510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K234052

B Applicant

Beckman Coulter, Inc

C Proprietary and Established Names

Access Ferritin

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JMG	Class II	21 CFR 866.5340 - Ferritin Immunological Test System	IM – Immunology

II Submission/Device Overview:

A Purpose for Submission:

Modification of the previously cleared device

B Measurand:

Ferritin

C Type of Test:

Quantitative chemiluminescent assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Access Ferritin assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of ferritin levels in human serum and plasma (heparin) using the Access Immunoassay Systems.

Ferritin is used as an aid in the diagnosis of iron deficiency or iron overload.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

DxI 9000 Access Immunoassay Analyzer (K221225).

IV Device/System Characteristics:

A Device Description:

Access Ferritin assay kit contains two Access Ferritin Reagent Pack. Each Access Ferritin Reagent Pack contains the following:

- Paramagnetic particles coated with goat anti mouse IgG: mouse monoclonal anti-ferritin complexes suspended in TRIS buffered saline, with surfactant, bovine serum albumin (BSA), < 0.1% sodium azide, and 0.1% ProClin 300.
- Goat anti-ferritin-alkaline phosphatase (bovine) conjugate in TRIS buffered saline, with surfactant, BSA, protein (goat, mouse), < 0.1% sodium azide, and 0.1% ProClin 300.

Other items needed but not supplied with reagent kit include:

- Access Ferritin Calibrators: at zero and approximately 10, 50, 200, 500 and 1,500 ng/mL
- Quality Control (QC) materials: commercial control material.
- Substrate: Lumi-Phos PRO
- UniCel DxI Wash Buffer II
- Access Sample Diluent A (optional)

The modification of the Access Ferritin includes: (a) a new substrate replacement (Lumi-Phos PRO); (b) run on DxI 9000 Access Immunoassay Analyzer

B Principle of Operation:

The Access Ferritin assay is a two-site immunoenzymatic (“sandwich”) assay. A sample is added to a reaction vessel with goat anti-ferritin-alkaline phosphatase conjugate, and paramagnetic

particles coated with goat anti-mouse: mouse anti-ferritin complexes. Serum or plasma (heparin) ferritin binds to the immobilized monoclonal anti-ferritin on the solid phase, while the goat anti-ferritin enzyme conjugate reacts with different antigenic sites on the ferritin molecules. 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 Ferritin Assay
Ferritin on the Access Immunoassay Systems

B Predicate 510(k) Number(s):

K926221
K052082

C Comparison with Predicate(s):

Device & Predicate Device(s):	K234052	K926221 (Predicate)	K052082 (Predicate)
Device Trade Name	Access Ferritin	Access Ferritin	Ferritin on the Access Immunoassay Systems
General Device Characteristic Similarities			
Intended Use/ Indications For Use	The Access Ferritin assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of ferritin levels in human serum and plasma (heparin) using the Access Immunoassay Systems. Ferritin is used as an aid in the diagnosis of iron deficiency or iron overload.	The Access Ferritin Assay is a magnetic particle chemiluminescent immunoassay for the quantitative detection of ferritin levels in human serum using the Access Immunoassay System	The Access Ferritin assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of ferritin levels in human serum and plasma (heparin) using the Access Immunoassay Systems.
Analyte	Ferritin	Same	Same

Traceability	WHO 94/572	Same	Same
Technology	Sandwich Immunoassay	Same	Same
Format	Chemiluminescent	Same	Same
Method	Automated	Same	Same
Calibration	Utilizes a stored calibration curve	Same	Same
Sample Type	Serum and Plasma (heparin)	Same	Same
Stability	28 days after opening	Same	Same
General Device Characteristic Differences			
Substrate	Lumi-Phos PRO substrate	Access Substrate	
Instrument	DxI 9000 Access Immunoassay Analyzer	Access 2 Immunoassay system	
Measuring Range	0.6 – 1500 ng/mL	0.2 – 1500 ng/mL	
Sample Volume	5 µL	10 µL	
Reagent Configurations	Two Configurations: • 100 determinations, 2 packs, 50 tests/pack • 200 determinations, 2 packs, 100 tests/pack	One Configuration: • 100 determinations, 2 packs, 50 tests/pack	

VI Standards/Guidance Documents Referenced:

The following Clinical and Laboratory Standards Institute (CLSI) guidelines were used:

- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline
- 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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

All results presented below met the manufacturer's pre-determined acceptance criteria.

1. Precision/Reproducibility:

   Precision testing was performed in accordance with CLSI Guideline EP05-A3.

a) *Within-Laboratory Precision:*

The studies were performed by testing six levels of human serum samples in a minimum of two replicates per run, two runs per day for 20 days, resulting a minimum of 80 datapoints for each sample. Three reagent lots and three instruments were used in the study. The data were analyzed for repeatability (within-run), between-run, between-day, and within-laboratory precision. The mean (ng/mL), standard deviation (SD) (ng/mL) and percent coefficient of variation (%CV) were calculated for each sample. The representative data of within-laboratory precision using one lot of reagents on one instrument are summarized in table below.

Sample	Mean (ng/mL)	N	Within-Run (Repeatability)		Between-Run		Between-Day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	1.2	80	0.2	16.5	0.0	0.0	0.1	5.3	0.2	17.3
2	13	80	0.4	3.1	0.2	1.3	0.4	3.2	0.6	4.7
3	147	80	4.5	3.0	2.0	1.4	6.0	4.1	7.7	5.3
4	289	80	8.6	3.0	0.0	0.0	9.1	3.1	12.5	4.3
5	560	80	17.2	3.1	10.0	1.8	16.2	2.9	25.7	4.6
6	1276	80	53.3	4.2	5.8	0.5	42.2	3.3	68.2	5.3

b) *Reagent Lot-to-Lot Precision:*

The study was performed using three lots of the modified Access Ferritin reagent on the DxI 9000 Access Immunoassay Analyzer. Five serum samples at different concentrations were tested in five replicates per run, one run per day over five days, resulting N=75 datapoints per sample on one instrument. The same study was also performed on two additional instruments. The representative data for the lot-to-lot precision are summarized in the table below.

Sample	Mean (ng/mL)	N	Within-Run (Repeatability)		Between-Day		Between-Reagent Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.91	75	0.0	4.6	0.0	5.1	0.0	2.5	0.1	7.3
2	12	75	0.3	2.8	0.2	1.8	0.2	1.9	0.4	3.8
3	135	75	3.4	2.5	3.0	2.2	1.4	1.0	4.8	3.5
4	345	75	13.7	4.0	12.5	3.6	4.7	1.4	19.2	5.6
5	881	75	36.5	4.1	18.2	2.1	14.1	1.6	43.1	4.9

c) *Instrument-to-Instrument Reproducibility:*

The instrument-to-instrument reproducibility was evaluated by testing five serum samples at different concentrations on three DxI 9000 Access Immunoassay Analyzers. Each sample was tested in five replicates per run, one run per day over five days, resulting N=75 datapoints using one lot of reagents. The same study was also repeated

using two additional reagent lots. The representative data of instrument-to-instrument reproducibility are summarized in the table below.

Sample	Mean (ng/mL)	N	Within-Run (Repeatability)		Between-Day		Between-Instrument		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.93	75	0.0	3.7	0.0	2.1	0.1	7.7	0.1	8.8
2	12	75	0.3	2.8	0.4	3.5	0.4	3.6	0.7	5.8
3	135	75	3.9	2.9	2.9	2.1	0.0	0.0	4.8	3.6
4	350	75	11.3	3.2	14.4	4.1	9.0	2.6	20.4	5.8
5	877	75	35.2	4.0	33.6	3.8	0.0	0.0	48.6	5.5

2. Linearity:

Linearity of the modified Access Ferritin on the DxI 9000 Access Immunoassay Analyzer was performed in accordance with CLSI Guideline EP06, 2nd Edition. Dilution series were prepared by mixing one High sample with a Low sample to provide eight dilution levels, spanning the analytical measuring interval (AMI) of the modified Access Ferritin. The Low sample was obtained from an individual native sample that was specifically depleted of ferritin to achieve a concentration below the lower limit of the AMI. The High sample is a pooled native sample at 1699 ng/mL. The low sample was run in replicates of eight, and all other dilution levels were run in replicates of four, and the mean (ng/mL) of each dilution level was compared to its predicted value for deviation percentage using a weighted linear regression analysis. This deviation was then compared to the allowable deviation from linearity. The results are summarized in table below.

Range (ng/mL)	Slope (95% CI)	Intercept (95% CI)	R^2	% Deviation* (Deviation**)
0.03 – 1698.57	1.005 (0.983, 1.027)	-0.0002 (-0.032, 0.031)	0.993	-7% – 5% (0.0001)

* % Deviation from Linearity for concentrations > 0.6 ng/mL
** Deviation (ng/mL) from Linearity for concentrations ≤ 0.6 ng/mL

The data support the linearity interval from 0.03 to 1658.57 ng/mL with the deviations from linearity within ±10%. The study results support the linearity of the claimed analytical measuring interval (AMI): 0.6 – 1500 ng/mL.

3. Analytical Specificity/Interference:

Refer to K926221

4. Assay Reportable Range:

0.6 – 1500 ng/mL

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

a) Traceability:

Refer to K926221. The Access Ferritin is traceable to the WHO reference material 94/572.

b) Stability:

The Access Ferritin Reagent kit and the Lumi-Phos PRO substrate are packaged separately. The stability of the Access Ferritin Reagent kit was established in K926221. The proposed change is to replace substrate (Lumi-Phos 530) of the Access Ferritin with a new substrate (Lumi-Phos PRO). The shelf-life claims and on-board stability claims of Lumi-Phos PRO substrate were established in K221225.

6. Detection Limit:

CLSI guideline EP17-A2 was followed to determine the Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) for the Access Ferritin.

LoB: The study was conducted on two DxI 9000 Immunoassay Systems with two Access Ferritin reagent lots and one calibrator lot. Five analyte depleted samples (prepared from five unique native serum samples) were tested over three days, with one run per day and five replicates per run, resulting in 75 datapoints for each reagent lot and each instrument. The LoB was determined as 0.2 ng/mL and 0.1 ng/mL based on the 95% nonparametric percentile of the replicates for each of the two reagent lots. The claimed LoB for the modified Access Ferritin on DxI 9000 Access Immunoassay Analyzer is 0.2 ng/mL.

LoD: For the determination of the LoD, three DxI 9000 Immunoassay Systems with three reagent lots were used to test five to nine serum samples containing low levels of ferritin. Samples were tested for five days with one run per day and nine replicates per run. LoD was calculated from LoB + "SD multiplied by the 95th percentile of the standard normal distribution" and resulted in 0.4 ng/mL for each reagent lot. The claimed LoD for the modified Access Ferritin on DxI 9000 Access Immunoassay Analyzer is 0.4 ng/mL.

LoQ: For the determination of the LoQ, eight to twelve serum samples containing low levels of ferritin were measured. Samples were tested in replicates of nine per run, one run per day, over five total days on each pack lot and instrument for a minimum of 40 total datapoints for each sample on each lot. A variance components model was used to estimate the within-run and within-laboratory (total) %CV for each sample on each instrument and reagent lot combination. The estimated LoQ of the modified Access Ferritin was set to be the ferritin concentration which met the within-laboratory imprecision of 20% CV. The claimed LoQ for the modified Access Ferritin on DxI 9000 Access Immunoassay Analyzer is 0.6 ng/mL.

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

CLSI Guideline EP09c, 3rd Edition was followed to compare the modified Access Ferritin on DxI 9000 Access Immunoassay Analyzer to the predicate device, the Access Ferritin on the Access 2 Immunoassay System. Patient samples falling within the analytical measuring interval of both Access Ferritin assays were evaluated. A total of 147 deidentified serum samples were tested with the modified Access Ferritin on three DxI 9000 instruments and three Access 2 instruments with three reagent pack lots and three calibrator lots. The comparison between paired measurements was analyzed by fitting the observed Access Ferritin Assay on DxI 9000 instrument (dependent variable, y) into a linear regression model, with the observed Access Ferritin Assay on Access 2 values as the only independent variable (x, predicate), using Passing-Bablok method. The results are summarized in the following table:

N	Range (ng/mL)	Slope (95% CI)	Intercept (95% CI)	R^2
147	2.2 – 1348	0.96 (0.95 – 0.97)	0.23 (-0.34 – 1.08)	0.99

2. Matrix Comparison:

Refer to K052082

C Clinical Studies:

Refer to K926221

D Clinical Cut-Off:

Refer to K926221

E Expected Values/Reference Range:

Refer to K926221

VIII Proposed Labeling:

The labeling supports finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.