



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

**I Background Information:**

**A 510(k) Number**

K252357

**B Applicant**

Abbott Ireland

**C Proprietary and Established Names**

Glucose2

**D Regulatory Information**

Product Code(s)	Classification	Regulation Section	Panel
CFR	Class II	21 CFR 862.1345 - Glucose Test System	CH - Clinical Chemistry

**II Submission/Device Overview:**

**A Purpose for Submission:**

New device

**B Measurand:**

Glucose

**C Type of Test:**

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

### **III Intended Use/Indications for Use:**

#### **A Intended Use(s):**

See Indications for Use below.

#### **B Indication(s) for Use:**

The Glucose2 assay is used for the quantitation of glucose in human serum, plasma, urine, or cerebrospinal fluid (CSF) on the ARCHITECT c System.

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.

#### **C Special Conditions for Use Statement(s):**

Rx - For Prescription Use Only

#### **D Special Instrument Requirements:**

ARCHITECT c8000

### **IV Device/System Characteristics:**

#### **A Device Description:**

The Glucose2 assay kit consists of two ready to use reagent solutions, R1 and R2.

R1: Buffer solution containing 6.300 g/L b-NADP, disodium salt, 2.420 g/L adenosine triphosphate (ATP) and sodium azide as a preservative.

R2: Substrate solution containing hexokinase 19.200 KU/L, glucose-6-phosphate dehydrogenase 6.400 KU/L and sodium azide as a preservative.

#### **B Principle of Operation:**

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.

**V Substantial Equivalence Information:****A Predicate Device Name(s):**

Glucose

**B Predicate 510(k) Number(s):**

K060383

**C Comparison with Predicate(s):**

<b>Device &amp; Predicate Device(s):</b>	<u>K252357</u>	<u>K060383</u>
Device Trade Name	Glucose2	Glucose
<b>General Device Characteristic Similarities</b>		
Intended Use/Indications For Use	The assay is used for the quantitation of glucose used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.	Same
Specimen type	Human serum, plasma, urine, or cerebrospinal fluid (CSF).	Same
Analytical Measuring Interval (AMI)	Serum/Plasma: 5–800 mg/dL Urine: 1–800 mg/dL	Same
<b>General Device Characteristic Differences</b>		
Analytical Measuring Interval (AMI)	CSF: 2–800 mg/dL	CSF: 1–800 mg/dL
Limits of Measurement	Serum/Plasma: Limit of Blank: 0.17 mg/dL Limit of Detection: 0.30 mg/dL Limit of Quantitation: 1.16 mg/dL  Urine Limit of Blank: 0.15 mg/dL Limit of Detection: 0.29 mg/dL	Serum: Limit of Detection: 2.5 mg/dL Limit of Quantitation: 5.0 mg/dL  Urine/CSF: Limit of Detection: 1.0 mg/dL

Device & Predicate Device(s):	<u>K252357</u>	<u>K060383</u>
	Limit of Quantitation: 0.47 mg/dL  CSF Limit of Blank: 0.23 mg/dL Limit of Detection: 0.35 mg/dL Limit of Quantitation: 1.25 mg/dL	Limit of Quantitation: 1.0 mg/dL

#### **Planned modifications by PCCP:**

In addition to the similarities and differences between the candidate and the predicate device listed in the table above, the candidate device has an authorized predetermined change control plan (PCCP) for modifications to the device to enable use of specimens collected in potassium fluoride/EDTA tubes. The PCCP included the testing protocol, comparator sample type (i.e., serum), proposal to support sample stability, and pre-defined acceptance criteria. The protocol to validate potassium fluoride/EDTA tubes in the PCCP was consistent with the study conducted for validation of other sample types claimed through a matrix comparison study (see section VII.B.2 below). The acceptance criteria reviewed included criteria for slope, intercept, and predicted differences at medical decision limits with confidence and it was determined that if the results meet the acceptance criteria, the use of samples collected in potassium fluoride/EDTA tubes on the candidate device (i.e., Glucose2 assay on ARCHITECT c8000) would remain as safe and effective as the predicate device. Following verification of this additional specimen collection tube, the device labeling will be updated in accordance with the authorized PCCP to provide users with current information regarding compatible specimen collection tubes for the Glucose2 assay on the ARCHITECT c8000.

#### **VI Standards/Guidance Documents Referenced:**

Clinical and Laboratory Standards Institute (CLSI) EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition.

CLSI EP06: Evaluation of the Linearity of Quantitative Measurement Procedures – Second Edition.

CLSI EP07: Interference Testing in Clinical Chemistry- Third Edition.

CLSI EP09c – Measurement Procedure Comparison and Bias Estimation Using Patient Samples. Third Edition.

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

CLSI EP37: Supplemental Tables for Interference Testing in Clinical Chemistry- First Edition

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

#### 1. Precision/Reproducibility:

The sponsor provided separate precision studies supporting use of: (1) serum, (2) urine, and (3) CSF. The Glucose2 assay was evaluated in accordance with CLSI EP05-A3.

#### Within-Laboratory Precision

Serum and Urine: Each of the five samples was tested on three ARCHITECT c8000 instruments for serum and urine and one ARCHITECT c8000 instrument for CSF using three lots of the Glucose2 reagents. Two controls and 3 human serum, urine, and CSF panels were tested in duplicates per run, two runs per day, over 20 days for a total of 80 measurements per instrument/lot, where a unique reagent lot and a unique calibrator lot are paired with one instrument. The performance from a representative combination is shown in the tables below. The within-laboratory SD and %CV includes within-run, between-run, and between-day variance components.

#### *Serum*

Sample	n	Mean (mg/dL)	Within-Run (Repeatability)		Within-Laboratory	
			SD	%CV	SD	%CV
Control Level 1	80	43	0.5	1.2	0.5	1.3
Control Level 2	80	132	1.0	0.8	1.3	1.0
Panel 1	80	10	0.1	1.1	0.1	1.1
Panel 2	80	20	0.2	1.3	0.4	1.9
Panel 3	80	740	4.1	0.5	5.9	0.8

#### *Urine*

Sample	n	Mean (mg/dL)	Within-Run (Repeatability)		Within-Laboratory	
			SD	%CV	SD	%CV
Control Level 1	80	41	0.4	1.0	0.5	1.2
Control Level 2	80	338	2.5	0.7	2.8	0.8
Panel 1	80	3	0.0	0.0	0.0	0.0
Panel 2	80	100	0.8	0.8	1.1	1.1
Panel 3	80	732	6.0	0.8	8.2	1.1

*CSF*

Sample	n	Mean (mg/dL)	Within-Run (Repeatability)		Within-Laboratory	
			SD	%CV	SD	%CV
Control Level 1	80	64	0.6	1.0	0.7	1.1
Control Level 2	80	32	0.4	1.2	0.5	1.5
Panel 1	80	10	0.1	1.1	0.1	1.1
Panel 2	80	253	1.9	0.8	2.4	1.0
Panel 3	80	744	5.3	0.7	7.0	0.9

Reproducibility

Each of the five samples was tested using one lot of the Glucose2 reagents on three ARCHITECT c8000 instruments. Each instrument was operated by a different technician, and each individual sample set was prepared independently. Two controls and 3 human serum, urine, and CSF panels were tested in 3 replicates at 2 separate times per day on 5 different days. Reproducibility study results are summarized below:

*Serum*

Sample	n	Mean (mg/dL)	Repeatability		Within-Laboratory <sup>a</sup>		Reproducibility <sup>b</sup>	
			SD	%CV	SD	%CV	SD	%CV
Control Level 1	90	42	0.4	1.0	0.5	1.2	0.8	1.8
Control Level 2	90	132	1.0	0.7	1.7	1.3	1.7	1.3
Panel 1	90	10	0.3	2.6	0.3	2.8	0.3	2.9
Panel 2	90	20	0.1	0.7	0.2	0.9	0.2	0.9
Panel 3	90	745	6.9	0.9	7.9	1.1	8.0	1.1

*Urine*

Sample	n	Mean (mg/dL)	Repeatability		Within-Laboratory <sup>a</sup>		Reproducibility <sup>b</sup>	
			SD	%CV	SD	%CV	SD	%CV
Control Level 1	90	40	0.6	1.4	0.6	1.5	0.8	1.9
Control Level 2	90	338	2.8	0.8	3.4	1.0	3.4	1.0
Panel 1	90	3	0.1	4.4	0.2	6.9	0.2	6.9
Panel 2	90	99	0.8	0.8	1.1	1.1	1.5	1.5
Panel 3	90	733	5.6	0.8	6.5	0.9	7.3	1.0

## CSF

Sample	n	Mean (mg/dL)	Repeatability		Within-Laboratory <sup>a</sup>		Reproducibility <sup>b</sup>	
			SD	%CV	SD	%CV	SD	%CV
Control Level 1	90	63	0.9	1.4	1.1	1.7	1.3	2.0
Control Level 2	90	32	0.4	1.4	0.6	1.8	0.6	1.9
Panel 1	90	10	0.1	1.1	0.1	1.1	0.1	1.1
Panel 2	90	244	2.3	0.9	2.9	1.2	2.9	1.2
Panel 3	90	751	5.9	0.8	7.5	1.0	7.6	1.0

<sup>a</sup> Includes within-run, between-run, and between-day variability

<sup>b</sup> Includes within-run, between-run, between-day, and between-instrument variability

## 2. Linearity:

Linearity studies were performed according to the CLSI EP06-2nd edition guideline. Thirteen (13) levels of samples were prepared by mixing different portions of high sample and a blank sample. Each sample was tested in replicates of four (serum), seven (urine), and eight (CSF) on a single instrument using three reagent lots (serum and urine) and one reagent lot (CSF) in a single run. The results were analyzed using weighted least squares linear regression analysis, with the intercept forced through zero. Results are summarized in the table below:

Sample	Slope	R	Range Tested (mg/dL)	Max absolute Deviation of samples (mg/dL) <sup>a</sup>	Max percent Deviation of samples <sup>b</sup>
Serum	1.0366	0.9995	2-844	0	5.2
Urine	1.0270	0.9996	1-866	0	3.0
CSF	1.0223	0.9996	2-850	0	2.7

<sup>a</sup>Samples <17 mg/dL (serum), < 10 mg/dL (urine), and <13 mg/dL (CSF) were evaluated against the absolute deviation from linearity.

<sup>b</sup>Samples ≥17 mg/dL (serum), ≥10 mg/dL (urine), and ≥13 mg/dL (CSF) were evaluated against the percent deviation from linearity.

Based on the results, the sponsor concluded that the Glucose2 test system demonstrated linearity over the claimed range of 5 - 800 mg/dL for serum, 2 - 800 mg/dL for CSF, and 1 - 800 mg/dL for urine.

## Dilution Recovery Study

A dilution study was performed to support the claimed extended measuring range. Five high concentration serum samples were diluted manually and by the instrument using saline in a 1:5 ratio. The data support the 1:5 dilution claim in the labeling.

### 3. Analytical Specificity/Interference:

The effect on the quantitation of analyte in the presence of potentially interfering substances using the Glucose2 assay was determined using serum and urine samples.

Glucose levels of approximately 40 mg/dL and 220 mg/dL in serum and approximately 15 mg/dL and 90 mg/dL in urine were tested. Each sample was assayed in 10 replicates. The tables below summarize the results for serum and urine samples indicating the highest interferent level at which the percent interference was within  $\pm 6\%$  for serum and  $\pm 10\%$  for urine. For any substance, if the difference between the test and control means was greater than the allowed difference, dose response testing and analysis was conducted to assess the highest concentration limit below which no significant interference is expected.

#### Endogenous Interference

##### *Serum*

Potential Interferent	Highest Concentration Tested Without Significant Interference
Unconjugated Bilirubin	40 mg/dL
Conjugated Bilirubin	40 mg/dL
Hemoglobin	1,000 mg/dL
Total Protein	12 g/dL
Triglycerides	1,070 mg/dL

##### *Urine*

Potential Interferent	Highest Concentration Tested Without Significant Interference
Ascorbate	200 mg/dL
Protein	50 mg/dL
Sodium Oxalate	60 mg/dL

#### Exogenous Interference

##### *Serum*

Potentially Interfering Substance	Highest Concentration Tested Without Significant Interference
Acetaminophen	16 mg/dL
Acetylcysteine	15 mg/dL
Acetylsalicylic acid	3 mg/dL
5-amino-4-imidazole-carboxamide (AIC)	0.3 mg/dL
Ampicillin-Na	8 mg/dL
Ascorbic acid	6 mg/dL
Biotin	3510 ng/mL



Potentially Interfering Substance	Highest Concentration Tested Without Significant Interference
Ca-dobesilate	6 mg/dL
Cefoxitin	660 mg/dL
Cyclosporine	0.2 mg/dL
Doxycycline	2 mg/dL
Eltrombopag	30 mg/dL
Ibuprofen	22 mg/dL
Levodopa	0.8 mg/dL
Methyldopa	2.5 mg/dL
3-methyl-(triazene-1-yl) imidazole-4-carboxamide (MTIC)	0.06 mg/dL
Metronidazole	13 mg/dL
Phenylbutazone	33 mg/dL
Rifampicin	5 mg/dL
Sodium heparin	4 U/mL
Sulfapyridine	30 mg/dL
Sulfasalazine	30 mg/dL
Temozolomide	2 mg/dL
Tetracycline	3 mg/dL
Theophylline (1,3-dimethylxanthine)	6 mg/dL

#### *Urine*

Potentially Interfering Substance	Highest Concentration Tested Without Significant Interference
Acetic acid (8.5N)	6.25 mL/dL
Boric acid	250 mg/dL
Hydrochloric acid (6N)	2.5 mL/dL
Nitric acid (6N)	5.0 mL/dL
Sodium carbonate	1.25 g/dL
Sodium fluoride	400 mg/dL

#### 4. Assay Reportable Range:

Assays reportable ranges are 5 - 800 mg/dL for serum, 2 - 800 mg/dL for CSF, and 1 - 800 mg/dL for urine.

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

This assay is traceable to SRM 965 National Institute of Standards and Technology (NIST) Standard Reference Material.

6. Detection Limit:

The limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) studies were performed in accordance with CLSI EP17-A2.

Limit of blank (LoB) study was performed by testing 5 blank samples, using 3 reagent lots over 3 days on 2 different instruments. Each day, for each reagent lot, 10 replicate measurements were recorded (60 results per reagent lot). The LoB was calculated non-parametrically at the 95th percentile for each lot. The higher LoB of the 3 reagent lots was chosen as the assay's LoB.

Limit of detection (LoD) study was performed by testing 5 low level samples using 3 reagent lots over 3 days on 2 instruments. Each day, for each reagent lot, 10 replicate measurements were recorded (60 results per reagent lot). LoD was calculated non-parametrically. The higher LoD of the 3 lots was chosen as the assay's LoD.

Limit of quantitation (LoQ) study was performed using 5 low level samples measured over 3 days on 2 instruments using 3 reagent lots. Each day, for each reagent lot, 10 replicate measurements were recorded (60 results total). The sponsor defined the LoQ as the lowest concentration at which the maximum allowable precision of 20 %CV was met.

The studies supported the following detection limit claims:

Sample Type	Units	LoB	LoD	LoQ
Serum	mg/dL	0.17	0.30	1.16
Urine	mg/dL	0.15	0.29	0.47
CSF	mg/dL	0.2	0.4	1.25

7. Assay Cut-Off:

Not applicable.

**B Comparison Studies:**

1. Method Comparison with Predicate Device:

Method comparison studies were performed in accordance with CLSI EP09c comparing the results from the candidate device to the predicate device. A minimum of 100 samples with analyte concentrations within the claimed analytical measurement ranges were evaluated for each sample matrix type respectively over four days. Passing-Bablok regression analysis was performed using the first replicate of the candidate device results compared to the mean of the duplicate results from the comparator device, and results are summarized in the table below.

Sample Type	N	Slope	Intercept	R	Concentration Range (mg/dL)
Serum	130	0.97	6	1.00	6 - 797
Urine	148	0.98	4	1.00	1- 800
CSF	135	1.00	3	1.00	3 - 772

## 2. Matrix Comparison:

A matrix comparison study was performed to evaluate the performance of K<sub>2</sub>EDTA, K<sub>3</sub>EDTA, Lithium heparin, Lithium heparin plasma separator, Sodium heparin, Sodium fluoride/EDTA, Sodium fluoride/potassium oxalate, and Potassium fluoride/citrate/EDTA samples compared to serum samples for the Glucose2 test. Sixty nine (69) paired samples were evaluated for each combination and less than 12% of the total samples were altered to cover the entire claimed measurement range. Each sample was assayed in duplicate and Passing-Bablok regression analysis was performed using the first replicate of the evaluation tube compared to the mean of the control serum measurement, and results are summarized in the table below.

Evaluation Tube Type	N	Concentration Range (mg/dL)	Correlation Coefficient (r)	Intercept	Slope
Dipotassium EDTA	69	5 - 755	1.00	3	1.00
Lithium heparin	69	5 - 740	1.00	3	1.00
Sodium heparin	69	5 - 750	1.00	2	1.01
Lithium heparin plasma separator	69	5 - 755	1.00	3	1.01
Serum separator, plastic	69	5 - 750	1.00	1	1.01
Tripotassium EDTA	69	5 - 757	1.00	1	1.01
Sodium fluoride/EDTA	69	5 - 758	1.00	2	1.01
Potassium Fluoride/Citrate/EDTA	69	5 - 755	1.00	5	1.00
Sodium Fluoride/Potassium Oxalate	69	5 - 756	1.00	0	1.02

## 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:**

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

**Reference Range (Serum/Plasma)\***

<b>Fasting</b>	<b>Range (mg/dL)</b>	<b>Range* (mmol/L)</b>
Cord	45–96	2.50–5.33
Premature	20–60	1.11–3.33
Neonate	30–60	1.67–3.33
Newborn 1 Day	40–60	2.22–3.33
Newborn > 1 Day	50–80	2.78–4.44
Child	60–100	3.33–5.55
Adult	74–100	4.11–5.55
Adult > 60 Years	82–115	4.55–6.38
Adult > 90 Years	75–121	4.16–6.72

**Urine**

	<b>Range</b>	<b>Range</b>
Random*	1–15 mg/dL	0.06–0.83 mmol/L*
24 Hour Urine Sample**	< 0.5 g/day	< 2.78 mmol/day

**CSF**

	<b>Range (mg/dL)</b>	<b>Range<sup>+</sup> (mmol/L)</b>
Infant, Child	60–80	3.33–4.44
Adult	40–70	2.22–3.89

<sup>+</sup> Alternate result units were calculated by Abbott.

\*Adeli K, Ceriotti F, Nieuwesteeg M. Reference information for the clinical laboratory. In: Rifai N, Horvath AR, Wittwer CT, editors. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. 6th ed. Elsevier; 2018:1745-1818.

\*\* Wu AHB, editor. *Tietz Clinical Guide to Laboratory Tests*. 4th ed. Saunders Elsevier; 2006:448.

## **24-Hour Urinary Excretion**

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

$$24\text{-hour excretion} = [(V \times c) \div 100\,000] \text{ g/day}$$

Where:

V = 24 hour urine volume (mL)

c = analyte concentration (mg/dL)

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

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

Where:

V = 24 hour urine volume (mL)

c = analyte concentration (mmol/L)

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

## **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.