510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K223038

B Applicant

Beckman Coulter, Inc

C Proprietary and Established Names

Access Cortisol

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

II Submission/Device Overview:

A Purpose for Submission:

Modified device

B Measurand:

Cortisol

C Type of Test:

Quantitative immunoenzymatic assay

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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For in vitro diagnostic use

D Special Instrument Requirements:

DxI 9000 Access Immunoassay Analyzer

IV Device/System Characteristics:

A Device Description:

The Access Cortisol assay consists of the following reagent pack and accessories:

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

Material needed but not supplied with the reagent kit include the Access Cortisol Calibrators, Quality Control (QC) materials, Lumi-Phos PRO, and UniCel DxI Wash Buffer II.

Materials required but not provided for the urine extraction procedure include Ethyl acetate (HPLC grade), 12 mm x 75 mm glass tubes, vortex mixer, pipettes capable of accurately delivering 200 and 1,000 µL, a centrifuge, and drying apparatus (either nitrogen or air).

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. The resulting antigen:antibody complexes bind to the capture antibody on the solid phase.

After incubation, 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 which reacts with the enzyme label in the bound immune complexes, resulting in the emission of light (chemiluminescence). Light generated by the reaction is measured with a luminometer. The light production is inversely proportional to the concentration of analyte in the sample. Analyte concentration is automatically determined from a stored calibration.

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):	K223038	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,	Same

	chemiluminescent immunoassay for the quantitative determination of cortisol levels in human serum, plasma (heparin, EDTA) and urine using the Access Immunoassay Systems.	
Solid Phase	Paramagnetic particles coated with goat anti-rabbit IgG	Same
Conjugate	Cortisol-alkaline phosphatase (bovine) conjugate	Same
Technology	Competitive binding	Same
Sample Type	Serum, plasma, or urine	Same
General Device Characteristic Differences		
Measuring Range	0.8 - 60 µg/dL	0.4 - 60 µg/dL
Instrument	DxI 9000 Access Immunoassay Analyzer	Access Immunoassay System
Substrate	Lumi-Phos PRO substrate	Access substrate

VI Standards/Guidance Documents Referenced:

Clinical and Laboratory Standards Institute (CLSI) EP17-A2 – Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition
CLSI EP06-2nd edition – Evaluation of Linearity of Quantitative Measurement Procedures
CLSI EP05-A3–Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition
CLSI EP09c 3rd Edition– Measurement Procedure Comparison and Bias Estimation Using Patient Samples.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

An imprecision study was performed based on CLSI EP05-A3 using 3 DxI 9000 Immunoassay Analyzers, 3 reagent pack lots, and 3 calibrator lots within one internal site. A total of 5 serum samples (3 native, 2 contrived) spanning the assay measuring range were assayed in duplicate with 2 runs per day, over 20 days for a total of 80 replicates (n=80) per

sample on each instrument and reagent lot combination. Within-run, between-run, between-day, and total imprecision were calculated. Results from multiple lots were similar. Results from one representative lot are provided in the table below:

Sample (n=80)	Mean (µg/dL)	Repeatability (Within-run)		Between Run		Between Day		Within-lab (total)	
		SD	% CV	SD	% CV	SD	% CV	SD	% CV
1	0.9	0.1	10.2	0.1	8.2	0.0	0.0	0.1	13.1
2	5.7	0.2	3.4	0.3	5.5	0.2	2.7	0.4	7.1
3	19	0.5	2.6	1.1	6.0	1.1	5.5	1.6	8.6
4	29	0.8	2.7	2.0	6.7	1.7	5.8	2.7	9.3
5	49	1.1	2.3	0.0	0.0	1.6	3.2	1.9	3.9

A separate reproducibility study was conducted using 3 reagent lots and 1 calibrator lot on each of 3 instruments with 5 replicates per run and one run per day over 5 days according to CLSI EP05-A3 (n=225 per sample). Within-run, between-day, between-lot, between-instrument, and reproducibility were calculated. Results are summarized below:

Sample (n=225)	Mean (µg/dL)	Repeatability (Within-run)		Between Day		Between Lot		Between Instrument		Reproducibility	
		SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
1	0.7	0.1	9.3	0.1	11.3	0.0	6.2	0.0	2.4	0.1	16
2	5.3	0.2	3.8	0.2	3.1	0.1	1.9	0.1	1.6	0.3	5.5
3	18	0.4	2.3	0.5	2.9	0.3	1.4	0.2	1.0	0.7	4.1
4	28	0.6	2.1	0.8	2.9	0.3	1.2	0.0	0.0	1.0	3.8
5	48	1.0	2.1	0.9	1.9	0.3	0.7	0.2	0.4	1.0	3.0

2. Linearity:

A linearity study was conducted according to CLSI EP06-2nd edition. A total of 9 levels of serum samples ranging from 0.104 to 69.295 µg/dL were prepared by mixing different proportions of a serum sample containing a high concentration of cortisol with a serum sample containing a low concentration of cortisol. The lowest sample was run in 8 replicates, and all other samples were run in 4 replicates. Samples were tested on one DxI 9000 Access Immunoassay Analyzer using 3 reagent lots and one calibrator lot in one day. The data was analyzed using a weighted linear regression model. The deviation from linearity did not exceed 0.02 µg/dL for concentrations <5 µg/dL or 8.6% for concentrations >5 µg/dL. The results support the claimed measuring interval of 0.8 - 60 µg/dL.

3. Analytical Specificity/Interference:

Interference was reviewed in K050202.

4. Assay Reportable Range:

   See Linearity section VII A.2 above.

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) were validated based on the CLSI guideline EP17-A2.

   To calculate the LoB, three DxI 9000 Immunoassay Analyzers were used with three reagent pack lots and one calibrator lot. Four S0 calibrator lots were used as blank samples for the LoB determination, over three days with one run per day, five replicates per run for each pack lot. LoB was determined using the 95% nonparametric percentile of the replicates for each of three reagent lots. The LoB was determined to be 0.2 µg/dL and the claimed LoB is 0.4 µg/dL.

   To calculate the LoD, three DxI 9000 Immunoassay Analyzers were used with three reagent lots and one calibrator lot. Nine native serum samples containing low levels of cortisol were tested over five days with one run per day and nine replicates per run for each pack lot. The LoD was determined to be 0.3 µg/dL and the claimed LoD is 0.4µg/dL.

   Limit of quantitation (LoQ) was determined using 13 serum samples containing low levels of cortisol. Samples were tested on three DxI 9000 Immunoassay Analyzers, using three reagent pack lots and one calibrator lot. Each of the samples were run in replicates of nine on three reagent pack lots with one run per day for five days on each pack lot. The LoQ (<20% within-laboratory CV) was determined to be 0.4 µg/dL and the claimed LoQ is 0.8 µg/dL.

   These studies support the claimed measuring range of 0.8-60 µg/dL.

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was conducted comparing the Access Cortisol assay on the DxI 9000 Analyzer to the comparator device, the Access Cortisol assay on the Access 2 Immunoassay System using a protocol based on CLSI EP09c-A3. A total of 116 serum samples were tested using three reagent pack lots and three calibrator lots on three DxI 9000

Immunoassay Analyzers and three predicate test systems. The Passing-Bablok regression analysis results between the candidate device (dependent variable, y) and the predicate device (x, comparator), are shown below:

N	Concentration range (µg/dL)	Intercept (95% CI)	Slope (95% CI)	Correlation Coefficient (r)
116	1.6 - 59	-0.2 µg/dL (-0.41, 0.056)	1.01 (0.99, 1.03)	1.00

2. Matrix Comparison:

Matrix comparison studies for serum, plasma (heparin), plasma (EDTA) and urine were reviewed in K050202.

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 reviewed in K050202.

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.