May 19, 2022

Abbott Laboratories Diagnostic Division
Judi Wallach
Regulatory Affairs Project Manager
Dept. 09AA, Bldg. Ap8, 100 Abbott Park Road
Abbott Park, Illinois 60064-6038

Re: K202525
Trade/Device Name: Alinity i STAT High Sensitivity Troponin-I
Regulation Number: 21 CFR 862.1215
Regulation Name: Creatine Phosphokinase/Creatine Kinase Or Isoenzymes Test System
Regulatory Class: Class II
Product Code: MMI
Dated: February 1, 2022
Received: February 2, 2022

Dear Judi Wallach:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K202525

Device Name
Alinity i STAT High Sensitivity Troponin-I

Indications for Use *(Describe)*
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).

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Section 5: 510(k) Summary

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of the Federal Food, Drug, and Cosmetic Act and 21 CFR 807.92.

I. 510(k) Number

K202525

II. Applicant Name

Date summary prepared: May 13, 2022

Abbott Laboratories Diagnostics Division
Dept. 9AA, CP01-2
100 Abbott Park Road
Abbott Park, IL 60064

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III. Device Name

Alinity i STAT High Sensitivity Troponin-I

Reagents

Trade Name: Alinity i STAT High Sensitivity Troponin-I
Device Classification: Class II
Classification Name: Creatine phosphokinase/creatine kinase or isoenzymes test system
Governing Regulation: 862.1215

Code: MMI

IV. Predicate Device

ARCHITECT STAT High Sensitivity Troponin-I (K191595)

V. Intended Use of the Device

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).

VI. Description of Device

The Alinity i STAT High Sensitivity Troponin-I Reagent Kit 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.

Principles of the Procedure

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 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.

VII. Comparison of Technological Characteristics

The Alinity i STAT High Sensitivity Troponin-I assay (subject device) utilizes a CMIA methodology for the quantitative *in vitro* determination of cTnI and is intended for use on the Alinity i system.

The similarities and differences between the subject device and the predicate device are presented in the following table.

Description	Subject Device **Alinity i STAT High Sensitivity Troponin-I**	Predicate Device **ARCHITECT STAT High Sensitivity Troponin-I (K191595)**
General Device Characteristic Similarities		
Intended Use / Indications for Use	The Alinity i STAT High Sensitivity Troponin-I assay is a CMIA used for the quantitative determination of 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 MI.	The ARCHITECT STAT High Sensitivity Troponin-I assay is a CMIA used for the quantitative determination of cTnI in human plasma (dipotassium [K_2] EDTA) on the ARCHITECT 2000SR System. The ARCHITECT STAT High Sensitivity Troponin-I assay is to be used as an aid in the diagnosis of MI.
Specific Analyte Detected	cTnI	Same
General Device Characteristic Differences		
Specimen Type	Plasma (lithium heparin)	Plasma (dipotassium 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

VIII. Performance Summary*

A. Nonclinical

1. Precision

Reproducibility

A study was performed using 1 lot of the Alinity i STAT High Sensitivity Troponin-I reagents, 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 to include lithium heparin separator plasma specimens within each of 5 target concentration ranges (> 3 to 6 ng/L, 10 to 20 ng/L, 30 to 50 ng/L, 100 to 300 ng/L, and 1000 ng/L to near the upper limit of the analytical measuring interval [AMI]). Only one specimen per concentration range was collected in a single day. 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) within 8 hours of collection.

		Mean (ng/L,	Within-Run		Between-Run		Within-Laboratory[a]		Reproducibility[b]	
Sample	n	pg/mL)	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	12	3.5	0.22	6.2	0.00	0.0	0.22	6.2	0.30	8.7
2	12	5.2	0.30	5.7	0.00	0.0	0.30	5.7	0.67	12.7
3	12	8.0	0.25	3.2	0.23	2.9	0.34	4.3	0.67	8.4
4	12	13.6	0.37	2.7	0.00	0.0	0.37	2.7	0.61	4.5
5	12	13.9	0.37	2.7	0.00	0.0	0.37	2.7	0.37	2.7
6	12	15.1	0.65	4.3	0.00	0.0	0.65	4.3	0.65	4.3
7	12	18.2	0.82	4.5	0.00	0.0	0.82	4.5	0.82	4.5
8	12	20.2	0.66	3.3	0.00	0.0	0.66	3.3	0.74	3.7
9	12	36.9	0.73	2.0	0.00	0.0	0.73	2.0	1.17	3.2
10	12	46.7	0.90	1.9	0.00	0.0	0.90	1.9	0.95	2.0
11	12	51.6	1.22	2.4	1.07	2.1	1.63	3.2	1.63	3.2
12	12	172.6	4.51	2.6	5.53	3.2	7.14	4.1	7.14	4.1
13	12	233.0	5.00	2.1	9.18	3.9	10.45	4.5	10.45	4.5

* Unless otherwise specified, all studies were performed on the Alinity i system.

Sample	n	Mean (ng/L, pg/mL)	Within-Run		Between-Run		Within-Laboratory[a]		Reproducibility[b]	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
14	12	300.0	11.00	3.7	5.61	1.9	12.35	4.1	12.35	4.1
15	12	1228.3	29.03	2.4	45.23	3.7	53.74	4.4	53.74	4.4
16	12	1974.6	49.46	2.5	57.97	2.9	76.21	3.9	76.21	3.9
17	12	2871.4	72.86	2.5	85.31	3.0	112.19	3.9	112.19	3.9

[a] Includes within-run and between-run variability.

[b] Includes within-run, between-run, and between-instrument variability.

Within-Laboratory Precision

A study was performed based on guidance from CLSI EP05-A3.* Testing was conducted using 3 lots of the Alinity i STAT High Sensitivity Troponin-I reagents, 2 lots of the Alinity i STAT High Sensitivity Troponin-I Calibrators, 1 lot of the Alinity i STAT High Sensitivity Troponin-I Controls, 1 lot of Bio-Rad Liquichek Cardiac Markers Plus Control LT (Level 2), and 2 instruments. Three controls were tested in duplicate, twice per day on 20 days (following the manufacturers' storage and handling requirements) on 6 reagent lot/calibrator lot/instrument combinations. The performance from a representative combination is shown in the following table.

Note: Patient samples can only be stored for 8 hours at room temperature; therefore, 20-day precision was conducted with quality controls.

Sample	n	Mean (ng/L, pg/mL)	Within-Run (Repeatability)		Within-Laboratory[a]	
			SD	%CV	SD (Range[b])	%CV (Range[b])
Low Control	80	19.9	0.73	3.7	0.81 (0.76-1.13)	4.1 (3.9-5.1)
Medium Control	80	199.8	6.14	3.1	7.25 (5.54-7.25)	3.6 (2.8-3.6)
Bio-Rad Level 2	80	1442.7	45.91	3.2	60.02 (49.50-69.39)	4.2 (3.3-4.5)

[a] Includes within-run, between-run, and between-day variability.

* Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Precision of Quantitative Measurement Procedures: Approved Guideline–Third Edition*. CLSI Document EP05-A3. Wayne, PA: CLSI; 2014.

[b] Minimum and maximum SD or %CV across all reagent lot and instrument combinations.

2. Lower Limits of Measurement

A study was performed based on guidance from CLSI EP17-A2.* Testing was conducted using 2 lots of the Alinity i STAT High Sensitivity Troponin-I reagents on each of 2 instruments (1 instrument for limit of blank [LoB]). The maximum observed LoB, limit of detection (LoD), and limit of quantitation (LoQ) values are summarized below. These representative data support the lower limit of the analytical measuring interval.

	ng/L (pg/mL)
LoB[a]	0.0
LoD[b]	0.9
LoQ[c]	2.7

[a] The LoB represents the 95th percentile from n ≥ 60 replicates of zero-analyte samples.

[b] The LoD represents the lowest concentration at which the analyte can be detected with 95% probability based on n ≥ 60 replicates of low-analyte level samples.

[c] The LoQ is defined as the lowest concentration at which a maximum allowable precision of 20 %CV was met and was determined from n ≥ 60 replicates of low-analyte level samples.

3. Linearity

A study was performed based on guidance from CLSI EP06-A.† This assay is linear across the analytical measuring interval of 2.7 to 3600.0 ng/L (pg/mL).

* Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline–Second Edition*. CLSI Document EP17-A2. Wayne, PA: CLSI; 2012.

† Clinical and Laboratory Standards Institute (CLSI). *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. CLSI Document EP06-A. Wayne, PA: CLSI; 2003.

4. Analytical Specificity

a. Interference

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.* 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).

No significant interference (interference within ± 10%) was observed at the following concentrations.

Potentially Interfering Substance	Interferent Level
Bilirubin (conjugated)	40 mg/dL
Bilirubin (unconjugated)	40 mg/dL
Hemoglobin	1000 mg/dL
Total protein	8.8 g/dL
Intralipid	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	-10.9%

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%.

* Clinical and Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry*. 3rd ed. CLSI Guideline EP07. Wayne, PA: CLSI; 2018.

Potentially Interfering Drugs

A study was performed based on guidance from CLSI EP07-A2* and EP07, 3rd ed. Each drug was tested at 2 levels of the analyte (approximately 15 ng/L and 500 ng/L).

No significant interference (interference within ± 10%) was observed at the following concentrations.

Potentially Interfering Drug	Interferent Level	Potentially Interfering Drug	Interferent Level
Acetaminophen	250 µg/mL	Ibuprofen	500 µg/mL
Acetylsalicylic Acid	1000 µg/mL	Levodopa	20 µg/mL
Adrenaline	0.37 µg/mL	Low MW Heparin	5 U/mL
Allopurinol	400 µg/mL	Methyldopa	25 µg/mL
Ambroxol	400 µg/mL	Methylprednisolone	80 µg/mL
Ampicillin	1000 µg/mL	Metronidazole	200 µg/mL
Ascorbic Acid	300 µg/mL	Nicotine	2 mg/dL
Atenolol	10 µg/mL	Nifedipine	60 µg/mL
Biotin	4250 ng/mL	Nitrofurantoin	64 µg/mL
Bivalirudin	42 µg/mL	Nystatin	7.5 µg/mL
Caffeine	100 µg/mL	Oxytetracycline	5 µg/mL
Captopril	50 µg/mL	Phenylbutazone	400 µg/mL
Carvedilol	150 µg/mL	Phenytoin	100 µg/mL
Cefoxitin	2500 µg/mL	Primidone	10 mg/dL
Cinnarizine	400 µg/mL	Propranolol	5 µg/mL
Clopidogrel	75 µg/mL	Quinidine	20 µg/mL
Cocaine	10 µg/mL	Rifampicin	60 µg/mL
Cyclosporine	5 µg/mL	Salicylic Acid	600 µg/mL
Diclofenac	50 µg/mL	Simvastatin	20 µg/mL
Digoxin	7.5 µg/mL	Sodium Heparin	8 U/mL
Dopamine	900 µg/mL	Streptokinase	31.3 U/mL
Doxycycline	50 µg/mL	Theophylline	75 µg/mL
Eptifibatide	7 µg/mL	TPA	2.3 µg/mL

* Clinical and Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry; Approved Guideline–Second Edition*. CLSI Document EP07-A2. Wayne, PA: CLSI; 2005.

Potentially Interfering Drug	Interferent Level	Potentially Interfering Drug	Interferent Level
Erythromycin	200 µg/mL	Trimethoprim	75 µg/mL
Fondaparinux	4 µg/mL	Verapamil	160 µg/mL
Furosemide	400 µg/mL	Warfarin	30 µg/mL

MW = Molecular weight
TPA = Tissue plasminogen activator

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

Potentially Interfering Drug	Interferent Level	Analyte Level	% Interference
Fibrinogen	1000 mg/dL	15 ng/L	24.3%

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

Potentially Interfering Other Conditions

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. The individual differences for samples near 2.7 ng/L ranged from -0.2 to 0.1 ng/L. The individual % differences for samples near 15 ng/L and 500 ng/L ranged from -8.9% to -0.5%. No significant interference (interference within ± 10%) was observed with specimens containing HAMA at concentrations up to 150 ng/mL.

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%.

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. For samples tested at an RF concentration of 1200 IU/mL, the difference for a sample near 2.7 ng/L was 0.3 ng/L, and the % differences for samples near 15 ng/L and 500 ng/L were -7.1% and -7.6%, respectively. For samples tested at an RF concentration of 1495 IU/mL, the difference for a sample near 2.7 ng/L was -0.1 ng/L, and the % differences for samples near 15 ng/L and 500 ng/L were -12.6% and -18.9%, respectively.

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.

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.

[*] Park JY, Jaffe AS. Troponin autoantibodies: from assay interferent to mediator of cardiotoxicity. *Clin Chem* 2017;63(1):30-32.

[†] Nussinovitch U, Shoenfeld Y. Anti-troponin autoantibodies and the cardiovascular system. *Heart* 2010;96:1518-1524.

b. Cross-Reactants

A study was performed based on guidance from CLSI EP07, 3rd ed. Samples with cTnI target concentrations of 2.7, 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. The observed % cross-reactivity was ≤ 1% for all cross-reactants evaluated at each analyte level.

Cross-Reactant	Cross-Reactant Concentration
Actin	1 000 000 ng/L
Cardiac troponin C	1 000 000 ng/L
Cardiac troponin T	1 000 000 ng/L
Creatine kinase-MB (CK-MB)	1 000 000 ng/L
Myoglobin	1 000 000 ng/L
Myosin	1 000 000 ng/L
Skeletal troponin I	1 000 000 ng/L
Tropomyosin	1 000 000 ng/L

5. Expected Values

This study was performed on the ARCHITECT i2000SR System.

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 normal levels of cardiac B-type natriuretic peptide (BNP) and HbA1c, and glomerular filtration rate (GFR) values ≥ 60 mL/min. Each specimen was stored frozen, thawed, and evaluated in replicates of one using the ARCHITECT STAT High Sensitivity Troponin-I assay. The 99th

[*] Clinical and Laboratory Standards Institute (CLSI). *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline–Third Edition*. CLSI document EP28-A3c. Wayne, PA: CLSI; 2010.

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, pg/mL)	90% CI (ng/L, pg/mL)
Female	763[a]	21 - 75	14	[12, 17]
Male	766	21 - 73	35	[27, 44]
Overall	1531	21 - 75	27	[22, 32]

[a] During the sex-specific analysis, 2 female subjects were identified as outliers. The subjects and results were excluded from the sex-specific analysis but were included in the overall analysis.

B. Clinical

The Alinity i STAT High Sensitivity Troponin-I results should be used in conjunction with other diagnostic information such as electrocardiogram (ECG), clinical observations and information, and patient symptoms to aid in the diagnosis of MI.

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 EDs from 6174 subjects presenting to the ED with chest discomfort or equivalent ischemic symptoms consistent with ACS. 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 adjudicators were blinded to the Alinity i STAT High Sensitivity Troponin-I assay results. The observed MI prevalence in this study was 7.0%.

- 891 specimens with serial sampling from 432 MI subjects (124 female subjects, 308 male subjects)
- 8975 specimens with serial sampling from 5742 non-MI subjects (2128 female subjects, 3614 male subjects)

[*] Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Eur Heart J* 2012;33(20):2551-2567.

The specimens were collected in lithium heparin or lithium heparin separator tubes. The specimens were evaluated using the Alinity i STAT High Sensitivity Troponin-I assay.

NOTE: The study population did not include type 4 or 5 MI subjects. Therefore, the ability of the assay to identify these patients was not evaluated.

The results were analyzed using the serial sampling time points collected as part of the ED visit.

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 results are summarized in the following table.

Cutoff (ng/L)	Time Point[a]	n[b]	Sensitivity[c]		Specificity[d]		PPV[e]		NPV[f]	
			%	95% CI	%	95% CI	%	95% CI	%	95% CI
14 (Female only)	0 to < 1 Hour	1574	85.29 (87/102)	77.15 - 90.88	84.04 (1237/1472)	82.08 - 85.82	27.02 (87/322)	22.46 - 32.12	98.80 (1237/1252)	98.03 - 99.27
	1 to < 3 Hours	841	93.62 (44/47)	82.84 - 97.81	85.64 (680/794)	83.03 - 87.91	27.85 (44/158)	21.45 - 35.30	99.56 (680/683)	98.72 - 99.85
	3 to < 6 Hours	854	98.46 (64/65)	91.79 - 99.73	82.00 (647/789)	79.17 - 84.53	31.07 (64/206)	25.14 - 37.69	99.85 (647/648)	99.13 - 99.97
	≥ 6 Hours[g, h]	284	98.15 (53/54)	90.23 - 99.67	69.13 (159/230)	62.89 - 74.75	42.74 (53/124)	34.38 - 51.54	99.38 (159/160)	96.55 - 99.89
35 (Male only)	0 to < 1 Hour	2917	72.20 (187/259)	66.45 - 77.30	88.98 (2365/2658)	87.73 - 90.11	38.96 (187/480)	34.70 - 43.39	97.05 (2365/2437)	96.30 - 97.65
	1 to < 3 Hours	1339	89.29 (75/84)	80.88 - 94.26	88.29 (1108/1255)	86.39 - 89.95	33.78 (75/222)	27.88 - 40.23	99.19 (1108/1117)	98.48 - 99.58
	3 to < 6 Hours	1480	90.85 (139/153)	85.23 - 94.47	84.33 (1119/1327)	82.27 - 86.18	40.06 (139/347)	35.04 - 45.30	98.76 (1119/1133)	97.94 - 99.26
	≥ 6 Hours[g, h]	576	92.06 (116/126)	86.01 - 95.63	74.22 (334/450)	69.99 - 78.05	50.00 (116/232)	43.62 - 56.38	97.09 (334/344)	94.73 - 98.41

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

Sex	Time Point[a]	n[b]	Sensitivity[c] %	Sensitivity[c] 95% CI	Specificity[d] %	Specificity[d] 95% CI	PPV[e] %	PPV[e] 95% CI	NPV[f] %	NPV[f] 95% CI
Female	0 to < 1 Hour	1574	78.43 (80/102)	69.50 - 85.30	89.95 (1324/1472)	88.30 - 91.38	35.09 (80/228)	29.19 - 41.48	98.37 (1324/1346)	97.54 - 98.92
	1 to < 3 Hours	841	91.49 (43/47)	80.07 - 96.64	92.57 (735/794)	90.53 - 94.20	42.16 (43/102)	33.03 - 51.85	99.46 (735/739)	98.62 - 99.79
	3 to < 6 Hours	854	93.85 (61/65)	85.22 - 97.58	88.34 (697/789)	85.91 - 90.40	39.87 (61/153)	32.45 - 47.78	99.43 (697/701)	98.54 - 99.78
	≥ 6 Hours[g, h]	284	94.44 (51/54)	84.89 - 98.09	75.65 (174/230)	69.71 - 80.75	47.66 (51/107)	38.45 - 57.04	98.31 (174/177)	95.14 - 99.42
Male	0 to < 1 Hour	2917	76.45 (198/259)	70.92 - 81.21	85.82 (2281/2658)	84.44 - 87.09	34.43 (198/575)	30.67 - 38.41	97.40 (2281/2342)	96.67 - 97.97
	1 to < 3 Hours	1339	91.67 (77/84)	83.78 - 95.90	85.02 (1067/1255)	82.94 - 86.89	29.06 (77/265)	23.92 - 34.79	99.35 (1067/1074)	98.66 - 99.68
	3 to < 6 Hours	1480	93.46 (143/153)	88.39 - 96.41	80.71 (1071/1327)	78.50 - 82.74	35.84 (143/399)	31.29 - 40.66	99.07 (1071/1081)	98.31 - 99.50
	≥ 6 Hours[g, h]	576	94.44 (119/126)	88.98 - 97.28	66.44 (299/450)	61.96 - 70.65	44.07 (119/270)	38.28 - 50.04	97.71 (299/306)	95.35 - 98.89

CI = confidence interval

[a] All time points are relative to ED presentation / ED triage.

[b] Some time points could not be collected for some subjects.

For footnotes c-f:

Alinity i STAT High Sensitivity Troponin-I	Diagnosis: MI	Diagnosis: Non-MI
cTnI Value > cutpoint	A	B
cTnI Value ≤ cutpoint	C	D

[c] Sensitivity = A/(A + C) × 100%

[d] Specificity = D/(B + D) × 100%

[e] Positive predictive value (PPV) = A/(A + B) × 100%

[f] Negative predictive value (NPV) = D/(C + D) × 100%

[g] The study design followed the standard of care at each site where few specimens would be obtained at later time points because most patients would not typically require further serial cTnI testing after 6 hours.[*] Therefore, the lower specificity at the ≥ 6 hour time point was the result of the disproportionate number of elevated and non-elevated specimens carried over from previous time points. The cTnI value should be used in conjunction with information available from clinical evaluation and other diagnostic procedures.

[h] Of the specimens collected at greater than or equal to 6 hours, all were collected within 19 hours from presentation to the ED, except for one specimen from a male collected at 35 hours.

[*] Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021;144:e368-e454.

Prevalence of adjudicated MI in the study population was 7.0% (5.5% for females and 7.9% for males).

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.

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.

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.

Troponin results should always be used in conjunction with clinical data, signs, and symptoms in accordance with the fourth universal definition of MI[*] requiring acute myocardial injury with clinical evidence of acute myocardial ischemia, detection of a rise and/or fall of cardiac troponin (cTn) values, at least one value above the 99th percentile upper reference limit (URL), and at least one of the following: symptoms of myocardial ischemia, new ischemic ECG changes, development of pathological Q waves, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology, identification of a coronary thrombus by angiography.

There are conditions other than MI that are known to cause myocardial injury and elevated troponin values. The Alinity i STAT High Sensitivity Troponin-I clinical trial enrolled all patients presenting to the ED with symptoms consistent with ACS. Some of these patients had an acute or chronic condition other than MI.

[*] Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol* 2018;72(18):2231-2264.

A sex difference in 99th percentile has been reported.[*, †, ‡]

In the clinical trial, 14.1% of patients without an MI diagnosis had at least one Alinity i STAT High Sensitivity Troponin-I test result above the sex-specific 99th percentile on one or more serial draws.

One or more of the following conditions were found in 94.2% of these patients:

Cardiac Conditions	Non-Cardiac Conditions
Atrial fibrillation	Cerebrovascular accidents and subarachnoid bleeds
Cardiotoxic drugs	Chronic obstructive pulmonary disease
Heart failure	Chronic renal insufficiency with or without hemodialysis
Hypertension	Cocaine user
Infiltrative cardiomyopathies	Diabetes mellitus
Left ventricular hypertrophy	Pulmonary embolism
Myocarditis	Rhabdomyolysis
Recent cardiac intervention and/or surgery	Sepsis
Recent MI	Vigorous exercise

The Area Under the Curve (AUC) results[§] are summarized in the following table.

Sex	Time Point[a]	n[b]	AUC	Standard Error	95% Wald CI
Female	0 to < 1 Hour	1574	0.9257	0.0129	[0.9003, 0.9510]
	1 to < 3 Hours	841	0.9582	0.0179	[0.9230, 0.9933]
	3 to < 6 Hours	854	0.9777	0.0056	[0.9666, 0.9888]
	≥ 6 Hours	284	0.9500	0.0148	[0.9210, 0.9790]
Male	0 to < 1 Hour	2917	0.8994	0.0106	[0.8787, 0.9202]

[*] Wu AHB, Christenson RH, Greene DN, et al. Clinical laboratory practice recommendations for the use of cardiac troponin in acute coronary syndrome: expert opinion from the Academy of the American Association for Clinical Chemistry and the Task Force on Clinical Applications of Cardiac Bio-Markers of the International Federation of Clinical Chemistry and Laboratory Medicine. *Clin Chem* 2018;64(4):645-655.

[†] Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol* 2018;72(18):2231-2264.

[‡] Apple FS, Ler R, Murakami MM. Determination of 19 cardiac troponin I and T assay 99th percentile values from a common presumably healthy population. *Clin Chem* 2012;58(11):1574-1581.

[§] Obuchowski NA. Fundamentals of clinical research for radiologists: ROC analysis. *Am J Roentgenol* 2005;184(2):364-372.

Sex	Time Point[a]	n[b]	AUC	Standard Error	95% Wald CI
	1 to < 3 Hours	1339	0.9455	0.0094	[0.9270, 0.9640]
	3 to < 6 Hours	1480	0.9489	0.0094	[0.9306, 0.9673]
	≥ 6 Hours	576	0.9243	0.0140	[0.8969, 0.9516]

[a] All time points are relative to ED presentation / ED triage.

[b] Some time points could not be collected for some subjects.

IX. Conclusion Drawn from Nonclinical Laboratory Studies and Clinical Performance

The results presented in this 510(k) demonstrate that the subject device (Alinity i STAT High Sensitivity Troponin-I) performance is substantially equivalent to the predicate device (ARCHITECT STAT High Sensitivity Troponin-I, K191595).

The similarities and differences between the subject device and predicate device are presented in section VII.

There is no known potential adverse effect to the operator when using this *in vitro* device according to the Alinity i STAT High Sensitivity Troponin-I reagent package insert instructions.