Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K191595

B Applicant

Abbott Laboratories Diagnostic Division

C Proprietary and Established Names

ARCHITECT STAT High Sensitivity Troponin-I

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:

New Device

B Measurand:

Cardiac Troponin I (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:

The ARCHITECT STAT High Sensitivity Troponin-I assay is a chemiluminescent microparticle immunoassay (CMIA) used for the quantitative determination of cardiac troponin I (cTnI) in human plasma (dipotassium [K2] EDTA) on the ARCHITECT i2000SR System.

The ARCHITECT STAT High Sensitivity Troponin-I assay is to be used as an aid in the diagnosis of myocardial infarction (MI).

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For in vitro diagnostic use

D Special Instrument Requirements:

ARCHITECT i2000SR

IV Device/System Characteristics:

A Device Description:

The ARCHITECT STAT High Sensitivity Troponin-I reagent kit contains:

- **Microparticles:** 1 bottle (6.6 mL per 100 test bottle / 29.0 mL per 500 test bottle) Anti-troponin I (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizer. Minimum concentration: 0.035% solids. Preservative: ProClin 300.

- **Conjugate:** 1 bottle (5.9 mL per 100 test bottle / 28.5 mL per 500 test bottle). Anti-troponin I (mouse-human chimeric, monoclonal) acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizer and human IgG. Minimum concentration: 0.1 mg/L. Preservative: ProClin 300.

B Principle of Operation:

The ARCHITECT STAT High Sensitivity Troponin-I assay is a two-step immunoassay for the quantitative determination of cardiac troponin I (cTnI) in human plasma using chemiluminescent microparticle immunoassay (CMIA) technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and anti-troponin I antibody-coated paramagnetic microparticles are combined. The cTnI present in the sample binds to the anti-troponin I coated microparticles.
2. After incubation and wash, anti-troponin I acridinium-labeled conjugate is added.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of cTnI in the sample and the RLUs detected by the ARCHITECT iSystem optics.

The cTnI concentration is read relative to a standard curve established with calibrators of known cTnI concentrations.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Elecsys Troponin T Gen 5 STAT Immunoassay

B Predicate 510(k) Number(s):

K162895

C Comparison with Predicate(s):

Device & Predicate Device(s):	K191595	K162895
Device Trade Name	**ARCHITECT STAT High Sensitivity Troponin-I**	**Roche cobas Elecsys Troponin T Gen 5 STAT**
General Device Characteristic Similarities		
Intended Use/Indications For Use	The assay is to be used as an aid in the diagnosis of myocardial infarction.	Same
General Device Characteristic Differences		
Specific Analyte Detected	cTnI	cTnT

Device & Predicate Device(s):	K191595	K162895
Specimen Type	Plasma (dipotassium [K2] EDTA)	Plasma (lithium heparin)
99th Percentile Cutoff / Expected Values from Apparently Healthy Individuals	Female: 17 ng/L (ng/L) Male: 35 ng/L (ng/L) Overall: 28 ng/L (ng/L)	Female: 14 ng/L Male: 22 ng/L Overall: 19 ng/L

VI Standards/Guidance Documents Referenced:

Clinical and Laboratory Standards Institute (CLSI) EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition

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

CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition

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

CLSI EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A study was performed using 1 lot of the ARCHITECT STAT High Sensitivity Troponin-I reagent, 1 lot of the ARCHITECT STAT High Sensitivity Troponin-I Calibrators, and 1 lot of the ARCHITECT STAT High Sensitivity Troponin-I Controls. The study was performed to include K_2 EDTA plasma specimens within each of 4 concentration ranges (> 3.5 to 6 ng/L, 10 to 20 ng/L, 30 to 50 ng/L, and 150 to 200 ng/L). Data was collected within the 8 hour stability claim for patient samples. The study was performed over a minimum of 3 days. Each specimen was stored at room temperature and tested in duplicate, twice in one day, on each of 3 instruments (for a total of 12 replicates per sample) within 8 hours of collection. Within laboratory precision includes within-run and between-run variability. Reproducibility includes within-run, between-run, and between-instrument variance components.

Sample	n	Mean (ng/L)	Within-Run		Between-Run		Within-Laboratory		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 3	12	5.3	0.12	2.2	0.23	4.2	0.25	4.8	0.25	4.8
Sample 4	12	11.2	0.47	4.2	0.00	0.0	0.47	4.2	0.62	5.5
Sample 5	12	17.5	0.50	2.9	0.23	1.3	0.55	3.1	0.81	4.6
Sample 6	12	18.8	0.60	3.2	0.22	1.2	0.64	3.4	0.75	4.0
Sample 7	12	34.6	0.84	2.4	0.00	0.0	0.84	2.4	1.10	3.2
Sample 8	12	38.8	1.00	2.6	1.10	2.8	1.48	3.8	1.92	5.0
Sample 9	12	45.0	1.52	3.4	1.42	3.2	2.08	4.6	3.16	7.0
Sample 10	12	163.7	5.00	3.1	6.23	3.8	7.99	4.9	11.68	7.1
Sample 11	12	167.5	6.82	4.1	2.82	1.7	7.38	4.4	11.09	6.6
Sample 12	12	179.6	6.76	3.8	0.00	0.0	6.76	3.8	8.19	4.6

Samples 1 and 2 were below the LoQ and were not included in the above analysis.

The sponsor also provided between-lot variability (which was similar to the reproducibility estimates described above) and between-instrument variability (which was similar to the within-run estimates described above) using patient samples.

A second study was performed following the recommendations in the EP05-A2 guideline. Testing was conducted using 3 lots of the ARCHITECT STAT High Sensitivity Troponin-I reagent, 2 lots of the ARCHITECT STAT High Sensitivity Troponin-I Calibrators, and 1 lot of the ARCHITECT STAT High Sensitivity Troponin-I Controls and 2 instruments. Five controls were tested in duplicate, twice per day on 20 days. Within-laboratory variability contains within-run, between-run, and between day variability. Patient samples can only be stored for 8 hours at room temperature; therefore, 20-day precision studies were conducted with quality control materials. On each day of testing a new vial of quality control material from the same lot was used.

Sample	Instrument	Reagent Lot	N	Mean (ng/L)	Within-Run		Within-Laboratory (Total)	
					SD	%CV	SD	%CV
Low Control	1	1	80	19.3	0.61	3.2	0.72	3.7
		2	80	20.3	0.61	3.0	0.78	3.9
		3	80	19.7	0.64	3.3	0.78	3.9
	2	1	80	20.4	0.84	4.1	0.85	4.1
		2	80	20.2	0.64	3.2	0.83	4.1
		3	80	20.0	0.66	3.3	0.87	4.3

Sample	Instrument	Reagent Lot	N	Mean (ng/L)	Within-Run		Within-Laboratory (Total)	
					SD	%CV	SD	%CV
Medium Control	1	1	80	190.7	4.21	2.2	5.54	2.9
		2	80	195.0	3.57	1.8	4.13	2.1
		3	80	191.2	4.27	2.2	4.49	2.3
	2	1	80	197.8	5.26	2.7	5.76	2.9
		2	80	196.8	4.65	2.4	5.36	2.7
		3	80	194.3	4.43	2.3	5.95	3.1
Commercial Control Level Low	1	1	80	43.3	1.27	2.9	1.46	3.4
		2	80	46.1	1.48	3.2	1.57	3.4
		3	80	45.4	1.27	2.8	1.51	3.3
	2	1	80	45.2	1.36	3.0	1.82	4.0
		2	80	46.4	1.80	3.9	1.84	4.0
		3	80	46.0	1.40	3.0	1.48	3.2
Commercial Control Level 2	1	1	80	1198.0	31.13	2.6	33.80	2.8
		2	80	1281.3	33.38	2.6	40.95	3.2
		3	80	1267.1	27.57	2.2	31.72	2.5
	2	1	80	1260.1	38.34	3.0	42.33	3.4
		2	80	1309.1	28.25	2.2	42.68	3.3
		3	80	1309.6	35.68	2.7	43.81	3.3
Commercial Control Level 3	1	1	80	2812.3	64.56	2.3	80.50	2.9
		2	80	3023.0	83.52	2.8	93.82	3.1
		3	80	3015.3	94.13	3.1	95.14	3.2
	2	1	80	2978.3	80.34	2.7	102.42	3.4
		2	80	3103.9	83.93	2.7	96.25	3.1
		3	80	3138.2	55.49	1.8	84.50	2.7

Below is the between-lot and between-instrument precision estimates for the five control materials. Overall variability contains within-run, between-run, between-day, between-lot, between-instrument, and instrument-lot interaction variance components.

			Between-Lot		Between-Instrument		Overall	
Sample	**N**	**Mean (ng/L)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Low Control	480	20.0	0.39	1.9	0.44	2.2	1.07	5.3
Medium Control	480	194.3	1.97	1.0	3.15	1.6	6.67	3.4
Commercial Control Level Low	480	45.4	1.11	2.4	0.82	1.8	2.21	4.9
Commercial Control Level 2	480	1270.9	37.01	2.9	32.33	2.5	63.97	5.0
Commercial Control Level 3	480	3011.8	102.59	3.4	89.69	3.0	166.88	5.5

2. Linearity:

Linearity was evaluated following the recommendations in the CLSI EP06-A guideline with 10 samples ranging in concentrations from < 10 ng/L to >5000 ng/L. The high samples and the low samples were native and the intermediate samples were prepared by mixing high and low concentration samples. Four replicates were measured for each sample, and the mean of these replicates was used to calculate the reported results. There were three sets of linearity samples made. Deviation from linearity within the claimed range was never observed to be greater than 14.1%.

The measuring range is 3.5 to 5000.0 ng/L with the upper end of the measuring range being defined by the upper linear range of the assay. See detection limits below for information supporting the lower end of the measuring range.

Hook Effect

The sponsor demonstrated that there is no hook effect with the assay up to 500,000 ng/L.

Dilution Recovery

The sponsor provided dilution studies which supported the measurement of samples above the measurement range diluted by a factor of 10.

3. Analytical Specificity/Interference:

Endogenous interference studies were performed following the recommendations in the CLSI EP07-A2 guideline. Two sample pools were tested. One sample pool had 20-60 ng/L cTnI and the second sample pool had 700-2000 ng/L cTnI. These sample pools were spiked with potential interferents. Test results from samples spiked with the potential interferent were compared to test results from the control samples lacking the potential interferent. At the tested concentrations, these compounds caused <10% interference.

Endogenous Substance	Highest Concentration Tested Without Significant Interference
Unconjugated Bilirubin	20 mg/dL
Conjugated Bilirubin	20 mg/dL
Hemoglobin	500 mg/dL
Total Protein	9.3 g/dL
Triglycerides	3000 mg/dL

Human anti-mouse antibodies (HAMA) and rheumatoid factor (RF)

The sponsor provided studies that evaluated the effect of HAMA and RF on the function of their device. The sponsor included the following information in the labeling to address the results:

"Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as ARCHITECT STAT High Sensitivity Troponin-I or others that employ mouse monoclonal antibodies.

Heterophilic antibodies and rheumatoid factor (RF) in human plasma can react with reagent immunoglobulins, interfering with in vitro immunoassays. The presence of heterophilic antibodies or RF in a patient specimen may demonstrate anomalous values. Additional information may be required for diagnosis.

Although the ARCHITECT STAT High Sensitive Troponin-I assay is specifically designed to minimize the effects of HAMA, heterophilic antibodies, and RF, assay results that are not consistent with other clinical observations may require additional information for diagnosis."

The same protocol described above was used to evaluate potential interference from therapeutic drugs. The results are summarized below. At the tested concentrations, all drugs caused <10% interference.

Compound	Highest Concentration Tested Without Interference
Abciximab	20 µg/mL
Acetaminophen	250 µg/mL
Acetylsalicylic Acid	1000 µg/mL
Adrenaline	0.37 µg/mL
Allopurinol	400 µg/mL
Ambroxol	400 µg/mL
Ampicillin	1000 µg/mL
Ascorbic Acid	300 µg/mL
Atenolol	10 µg/mL
Biotin	290 ng/mL
Bivalirudin	42 µg/mL
Caffeine	100 µg/mL
Captopril	50 µg/mL
Carvedilol	150 µg/mL
Cefoxitin	2500 µg/mL
Cinnarizine	400 µg/mL
Clopidogrel	75 µg/mL
Cocaine	10 µg/mL
Cyclosporine	5 µg/mL
Diclofenac	50 µg/mL
Digoxin	7.5 µg/mL
Dopamine	900 µg/mL
Doxycycline	50 µg/mL
Eptifibatide	7 µg/mL
Erythromycin	200 µg/mL
Fibrinogen	100 mg/dL
Fondaparinux	4 µg/mL
Furosemide	400 µg/mL
Ibuprofen	500 µg/mL
Levodopa	20 µg/mL
Low MW Heparin	5 U/mL
Methyldopa	25 µg/mL
Methylprednisolone	80 µg/mL
Metronidazole	200 µg/mL
Nicotine	2 mg/dL
Nifedipine	60 µg/mL
Nitrofurantoin	64 µg/mL
Nystatin	7.5 µg/mL
Oxytetracycline	5 µg/mL
Phenobarbital	15 mg/dL
Phenylbutazone	400 µg/mL
Phenytoin	100 µg/mL
Primidone	10 mg/dL
Propranolol	5 µg/mL
Quinidine	20 µg/mL

Compound	Highest Concentration Tested Without Interference
Rifampicin	60 µg/mL
Salicylic Acid	600 µg/mL
Simvastatin	20 µg/mL
Sodium Heparin	8 U/mL
Streptokinase	31.3 U/mL
Theophylline	75 µg/mL
TPA	2.3 µg/mL
Trimethoprim	75 µg/mL
Verapamil	160 µg/mL
Warfarin	30 µg/mL

Interference beyond ± 10% was observed at the concentrations shown below for the following drug.

Potentially Interfering Substance	Interferent Level		Analyte Level	% Interference
	Therapeutic	High		
Fibrinogen	NA	1000 mg/dL	15 ng/L	11.6

Cross-Reactivity

Potential cross-reactivity was evaluated following the recommendations in the CLSI guideline EP07-A2.

To evaluate cross reactivity, the substances shown in the following table were added to K_2EDTA plasma patient samples at two cTnI concentrations (~ 0 and ~ 40 ng/L). Test results from samples spiked with the cross-reactant were compared to test results from samples without cross-reactant added. Samples were measured using three lots. There was no observed cross-reactivity at the concentrations tested below.

Potential Cross-Reacting Substance	Highest Concentration Tested (ng/mL)
Cardiac Troponin T	1000
Skeletal Troponin I	1000
Tropomyosin	1000
Actin	1000
Troponin C	1000
Myosin Light Chain	1000
Myoglobin	1000
CK-MB	1000

The following interferences are also described in the labeling:
Specimens from individuals with elevated levels of fibrinogen may demonstrate falsely elevated values.

Total protein at 12.4 g/dL decreases troponin values at 15 ng/L and 500 ng/L by -12.0% and -18.4%, respectively.

Potential interference has not been evaluated for substances other than those described in the SPECIFIC PERFORMANCE CHARACTERISTICS, Interference section of this package insert.

Troponin autoantibodies have been reported to be present in approximately 10% to 20% of patients presenting to the emergency department (ED) and may lead to falsely low troponin assay results and delay in treatment of acute coronary syndrome (ACS). Therefore, a test result that is inconsistent with the clinical picture and patient history should be interpreted with caution.

4. Assay Reportable Range:

   3.5 to 5000.0 ng/L cTnI

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

   The Abbott ARCHITECT STAT High Sensitivity Troponin-I is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material SRM2921. The sponsor's traceability scheme was reviewed and found acceptable.

6. Detection Limit:

   Limit of Blank (LoB) Test Protocol

   The LoB was determined as described in the CLSI EP17-A2 guideline. Testing was performed using two sets of 4 zero-analyte samples tested with 3 replicates on 5 runs over the course of 3 days. Testing was performed using 4 reagent lots and 5 instruments. 60 determinations were obtained for each reagent lot / instrument combination. LoB was calculated parametrically. The largest estimate across all reagent lot-instrument combinations tested was 0.9 ng/L.

   Limit of Detection (LoD) Test Protocol

   The LoD was determined following the recommendations in the CLSI EP17-A2 guideline. Testing was performed using three reagent lots and one instrument. For the three lots tested, seven to ten native low analyte K_2EDTA plasma samples were tested every day, respectively, with four replicates for each test, for three days.

   The parametric approach described in EP17-A2 was followed to determine the LoD. The largest estimate across all reagent lot-instrument combinations tested was 1.7 ng/L.

   Limit of Quantitation (LoQ) Protocol

   The Limit of Quantitation (LoQ) was determined as the analyte level with a within-lab CV of less than or equal to 20% following the recommendations in the CLSI EP17-A2 guideline. Testing was completed two times a day (n=2) for at least 20 days for a total of 60 replicates

with eight to 10 native K_2EDTA plasma pools measured on one instrument using three reagent lots. For each reagent lot-instrument combination, the within-laboratory precision for each sample, expressed as %CV, was plotted against the mean concentration obtained for each sample. LoQ was determined by this precision profile as the concentration where the %CV was less than 20%. The largest estimate across all reagent lot-instrument combinations tested was 2.3 ng/L.

The sponsor claims a LoB of 0.9 ng/L, and LoD of 1.7 ng/L, and an LoQ of 3.5 ng/L.

7. Assay Cut-Off:

See Expected Values/Reference Range Section below.

8. Carry-Over:

Potential sample carryover was evaluated using EDTA plasma.

Potential sample carryover was evaluated by comparing the results of an unprotected low sample to a protected low sample. The protected low sample was tested before the high sample, and the unprotected low sample was tested after the high sample. The low sample had a native cTnI concentration of ≤ 10 ng/L. The high sample had a recombinant cTnI concentration ≥ 500,000 ng/L. The carry-over observed was approximately 0.3 ng/L cTnI going from a high sample to a low sample.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Not applicable.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

A multi-center prospective study was performed to assess the diagnostic accuracy of the ARCHITECT STAT High Sensitivity Troponin-I assay. Specimens were collected at 11 emergency departments (ED) from 1065 subjects presenting to the ED with symptoms consistent with acute coronary syndrome (ACS). All subject diagnoses were adjudicated by three board certified cardiologists based on the 2007 ACC/AHA/ESC guidelines for MI. Serial samples were collected from patients presenting to the emergency department. The number of patients adjudicated with an MI was 10.8% (116/1065). The sample collection times were at 0 – 2 hours from presentation to the ED and at the following time-point relative to the time from presentation: 2 – 4 hours and 4 – 9 hours. Investigators and adjudicators were blinded to the proposed device's results. Adjudicators were also blinded to site diagnoses. All results presented below were based on the adjudicated diagnoses. Clinical

performance was estimated at an overall cut-off (male and female combined 99th percentile upper reference limit (URL) cut-off) and male- and female-specific URL cut-offs, calculated as described in Expected values/Reference range (in Section E below).

The samples collected in the study were frozen and stored prior to analysis. Abbott provided additional information to confirm that the performance estimates in the labeling were not affected by the freezing of these clinical samples. The results are summarized below.

An analysis for both females and males was performed using the overall 99th percentile cutoff (28 ng/L). The results are summarized in the following table.

Sex	Time Point	N	Sensitivity		Specificity	
			%	95% CI	%	95% CI
Female	Baseline	412	91.7 (22/24)	73.0 - 99.0	92.0 (357/388)	88.9 - 94.5
	2 - 4 Hours	418	94.4 (17/18)	72.7 - 99.9	89.3 (357/400)	85.8 - 92.1
	4 - 9 Hours	372	94.1 (16/17)	71.3 - 99.9	87.0 (309/355)	83.1 - 90.4
Male	Baseline	519	81.8 (54/66)	70.4 - 90.2	81.5 (369/453)	77.6 - 84.9
	2 - 4 Hours	526	91.7 (55/60)	81.6 - 97.2	83.5 (389/466)	79.8 - 86.7
	4 - 9 Hours	489	93.7 (59/63)	84.5 - 98.2	81.0 (345/426)	76.9 - 84.6

Sex	Time Point	N	PPV		NPV	
			%	95% CI	%	95% CI
Female	Baseline	412	41.5 (22/53)	28.1 - 55.9	99.4 (357/359)	98.0 - 99.9
	2 - 4 Hours	418	28.3 (17/60)	17.5 - 41.4	99.7 (357/358)	98.5 - 100.0
	4 - 9 Hours	372	25.8 (16/62)	15.5 - 38.5	99.7 (309/310)	98.2 - 100.0
Male	Baseline	519	39.1 (54/138)	30.9 - 47.8	96.9 (369/381)	94.6 - 98.4
	2 - 4 Hours	526	41.7 (55/132)	33.2 - 50.6	98.7 (389/394)	97.1 - 99.6

Sex	Time Point	N	PPV		NPV	
			%	95% CI	%	95% CI
	4 - 9 Hours	489	42.1 (59/140)	33.9 - 50.8	98.9 (345/349)	97.1 - 99.7

The following limitation is in the labeling regarding the clinical performance of this device.

Using the established overall 99th percentile (28 ng/L), the lower end of the confidence interval (CI) for positive predictive value (PPV) for female subjects was as low as 15.5% and for male subjects was as low as 30.9% in the clinical validation study. Up to 84.5% and 69.1% of positive troponin results could come from females and males, respectively, without an MI.

The results using the sex-specific 99th percentile cutoffs (female 17 ng/L, male 35 ng/L) are summarized in the following tables.

Cutoff (ng/L)	Time Point	N	Sensitivity		Specificity	
			%	95% CI	%	95% CI
17 (Female only)	Baseline	412	95.8 (23/24)	78.9 - 99.9	87.6 (340/388)	83.9 - 90.7
	2 - 4 Hours	418	94.4 (17/18)	72.7 - 99.9	85.3 (341/400)	81.4 - 88.6
	4 - 9 Hours	372	94.1 (16/17)	71.3 - 99.9	82.8 (294/355)	78.5 - 86.6
35 (Male only)	Baseline	519	78.8 (52/66)	67.0 - 87.9	84.5 (383/453)	80.9 - 87.8
	2 - 4 Hours	526	90.0 (54/60)	79.5 - 96.2	86.1 (401/466)	82.6 - 89.1
	4 - 9 Hours	489	93.7 (59/63)	84.5 - 98.2	84.3 (359/426)	80.5 - 87.6

Cutoff (ng/L)	Time Point	N	PPV		NPV	
			%	95% CI	%	95% CI
17 (Female only)	Baseline	412	32.4 (23/71)	21.8 - 44.5	99.7 (340/341)	98.4 - 100.0
	2 - 4 Hours	418	22.4 (17/76)	13.6 - 33.4	99.7 (341/342)	98.4 - 100.0
	4 - 9 Hours	372	20.8 (16/77)	12.4 - 31.5	99.7 (294/295)	98.1 - 100.0
35 (Male only)	Baseline	519	42.6 (52/122)	33.7 - 51.9	96.5 (383/397)	94.2 - 98.1
	2 - 4 Hours	526	45.4 (54/119)	36.2 - 54.8	98.5 (401/407)	96.8 - 99.5
	4 - 9 Hours	489	46.8 (59/126)	37.9 - 55.9	98.9 (359/363)	97.2 - 99.7

The following limitations are in the labeling regarding the clinical performance of this device.

Using the established sex-specific 99th percentiles in the same study (female 17 ng/L, male 35 ng/L), the lower end of the CI for PPV for female subjects was as low as 12.4% and for male subjects was as low as 33.7%. Up to 87.6% and 66.3% of positive troponin results could come from females and males, respectively, without an MI.

2. Clinical Specificity:

See Clinical Sensitivity above (Section C).

D Clinical Cut-Off:

The cut-offs for this assay were determined based on the 99th percentile upper reference limit in apparently healthy adults. Please see Expected Values/Reference Range below (Section E) for the determination of the clinical cut-offs.

E Expected Values/Reference Range:

A reference range study was conducted based on guidance from CLSI EP28-A3c. Specimens were collected from 1531 apparently healthy individuals in a US population with the following levels of biomarkers:

Biomarker	Male	Female
Cardiac BNP (pg/mL)	≤ 25	≤ 40
HbA_{1c} (%)	≤ 6	
GFR (mL/min/1.73 m2)	≥ 60	

Each specimen was stored frozen, thawed, and evaluated in replicates of one using the ARCHITECT STAT High Sensitivity Troponin-I assay. The 99th percentiles described in the following table for this population were determined using the robust statistical method described in CLSI EP28-A3c.

Apparently Healthy Population	N	Age Range (years)	99th Percentile (ng/L)	90% CI (ng/L)
Female	765	21 - 75	17	[14, 20]
Male	766	21 - 73	35	[27, 44]
Overall	1531	21 - 75	28	[22, 33]

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.