510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k041192

B. Purpose of Submission:
New Device

C. Analyte:
Troponin-I

D. Type of Test:
Quantitative Immunoassay

E. Applicant:
Fisher Diagnostics

F. Proprietary and Established Names:
ARCHITECT® *STAT* Troponin-I Immunoassay and STAT Troponin-I Calibrator

G. Regulatory Information:

1. Regulation section:
   21 CFR §862.1215 Creatine phosphokinase/creatine kinase or isoenzymes test system
   21 CFR §862.1150 Calibrator

2. Classification:
   Class II

3. Product Code:
   MMI and JIT

4. Panel:
   75

H. Intended Use:

1. Intended use(s):

ARCHITECT®*STAT* Troponin-I is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of cardiac troponin-I (cTnI) in human serum and plasma on the ARCHITECT *i* System with STAT protocol capability. Troponin-I values are used to assist in the diagnosis of myocardial infarction (MI).

The ARCHITECT®*STAT* Troponin-I Calibrators are for calibration of the ARCHITECT *i*2000SR System when used for the quantitative determination of cardiac Troponin-I in human serum or plasma.

2. Indication(s) for use:

ARCHITECT®*STAT* Troponin-I is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of cardiac troponin-I (cTnl) in human serum and plasma on the ARCHITECT *i* System with STAT protocol capability. Troponin-I values are used to assist in the diagnosis of myocardial infarction (MI).

3. Special condition for use statement(s):
   Prescription use

4. Special instrument Requirements:
   ARCHITECT *i*2000SR

I. Device Description:

The ARCHITECT®*STAT* Troponin-I assay, including calibrators and controls are designed to be used on the ARCHITECT *i*2000SR instrument platform. Each ARCHITECT®*STAT* Troponin-I assay is a two-step assay to determine the presence of cardiac troponin-I in human serum and plasma using Chemiluminescent Microparticle Immunoassay (CMIA) technology with flexible assay protocols, referred to as Chemiflex.

Each ARCHITECT®*STAT* Troponin-I assay consists of a reagent kit, other reagents, calibrator kit and a CD-ROM. The reagent kit contains 1 or 4 bottles each of a) microparticle, b) conjugate, and c) assay diluent. The other reagents are a) pre-trigger solution, b) trigger solution, and c) wash buffer. The Calibrator Kit contains: a) calibrator A in human serum, nonreactive for HBsAg, HIV-1 Ag or HIV-I NAT, anti-HCV, and anti-HIV/HIV-2 and sodium azide as a preservative, and b) calibrators B through F contain a recombinant human cardiac troponin IC complex in a phosphate buffer with protein stabilizer and Proclin® 300 as a preservative. The assay CD addition B, version 1.0 is compatible with other ARCHITECT *i* System software (compatible to 21 CFR 820).

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Beckman's ACCESS® AccuTnI Assay

2. Predicate K number(s):
   k021814

3. Comparison with predicate:

See the table below:

Characteristics	**ARCHITECT**	**ACCESS**	**Comparison**
Product Type	Troponin-I immunoassay	Troponin-I immunoassay	Same
Specimen Type	Human serum or plasma	Human serum or plasma	Same
Intended Use or indications for Use	ARCHITECT®*STAT* Troponin-I is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of cardiac troponin-I (cTnI) in human serum and plasma on the ARCHITECT *i* System with STAT capability. Troponin-I values are used to assist in the diagnosis of myocardial infarction (MI).	The Access AccuTnI assay is a paramagnetic particle, Chemiluminescent Immunoassay for the quantitative determination of cardiac Troponin-I (cTnI) levels in human serum and plasma using the Access Immunoassay Systems to aid in the diagnosis and treatment of myocardial infarction and cardiac muscle damage.	• Similar assay technology • Both quantitatively determine cTnI using human serum and plasma • Both assays are used in the diagnosis of myocardial infarction (MI).
Where Used	Clinical Laboratories	Clinical Laboratories	Same
Components	• Mouse monoclonal anti-Troponin I coated microparticles in TRIS buffer with protein (bovine and goat) stabilizers. Preservative: Antimicrobial agents. • Diluent containing protein (bovine and goat) stabilizers in phosphate buffer. Preservative: Proclin 300. • Anti-troponin-I (mouse, monoclonal) acridinium conjugate in MES buffer with protein (bovine) stabilizer. Preservative: Proclin 300.	• Paramagnetic particles coated with mouse monoclonal anti-human cardiac Troponin-I (cTnI) suspended in TRIS buffer saline, with surfactant, bovine serum albumin (BSA) matrix, <0.1% sodium azide and 0.1% Proclin 300. • Diluent A containing buffered BSA matrix with buffered surfactant, <0.1% sodium azide, 0.5% Proclin 300. • Mouse monoclonal anti-human cTnI alkaline phosphatase conjugate diluted in ACES buffered saline, with surfactant, BSA matrix, protein (bovine, goat, mouse), <0.1% sodium azide, 0.25% Proclin 300.	• Microparticles are both coated with mouse monoclonal anti-troponin I in TRIS buffer. The Access assay, however, uses a Proclin 300 preservative. • Both diluents contain a bovine component and Proclin 300 as a preservative. Unlike the Access assay, the ARCHITECT assay uses bovine and goat stabilizers. • Both conjugates contain mouse monoclonal anti-troponin I and Proclin 300 as a preservative. The Access assay contains bovine, goat and mouse proteins whereas the ARCHITECT assay contains bovine protein as a stabilizer.

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

FDA guidance "Points to Consider Guidance Document on Creatine phosphokinase/creatine kinase or isoenzymes test system."
NCCLS EP5-A, NCCLS EP7-A, NCCLS GP10-A

L. Test Principle:

The ARCHITECT®*STAT* Troponin-I is a based on Chemiluminescent Microparticle Immunoassay (CMIA) technology with flexible assay protocols, referred to as Chemiflex.

In the first step, sample, assay diluent and anti-troponin-I antibody-coated paramagnetic microparticles are combined. After incubation and washing, anti-troponin-I acridinium labeled conjugate is added and incubated, followed by wash and then pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of troponin-I in the sample and the RLUs detected by the ARCHITECT *I* system optics. The concentration of troponin-I is read relative to a standard curve established with calibrators of known troponin-I concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility: Precision studies were performed on the ARCHITECT®*STAT* Troponin-I assay for 20 days to determine variability over time. Three lots of ARCHITECT®*STAT* Troponin-I reagents were used on two ARCHITECT instruments with 2 specimen assay panels and troponin-I controls (low, medium and high). Replicates of each troponin-I assay panel and control samples were run on 2 instruments. The study was conducted under the guidance of NCCLS standard, "EP5-A".

Comparable results indicated that all three reagent lots on each instrument performed within the acceptance criteria of ≤ 10% CV (2.3% to 5.8%). Total imprecision of the ARCHITECT®*STAT* Troponin-I assay was substantially equivalent to that of the ACCESS AccuTnl assay (≤5.8% CV vs ≤6.90% CV, respectively).

b. Linearity/assay reportable range:
The dilution linearity of the ARCHITECT *STAT* Troponin-I assay using 12 patient samples (with mean expected values ranging from 0.199 ng/mL-21.870) with analyte concentrations across the dynamic range was calculated. The samples were diluted with human serum to the lower end of the detection range, between 0.2 and 1.0 ng/mL in concentration, to demonstrate linearity across the full range of the calibration curve.

The results indicated that the dilution linearity of the ARCHITECT *STAT* Troponin-I assay met the acceptance criteria of ±20% of the undiluted troponin-I concentration (the recovery ranged from 85.8% to 114.7%).

c. Traceability (controls, calibrators, or method):
The calibrators are prepared gravimetrically using a recombinant Troponin IC complex. The concentrations of the Internal Secondary Reference Calibrators are traceable near the MI medical decision point to a NIST candidate reference material, cRM A HyTest native Troponin lot 00/12-8T62.

Calibrator Stability: The calibrator stability study was designed to determine the minimum expiration dating/shelf life based upon accelerated and real-time data with adverse environmental and shipping conditions.

Stability studies were performed using three lots of calibrator using intended primary containers at 5, 25, 30 and 40 °C for 0 to 13 months. In addition, calibrators were evaluated using MCC and assay panels. The ARCHITECT®*STAT* Troponin-I assay recommended storage temperature at 2-8 °C. The performance of the calibrators over time was evaluated to verify the shelf life using the Arrhenius method. The data confirmed a shelf life of 12 months for product stored at 2-8 °C for calibrators tested.

The ARCHITECT®*STAT* Troponin-I assay demonstrated on-board reagent stability in excess of 30 days with both 100- and 500-test kits. All % CV was less than 10%. In addition, there was no ring formation in the microparticle bottles, in confirmation that the microparticles remained adequately suspended.

d. Detection limit:
The lowest detection limit for the ARCHITECT *STAT* Troponin-I assay at 10% CV is 0.032 ng/mL, and analytical sensitivity is ≤0.01 ng/mL at the 95% level of confidence. The analytical sensitivity was determined by assaying calibrator A in 36 runs in replicates of 10 and assaying calibrator B in 36 runs in replicates of 4. The calculation of the grand mean for calibrator A (0.0 ng/mL) and 2 standard deviations resulted in a value of ≤0.01 ng/mL. The ARCHITECT *STAT* Troponin-I assay diagnostic cutoff is 0.30 ng/mL based on the clinical performance.

e. *Analytical specificity:*
The ARCHITECT *STAT* Troponin-I assay analytical specificity is ≤ 0.1% cross-reactivity with skeletal troponin-I and ≤ 1% with cardiac troponin-C and cardiac troponin-T. Based on the NCCLS Protocol EP7-

A, a study was performed for ARCHITECT STAT Troponin-I assay. Specificity of the assay was determined by studying the cross-reactivity of the following compounds in normal human serum. The representative data is presented below; results in individual laboratories may vary from these data.

Cross-reactant	Cross-reactant Concentration (ng/mL)	% Cross-reactivity
Skeletal troponin-I	100	0.07
Cardiac troponin-C	1000	0.00
Cardiac troponin-T	1000	0.32

Drug Interference: The drug interference verification study was performed to determine the susceptibility of the ARCHITECT STAT Troponin-I assay to drug interferences. Base pools of negative and positive cardiac troponin-I concentrations were divided between a test and control sample. The test sample was spiked with formulated drug stock solution and the controls were spiked with equal volume of the solvent or diluent.

All tested drug compounds reflected values <0.01 ng/mL in the unspiked and <15% interference for the spiked samples except for two confirmed failures with Streptokinase and tPA. Repeat testing were performed using different concentrations of 31 U/mL and 2.3 ug/mL for Streptokinase and tPA, respectively at 1.5 and 1.2 hours post therapy. Based on the half-life information for Streptokinase and tPA, and the results of interference, Streptokinase and tPA do not produce interference in the ARCHITECT *STAT* Troponin-I assay when evaluated through *in vitro* testing.

Evaluation of Potentially Interfering Clinical Conditions: The ARCHITECT *STAT* Troponin-I assay was evaluated using specimens with HAMA and Rheumatoid Factor (RF) to assess the clinical specificity. A total of 11 specimens positive for HAMA and 10 sample positive for RF were evaluated for % interference with troponin-I levels spiked between 0.5 and 1.0 ng/mL; % interference results are summarized below, which are representative data; results in individual laboratories may vary from these data. The results indicated that HAMA and RF interferences for the ARCHITECT *STAT* Troponin-I assay were absolute mean of 6.0% for HAMA and 5.1% for RF.

Clinical Condition	Number of Specimens	% Interference	% Absolute Mean
HAMA	11	-4.5	6.0%
RF	10	-3.5	5.1%

Endogenous Interference: Interference was evaluated for four endogenous substances (bilirubin, hemoglobin, triglycerides, and total proteins), using specimens both positive and negative for troponin-I with the ARCHITECT *STAT* Troponin-I assay. Acceptance criteria of ≤ 15% interference of endogenous compounds were confirmed.

f. Assay cut-off:

A study was performed for the ARCHITECT *STAT* Troponin-I assay with specimens collected from four clinical sites. A total of 174 specimens from 77 AMI patients and a total of 778 specimens from 367 non-AMI patients were collected and assayed using ARCHITECT *STAT* Troponin-I assay. All troponin-I values were used to determine the diagnostic cutoff by ROC (receiver operator characteristics) curve analysis and clinical sensitivity and specificity was determined. The optimal cutoff value of 0.30 ng/mL was selected and optimal sensitivity and specificity was determined at various time intervals.

2. Comparison studies:

g. Method comparison with predicate device:

A study was performed where 460 samples were tested in replicates of one using ARCHITECT *STAT* Troponin-I over a period of three calibration cycles with three reagent lots on three instruments and compared to Beckman ACCESS instrument diagnostic kit. Data analyzed using the Passing-Bablok regression method indicated the following regression equation: slope = 1.1437 (1.092 to 1.190) , intercept = – 0.003 (-0.004 to -0.002), R2 = 0.98. The ARCHITECT *STAT* Troponin-I assay concentration ranged from 0-469 ng/mL, and ACCESS AccuTnl ranged from 0-277 ng/mL.

h. Matrix comparison:

The matrix comparison was performed by comparing plasma and serum interference in different tubes. The anticoagulant mean % interference was compared to serum uncoated glass tubes. All anticoagulants tested meet the PDR acceptance criteria of less than 10% interference.

3. Clinical studies:

a. Clinical sensitivity:

A study based on guidance from NCCLS Protocol GP10-A was performed for the ARCHITECT *STAT* Troponin-I assay. Specimens from the following populations were collected from four clinical sites and evaluated using the ARCHITECT *STAT* Troponin-I assay:

- 174 specimens from 77 AMI patients as diagnosed according to WHO criteria.
- 778 specimens from 367 non-AMI patients as diagnosed according to WHO criteria.

All troponin-I values were used to determine the diagnostic cutoff by receiver operator characteristics (ROC) curve analysis. From the ROC analysis, the optimal cutoff value of 0.30 ng/mL was selected to provide optimal clinical sensitivity and specificity. The data was further analyzed using time stratification from time of admission to the medical center and compared to another commercially available cTnI diagnostic assay. The representative data is presented below; results in individual laboratories may vary from these data.

		Hours Post admission 0-6	Hours Post admission 6-12	Hours Post admission 12-24
ARCHITECT *STAT* Troponin-I (cutoff= 0.30 ng/mL)	% Sensitivity % Specificity	60.0 95.4	78.6 94.6	91.7 96.5
Beckman's ACCESS Troponin-I (cutoff=0.50 ng/mL)	% Sensitivity % Specificity	50.0 98.3	67.9 98.5	72.9 98.8
WHO AMI Positive (n)		70	56	48
WHO AMI Negative (n)		346	259	173
Total Specimens (n)		416	315	221

b. Clinical specificity: The ARCHITECT *STAT* Troponin-I assay demonstrated sensitivity and specificity that is substantially equivalent to the ACCESS AccTnI assay, using the AMI "cut-off" of 0.30 ng/mL. The acceptance criteria for this study were met. The results are summarized below:

Assay System	Number of samples (Positive/Negative)	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)
ARCHITECT cardiac Troponin-I	174/778	74.7% (67.6-81.0%)	95.5% (93.7-96.7%)
Beckman Access Troponin-I		73.0% (65.7-79.4%)	96.5% (95.0-97.7%)

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

4. Clinical cut-off:
The ARCHITECT *STAT* Troponin-I assay diagnostic cutoff is 0.30 ng/mL based on the clinical sensitivity and specificity (described above).

5. Expected values/Reference range:
The normal range study for ARCHITECT *STAT* Troponin-I was performed to establish a reference interval for specimens from normal population. Three different reagent lots and instrument systems were utilized and each specimen was tested in replicate. A total of 224 specimens from donors were evaluated.

From the data the normal range for the ARCHITECT *STAT* Troponin-I assay was established and the 99th percentile concentration of troponin-I is 0.012 ng/mL.

The labeling recommends that each laboratory establish its own diagnostic cut-off to assure proper representation of specific populations and to reflect current practice and criteria for AMI diagnosis at their institution.

N. Conclusion:

The submitted material in this premarket notification for ARCHITECT® *STAT* Troponin-I Assay is complete and supports a substantially equivalence decision.