510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K234005

B Applicant

Beckman Coulter, Inc

C Proprietary and Established Names

Access CK-MB

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JHX	Class II	21 CFR 862.1215 - Creatine Phosphokinase/Creatine Kinase Or Isoenzymes Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modified device

B Measurand:

Creatine kinase, isoenzyme MB (CK-MB)

C Type of Test:

Quantitative solid phase immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Access CK-MB assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of CK-MB levels in human serum and plasma using the Access Immunoassay Systems to aid in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

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 (K221225)

IV Device/System Characteristics:

A Device Description:

The Access CK-MB assay consists of the following reagents:

- R1a: Paramagnetic particles coated with goat anti-biotin antibodies and biotinylated anti-human CK-BB mouse monoclonal antibodies suspended in buffered solution, with bovine serum albumin (BSA), 0.2% ProClin* 950, and < 0.1% sodium azide.
- R1b: Purified mouse IgG and purified goat IgG in buffered solution with BSA, 0.1% ProClin 300, and < 0.1% sodium azide.
- R1c: Mouse monoclonal anti-human CK-MB antibody alkaline phosphatase conjugate in buffered solution with BSA, 0.1% ProClin 300, and < 0.1% sodium azide.

Other items needed to run the assay include the Access CK-MB 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 CK-MB assay is a two-site immunoenzymatic ("sandwich") assay.

Patient sample is added to a reaction vessel with mouse monoclonal anti-human CK-MB antibody-alkaline phosphatase conjugate and paramagnetic particles coated with mouse monoclonal anti-human CK-BB. Human serum CK-MB binds to the anti-CK-MB conjugate and is immobilized on the paramagnetic particle coated with anti-CK-BB. The CK-MB in the human serum or plasma binds to the immobilized anti-CK-BB on the solid phase by the sub-unit B epitope (common to CK-BB and CK-MB isoforms), while the mouse anti-CK-MB conjugate reacts specifically with the serum or the plasma CK-MB (no reaction with CK-MM or CK-BB isoforms).

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):
CK-MB and CK-MB Calibrators on the Access® Immunoassay Systems

B Predicate 510(k) Number(s):
K030012

C Comparison with Predicate(s):

Device & Predicate Device(s):	K234005	K030012
Device Trade Name	Access CK-MB	CK-MB and CK-MB Calibrators On The Access® Immunoassay Systems
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Access CK-MB assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of CK-MB levels in human serum and plasma using the Access Immunoassay Systems.	Same
Technology	The Access CK-MB assay is a two-site immunoenzymatic ("sandwich") assay. Patient sample is added to a reaction vessel with mouse monoclonal anti-human CK-MB antibody-alkaline phosphatase conjugate and paramagnetic particles coated with	Same

	mouse monoclonal anti-human CK-BB.	
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 2nd Edition – Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
CLSI EP06 2nd Edition – Evaluation of Linearity of Quantitative Measurement Procedures
CLSI EP05-A3 3rd Edition –Evaluation of Precision of Quantitative Measurement Procedures
CLSI EP09c 3rd Edition – Measurement Procedure Comparison and Bias Estimation Using Patient Samples
CLSI EP28-A3c 3rd Edition– 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:

Precision was evaluated according to CLSI EP05-A3. The study was run on three DxI 9000 Access Immunoassay Analyzers using three reagent lots and three calibrator lots. Five lithium heparin plasma samples, with varying CK-MB concentrations, were tested in replicates of two with two runs per day, over 20 days, for a total of 80 replicates per sample on each instrument and reagent lot combination. One commercial quality control sample was run in duplicate on each day.

Results from one representative lot:

Concentration (ng/mL [µg/L])			**Repeatability (Within-Run)**		**Between-Run**		**Between-Day**		**Within-Laboratory (Total)**	
Sample	**N**	**Mean**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sample 1	80	0.2	0.01	5.2	0.01	3.4	0.003	1.9	0.01	6.5
Sample 2	80	9.2	0.2	2.2	0.2	2.6	0.00	0.0	0.3	3.4
Sample 3	80	54	1.1	2.0	1.1	2.0	0.5	1.0	1.6	3.0
Sample 4	80	120	3.0	2.5	1.6	1.4	1.3	1.1	3.6	3.0
Sample 5	80	220	4.5	2.0	2.9	1.3	1.3	0.6	5.4	2.5

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 or nine lithium heparin samples ranging from 0.03 ng/mL (native) to 378.06 ng/mL were prepared by mixing a high sample spiked with CK-MB antigen 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 three or four. The study was run using three reagent lots and three calibrator lots. The results were analyzed using a weighted linear regression model and the deviation from linearity did not exceed 5%. The data support that the assay is linear over the claimed measuring range of 0.2 ng/mL to 300 ng/mL CK-MB.

3. Analytical Specificity/Interference:

Interference was reviewed in K030012 and the claims are unchanged. The sponsor provided information to support that biotin up to 3500 ng/mL does not interfere with the test. The following statement is included in the labeling. "Biotin was added to samples containing approximately 0.75 ng/mL (µg/L) and 5.0 ng/mL (µg/L) of CK-MB. CK-MB values obtained in the presence of biotin up to 3500 ng/mL were within ± 10% of the controls."

4. Assay Reportable Range:

The claimed assay reportable range is 0.2 ng/mL - 300 ng/mL.

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

The traceability of the Access CK-MB assay is unchanged since the clearance in K030012.

6. Detection Limit:

The limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) were determined for the Access CK-MB assay based upon recommendations in the CLSI EP17-A2 guideline. The LoB was determined to be 0.01 ng/mL. The LoD was determined to be 0.02 ng/mL. The LoQ was determined to be 0.03 ng/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 conducted using a protocol based on CLSI EP09c, 3rd Edition. A total of 146 lithium heparin plasma samples were evaluated, of which 132 were native samples and 14 were native samples supplemented with CK-MB antigen.

The study was run using three DxI 9000 Access Immunoassay Analyzers and three Access 2 instruments with three reagent lots and three calibrator lots. The concentrations in the

samples ranged from 0.29-271 ng/mL, as determined by the comparator device. Each sample was run in singleton. Weighted Deming regression analysis was performed. The regression analysis summary is shown below:

N	Concentration Range (ng/mL)	Slope (95% CI) (ng/mL)	Intercept (95% CI)	Correlation Coefficient (r)
146	0.29 - 271	1.04 (1.03 to 1.05)	0.0066 (-0.019 to 0.032)	1.00

2. Matrix Comparison:

The matrix claims are unchanged since the device was cleared in K030012.

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 sponsor provided the following information in the package insert:
"A study performed by Beckman Coulter, Inc. on serum and lithium heparin plasma samples produced the following reference interval (95% central fraction). The reference interval was calculated using CLSI C28-A2 and verified with EDTA plasma samples using CLSI EP28-A3c."

n	Median Age	Age Range	Reference Interval (ng/mL)
242	48	23 - 78	0.6 - 6.3

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.