September 13, 2019

Abbott Laboratories Diagnostic Division
Judi Wallach
Regulatory Affairs Project Manager
Dept. 09AA, Bldg, AP8-1, 100 Abbott Park Road
Abbott Park, IL 60064-6038

Re: K191595
Trade/Device Name: ARCHITECT 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: June 13, 2019
Received: June 17, 2019

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,

Kellie Kelm, Ph.D.
Acting Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K191595

Device Name
ARCHITECT STAT High Sensitivity Troponin-I

Indications for Use *(Describe)*
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).

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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510(k) Summary (Summary of Safety and Effectiveness)

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

I. 510(k) Number

K191595

II. Applicant Name

Abbott Laboratories Diagnostics Division
Dept. 9AA, AP8-1
100 Abbott Park Road
Abbott Park, IL 60064

Primary contact person for all communications:

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Date summary prepared: August 14, 2019

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III. Device Name

ARCHITECT STAT High Sensitivity Troponin-I

Reagents

Trade Name: ARCHITECT 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

Reagents

Elecsys Troponin T Gen 5 STAT Immunoassay (K162895)

V. Description of Device

Reagents

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.

Principles of the Procedure

The ARCHITECT STAT High Sensitivity Troponin-I assay is a two-step immunoassay for the quantitative determination of cardiac troponin I in human plasma (dipotassium EDTA) using chemiluminescent microparticle immunoassay 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.

VI. Intended Use of the Device

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 [K_2] 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).

VII. Comparison of Technological Characteristics

The ARCHITECT STAT High Sensitivity Troponin-I assay (candidate assay) utilizes a CMIA methodology for the quantitative *in vitro* determination of cTnI and is intended for use on the ARCHITECT i2000SR System.

The similarities and differences between the candidate assay and the predicate assay are presented in the following table.

Similarities and Differences

Characteristics	**Candidate Device** **ARCHITECT STAT High Sensitivity Troponin-I**	**Predicate Device** **Roche cobas Elecsys Troponin T Gen 5 STAT** **(K162895)**
Platform	ARCHITECT i2000SR	cobas e 411 and e 601 immunoassay analyzers
Methodology	CMIA	Electrochemiluminescence Immunoassay (ECLIA)
Intended Use and Indications 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 [K_2] 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).	Immunoassay for the in vitro quantitative determination of cardiac troponin T (cTnT) in lithium heparin plasma. The immunoassay is intended to aid in the diagnosis of myocardial infarction. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas system analyzers.
Specific Analyte Detected	cTnI	cTnT

Characteristics	Candidate Device ARCHITECT STAT High Sensitivity Troponin-I	Predicate Device Roche cobas Elecsys Troponin T Gen 5 STAT (K162895)
Specimen Type	Plasma (K_2 EDTA)	Plasma (lithium heparin)
Reagent Components	Microparticles – Anti-troponin I (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizer. Minimum concentration: 0.035% solids. Preservative: ProClin 300. Conjugate – 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.	M – Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative. R1 – Anti-troponin T-Ab~biotin (gray cap), 1 bottle, 8 mL: Biotinylated monoclonal anti-cardiac troponin T-antibody (mouse) 2.5 mg/L; phosphate buffer 100 mmol/L, pH 6.0; preservative; inhibitors. R2 – Anti-troponin T-Ab~Ru(bpy)$_3^{2+}$ (black cap), 1 bottle, 8 mL: Monoclonal chimeric anti-cardiac troponin T-antibody (mouse/human) labeled with ruthenium complex 2.5 mg/L; phosphate buffer 100 mmol/L, pH 6.0; preservative.
Limit of Quantitation (LoQ)	The LoQ is 3.5 ng/L.	The LoQ at ≤ 20 %CV is 6.0 ng/L.
Measurement Range	Analytical measuring interval (AMI): 3.5 to 5000.0 ng/L (pg/mL)	6.0 to 10,000 ng/L
Potentially Interfering Endogenous Substances and Clinical Conditions	Samples targeted to 15 and 500 ng/L cTnI were evaluated with unconjugated and conjugated bilirubin (20 mg/dL), hemoglobin (500 mg/dL), total protein (9.3 g/dL) and triglycerides (3000 mg/dL). No significant interference (interference within ± 10%) was observed.	Samples from approximately 13 to 8500 ng/L cTnT were evaluated with bilirubin (25 mg/dL), hemoglobin (100 mg/dL), lipemia / Intralipid (1500 mg/dL), human serum albumin (7 g/dL), cholesterol (310 mg/dL), biotin (20 ng/mL), rheumatoid factor (RF) (900 IU/mL), and human anti-mouse antibodies (HAMA) (322 µg/L). Bias less than 10% was observed.
Drug Interferences (General Drug and Cardiac Drug Panel)	Commonly used pharmaceuticals and cardiac-specific drugs were evaluated with samples targeted to 15 and 500 ng/L cTnI. No significant interference (interference within ± 10%) was observed at therapeutic levels, and no significant interference (interference within ± 10%) was observed at high levels, with the exception of fibrinogen.	Commonly used pharmaceuticals were evaluated in samples with cTnT concentrations of 15 ng/L and 9800 ng/L. Cardiac-specific drugs were tested in samples with cTnT concentrations of 15 ng/L and 1900 ng/L. Bias less than ± 10% was observed.

Characteristics	Candidate Device ARCHITECT STAT High Sensitivity Troponin-I	Predicate Device Roche cobas Elecsys Troponin T Gen 5 STAT (K162895)
99th Percentile Cutoff / Expected Values from Apparently Healthy Individuals	Female: 17 ng/L (pg/mL) Male: 35 ng/L (pg/mL) Overall: 28 ng/L (pg/mL)	Female: 14 ng/L Male: 22 ng/L Overall: 19 ng/L

VIII. Summary of Nonclinical Performance

A. 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 (> LoQ to 6 ng/L, 10 to 20 ng/L, 30 to 50 ng/L, and 150 to 200 ng/L). 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.

			Within-Run		Between-Run		Within-Laboratory[a]		Reproducibility[b]	
Sample	n	Mean (ng/L)	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	12	5.3	0.12	2.2	0.23	4.2	0.25	4.8	0.25	4.8
Sample 2	12	11.2	0.47	4.2	0.00	0.0	0.47	4.2	0.62	5.5
Sample 3	12	17.5	0.50	2.9	0.23	1.3	0.55	3.1	0.81	4.6
Sample 4	12	18.8	0.60	3.2	0.22	1.2	0.64	3.4	0.75	4.0
Sample 5	12	34.6	0.84	2.4	0.00	0.0	0.84	2.4	1.10	3.2
Sample 6	12	38.8	1.00	2.6	1.10	2.8	1.48	3.8	1.92	5.0
Sample 7	12	45.0	1.52	3.4	1.42	3.2	2.08	4.6	3.16	7.0
Sample 8	12	163.7	5.00	3.1	6.23	3.8	7.99	4.9	11.68	7.1
Sample 9	12	167.5	6.82	4.1	2.82	1.7	7.38	4.4	11.09	6.6
Sample 10	12	179.6	6.76	3.8	0.00	0.0	6.76	3.8	8.19	4.6

[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 Clinical and Laboratory Standards Institute (CLSI) EP05-A2.[*] 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, 1 lot of the ARCHITECT STAT High Sensitivity Troponin-I Controls, 1 lot each of Bio-Rad Liquichek Cardiac Markers Plus Control LT (Level Low, 2, and 3), and 2 instruments. Five controls were tested in duplicate, twice per day on 20 days, following the manufacturers' storage and handling requirements.

Note: Patient samples can only be stored for 8 hours at room temperature; therefore, 20-day precision was conducted with quality controls. Bio-Rad controls were thawed and tested each day of the precision study.

[*] Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition*. CLSI Document EP05-A2. Wayne, PA: CLSI; 2004.

Sample	Instrument	Reagent Lot	n	Mean (ng/L)	Within-Run		Within-Laboratory (Total)[a]	
					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
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
Bio-Rad 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
Bio-Rad 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
Bio-Rad 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

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

B. Lower Limits of Measurement

A study was performed based on guidance from CLSI EP17-A2.[†] Testing of zero-analyte samples was conducted using 4 lots of the ARCHITECT STAT High Sensitivity Troponin-I reagent kit across 5 instruments over a minimum of 3 days. Testing of low-analyte samples was conducted using 2 lots of the ARCHITECT STAT High Sensitivity Troponin-I reagent kit on each of 2 instruments over a minimum of 3 days. The limit of blank (LoB), limit of detection (LoD), and LoQ values are summarized below.

	ng/L (pg/mL)
LoB[a]	0.9
LoD[b]	1.7
LoQ[c]	3.5

[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 presented in the table is in alignment with the low end of the AMI for the ARCHITECT STAT High Sensitivity Troponin-I assay. The observed LoQ on the ARCHITECT i2000SR System was 2.3 ng/L (2.3 pg/mL). This 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.

C. Linearity

A study was performed based on guidance from CLSI EP06-A.[‡] This assay is linear across the analytical measuring interval of 3.5 to 5000.0 ng/L (3.5 to 5000.0 pg/mL).

D. Measuring Interval

Based on representative data for the LoQ, the ranges over which results can be quantified are provided below.

[†] 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.

	ng/L (pg/mL)
AMI[a]	3.5 - 5000.0
Extended Measuring Interval (EMI)[b]	5000.0 - 50,000.0

[a] AMI: The AMI extends from the LoQ to the upper limit of quantitation (ULoQ).

[b] EMI: The EMI extends from the ULoQ to the ULoQ × dilution factor. The value reflects a 1:10 dilution factor.

E. Analytical Specificity

1. Interference

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07-A2.[§] Each substance 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 Substance	Interferent Level
Unconjugated Bilirubin	≤ 20 mg/dL
Conjugated Bilirubin	≤ 20 mg/dL
Hemoglobin	≤ 500 mg/dL
Total Protein	≤ 9.3 g/dL
Triglycerides	≤ 3000 mg/dL

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

Potentially Interfering Substance	Interferent Level	Analyte Level	% Interference
Total Protein	12.4 g/dL	15 ng/L	-12.0%
Total Protein	12.4 g/dL	500 ng/L	-18.4%

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

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.

Potentially Interfering Drugs

A study was performed based on guidance from CLSI EP07-A2. 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	
	Therapeutic	High		Therapeutic	High
Abciximab	4 µg/mL	20 µg/mL	Ibuprofen	40 µg/mL	500 µg/mL
Acetaminophen	20 µg/mL	250 µg/mL	Levodopa	1.8 µg/mL	20 µg/mL
Acetylsalicylic Acid	260 µg/mL	1000 µg/mL	Low MW Heparin	1.8 U/mL	5 U/mL
Adrenaline	60 ng/mL	0.37 µg/mL	Methyldopa	4 µg/mL	25 µg/mL
Allopurinol	12 µg/mL	400 µg/mL	Methylprednisolone	8 µg/mL	80 µg/mL
Ambroxol	0.1 µg/mL	400 µg/mL	Metronidazole	23 µg/mL	200 µg/mL
Ampicillin	10 µg/mL	1000 µg/mL	Nicotine	37 ng/mL	2 mg/dL
Ascorbic Acid	12 µg/mL	300 µg/mL	Nifedipine	125 ng/mL	60 µg/mL
Atenolol	1 µg/mL	10 µg/mL	Nitrofurantoin	2.0 µg/mL	64 µg/mL
Biotin	10 ng/mL	290 ng/mL	Nystatin	2 µg/mL	7.5 µg/mL
Bivalirudin	11 µg/mL	42 µg/mL	Oxytetracycline	2 µg/mL	5 µg/mL
Caffeine	12 µg/mL	100 µg/mL	Phenobarbital	25 µg/mL	15 mg/dL
Captopril	1.0 µg/mL	50 µg/mL	Phenylbutazone	30 µg/mL	400 µg/mL
Carvedilol	5 µg/mL	150 µg/mL	Phenytoin	12 µg/mL	100 µg/mL
Cefoxitin	120 µg/mL	2500 µg/mL	Primidone	10 µg/mL	10 mg/dL
Cinnarizine	4 µg/mL	400 µg/mL	Propranolol	1 µg/mL	5 µg/mL
Clopidogrel	15 µg/mL	75 µg/mL	Quinidine	4 µg/mL	20 µg/mL
Cocaine	0.1 µg/mL	10 µg/mL	Rifampicin	7 µg/mL	60 µg/mL
Cyclosporine	0.8 µg/mL	5 µg/mL	Salicylic Acid	199 µg/mL	600 µg/mL
Diclofenac	2.5 µg/mL	50 µg/mL	Simvastatin	4 µg/mL	20 µg/mL
Digoxin	1 ng/mL	7.5 µg/mL	Sodium Heparin	2 U/mL	8 U/mL
Dopamine	0.3 µg/mL	900 µg/mL	Streptokinase	4 U/mL	31.3 U/mL
Doxycycline	10 µg/mL	50 µg/mL	Theophylline	12 µg/mL	75 µg/mL
Eptifibatide	2 µg/mL	7 µg/mL	TPA	0.52 µg/mL	2.3 µg/mL
Erythromycin	11 µg/mL	200 µg/mL	Trimethoprim	12 µg/mL	75 µg/mL
Fibrinogen	100 mg/dL	NA	Verapamil	325 ng/mL	160 µg/mL
Fondaparinux	1.2 µg/mL	4 µg/mL	Warfarin	2 µg/mL	30 µg/mL
Furosemide	20 µg/mL	400 µg/mL			

MW = Molecular weight, NA = Not applicable, TPA = Tissue plasminogen activator

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

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

Potentially Interfering Clinical Conditions

Twenty-three specimens positive for HAMA and 23 specimens positive for RF were evaluated for potential interference.

Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain 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.[**, ††] Specimens containing HAMA may show either falsely elevated or depressed values when tested with the ARCHITECT STAT High Sensitivity Troponin-I assay.

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.[‡‡]

RF in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[‡‡] Specimens containing RF may show either falsely

[**] Primus FJ, Kelley EA, Hansen HJ, et al. "Sandwich"-type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy. *Clin Chem* 1988;34(2):261-264.

[††] Schroff RW, Foon KA, Beatty SM, et al. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45(2):879-885.

[‡‡] Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.

elevated or depressed values when tested with the ARCHITECT STAT High Sensitivity Troponin-I assay.

Although the ARCHITECT 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.

2. Cross-Reactants

A study was performed based on guidance from CLSI EP07-A2. Samples with cTnI concentrations from 3.5 to 5000 ng/L containing the cross-reactants listed in the following table were tested with the ARCHITECT STAT High Sensitivity Troponin-I assay.

The observed % cross-reactivity was ≤ 0.1% for skeletal troponin I and ≤ 1% for all other cross-reactants.

Cross-Reactant	Cross-Reactant Concentration
Actin	1,000,000 ng/L
Cardiac troponin T	1,000,000 ng/L
Creatine kinase-muscle/brain (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
Troponin C	1,000,000 ng/L

[§§] 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.

F. Expected Values

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 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	765	21 - 75	17	[14, 20]
Male	766	21 - 73	35	[27, 44]
Overall	1531	21 - 75	28	[22, 33]

* CI = Confidence Interval

IX. Summary of Clinical Performance

A multi-center prospective study was performed to assess diagnostic accuracy of the ARCHITECT STAT High Sensitivity Troponin-I assay. Specimens were collected at 11 EDs from 1065 subjects presenting to the ED with symptoms consistent with ACS. The specimen collection sites represented geographically diverse EDs associated with primary care hospitals and medical centers, reflecting regional, urban, suburban, and rural patient populations. All subject diagnoses were adjudicated by three board certified cardiologists according to the 2007 universal definition of MI[‡‡‡] before the ARCHITECT STAT High Sensitivity Troponin-I assay results were available. The final adjudicated diagnosis was made by majority agreement of the 3 board-certified cardiologists. The observed MI prevalence in this study was 10.89%.

[†††] 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.

[‡‡‡] Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. *Eur Heart J* 2007;28(20):2525-2538.

- 248 specimens with serial sampling from 116 MI subjects (31 female subjects, 85 male subjects)
- 2488 specimens with serial sampling from 949 non-MI subjects (440 female subjects, 509 male subjects)

The specimens were collected in K_2 EDTA tubes and frozen. The specimens were thawed and evaluated using the ARCHITECT 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 during the ED visit.

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.

			Sensitivity[c]		**Specificity[d]**		**PPV[e]**		**NPV[f]**	
Sex	**Time Point[a]**	**N[b]**	**%**	**95% CI**	**%**	**95% CI**	**%**	**95% CI**	**%**	**95% CI**
Female	Baseline	412	91.7 (22/24)	73.0 - 99.0	92.0 (357/388)	88.9 - 94.5	41.5 (22/53)	28.1 - 55.9	99.4 (357/359)	98.0 - 99.9
	2 - 4 Hours	418	94.4 (17/18)	72.7 - 99.9	89.3 (357/400)	85.8 - 92.1	28.3 (17/60)	17.5 - 41.4	99.7 (357/358)	98.5 - 100.0
	4 - 9 Hours	372	94.1 (16/17)	71.3 - 99.9	87.0 (309/355)	83.1 - 90.4	25.8 (16/62)	15.5 - 38.5	99.7 (309/310)	98.2 - 100.0
Male	Baseline	519	81.8 (54/66)	70.4 - 90.2	81.5 (369/453)	77.6 - 84.9	39.1 (54/138)	30.9 - 47.8	96.9 (369/381)	94.6 - 98.4
	2 - 4 Hours	526	91.7 (55/60)	81.6 - 97.2	83.5 (389/466)	79.8 - 86.7	41.7 (55/132)	33.2 - 50.6	98.7 (389/394)	97.1 - 99.6
	4 - 9 Hours	489	93.7 (59/63)	84.5 - 98.2	81.0 (345/426)	76.9 - 84.6	42.1 (59/140)	33.9 - 50.8	98.9 (345/349)	97.1 - 99.7

[a] All time points are relative to ED presentation / ED triage; baseline is within 2 hours of ED presentation / ED triage.

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

For footnotes c-f:

	Diagnosis	
ARCHITECT STAT High Sensitive Troponin-I	**MI**	**Non-MI**
cTnI Value > cutpoint	A	B
cTnI Value ≤ cutpoint	C	D

[c] Sensitivity = $A/(A + C) \times 100$

[d] Specificity = D/(B + D) × 100

[e] Positive Predictive Value (PPV) = A/(A + B) × 100

[f] Negative Predictive Value (NPV) = D/(C + D) × 100

The lower end of the CI for PPV demonstrated for female subjects using the established overall 99th percentile was as low as 15.5%. Taking into consideration the lower bound of the 95% CI, up to 71.9% (baseline), 82.5% (at 2 to 4 hours), and 84.5% (at 4 to 9 hours) of positive troponin results could come from females that are not having an MI.

The lower end of the CI for PPV demonstrated for male subjects using the established overall 99th percentiles was as low as 30.9%. Taking into consideration the lower bound of the 95% CI, up to 69.1% (baseline), 66.8% (at 2 to 4 hours), and 66.1% (at 4 to 9 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 signs and symptoms in accordance with the fourth universal definition of MI[§§§] requiring myocardial injury represented by a rise and/or fall of cTn values with at least one value above the 99th percentile URL and at least one of the following: symptoms of myocardial ischaemia, new ischaemic 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 ischaemic aetiology, identification of a coronary thrombus by angiography or autopsy.

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

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

Cutoff (ng/L)	Time Point[a]	N[b]	Sensitivity[c]		Specificity[d]		PPV[e]		NPV[f]	
			%	95% CI	%	95% CI	%	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	32.4 (23/71)	21.8 - 44.5	99.7 (340/341)	98.4 - 100.0
	2 - 4 Hours	418	94.4 (17/18)	72.7 - 99.9	85.3 (341/400)	81.4 - 88.6	22.4 (17/76)	13.6 - 33.4	99.7 (341/342)	98.4 - 100.0
	4 - 9 Hours	372	94.1 (16/17)	71.3 - 99.9	82.8 (294/355)	78.5 - 86.6	20.8 (16/77)	12.4 - 31.5	99.7 (294/295)	98.1 - 100.0
35 (Male only)	Baseline	519	78.8 (52/66)	67.0 - 87.9	84.5 (383/453)	80.9 - 87.8	42.6 (52/122)	33.7 - 51.9	96.5 (383/397)	94.2 - 98.1
	2 - 4 Hours	526	90.0 (54/60)	79.5 - 96.2	86.1 (401/466)	82.6 - 89.1	45.4 (54/119)	36.2 - 54.8	98.5 (401/407)	96.8 - 99.5
	4 - 9 Hours	489	93.7 (59/63)	84.5 - 98.2	84.3 (359/426)	80.5 - 87.6	46.8 (59/126)	37.9 - 55.9	98.9 (359/363)	97.2 - 99.7

[a] All time points are relative to ED presentation / ED triage; baseline is within 2 hours of ED presentation / ED triage.

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

For footnotes c-f:

	Diagnosis	
ARCHITECT STAT High Sensitive Troponin-I	MI	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] PPV = A/(A + B) × 100

[f] NPV = D/(C + D) × 100

The lower end of the CI for PPV demonstrated for female subjects using the established female 99th percentile was as low as 12.4%. Taking into consideration the lower bound of the 95% CI, up to 78.2% (baseline), 86.4% (at 2 to 4 hours), and 87.6% (at 4 to 9 hours) of positive troponin results could come from females that are not having an MI.

The lower end of the CI for PPV demonstrated for male subjects using the established male 99th percentile was as low as 33.7%. Taking into consideration the lower bound of the 95% CI, up to 66.3% (baseline), 63.8% (at 2 to 4 hours), and 62.1% (at 4 to 9 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 signs and symptoms in accordance with the fourth universal definition of MI requiring myocardial injury

represented by a rise and/or fall of cTn values with at least one value above the 99th percentile URL and at least one of the following: symptoms of myocardial ischaemia, new ischaemic 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 ischaemic aetiology, identification of a coronary thrombus by angiography or autopsy.

There are conditions other than MI that are known to cause myocardial injury and elevated troponin values. The ARCHITECT 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.

In the clinical trial, 16.5% of patients without an MI diagnosis had at least one ARCHITECT 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 71.3% of these patients:

Cardiac Conditions	**Non-Cardiac Conditions**
Angina	Cardiac contusion related to a traumatic injury
Atrial fibrillation	Chronic lung disease
Cardiomyopathy	Pneumonia
Coronary artery disease	Pulmonary embolism
Heart failure	Renal failure
Hypertensive urgency	Shock
Pericarditis	Systemic sclerosis
Recent cardiac intervention	
Severe valvular heart disease	
Tachycardia	

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

[****] 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
F	Baseline	412	0.9458	0.0367	[0.8738, 1.0000]
	2 - 4 Hours	418	0.9402	0.0521	[0.8381, 1.0000]
	4 - 9 Hours	372	0.9404	0.0544	[0.8339, 1.0000]
M	Baseline	519	0.9136	0.0162	[0.8818, 0.9453]
	2 - 4 Hours	526	0.9388	0.0184	[0.9028, 0.9747]
	4 - 9 Hours	489	0.9479	0.0191	[0.9105, 0.9854]

[a] All time points are relative to ED presentation / ED triage; baseline is within 2 hours of ED presentation / ED triage.

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

X. Conclusion Drawn from Nonclinical Laboratory Studies and Clinical Performance

The results presented in this 510(k) premarket notification demonstrate that the candidate assay (ARCHITECT STAT High Sensitivity Troponin-I) performance is substantially equivalent to the predicate Elecsys Troponin T Gen 5 STAT Immunoassay (K162895).

The similarities and differences between the candidate assay and the predicate assay are presented in section VII. The results presented in this 510(k) provide reasonable assurance that the ARCHITECT STAT High Sensitivity Troponin-I assay is safe and effective for the stated intended use. Any differences between the candidate assay and the predicate assay shown in the tables do not affect the safety and effectiveness of the candidate assay.

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