510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K221990

B Applicant

Beckman Coulter, Inc

C Proprietary and Established Names

Access Total ßhCG (5th IS)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DHA	Class II	21 CFR 862.1155 - Human Chorionic Gonadotropin (hCG) Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification to a previously cleared device

B Measurand:

Total beta human chorionic gonadotropin (βhCG)

C Type of Test:

Quantitative chemiluminescent immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Access Total βhCG (5th IS) assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of total βhCG levels in human serum and plasma using the Access Immunoassay Systems. This assay is intended for use as an aid in the early detection of pregnancy.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

DxI 9000 Access Immunoassay Analyzer

IV Device/System Characteristics:

A Device Description:

The Access Total βhCG (5th IS) assay is provided in two configurations, A85264 which includes tests for 100 determinations, and C28645 which includes tests for 200 determinations.

Part Number	Description
A85264	Access Total βhCG (5^{th} IS) Reagent Pack: 100 determinations, 2 packs, 50 tests/pack
C28645	Access Total βhCG (5^{th} IS) Reagent Pack: 200 determinations, 2 packs, 100 tests/pack

A description of both reagent pack part numbers are provided below:

Well	Contents	Ingredients
R1a:	3.37 mL	Paramagnetic particles coated with goat anti-mouse IgG: mouse monoclonal anti-βhCG complexes suspended in TRIS buffered saline, with surfactant, bovine serum albumin (BSA), < 0.1% sodium azide, and 0.1% Pro Clin 300.
R1b:	3.1 mL	Protein (goat, murine, and recombinant) diluted in citrate buffered saline, with surfactant, < 0.1% sodium azide, and 0.1% ProClin 300

R1c:	3.1 mL	Rabbit anti-βhCG alkaline phosphatase (recombinant) conjugate diluted in MES buffered saline, with surfactant, BSA, protein (rabbit) < 0.1% sodium azide, and 0.25% ProClin 300

Materials needed but not supplied with reagent kit include Access Total βhCG (5th IS) Calibrators, Quality Control (QC) materials, Lumi-Phos PRO, UniCel DxI Wash Buffer II and optional Access Wash Buffer II for dilution.

B Principle of Operation:

The Access Total βhCG (5th IS) assay is a sequential two-step immunoenzymatic ("sandwich") assay. A sample is added to a reaction vessel along with citrate buffer. After an initial incubation, rabbit anti-βhCG alkaline phosphatase conjugate and paramagnetic particles coated with goat anti-mouse IgG: mouse monoclonal anti-βhCG complexes are added. The hCG binds to the immobilized monoclonal anti-βhCG on the solid phase while, at the same time, the rabbit anti-βhCG alkaline phosphatase conjugate reacts with different antigenic sites on the hCG.
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 and light generated by the reaction is measured with a luminometer. The light production is directly 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):

Access Total βhCG (5th IS)

B Predicate 510(k) Number(s):

K130020

C Comparison with Predicate(s):

Device & Predicate Device(s):	K221990	K130020
Device Trade Name	Access Total βhCG (5th IS)	Access Total βhCG (5th IS)
General Device Characteristic Similarities		
Intended Use/Indications For Use	A paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of human total βhCG levels in	Same

	human serum and plasma. This assay is intended for use as an aid in the early detection of pregnancy.	
Analyte	Total βhCG	Same
Sample Type	Serum or lithium heparin plasma	Same
Measuring Range	0.6 to approximately 1350 mIU/mL	Same
Standardization	World Health Organization (WHO) 5th International Standard (IS) for hCG (NIBSC Code 07/364)	Same
General Device Characteristic Differences		
Instrument	DxI 9000 Access Immunoassay Analyzer	UniCel DxI 800 Access Immunoassay System
Substrate	Lumi-Phos PRO substrate	Access Substrate
Reagent Configurations	Two Configurations: 1) 100 determinations, 2 packs, 50 tests/pack (for predicate and candidate instrument) 2) 200 determinations, 2 packs, 100 tests/pack (for candidate instrument only)	One Configuration: 100 determinations, 2 packs, 50 tests/pack

VI Standards/Guidance Documents Referenced:

- CLSI EP17- A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition.
- CLSI EP05-A3,Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition.
- CLSI EP06-Ed2, Evaluation of the Linearity of Quantitative Measurement Procedures; Approved Guideline.
- CLSI EP09c-A3, Method Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline - Third Edition.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were conducted to estimate repeatability and within-laboratory precision. The study was run on three DxI 9000 Immunoassay Analyzers and three reagent pack lots. Seven serum samples with approximate hCG concentrations of 0.5, 7, 25, 100, 800, 1,000 and 120,000 mIU/mL were used in the determination of imprecision. Each sample was assayed in duplicate, in two runs per day, over twenty days for a total of 40 runs and 80 replicates per instrument. Each instrument was evaluated with one reagent lot. The within-run, between-run, between-day, and total imprecision was calculated. Results from multiple lots were similar. Results from one representative lot are provided in the table below:

Access Total βhCG (5th IS) Precision Results

Concentration (mIU/mL)			**Repeatability (Within-run)**		**Between-run**		**Between-day**		**Within-Laboratory (Total)**	
Serum Sample	**N**	**Mean (mIU/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sample 1	80	0.49	0.04	7.5	0.02	3.4	0.00	1.0	0.04	8.3
Sample 2	80	7.2	0.15	2.1	0.00	0.0	0.17	2.3	0.23	3.1
Sample 3	80	23	0.50	2.1	0.00	0.0	0.6	2.5	0.80	3.3
Sample 4	80	100	2.00	2.0	0.00	0.0	2.0	2.0	2.80	2.8
Sample 5	80	791	17.10	2.2	0.00	0.0	11.3	1.4	20.5	2.6
Sample 6	80	1060	25.8	2.4	0.0	0.0	18.7	1.8	31.8	3.0

A reproducibility study was conducted to assess instrument-to-instrument variability. Five serum samples with different hCG concentrations were run on three DxI 9000 Immunoassay Analyzers. The samples were tested across three reagent lots and one calibrator lot on each instrument with five replicates per run and one run per day over five days. The within-run, between-day, between-instrument, and reproducibility was calculated for each reagent lot. Results from multiple lots were similar. Results from one representative lot are provided below:

Concentration (mIU/mL)			Repeatability (Within-run)		Between-day		Between - instrument		Reproducibility	
Sample	**N**	**Mean**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sample 1	75	0.46	0.02	4.8	0.02	5.4	0.04	9.9	0.06	12.2
Sample 2	75	7.3	0.12	1.6	0.10	1.4	0.09	1.2	0.18	2.4
Sample 3	75	24	0.5	2.3	0.3	1.2	0.1	0.4	0.6	2.6
Sample 4	75	103	1.8	1.7	1.6	1.6	0.0	0.0	2.4	2.3
Sample 5	75	806	15.6	1.9	15.3	1.9	11.3	1.4	24.6	3.1

2. Linearity:

   Linearity was evaluated based upon recommendations in CLSI EP06-Ed2. Seven sample dilutions at concentrations across the measuring range of the Access Total βhCG (5th IS) (0.07 to approximately 1598.5 mIU/mL) were prepared by mixing different proportions of a serum sample containing high concentrations of βhCG and a serum samples containing low concentrations of βhCG. The low concentration serum sample was run in eight replicates, and all other samples were run in replicates of four. This study was run on one DxI 9000 Immunoassay System, using three reagent lots and one calibrator lot. Three quality controls were run in replicates of two to verify the system was in control. The data was analyzed using a weighted linear regression model as described in the guideline. The results from the linearity study supports the sponsor's claimed analytical measuring interval of 0.6 to approximately 1350 mIU/mL. The maximum deviation from linearity was found to be acceptable and supported by the results.

3. Analytical Specificity/Interference:

   Potential cross-reactivity, interference, and high dose effect were evaluated in k130020. No cross reactivity, interference, or high dose effect was observed.

4. Assay Reportable Range:

   The assay reportable range is 0.6 – 1350 mIU/mL.

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

   This assay is traceable to the WHO 5th International Standard for human Chorionic Gonadotropin (NIBSC Code 07/364).

6. Detection Limit:

   The LoB, LoD, LoQ were determined based upon recommendations in CLSI EP17-A2.

   Limit of blank (LoB) is the highest concentration that is likely to be observed for a blank sample. To calculate the LoB, three DxI 9000 Immunoassay Systems were used with three reagent pack lots and one calibrator lot. Four S0 (hCG free)calibrator lots were used for the

LoB determination. Samples were tested over three days one run per day, five replicates per run, for each reagent pack lot. Three quality controls were run in duplicate on each day.. LoB was determined using the 95% nonparametric percentile of the replicates for each of three reagent lots. The LoB was determined to be 0.1 mIU/mL.

Limit of detection (LoD) is the lowest concentration of analyte that can be detected reliably. To calculate the LoD, three DxI 9000 Immunoassay Systems were used with three reagent lots and one calibrator lot. Seven serum samples containing low levels of total βhCG (5th IS) analyte were prepared. Samples were tested in nine replicates per day over five days for each reagent pack lot. Three quality controls were run in replicates of two on each day.. The LoD was determined to be 0.2 mIU/mL.

Limit of quantitation (LoQ) is the lowest concentration which is the design requirements of TEa% (Total Error Allowance) of ≤30%. To calculate LoQ, three DxI 9000 Immunoassay Systems were used with three reagent pack lots and one calibrator lot. Thirteen native serum samples containing low levels of total βhCG analyte were prepared. Each of the samples were run in replicates of nine, in one run per day, for five days on three reagent pack lots (45 replicates of each sample on each reagent lot). Three quality controls were run in replicates of two on each day to verify the systems were in control. The LoQ was determined to be 0.6 mIU/mL.

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was performed comparing the Access Total βhCG (5th IS) assay on the DxI 9000 Access Immunoassay Analyzer to the comparator device, the Access Total βhCG (5th IS) assay run on the Access 2 Immunoassay System using a protocol based on CLSI EP09c-A3. A total of one hundred eleven (111) human serum samples were run on three DxI 9000 instruments and three Access 2 instruments with three reagent pack lots and three calibrator lots. Three commercial quality controls were run in triplicate each day. The Passing Bablok regression analysis between Access Total βhCG (5th IS) DxI 9000 analyzer values (dependent variable, y) and the Access Total βhCG (5th IS) Access 2 Immunoassay system values (x, comparator), are shown below:

Passing Bablok Regression Analysis

N	**Range Tested (Candidate)**	**Range Tested (Comparator)**	**Slope**	**Slope 95% CI**	**Intercept**	**Intercept 95% CI**	**Correlation Coefficient R**
111	[0.58,1293]	[0.59,1335]	0.97	[0.96, 0.98]	0.19	[0.0043, 1.7]	1.00

2. Matrix Comparison:

A matrix comparison study was conducted in k130020 and demonstrates equivalent performance between serum and lithium heparin 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:

The reference range information was reviewed in K130020.

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.