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

A. 510(k) Number:
k041811

B. Purpose for Submission:
New device

C. Analyte:
Troponin I

D. Type of Test:
Quantitative

E. Applicant:
Abbott Diagnostics

F. Proprietary and Established Names:
Abbott AxSYM® Troponin-I ADV
Abbott AxSYM® Troponin-I ADV Standard Calibrators
Abbott AxSYM® Troponin-I ADV Controls

G. Regulatory Information:

1. Regulation section:
   21 CFR 862.1215, Immunoassay method, troponin subunit
   21 CFR 862.1150, Calibrator, Secondary
   21 CFR 862.1660, Single (specified) analyte controls (assayed and unassayed)
2. Classification:
   Class II, Class I
3. Product Code:
   MMI, JIT, JJX
4. Panel:
   75

H. Intended Use:

1. Intended use(s):
   See Indications for Use

2. Indication(s) for use:
   The AxSYM® Troponin-I ADV assay is a Microparticle Enzyme Immunoassay (MEIA) for the quantitative determination of cardiac troponin-I (cTnI) in human serum or plasma on the AxSYM System. Troponin-I values are used to assist in the diagnosis of myocardial infarction (MI).

The AxSYM Troponin-I ADV Standard Calibrators are for the standard calibration of the AxSYM System when used for the quantitative determination of cardiac troponin-I in human serum or plasma.

The AxSYM Troponin-I ADV Controls are for the estimation of test precision and the detection of systematic analytical deviations of the AxSYM System (reagents, calibrators, and instrument) when used for the quantitative measurement of cardiac troponin-I in human serum or plasma.

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

4. Special instrument Requirements:
   Abbott AxSYM System

I. Device Description:

The AxSYM® Troponin-I ADV assay is supplied as a 100 test reagent pack consisting of Reagent Bottles 1 – 4 as follows:

Reagent Bottle 1	Conjugate 2, Anti-biotin (mouse monoclonal): alkaline phosphatase (E. coli) conjugate in TRIS buffer with protein (mouse and bovine) stabilizers
Reagent Bottle 2	Microparticles, Anti-troponin-I (mouse monoclonal) coated microparticles in TRIS buffer with protein (mouse, goat, and bovine) stabilizers
Reagent Bottle 3	Conjugate 1, Anti-troponin-I (mouse monoclonal): biotin conjugate in TRIS buffer with protein (mouse and bovine) stabilizers
Reagent Bottle 4	Pre-incubation diluent, diluent containing protein (mouse, goat, bovine, and E coli lysate) stabilizers in TRIS buffer

AxSYM® Troponin-I ADV Standard Calibrators are supplied as 6 x 4 mL bottles, Calibrator A contains gelatin (porcine) solution and Calibrator B through F contain a recombinant human cardiac troponin-I-C complex in a protein (bovine) solution. AxSYM® Troponin-I ADV Controls are supplied as 3 x 8 mL bottles containing a recombinant human cardiac troponin-I-C complex in a protein (bovine) solution.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   AccuTnI on the Access Immunoassay Systems

2. Predicate K number(s):
   k021814

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Analyte measured	Cardiac Troponin I	Same
Antibodies used	Monoclonal	Same
Sample type	Serum or plasma	Same
Differences		
Item	**Device**	**Predicate**
Assay principle	Microparticle enzyme immunoassay (MEIA)	Chemiluminescent immunoassay
Instrumentation	AxSYM system	Access Immunoassay Systems
Assay range	0.02 to 22.78 ng/mL	0.01 to 100 ng/mL

K. Standard/Guidance Document Referenced (if applicable):
NCCLS C28-A2, NCCLS EP5-A, NCCLS EP7-A, NCCLS GP10-A

L. Test Principle:
AxSYM Troponin-I ADV assay is a three step microparticle enzyme immunoassay (MEIA). Cardiac Troponin-I (cTnI) in the sample and pre-incubation diluent are combined in a well of the reaction vessel (RV). Components in the diluent inactivate factors in the sample to block elements which might cause falsely elevated or falsely depressed troponin readings. An aliquot of the sample/diluent is mixed with microparticles coated with monoclonal antibodies recognizing the cTnI molecule. The cTnI in the sample binds to the microparticles forming an antigen-antibody complex. An aliquot of the sample/diluent/microparticle complex is transferred to the matrix cell. The microparticles bind irreversibly to the glass fiber matrix. Conjugate 1 is dispensed onto the matrix cell and allowed to bind to the troponin-I of the antibody-antigen complex, forming an antibody-antigen-antibody complex. The matrix cell is washed to remove unbound materials. Conjugate 2 is then dispensed onto the matrix cell and allowed to bind to the biotin of the antibody-antigen-antibody complex, forming an antibody-antigen-antibody-antibody complex. The matrix cell is washed to remove unbound materials. Substrate is added to the matrix cell and the fluorescent product is measured by the MEIA optical assembly.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. *Precision/Reproducibility:*
   A study was performed based on NCCLS EP5-A. The AxSYM Troponin-I ADV Controls and three other cardiac controls were assayed in replicates of two at two separate times of day for 20 days. Testing was performed on three instruments using three lots of reagents. For within run precision, % CV ranged from 3.9 % to 9.0 %; for total precision, % CV ranged from 4.3 % to 10.5 %. In five

studies, the median AxSYM Troponin-I ADV concentration that demonstrated a 10% CV was 0.16 ng/mL with a range of 0.16 ng/mL to 0.27 mg/dL. These studies were performed based on guidance from the Committee on Standardization of Markers of Cardiac Damage of the IFCC.

b. Linearity/assay reportable range:
A high sample pool with a troponin concentration of approximately 26 ng/mL was prepared from specimens with endogenous troponin-I. A low sample pool was prepared form a normal serum pool with an undetectable troponin concentration. A dilution set with 12 levels of troponin-I was prepared . The dilutions were tested in replicates of five. The data support the assay's linearity form 0.02 ng/mL to 22.78 ng/mL.

c. Traceability (controls, calibrators, or method):
The AxSYM Troponin-I ADV assay standardization is traceable to material with a NIST assigned value. AxSYM Troponin-I Calibrators are gravimetrically prepared from recombinant troponin I-C complex and tested against internal working calibrators. The AxSYM internal working calibrators were value assigned by specimen correlation to the Abbott ARCHITECT STAT Troponin-I assay calibrated using its internal working calibrators. The Abbott ARCHITECT STAT Troponin-I internal working calibrators were prepared from recombinant troponin-I-C complex which has a concentration traceable near the AMI medical decision point to a NIST value assigned native human troponin-I-C complex.

d. Detection limit:
The analytical sensitivity of the AxSYM Troponin-I ADV assay, defined as the concentration at two standard deviations above the AxSYM Troponin-I ADV Standard Calibrator A (0 ng/mL) was calculated to be 0.02 ng/mL at the 95% level of confidence (n = 21 runs, 10 replicates of Calibrator A and 4 replicates of Calibrator B per run).

e. Analytical specificity:
The AxSYM Troponin-I ADV assay is $\leq$ 0.1 % cross-reactivity with skeletal troponin-I and is $\leq$ 1 % cross-reactivity with cardiac troponin-C and cardiac troponin-T at the concentrations indicated below.

Cross-reactant	Cross-reactant Concentration % (ng/mL)	% Cross-reactivity
Skeletal troponin-I	100	0.0
Cardiac troponin-C	1000	0.0
Cardiac troponin-T	1000	0.0

Potential interference from bilirubin, hemoglobin, red blood cells, total protein and triglycerides at the levels indicated below is ≤ 10 % for specimens containing troponin-I concentrations between 0.27 and 3.00 ng/mL and is ≤ 15 % for specimens containing troponin-I concentrations ≥ 3.00 ng/mL as demonstrated by a study based on NCCLS EP7-A. In addition, various drugs were tested and showed no interference.

Potential Interferent	Potential Interferent Concentration
Triglycerides	1000 mg/dL
Hemoglobin	500 mg/dL
Bilirubin	20 mg/dL
Red Blood Cells	0.4% (v/v)
Total Protein	9g/dL

f. Assay cut-off:

See clinical cut-off below.

2. Comparison studies:

a. Method comparison with predicate device:

A total of 546 human serum and plasma specimens were tested using the AxSYM Troponin-I ADV assay and the Access AccuTnI assay. Of the 546 specimens, 531 were within the linear limit of the AxSYM Troponin-I ADV assay. Passing-Bablok regression analysis was performed on these 531 specimens and on the entire group of 546 samples. The slope and intercept of the regression line, the 95% confidence interval around the slope and intercept, and the specimen correlation coefficient were calculated. The data are summarized in the following tables and graph:

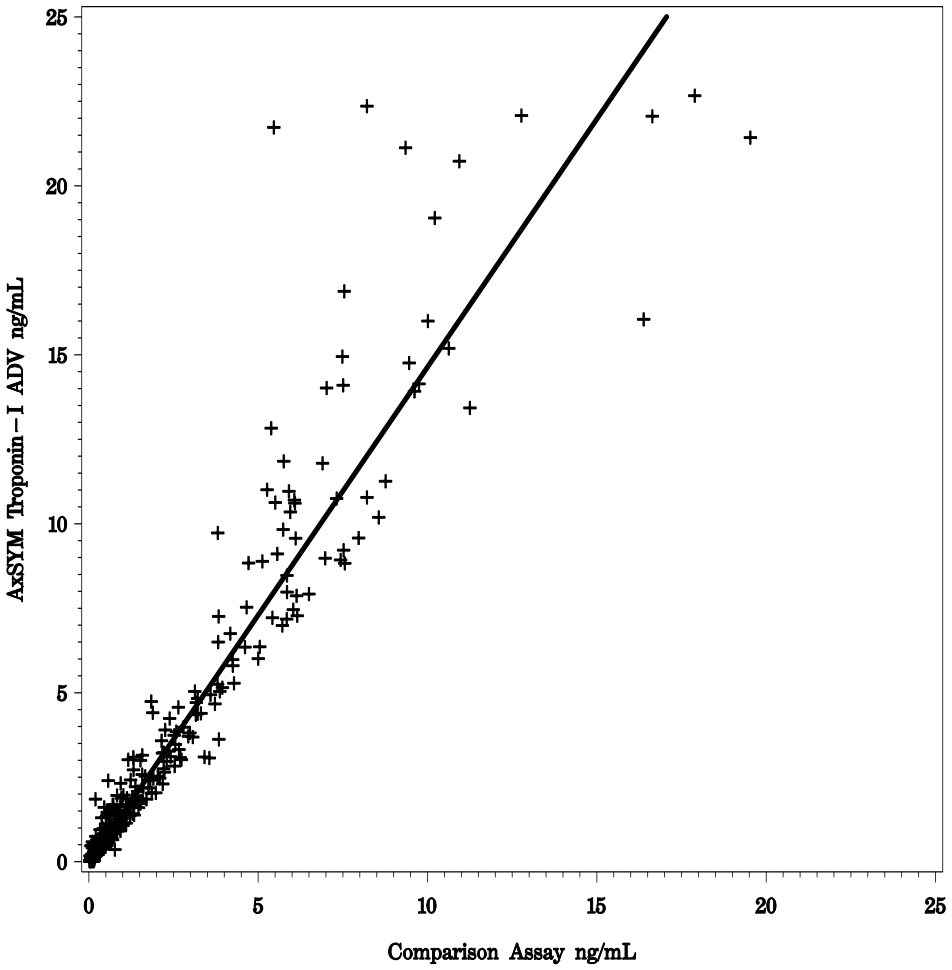
n	**Slope (95% CI)**	**Intercept (ng/mL) (95% CI)**	**Correlation Coefficient (r)**
531	1.47 (1.43, 1.51)	-0.05 (-0.06, -0.04)	0.95

Sample Range (AxSYM Troponin-I *ADV*): 0.02 to 22.67 ng/mL

n	Slope (95% CI)	Intercept (ng/mL) (95% CI)	Correlation Coefficient (r)
546	1.47 (1.44, 1.52)	-0.05 (-0.06, -0.04)	0.97

Sample Range (AccuTnI): 0.03 to 19.53 ng/mL

Sample Range (AxSYM Troponin-I *ADV*): 0.02 to 67.32 ng/mL analyzed with auto-dilution of the samples with troponin-I > 22.67 ng/mL
Sample Range (AccuTnI): 0.03 to 59.56 ng/mL



b. Matrix comparison:
A study was conducted to compare the results of human specimens collected in various serum and plasma tubes to glass serum tubes

with no additives. Specimens were divided into two groups. Group 1 had specimens with troponin-I concentrations between 0.27 and 3.00 ng/mL. Group 2 had specimens with troponin-I concentrations ≥ 3.00 ng/mL. No significant differences were found between tube types. The data is summarized in the following table.

Sample tube type	n	Group 1 mean % difference	n	Group 2 mean % difference
Glass lithium heparin	27	-3	24	-2
Glass lithium heparin separator	27	1	24	2
Plastic lithium heparin	27	3	24	5
Plastic lithium heparin separator	27	2	24	0
Plastic serum separator	27	0	24	-1
Plastic sodium heparin	27	3	24	4

3. Clinical studies:

a. Clinical sensitivity:

A study based on guidance from NCCLS GP10-A was performed. Specimens from the following populations were collected from 5 clinical sites and evaluated using the AxSYM troponin-I ADV assay: 174 specimens from 77 AMI patients diagnosed according to WHO criteria, 778 specimens from 336 non-AMI patients diagnosed according to WHO criteria. The maximum troponin-I value for each patient was used to determine the diagnostic cut-off by receiver operator characteristics (ROC) curve analysis and to determine the optimum clinical sensitivity and specificity. The area under the curve (AUC) was 0.94. All troponin-I values for each patient were analyzed using time stratification from time of admission and compared to the Access AccuTnI assay (using the manufacturer's recommended AMI cut-off). Data from the study are summarized in the following tables.

		Hours post admission		
		0-6	6-12	12-24
AxSYM Troponin-I ADV	% Sensitivity	60.0	78.6	91.7
Cut-off = 0.40 ng/mL	% Specificity	97.4	96.1	98.3
AccuTnI	% Sensitivity	50.0	67.9	72.9
Cut-off = 0.50 ng/mL	% Specificity	98.3	98.5	98.8
WHO AMI Positive Specimens		70	56	48
WHO AMI Negative Specimens		346	259	173
Total Specimens		416	315	221

	WHO Diagnosis		
	non-AMI	AMI	Total
AxSYM® Troponin-I *ADV*			
less than 0.40 ng/mL	353	12	365
0.40 ng/mL or greater	13	65	78
Total	366	77	443
Agreement	418 / 443 = 94.4%		
Access® AccuTnI			
less than 0.50 ng/mL	359	19	378
0.50 ng/mL or greater	7	58	65
Total	366	77	443
Agreement	417 / 443 = 94.1%		

b. Clinical specificity:
See Clinical sensitivity. In addition, specimens from patients with the following potential interferents were evaluated to further assess the clinical specificity of the assay.

Potential Interferent	n	% ≤ 0.27 ng/mL (10% CV value)
Anti-E. coli antibodies	20	100
Chronic renal failure	119	99
HAMA	14	100
Rheumatoid factor	20	100
Skeletal muscle injury	120	100

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

4. Clinical cut-off:
The AxSYM Troponin-I assay diagnostic cut-off for AMI (WHO criteria) is 0.40 ng/mL. See clinical sensitivity studies above.

5. Expected values/Reference range:
A reference range study was conducted based on NCCLS C28-A2. 550 samples from apparently healthy subjects were evaluated using the AxSYM Troponin-I ADV assay. The value obtained for the 99th percentile was 0.04 ng/mL based on a one-sided distribution-free conservative upper 95 % confidence limit for the 99th percentile of all of the apparently healthy subjects.

N. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.