

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

A. 510(k) Number:

k060383

B. Purpose for Submission:

New device

C. Measurand:

Glucose

D. Type of Test:

Quantitative enzymatic assay based on Hexokinase/G-6-PDH methodology

E. Applicant:

Abbott Laboratories

F. Proprietary and Established Names:

Glucose Reagent

G. Regulatory Information:

1. Regulation section:

21 CFR §862.1345, Hexokinase, Glucose

2. Classification:

Class II

3. Product code:

CFR

4. Panel:

75 (Chemistry)

H. Intended Use:

1. Intended use(s):

See Indications for use.

2. Indication(s) for use:

A glucose test system is a device intended to measure glucose quantitatively in blood and other bodily fluids. 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.

3. Special conditions for use statement(s):

For Prescription use only.

4. Special instrument requirements:

Abbott AEROSSET® and Abbott ARCHITECT® c8000®

I. Device Description:

The Glucose reagent is supplied as a liquid, ready-to-use, single reagent kit which contains:

Ref 3L82-20, **R1** 10 x 55 mL – estimated test per kit: 9,000
Ref 3L82-40, **R1** 10 x 90 mL – estimated test per kit: 15,000

<u>Reactive Ingredients</u>	<u>Concentration</u>
NAD	5.0 mg/mL
G-6-PDH	3,000 U/L
Hexokinase	15,000 U/L
ATP 2Na	9.0 mg/mL

The calibrator recommended for this assay was cleared under k981706.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Glucose/HK on the Hitachi 917 Analyzer

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

k953847

3. Comparison with predicate:

Assay Characteristics	New Device Glucose (k060383)	Glucose/HK on Hitachi 917 Analyzer (k032377)
Analyte Measured	Carbon Dioxide	Carbon Dioxide
Intended Use	The Glucose assay is used for the quantitation of glucose in human serum, plasma, urine, or cerebrospinal fluid (CSF).	The Glucose assay is used for the quantitation of glucose in human serum, plasma, urine, or cerebrospinal fluid (CSF).
Assay Principle	Glucose 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) specifically oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD) to nicotinamide adenine dinucleotide reduced (NADH). One micromole of NADH is produced for each micromole of glucose consumed. The NADH produced absorbs light at 340 nm and can be detected spectrophotometrically as an increased absorbance	Glucose 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) specifically oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD) to nicotinamide adenine dinucleotide reduced (NADH). One micromole of NADH is produced for each micromole of glucose consumed. The NADH produced absorbs light at 340 nm and can be detected spectrophotometrically as an increased absorbance
Detection of Analyte	Endpoint	Endpoint
Samples	Serum, plasma, urine, or cerebrospinal fluid (CSF)	Serum, plasma, urine, or cerebrospinal fluid (CSF)
Assay Range	Serum/ Plasma: 5 to 800 mg/dL Urine/CSF: 1 to 800 mg/dL	Serum/ Plasma: 2 to 750 mg/dL Urine/CSF: 2 to 750 mg/dL
Analysis Medium	Aqueous solution	Aqueous solution
Use of Calibrators	Yes	Yes
Use of Controls	Yes	Yes

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

EP5-A2 CLSI: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition 2004

EP6-A CLSI: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline Evaluation of Matrix Effects; Approved Guideline, Second Edition 2003

EP7-P CLSI: Interference Testing in Clinical Chemistry; Approved Guideline. Vol 6, No. 13, 1986

EP9-A CLSI: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline. Vol. 15, No. 17, 1995

L. Test Principle:

Glucose 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) specifically oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD) to nicotinamide adenine dinucleotide reduced (NADH). One micromole of NADH is produced for each micromole of glucose consumed. The NADH produced absorbs light at 340 nm and can be detected spectrophotometrically as an increased absorbance

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Serum Application:

The sponsor conducted a total precision study in accordance with CLSI EP5-A for each component of variation (between-day, between-run, and within-run) per protocol. Two control levels (Level 1 and Level 2) at normal and abnormal analyte concentrations were tested. These controls were evaluated over 20 days, two runs per day, and two replicates per run. Precision was reported as the total %CV. Serum precision results are summarized in the below table.

AEROSET Serum Precision

Control		Level 1	Level 2
N		80	80
Mean (mg/dL)		82.28	292.19
Within Run	SD	0.59	1.50
	%CV	0.72	0.51
Between Run	SD	0.57	3.84
	%CV	0.69	1.31
Between Day	SD	0.30	0.00
	%CV	0.36	0.00
Total	SD	0.87	4.12
	%CV	1.06	1.41

ARCHITECT Serum Precision

Control		Level 1	Level 2
N		80	80
Mean (mg/dL)		79.58	281.26
Within Run	SD	1.58	1.83
	%CV	1.98	0.65
Between Run	SD	0.67	2.62
	%CV	0.84	0.93
Between Day	SD	0.00	2.80
	%CV	0.00	0.99
Total	SD	1.71	4.24
	%CV	2.15	1.51

Urine and CSF Applications:

The sponsor also conducted a five day precision study in accordance with CLSI EP10-A. This study was intended to supplement data obtained from the twenty-day serum precision study and provides a limited assessment of the performance of the assay with the urine and CSF matrices. Two control levels (Level 1 and Level 2) at normal and abnormal analyte concentrations were tested for the urine and CSF applications. These controls were evaluated over five days, two runs per day, and five replicates per run. Precision was reported as the total %CV. Urine and CSF precision results are summarized in the below tables.

AEROSET Urine Precision

Control		Level 1	Level 2
N		50	50
Mean (mg/dL)		29.86	305.94
Within Run	SD	0.30	2.12
	%CV	0.99	0.69
Between Run	SD	0.40	3.55
	%CV	1.33	1.16
Between Day	SD	0.00	0.00
	%CV	0.00	0.00
Total	SD	0.49	4.13
	%CV	1.66	1.35

ARCHITECT Urine Precision

Control		Level 1	Level 2
N		50	50
Mean (mg/dL)		29.37	300.66
Within Run	SD	0.25	2.28
	%CV	0.85	0.76
Between Run	SD	0.16	0.76
	%CV	0.54	0.25
Between Day	SD	0.00	0.00
	%CV	0.00	0.00
Total	SD	0.30	2.40
	%CV	1.01	0.80

AEROSET CSF Precision

Control		Level 1	Level 2
N		50	50
Mean (mg/dL)		60.40	28.98
Within Run	SD	0.57	0.41
	%CV	0.95	1.41
Between	SD	0.74	0.27

Run	%CV	1.23	0.92
Between Day	SD	0.00	0.00
	%CV	0.00	0.00
Total	SD	0.94	0.49
	%CV	1.55	1.69

ARCHITECT CSF Precision

Control		Level 1	Level 2
N		50	50
Mean (mg/dL)		59.25	28.45
Within Run	SD	0.46	0.20
	%CV	0.78	0.70
Between Run	SD	0.43	0.27
	%CV	0.72	0.94
Between Day	SD	0.00	0.00
	%CV	0.00	0.00
Total	SD	0.63	0.33
	%CV	1.07	1.17

b. Linearity/assay reportable range:

To determine the linear range of analyte concentrations of the Glucose assay on the AEROSSET and ARCHITECT c8000 Systems the sponsor assayed ten samples at various concentrations spanning the desired linear range of the assay with four replicates per concentration. At least one level was included which exceeded the desired linear range. The percent recovery for each sample was determined by dividing the mean observed result by the expected value. The sponsor's acceptance criteria were the acceptable difference between the observed result and expected value be within $\pm 6\%$ or ± 1 mg/dL, whichever is greater, for serum; and $\pm 10\%$ or ± 1 mg/dL, whichever is greater, for urine.

Serum linearity results are presented in the tables below.

Glucose – Serum
AEROSET Linearity

Mean Conc. (mg/dL)	Expected Conc. (mg/dL)	% Recovery
899.853	864.506	104.09
804.023	778.055	103.34
720.345	691.605	104.16
532.258	518.704	102.61
432.253	432.253	100.00
336.563	345.802	97.328
162.675	172.901	94.086
86.935	86.451	100.56
41.320	43.225	95.592
8.703	8.645	100.66
4.553	4.323	105.32
2.700	2.161	124.93

Glucose – Serum
ARCHITECT Linearity

Mean Conc. (mg/dL)	Expected Conc. (mg/dL)	% Recovery
897.031	876.5	102.35
812.504	788.9	103.00
714.763	701.3	101.92
534.571	526.1	101.62
438.236	438.5	99.946
340.989	350.9	97.183
165.448	175.7	94.180
87.741	88.07	99.624
42.090	44.27	95.071
8.746	9.232	94.738
4.591	4.852	94.628
2.601	2.662	97.716

The data presented indicate acceptable linearity over the claimed measuring range (5 to 800 mg/dL) for serum.

Urine linearity results are presented in the tables below.

Glucose – Urine
AEROSSET Linearity

Mean Conc. (mg/dL)	Expected Conc. (mg/dL)	% Recovery
881.710	841.3	104.81
785.773	757.1	103.78
702.290	673.0	104.35
541.753	504.8	107.33
420.628	420.6	100.00
330.135	336.5	98.108
162.968	168.3	96.860
82.800	84.13	98.424
40.370	42.06	95.976
8.118	8.413	96.493
4.045	4.206	96.166
2.080	2.103	98.900
0.918	0.841	109.06

Glucose – Urine
ARCHITECT Linearity

Mean Conc. (mg/dL)	Expected Conc. (mg/dL)	% Recovery
895.497	858.000	104.37
801.910	772.200	103.85
706.534	686.400	102.93
549.767	514.800	106.79
429.000	429.000	100.00
339.807	343.200	99.011
166.934	171.600	97.281
84.825	85.800	98.864

Mean Conc. (mg/dL)	Expected Conc. (mg/dL)	% Recovery
41.618	42.900	97.012
8.205	8.580	95.629
3.928	4.290	91.559
2.043	2.145	95.222
0.733	0.858	85.456

The data presented indicate acceptable linearity of urine over the claimed measuring range (1 to 800 mg/dL) for urine/ CSF.

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

The reagent calibration stability was determined by the recovery method of Glucose reagent. Fresh reagent was calibrated with fresh calibrators on Day 0. Control material and a prepared test sample near the linear high were analyzed on Day 0, 1, 7, 14, 15, 21, 28, 29, 32, and 33. The sponsor's acceptance criteria were the target for % recovery was 94 to 106% of the Day 0 results. All test points up to and including Day 33 met the target for % recovery. The resulting calibration stability claim is 30 days.

The reagent open onboard stability was also determined by the recovery method on multiple lots of Glucose reagent. Fresh reagent was calibrated with fresh calibrators on Day 0. Control material and a prepared test sample near the linear high were analyzed on Day 0, 1, 7, 14, 15, 21, 28, 29, 32 and, 33. The open onboard stability claim is 30 days. The sponsor claims a product shelf-life/expiration of 12 months. Protocols and acceptance criteria were reviewed.

d. Detection limit:

The sponsor determined the functional sensitivity of the Glucose assay based on the Limit Of Quantitation (LOQ) on the AEROSSET and the ARCHITECT c8000 Systems. To determine the LOQ, test levels near the linear low for the Glucose assay were run in replicates of 10, on three instruments, two runs per instrument. 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 internal verification study supported an LOQ of 5.0 mg/dL (0.278 mmol/L) for the serum application and 1.0 mg/dL (0.056 mmol/L) for the urine/CSF application. The LOD testing for Glucose was performed using a study design based on CLSI EP17-A. An internal verification study by the sponsor supported an LOD of 2.5 mg/dL (0.139 mmol/L) for the serum application, and 1.0 mg/dL (0.056 mmol/L) for the urine/CSF application. The proportions of false positives (α) and false negatives (β) were less than 5% and the limit of blank (LOB) was 0.33 mg/dL.

e. *Analytical specificity:*

The sponsor conducted interference studies to evaluate any interference in the Glucose assay caused by bilirubin, hemoglobin, and triglyceride (Intralipid) for serum samples on the AEROSET and ARCHITECT c8000 Systems. For urine samples, testing for interference was performed using hydrochloric acid, sodium fluoride, acetic acid, ascorbate, boric acid, nitric acid, protein, sodium carbonate, and sodium oxalate. Interferents which may falsely elevate or reduce the concentration of an analyte were tested per the work instruction protocol for Glucose. Human serum samples (reference) at two glucose concentrations (Medical Decision Level 1 and 2) and urine samples (reference) were spiked with various levels of interferents.

According to the sponsor, four replicates of each interferent level and four replicates of reference sample were run. The percent recovery was determined by dividing the mean result of each interferent sample by the mean result of the reference sample. The sponsor's acceptance criteria were the level of interference was considered acceptable if there was no more than $\pm 6\%$ difference between the interferent result and the reference result (serum) or no more than $\pm 10\%$ difference between the interferent result and the reference result (urine). Testing was performed using the AEROSET System.

The tables below summarize the results for serum samples, at each decision level, and urine samples, respectively, indicating the highest interferent level at which the percent interference was within $\pm 6\%$ for serum and $\pm 10\%$ for urine.

Glucose - Serum
Interfering Substances – Medical Decision Level 1

Interfering Substance	Interfering Substance Concentration	Target (mg/dL)	Observed (% of Target)
Bilirubin	30 mg/dL	83.1	99.89
	60 mg/dL	83.1	100.11
Hemoglobin	1,000 mg/dL	78.2	95.59
	2,000 mg/dL	78.2	91.74
Intralipid	1,000 mg/dL	81.0	98.21
	2,000 mg/dL	81.0	97.84

Glucose - Serum
Interfering Substances – Medical Decision Level 2

Interfering Substance	Interfering Substance Concentration	Target (mg/dL)	Observed (% of Target)
Bilirubin	30 mg/dL	126.3	100.66
	60 mg/dL	126.3	101.14
Hemoglobin	1,000 mg/dL	118.3	98.29
	2,000 mg/dL	118.3	96.03
Intralipid	1,000 mg/dL	119.1	99.70
	2,000 mg/dL	119.1	99.58

Glucose - Urine
Interfering Substances

Interfering Substance	Interfering Substance Concentration	Target (mg/dL)	Observed (% of Target)
Hydrochloric Acid (6 N)	2.5 ml/dL	16.140	101.81
Sodium Fluoride	400 mg/dL	16.293	100.12
Acetic Acid (8.5 N)	6.25 ml/dL	15.948	105.55
Ascorbate	200 mg/dL	14.995	99.53
Boric Acid	250 mg/dL	16.050	99.58
Nitric Acid (6 N)	5.0 ml/dL	15.860	105.47
Protein	50 mg/dL	15.968	102.16
Sodium Carbonate	1.25 g/dL	15.930	100.86
Sodium Oxalate	60 mg/dL	15.705	103.87

f. Assay cut-off:

Not applicable for this type of device.

2. Comparison studies:

a. Method comparison with predicate device:

The sponsor performed comparative performance studies using the AEROSSET[®] and

ARCHITECT® c8000® Systems compared to the Glucose/HK assay on the Hitachi 917 Analyzer. The study was conducted in accordance with CLSI EP9-A2 by testing 102 serum samples, 41 urine samples, and 52 CSF samples using each method. A total of 3 serum samples, 12 urine samples, and 12 CSF samples were spiked with NIST SRM917 to generate high analytical levels. A linear regression was performed comparing the results for each method. The ranges of samples tested were as follows - 13.3 to 663.9 mg/dL (Serum), 13.3 to 663.9 mg/dL (Urine), and 10.5 to 697.7 mg/dL (CSF).

Serum application:

	AEROSET vs. Hitachi	ARCHITECT vs. Hitachi	AEROSET vs. ARCHITECT
N	102	102	102
Y - Intercept	-5.50	-4.54	0.85
Correlation Coefficient	0.9995	0.9993	0.9996
Slope	1.09	1.06	0.97

Urine application:

	AEROSET vs. Hitachi	ARCHITECT vs. Hitachi	AEROSET vs. ARCHITECT
N	41	41	41
Y - Intercept	-1.35	-2.67	-1.36
Correlation Coefficient	0.9998	0.9998	0.9999
Slope	1.09	1.04	0.96

CSF application:

	AEROSET vs. Hitachi	ARCHITECT vs. Hitachi	AEROSET vs. ARCHITECT
N	52	52	52
Y - Intercept	-4.29	-3.89	0.22
Correlation Coefficient	0.9998	0.9997	0.9998
Slope	1.09	1.04	0.95

b. *Matrix comparison:*

Ten (10) subjects were tested using each of the collection tubes to be evaluated. The serum tube used for the baseline was the only glass tube; all other specimen tubes were plastic. Data were analyzed for statistical differences between different tube types. The sponsor's acceptance criteria were acceptability of each anticoagulant is based on a difference of less than $\pm 6\%$ difference between the mean values of all samples/ replicates for each tube type in question and the plain glass serum tube.

Testing was performed using the AEROSSET System. The table below summarizes the results of the specimen tube study.

**Glucose
Specimen Tube – Data Summary**

Substance	N	Differences			Percent Differences			Recoveries		
		Mean	Min	Max	Mean	Min	Max	Mean	Min	Max
Li Hep Plasma	15	3.000	-1.602	7.330	3.362	-1.538	8.043	103.36	98.462	108.04
Li Hep PST	15	4.468	0.250	8.798	4.696	0.292	11.030	104.70	100.29	111.03
Na Hep Plasma	15	3.334	0.302	8.355	3.533	0.318	8.812	103.53	100.32	108.81
EDTA Plasma	15	5.205	1.135	9.283	5.421	1.325	10.820	105.42	101.32	110.82
NaFl/Potassium Oxalate Plasma	14	1.210	-1.597	3.463	1.238	-2.078	3.469	101.24	97.922	103.47
SST Serum	15	3.104	1.285	7.590	3.127	1.352	6.378	103.13	101.35	106.38

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):

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The sponsor's claimed Expected values/ Reference range were derived from literature.

The sponsor states that the American Diabetes Association recommends use of a fasting glucose concentration of 109 mg/dL (6.0 mmol/L) as the upper limit of "normal." Population reference ranges in various texts and publications may differ.

Serum/ Plasma

<u>Fasting</u>	<u>Range (mg/dL)</u>	<u>Range (mmol/L)</u>
Cord	45 to 96	2.50 to 5.33
Premature	20 to 60	1.11 to 3.33
Neonate	30 to 60	1.67 to 3.33
Newborn, 1 day	40 to 60	2.22 to 3.33
Newborn, > 1 day	50 to 80	2.78 to 4.44
Child	60 to 100	3.33 to 5.55
Adult	70 to 105	3.89 to 5.83
> 60 years	80 to 115	4.44 to 6.38
> 70 years	83 to 110	4.61 to 6.10

Urine

	<u>Range</u>	<u>Range</u>
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

	<u>Range</u>	<u>Range</u>
Infant, Child	60 to 80	3.33 to 4.44
Adult	40 to 70	2.22 to 3.89

24 Hour Urinary Excretion

To convert results from mg/dL to g/day (24 hour urinary excretion)

Where:

$$V = 24 \text{ hour urine volume (mL)}$$

c = analyte concentration (mg/dL)

$$\text{24 hour excretion} = [(V \times c) \div 100,000] \text{ mmol/day} \underline{\hspace{2cm}}$$

To convert results from mmol/L to mmol/day (24 hour urinary excretion)

Where:

V = 24 hour urine volume (mL)

c = analyte concentration (mmol/L)

$$\text{24 hour excretion} = [(V \times c) \div 1000] \text{ mmol/ day} \underline{\hspace{2cm}}$$

The sponsor recommends that each laboratory determine its own reference range based upon its particular locale and population characteristics.

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.