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

I Background Information:

A 510(k) Number

K220977

B Applicant

Beckman Coulter Laboratory Systems (Suzhou) Co., Ltd.

C Proprietary and Established Names

ISE Reagents, Glucose, CRP Latex, DxC 500 AU Clinical Chemistry Analyzer

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JGS	Class II	21 CFR 862.1665 - Sodium Test System	CH - Clinical Chemistry
CEM	Class II	21 CFR 862.1600 - Potassium test system	CH - Clinical Chemistry
CGZ	Class II	21 CFR 862.1170 - Chloride test system	CH - Clinical Chemistry
CFR	Class II	21 CFR 862.1345 - Glucose test system	CH - Clinical Chemistry
NQD, DCN	Class II	21 CFR 866.5270 - C-reactive protein immunological test system	IM - Immunology
JJE	Class I	21 CFR 862.2160 - Discrete photometric chemistry analyzer for clinical use	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Sodium, Potassium, Chloride, Glucose, C-Reactive Protein

C Type of Test:

Sodium, Potassium, and Chloride: Quantitative, ion selective electrodes
C-Reactive Protein: Quantitative, latex agglutination
Glucose: Quantitative, colorimetric enzymatic assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Beckman Coulter DxC 500 AU Clinical Chemistry Analyzer is an automated chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. This system is for in vitro diagnostic use only.

The Glucose test system is for the quantitative measurement of glucose in human serum, plasma, urine and cerebrospinal fluid on Beckman Coulter AU/DxC AU analyzers. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and pancreatic islet cell carcinoma.

System reagent for the quantitative determination of C-Reactive Protein in human serum and plasma on Beckman Coulter AU/DxC AU analyzers. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases. Measurements may also be useful as an aid in the identification of individuals at risk for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events, in patients with stable coronary disease or acute coronary syndromes.

Reagents for the quantitative determination of Sodium, Potassium and Chloride concentrations in human serum, plasma and urine on the Beckman Coulter ISE modules.

The sodium test system is intended for the quantitative measurement of sodium in serum, plasma, and urine. Measurements obtained by this device are used in the diagnosis and treatment of aldosteronism (excessive secretion of the hormone aldosterone), diabetes insipidus (chronic excretion of large amounts of dilute urine, accompanied by extreme thirst), adrenal hypertension,

Addison's disease (caused by destruction of the adrenal glands), dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance.

The potassium test system is intended for the quantitative measurement of potassium in serum, plasma and urine. Measurements obtained by this device are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels.

The chloride test system is intended for the quantitative measurement of the level of chloride in plasma, serum, and urine. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

DxC 500 AU Clinical Chemistry Analyzer

IV Device/System Characteristics:

A Device Description:

DxC 500 AU Clinical Chemistry Analyzer

The Beckman Coulter DxC 500 AU Clinical Chemistry Analyzer is a fully automated random access analyzer used for the analysis of serum, plasma, urine, CSF and other body fluids. The DxC 500 AU is designed for use in low- to mid-volume laboratory settings. The DxC 500 AU Clinical Chemistry Analyzer measures analytes in samples using the same reagents, calibrators, quality control materials and other consumables used within the AU series of instruments. Applications include colorimetric, latex agglutination, and ion selective electrode.

The ISE Reagent consists of the following**:**

ISE Low Serum Standard: 130 mmol/L Na^+, 3.5 mmol/L K^+, 85 mmol/L Cl^-
ISE Mid-Standard: 4.3 mmol/L Na^+, 0.13 mmol/L K^+, 3.1 mmol/L Cl^-
ISE High Serum Standard: 160 mmol/L Na^+, 6 mmol/L K^+, 120 mmol/L Cl^-
ISE Low Urine Standard: 50 mmol/L Na^+, 10 mmol/L K^+, 50 mmol/L Cl^-
ISE High Urine Standard: 200 mmol/L Na^+, 100 mmol/L K+, 180 mmol/L Cl^-

ISE Buffer: Triethanolamine, 0.1 mol/L
ISE Reference: Potassium Chloride, 1.00 mol/L
ISE Na+ Selectivity Check: 150 mmol/L Na^+
ISE K+ Selectivity Check: 5 mmol/L K^+
ISE Internal Reference: Potassium Chloride, 3.3 mol/L and saturated silver chloride

The Glucose reagent consists of the following**:**

Reactive Ingredients: PIPES- buffer (pH 7.6), 24.0 mmol/L; NAD+, ≥ 1.32 mmol/L; Hexokinase, ≥ 0.59 KU/L; ATP, ≥ 2.0 mmol/L, Mg^{2+}, 2.37 mmol/L; and, G6P-DH, ≥1.58 KU/L

The CRP Latex reagent consists of the following**:**

Reactive Ingredients: Glycine buffer, 100 mmol/L; Latex coated with rabbit anti-CRP Antibodies, <0.5%

Materials needed but not supplied with the CRP reagent kit : CRP Latex Calibrator Normal (N) set for the Normal Application; CRP Latex Highly Sensitive (HS) Calibrator for the Highly Sensitive Application; 0.9% Saline.

B Principle of Operation:

ISE Reagents

The Ion Selective Electrode (ISE) module for Na^+, K^+, and Cl^- measurement employs crown ether membrane electrodes for sodium and potassium and a molecular oriented PVC membrane for chloride that are specific for each ion of interest in the sample. An electrical potential is developed according to the Nernst Equation for a specific ion. When compared to the Internal Reference Solution, this electrical potential is translated into voltage and then into the ion concentration of the sample.

Glucose

In this procedure, 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 (G6P-DH) specifically oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD^+) to nicotinamide adenine dinucleotide, reduced (NADH). The change in absorbance at 340/660 nm is proportional to the amount of glucose present in the sample.

CRP Latex

The CRP Latex reagent is an in vitro diagnostic device that consists of ready to use buffer and latex particles coated with rabbit anti-CRP antibodies. Immune complexes formed in solution scatter light in proportion to their size, shape, and concentration. Turbidimeters measure the reduction of incident light due to reflection, absorption or scatter. In this procedure, the measurement of the rate of decrease in light intensity transmitted (increase in absorbance) through particles suspended in solution is the result of complexes formed during the immunological reaction between the CRP of the patient serum and rabbit anti-CRP-antibodies covered on latex particles.

The same CRP Latex reagent have two different applications on the instrument: Normal Application (CRP concentrations ranging between 5.0-480 mg/L) and Highly Sensitive (Cardiac) Application (CRP concentrations ranging between 0.2- 80 mg/L).These two applications require separate calibrators and instrument workflows.

C Instrument Description Information:

1. Instrument Name:

   DxC 500 AU Clinical Chemistry Analyzer

2. Specimen Identification:

   The specimen is in a sample container with a barcode label. The analyzer identifies the specimen by scanning the barcode. This is the primary use case for sample identification. The analyzer also supports manual entry of sample IDs to support the needs of the customer.

3. Specimen Sampling and Handling:

   Specimen sampling and handling procedures are described in the DxC 500AU Chemistry Analyzer's instruction for use manual. Assay specific specimen collection and preparation procedure can be found in the respective reagent instruction for use manual.

4. Calibration:

   Calibration methods and procedures can be found in the DxC 500AU Chemistry Analyzer's instruction for use manual. Assay specific calibration information can be found in the respective reagent instruction for use manual.

5. Quality Control:

   Quality control procedures are analyte specific and details can be found in the respective reagent Instructions for Use (IFU) document.

V Substantial Equivalence Information:

A Predicate Device Name(s):
ISE Reagents, Glucose, CRP Latex, DxC 700 AU Clinical Chemistry Analyzer

B Predicate 510(k) Number(s):
K161837

C Comparison with Predicate(s):

Device & Predicate Device(s):	K220977	K161837
Device Trade Name	ISE Reagents, Glucose, CRP Latex, DxC500AU Clinical Chemistry Analyzer	ISE Reagents, Glucose, CRP Latex, DxC 700 AU Clinical Chemistry Analyzer
General Device Characteristic Similarities		
Intended Use/Indications For Use	Analyzer: An automated chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. The system is for in vitro diagnostic use only. ISE reagents: The sodium, potassium, and chloride test systems are intended for the quantitative measurement of sodium, potassium, and chloride in serum, plasma, and urine. Glucose: The glucose test system is for the quantitative measurement of glucose in human serum, plasma, urine and cerebrospinal fluid. C-Reactive Protein: System reagent for the quantitative determination of C-Reactive Protein in human serum and plasma.	Same
Single Sample Replicate Analysis	Ability to request test replicates for one sample, up to 20 replicates per sample per test.	Same
Wavelengths (nm)	Halogen Lamp	Same

	340 to 800 nm 13 wavelengths: 340, 380, 410, 450, 480, 520, 540, 570, 600, 660, 700, 750, and 800 nm (maximum of 2 wavelengths)	
Sample Types	ISE reagents: Serum, plasma, urine Glucose: Serum, plasma, urine, and cerebrospinal fluid (CSF) CRP latex: Serum, plasma	Same
General Device Characteristic Differences		
Assay Volume Requirements	CRP latex (normal application) Sample volume – 1.6 µL Reagent 1 – 120 µL Reagent 2 – 120 µL Diluent 2 - 10 µL Glucose serum and CSF Sample volume – 1.6 µL Reagent 1 – 40 µL Diluent 1 – 120 µL Reagent 2 – 20 µL Diluent 2 – 20 µL Glucose urine Sample volume – 3.0 µL Reagent 1 – 50 µL Diluent 1 – 150 µL Reagent 2 – 25 µL Diluent 2 – 25 µL	CRP latex (normal application) Sample volume – 1.2 µL Reagent 1 – 90 µL Reagent 2 – 90 µL Diluent 2 - 10 µL Glucose serum and CSF Sample volume – 1.2 µL Reagent 1 – 30 µL Diluent 1 – 90 µL Reagent 2 – 15 µL Diluent 2 – 15 µL Glucose urine Sample volume – 1.8 µL Reagent 1 – 30 µL Diluent 1 – 90 µL Reagent 2 – 15 µL Diluent 2 – 15 µL
Sample Input	Sample Rack, STAT Table	Sample Rack, STAT Table, Direct-line Sample Aspiration (for automation connections)
Throughput	Maximum 400 photometric tests/hour or 800 tests/hour (photometric + ISE)	Maximum 800 photometric tests/hour or 1200 tests/hour (photometric + ISE)

Refrigerated Reagent On-board capacity	System has one Reagent Refrigerator with 76 bottle capacity (Reagent 1+ Reagent 2)	System has two Reagent Refrigerators: Reagent 1: 60 bottle capacity Reagent 2: 48 bottle capacity

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 EP34: Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking. – First Edition. This is a partially recognized standard.

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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Repeatability and within-laboratory precision studies were designed in accordance with the CLSI EP05-A3 guideline. Per assay type, each sample was assayed in duplicate per run, two (2) runs per day for twenty (20) days in random order (N=80 for each sample) using one (1) lot of reagent, one (1) lot of calibrator on one (1) instrument.

   The precision performance for ISE reagents (Na^+, K^+ and Cl^-) was evaluated by testing spiked serum pools and urine pools. The precision performance for the glucose assay was evaluated by testing spiked serum pools, urine pools and CSF pools. The precision performance for the CRP latex (highly sensitive (cardiac) application) and CRP latex (normal application) was evaluated by testing spiked serum pools. The within-laboratory precision includes the within-run, between-run and between-day components. The precision study results are summarized in the tables below:

Analyte and Units	Sample Levels	Mean (n=80)	Repeatability (Within Run)		Within Laboratory (Total)	
			SD	%CV	SD	%CV
Sodium (mEq/L)	Serum 1	60	0.23	0.4	0.48	0.8
	Serum 2	110	0.24	0.2	0.53	0.5
	Serum 3	140	0.28	0.2	0.40	0.3
	Serum 4	172	0.36	0.2	0.57	0.3
Sodium (mEq/L)	Urine 1	21	0.24	1.1	0.37	1.7
	Urine 2	99	0.26	0.3	0.40	0.4
	Urine 3	251	0.69	0.3	1.17	0.5
	Urine 4	352	1.42	0.4	2.18	0.6
Potassium (mEq/L)	Serum 1	2.5	0.01	0.2	0.01	0.3
	Serum 2	4.5	0.01	0.2	0.01	0.3
	Serum 3	6.4	0.01	0.2	0.02	0.4
	Serum 4	8.5	0.02	0.2	0.05	0.5
Potassium (mEq/L)	Urine 1	10	0.03	0.3	0.05	0.5
	Urine 2	32	0.13	0.4	0.25	0.8
	Urine 3	100	0.27	0.3	1.02	1.0
	Urine 4	178	0.77	0.4	1.85	1.0
Chloride (mEq/L)	Serum 1	51	0.21	0.4	0.26	0.5
	Serum 2	76	0.23	0.3	0.28	0.4
	Serum 3	104	0.35	0.3	0.47	0.5
	Serum 4	150	0.70	0.5	0.81	0.5
Chloride (mEq/L)	Urine 1	26	0.20	0.8	0.28	1.1
	Urine 2	87	0.30	0.3	0.36	0.4
	Urine 3	152	0.49	0.3	0.72	0.5
	Urine 4	303	1.38	0.5	1.88	0.6
	Urine 5	375	1.59	0.4	2.32	0.6
Glucose (mg/dL)	Serum 1	51.1	0.20	0.4	0.50	0.9
	Serum 2	121.4	0.40	0.3	1.10	0.9
	Serum 3	288.9	0.70	0.3	2.90	1.0
Glucose (mg/dL)	CSF 1	36.9	0.20	0.5	0.40	1.2
	CSF 2	122.7	0.40	0.4	1.00	0.8
	CSF 3	317.2	1.30	0.4	3.20	1.0
Glucose (mg/dL)	Urine 1	56.8	0.30	0.5	0.40	0.7
	Urine 2	131.4	0.60	0.4	1.70	1.3
	Urine 3	341.8	1.50	0.4	3.00	0.9
CRP latex (highly sensitive (cardiac) application) (mg/L)	Serum 1	1.00	0.01	1.4	0.04	3.8
	Serum 2	3.01	0.02	0.6	0.03	0.8
	Serum 3	10.5	0.10	0.9	0.15	1.5
	Serum 4	70.0	0.53	0.8	0.73	1.0
	Serum 1	5.62	0.04	0.7	0.06	1.1

Analyte and Units	Sample Levels	Mean (n=80)	Repeatability (Within Run)		Within Laboratory (Total)	
			SD	%CV	SD	%CV
CRP latex (normal application) (mg/L)	Serum 2	10.12	0.06	0.6	0.11	1.1
	Serum 3	36.18	0.35	1.0	0.56	1.5
	Serum 4	248.10	1.49	0.6	2.70	1.1
	Serum 5	422.85	3.34	0.8	4.33	1.0

2. Linearity:

Linearity studies were performed in accordance with the CLSI EP-06 2nd Edition guideline. For each analyte per specimen type, equally spaced samples were prepared by mixing high and low concentration sample pools to cover the claimed measuring range. Each sample was measured in four replicates on one (1) DxC 500 AU Clinical Chemistry Analyzer using one (1) reagent lot. The data were analyzed using weighted least square regression and the regression results are summarized in the table below:

Analyte	Level of Samples	Sample Range Tested	Slope	Intercept	R^2	Claimed Measuring Range
Sodium (serum)	9	47.11 to 205.70 mEq/L	1.005	-0.691	1.000	50 to 200 mEq/L
Sodium (urine)	11	7.93 to 441.48 mEq/L	0.964	-0.658	1.000	10 to 400 mEq/L
Potassium (serum)	9	0.73 to 10.91 mEq/L	0.993	-0.055	1.000	1 to 10 mEq/L
Potassium (urine)	11	0.99 to 222.06 mEq/L	1.025	0.000	1.000	2 to 200 mEq/L
Chloride (serum)	9	25.41 to 228.69 mEq/L	0.965	0.000	1.000	50 to 200 mEq/L
Chloride (urine)	11	11.42 to 443.78 mEq/L	0.985	-0.926	1.000	15 to 400 mEq/L
Glucose, (serum)	11	7.68 to 879.73 mg/dL	1.003	0.054	1.000	10 to 800 mg/dL

Analyte	Level of Samples	Sample Range Tested	Slope	Intercept	R^2	Claimed Measuring Range
Glucose (urine)	11	7.39 to 760.22 mg/dL	1.003	-0.011	1.000	10 to 700 mg/dL
Glucose (CSF)	11	7.23 to 901.37 mg/dL	1.002	0.109	1.000	10 to 800 mg/dL
CRP latex (normal application)	15	0.78 to 516.08 mg/L	1.020	0.076	1.000	5 to 480 mg/L
CRP latex (highly sensitive (cardiac) application)	10	0.12 to 11.45 mg/L	0.967	0.061	0.998	0.2 to 80 mg/L
	10	0.12 to 81.32 mg/L	1.008	0.007	1.000	

3. Analytical Specificity/Interference:

Interference studies were performed in accordance with the CLSI EP07, 3rd Edition guideline. Common endogenous substances were evaluated for each candidate assay to determine the potential interference effects to the assay performance.

For each assay type, samples at high and low concentrations were prepared (see table below) and each sample was further divided into two aliquots: test samples (with added interference substances) and control samples (without interference substances). Each sample was assayed in five (5) replicates. The results of the spiked samples were compared to the results of non-spiked samples for each assay. At the following concentrations, the percentage difference was less than ± 10% between the test samples results and control samples results.

Analyte	Analyte Concentrations Tested	Interferent Substances	Highest Concentration Tested Without Significant Interference
Na^+ (serum)	130 mEq/L 150 mEq/L	Intralipid	500 mg/dL
		Bilirubin	40 mg/dL
		Hemoglobin	250 mg/dL
K^+ (serum)	3 mEq/L 5 mEq/L	Intralipid	500 mg/dL
		Bilirubin	40 mg/dL
		Hemoglobin	70 mg/dL
Cl^- (serum)	90 mEq/L 110 mEq/L	Intralipid	500 mg/dL
		Bilirubin	40 mg/dL
		Hemoglobin	500 mg/dL
Glucose (serum)	40 mg/dL 220 mg/dL	Intralipid	700 mg/dL
		Bilirubin	40 mg/dL
		Hemoglobin	500 mg/dL
Glucose (urine)	36 mg/dL 216 mg/dL	Bilirubin	40 mg/dL
		Hemoglobin	500 mg/dL

Analyte	Analyte Concentrations Tested	Interferent Substances	Highest Concentration Tested Without Significant Interference
Glucose (CSF)	36 mg/dL 216 mg/dL	Bilirubin	40 mg/dL
		Hemoglobin	500 mg/dL
CRP latex (highly sensitive (cardiac) application) (serum)	1 mg/L 20 mg/L	Intralipid	1000 mg/dL
		Bilirubin	40 mg/dL
		Hemoglobin	500 mg/dL
		Rheumatoid Factor	500 IU/mL
CRP latex (highly sensitive (cardiac) application) (serum)	1 mg/L 3 mg/L 20 mg/L	Triglyceride	500 mg/dL
CRP latex (normal application) (serum)	15 mg/L 100 mg/L 200 mg/L	Triglyceride	500 mg/dL
	15 mg/L 200 mg/L	Rheumatoid Factor	500 IU/mL

CRP Latex exogenous interference study

Sixteen (16) commonly used drugs were assessed for potential exogenous interference for the CRP latex (highly sensitive (cardiac) application) and the CRP latex (normal application). The exogenous substances were tested at approximately three (3) times the peak therapeutic concentrations as recommended by the CLSI EP37 guideline. Samples with three (3) analyte levels were divided into paired control samples (without interference substances) and test samples (with interference substances). Each test sample and control sample was assayed in 5 replicates with two (2) lot of reagents and calibrators on one DxC 500AU Analyzer. The results of the test samples were compared to the results of the control samples. At the following concentrations, the percent difference between the results of the spiked samples compared to the results of the control samples was less than ± 4%.

Analyte Concentrations Tested	Interferent Substances	Highest Concentration Tested Without Significant Interference
CRP latex(highly sensitive (cardiac) application) 1 mg/L 3 mg/L 20 mg/L	Acetaminophen	15.6 mg/dL
	Acetylsalicylic	3 mg/dL
	Amoxicillin	5.4 mg/dL
	Ascorbic Acid	5.25 mg/dL
	Atorvastatin	0.075 mg/dL
	Azithromycin	1.11 mg/dL
	Cephalexin	12.6 mg/dL
	Ciprofloxacin	1.2mg/dL

Analyte Concentrations Tested	Interferent Substances	Highest Concentration Tested Without Significant Interference
CRP latex (normal application) 15 mg/L 100 mg/L 200 mg/L	Fluconazole	2.55 mg/dL
	Ibuprofen	21.9 mg/dL
	Lisinopril	0.0246 mg/dL
	Metformin	1.2 mg/dL
	Methotrexate	136 mg/dL
	Naproxen	36 mg/dL
	Omeprazole	0.84 mg/dL
	Prednisone	0.0099 mg/dL

The following is a new limitation for the Glucose reagent:

"Eltrombopag and its metabolites may interfere with this assay causing erroneously high patient results."

The other limitations remain the same as described in K161837.

4. Assay Reportable Range:

Assays reportable ranges are described in the linearity section (VII.A.2 above).

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

The traceability of the ISE Reagents and Glucose is unchanged (cleared in K921718 and K043460, respectively).

CRP Latex: Assay is traceable to ERM DA472/IFCC.

6. Detection Limit:

Detection limit studies were designed in accordance with the CLSI EP17-A2 guideline. The limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) for the Glucose assay, the CRP Latex (highly sensitive (cardiac) application) and the CRP Latex (normal application) were determined by running replicate measurements on blank and low-level samples across multiple days using two (2) reagent lots on one DxC 500 AU Analyzer, with each lot evaluated separately for each parameter. Per assay and specimen type, a total of 72 blank replicates were generated per reagent lot (4 blank samples ran in replicates of 6 for 3 days) to determine the LoB. For LoD and LoQ determinations, 250 low-level sample replicates were generated per Glucose assay specimen type per reagent lot (10 low-level samples ran in replicates of 5 for 5 days), 325 low-level sample replicates were generated for the CRP Latex (highly sensitive (cardiac) application) per reagent lot (13 low-level samples ran in replicates of 5 for 5 days), and 500 low-level sample replicates were generated for the CRP Latex (normal application) per reagent lot (10 low-level samples ran in replicates of 10 for 5 days). The LoB was determined following the classic approach and the LoD and LoQ were determined following the precision profile approach described in the guideline. The sponsor defines the LoQ as the lowest concentration with a within-laboratory precision of ≤

20% CV. The claimed LoB, LoD, and LoQ are the highest estimates across the two (2) lots. The detection limits for glucose, CRP latex (highly sensitive (cardiac) application) and CRP latex (normal application) are summarized below:

Analyte	Sample Type	Units	LoB	LoD	LoQ	Claimed measuring Range
CRP latex (highly sensitive (cardiac) application)	Serum	mg/L	0.01	0.03	0.06	0.2 – 80
CRP latex (normal application)	Serum	mg/L	0.28	0.48	0.89	5 – 480
Glucose	Serum	mg/dL	0.55	1.02	1.42	10 – 800
	Urine	mg/dL	0.48	0.92	1.41	10 – 700
	CSF	mg/dL	0.4	0.7	1.10	10 – 800

The lower limits of the measuring range for the ISE Reagents (Na^+, K^+, Cl^-) are supported by the linearity studies.

7. Assay Cut-Off:

   Not applicable.

8. Accuracy (Instrument):

   Refer to the method comparison study.

9. Carry-Over:

   Carry-over study was performed for the CRP Latex (highly sensitive (cardiac) application) with the DxC 500AU contamination parameters that provide additional cleaning of the sample probe before and after each CRP sample is tested. The study supports the carry-over information provided in the CRP assay Instruction-for-Use.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   Method comparison studies were performed in accordance with the CLSI EP09c guideline comparing the results from the candidate devices to the predicate devices. A minimum of 100 samples with analyte concentrations within the claimed analytical ranges were evaluated for the ISE Reagents, Glucose, CRP Latex (highly sensitive (cardiac) application) and CRP Latex (normal application) for each sample type respectively. Each sample was assayed in duplicate by the candidate method and the comparator method on the same day. Weighted Deming regression analysis was performed using the first replicate result only, and results are summarized in the table below.

Analyte (Unit)	Sample Type	N	Slope	Intercept	R	Tested Range by Comparator	Claimed Measuring Range
Sodium (mEq/L)	Serum	120	1.018	-2.077	0.9995	62-194	50-200
Potassium (mEq/L)	Serum	119	1.015	-0.048	0.9998	1.4-9.3	1.0 - 10.0
Chloride (mEq/L)	Serum	120	1.007	-0.379	0.9997	54-186	50 – 200
Sodium (mEq/L)	Urine	117	1.008	-0.150	0.9999	11-396	10 – 400
Potassium (mEq/L)	Urine	120	1.000	0.194	0.9998	2.1-182.8	2.0 – 200.0
Chloride (mEq/L)	Urine	114	1.002	-0.291	0.9999	18-379	15 – 400
Glucose (mg/dL)	Serum	133	0.986	0.227	0.9999	14-773	10 – 800
	Urine	113	1.001	-0.216	1.000	11 – 688	10 –700
	CSF	111	1.009	0.891	0.9998	34 - 772	10 – 800
CRP Latex (highly sensitive (cardiac) application) (mg/L)	Serum	101	0.968	0.009	0.9996	0.21-9.38	0.2 – 80
	Serum	115	0.99	0.0421	0.9997	0.21 - 72.99	
CRP Latex(normal application) (mg/L)	Serum	120	0.993	0.606	0.9995	5.16 to 470.45	5 – 480

2. Matrix Comparison:

ISE reagents (Na^+, K^+, Cl^-):

A matrix comparison study was performed to demonstrate the equivalence between serum and plasma samples when measuring sodium, potassium and chloride on the DxC 500 Analyzer. Each study utilized freshly drawn paired serum and plasma samples from over forty (40) donors. Less than 20% of the total samples were altered by diluting or spiking in order to cover the claimed measuring range. For each pair of samples, only one measurement was obtained for the evaluation tube and one measurement for the serum control tube. Weighted Deming regression analysis was performed, and the results are summarized below:

Analyte	Matrix	N	Test Range (serum) (mEq/L)	Slope	Intercept	R
Na+	Serum vs LiHep	47	53.85 - 188.38	0.99	1.953	1.00
K+	Serum vs LiHep	46	1.39 – 9.39	0.98	-0.127	0.98
Cl-	Serum vs LiHep	47	50.30 – 189.59	1.01	0.100	1.00
Na+	Serum vs AmHep	47	53.85 - 188.38	1.00	0.908	0.99
K+	Serum vs AmHep	46	1.39 – 9.39	0.96	0.027	0.99
Cl-	Serum vs AmHep	47	50.31 – 189.59	1.00	0.605	1.00

The results of the matrix comparison studies support the sponsor's claim that serum, lithium heparin, and ammonium heparin plasma samples are suitable for use on the candidate ISE Reagents.

Glucose :

A matrix comparison study was performed on the DxC AU 500 Analyzer to evaluate the performance of K_2EDTA, K_3EDTA, Fluoride Oxalate, and Lithium Heparin plasma samples compared to serum samples for the Glucose test. Fifty-nine (59) paired samples were evaluated for each combination and less than 16% of the total samples were altered to cover the entire claimed measurement range. For each set of samples, only one measurement was obtained for the evaluation tube and one measurement for the serum sample control. Weighted Deming regression analysis was performed, and the results are summarized below:

Matrix	N	Test Range (mg/dL) (serum)	Slope	Intercept	R
Serum vs Sodium Fluoride Oxalate	59	15.28 – 727.74	0.996	2.112	0.9998
Serum vs K_2-EDTA	59		1.000	1.198	0.9999
Serum vs K_3-EDTA	59		1.008	-1.069	0.9998
Serum vs Lithium Heparin	59		1.003	1.207	0.9999

The results of the matrix comparison studies support the claim that serum, K2-EDTA, K3-EDTA lithium heparin, and sodium fluoride oxalate plasma samples are suitable for use on the candidate Glucose test.

CRP Latex (highly sensitive (cardiac) application)

Matrix comparison studies were performed on the DxC AU 500 Analyzer to evaluate the performance of K_2-EDTA, K_3 EDTA and Lithium Heparin plasma samples versus serum samples on the CRP Latex (highly sensitive (cardiac) application). Forty-six (46) paired samples were evaluated for each combination and less than 7% of the total samples were

altered. For each set of samples, only one measurement was obtained for the evaluation tube and one measurement for the serum sample control. Weighted Deming regression analysis was performed. The results support the use of K_2-EDTA, K_3 EDTA, lithium heparin plasma samples on the candidate CRP Latex (highly sensitive (cardiac) application).

CRP Latex (normal application)

Matrix comparison studies were performed on the DxC AU 500 Analyzer to evaluate the performance of K_2-EDTA, K_3 EDTA and Lithium Heparin plasma samples versus serum samples for the CRP Latex (normal application). Forty (40) paired samples were evaluated for each combination. For each set of samples, only one measurement was obtained for the evaluation tube and one measurement for the serum sample control. Weighted Deming regression analysis was performed. The results support the use of K_2-EDTA, K_3 EDTA, and lithium heparin plasma samples on the candidate CRP Latex (normal application).

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 following information, cited from literature, will be included in the labeling for the candidate devices.

Sodium, serum and plasma: 136-145 mEq/L[1]
Sodium, urine: 40-220 mEq/day[1]

Potassium, serum: 3.5-5.1 mEq/L[1]
Potassium, plasma: 3.4-4.53 mEq/L[1]
Potassium, urine: 25-125 mEq/day [1]

Chloride, serum and plasma: 98-107 mEq/L[1]
Chloride, urine: 110-250 mEq/day[1]

Glucose, serum, adult: 74-109 mg/dL[2]

Glucose, serum, newborn: 36-99 mg/dL[2]
Glucose, cerebrospinal fluid, adult: 40-70 mg/dL[1]
Glucose, cerebrospinal fluid, child: 60-80 mg/dL[1]

CRP latex (highly sensitive (cardiac) application): Recommended Cardiac risk assessment categories by the America Heart Association (AHA): low < 1 mg/L, Average 1.0 to 3.0 mg/L, high > 3 mg/L. [3]

CRP latex (normal application):
10-50 mg/L indicates mild inflammation, 50 – 100 mg/L indicates more severe inflammation and > 100 mg/L represents serious process and frequently indicates the presence of a bacterial infection. [3]

Reference:

1. Tietz, N.W., editor, Clinical Guide to Laboratory Tests, 5th Edition, W.B Saunders 2012.
2. Thomas L, ed. Blutglucose. In: Thosmas L. ed. Laboratory and Diagnosis, 6th ed., Frankfurt/Main: TH-Books 2005; 193-199.
3. Thomas, L., Clinical Laboratory Diagnostics Use and Assessment of Clinical Laboratory Result, 1st Edition, TH-Books Verlagsgesellschaft, Frankfurt, Germany, 1998.

F Other Supportive Instrument Performance Characteristics Data:

Not applicable.

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.