510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K242870

B Applicant

Beckman Coulter, Inc.

C Proprietary and Established Names

Access hsTnI

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MMI	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:

Addition of previously cleared assay to a new instrument

B Measurand:

Cardiac Troponin (cTnI)

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:
Access hsTnI is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of cardiac troponin I (cTnI) levels in human serum and plasma using the Access 2 Immunoassay Systems to aid in the diagnosis of myocardial infarction (MI).

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

DxC 500i Clinical Analyzer

IV Device/System Characteristics:

A Device Description:

The Access hsTnI reagent packs contain specific reagents for the in vitro diagnostic measurement of cTnI including:

- R1a: Dynabeads paramagnetic particles coated with mouse monoclonal anti-human cTnI antibody suspended in TRIS buffered saline, with surfactant, bovine serum albumin (BSA), < 0.1% sodium azide, and 0.1% ProClin 300.
- R1b: 0.1 N NaOH
- R1c: TRIS buffered saline, surfactant, protein (mouse), < 0.1% sodium azide, and 0.1% ProClin 300.
- R1d: Sheep monoclonal anti-human cTnI alkaline phosphatase conjugate diluted in ACES buffered saline, with surfactant, BSA matrix, protein (bovine, sheep, mouse), <0.1% sodium azide, and 0.25% ProClin 300.

B Principle of Operation:

The Access hsTnI assay is a two–site immunoenzymatic (“sandwich”) assay. Monoclonal anti–cTnI antibody conjugated to alkaline phosphatase is added to a reaction vessel along with a surfactant–containing buffer and sample. After a short incubation, paramagnetic particles coated with monoclonal anti–cTnI antibody are added. The human cTnI binds to the anti–cTnI antibody on the solid phase, while the anti–cTnI antibody–alkaline phosphatase conjugate reacts with different antigenic sites on the cTnI 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 hsTnI

B Predicate 510(k) Number(s):
K230648

C Comparison with Predicate(s):

Device & Predicate Device(s):	K242870	K230648
Device Trade Name	Access hsTnI	Access hsTnI
General Device Characteristic Similarities		
Intended Use/Indications For Use	Quantitative determination of cardiac troponin I (cTnI) levels in human serum and plasma to aid in the diagnosis of myocardial infarction (MI).	Same
Assay Principle	Chemiluminescent sandwich assay	Same
Sample Type	Serum and Lithium Heparin plasma	Same
Analytical Measuring Range	2.0 pg/mL to 27,027 pg/mL	Same
Sample Volume	55 µL	Same
Open pack stability	Stable at 2 to 10°C for 64 days after opening	Same
Extended Range	1:5 dilution factor and limitation statement related to carryover	Same
General Device Characteristic Differences		
Instrument Required	DxC 500i Clinical Analyzer	Access 2 Immunoassay System
Wash Buffer	A16793 (10L container)	A16792 (2L container)

VI Standards/Guidance Documents Referenced:

1. CLSI EP06-Ed2: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
2. CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
3. CLSI EP05-A3: Evaluation of Precision of Qualitative Measurement Methods Procedures; Approved Guideline – Third Edition
4. CLSI EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Repeatability and Within-Laboratory Precision study

The sponsor evaluated precision of the Access hsTnI assay on the DxC 500i Clinical Analyzer in several studies following the recommendations in CLSI EP05-A3. Six levels of lithium heparin plasma and serum pools, and serum-based commercial control materials with troponin concentrations spanning the measuring range were each tested on a single DxC 500i instrument using a single reagent pack lot and calibrator lot at a single site. Each sample was assayed in duplicate, in two runs per day, over 20 days for a total of 40 runs and a minimum of 80 measurement per sample. The within-laboratory (total) imprecision and within-run (repeatability) %CV and SD results for this study are shown below:

DxC 500i Serum Results					
Sample	Mean (pg/mL)	Within-Run (Repeatability)		Within-Laboratory (Total)	
		SD	CV%	SD	CV%
Control L1	46.7	0.8	1.8	1.2	2.5
Control L2	1500.0	27.6	1.8	34.8	2.3
Control L3	17400.7	448.3	2.6	466.1	2.7
Pool 1	3.2	0.2	5.5	0.3	9.3
Pool 2	8.7	0.3	3.7	0.5	5.2
Pool 3	15.9	0.4	2.3	0.9	5.8
Pool 4	77.7	1.7	2.2	2.2	2.8
Pool 5	4001.7	63.3	1.6	120.3	3.0
Pool 6	17289.2	414.7	2.4	572.3	3.3

DxC 500i Lithium Heparin					
Sample	Mean (pg/mL)	Within-Run (Repeatability)		Within-Laboratory (Total)	
		SD	CV%	SD	CV%
Control L1	47.7	1.8	3.8	2.3	4.8
Control L2	1502.7	36.2	2.4	73.2	4.9
Control L3	18246.1	654.5	3.6	838.9	4.6
Pool 1	10.5	0.4	3.6	0.5	4.8
Pool 2	16.4	0.7	4.0	0.9	5.4
Pool 3	110.3	3.8	3.4	5.5	5.0
Pool 4	4605.6	166.3	3.6	283.6	6.2
Pool 5	19027.4	778.9	4.1	1334.0	7.0
Pool 6	2.6	0.3	11.6	0.3	12.9

Reproducibility Study

Reproducibility of the Access hsTnI assay was evaluated on the DxC 500i instrument platform following CLSI EP05-A3 guideline. Reproducibility panel testing consisted of six serum samples and six lithium heparin plasma samples with troponin concentrations across the measuring range tested in replicates of three, in two runs per day, separated by at least 2 hours between runs, for five (5) days, generating thirty measurements for each panel at each of three sites with a single instrument per site, for a total of 90 measurements per panel overall. The reproducibility %CV and SD results for this study are shown below:

DxC 500i Reproducibility - Serum													
Sample	Mean (pg/mL)	Reproducibility		Repeatability		Between-Site		Between-Lot		Between-Day		Between-Run	
		SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Panel 1	10.32	0.40	3.9	0.37	3.6	0.13	1.2	0.003	0.0	0.108	1.0	0	0
Panel 2	21.30	0.80	3.8	0.69	3.2	0.32	1.5	0.063	0.3	0.246	1.2	0	0
Panel 3	97.27	4.38	4.5	3.06	3.1	2.19	2.3	0.750	0.8	2.114	2.2	0	0
Panel 4	4813	148.46	3.1	143.1	3.0	25.4	0.5	0.414	0.0	0	0	30.49	0.6
Panel 5	23125	753.33	3.3	706	3.1	262.9	1.1	5.697	0.0	0	0	0	0
DxC 500i Reproducibility – Lithium Heparin Plasma													
Sample	Mean (pg/mL)	Reproducibility		Repeatability		Between-Site		Between-Lot		Between-Day		Between-Run	
		SD	CV	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Panel 0	2.509	0.269	10.7	0.183	7.3	0.17	6.7	0.010	0.4	0.047	1.9	0.088	3.5
Panel 1	11.831	0.572	4.8	0.412	3.5	0	0	0	0	0.230	1.9	0.326	2.7
Panel 2	19.035	0.688	3.6	0.576	3.0	0.30	1.6	0.010	0.1	0.216	1.1	0.067	0.4
Panel 3	83.689	4.562	5.5	3.906	4.7	0.83	1.0	0.117	0.1	2.148	2.6	0.477	0.6
Panel 4	5006.95	223.10	4.5	131.20	2.6	176.6	3.5	33.86	0.7	15.168	0.3	0	0
Panel 5	23731.3	888.95	3.7	864.50	3.6	155.4	0.7	17.41	0.1	135.67	0.6	0	0

Multiple temperature (run and calibration) within laboratory study: The hsTnI assay imprecision was evaluated using lithium heparin plasma samples, under the following temperature conditions:

Calibrating at 18°C and running samples at 18°C, 23°C and 28°C
Calibrating at 23°C and running samples at 18°C, 23°C and 28°C
Calibrating at 28°C and running samples at 18°C, 23°C and 28°C

For each set of temperature conditions, six lithium heparin plasma samples with TnI concentrations of approximately 3, 10, 18, 80, 4000, and 18,000 pg/mL were used in the determination of imprecision. Each sample was assayed in duplicate, in two runs per day, over at least 20 days for a total of 40 runs and 80 replicates for each sample at each of the nine combinations of temperature conditions noted above. Testing was performed on one DxC 500i instrument using one reagent lot and one calibrator lot. The following results from one set of temperature conditions are representative of the results from this precision study:

Thermal Imprecision Study Results: DxC 500i; Calibration at 18°C; Run at 18°C										
Sample	N	Mean	Repeatability (within-run)		Between-Run		Between-Day		Total (Within-Lab)	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%
Sample 1	80	3	0.22	7.2	0.20	6.6	0.00	0.0	0.3	9.8
Sample 2	80	12	0.30	2.6	0.20	1.8	0.20	1.4	0.4	3.5
Sample 3	80	19	0.6	3.0	0.0	0.0	0.2	0.9	0.6	3.1
Sample 4	80	93	2.0	2.2	1.2	1.3	0.4	0.4	2.4	2.6
Sample 5	80	4413	116.4	2.6	0.1	0.0	68.5	1.6	135.1	3.1
Sample 6	80	19786	700.6	3.5	11.2	0.1	232.8	1.2	738.3	3.7

2. Linearity:
   The linearity of the Access hsTnI assay on the DxC 500i instrument was evaluated following the recommendations in CLSI EP06-A2 using lithium heparin plasma samples covering the full range of the assay. Testing consisted of 9 sample panels across the measuring range, performed on two instruments using 2 reagent lots and a single calibrator lot. A minimum of seven test replicates per linearity sample were measured using two test runs, four replicates per sample per run. The results are summarized below:

   Results; Linear regression equation:
   $y = 0.964x + 0.066$ (range tested 1.83 to 35152.97 pg/mL)

   The largest deviations in recovery in the full AMR results was 5.67%.

3. Analytical Specificity/Interference:

   The Analytical Specificity/Interference performance was evaluated in K172787 and the claims are unchanged.

4. Assay Reportable Range:

2.0 – 27,027 pg/mL.

The sponsor performed studies to evaluate total carryover (intra-assay carryover and inter-module carryover (carryover from the clinical chemistry module to the immunoassay module)) and included a limitation in the labeling describing the carryover observed.

Studies indicate that if a sample with cTnI > 150,000 pg/mL (ng/L) is tested on an Access 2 system, intra-assay carryover may be observed if Access hsTnI is tested after the high cTnI sample. The extent of carryover observed is directly proportional to the cTnI concentration that is present in the high sample. In studies, the estimated carryover was 3-5 pg/mL (ng/L) from a high sample at 270,000 pg/mL (ng/L) and 5-8 pg/mL (ng/L) from a high sample at 500,000 pg/mL (ng/L).

Additionally, BEC included a second limitation statement to address the inter-assay carryover:

When a sample containing high cardiac troponin (cTnI) >27,000 pg/mL is tested on an Access Immunoassay other than Access hsTnI, carryover of cTnI may be observed if the next test(s) performed is Access hsTnI. This form of carryover has been observed ***in the sample immediately following, and up to the third subsequent sample*** *processed after the high cTnI sample. The magnitude of carryover observed is directly proportional to the cTnI concentration present in the high sample. Representative data for the potential magnitude of carryover from samples with different concentrations of cTnI tested is provided below:*

High cTnI Concentration (pg/mL)	*Observed Carryover Magnitude (pg/mL)*
~27,000	*3.2*
~50,000	*4.5*
~110,000	*9.3*
~150,000	*19.6*
~270,000	*22.3*
~500,000	*44.9*
~1,000,000	*77.8*

To reduce the risk of inter-assay carryover when testing Access hsTnI on the DxC 500i Clinical Analyzer, it is strongly recommended to test all Access hsTnI samples on a dedicated instrument, separate from other Access Immunoassays.

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

Traceability and stability are the same as described in K222881.

6. Detection Limit:

Studies were performed to determine the Limit of Blank (LoB), Limit of Detection

(LoD) and Limit of Quantitation (LoQ) for the Access hsTnI assay on the DxC 500i instrument following the recommendations in CLSI EP17-A2.

The study protocol was carried out on three DxC 500i analyzers, which tested one reagent lot each. The LoB evaluation required a total of 60 replicates on each instrument by running four test samples, five replicates in a single test run, one run per day for three days. Four separate lots of zero-level (S0) Access hsTnI calibrator served as the four LoB test samples. For the LoD and LoQ experiment, a total of 45 replicates were generated per test sample on each instrument by testing nine replicates per sample per test run and completing one run per day for five days. For estimation of LoD and LoQ, 13 lithium heparin plasma samples containing low levels of hsTnI analyte were measured. These studies support the sponsor's claimed measuring range of 2.0 pg/mL to 27,027 pg/mL.

Thermal Sensitivity Study
A second study was performed to evaluate the LoQ of the Access hsTnI assay across various calibration and run temperatures. 13 lithium heparin plasma samples containing low concentrations of Troponin I analyte were tested on one DxC 500i analyzer at each of three ambient run and calibration temperatures (18°C, 23°C, and 28°C). A total of 45 replicates were generated per test sample per temperature on each instrument by testing nine replicates per sample per test run and completing one run per day for five days.

These studies support the sponsor's claimed measuring range of 2.0 pg/mL to 27,027 pg/mL.

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A Method Comparison study conducted at three (3) testing sites evaluated 208 unique intended use lithium heparin samples with two (2) lots of reagents used at each site. One (1) calibrator lot was used for all testing. Results of this method comparison study were analyzed using Weighted Deming regression model and representative results of a single site are summarized below:

N	Intercept [95% CI]	Slope [95% CI]	Correlation Coefficient (r)
208	0.49 [0.30 - 0.77]	0.97 [0.95 - 0.98]	0.999

A second method comparison study was conducted to determine the equivalency of serum. Testing occurred over multiple days using DxC 500i clinical analyzer-Access 2 instrument pairs, with a single lot of hsTnI and calibrator. Representative results of the study are summarized below:

Range	N	Passing Bablok Regression				
		Slope		Intercept		Correlation Coefficient
		Estimate	95% CI	Estimate	95% CI	
2.12 – 23,211	98	1.0	(0.99, 1.02)	-0.245	(-0.670, 0.068)	1.0

Thermal Method Comparison Study:
The sponsor also performed thermal method comparison studies that show that the performance of the candidate device at different calibration and run temperature conditions is unchanged from K172787.

Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

   The sponsor provided information to support that the modification to the candidate device did not impact the clinical performance claims described in K172787.

2. Clinical Specificity:

   See clinical sensitivity above.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not applicable.

D Clinical Cut-Off:

The sponsor provided information to support that the modification to the candidate device did not impact the clinical cutoffs described in K172787.

E Expected Values/Reference Range:

The sponsor provided information to support that the modification to the candidate device did not impact the 99th percentile upper reference limits described in K172787.

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.