July 20, 2023

Beckman Coulter Laboratory Systems (Suzhou) Co., Ltd.
Tracy Jin
Sr. Regulatory Affairs
No. 181 West Su Hong Road, Suzhou Industrial Park
Suzhou, Jiangsu, CN 215021
China

Re: K220977
Trade/Device Name: ISE Reagents, Glucose, CRP Latex, DxC 500 AU Clinical Chemistry Analyzer
Regulation Number: 21 CFR 862.1665
Regulation Name: Sodium Test System
Regulatory Class: Class II
Product Code: JGS, CEM, CGZ, CFR, NQD, DCN, JJE
Dated: January 12, 2023
Received: January 12, 2023

Dear Tracy Jin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Paula V. Caposino -S

Paula Caposino, Ph.D.
Acting Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K220977

Device Name
DxC 500 AU Clinical Chemistry Analyzer;
Glucose; CRP Latex; ISE Reagents

Indications for Use *(Describe)*
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 of 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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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1.0 Submitted By

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2.0 Date of Preparation

July 19, 2023

3.0 Device Name(s)

3.1 DxC 500 AU Clinical Chemistry Analyzer

Proprietary Name: DxC 500 AU Clinical Chemistry Analyzer
Common Name: DxC 500 AU

510 (K) Number: K220977
Class: Class I
Classification Name: Discrete photometric chemistry analyzer for clinical use
Regulation Number: 21 CFR § 862.2160
Product Code: JJE

3.2 ISE Reagents

Proprietary Name: ISE Reagents
Common Name: ISE Reagents

Class: Class II
Classification Name/Regulation Number/Product Code:
Sodium test system 21 CFR § 862.1665 [JGS]
Potassium test system 21 CFR § 862.1600 [CEM]
Chloride test system 21 CFR § 862.1170 [CGZ]

3.3 Glucose

Proprietary Name: Glucose
Common Name: Glucose
Class: Class II
Classification Name: Glucose test system
Regulation Number: 21 CFR § 862.1345
Product Code: CFR

3.4 CRP Latex

Proprietary Name: CRP Latex
Common Name: CRP Latex
Class: Class II
Classification Name: C-reactive protein immunological test system
Regulation Number: 21 CFR § 866.5270
Product Code: DCN, NQD

4.0 Predicate Devices

Candidate(s)	Predicate	Manufacturer
DxC 500 AU Clinical Chemistry Analyzer	DxC 700 AU Clinical Chemistry Analyzer (K161837)	Beckman Coulter, Inc.
ISE Reagents: Sodium, Potassium and Chloride	ISE Reagents: Sodium, Potassium and Chloride (K161837)	
Glucose	Glucose (K161837)	
CRP Latex	CRP Latex (K161837)	

5.0 Device Description

5.1 DxC 500 AU Clinical Chemistry Analyzer

The Beckman Coulter DxC 500 AU Clinical Chemistry Analyzer carries out automated analysis of serum, plasma, urine samples and other body fluids and automatically generates results. The device is an automated photometric clinical 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. Electrolyte measurement is performed using a single cell Ion Selective Electrode (ISE) which is also common among the other members of the AU family.

5.2 ISE Reagents

The ISE module for Na+, K+, and Cl- 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.

5.3 Glucose

In this Beckman Coulter 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.

5.4 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. In this procedure, the measurement of the rate of decrease in light intensity transmitted 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 coated on latex particles. Two measuring range settings are available: Normal application (CRP Concentrations ranging between 5.0-480 mg/L) and Highly Sensitive (Cardiac) Application- (CRP concentrations ranging between 0.2-80mg/L).

6.0 Indications for Use

6.1 DxC 500 AU Clinical Chemistry Analyzer

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.

6.2 ISE Reagents (Sodium, Potassium and Chloride)

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.

6.3 Glucose

The Glucose test system is for the quantitative measurement of glucose in human serum, plasma, urine and cerebrospinal fluid on Beckman Coulter AU/DxC analyzers. 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.

6.4 CRP Latex

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.

7.0 Comparison to the Predicate

The DxC 500 AU Clinical Chemistry Analyzer is a member of Beckman Coulter's AU/DxC AU series of automated photometric analyzers that includes the DxC 700 AU Clinical Chemistry Analyzer (K161837) to which the substantial equivalence is claimed. The devices share common design characteristics and modes of operation. The key features are summarized in Tables 7.1 through 7.4.

Table 7.1 Predicate Device Comparison

Feature	Predicate Device: DxC 700 AU Clinical Chemistry Analyzer (K161837)	Predicate Device: DxC 500 AU Clinical Chemistry Analyzer (K220977)
Intended Use:	Automated chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. For in vitro diagnostic use only. Applications include colorimetric, latex agglutination and ion selective electrode.	Same (removal of test applications only): 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.
Classification:	Analyzer, chemistry (photometric, discrete), for clinical use has been classified as Class I, JJE by the Clinical Chemistry and Clinical Toxicology Devices Panel, (21 CFR 862.2160).	Same
Sample Handling		
Sample Containers	10 sample tubes on a Rack	7 sample tubes on a Rack
Sample Volume	1.0 to 25.0 µL	Same
Sample Types	Serum, plasma, urine, CSF, and whole blood (HbA1c only)	Same
Sample Input	Sample Rack, STAT Table, Direct-line Sample Aspiration (For Automation Connections)	Sample Rack, STAT Table

Feature	Predicate Device: DxC 700 AU Clinical Chemistry Analyzer (K161837)	Candidate Device: DxC 500 AU Clinical Chemistry Analyzer (K220977)
Single Sample Replicate Analysis	Ability to request test replicates for one sample, up to 20 replicates per sample per test.	Same
Sample Analysis		
Wavelength (nm)	Halogen Lamp 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)	Same
Type of Measurement	• End-point assay • Rate assay • Fixed point assay • Electrode method (ISE)	Same
Throughput	Maximum 800 photometric tests/hour or 1200 tests/hour (photometric + ISE)	Maximum 400 photometric tests/hour or 800 tests/hour (photometric + ISE)
Reagent Handling		
Reagent Identification	Barcode and fixed position in the reagent carousel	Same
Refrigerated Reagent On-board Capacity	System has two Reagent Refrigerators: Reagent 1: 60 bottle capacity Reagent 2: 48 bottle capacity	System has one Reagent Refrigerator with 76 bottle capacity (Reagent 1+Reagent 2)

Feature	Predicate Device: DxC 700 AU Clinical Chemistry Analyzer (K161837)	Candidate Device: DxC 500 AU Clinical Chemistry Analyzer (K220977)
ISE Reagents	Three ISEs	Same
Reagent Storage Temperature	Refrigeration temperature: 4 to 12 °C (39.2 to 53.6 °F)	Same
Reagent Loading during Analysis	Reagent bottles can be changed while the instrument continues to measure patient samples. A reagent bottle can be added or changed within 5 minutes of request.	Reagent bottles can be changed while the instrument continues to measure patient samples. A reagent bottle can be added or changed within 5 minutes 30 seconds of request.
Computers/OS		
CPU	Intel Processor running Windows 7 64bit	Intel Processor running Windows 10 64bit
Display/Monitor	24” display with touch screen	21.5” display with touch screen
Handheld Barcode Reader	Provided for reading 1D and 2D barcodes	Same
Software		
GUI Application	User interface which will be common to new Beckman Coulter IVD systems	Re-engineered GUI; Latest common GUI design to Beckman Coulter IVD systems
User Help	HTML version of IFU is accessible with built-in interactive video.	HTML version of IFU is accessible in User Help

Feature	Predicate Device: DxC 700 AU Clinical Chemistry Analyzer (K161837)	Candidate Device: DxC 500 AU Clinical Chemistry Analyzer (K220977)
Laboratory Information System (LIS) Interfaces	Similar with LIS ASTM 1394 and AU unique LIS protocol	Similar with LIS ASTM 1394 protocol
Laboratory Automation System (LAS) Interfaces	Beckman LAS interface for Direct Track Sampling system	Not supported
Real-Time Solutions (RTS) support	Interface to RTS via PRO*Service* protocol which is made by Beckman Coulter Remote software installation capabilities.	Interface to RTS via remote service protocol which is made by Beckman Coulter
External printers	USB and LAN interfaced printers	USB interfaced printers

Table 7.2 ISE (Sodium, Potassium & Chloride) Predicate Device Comparison

Feature	Predicate Device: ISE – Sodium, Potassium and Chloride (K161837)	Candidate Device: ISE –Sodium, Potassium and Chloride (K220977)
Intended Use	Reagent for the quantitative determination of Sodium, Potassium and Chloride concentrations in human serum and urine on the Beckman Coulter ISE modules.	Same
Measurement	Quantitative	Same
Instrument Required	DxC 700 AU Beckman Coulter Analyzer	DxC 500 AU Beckman Coulter Analyzer
Methodology	Indirect ISE	Same
Reagent form and storage	Liquid, on-board storage	Same
Specimen Type	Serum, plasma, and urine	Same
Calibrator	Low Serum Standard (Cat # AUH1014) and High Serum Standard (Cat # AUH1015) Low/High Urine Standard (Cat # AUH1016)	Same
Calibration Stability	Calibrate daily.	Same
Reagent stability	ISE reagents are stable up to 90 days when stored in accordance with the IFU instructions.	Same

Feature	Predicate Device: ISE – Sodium, Potassium and Chloride (K161837)	Candidate Device: ISE –Sodium, Potassium and Chloride (K220977)
Analytical Range	Serum Na^+ 50 – 200 mEq/L K^+ 1.0 – 10.0 mEq/L Cl^- 50 – 200 mEq/L Urine Na^+ 10 – 400 mEq/L K+ 2.0 – 200.0 mEq/L Cl^- 15 – 400 mEq/L	Same
Interferences	Bilirubin (Na/K/Cl): NSI* up to 40 mg/dL. Lipemia (Na/K/Cl): NSI up to 500 mg/dL. Hemoglobin (Na): NSI up to 250 mg/dL. Hemoglobin (K): NSI up to 70 mg/dL. Hemoglobin (Cl): NSI up to 500 mg/dL.	Same
Precision (serum, urine)	Within-run CV < 3% Total Precision CV < 5%.	Same

*NSI – No significant interference (Chloride ±2.5%, Potassium ±0.25 mEq/L, Sodium ±2mEq/L)

Table 7.3 Glucose Predicate Device Comparison

Feature	Predicate Device: Glucose (K161837)	Candidate Device: Glucose (K220977)
Intended Use	The Glucose test system is for the quantitative measurement of glucose in human serum, plasma, urine, and cerebrospinal fluid on Beckman Coulter AU analyzers.	Same; updated instrument family branding 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.
Measurement	Quantitative	Same
Instrument Required	DxC 700 AU Beckman Coulter Analyzer.	DxC 500 AU Beckman Coulter Analyzer
Methodology	Photometric	Same
Reagent form and storage	Liquid, on-board storage	Same
Specimen Type	Serum, plasma, urine, and cerebrospinal fluid	Same
Calibrator	Chemistry Calibrator (Cat # DR0070) Urine Calibrator (Cat # DR0090)	Same
Calibration Stability	30 days	Same
Onboard Stability	30 days refrigerated	Same

Feature	Predicate Device: Glucose (K161837)	Candidate Device: Glucose (K220977)
Analytical Range	Serum, plasma, and CSF: 10 - 800 mg/dL Urine: 10 - 700 mg/dL	Same
Interferences	Bilirubin: NSI* up to 40 mg/dL. Lipemia: NSI up to 700 mg/dL. Hemoglobin: NSI up to 500 mg/dL	Same
Precision (serum, urine)	Within-run CV < 3% Total Precision CV < 3%.	Same

*NSI – No significant interference designates recovery within 10% of the initial value.

Table 7.4 CRP Predicate Device Comparison

Feature	Predicate Device: CRP Latex (K161837)	Candidate Device: CRP Latex (K220977)
Intended Use	System reagent for the quantitative determination of C-Reactive Protein in human serum and plasma on *Beckman Coulter 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.	Same; updated instrument family branding only. 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.

Feature	Predicate Device: CRP Latex (K161837)	Candidate Device: CRP Latex (K220977)
Measurement	Quantitative	Same
Instrument Required	DxC 700 AU Beckman Coulter Analyzer	DxC 500 AU Beckman Coulter Analyzer
Methodology	Latex enhanced Immunoturbidimetric	Same
Antibody	Rabbit Anti-CRP Antibodies	Same
Reagent form and storage	Liquid, on-board storage	Same
Specimen Type	Serum and plasma	Same
Calibrator	CRP Latex Highly Sensitive Calibrator (Cat # ODC0027) for the Highly Sensitive (Cardiac) Application. CRP Latex Normal Calibrator (Cat # ODC0026) for the Normal Application	Same
Calibration Stability	90 days refrigerated	Same
Onboard Stability	90 days refrigerated	Same
Analytical Range	CRP High Sensitivity 0.2 - 80 mg/L CRP Normal 1.0 – 480 mg/L	CRP High Sensitivity 0.2 - 80 mg/L CRP Normal 5.0 – 480 mg/L

Feature	Predicate Device: CRP Latex (K161837)	Candidate Device: CRP Latex (K220977)
Interferences	Bilirubin: <5% at CRP concentrations of 1 mg/L up to 40 mg/dL bilirubin Lipemia: <10% at CRP concentrations of 1 mg/L up to 1000 mg/dL intralipid Hemoglobin: <5% at CRP concentrations of 1 mg/L up to 500 mg/dL hemoglobin	Same
Precision (serum)	Within-run: SD ≤0.20 mg/L Total Precision: SD ≤0.02 mg/L	Same

8.0 Comparison Testing

Substantial equivalence was demonstrated through non-clinical (bench) studies as listed below. CLSI study protocols were used to verify the performance claims stated in the reagent IFUs and ensure that the technological differences between the candidate and predicate analyzer models did not adversely affect safety and effectiveness.

Method Comparison
Linearity
Precision
Sensitivity
Reference Interval
Interference

9.0 Summary of Performance Data

The data contained in the Premarket Notification supports a finding of substantial equivalence to the measurand test systems already in commercial distribution.

9.1 Method Comparison with Predicate Device

Method comparison and bias estimation experiments were designed in accordance with the CLSI Guideline EP09C-ED3 *"Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Third Edition"*. The patient correlation studies demonstrated equivalence between the representative assays on the candidate DxC 500 AU analyzer and the predicate DxC 700 AU analyzer. The study results in Table 9.1 are based on Weighted Deming regression analysis.

Table 9.1 Method Comparison Data Summary

Reagent/ ISE	Sample Type	N	Slope	Bias	Intercept	R
hsCRP (Cardiac)	Serum	115	0.990	0.4% at 3mg/L	0.0421	0.9997
CRP Normal	Serum	120	0.993	5.4% at 10 mg/L	0.606	0.9995
Glucose	Serum	133	0.986	-1% at 100 mg/dL	0.227	0.9999
Glucose	Urine	113	1.001	-0.3% at 50 mg/dL	-0.216	1.0000
Glucose	CSF	111	1.009	3% at 50 mg/dL	0.891	0.9998
ISE Sodium	Serum	120	1.018	0.2% at 130 mEq/L 0.5% at 160 mEq/L	-2.077	0.9995
ISE Potassium	Serum	119	1.015	-0.1% at 3 mEq/L 0.7% at 6 mEq/L	-0.048	0.9998
ISE Chloride	Serum	120	1.007	0.3% at 90 mEq/L 0.4% at 120 mEq/L	-0.379	0.9997
ISE Sodium	Urine	117	1.008	0.6% at 60 mEq/L 0.7% at 180 mEq/L	-0.150	0.9999
ISE Potassium	Urine	120	1.000	1.3% at 15 mEq/L 0.2% at 80 mEq/L	0.194	0.9998
ISE Chloride	Urine	114	1.002	-0.4% at 50 mEq/L 0.05% at 170 mEq/L	-0.291	0.9999

9.2 Linearity/Reportable Range:

Analytical range (linearity) studies were designed in accordance with the CLSI guideline EP06-ED2 *"Evaluation of the Linearity of Quantitative Measurement Procedures".*

High and low sample pools were prepared and inter-diluted to achieve analyte concentrations spanning the claimed linear range of each assay. Test samples were assayed in quadruplicate on the DxC 500 AU analyzer. The study data demonstrates linearity throughout the claimed analytical measuring range of each assay, as represented in the Table 9.2 below.

Table 9.2 Linearity Data Summary

Reagent and Sample Type	Units	Acceptance Criteria		Results		Pass/ Fail
		Linear Range	Allowable Difference (±)	Linear From	Linear To	
hsCRP (Cardiac) Serum	mg/L	0.2 - 80	12% or 0.15 mg/L	0.124	81.35	Pass
CRP Normal Serum	mg/L	1.0 - 480	12% or 0.2 mg/L	0.78	516.408	Pass
Glucose Serum	mg/dL	10 - 800	5% or 0.5 mg/dL	7.68	879.73	Pass
Glucose CSF	mg/dL	10 - 800	5% or 0.5 mg/dL	7.23	901.37	Pass
Glucose Urine	mg/dL	10 - 700	5% or 0.5 mg/dL	7.39	760.22	Pass
Sodium Serum	mEq/L	50 - 200	2.5% or 3.25 mEq/L	47.11	205.87	Pass
Potassium Serum	mEq/L	1.0 - 10.0	4% or 0.12 mEq/L	0.727	10.835	Pass
Chloride Serum	mEq/L	50 - 200	4% or 3.6 mEq/L	27.66	223.58	Pass
Sodium Urine	mEq/L	10 - 400	5% or 1.2 mEq/L	7.93	441.48	Pass
Potassium Urine	mEq/L	2.0 - 200.0	7% or 1 mEq/L	1.066	225.165	Pass
Chloride Urine	mEq/L	15-400	6% or 3.6 mEq/L	11.42	433.78	Pass

9.3 Sensitivity (Detection Limits):

LOD and LOQ studies were designed in accordance with CLSI guideline EP17-A2 "*Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures Approved Guideline - Second Edition"*. The experimental design consisted of replicate measurements on blank and low-level samples across multiple days using multiple reagent lots.

The LOB, LOD, and LOQ results are summarized in the Table 9.3 below. The representative reagents met the established LOQ specifications when tested on the DxC 500 AU analyzer, and the LOQ results were below the claimed measuring range for each assay.

Table 9.3 Reagent Sensitivity Data Summary

Reagent and Sample Type	Units	Low End of Measuring Range	LOD Spec	LOQ Spec	LOB	LOD	LOQ
CRP Normal Serum	mg/L	5.00	≤5.0	≤ 5.0 at ≤ 20% CV	0.28	0.48	0.89
hsCRP (Cardiac) Serum	mg/L	0.20	≤ 0.2	≤ 0.2 at ≤ 20% CV	0.01	0.03	0.06
Glucose Serum	mg/dL	10	≤ 10	≤ 10 at ≤ 20% CV	0.55	1.02	1.42
Glucose Urine	mg/dL	10	≤ 10	≤ 10 at ≤ 20% CV	0.48	0.92	1.41
Glucose CSF	mg/dL	10	≤ 10	≤ 10 at ≤ 20% CV	0.4	0.7	1.1

9.4 Precision/Reproducibility:

Repeatability (within-run) and within-laboratory (total) precision studies were designed from the CLSI guideline EP05-A3 *"Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition".* The precision was verified on the DxC 500 AU using one lot of reagent and one lot of calibrator and utilized duplicate sample analysis, twice daily, over the course of 20 days (n=80) for multiple sample levels.

All assays met the performance precision specifications and provided data to support the precision claims in the IFUs. The results are summarized in Tables 9.4.1 and 9.4.2 below:

Table 9.4.1 Reagent Precision Data Summary

Reagent and Units	Sample Levels	Mean (n=80)	Repeatability (Within Run)		Within Laboratory (Total)	
			SD	% CV	SD	% CV
hsCRP (Cardiac) (mg/L)	Serum 1	1.06	0.01	1.2	0.01	1.3
	Serum 2	3.01	0.02	0.6	0.03	0.8
	Serum 3	9.10	0.08	0.9	0.09	1.0
	Serum 4	10.5	0.10	0.9	0.15	1.5
	Serum 5	70.0	0.53	0.8	0.73	1.0
CRP Normal (mg/L)	Serum 1	5.62	0.04	0.7	0.06	1.1
	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
Glucose (mg/dL)	Serum 1	51.1	0.2	0.4	0.5	0.9
	Serum 2	121.4	0.4	0.3	1.1	0.9
	Serum 3	288.9	0.7	0.3	2.9	1.0
Glucose (mg/dL)	CSF 1	36.9	0.2	0.5	0.4	1.2
	CSF 2	122.7	0.4	0.4	1.0	0.8
	CSF 3	317.2	1.3	0.4	3.2	1.0
Glucose (mg/dL)	Urine 1	56.8	0.3	0.5	0.4	0.7
	Urine 2	131.4	0.6	0.4	1.7	1.3
	Urine 3	341.8	1.5	0.4	3.0	0.9

Table 9.4.2 ISE Precision Data Summary

Reagent 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
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
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
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)	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)	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

9.5 Interferences (Analytical Specificity):

Interference studies were designed in accordance with CLSI Guideline EP07, 3rd Edition *"Interference Testing in Clinical Chemistry; Approved Guideline"*. All test samples were assayed (n=5) at two analyte levels. The sample pools were tested at different levels of interferents to determine the magnitude of their effect. The data analysis involved calculating the recovery difference between samples with and without the potential interfering substances. The results for Glucose and ISE are summarized in Table 9.5 below. The results for CRP Normal and CRP Highly Sensitive (Cardiac) applications are summarized on page 5-27 and 5-28. All assays met the performance specifications and provided data to support the interference claims in the IFUs.

Table 9.5 Interference Data Summary

Reagent/ Sample Type	Interference Threshold			
	Lipemic[1]	Icteric[2]	Hemolytic[3]	Results
Glucose Serum	Intralipid (700 mg/dL) intf. ≤10% at Glucose conc. of 40 & 220 mg/dL	Bilirubin (40 mg/dL) intf. ≤10% at Glucose conc. of 40 & 220 mg/dL	Hemolysate (500 mg/dL) intf. ≤10% at Glucose conc. of 40 & 220 mg/dL	Pass
Glucose CSF	N/A	Bilirubin (40 mg/dL) intf. ≤10% at Glucose conc. of 36 & 216 mg/dL	Hemolysate (500 mg/dL) intf. ≤10% at Glucose conc. of 36 & 216 mg/dL	Pass
Glucose Urine	N/A	Bilirubin (40 mg/dL) intf. ≤10% at Glucose conc. of 20 & 200 mg/dL	Hemolysate (500 mg/dL) intf. ≤10% at Glucose conc. of 20 & 200 mg/dL	Pass
Sodium Serum	Intralipid (500 mg/dL) intf. ≤2 mEq/L at Sodium conc. of 130 & 150 mEq/L	Bilirubin (40 mg/dL) intf. ≤2 mEq/L at Sodium conc. of 130 & 150 mEq/L	Hemolysate (250 mg/dL) intf. ≤2 mEq/L at Sodium conc. of 130 & 150 mEq/L	Pass
Chloride Serum	Intralipid (500 mg/dL) intf. ≤2.5 mEq/L at Chloride conc. of 90 & 110 mEq/L	Bilirubin (40 mg/dL) intf. ≤2.5 mEq/L at Chloride conc. of 90 & 110 mEq/L	Hemolysate (500 mg/dL) intf. ≤2.5 mEq/L at Chloride conc. of 90 & 110 mEq/L	Pass
Potassium Serum	Intralipid (500 mg/dL) intf. ≤0.25 mEq/L at Potassium conc. of 3 & 5 mEq/L	Bilirubin (40 mg/dL) intf, ≤0.25 mEq/L at Potassium conc. of 3 & 5 mEq/L	Hemolysate (70 mg/dL) intf ≤0.25 mEq/L at Potassium conc. of 3 & 5 mEq/L	Pass

[1] Intralipid is a 20% fat emulsion used to emulate extremely turbid samples.
[2] Unconjugated bilirubin, (porcine source)
[3] Lysed human red blood cells

CRP Normal and CRP Highly Sensitive (Cardiac) Applications

Results of studies show that the following substances may interfere with this C-reactive protein procedure.

Normal Application

Icterus: Interference less than 5% up to 40 mg/dL bilirubin

Haemolysis: Interference less than 5% up to 5 g/L haemoglobin

Lipemia: Interference less than 10% up to 1,000 mg/dL Intralipid

Rheumatoid Factor: Interference less than 10% up to 500 IU/mL Rheumatoid Factor

Triglyceride: Interference less than 10% up to 500 mg/dL Triglyceride

Highly Sensitive (Cardiac) Application

Icterus: Interference less than 5% up to 40 mg/dL bilirubin

Haemolysis: Interference less than 5% up to 5 g/L haemoglobin

Lipemia: Interference less than 10% up to 1,000 mg/dL Intralipid

Rheumatoid Factor: Interference less than 10% up to 500 IU/mL Rheumatoid Factor

Triglyceride: Interference less than 10% up to 500 mg/dL Triglyceride

* Intralipid, manufactured by Pharmacia, is a 20% fat emulsion used to emulate extremely turbid samples.

Results of studies conducted to evaluate the susceptibility of the method to interference from common or known drugs that could interfere with the CRP (Normal and CRP Highly Sensitive (Cardiac) Applications) are listed below. The criteria for no significant interference is recovery within 10% of the initial value (sample containing no interferent).

No significant interference is observed from substances up to the following concentrations:

Acetaminophen	15.6 mg/dL
Acetylsalicylic Acid	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	1.2 mg/dL
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

9.6 Reference Interval

The Reference Interval study utilized a transference approach in accordance with the CLSI guideline EP028-A3c "*Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition".* The purpose of the study was to validate the acceptability of the original adult reference intervals for use on the candidate DxC 500 AU analyzer. The use of a transference approach was based on the demonstrated comparability between the candidate and predicate tests systems via the CLSI EP09c study. The approach used a sampling of at least 20 reference individuals to verify that ≥ 90% of the test samples recovered within the reference intervals cited in the respective assay IFUs. Verification studies were not performed for sample types difficult to source (CSF and 24-hour urine collections); these applications are supported by the original literature references in their IFUs. Refer to Table 9.6 below for a summary of results.

Table 9.6 Reference Interval Summary

Product and Sample Type	Units	Reference Range	Within Range	Result
CRP Latex Serum	mg/L	<10	96% (24/25)	Pass
Glucose Serum (Adult)	mg/dL	74 - 109	91% (21/23)	Pass
Glucose Urine	mg/dL	No detectable Glucose	100% (24/24)	Pass
Glucose CSF (Adult)	mg/dL	40 - 70	N/A*	N/A*
ISE Na Serum	mEq/L	136 - 145	100% (20/20)	Pass
ISE K Serum	mEq/L	3.5 - 5.1	100% (20/20)	Pass
ISE Cl Serum	mEq/L	98 - 107	95% (19/20)	Pass
ISE Na Urine	mEq/day	40 – 220	N/A*	N/A*
ISE K Urine	mEq/day	25 – 125	N/A*	N/A*
ISE Cl Urine	mEq/day	110 - 250	N/A*	N/A*

**Literature reference used*

10.0 Substantial Equivalence Conclusion

The data contained in the Premarket Notification supports a finding of substantial equivalence to the measurand test systems already in commercial distribution. The performance testing on the DxC 500 AU Clinical Chemistry Analyzer presented in this submission demonstrates that the measurand test systems continue to be safe and effective in their Intended Use.