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

A. 510(k) Number:

k042924

B. Purpose for Submission:

New Device

C. Measurand:

Myoglobin (MYO) and calibrators

D. Type of Test:

Quantitative, Chemiluminescent Microparticle Immunoassay (CMIA)

E. Applicant:

Fisher Diagnostics

F. Proprietary and Established Names:

ARCHITECT® Stat Myo Immunoassay and ARCHITECT® STAT Myoglobin Calibrators A-F

G. Regulatory Information:

1. Regulation section:

   21 CFR §866.5680, Myoglobin immunological test system

   21 CFR §862.1150, Calibrator

2. Classification:

   Class II for both

3. Product code:

   DDR Myoglobin immunological test system

   JIS Calibrator, Primary

4. Panel:

   82, Immunology and 75, Chemistry

H. Intended Use:

1. Intended use(s):

   See indications for use.

2. Indication(s) for use:

   ARCHITECT® STAT Myoglobin (MYO) is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of myoglobin in human serum and plasma on the ARCHITECT® i System with STAT protocol capability. Myoglobin values are used to assist in the diagnosis of myocardial infarction (MI).

   The ARCHITECT® STAT Myoglobin Calibrators are for calibration of the ARCHITECT® i System with STAT protocol capability when used for the quantitative determination of myoglobin in human serum or plasma.

3. Special conditions for use statement(s):

   For Prescription use only

4. Special instrument requirements:

   ARCHITECT® i System

I. Device Description:

ARCHITECT® STAT MYO is a 2-step quantitative chemiluminescent microparticle immunoassay that determines the presence of myoglobin in human serum and plasma. The device uses 2 reagents that are provided as microparticles, anti-myoglobin (mouse, monoclonal) coated microparticles in TRIS buffer and conjugate anti-myoglobin (mouse, monoclonal) acridinium labeled conjugate in MES buffer with protein. Also, the device uses calibrators and controls (controls have been cleared k040880). Trigger and pre-trigger solutions and wash buffers are not provided with the conjugate and microparticles. The calibrators can be purchased separately. The assay CD addition B, version 3.01 is compatible with the ARCHITECT System soft versions 2.0 or high and is compatible to 21 CFR 820.

Human source material was tested for HBV, HCV and HIV I and 2 and found negative using FDA approved methods.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Abbott AxSYM® myoglobin assay

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

   k983848

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	ARCHITECT® STAT Myoglobin is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of myoglobin in human serum and plasma on the ARCHITECT® I System with Stat protocol capability.	The Abbott AxSYM® MYO is a Microparticle Enzyme Immunoassay (MEIA) for the quantitative determination of myoglobin in human serum and plasma using the AxSYM Immunoassay System
Components	• Microparticles: Anti-MYO (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizers. • Conjugate: Anti-MYO (mouse, monoclonal) acridinium conjugate in MES buffer with protein (bovine) stabilizer. • Calibrator A-F • Controls (k040880)	• Microparticles: Anti-MYO (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizers. • Conjugate: Anti- MYO (goat) Alkaline Phosphatase in TRIS buffer with protein stabilizers. • Calibrator A-F • Controls
Storage	Reagents at 2-8º C Calibrators at -10º C	2-8º C

Differences		
Item	Device	Predicate
Instrumentation Required	ARCHITECT® i System	AxSYM System
Test Principle	Chemiluminescence Microparticle Immunoassay (CMIA)	Microparticle Enzyme Immunoassay (MEIA)

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

NCCLS' Guideline, "C28-A2: How to Define and Determine Reference interval in the Clinical"
NCCLS' Guideline, "EP7-A: Interference testing in Clinical Chemistry"
NCCLS' Guideline, "EP5-A: Evaluation of Precision Performance of Clinical Chemistry".
NCCLS' Guideline, "EP9-A2: Method Comparison and Bias Estimation Using Patient Samples".
FDA Document-Shelf Life of Medical Devices, April 1, 1991
HIMA Stability Testing Programs for In Vitro Diagnostic Products July 1983
BSI: EN 13640 Stability Testing Programs for In Vitro Diagnostic Medical Devices 13/08/99
ICH Guideline: Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products (Annex to the Tripartite ICH Guideline for the Stability Testing of New Drug Substances ND Products) March 1995.

L. Test Principle:

ARCHITECT® STAT MYO immunoassay uses two steps to determine the presence of myoglobin in human serum or plasma. The first step is combining the sample with the anti MYO coated paramagnetic particles which is followed by incubation and washing. In the second step, the anti MYO acridinium conjugate is added. The pre-trigger and trigger solutions are added to produce a chemiluminescent reaction. This reaction is measured in relative light units (RLUs). The ARCHITECT® i System is an optical system that is capable of measuring the amount of myoglobin in a serum or plasma sample based on the RLUs.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Three lots of reagent assays were run in replicates of two at two separate times per day for twenty days on two instruments to determine reagent lot differences and variation in controls (low, medium and high). All three lots met their acceptance criteria of < 10%. The total imprecision CV ranged from 3.2% to 6.3 %.

Sample	Instrument	Reagent lot	Number of samples	Mean Conc. (ng/mL)	Within Run		Total	
					SD	%CV	SD	%CV
		A	80	56.9	2.0	3.6%	2.2	3.9%
	1	B	80	56.7	1.9	3.4%	2.0	3.5%
Low Control		C	80	62.3	2.2	3.5%	2.6	4.2%
		A	80	57.8	1.8	3.2%	2.7	4.6%
	2	B	80	60.8	2.0	3.4%	2.3	3.8%
		C	80	60.1	2.3	3.8%	2.4	3.9%
		A	80	324.9	13.3	4.1%	15.1	4.6%
	1	B	80	329.6	9.5	2.9%	12.0	3.6%
Medium Control		C	80	353.0	11.0	3.1%	12.8	3.6%
		A	80	354.9	10.3	2.9%	12.4	3.5%
	2	B	80	337.2	10.4	3.1%	11.3	3.4%
		C	80	337.6	12.0	3.6%	12.7	3.8%
		A	80	785.2	25.3	3.2%	25.3	3.2%
	1	B	80	803.5	36.0	4.5%	37.9	4.7%
High Control		C	80	848.1	29.3	3.5%	32.9	3.9%
		A	80	924.8	26.9	3.3%	32.4	3.9%
	2	B	80	813.3	29.6	3.6%	32.7	4.0%
		C	80	821.7	38.3	4.7%	11.8	5.4%
		A	80	42.7	1.6	3.8%	1.9	4.6%
	1	B	80	41.3	1.3	3.1%	1.7	4.1%
MCC Low Control		C	80	45.7	2.0	4.5%	2.2	4.8%
		A	80	42.6	1.7	3.9%	2.7	6.3%
	2	B	80	44.4	1.4	3.1%	1.8	4.1%
		C	80	44.7	2.1	4.6%	2.3	5.1%
		A	80	111.6	3.7	3.4%	5.1	4.6%
	1	B	80	110.1	4.4	4.0%	4.7	4.3%
MCC Medium Control		C	80	118.5	4.6	3.9%	5.3	4.5%
		A	80	117.2	3.8	3.3%	6.0	5.1%
	2	B	80	114.3	2.9	2.5%	4.1	3.6%
		C	80	114.2	4.5	3.9%	5.1	4.4%
		A	80	297.1	12.6	4.2%	15.5	5.2%
	1	B	80	293.2	12.9	4.4%	13.4	4.6%
MCC High Control		C	80	312.6	13.8	4.4%	15.6	5.0%
		A	80	320.7	7.4	2.3%	14.5	4.5%
	2	B	80	299.5	9.6	3.2%	11.7	3.9%
		C	80	299.0	12.6	4.2%	15.2	5.1%
		A	80	51.3	2.6	5.1%	3.5	6.7%
	1	B	80	49.7	2.8	5.7%	3.5	6.9%
Panel 1		C	80	54.0	2.1	3.8%	4.0	7.4%
		A	80	51.2	1.5	2.9%	3.1	6.1%
	2	B	80	53.4	2.2	4.2%	2.9	5.4%
		C	80	52.3	2.5	4.8%	3.3	6.3%
		A	80	116.6	3.8	3.3%	6.3	5.4%
	1	B	80	116.2	5.6	4.8%	7.5	6.4%
Panel 2		C	80	122.3	5.0	4.1%	6.7	5.5%
		A	80	121.7	3.4	2.8%	6.5	5.4%
	2	B	80	120.1	3.6	3.0%	7.6	6.3%
		C		118.1	5.7	4.8%	6.9	5.8%

b. Linearity/assay reportable range:

Ten samples with analyte concentrations between 914 ng/mL and 1100.7 ng/mL were diluted 50 fold with Calibrator A to obtain the lower end of the detection. The diluted samples ranged between 21.8 to 1171.2 ng/mL. The dilution linearity of ARCHITECT® STAT MYO immunoassay met their acceptance criteria of +/- 20 % of the undiluted MYO concentration with a mean of 117.7 % recovery and ranged from 80.0% to 120%.

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

Purified human cardiac myoglobin reference material (primary reference) is a purchased product which is prepared by taking human heart tissue and mixing it in a buffer solution. The primary calibrator is then run on a commercially available assay to determine its concentration. Internal Secondary Reference Calibrators (master calibrators B-F) are prepared by taking the primary calibrator and gravimetrically adding it to calibrator diluent at appropriate target values which are assigned by a commercially available assay. The ARCHITECT STAT Myoglobin is matched within +/-2.5 % to of the target concentration. The calibrator concentrations are:

CAL A- 0.00 ng/mL	CAL D- 300.0 ng/mL
CAL B- 30.0 ng/mL	CAL E- 600.0 ng/mL
CAL C- 100.0 ng/mL	CAL F- 1200.0ng/mL

Calibrator A contains TRIS buffer with protein (bovine) stabilizer.

Stability:

Calibrator stability studies were conducted (stress, open and closed vial) on three lots of calibrators from the ARCHITECT® STAT Myoglobin immunoassay. Storage of the calibrators at -10º C demonstrated stability of 8 weeks. The open vial stability demonstrated acceptable stability for 30 days at 2-8ºC. Accelerated studies, along with real-time intended storage (-10ºC) and real-time at intended thawed condition (2-8º C) confirm their dating of 12 months.

Sample stability:

The sample stability study evaluates the sample stability of the ARCHITECT® Stat MYO assay using Lithium Heparin and Serum Separator collection tubes. One reagent lot was used to calibrate one ARCHITECT® system. The storage conditions tested were: Room temperature ON-Board 1 hr, 3 hr and 8 hr; Refrigerated stability 2-8ºC 24 hrs and 2-8ºC 72 hrs; Freeze/Thaw stability – freeze for 24 hrs immediately after draw and 2-8ºC 24 hrs after thaw; and frozen stability –

frozen 14 days and 30-33 days. Data was evaluated as the % recovery difference for each sample from baseline (time=0). Acceptance criteria are +/- 20% of the mean difference for each sample type. The sample stability for each type and storage condition was +/- 10 % with a range of -1.3% to 9.3%.

d. Detection limit:

The ARCHITECT® STAT Myoglobin analytical sensitivity is <1.0 ng/mL at the 95% level of confidence (36 runs and 10 replicates of Calibrator A and 4 replicates of Calibrator B per run). Analytical sensitivity is defined as the concentration at two standard deviations above the ARCHITECT® STAT Myoglobin calibrator A (0.0ng/mL) grand mean and represents the lowest concentration of Myoglobin that can be distinguished from zero. The calibration range is 0.0 to1200.0 ng/mL. In the labeling, it is recommended that a single sample of all levels of myoglobin controls be tested to evaluate the assay calibration.

e. Analytical specificity:

Potentially cross-reactive substances were evaluated by spiking samples with different concentrations of myoglobin using NCCLS's "EP7-A: Interference Testing in Clinical Chemistry". One reagent lot and one instrument was used to determine the interferences of bilirubin (20 mg/dL), hemoglobin (500 mg/dL), triglycerides (1000 mg/dL) and total protein (4 and 10 g/dL) using high and low interference levels. The % interference was evaluated using the equation:

$$\% \text{ interference} = \frac{(\text{Test Conc.} - \text{Control Conc.})}{\text{Control Conc.}} \times 100$$

The compounds appear to have no significant cross reactivity (<10%) with the ARCHITECT® STAT Myoglobin immunoassay and reflected values of between -1.9% and 9.8% percent interference.
A total of 10 sample pairs were tested for HAMA interference and 10 sample pairs were tested for RF interference using one reagent lot and one instrument system according to the guidelines from NCCLS EP7. Each sample was assayed five times and a mean concentration was used to calculate the % interference. The amount of interference for HAMA was less than 10% based on absolute values. The average absolute HAMA interference was 7.74% with a range of 3.63% to 11.86%. The amount of interference for RF was less than 15% based on absolute values. The average absolute RF interference was 12.60% with a range of 11.00% to 14.19%

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:
238 serum and plasma samples were tested using both the Architect and the AxSYM myoglobin assays.

The Passing-Bablok regression analysis was conducted on the 238 plasma and serum samples. The Architect assay ranged from 7.6 to 1188.7 ng/mL and the AxSYM ranged from 7.6 to 1167.1 ng/mL. The regression analysis obtained a y-intercept of 2.88 (95% CI of 2.05 – 3.36), slope of 0.99 (95% of 0.97 to 1.01) and a correlation coefficient (r) of 0.989.

b. Matrix comparison:

A serum and plasma comparison study was conducted to compare tube interference. Absolute interference from all tubes ranged from 2.1 to 4.6% for spiked donor samples and ranged from 1.8 to 5.2% for endogenous donor specimens. Actual interference from all tubes ranged from -4.6 to -1.0% for spiked donor specimens and from -4.6 to -0.3% for endogenous donor specimens. The acceptance criteria for interference is less than or equal to 10% interference.

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:

160 specimens from donors were tested with the ARCHITECT® MYO assay to establish a normal range from normal population.
The 99th percentile concentration for plasma specimens is 146.9 ng/mL. The 99th percentile concentration for plasma male and female specimens is 138.8 ng/mL and 107.2 ng/mL, respectively. Guidelines and principles from NCCLS' standard, "C28-A2: How to Define and Determine Reference Intervals in the Clinical Laboratory" was used.

Table11: Plasma Summary Table

Statistic	Myoglobin (ng/mL)
Number	160
Mean	37.7
Median	30.1
97.5 Percentile	107.8
99 Percentile	146.9
Minimum	7.6
Maximum	195.6

Table 12: Male Summary Table

Statistic	Myoglobin (ng/mL)
Number	80
Mean	49.1
Median	41.1
97.5 Percentile	116.6
99 Percentile	138.8
Minimum	15.4
Maximum	195.6

Table 13: Female Summary Table

Statistic	Myoglobin (ng/mL)
Number	80
Mean	26.2
Median	20.8
97.5 Percentile	55.2
99 Percentile	107.2
Minimum	7.6
Maximum	180.4

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.