assessment of linearity was performed using polynomial regression analysis for 1st, 2nd, and 3rd order polynomials. The i-STAT Alinity Glucose test results were plotted against the expected concentrations. Analysis of the regression coefficients (using a significance level of 0.05) showed that the nonlinear coefficients in both the second and third order were significant with p-values of the coefficients less than 0.05. The 2nd order was determined to have the best fit and was used for the assessment of degree of non-linearity. The degree of nonlinearity acceptance criteria analysis results are as follows:

Sample ID	Expected Values (mg/dL)	Acceptance criteria	Absolute Degree of Nonlinearity	Pass/Fail
B1	787.8	39.4	23.8	Pass
B2	691.6	34.6	15.6	Pass
B3	595.3	29.8	8.9	Pass
B4	499.0	25.0	3.7	Pass
B5	393.5	19.7	0.0	Pass
B6	287.2	14.4	1.8	Pass
B7	180.1	9.0	1.7	Pass
B8	120.0	6.0	0.7	Pass
B9	85.4	4.3	0.1	Pass
B10	45.3	3	1.3	Pass
B11	17.6	3	2.4	Pass

For all test samples, the absolute value of the degree of non-linearity met the pre-defined acceptance criterion of less than or equal to the greater of 3 mg/dL or 5% of expected value (glucose concentration, mg/dL). The degree of nonlinearity analysis demonstrates that the i-STAT Glucose test used with the i-STAT Alinity instrument is linear over the claimed reportable range of the glucose test of 20 - 700 mg/dL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The i-STAT glucose test and glucose values assigned to i-STAT controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material SRM965.

The stability of the glucose test was previously cleared in k103195.

The instrument calibration is a one-point on board calibration and is performed each time a cartridge requiring calibration is used. This one-point calibration adjusts the offset of the stored calibration curve.

The i-STAT Controls and i-STAT Calibration Verification Material were previously cleared in k972868 and stability/value assignment information can be found in k972868.

d. *Detection limit:*

The detection limits are supported by the linearity study (see M.1.b. above). In addition, a LoQ study was performed to verify the low end of the claimed measuring range.

The study was based on the CLSI EP17-A2 guideline. The LoQ of the i-STAT Glucose test on the i-STAT Alinity System was evaluated on 36 instruments using whole blood that was altered to low glucose concentrations (< 20 mg/dL) and two EC4+ test cartridge lots over four days by three operators. The LoQ for the i-STAT Glucose test on the i-STAT Alinity System was determined to be 5.558 mg/dL.

The i-STAT Glucose test on the i-STAT Alinity system has a measuring range of 20–700 mg/dL.

e. *Analytical specificity:*

The interference performance of the i-STAT Glucose test on the i-STAT Alinity System was evaluated based on CLSI EP07-A2 guideline. The interference performance was evaluated using whole blood samples at two glucose concentrations (low 70 – 90 mg/dL and high 110-130 mg/dL glucose concentrations). The effect of each potentially interfering compound was evaluated by comparing the performance of a test sample spiked to a high concentration of the compound and a control test sample spiked with an equal volume of solvent. A compound was identified as an interferent if the difference between the spiked test sample and the control was > 10% of the mean of glucose test results for the control sample.

Compound	Highest concentration tested with no observed significant interference	
	mmol/L (unless specified)	mg/dL**
Acetaminophen	1.33	20.10
Acetaldehyde	0.045	0.20
Acetoacetate	2.0	21.60
L-Ascorbic Acid	0.342	6.02
Acetyl Cysteine	10.2	166.45
Ammonium Chloride	2.0	10.70
Bromide	37.5	325.69
β-Hydroxybutyric Acid	6.00	62.47
Dopamine	0.006	0.09
Ethanol	86.8	399.89
Fluoride	0.105	0.27
Formaldehyde	0.133	0.40
Glycolic Acid	10.0	76.05
Gentamicin	0.021	3.13
Glucosamine	0.030	0.54
Glutathione, reduced	3	92.20
Guaifenesin	15	297.33
Hemoglobin*	2 g/L	200
Heparin	3 U/mL	n/a
Ibuprofen	2.425	50.03
Isoniazid	0.292	4.00
Lactate	6.6	63.37
Mannose	1.00	18.02
Maltose	13.3	455.26
pH	8.0	n/a
Pyruvate	0.309	2.90
Salicylate	4.34	62.52
Thiocyanate	6.9	44.86
Triglyceride	37	3233.80
Uric Acid	1.4	23.54
Sodium Thiosulfate	16.7	264.04
Bilirubin	0.342	19
Cholesterol	13	503
Creatinine	0.442	5
Fructose	1	18
Galactose	0.84	15
Xylose	3	45

*Tested in g/L
**The molecular weight of the substance tested was used to convert the test concentration from mmol/L to mg/dL. The molecular weight of each substance could vary depending on the form chosen.

Hydroxyurea at a concentration of 0.92 mmol/L (7.0 mg/dL) interferes with the i-STAT Glucose test on the i-STAT Alinity System. Hydroxyurea dose response testing was performed and results showed that hydroxyurea concentration above 0.43 mmol/L may give a falsely elevated i-STAT glucose test result of more than 10%.

The sponsor includes the following limitations in the labeling:

"An alternative method should be used if it is suspected that the patient have been administered hydroxyurea. A hydroxyurea concentration above 0.43 mmol/L may give a falsely elevated i-STAT glucose test results of more than 10%.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The method comparison study compared the results of the i-STAT Glucose Test on the i-STAT Alinity System to the i-STAT Glucose Test performance on the i-STAT 1 Wireless Analyzer (predicate). This study was conducted across 3 point of care sites, performed in the intensive care unit (ICU), blood gas lab, emergency department (ED) and general hospital wards. A total of 145 lithium heparin venous whole blood specimens and 92 lithium heparin arterial whole blood specimens were tested using one lot of i-STAT EC4+ cartridges. Twelve specimens were contrived (5.1%). Weighted Deming regression analysis comparing the first replicate of the candidate device results to the mean of the predicate device results yielded the following results:

Individual POC Sites

Site	N	Sample Range tested mg/dL	Regression Equation	"r"
1	77	46 - 673	y = 0.996x + 1.527	1.000
2	92	45 - 653	y = 1.000x + 1.077	1.000
4	68	24 - 620	y = 0.999x + 1.050	1.000

All Sites Combined

N	Sample Range tested mg/dL	Regression Equation	"r"
237	24 - 673	y = 0.999x + 1.164	1.000

b. Matrix comparison:

A matrix comparison study comparing non-anticoagulated venous whole blood and anti-coagulated venous whole blood (lithium heparin) was performed. The reference matrix for this study is heparinized venous whole blood (lithium heparin collection tubes) and the test condition is the non-anticoagulant venous whole blood sample collected without anticoagulant. A total of 40 matched venous whole blood samples were tested using the i-STAT Glucose test on 8 i-STAT Alinity Systems. Deming regression analysis between first individual non-anticoagulated result and the heparinized mean result yielded the following regression results.

N	Sample Range	Regression Equation	"r"
40	41 - 493 mg/dL	y = 1.000x + 0.34	1.000

Non-anticoagulated venous whole blood and anticoagulated (lithium heparin) venous whole blood samples are acceptable for use with the i-STAT Alinity System with the i-STAT Glucose test.

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:

Test/Abbreviation	Units	Reference Range[1]
Glucose/Glu (fasting)	mg/dL	70 - 105
	mmol/L	3.9 – 5.8
	g/L	0.70 – 1.05

[1]P.C. Painter, J.Y. Cope, J.L. Smith, "Reference Ranges, table 41-20" in Tietz Textbook of Clinical Chemistry – Second Edition, C.A. Burtis and E.R Ashwood, eds. (Philadelphia: W.B. Saunders Company, 1994).

The reference range for whole blood with the i-STAT Glucose test on the i-STAT Alinity System listed above is similar to reference ranges derived from serum or plasma measurements with standard laboratory methods. The reference range shown above is intended to be used as a guide for the interpretation of results. Since reference ranges may vary with demographic factors such as age, gender and heritage, it is recommended that reference ranges be determined for the population being tested. Each facility should establish its own reference range to assure proper representation of specific populations.

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.