

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k080481

B. Purpose for Submission:

Provide performance characteristics for use of a marketed device on the UniCel DxI 800

C. Measurand:

Myoglobin

D. Type of Test:

Quantitative, immunoassay

E. Applicant:

Beckman Coulter

F. Proprietary and Established Names:

Access[®] Myoglobin and Access Myoglobin Calibrators on the Access Immunoassay Systems

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5680 - Myoglobin immunological test system

21CFR 862.1150 - Calibrator

2. Classification:

Class II

3. Product code:

DDR, JIT

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indication for use below.

2. Indication(s) for use:

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.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Access immunoassay system

I. Device Description:

The Access Myoglobin assay consists of the following:

1. Reagent 1a: 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. It is provided as a ready to use suspension.
2. Reagent 1b: 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. It is provided as a ready to use suspension.
3. Access Myoglobin calibrators: Six levels- zero and approximately 50, 200, 800, 2000, and 4000 ng/mL of human myoglobin in buffered BSA matrix with surfactant, <0.1% sodium azide, and 0.5% ProClin 300. It is provided as a ready to use calibrators in a 1.0 mL vial each.

All human source materials were tested and found to be negative for HIV 1/2,

HBsAg, and HCV.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Access Myoglobin Assay

2. Predicate 510(k) number(s):

k021229

3. Comparison with predicate:

Attribute	Access Myoglobin (Predicate device)	Access Myoglobin (With Modification)
Intended Use	For the quantitative determination of myoglobin levels in human serum and plasma.	For the quantitative determination of myoglobin levels in human serum and plasma.
Assay principles	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-myoglobinbiotin conjugate, and paramagnetic particles coated with goat anti-biotin	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-myoglobinbiotin conjugate, and paramagnetic particles coated with goat anti-biotin
Solid Support	Paramagnetic particles.	Paramagnetic particles.
Detection System	Chemiluminescent substrate.	Chemiluminescent substrate.
Calibrator	Liquid calibrators (frozen) prepared from buffered bovine serum albumin matrix with human cardiac Myoglobin at specified levels	Liquid calibrators (frozen) prepared from buffered bovine serum albumin matrix with human cardiac Myoglobin at specified levels
Analytical Range	1- 4000ng/mL	1- 4000ng/mL
Imprecision	This assay exhibits total imprecision of 3.03% to 4.54% for the Access instruments.	This assay exhibits total imprecision of 7.32% to 9.25% for the UniCel DxI 800 system.

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2, Evaluation of Precision Performance of Clinical Chemistry Devices;
Approved Guideline- Second edition, 2004

CLSI EP7-A2, Interference Testing in Clinical Chemistry; Approved Guideline-
Second edition, 2003

L. Test Principle:

The Access Myoglobin assay is a two-site immunoenzymatic (“sandwich”) assay. A sample is added to a reaction vessel with the mouse monoclonal anti-myoglobin alkaline phosphatase conjugate, mouse monoclonal anti-myoglobin-biotin conjugate, and paramagnetic particles coated with a goat polyclonal anti-biotin. Human serum myoglobin binds to 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 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 Lumi-Phos 530 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 myoglobin in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were designed according to the CLSI EP5-A2 guideline. Five levels of control materials were measured twice a day in duplicate on two separate UniCel DxI 800 analyzers for 20 days. The results from one of the two instruments (N=80) are summarized below:

Sample ID	Mean (ng/mL)	Within-run (CV %)	Between-run (CV %)	Total precision (CV %)
Level 1	78.73	3.55	6.49	7.39
Level 2	177.97	3.05	7.34	7.32
Level 3	427.74	4.32	7.44	8.60
Level 4	1624.61	3.45	8.58	9.25
Level 5	2404.64	3.11	7.51	8.13

b. Linearity/assay reportable range:

A linearity study across the entire measuring range was assessed using the UniCel DxI 800 analyzer. Two previously frozen spiked serum samples were analyzed in this study, one sample at greater than 4000 ng/mL and a second lower sample at approximately 70 ng/mL. Five dilutions were prepared from both of these samples using Sample Diluent A as the diluent. All samples were tested in replicates of seven in random order. The range of the samples tested was from 0.64 – 4179 ng/mL. The values were plotted for the expected concentrations (X) versus the observed concentrations (Y) and an appropriate line fitted by standard linear regressions was calculated. The linear regression correlation is $Y = 1.012X + 6.641$, (95% CI for slope is 0.98 to 1.043 and intercept is -36.9 to 50.19).

The data provided support the sponsor's claims that the reportable range of this assay is 1- 4000ng/mL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Access Myoglobin Calibrators is traceable to the in-house calibrations. See k021229

d. Detection limit:

The Limit of Blank (LoB) determination was based on multiple measurements of the Myoglobin calibrator, S0, on multiple instruments. The mean, SD, and % CV were calculated. The limit of blank for Myoglobin as determined by being distinguishable from zero with 95% confidence is 0.215 ng/mL on DxI 800. Limit of Detections (LoD) determination was based on measurements of 4 low samples in replicates of 7 on a DxI 800 analyzer according to CLSI EP17-A. The sponsor claimed that the LoD is 0.762 ng/mL.

The Access Myoglobin assay has a reportable range of 1-4000 ng/mL.

e. Analytical specificity:

Interference studies were designed according to the CLSI EP7-A guideline. A normal human serum was spiked with the known interference substances and analyzed in replicate of ten on the DxI 800 analyzer. No significant interference was defined as the observed value <10% of the expected value (neat sample). The sponsor claimed that there was no significant interference (<10%) by the following interferents:

- Hemoglobin up to 500 mg/dL
- Bilirubin up to 40 mg/dL
- Triglycerides (triolein) up to 3000 mg/dL

- Human serum albumin up to 6000 mg/dL

The sponsor has the following limitations in their labeling:

“For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interferes with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples. Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.”

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed at an internal site. A total of 110 serum samples were evaluated using UniCel DxI 800 (candidate) and Access 2 (predicate). Deming regression analyses were used to evaluate the correlations between results obtained using the UniCel DxI 800 and Access 2. Correlation regression is summarized below:

$$Y = 0.93X + 7.47, r^2 = 0.99, \text{ range of sample tested} = 32.3 - 3748 \text{ ng/mL}$$

(X= Access 2 and Y= UniCel DxI 800)

b. Matrix comparison:

In the labeling, the sponsor recommends serum, EDTA and heparinized plasma as the samples to use. Matrix comparisons between all the sample types were previously performed on the Access 2 analyzer. See previously cleared submission, k021229

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

A reference range study was performed by evaluating 277 healthy subjects (140 males and 137 females, age range from 22-93) on the Access 2 analyzer. The cen

tral 95% reference intervals for different sample types were determined as follows:

Sample type	Sex	Reference intervals (ng/mL)
Heparin plasma and serum	Females	14.3-65.8
	Males	17.4-105.7
EDTA plasma	Females	11.1-57.5
	Males	15.2 – 91.2

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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