510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k170316

B. Purpose for Submission:

Adding a previously cleared assay to a new instrument platform

C. Measurand:

Glucose

D. Type of Test:

Quantitative, colorimetric, enzymatic (hexokinase)

E. Applicant:

Abbott Laboratories

F. Proprietary and Established Names:

Alinity c Glucose Reagent Kit
Alinity c System

G. Regulatory Information:

1. Regulation section:

Device	Product Code	Classification	Regulation	Panel
Alinity c Glucose Reagent Kit	CFR	Class II	CFR 862.1345 Glucose test system	Clinical Chemistry (75)
Alinity c System	JJE	Class I	CFR 862.2160 Discrete photometric chemistry analyzer for clinical use	

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use.

2. Indication(s) for use:

   Alinity c Glucose Reagent Kit
   The Alinity c Glucose Reagent Kit is used for the quantitation of glucose in human serum, plasma, urine, or cerebrospinal fluid (CSF) on the Alinity c analyzer. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

   The Alinity c System
   The Alinity c System is a fully automated, random/continuous access, clinical chemistry analyzer intended for the in vitro determination of analytes in body fluids.

3. Special conditions for use statement(s):

   For prescription use only.
   For in vitro diagnostic use only.

4. Special instrument requirements:

   Alinity c System

I. Device Description:

Alinity c Glucose Reagent Kit
The Alinity c Glucose Reagent Kit has the same bulk reagents as the reagent cleared for use with the predicate device: Glucose Assay for use on the Abbott ARCHITECT c8000 and Abbott AEROSET systems (k060383). The reagent container for Alinity c Glucose Reagent Kit has changed and performance has been established on the Alinity c System as the candidate test system in this submission.

The Alinity c Glucose Reagent Kit consists of ATP•2Na (9.0 mg/mL), NAD (5.0 mg/mL), G-6-PDH (3000 U/L), hexokinase (15 000 U/L), and preservative: sodium azide (0.05%).

Alinity c Multiconstituent Calibrator Kit
The calibration of the Alinity c Glucose Reagent Kit on the Alinity c System uses the Alinity c Multiconstituent Calibrator Kit.

Alinity c System
The Alinity c System is a fully automated, random access chemistry analyzer using detection technologies to determine analyte concentrations in body fluids.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Abbott Glucose Reagent
   Abbott AEROSET System

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

   k060383
   k980367

3. Comparison with predicate:

Alinity c Glucose Reagent Kit

Item	Candidate Device Alinity c Glucose Reagent Kit k170316	Predicate Device Glucose Reagent k060383
Similarities		
Intended Use	For the quantitation of glucose in human serum, plasma, urine, or cerebrospinal fluid (CSF).	Same
Assay principle	Glucose hexokinase method	Same
Detection of analyte	End-point colorimetric	Same
Reagent formulation	R1: Active ingredients: ATP•2Na, NAD, G-6-PDH, and Hexokinase.	Same
Specimen Type	Human serum, plasma, urine or CSF	Same
Assay range	Serum/Plasma: 5-800 mg/dL (0.28-44.4 mM) Urine/CSF: 1-800 mg/dL (0.06-44.4 mM)	Same
Tube types	Serum: serum tubes (with or without gel barriers) Plasma: acceptable anticoagulants in collection tubes are lithium heparin (with or without gel barrier), sodium heparin, sodium fluoride/potassium oxalate, EDTA	Same
Use of calibrators	Yes	Same
Use of controls	Yes, commercially available controls	Same

Item	Candidate Device Alinity c Glucose Reagent Kit k170316	Predicate Device Glucose Reagent k060383
Differences		
Reagent container	Polypropylene; black color	High density polyethylene; white colorant
Closure material for reagent container	High density polyethylene; black color	F217 cap liner; polyethylene foam between low-density polyethylene liners; green color

Alinity c System

Item	Candidate Device Alinity c System k170316	Predicate Device AEROSET System k980367
Similarities		
Intended use	For in vitro determination of analytes in body fluids.	Same
Detection Technology	Potentiometric/photometric	Same
Sample Handling	Robotic sample handler (RSH), transport system that has random and continuous access to samples. Autoretest Capability. Priority and batch sample loading.	Same
Reagent Handling	The on-board storage area cooler provides evaporation control. Continuous Reagent Access.	Same
Differences		
Calibrator/Control Automation	Direct aspiration from the calibrator/control bottles	None
Reagent access	Continuous reagent access	Scheduled reagent access
Bulk solutions replenishment	Continuous bulk solution access	Scheduled bulk solution access
Priority sample loading	All carrier positions are available to have a priority sample loading designation.	Select positions available for priority loading.

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

CLSI EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition.

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– Third Edition.

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline– Second Edition.

CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.

IEC/EN 61010-1:2010 (3rd Edition) Safety Requirements for Electrical Equipment for Measurement Control and Laboratory Use – Part 1 General Requirements.

L. Test Principle:

The concentration of glucose is determined by the glucose hexokinase method. Glucose in the specimen is phosphorylated by hexokinase (HK) in the presence of adenosine triphosphate (ATP) and magnesium ions to produce glucose-6-phosphate (G-6-P) and adenosine diphosphate (ADP). Glucose-6-phosphate dehydrogenase (G-6-PDH) oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD) to nicotinamide adenine dinucleotide reduced (NADH). The NADH produced is detected spectrophotometrically at 340 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Precision studies to derive repeatability and within-laboratory precision were performed in accordance with CLSI EP05-A2 guideline.

   Serum glucose:
   The samples were three levels of control material and three levels of spiked human serum (Panels A, B, and C). Precision for spiked human serum was evaluated using two instruments and two reagent lots per instrument in 3 replicates per run, 2 runs per day across 22 days for 528 total results. Control samples were tested using two instruments and two reagent lots with only one reagent lot per instrument in 3 replicates per run, 2 runs per day across 22 days for 264 results per instrument/reagent lot; one representative lot is shown below. Estimates for repeatability and within-laboratory precision were analyzed by ANOVA and the results are summarized as follows. The number of actual results was slightly reduced due to instrument errors.

			Repeatability		Within-Laboratory*	
Sample	**N**	**Mean (mg/dL)**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	264	55	0.6	1.1	0.7	1.2
Control Level 2	263	128	0.9	0.7	1.3	1.0
Control Level 3	260	311	2.1	0.7	2.5	0.8
Panel A	527	7	0.1	1.9	0.1	1.9
Panel B	528	106	0.8	0.8	1.0	0.9
Panel C	523	728	5.6	0.8	5.9	0.8

*includes within run, between run, and between day variances.

Urine glucose:
The samples were two levels of control material and four synthetic urine samples spiked with glucose urine stock solution (Panel A, B, C, and D). Precision for spiked urine samples was evaluated using two instruments and two reagent lots per instrument in 3 replicates per run, 2 runs per day across 22 days for 528 total results. Control samples were tested using two instruments and two reagent lots with only one reagent lot per instrument in 3 replicates per run, 2 runs per day across 22 days for 264 results per instrument/reagent lot; one representative lot is shown below. Estimates for repeatability and within-laboratory precision were analyzed by ANOVA and the results are summarized as follows. The number of actual results was slightly reduced due to instrument errors.

			Repeatability		Within-Laboratory*	
Sample	**N**	**Mean (mg/dL)**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	263	38	0.3	0.9	0.6	1.4
Control Level 2	260	359	2.9	0.8	3.4	1.0
Panel A	527	3	0.1	3.8	0.1	3.8
Panel B	526	60	1.0	1.6	1.2	2.1
Panel C	528	110	2.4	2.2	3.1	2.8
Panel D	525	712	6.2	0.9	8.1	1.1

*includes within run, between run, and between day variances.

CSF glucose:
The samples were two levels of control material and four human CSF pools spiked with glucose CSF stock solution (Panel A, B, C, and D). Precision for spiked human CSF samples was evaluated using two instruments and two reagent lots per instrument in 3 replicates per run, 2 runs per day across 22 days for 528 total results. Control samples were tested using two instruments and two reagent lots with only one reagent lot per instrument in 3 replicates per run, 2 runs per day across 22 days for 264 results per instrument/reagent lot; one lot representative is shown below. Estimates for repeatability and within-laboratory precision were analyzed by ANOVA and the results are summarized as follows. The number of actual results

was slightly reduced due to instrument errors.

			Repeatability		Within-Laboratory*	
Sample	**N**	**Mean (mg/dL)**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	264	60	0.5	0.9	0.6	1.1
Control Level 2	263	31	0.4	1.1	0.4	1.3
Panel A	527	3	0.1	4.8	0.1	4.8
Panel B	528	57	0.4	0.8	0.5	0.9
Panel C	527	107	0.7	0.7	0.8	0.8
Panel D	526	700	3.8	0.5	4.8	0.7

*includes within run, between run, and between day variances.

b. *Linearity/assay reportable range:*

Linearity was evaluated in accordance with CLSI EP06-A guideline.

Serum glucose:
One low-level glucose sample, SeraSub (synthetic serum) and one high-level serum glucose sample were inter-diluted to prepare 13 test sample concentrations (828, 796, 777, 730, 560, 361, 189, 93, 48, 22, 4, 2, and 0 mg/dL) spanning the claimed measuring range. Test samples were assayed in a minimum of two replicates using one instrument, reagent lot, calibrator lot, and control lot.

Urine glucose:
One low-level glucose sample, UriSub (synthetic urine) and one high-level urine glucose sample were inter-diluted to prepare 15 test sample concentrations (843, 814, 794 745, 551, 369, 198, 98, 25, 10, 6, 1, 0 mg/dL) spanning the claimed measuring range. Test samples were assayed in a minimum of two replicates using one instrument, reagent lot, calibrator lot, and control lot.

CSF glucose:
One low-level glucose sample, UriSub and one high-level human CSF glucose sample were inter-diluted to prepare 15 concentrations (887, 846, 825, 783, 574, 365, 209, 105, 26, 11, 5, 1.1, 1.0, 0.6, 0.1 mg/dL) spanning the claimed measuring range. Test samples were assayed in a minimum of two replicates using one instrument, reagent lot, calibrator lot, and control lot.

For each specimen type, the mean sample concentration result for each test sample was compared to the expected result determined by the dilution factor and analyzed by regression analysis. Results of the linear regression analysis per sample type are presented in the table below.

Sample	Slope	Intercept	R^2
Serum	0.9903	-0.1	0.9993
Urine	0.9616	-0.2	0.9988
CSF	0.9476	-0.4	0.9986

The observed linear range supports the claim that the Alinity c Glucose Reagent is linear across the measuring interval of 5 to 800 mg/dL for serum and 1 to 800 mg/dL for urine and CSF.

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

Traceability: The Alinity c Glucose Reagent Kit is traceable to NIST standard reference material 965b.

Stability: The shelf life stability and open on-board reagent stability of the Alinity c Glucose Reagent Kit was previously established in k060383. The open onboard stability claim is 30 days. The sponsor claims a product shelf-life/expiration of 12 months.

d. Detection limit:

Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were evaluated in accordance with CLSI EP17-A2 guideline.

To determine LoB, one blank sample was assayed a minimum of 5 replicates over 3 days. The LoB was calculated as the 95th percentile of the zero-analyte measurements. The sponsor's study supported a LoB of 0.33 mg/dL for the serum application and 0.23 mg/dL for the urine/CSF application.

To determine LoD, five low-level samples were prepared by diluting a glucose serum stock solution and assaying 10 replicates over 3 days. LoD was evaluated from the lowest analyte level that had at least 95% of the replicates greater than the LoB. The sponsor's study supported an LOD of 0.55 mg/dL for the serum application and 0.40 mg/dL for the urine/CSF application. The sponsor determined the functional sensitivity of the Alinity c Glucose Reagent Kit based on the LOQ on the Alinity c System.

To determine the LoQ, test levels near the linear low limit for the glucose assay were run in replicates of 10 on three instruments over 3 days. The limit of quantitation was defined as the lowest concentration of analyte which has imprecision less than or equal to 20% CV. The sponsor's study supported a LoQ of 2.25 mg/dL for the serum application and 0.86 mg/dL for the urine/CSF application. *e. Analytical specificity:*

Potential interference was in accordance with CLSI EP07-A2 guideline.

Serum glucose:
Interference from six drugs and four endogenous substances was evaluated using Technopath Serum Matrix spiked with high (135 mg/dL) or low (93 mg/dL) glucose levels. Test samples were prepared by spiking each drug (one concentration per interferent) or endogenous substance (two concentrations per interferent) into the low and high glucose samples, and comparing to control samples containing no interferent. The sponsor defined significant interference as bias >6% or >1 mg/dL between the test and control samples.

Potentially Interfering Substance	**Highest concentration tested that did not show significant interference**
Unconjugated Bilirubin	30 mg/dL
Conjugated Bilirubin	60 mg/dL
Hemoglobin	2,000 mg/dL
Triglycerides	2,000 mg/dL
Ascorbic Acid	6 mg/dL
Acetaminophen	20 mg/dL
Ibuprofen	50 mg/dL
Acetylcysteine	167 mg/dL
Acetylsalicylic Acid	66 mg/dL
Sodium Salicylate	70 mg/dL

Urine glucose:
Interference was evaluated using UriSub spiked with high (135 mg/dL) or low (93 mg/dL) glucose levels. Test samples were prepared by spiking each potential interferent into the low and high glucose samples, and results compared to control samples containing no interferent. The sponsor defined significant interference as bias >10% or >1 mg/dL between the test and control samples.

Potentially Interfering Substance	**Highest concentration of interferent tested that did not show significant interference**
Protein	50 mg/dL
Ascorbate	200 mg/dL
8.5 N Acetic Acid	6.25 mL/dL
Boric Acid	250 mg/dL
6 N Hydrochloric Acid	2.5 mL/dL
6 N Nitric Acid	5 mL/dL
Sodium Oxalate	60 mg/dL
Sodium Carbonate	1.25 g/dL
Sodium Fluoride	400 mg/dL
Acetaminophen	20 mg/dL
Ibuprofen	50 mg/dL
Acetylcysteine	167 mg/dL

The sponsor included the following limitation in the labeling:

"The Alinity c Glucose assay using the serum application is susceptible to interference effects from unconjugated bilirubin at > 30 mg/dL."

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed in accordance with CLSI EP09-A3 guideline. Serum, urine, and CSF glucose samples were measured using two Alinity c Systems and an ARCHITECT c8000 System (k060383) as the comparator method. Samples were tested in duplicate on each system. The first replicate for the Alinity c System was compared to the mean concentration from the ARCHITECT c System. The number and range of samples tested for each matrix are listed in the table below with representative results using a Passing-Bablok linear regression. Less than 15% of samples were prepared by diluting or spiking specimens.

Matrix	N	Slope	y-intercept	Correlation Coefficient	Test Range (mg/dL)
Serum	98	1.00	-1.78	1.00	8-791
Urine	118	0.99	0.25	0.99	4-785
CSF	90	1.00	0.50	1.00	4-740

b. Matrix comparison:

A matrix comparison study was performed to evaluate collection tube types suitable for use with the Alinity c Glucose Reagent Kit on the Alinity c System. A minimum of 40 sets of matched samples were tested in duplicate using one instrument, reagent lot, calibrator lot, and control lot. For each set of samples, the first replicate for the evaluation collection tube type was compared to the mean concentration for the serum sample control and analyzed using a Passing-Bablok linear regression. Results are summarized in the table below:

Sample type	N	Slope	y-intercept	Correlation Coefficient	Test Range (mg/dL)
Serum Separator	46	1.00	-0.13	1.00	10-757
Dipotassium EDTA	43	1.00	1.29	1.00	
Lithium heparin	46	0.99	1.22	1.00	
Sodium heparin	46	0.99	1.26	1.00	
Sodium fluoride/Potassium oxalate	43	0.99	1.32	1.00	

Sample type	N	Slope	y-intercept	Correlation Coefficient	Test Range (mg/dL)
Lithium heparin plasma separator	46	0.99	1.66	1.00	

The results of the matrix comparison study support the claim that serum, dipotassium EDTA, sodium heparin, lithium heparin, and sodium fluoride/potassium oxalate plasma anti-coagulants are suitable for use with the Alinity c Glucose Reagent Kit.

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:

Serum (fasting)		
	Range (mg/dL)	Range (mmol/L)
Cord	45 to 96	2.5 to 5.3
Premature	20 to 60	1.1 to 3.3
Neonate	30 to 60	1.7 to 3.3
Newborn, 1 day	40 to 60	2.2 to 3.3
Newborn, > 1 day	50 to 80	2.8 to 4.5
Child	60 to 100	3.3 to 5.6
Adult	74 to 100	4.1 to 5.6
>60 yeas	82 to 115	4.1to 5.6
>90 years	75 to 121	4.2 to 6.7
Urine		
	Range	Range
Random	1 to 15 mg/dL	0.1 to 0.8 mmol/L
24 hour	< 0.5 g/day	< 2.8 mmol/day
Cerebrospinal Fluid		
Infant, child	60 to 80 mg/dL	3.3 to 4.5 mmol/L
Adult	40 to 70 mg/dL	2.2 to 3.9 mmol/L

The reported reference ranges are from: Burtis CA, Ashwood ER, Bruns DE, editors. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics,* 5th ed. St. Louis, MO: Elsevier Saunders; 2012:2149.

N. Instrument Name:

Alinity c System

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X___ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___X___

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X___ or No _____

3. Specimen Identification:

   Sample barcode, rack barcode

4. Specimen Sampling and Handling:

   Instructions on specimen handling, storage, and shipping is provided in the package insert for the reagents.

5. Calibration:

   Instruction for calibration is provided in the package insert for the assays and in the operator's manual for the Alinity c System. Calibration is required with each change in reagent lot. Calibration verification should be conducted with at least 2 levels of controls according to the established quality control requirements for the laboratory. If control results fall outside acceptable ranges, recalibration may be necessary.

6. Quality Control:

   The sponsor recommends that two levels of controls (normal and abnormal) should be tested every 24 hours. Two levels of controls should be used to verify each calibration. The Alinity c System is equipped with quality control analysis software to monitor quality control data with Levey-Jennings graphs, Westgard rules, control range tracking, and quality control data summaries. The sponsor also recommends verification procedures be performed to verify Alinity ci series claims. Quality control testing should be performed in accordance with regulatory requirements and each laboratory's standard procedure.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In the "Performance Characteristics" Section above:

EMC and Electrical Safety: The Alinity c System was tested and passed for compliance to EMC and Electrical Safety standards.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.