510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K231832

B Applicant

Beckman Coulter, Inc.

C Proprietary and Established Names

Access Myoglobin

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DDR	Class II	21 CFR 866.5680 - Myoglobin Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

Modified device

B Measurand:

Myoglobin

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 Myoglobin assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of myoglobin levels in human serum and plasma using the Access Immunoassay Systems. Measurement of myoglobin aids in the rapid diagnosis of heart and renal diseases.

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 Myoglobin assay consists of the following:

Well	Contents	Ingredients
R1a:	3.25 mL	Paramagnetic particles coated with goat anti-biotin antibody suspended in MES buffered saline, with bovine serum albumin (BSA), 0.25% ProClin* 300, and < 0.1% sodium azide.
R1b:	3.1 mL	Mouse monoclonal anti-human myoglobin antibody-biotin conjugate and mouse monoclonal anti-human myoglobin antibody-alkaline phosphatase conjugate in phosphate buffered saline with BSA, purified mouse IgG, purified goat IgG, 0.25% ProClin 300, and < 0.1% sodium azide.

Other items needed to run the assay include the Access Myoglobin reagent packs, Access Myoglobin Calibrators, along with the UniCel DxI wash buffer II, and Lumi-Phos PRO substrate. It is intended for use on the DxI 9000 Access Immunoassay Analyzer in a clinical laboratory setting.

B Principle of Operation:

The Access Myoglobin assay is a two-site immunoenzymatic (“sandwich”) assay.

A sample is added to a reaction vessel with mouse monoclonal anti-myoglobin-alkaline phosphatase conjugate, mouse monoclonal anti-myoglobin-biotin conjugate, and paramagnetic

particles coated with goat anti-biotin. Human serum myoglobin binds to the anti-myoglobin biotin conjugate and is immobilized on paramagnetic particles coated with goat anti-biotin antibody, while the mouse anti-myoglobin-alkaline phosphatase conjugate reacts specifically with a different antigenic site on the myoglobin molecule.

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):
Myoglobin And Myoglobin Calibrators On The Access Immunoassay System

B Predicate 510(k) Number(s):
K021229

C Comparison with Predicate(s):

Device & Predicate Device(s):	K231832	K021229
Device Trade Name	Access Myoglobin	Myoglobin and Myoglobin Calibrators On the Access Immunoassay System
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Access Myoglobin assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of myoglobin levels in human serum and plasma using Access Immunoassay Systems.	Same
Assay Principles	The Access Myoglobin assay is a two-site immunoenzymatic (“sandwich”) assay. A sample is added to a reaction vessel with mouse monoclonal anti-myoglobin-alkaline	Same

Device & Predicate Device(s):	K231832	K021229
	phosphatase conjugate, mouse monoclonal anti-myoglobin-biotin conjugate, and paramagnetic particles coated with goat anti-biotin.	
Solid Support	Paramagnetic particles	Same
Detection System	Chemiluminescence	Same
Calibrators	Liquid calibrators prepared from buffered bovine protein matrix and human skeletal Myoglobin at various levels	Same
General Device Characteristic Differences		
Instrument	DxI 9000 Access Immunoassay Analyzer	Access Immunoassay System
Substrate	Lumi-Phos PRO substrate	Access Substrate

VI Standards/Guidance Documents Referenced:

CLSI EP17-A2 – Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
CLSI EP06 2nd Edition – Evaluation of Linearity of Quantitative Measurement Procedures
CLSI EP05-A3 – Evaluation of Precision of Quantitative Measurement Procedures
CLSI EP09c 3rd Edition – Measurement Procedure Comparison and Bias Estimation Using Patient Samples
CLSI EP28-A3c – Defining Establishing and Verifying Reference Intervals in the Clinical Laboratory
CLSI EP35 1st Edition – Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Studies were performed to determine the imprecision of the candidate device using a protocol based on CLSI EP05-A3.

The study was run on three DxI 9000 Access Immunoassay Analyzers using three reagent lots, and three calibrator lots. Five (5) lithium heparin samples, with varying myoglobin

concentrations were tested across two runs per day, over 20 or more days. The study met the minimum requirement of 80 replicates per sample on each instrument and reagent lot combination. Three commercial quality controls were run in duplicate on each day to verify the system was in control.

Results from one representative lot:

Concentration (ng/mL)			**Repeatability (Within-run)**		**Between-run**		**Between-day**		**Within-Laboratory (Total)**	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	80	101	2.2	2.1	4.0	4.0	3.0	3.0	5.5	5.4
2	80	465	8.0	1.7	15.1	3.2	0.0	0.0	17.0	3.7
3	80	1763	35.0	2.0	57.5	3.3	0.1	0.0	67.3	3.8
4	80	2719	54.8	2.0	85.9	3.2	0.0	0.0	101.9	3.7
5	80	7.9	0.18	2.3	0.18	2.2	0.17	2.2	0.31	3.9

2. Linearity:

A study was performed to determine the linearity of the candidate device based on the recommendations in the CLSI EP06-2nd Edition guideline. Eight lithium heparin samples ranging from 0.152ng/mL (native) to 4778.10ng/mL were prepared by mixing a high sample spiked with human myoglobin and a native sample with a low concentration. The low sample was run in replicates of eight, and all other samples were run in replicates of four. The study was run using three reagent lots and three calibrator lots. The data were analyzed using a weighted linear regression model and the deviation from linearity did not exceed 10%. The data supports the claimed reportable range of 3.0ng/L to 400ng/L of myoglobin.

3. Analytical Specificity/Interference:

Interference was reviewed in K021229. The sponsor also provided information to support that biotin up to 1200 ng/mL does not interfere with the test. The following statement is included in the labeling. "Specimens that contain biotin at a concentration of ≤ 1,200 ng/mL demonstrate a less than or equal to 10% change in results. Biotin concentrations greater than this may lead to incorrect Access Myoglobin results for patient samples."

4. Assay Reportable Range:

The data provided support the sponsor's claims that the reportable range of this assay is 3.0ng/mL – 4,000ng/mL.

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

Traceability was reviewed in k021229.

6. Detection Limit:

Studies were performed to determine the Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation using protocols based on CLSI EP17-A2. LoB was determined to

be 0.3ng/mL. The LoD was determined to be 0.8ng/mL. The LoQ was determined to be 1.0ng/mL based on a 20% CV performance goal.

7. Assay Cut-Off:

   Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was completed to compare the candidate device compared to the predicate device using a protocol based on CLSI EP09c-A3. A total of one hundred and fifty-five (155) lithium heparin plasma samples (11 were contrived with human myoglobin and 144 were native samples including 15 that were native pools) were evaluated in the method comparison study.

   The study was run 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 Myoglobin Assay on DxI 9000 instrument (dependent variable, y) into a linear regression model, with the observed Access Myoglobin Assay on Access 2 values as the only independent variable (x, predicate) are shown below:

N	Concentration Range* (ng/mL)	Slope	Slope 95% CI	Intercept	Intercept 95% CI	R
155	8.2 – 3900	0.99	0.98 – 1.00	0.47	-0.10 – 1.0	1.00

*Range is Access 2 values

2. Matrix Comparison:

   For sample type comparison, two studies were run to compare each of the allowed sample types (LiHep vs Serum and LiHep vs EDTA). For each study, one DxI 9000 Access Immunoassay Analyzer was used with one reagent lot and one calibrator lot.

Sample Type	**N**	**LiHep Range (ng/mL)**	**Serum Range (ng/mL)**	**Slope**	**Slope 95% CI**	**Intercept**	**Intercept 95% CI**	**R**
LiHep v EDTA	42	8.3 – 3974	8.3 – 3846	1.01	0.99, 1.03	-0.11	-0.95, 1.14	0.99
LiHep v Serum	54	13.3 - 3650	13.6 – 3681	1.03	1.01, 1.07	-0.74	-1.92, 0.48	1.00

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 K021229.

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.