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

I Background Information:

A 510(k) Number

K242190

B Applicant

Beckman Coulter, Inc.

C Proprietary and Established Names

Access Cortisol; DxC 500i Clinical Analyzer

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CGR	Class II	21 CFR 862.1205 - Cortisol (Hydrocortisone and Hydroxycorticosterone) Test System	CH - Clinical Chemistry
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:

Cortisol

C Type of Test:

Quantitative immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Access Cortisol assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of cortisol levels in human serum, plasma (heparin, EDTA) and urine using the Access Immunoassay Systems. A cortisol (hydrocortisone and hydroxycorticosterone) test system is a device intended to measure the cortisol hormones secreted by the adrenal gland in serum, plasma and urine. Measurements of cortisol are used in the diagnosis and treatment of disorders of the adrenal gland.

The DxC 500i Clinical Analyzer combines the DxC 500 AU Clinical Chemistry Analyzer and the Access 2 Immunoassay System into a single instrument presentation. The system is for in vitro diagnostic use only. The chemistry module of the DxC 500i Clinical Analyzer is an automated chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. The immunoassay module of the DxC 500i Clinical Analyzer is an in-vitro diagnostic device used for the quantitative, semi-quantitative, or qualitative determination of various analyte concentrations found in human body fluids.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

DxC 500i Clinical Analyzer

IV Device/System Characteristics:

A Device Description:

The Access Cortisol assay consists of the following:

- R1a well 3.25 ml — Cortisol-alkaline phosphatase (bovine) conjugate and paramagnetic particles coated with goat anti-rabbit IgG in TRIS buffered saline, with surfactant, BSA matrix, and < 0.1% sodium azide.
- R1b well 13.25 ml — Rabbit antiserum to cortisol in TRIS buffered saline, with surfactant, BSA matrix, and < 0.1% sodium azide.

The DxC 500i Clinical Analyzer is an integrated chemistry-immunoassay work cell that combines Beckman Coulter's DxC 500 AU Clinical Chemistry Analyzer and the Access 2 Immunoassay System into a single instrument presentation. The DxC 500i instrument has a single user interface and common point of entry for sample racks; the sample handling unit operates as a parallel processor and sample manager for both sides of the instrument.

B Principle of Operation:

The Access Cortisol assay is a competitive binding immunoenzymatic assay. A sample is added to a reaction vessel with rabbit antibody to cortisol, cortisol-alkaline phosphatase conjugate, and paramagnetic particles coated with goat anti-rabbit capture antibody. Cortisol in the sample competes with the cortisol-alkaline phosphatase conjugate for binding sites on a limited amount of specific anti-cortisol antibody. Resulting antigen: antibody complexes bind to the capture antibody on the solid phase.

After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is inversely proportional to the concentration of cortisol in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

C Instrument Description Information:

1. Instrument Name:

   DxC 500i Clinical Analyzer

2. Specimen Identification:

   Samples are identified by a barcode label on the sample container that is associated with a test order. Alternatively, for manually entered test orders, which do not require a barcode label, samples may be identified and associated with the test order by rack ID and sample ID, or by rack position.

3. Specimen Sampling and Handling:

   The analyzer sample handler manages and routes the racks for processing samples. After loading racks, the loading door is closed, which triggers the rack transfer for sample processing. When a rack is transferred to the sample dispensing lane for a given analyzer module, the analyzer sample probe aspirates samples from the sample container and dispenses it into the reaction vessel (immunoassay module) or cuvette (chemistry module). The sample probe is rinsed at a probe wash station between each sample dispense.

4. Calibration:

   Calibrations either pass or fail according to the calibration acceptance criteria that are defined in the calibration parameters for a given test. When a calibration passes, the calibration result becomes the active calibration for processing samples. A calibration remains active for the duration of the calibration stability period, at the end of which the point of calibration expires

and can no longer be used to calculate results. The analyzer alerts the user when calibration tasks are due. For the Access Cortisol assay, calibration is required every 28 days.

Since the DxC 500i Cortisol assay is sensitive to temperature the sponsor included the following information in the labeling:

The DxC 500i cortisol assay is sensitive to temperature. The temperature sensitivity of the DxC 500i cortisol assay was evaluated at 18ºC, 23ºC and 28ºC. When the DxC 500i analyzer is calibrated at 23ºC, expect up to ±11% bias if patient samples are tested at temperature different from calibration temperature. When calibrated at 18°C or 28°C, the estimated biases could be greater. Therefore, ensure the ambient laboratory temperature is around 23°C ±2°C at the time of calibration.

5. Quality Control:

The analyzer provides a quality control (QC) management system in the software to help the user monitor test performance. The QC information (material lot, expiration, frequency, etc.,) must be configured before a specific QC test can be run. The QC tests generate alerts based on the rules that are configured for the control lot or test, which may signal the need for further investigation. The analyzer orders QC tests automatically when the QC tests are due based on the configured frequency. For the Access Cortisol assay, quality control materials should be included in each 24-hour time period and should cover at least two levels of analyte. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Cortisol and Cortisol Calibrators On The Access Immunoassay Systems

B Predicate 510(k) Number(s):
K050202

C Comparison with Predicate(s):

Device & Predicate Device(s):	K242190	K050202
Device Trade Name	Access Cortisol	Cortisol and Cortisol Calibrators on the Access Immunoassay Systems
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Access Cortisol assay is a paramagnetic particle, chemiluminescent	Same

	immunoassay for the quantitative determination of cortisol levels in human serum, plasma (heparin, EDTA) and urine using the Access Immunoassay Systems. A cortisol (hydrocortisone and hydroxycorticosterone) test system is a device intended to measure the cortisol hormones secreted by the adrenal gland in serum, plasma and urine. Measurements of cortisol are used in the diagnosis and treatment of disorders of the adrenal gland.	
Specimen types	Human serum, plasma (heparin, EDTA), urine	Same
Methodology	Paramagnetic particle, chemiluminescent immunoassay	Same
Reagent formulation	• Solid phase: paramagnetic particles coated with goat anti-rabbit IgG • Conjugate: Cortisol-alkaline phosphatase (bovine) conjugate	Same
General Device Characteristic Differences		
Instrument platform	Beckman Coulter DxC 500i Clinical Analyzer	Beckman Coulter Access 2 Immunoassay System
Measuring range	2.3 to 60.0 µg/dL	0.4 to 60.0 µg/dL

VI Standards/Guidance Documents Referenced:

- ISO 14971 Third Edition 2019-12: Medical devices – Application of risk management to medical devices.

- ISO 15223-1 Fourth edition 2021-07: Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements.
- ISO 7010 Third edition 2019-07: Graphical symbols – Safety colours and safety signs – Registered safety signs.
- IEC 62304 Edition 1.1 2015-06 CONSOLIDATED VERSION: Medical device software – Software life cycle processes.
- IEC 61326-1 Edition 3.0 2020-10: Electrical equipment for measurement, control and laboratory use – EMC requirements – Part 1: General requirements.
- IEC 61326-2-6 Edition 3.0 2020-10: Electrical equipment for measurement, control and laboratory use – EMC requirements – Part 2-6: Particular requirements – In vitro diagnostic (IVD) medical equipment.
- CLSI EP05-A3 (Reaffirmed: September 2019): Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition.
- CLSI EP06 2nd Edition: Evaluation of the Linearity of Quantitative Measurement Procedures.
- CLSI EP09c 3rd Edition: Measurement Procedure Comparison and Bias Estimation Using Patient Samples.
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A precision study was performed based on the CLSI guideline EP05-A3 to assess the imprecision of the Access Cortisol assay on the DxC 500i Clinical Analyzer. A human serum pool and three serum controls were run on two instruments using one reagent lot and one calibrator lot at one site. Each sample was assayed in duplicate per run over two runs per day and twenty days for a total of 80 replicates per sample. Performance for precision were similar between two instruments. Shown in the table below is representative data from one of the two instruments.

Sample	N	Mean (µg/dL)	Repeatability (Within-run)		Total (Within-laboratory)	
			SD (µg/dL)	CV (%)	SD (µg/dL)	CV (%)
Control L1	80	2.95	0.16	5.6	0.21	7.2
Control L2	80	17.7	0.50	2.8	0.72	4.1
Control L3	80	26.8	0.77	2.9	0.98	3.6
Serum Pool	80	47.2	1.40	3.0	2.34	5.0

2. Linearity:

A linearity study was conducted according to the CLSI guideline EP06 2nd Edition to assess the linearity of the Access Cortisol assay on the DxC 500i Clinical Analyzer. Nine levels of serum ranging from 0.11 to 72.0 µg/dL were prepared by mixing different proportions of a high cortisol-containing serum sample pool and a low cortisol-containing serum sample pool. The lowest sample was run in replicates of eight and all other samples were run in replicates of four. Samples were tested on two instruments using two lots of reagent (one per instrument) and one lot of calibrators. The data was analyzed using a linear regression model. The deviation from linearity did not exceed 8%. The results support the claimed measuring interval of 2.3 to 60.0 µg/dL.

3. Analytical Specificity/Interference:

Analytical specificity was established in K050202.

4. Assay Reportable Range:

2.3 – 60 µg/dL

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

The measurand (cortisol) in the Access Cortisol Calibrators is traceable to USP reference material. The method for value assignment is based on EN ISO 17511.

6. Detection Limit:

Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) studies were conducted on the DxC 500i in general accordance with the CLSI guideline EP17-A2. The data support LOB of 0.4 µg/dL, LOD of 0.4 µg/dL and LOQ of 0.8 µg/dL.

Due to thermal sensitivity of the DxC 500i Cortisol Assay, sample concentrations < 2.3 µg/dL) will not be reported by the analyzer. The 20% CV criteria for LoQ was met at a cortisol concentration of 2.3 µg/dL.

7. Assay Cut-Off:

Not applicable.

8. Accuracy (Instrument):

See Method Comparison section VII.B.1. below.

9. Carry-Over:

Information was provided demonstrating that the risk of carry-over on the DxC 500i Clinical Analyzer and Access Cortisol was adequately mitigated.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was conducted in accordance with the CLSI guideline EP09c 3rd Edition to compare the Access Cortisol assay on the DxC 500i Clinical Analyzer to the predicate device (Access Cortisol assay on the Access 2 Immunoassay System, K050202). A total of 113 serum samples and 120 urine samples were tested using one lot of Access Cortisol assay reagent and one lot of calibrators on two DxC 500i Clinical Analyzers and two predicate device systems. The weighted Deming regression analysis results between the candidate device and predicate device are shown below:

Sample type	N	Sample range (µg/dL)	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)
Serum	104	2.3 to 56.2	0.974 (0.95 – 1.00)	0.33 (0.08 – 0.59)	0.99
Urine	115	3.1 – 59.0	1.002 (0.98 – 1.03)	0.18 (-0.15 – 0.51)	0.99

2. Matrix Comparison:

   Matrix comparison studies were reviewed in K050202 and established the equivalence of serum, heparin plasma and EDTA plasma.

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:

Reference range information was established in K050202.

F Other Supportive Instrument Performance Characteristics Data:

Information was provided that demonstrated adequate instrument and assay performance. The following thermal sensitivity information for the DxC 500i Clinical Analyzer are included in the packet insert for the Access Cortisol.

Thermal Sensitivity:
The DxC 500i cortisol assay is sensitive to temperature. The temperature sensitivity of the DxC 500i cortisol assay was evaluated at 18ºC, 23ºC and 28ºC. When the DxC 500i analyzer is calibrated at 23ºC, expect up to ±11% bias if patient samples are tested at temperature different from calibration temperature. When calibrated at 18°C or 28°C, the estimated biases could be greater. Therefore, ensure the ambient laboratory temperature is around 23°C ±2°C at the time of calibration.

The following are observations from studies with Patient Samples:

The following thermal bias estimates were observed with patient specimens at representative concentrations across the analytical measuring interval including medical decision levels.19, 20 The bias estimates were calculated using Passing-Bablok regression analysis applied separately to the concentration intervals < 12 µg/dL (331 nmol/L) and =12 µg/dL (331 nmol/L).

Calibration Temperature 23ºC

Run Temperature	Concentration (MDL)	Relative Bias (%)
18ºC	2.3 µg/dL (63 nmol/L)	-7.1%
	2.6 µg/dL (72 nmol/L)	-7.3%
	5 µg/dL (138 nmol/L)	-8.1%
	6.7 µg/dL (185 nmol/L)	-8.3%
	10 µg/dL (276 nmol/L)	-8.5%
	18 µg/dL (497 nmol/L)	-10.7%
	22.6 µg/dL (624 nmol/L)	-9.3%
	50 µg/dL (1380 nmol/L)	-6.2%
28ºC	2.3 µg/dL (63 nmol/L)	-3.6%
	2.6 µg/dL (72 nmol/L)	-1.6%
	5 µg/dL (138 nmol/L)	5.7%
	6.7 µg/dL (185 nmol/L)	7.7%
	10 µg/dL (276 nmol/L)	9.6%
	18 µg/dL (497 nmol/L)	6.6%
	22.6 µg/dL (624 nmol/L)	5.5%
	50 µg/dL (1380 nmol/L)	3.3%

Calibration Temperature 18ºC

Run Temperature	Concentration (MDL)	Relative Bias (%)
23ºC	2.3 µg/dL (63 nmol/L)	-10.0%
	2.6 µg/dL (72 nmol/L)	-6.8%
	5 µg/dL (138 nmol/L)	5.2%
	6.7 µg/dL (185 nmol/L)	8.5%
	10 µg/dL (276 nmol/L)	11.7%

Run Temperature	Concentration (MDL)	Relative Bias (%)
	18 µg/dL (497 nmol/L)	9.9%
	22.6 µg/dL (624 nmol/L)	9.0%
	50 µg/dL (1380 nmol/L)	6.9%
28ºC	2.3 µg/dL (63 nmol/L)	3.8%
	2.6 µg/dL (72 nmol/L)	6.2%
	5 µg/dL (138 nmol/L)	5.0%
	6.7 µg/dL (185 nmol/L)	17.7%
	10 µg/dL (276 nmol/L)	20.1%
	18 µg/dL (497 nmol/L)	18.3%
	22.6 µg/dL (624 nmol/L)	15.0%
	50 µg/dL (1380 nmol/L)	8.1%

Calibration Temperature 28 ºC

Run Temperature	Concentration (MDL)	Relative Bias (%)
23ºC	2.3 µg/dL (63 nmol/L)	-26.0%
	2.6 µg/dL (72 nmol/L)	-23.0%
	5 µg/dL (138 nmol/L)	-11.8%
	6.7 µg/dL (185 nmol/L)	-8.7%
	10 µg/dL (276 nmol/L)	-5.7%
	18 µg/dL (497 nmol/L)	-8.3%
	22.6 µg/dL (624 nmol/L)	-6.6%
	50 µg/dL (1380 nmol/L)	-3.1%
18ºC	2.3 µg/dL (63 nmol/L)	-18.7%
	2.6 µg/dL (72 nmol/L)	-17.9%
	5 µg/dL (138 nmol/L)	-15.2%
	6.7 µg/dL (185 nmol/L)	-14.4%
	10 µg/dL (276 nmol/L)	-13.7%
	18 µg/dL (497 nmol/L)	-16.1%
	22.6 µg/dL (624 nmol/L)	-13.5%
	50 µg/dL (1380 nmol/L)	-8.0%

VIII Proposed Labeling:

The labeling support 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.