510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K202525

B Applicant

Abbott Laboratories Diagnostic Division

C Proprietary and Established Names

Alinity i 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 Alinity i 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 (lithium heparin) on the Alinity i system.

The Alinity i 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:

Alinity i System

IV Device/System Characteristics:

A Device Description:

The following are needed to conduct testing:

Alinity i STAT High Sensitivity Troponin-I Reagent Kit which contains:

Microparticles: 1 bottle (6.6 mL per 100 test cartridge / 33.8 mL per 600 test cartridge). 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 (6.1 mL per 100 test cartridge / 33.8 mL per 600 test cartridge). 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.

The following are also required to conduct testing but are not provided with the kit:

- Alinity i STAT High Sensitivity Troponin-I assay file
- 04Z2101 Alinity i STAT High Sensitivity Troponin-I Calibrators
- 04Z2110 Alinity i STAT High Sensitivity Troponin-I Controls or other control material containing cTnI

- Alinity Pre-Trigger Solution
- Alinity Trigger Solution
- Alinity i-series Concentrated Wash Buffer
- 09P1540 Alinity i Multi-Assay Manual Diluent

B Principle of Operation:

The Alinity i STAT High Sensitivity Troponin-I assay is an automated, two-step immunoassay for the quantitative determination of cTnI in human plasma (lithium heparin) using CMIA technology.

Sample and anti-troponin I antibody-coated coated paramagnetic microparticles are combined and incubated. The cTnI present in the sample binds to the anti-troponin I coated microparticles. The mixture is washed. Anti-troponin I acridinium-labeled conjugate is added to create a reaction mixture and incubated. Following a wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as a relative light unit (RLU). There is a direct relationship between the amount of cTnI in the sample and the RLU detected by the system optics.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ARCHITECT STAT High Sensitivity Troponin-I

B Predicate 510(k) Number(s):

K191595

C Comparison with Predicate(s):

Device & Predicate Device(s):	K202525	K191595
Device Trade Name	Alinity i STAT High Sensitivity Troponin-I	ARCHITECT STAT High Sensitivity Troponin-I
General Device Characteristic Similarities		
Intended Use/Indications For Use	The assay is for the quantitative determination of cardiac troponin I used as an aid in the diagnosis of myocardial infarction.	Same

General Device Characteristic Differences		
Specimen Type	Plasma (lithium heparin)	Plasma (dipotassium [K2] EDTA)
99th Percentile Cutoff / Expected Values from Apparently Healthy Individuals (ng/L, pg/mL)	Female: 14 Male: 35 Overall: 27	Female: 17 Male: 35 Overall: 28

VI   Standards/Guidance Documents Referenced:

- Clinical and Laboratory Standards Institute (CLSI) EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline–Third Edition
- CLSI EP07, 3rd ed., Interference Testing in Clinical Chemistry
- 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
- CLSI EP35, 1st ed., Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures

VII   Performance Characteristics (if/when applicable):

A   Analytical Performance:

1. Precision/Reproducibility:

   A study was performed using 1 lot of the Alinity i STAT High Sensitivity Troponin-I reagent, 1 lot of the Alinity i STAT High Sensitivity Troponin-I Calibrators, and 1 lot of the Alinity i STAT High Sensitivity Troponin-I Controls. The study was performed using fresh, native lithium heparin plasma specimens within each of 5 concentration ranges (> 3 to 6 ng/L, 10 to 20 ng/L, 30 to 50 ng/L, and 100 to 300 ng/L, and 1000 to 4500 ng/L). Testing for each sample was performed 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 SD	Within-Run %CV	Between-Run SD	Between-Run %CV	Within-Laboratory SD	Within-Laboratory %CV	Reproducibility SD	Reproducibility %CV
Sample 1	12	3.5	0.22	6.2	0.00	0.0	0.22	6.2	0.30	8.7
Sample 2	12	5.2	0.30	5.7	0.00	0.0	0.30	5.7	0.67	12.7
Sample 3	12	8.0	0.25	3.2	0.23	2.9	0.34	4.3	0.67	8.4

Sample	n	Mean (ng/L)	Within-Run SD	Within-Run %CV	Between-Run SD	Between-Run %CV	Within-Laboratory SD	Within-Laboratory %CV	Reproducibility SD	Reproducibility %CV
Sample 4	12	13.6	0.37	2.7	0.00	0.0	0.37	2.7	0.61	4.5
Sample 5	12	13.9	0.37	2.7	0.00	0.0	0.37	2.7	0.37	2.7
Sample 6	12	15.1	0.65	4.3	0.00	0.0	0.65	4.3	0.65	4.3
Sample 7	12	18.2	0.82	4.5	0.00	0.0	0.82	4.5	0.82	4.5
Sample 8	12	20.2	0.66	3.3	0.00	0.0	0.66	3.3	0.74	3.7
Sample 9	12	36.9	0.73	2.0	0.00	0.0	0.73	2.0	1.17	3.2
Sample 10	12	46.7	0.90	1.9	0.00	0.0	0.90	1.9	0.95	2.0
Sample 11	12	51.6	1.22	2.4	1.07	2.1	1.63	3.2	1.63	3.2
Sample 12	12	172.6	4.51	2.6	5.53	3.2	7.14	4.1	7.14	4.1
Sample 13	12	233.0	5.00	2.1	9.18	3.9	10.45	4.5	10.45	4.5
Sample 14	12	300.0	11.00	3.7	5.61	1.9	12.35	4.1	12.35	4.1
Sample 15	12	1228.3	29.03	2.4	45.23	3.7	53.74	4.4	53.74	4.4
Sample 16	12	1974.6	49.46	2.5	57.97	2.9	76.21	3.9	76.21	3.9
Sample 17	12	2871.4	72.86	2.5	85.31	3.0	112.19	3.9	112.19	3.9

A second study was performed following the recommendations in the EP05-A3 guideline. Testing was conducted using 3 lots of the Alinity i STAT High Sensitivity Troponin-I reagent, 2 lots of the Alinity i STAT High Sensitivity Troponin-I Calibrators, and 1 lot of the Alinity i STAT High Sensitivity Troponin-I Controls using 2 instruments. Three controls were tested in duplicate, twice per day over 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.

Sample	Instrument	Reagent Lot	N	Mean (ng/L)	Within-Run SD	Within-Run %CV	Within-Laboratory (Total) SD	Within-Laboratory (Total) %CV
Low Control	1	1	80	20.1	0.59	2.9	0.87	4.3
		2	80	20.0	0.61	3.0	0.91	4.5
		3	80	22.0	0.72	3.3	1.13	5.1
	2	1	80	19.6	0.67	3.4	0.76	3.9
		2	80	19.9	0.73	3.7	0.81	4.1
		3	80	18.3	0.67	3.7	0.77	4.2
Medium Control	1	1	80	195.2	4.55	2.3	5.54	2.8
		2	80	194.7	4.18	2.1	6.60	3.4
		3	80	210.3	4.82	2.3	7.00	3.3
	2	1	80	191.9	4.42	2.3	6.72	3.5
		2	80	199.8	6.14	3.1	7.25	3.6
		3	80	191.9	5.22	2.7	6.05	3.2
Commercial Control	1	1	80	1484.6	41.19	2.8	49.50	3.3
		2	80	1392.9	45.11	3.2	61.56	4.4
		3	80	1624.9	40.02	2.5	63.56	3.9
	2	1	80	1475.4	36.28	2.5	63.39	4.3

Sample	Instrument	Reagent Lot	N	Mean (ng/L)	Within-Run		Within-Laboratory (Total)	
					SD	%CV	SD	%CV
		2	80	1442.7	45.91	3.2	60.02	4.2
		3	80	1542.3	53.36	3.5	69.39	4.5

Reproducibility analysis was performed using single reagent lots of the Alinity i STAT High Sensitivity Troponin-I reagent, the Alinity i STAT High Sensitivity Troponin-I Calibrators, and the Alinity i STAT High Sensitivity Troponin-I Controls at three sites using 4 replicates per run, 2 runs per day, for 5 days at each site. Below are the between-site and reproducibility precision estimates for the three control materials. Reproducibility includes within-run, between-run, between-day, and between-site variance components.

Sample	N	Mean (ng/L)	Between-Site		Reproducibility	
			SD	%CV	SD	%CV
Low Control	480	20	1.34	7.2	1.55	8.3
Medium Control	480	197.3	5.69	2.9	7.65	3.9
Commercial Control	480	1493.8	42.18	2.7	80.58	5.2

2. Linearity:

Linearity was evaluated using 10 lithium heparin plasma samples ranging in concentrations from <2.7 pg/mL to >3,600 ng/L. The high samples and the low samples were native and the intermediate samples were prepared by mixing high and low concentration samples. At least four replicates were measured for each sample, and the mean of these replicates was used to calculate the reported results. Deviations from linearity within the claimed range were never observed to be greater than 15%.

Hook Effect

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

3. Analytical Specificity/Interference:

Potentially Interfering Endogenous Substances

A study was performed based on the recommendations in the CLSI EP07, 3rd ed. guideline. Each substance was tested at 2 levels of the analyte (approximately 15 ng/L and 500 ng/L for bilirubin, total protein, and Intralipid and 15 ng/L and 200 ng/L for hemoglobin). Test results from samples spiked with the potential interferent were compared to test results from the control samples lacking the potential interferent. No significant interference (results of the

sample with the potential interferent within ± 10% of the control sample) was observed at the following concentrations.

Endogenous Substance	Highest Concentration Tested without Significant Interference
Unconjugated Bilirubin	40 mg/dL
Conjugated Bilirubin	40 mg/dL
Hemoglobin	1000 mg/dL
Total Protein	8.8 g/dL
Triglycerides	3000 mg/dL

Interference beyond ± 10% was observed at the concentration shown below for the following substance.

Potentially Interfering Substance	Interferent Level	Analyte Level	% Interference
Total Protein	9.0 g/dL	500 ng/L	-10.90%

Potentially Interfering Drugs and other Compounds

A study was performed based on the recommendations in the CLSI EP07 3rd ed. guideline. Each drug was tested at 2 levels of the analyte (approximately 15 ng/L and 500 ng/L). Test results from samples spiked with the potential interferent were compared to test results from the control samples lacking the potential interferent. No significant interference (results of the sample with the potential interferent within ± 10% of the control sample) was observed at the following concentrations.

Compound	Highest Concentration Tested Without Interference
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	3510 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

Compound	Highest Concentration Tested Without Interference
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
Fondaparinux	4 µg/mL
Furosemide	400 µg/mL
Ibuprofen	500 µg/mL
Low MW Heparin	5 U/mL
Methyldopa	25 µg/mL
Methylprednisolone	80 µg/mL
Metronidazole	200 µg/mL
Nicotine	2 µg/mL
Nifedipine	60 µg/mL
Nitrofurantoin	64 µg/mL
Nystatin	7.5 µg/mL
Oxytetracycline	5 µg/mL
Phenylbutazone	400 µg/mL
Phenytoin	100 µg/mL
Primidone	10 µg/mL
Propranolol	5 µg/mL
Quinidine	20 µg/mL
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 concentration shown below for the following compound.

Compound	Interferent Level	Analyte Level	% Interference
Fibrinogen	1000 mg/dL	15 ng/L	24.30%

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

Samples at 3 levels of the analyte (approximately 2.7, 15, and 500 ng/L) were spiked with rheumatoid factor (RF) to concentrations of 1200 IU/mL and 1495 IU/mL and tested with the Alinity i STAT High Sensitivity Troponin-I assay. RF at 1495 IU/mL decreased troponin values up to -18.9%.

Specimens containing human anti-mouse antibodies (HAMA) were evaluated at 3 levels of the analyte (approximately 2.7, 15, and 500 ng/L) with the Alinity i STAT High Sensitivity Troponin-I assay. HAMA at 225 ng/mL decreased troponin values up to -11.0%.

Cross Reactants

A study was performed based on guidance from CLSI EP07, 3rd ed. Samples with cTnI target concentrations of 2.3, 15, and 500 ng/L containing the cross-reactants at the concentrations listed below were tested with the Alinity i STAT High Sensitivity Troponin-I assay. Test results from samples spiked with the potential interferent were compared to test results from the control samples lacking the potential interferent. There was no observed cross-reactivity at the concentrations tested below.

Potential Cross-Reacting Substance	Highest Concentration Tested (ng/L)
Actin	1,000,000
Cardiac Troponin C	1,000,000
Cardiac Troponin T	1,000,000
CK-MB	1,000,000
Myoglobin	1,000,000
Myosin	1,000,000
Skeletal Troponin I	1,000,000
Tropomyosin	1,000,000

The following additional interferences are described in the labeling:

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.

Limitations

The following limitations are included in the labeling:

The Alinity i STAT High Sensitivity Troponin-I assay is susceptible to interference effects from total protein > 8.8 g/dL. Total protein from 9.0 to 12.0 g/dL decreased troponin values at 500 ng/L by up to -16.3%.

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 depressed values when tested with assay kits such as Alinity i STAT High Sensitivity Troponin-I that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.

Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed. Additional information may be required for diagnosis.

The Alinity i STAT High Sensitivity Troponin-I assay is susceptible to interference effects from HAMA > 150 ng/mL. HAMA at 225 ng/mL decreased troponin values up to -11.0%.

The Alinity i STAT High Sensitivity Troponin-I assay is susceptible to interference effects from RF > 1200 IU/mL. RF at 1495 IU/mL decreased troponin values up to -18.9%.

Although the Alinity i STAT High Sensitivity Troponin-I assay is specifically designed to minimize the effects of HAMA, heterophilic antibodies, and RF, assay results may be impacted by these proteins.

Specimens from individuals with elevated levels of fibrinogen may demonstrate falsely elevated values.

4. Assay Reportable Range:

2.7 to 3600.0 ng/L (ng/L) cTnI

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

Traceability:

The Abbott Alinity i 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 4 sets of 4 zero-analyte samples tested with 5 replicates on 5 runs over the course of 3 days. Testing was performed using 2 reagent lots and 1 instrument. Sixty determinations were obtained for each reagent lot/instrument combination. LoB was calculated using non-parametric analysis. The largest estimate across all reagent lot-instrument combinations tested was 0.0 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 2 reagent lots and 2 instruments. For each lot and instrument combination, at least 5 native low-analyte lithium heparin plasma samples were tested over at least 3 days, with 12 replicates per sample.

The parametric approach described in EP17-A2 was followed to determine the LoD. The largest estimate across all reagent lot-instrument combinations tested was 0.9 ng/L.

Limit of Quantitation (LoQ) Protocol

The LoQ was determined as the analyte level with a within-lab CV of $\leq$ 20% following the recommendations in the CLSI EP17-A2 guideline. Testing was completed using the same parameters and sampling plan as described above in the LoD Test Protocol. 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 2.7 ng/L

The sponsor claims a LoB of 0.0 ng/L, and LoD of 0.9 ng/L, and an LoQ of 2.7 ng/L.

7. Assay Cut-Off:

See Clinical Cut-off Section below

B Comparison Studies:

1. Method Comparison with Predicate Device:

Not applicable

2. Matrix Comparison:

A tube type comparison study was carried out following guidance from EP35, 1st Edition on the Alinity i STAT High Sensitivity Troponin-I assay to determine if samples collected in lithium heparin and lithium heparin separator blood collection tubes are equivalent. At least 40 fresh samples were collected in each tube type and then supplemented with native heparin plasma samples to spike concentrations ranging from 2.7 ng/L to 3,500 ng/L. The results indicate concentrations of samples are equivalent when heparin plasma is collected in lithium heparin and lithium heparin separator blood collection tubes.

C Clinical Studies:

1. Clinical Sensitivity:

A multi-center prospective study was performed to assess diagnostic accuracy of the Alinity i STAT High Sensitivity Troponin-I assay. Specimens were collected at 23 emergency departments (EDs) from diverse locations within the US (i.e., rural and urban, small and

large, research and non-research) from 6171 subjects presenting to the ED with chest discomfort or equivalent ischemic symptoms consistent with acute coronary syndrome. The specimen collection sites represented geographically diverse EDs associated with primary care hospitals and medical centers, reflecting regional, urban, and rural patient populations. All subject diagnoses were adjudicated by a panel of board-certified cardiologists based on the third universal definition of MI. The sample collection times were at 0 – 1 hour from presentation to the ED and at the following time-point relative to the time from presentation: 1 – 3 hours, 3 – 6 hours, and ≥6 hours. Investigators and adjudicators were blinded to the Alinity i STAT High Sensitivity Troponin-I assay device's results. Adjudicators were also blinded to site diagnoses. The observed MI prevalence in this study was 7.0%.

The specimens were collected in lithium heparin or lithium heparin separator tubes and tested within 8 hours of sample collection. The specimens were evaluated using the Alinity i STAT High Sensitivity Troponin-I assay. The results were analyzed using the serial sampling time points collected as part of the ED visit.

The sensitivity and specificity results using the overall 99th percentile cutoff (27 ng/L) are summarized in the following table.

Sex	Time Point	n	Sensitivity		Specificity	
			%	95% CI	%	95% CI
Female	0 to < 1 Hours	1,574	78.43 (80/102)	69.50 - 85.30	89.95 (1324/1472)	88.30 - 91.38
	1 to < 3 Hours	841	91.49 (43/47)	80.07 - 96.64	92.57 (735/794)	90.53 - 94.20
	3 to < 6 Hours	854	93.85 (61/65)	85.22 - 97.58	88.34 (697/789)	85.91 - 90.40
	≥ 6 Hours	284	94.44 (51/54)	84.89 - 98.09	75.65 (174/230)	69.71 - 80.75
Male	0 to < 1 Hours	2,917	76.45 (198/259)	70.92 - 81.21	85.82 (2281/2658)	84.44 - 87.09
	1 to < 3 Hours	1,339	91.67 (77/84)	83.78 - 95.90	85.02 (1067/1255)	82.94 - 86.89
	3 to < 6 Hours	1,480	93.46 (143/153)	88.39 - 96.41	80.71 (1071/1327)	78.50 - 82.74
	≥ 6 Hours	576	94.44 (119/126)	88.98 - 97.28	66.44 (299/450)	61.96 - 70.65

The positive predictive value (PPV) and negative predictive value (NPV) results using the overall 99th percentile cutoff (27 ng/L) are summarized in the following table.

Sex	Time Point	n	PPV		NPV	
			%	95% CI	%	95% CI
Female	0 to < 1 Hours	1,574	35.09 (80/228)	29.19 - 41.48	98.37 (1324/1346)	97.54 - 98.92
	1 to < 3 Hours	841	42.16 (43/102)	33.03 - 51.85	99.46 (735/739)	98.62 - 99.79

Sex	Time Point	n	PPV		NPV	
			%	95% CI	%	95% CI
	3 to < 6 Hours	854	39.87 (61/153)	32.45 - 47.78	99.43 (697/701)	98.54 - 99.78
	≥ 6 Hours	284	47.66 (51/107)	38.45 - 57.04	98.31 (174/177)	95.14 - 99.42
Male	0 to < 1 Hours	2,917	34.43 (198/575)	30.67 - 38.41	97.40 (2281/2342)	96.67 - 97.97
	1 to < 3 Hours	1,339	29.06 (77/265)	23.92 - 34.79	99.35 (1067/1074)	98.66 - 99.68
	3 to < 6 Hours	1,480	35.84 (143/399)	31.29 - 40.66	99.07 (1071/1081)	98.31 - 99.50
	≥ 6 Hours	576	44.07 (119/270)	38.28 - 50.04	97.71 (299/306)	95.35 - 98.89

An analysis for both females and males was performed using the sex-specific 99th percentile cutoffs (female 14 ng/L, male 35 ng/L). The sensitivity and specificity results are summarized in the following table.

Cutoff (ng/L)	Time Point	n	Sensitivity		Specificity	
			%	95% CI	%	95% CI
14 (Female only)	0 to < 1 Hours	1,574	85.29 (87/102)	77.15 - 90.88	84.04 (1237/1472)	82.08 - 85.82
	1 to < 3 Hours	841	93.62 (44/47)	82.84 - 97.81	85.64 (680/794)	83.03 - 87.91
	3 to < 6 Hours	854	98.46 (64/65)	91.79 - 99.73	82.00 (647/789)	79.17 - 84.53
	≥ 6 Hours	284	98.15 (53/54)	90.23 - 99.67	69.13 (159/230)	62.89 - 74.75
35 (Male only)	0 to < 1 Hours	2,917	72.20 (187/259)	66.45 - 77.30	88.98 (2365/2658)	87.73 - 90.11
	1 to < 3 Hours	1,339	89.29 (75/84)	80.88 - 94.26	88.29 (1108/1255)	86.39 - 89.95
	3 to < 6 Hours	1,480	90.85 (139/153)	85.23 - 94.47	84.33 (1119/1327)	82.27 - 86.18
	≥ 6 Hours	576	92.06 (116/126)	86.01 - 95.63	74.22 (334/450)	69.99 - 78.05

An analysis for both females and males was performed using the sex-specific 99th percentile cutoffs (female 14 ng/L, male 35 ng/L). The PPV and NPV results are summarized in the following table.

Cutoff (ng/L)	Time Point	n	PPV		NPV	
			%	95% CI	%	95% CI
14 (Female only)	0 to < 1 Hours	1,574	27.02 (87/322)	22.46 - 32.12	98.80 (1237/1252)	98.03 - 99.27
		841	27.85		99.56	

Cutoff (ng/L)	Time Point	n	PPV		NPV	
			%	95% CI	%	95% CI
	1 to < 3 Hours		(44/158)	21.45 - 35.30	(680/683)	98.72 - 99.85
	3 to < 6 Hours	854	31.07 (64/206)	25.14 - 37.69	99.85 (647/648)	99.13 - 99.97
	≥ 6 Hours	284	42.74 (53/124)	34.38 - 51.54	99.38 (159/160)	96.55 - 99.89
35 (Male only)	0 to < 1 Hours	2,917	38.96 (187/480)	34.70 - 43.39	97.05 (2365/2437)	96.30 - 97.65
	1 to < 3 Hours	1,339	33.78 (75/222)	27.88 - 40.23	99.19 (1108/1117)	98.48 - 99.58
	3 to < 6 Hours	1,480	40.06 (139/347)	35.04 - 45.30	98.76 (1119/1133)	97.94 - 99.26
	≥ 6 Hours	576	50.00 (116/232)	43.62 - 56.38	97.09 (334/344)	94.73 - 98.41

The sponsor provided the following information in their labeling:

When using the female cutoff of 14 ng/L, the lower bound of the 95% CI for the PPV was as low as 21.45%. Taking into consideration the lower bound of the 95% CI, up to 77.54% (at 0 to < 1 hour), 78.55% (at 1 to < 3 hours), 74.86% (at 3 to < 6 hours), and 65.62% (at ≥ 6 hours) of positive troponin results could come from females that are not having an MI. When using the overall cutoff of 27 ng/L, the lower bound of the 95% CI for PPV was as low as 29.19%. Taking into consideration the lower bound of the 95% CI, up to 70.81% (at 0 to < 1 hour), 66.97% (at 1 to < 3 hours), 67.55% (at 3 to < 6 hours), and 61.55% (at ≥ 6 hours) of positive troponin results could come from females that are not having an MI. Troponin results should always be used in conjunction with clinical data, signs, and symptoms.

When using the male cutoff of 35 ng/L, the lower bound of the 95% CI for the PPV was as low as 27.88%. Taking into consideration the lower bound of the 95% CI, up to 65.30% (at 0 to < 1 hour), 72.12% (at 1 to < 3 hours), 64.96% (at 3 to < 6 hours), and 56.38% (at ≥ 6 hours) of positive troponin results could come from males that are not having an MI. When using the overall cutoff of 27 ng/L, the lower bound of the 95% CI for PPV was as low as 23.92%. Taking into consideration the lower bound of the 95% CI, up to 69.33% (at 0 to < 1 hour), 76.08% (at 1 to < 3 hours), 68.71% (at 3 to < 6 hours), and 61.72% (at ≥ 6 hours) of positive troponin results could come from males that are not having an MI. Troponin results should always be used in conjunction with clinical data, signs, and symptoms.

In the Alinity i STAT High Sensitivity Troponin-I clinical study, the percent of false negatives for males using the sex-specific cutoff (35 ng/L) was up to 1.63% higher when compared to the false negative rate for males when using the overall cutoff of 27 ng/L. When using the male cutoff of 35 ng/L, 8.12% of males with MI had non elevated Alinity i STAT High Sensitivity Troponin-I test results. When using the overall cutoff of 27 ng/L, 6.49% of males with MI had non-elevated Alinity i STAT High Sensitivity Troponin-I test results. Troponin results should always be used in conjunction with clinical data, signs, and symptoms.

In the Alinity i STAT High Sensitivity Troponin-I clinical study, the percent of false negatives for females using the sex-specific cutoff (14 ng/L) was up to 2.41% lower when compared to the false negative rate for females when using the overall cutoff of 27 ng/L. When using the female cutoff of 14 ng/L, 5.65% of females with MI had non-elevated Alinity i STAT High Sensitivity Troponin-I test results. When using the overall cutoff of 27 ng/L, 8.06% of females with MI had non-elevated Alinity i STAT High Sensitivity Troponin-I test results. Troponin results should always be used in conjunction with clinical data, signs, and symptoms.

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

Using the established overall 99th percentile (27 ng/L), the lower end of the 95% confidence interval (CI) for positive predictive value (PPV) for female subjects was as low as 29.19%, and for male subjects was as low as 23.92% in the clinical validation study. Up to 70.81% and 76.08% of positive troponin results could come from females and males, respectively, without an MI.

Using the established sex specific 99th percentiles in the same study (female 14 ng/L, male 35 ng/L), the lower end of the 95% CI for PPV for female subjects was as low as 21.45% and for male subjects was as low as 27.88%. Up to 78.55% and 72.12% of positive troponin results could come from females and males, respectively, without an MI.

False negative rates using the overall cutoff for females and sex-specific cutoff for males were higher compared to the false negative rates using the sex-specific cutoff for females and overall cutoff for males. Refer to the SPECIFIC PERFORMANCE CHARACTERISTICS, Clinical Results section of this package insert.

2. Clinical Specificity:

See Clinical Sensitivity above (Section VII. C. 1.).

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 VII. 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
HbA1c (%)	≤ 6	
GFR (mL/min/1.73 m^2)	≥ 60	

Each specimen was stored frozen, thawed, and evaluated in replicates of one using the Abbott 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	763	21-75	14	[12, 17]
Male	766	21-73	35	[27, 44]
Overall	1531	21-75	27	[22, 32]

VIII   Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

IX   Conclusion:

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