# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
ASSAY ONLY

## I Background Information:

### A 510(k) Number

K222881

### 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:

Modification of an existing device

### B Measurand:

Cardiac Troponin I

### 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 DxI Access Immunoassay Analyzers 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:**

DxI 9000 Access Immunoassay Analyzer

## IV Device/System Characteristics:

**A Device Description:**

The candidate device is the same as described in K172787 except for the chemiluminescent substrate, which was changed from the Lumi-Phos 530 substrate to the Lumi-Phos PRO substrate to support use on the new DxI 9000 Access Immunoassay Analyzer.

**B Principle of Operation:**

The principle of operation is unchanged from the previous clearance described in K172787. The device has been modified to now use the Lumi-Phos PRO substrate to support use on the DxI 9000 Access Immunoassay Analyzer.

## V Substantial Equivalence Information:

**A Predicate Device Name(s):**
Access hsTnI

**B Predicate 510(k) Number(s):**
K172787

**C Comparison with Predicate(s):**

| **Device & Predicate Device(s):** | K222881 | K172787 |
|---|---|---|
| Device Trade Name | Access hsTnI | Access hsTnI |
| **General Device Characteristic Similarities** | | |
| Intended Use/Indications For Use | Paramagnetic particle, chemiluminescent immunoassay for the 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 |
| Automated Dilution (Dilution Recovery) | Up to approximately 270,270 pg/mL | Same |
| Open Reagent Pack Stability | Stable at 2 to 10°C for 64 days after opening | Same |
| Thermal Susceptibility/ Assay Protocol File (APF) | hsTnI APF does not include thermal algorithm | Same |
| **General Device Characteristic Differences** | | |
| Immunoassay Instrument | DxI 9000 Access Immunoassay Analyzer | Access 2 Immunoassay system |
| Chemiluminescent Substrate | Lumi-Phos PRO substrate | Lumi-Phos 530 substrate |

## VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Evaluation of Precision of Qualitative Measurement Methods Procedures; Approved Guideline – Third Edition

CLSI EP06-Ed2: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition

CLSI EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition

CLSI EP07; Interference Testing in Clinical Chemistry; Approved Guideline – Third Edition

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

*Repeatability and Within-Laboratory Precision study*

Repeatability (within-run precision) and intermediate precision (within-laboratory precision) studies were conducted according to the CLSI EP05-A3 guideline. For lithium heparin plasma samples, the study was run on five DxI 9000 Access Immunoassay Analyzers, using three reagent lots and five calibrator lots. Eight lithium heparin plasma samples consisting of an individual native lithium heparin plasma sample, pooled native lithium heparin plasma samples, and native lithium heparin samples spiked with purified human cardiac troponin I antigen, with varying concentrations spanning the assay range were each tested in duplicate, in two runs per day, over 20 days for a total of 40 runs and a minimum of 80 replicates.

For serum samples, the study was run on three DxI 9000 Access Immunoassay Analyzers, using three reagent lots and three calibrator lots. Five serum samples with TnI concentrations spanning the range of the assay (Samples 2, 3, 4 = pool of native serum samples and Samples 5 and 6 = native serum sample spiked with purified human cardiac troponin I antigen) were each tested in duplicate, in two runs per day over 20 days on each instrument and reagent lot combination.

The within-laboratory (total) imprecision includes within-run (repeatability), between-run, and between-day variance components. Results for this study for one representative reagent lot are shown below:

Lithium Heparin Plasma Results

| Sample Material | N | Mean (pg/mL) | Repeatability (Within-run) | | Between-run | | Between-day | | Within-Laboratory | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Ind. Native #1 | 80 | 2.4 | 0.24 | 10.0 | 0.04 | 1.7 | 0.00 | 0.1 | 0.24 | 10.1 |
| Native Pool #1 | 80 | 7.7 | 0.37 | 4.8 | 0.12 | 1.6 | 0.10 | 1.3 | 0.40 | 5.2 |
| Native Pool #2 | 80 | 9.5 | 0.26 | 2.7 | 0.12 | 1.3 | 0.00 | 0.0 | 0.28 | 3.0 |
| Native Pool #3 | 80 | 13 | 0.4 | 2.8 | 0.2 | 1.6 | 0.0 | 0.0 | 0.4 | 3.2 |
| Native Pool #4 | 80 | 20 | 0.4 | 1.9 | 0.2 | 0.8 | 0.3 | 1.7 | 0.5 | 2.7 |
| Native Pool #5 | 80 | 100 | 1.4 | 1.4 | 1.4 | 1.4 | 0.6 | 0.6 | 2.1 | 2.1 |

| Sample Material | N | Mean (pg/mL) | Repeatability (Within-run) | | Between-run | | Between-day | | Within-Laboratory | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Contrived #1 | 80 | 4814 | 62.1 | 1.3 | 0.4 | 0.0 | 61.7 | 1.3 | 87.5 | 1.8 |
| Contrived #2 | 80 | 24700 | 356.8 | 1.4 | 141.1 | 0.6 | 169.1 | 0.7 | 419.3 | 1.7 |

Serum Results

| Sample # | N | Mean (pg/mL) | Repeatability (Within-run) | | Between-run | | Between-day | | Within-Laboratory | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Native Pool # 2 | 80 | 9.6 | 0.26 | 2.7 | 0.11 | 1.1 | 0.12 | 1.2 | 0.31 | 3.2 |
| Native Pool # 3 | 80 | 24 | 0.6 | 2.3 | 0.2 | 0.7 | 0.2 | 1.0 | 0.6 | 2.6 |
| Native Pool # 4 | 80 | 88 | 1.3 | 1.4 | 0.8 | 0.9 | 1.6 | 1.8 | 2.2 | 2.5 |
| Contrived # 5 | 80 | 4889 | 62.4 | 1.3 | 75.9 | 1.6 | 92.6 | 1.9 | 135.0 | 2.8 |
| Contrived # 6 | 80 | 22963 | 404.1 | 1.8 | 557 | 2.4 | 1211 | 5.3 | 1393.2 | 6.1 |

*Reproducibility study*

Reproducibility was evaluated on three instruments at three external clinical laboratories following recommendations described in CLSI EP05-A3. Five serum and six lithium heparin samples with hsTnI concentrations covering the measuring range were analyzed on instruments in replicates of three over a five-day period with two runs per day, three reagent lots per run, generating a maximum of 90 measurements per sample per platform per site; 270 total measurements per instrument. One calibrator lot was used in the studies. The results are summarized below.

Lithium Heparin Plasma Results

| Concentration pg/ml (ng/L) | | | Repeatability (Within-Run) | | Between-Run | | Between-Day | | Between-Site | | Reproducibility | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sample # | N | Mean | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Sample 1 | 270 | 2.6 | 0.19 | 7.5 | 0.21 | 8.1 | 0.08 | 3.1 | 0.26 | 10.0 | 0.40 | 15.5 |
| Sample 2 | 269 | 11.3 | 0.31 | 2.7 | 0.21 | 1.1 | 0.16 | 1.4 | 0.05 | 0.5 | 0.43 | 3.8 |
| Sample 3 | 270 | 18.9 | 0.31 | 1.6 | 0.15 | 0.8 | 0.14 | 0.8 | 0.33 | 1.8 | 0.58 | 3.1 |
| Sample 4 | 270 | 105 | 1.9 | 1.8 | 1.1 | 1.0 | 1.0 | 1.0 | 1.1 | 1.0 | 3.2 | 3.0 |
| Sample 5 | 270 | 4846 | 116.4 | 2.4 | 57.5 | 1.2 | 0.0 | 0.0 | 74.1 | 1.5 | 169.5 | 3.5 |
| Sample 6 | 270 | 22045 | 357.1 | 1.6 | 308.2 | 1.4 | 293.3 | 1.3 | 311.4 | 1.4 | 691.5 | 3.1 |

Serum Results

| Concentration pg/ml (ng/L) | | | Repeatability (Within-Run) | | Between-Run | | Between-Day | | Between-Site | | Reproducibility | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sample # | N | Mean | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Sample 2 | 270 | 10.6 | 0.34 | 3.3 | 0.20 | 1.9 | 0.00 | 0.0 | 0.00 | 0.0 | 0.44 | 4.2 |
| Sample 3 | 270 | 19.2 | 0.43 | 2.2 | 0.31 | 1.6 | 0.22 | 1.1 | 0.00 | 0.0 | 0.59 | 3.1 |
| Sample 4 | 270 | 105 | 2.3 | 2.2 | 1.7 | 1.7 | 0.1 | 0.1 | 2.4 | 2.3 | 3.9 | 3.7 |
| Sample 5 | 270 | 4548 | 78.6 | 1.7 | 83.9 | 1.8 | 0.0 | 0.0 | 8.4 | 0.2 | 134.4 | 3.0 |
| Sample 6 | 270 | 21567 | 409.0 | 1.9 | 307.3 | 1.4 | 197.2 | 0.9 | 200.1 | 0.9 | 712.0 | 3.3 |

Thermal imprecision study:
The study was run on two instruments, using three reagent lots and two calibrator lots. Seven lithium heparin plasma samples, with varying hsTnI concentrations, were assayed in duplicate with two runs per day, over 30 days 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

Samples were tested at each temperature for a period of 10 days for a total of 40 replicates for each temperature condition. Imprecision was evaluated for all combinations of calibration and result temperature for each sample on each of two instruments.

The within-laboratory (total) imprecision includes within-run (repeatability), between-run, and between-day variance components. The following results from one set of temperature conditions are representative of the results from this precision study:

| Sample | N | Mean (pg/ml) | Repeatability (Within-run) | | Between-run | | Between-day | | Within-Laboratory | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| 1 | 40 | 2.4 | 0.35 | 14.4 | 0.14 | 5.7 | 0.00 | 0.0 | 0.38 | 15.4 |
| 2 | 40 | 7.8 | 0.27 | 3.5 | 0.00 | 0.0 | 0.00 | 0.0 | 0-27 | 3.5 |
| 3 | 40 | 9.7 | 0.32 | 3.3 | 0.00 | 0.0 | 0.11 | 1.2 | 0.34 | 3.5 |
| 4 | 40 | 13 | 0.4 | 2.8 | 0.0 | 0.0 | 0.2 | 1.2 | 0.4 | 3.1 |
| 5 | 40 | 21 | 0.6 | 3.0 | 0.0 | 0.0 | 0.8 | 3.6 | 1.0 | 4.7 |
| 6 | 40 | 100 | 2.3 | 2.3 | 0.7 | 0.7 | 00 | 0.0 | 2.4 | 2.4 |
| 7 | 40 | 4750 | 61.2 | 1.3 | 47.3 | 1.0 | 36.9 | 0.8 | 85.7 | 1.8 |

2. Linearity:
Two studies were performed to determine the linearity of the modified device following the recommendations in CLSI EP06-A2. One study evaluated the full range and the second study evaluated the low range of the assay. The low sample was a native sample containing a concentration of hsTnI at the low end of the measuring interval and the high sample was prepared using purified human cardiac troponin. Using these low and high samples, admixtures were prepared by using incrementally larger proportions of the high sample

diluted with the low sample, in order to achieve concentrations that span the range of the assay or span the low range of the assay. These studies were run on one instrument using three reagent pack lots and one calibrator lot.

The data was analyzed based on CLSI EP06-A2 using a weighted linear regression comparing the observed results to the expected results based on the proportion of high sample in the linearity panel level. The deviation from linearity was derived for each sample by calculating the difference between the observed result and the corresponding value from the linear fit. The maximum deviation from linearity for these studies was 10% for study one (full range study) and 8% for study two (low range study). Representative results for weighted linear regression are shown below:

Study One: Full AMR

| Sample Type | Range Tested (pg/mL) | Regression Equation |
|---|---|---|
| Lithium Heparin Plasma | 1.660 – 31,522 | y=0.9533x+0.0768 |
| Serum | 0.982 – 30,419 | y=1.006x-0.006 |

Study Two: Low End of AMR

| Sample Type | Range Tested (pg/mL) | Regression Equation |
|---|---|---|
| Lithium Heparin Plasma | 1.645 – 122 | y=0.9919x-0.0048 |
| Serum | 1.249 – 100 | y=0.9283x+0.0858 |

These studies support the sponsor's measuring range claim of 2.0 to 27,027 pg/mL which is the same as the predicate.

Hook Effect:
Same as described in K172787.

Dilution:
A dilution study was performed and supports a 1:10 auto-dilution claim which is the same as the predicate.

3. Analytical Specificity/Interference:

Interference:
The sponsor conducted studies to support that the interference claims of the candidate device are unchanged from K172787.

Cross-Reactivity:
The sponsor conducted studies to support that the cross-reactivity claims of the candidate device are unchanged from K172787.

4. Assay Reportable Range:

2.0 – 27,027 pg/mL.

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

Traceability and stability are the same as described in K172787, except for the stability of frozen samples which has been updated to support the storage of frozen samples at -20°C for up to 180 days.

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 DxI 9000 Access Immunoassay Analyzer using the recommendations in CLSI EP17-A2.

For the estimation of LoB, three DxI 9000 Immunoassay Analyzers were used in the study design with three reagent lots and one calibrator lot. Four S0 calibrators were used for the LoB determination. Samples were tested over three days with one run per day and five replicates per run, for each pack lot.

For estimation of LoD, three DxI 9000 Immunoassay System were used in the study with three reagent lots and one calibrator lot. Eight serum and nine lithium heparin plasma samples containing low levels of hsTnI analyte were measured. Samples were tested over five days with one run per day, nine replicates per run, for each pack lot. The maximum observed LoD across the lots was taken as the reported value for the measurement procedure.

For estimation of LoQ, 12-13 serum and lithium heparin (plasma) samples containing low levels of hsTnI analyte were measured. Samples were tested in replicates of nine per run with one run per day and five total days on each pack lot and instrument. This resulted in a maximum of 45 replicates for each sample on each pack lot tested. 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.

A second study was performed to evaluate LoQ of the Access hsTnI assay across various calibration and run temperatures. Multiple LoQ studies were completed across two DxI 9000 instruments, two reagent lots, and three ambient temperatures. A panel of native serum samples containing low concentrations of troponin I analyte were measured in replicates of 5 per run with 2 runs per day over 5 days. This study was repeated at each of three ambient run and calibration temperatures (18 °C, 25 °C, and 32 °C). This same study design was completed for each instrument and reagent lot combination. A variance components model was used to estimate the within-laboratory (total) %CV for each sample on each instrument and reagent lot combination at each calibration and run temperature combination.

The results of the studies support the unchanged claimed measuring range of 2.0-27,027 pg/mL.

7. Assay Cut-Off:

Not applicable.

## B Comparison Studies:

1. Method Comparison with Predicate Device:

   The sponsor performed method comparison studies to demonstrate equivalence between the unmodified assay (K172787) and the candidate assay.

   A method comparison study was conducted by comparing the results for the Access hsTnI assay on the DxI 9000 Access Immunoassay Analyzer to the predicate device, the Access hsTnI assay on the Access 2 Immunoassay Analyzer. Lithium heparin and serum samples from the intended use population were evaluated using the predicate device and the candidate device across three reagent pack lots at multiple sites. Trilevel quality controls were also evaluated daily in duplicates to verify systems were in specifications. Results of this method comparison study were analyzed using both Passing-Bablok and Weighted Deming regression models. Representative results (based on Passing Bablok) are summarized below:

   Method Comparison: Access hsTnI (DxI 9000 vs. Access 2)

| Sample Type | N | Range of samples | Slope [95% CI] | Intercept [95% CI] | R |
|---|---|---|---|---|---|
| Lithium heparin Plasma | 184 | 2.1 – 24,557 | 1.08 [1.07-1.09] | -0.37 [-0.69 – -0.02] | 0.999 |
| Serum | 328 | 2.7 – 24,135 | 1.06 [1.06 - 1.07] | -0.76 [-1.09 – -0.42] | 0.998 |

2. Thermal Method Comparison with Predicate Device:

   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:

The sponsor provided data to support the use of lithium heparin samples and serum samples.

## 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.