January 3, 2025

Abbott Point of Care Inc.
Jacquelyn Gesumaria
Manager Regulatory Affairs
400 College Road East
Princeton, New Jersey 08540

Re: K240984
Trade/Device Name: i-STAT hs-TnI Cartridge with the i-STAT 1 System
Regulation Number: 21 CFR 862.1215
Regulation Name: Creatine Phosphokinase/Creatine Kinase Or Isoenzymes Test System
Regulatory Class: Class II
Product Code: MMI, JJE
Dated: November 29, 2024
Received: December 2, 2024

Dear Jacquelyn Gesumaria:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Paula V. Caposino -S

Paula Caposino, Ph.D.
Deputy Division 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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K240984

Device Name
i-STAT hs-TnI cartridge with the i-STAT 1 System

Indications for Use *(Describe)*

The i-STAT hs-TnI cartridge with the i-STAT 1 System is intended for use in the in vitro quantification of cardiac troponin I (cTnI) in whole blood or plasma samples in point of care or clinical laboratory settings.

The i-STAT hs-TnI cartridge with the i-STAT 1 System is intended 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

The information in this 510(k) summary is being submitted in accordance with the requirements of 21 CFR 807.92.

1. Submitter Information

Owner	Abbott Point of Care Inc. 400 College Road East Princeton, NJ 08540
Contact	Primary: Jacquelyn Gesumaria Manager Regulatory Affairs Phone: 609-454-9384 Secondary: Mojgan Soleimani Director, Regulatory Strategy and Design Quality Phone: 613-295-0932
Date Prepared	January 03, 2025

2. Device Information

Proprietary Names: *i-STAT hs-TnI* Cartridge with the *i-STAT 1 System*

Common Name: High Sensitivity Cardiac Troponin-I (hs-TnI)

510(k) Number: K240984

Product Code	Device Classification Name	Regulation Number	Class	Panel
MMI	Creatine phosphokinase/creatine kinase or isoenzymes test system	862.1215	II	CH - Clinical Chemistry
JJE	Discrete photometric chemistry analyzer for clinical use	862.2160	I	CH - Clinical Chemistry

3. Predicate Device

Proprietary Name: PATHFAST hs-cTnI-II Test

510(k) Number: K231974

Product Code	Device Classification Name	Regulation Number	Class	Panel
MMI	Creatine phosphokinase/creatine kinase or isoenzymes test system	862.1215	II	CH - Clinical Chemistry

4. Device Description

The *i-STAT hs-TnI* cartridge is an *in vitro* diagnostic test for the quantitative measurement of cardiac troponin I (cTnI) in whole blood or plasma samples using the *i-STAT 1* analyzer in point of care or clinical laboratory settings.

The i-STAT hs-TnI test uses an enzyme-linked immunosorbent assay (ELISA) method with electrochemical detection of the resulting enzyme signal. The test reports a quantitative measurement of the sample concentration of cTnI in units of ng/L in approximately 15 minutes.

The i-STAT hs-TnI immunoassay test method uses anti-cTnI antibodies for labeling and capture. The capture antibodies are coated on para-magnetic microparticles. Both label and capture antibodies are contained within the cartridge on a biosensor chip. The ELISA is initiated when the test cartridge is inserted into the analyzer. The sample is positioned over the biosensor chip to dissolve the reagents. This forms the ELISA sandwich (detection antibody-label/antigen/capture antibody). The sample and excess antibody-conjugate are then washed off the sensors. An enzyme within the ELISA sandwich generates an electrochemically detectable product. The biosensor chip measures the enzyme product which is proportional to the concentration of cTnI within the sample.

The *i-STAT hs-TnI* cartridge is a single use test cartridge. The cartridge contains a biosensor chip and all reagents required to execute the test cycle. All fluid movements within the cartridge (test sample or reagent) are automatically controlled by the *i-STAT 1* analyzer by electro-mechanical interaction with the cartridge. The analyzer executes the test cycle, acquires and processes the electrical sensor signals converting the signals into quantitative results. These functions are controlled by a microprocessor.

The *i-STAT 1 System* is comprised of the *i-STAT 1* analyzer and accessories (*i-STAT 1 Downloader/Recharger*, *i-STAT Electronic Simulator*, *i-STAT Printer* and *i-STAT 1 9V NiMH Rechargeable Battery*).

Assay quality control materials are also available for use with the *i-STAT hs-TnI* cartridge and include *i-STAT hs-TnI Control Level 1, i-STAT hs-TnI Control Level 2, i-STAT hs-TnI Control Level 3*, and the *i-STAT hs-TnI Calibration Verification Levels 1-3*.

5. Intended Use Statement

<u>i-STAT hs-TnI Cartridge</u>

The *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* is intended for use in the *in vitro* quantification of cardiac troponin I (cTnI) in whole blood or plasma samples in point of care or clinical laboratory settings.

The *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* is intended to be used as an aid in the diagnosis of myocardial infarction (MI).

6. Summary Comparison of Technological Characteristics

Table 1: Similarities and Differences: System (Test and Instrument)		
Feature or Characteristic	**Predicate Device: PATHFAST hs-cTnI-II Test (K231974)**	**Candidate Device: i-STAT hs-TnI cartridge with the i-STAT 1 System**
Intended Use	PATHFAST hs-cTnI-II is an *in vitro* diagnostic test for the quantitative measurement of cardiac Troponin I (cTnI) in heparinized or EDTA whole blood and plasma. Measurements of cardiac Troponin I are used to aid in the diagnosis of acute myocardial infarction (AMI). PATHFAST hs-cTnI-II is for use in clinical laboratory or point of care (POC) settings.	The *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* is intended for use in the *in vitro* quantification of cardiac troponin I (cTnI) in whole blood or plasma samples in point of care or clinical laboratory settings. The *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* is intended to be used as an aid in the diagnosis of myocardial infarction (MI).
Intended Use Setting	Clinical Laboratory and Point of Care	Same
Device Classification	Class II	Same
Product Code	MMI	Same
Regulation Number	862.1215	Same
Measurands	Cardiac Troponin I (cTnI)	Same
Assay Technology	Chemiluminescent enzyme immunoassay	Enzyme-linked immunosorbent assay
Assay Format	Single use cartridge	Same
Detection Technology	Chemiluminescent	Electrochemical
Sample Type	Heparinized and EDTA whole blood and plasma	Whole blood and plasma
Sample Volume	100 µL	~22 µL
Sample Preparation	Ready to Use	Same
Sample Collection	• With Na-heparin, Li-heparin or EDTA anticoagulant	• With lithium heparin anticoagulant ○ With lithium heparin tube with plasma separator gel • Without anticoagulant

Table 1: Similarities and Differences: System (Test and Instrument)		
Feature or Characteristic	**Predicate Device: PATHFAST hs-cTnI-II Test (K231974)**	**Candidate Device: i-STAT hs-TnI cartridge with the i-STAT 1 System**
Time to Result	Within 17 minutes	~ 15 minutes
Reportable Result	Quantitative results	Same
Instrument Platform	PATHFAST Analyzer	*i-STAT 1* analyzer
Calibration	Reagent lot: Initially by master calibration code, then by user with enclosed calibrators. Recalibration required every four weeks.	No calibration needed by the end user; calibration is pre-set during manufacture of the cartridge.
Traceability	The calibrator for PATHFAST hs-cTnI is traceable to the reference material NIST Standard Reference Material for Human Cardiac Troponin Complex SRM2921 of the National Institute of Standard and Technology in USA which certified concentration for human cTnI.	Cardiac troponin I values assigned to i-STAT controls and calibration verification materials are traceable to i-STAT's working calibrators prepared from human cardiac troponin-ITC complex (NIST SRM2921).
Assay Cut-off	99th percentile cutoff: 0.029 ng/mL (29 ng/L)	99th percentile cutoff: Female: 13 ng/L Male: 28 ng/L Overall: 21 ng/L
Reportable Range	4.1 – 50,000 ng/L	2.9 – 1000.0 ng/L
Time to Test/ Sample Stability (Time from collection to cartridge fill)	Whole Blood: **With Heparin Anticoagulant:** Within 4 hours Plasma: **With Heparin Anticoagulant:** within 24 hours	Whole Blood: **With Lithium Heparin Anticoagulant:** Within 4 hours **Without Anticoagulant:** Within 3 minutes Plasma: **With Lithium Heparin Anticoagulant:** within 4 hours
Storage Conditions	Refrigerated at 2 to 8°C (35 to 46°F) until expiration date.	Refrigerated at 2 to 8°C (35 to 46°F) until expiration date. Room Temperature at 18-30°C (64-86°F) for up to 14 days.

7. Performance Characteristics

A. Analytical Performance

a. Precision/Reproducibility:

i. 20-Day Precision

The precision performance of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* was evaluated using a panel of six (6) frozen plasma samples with concentrations across the reportable range of the test. This 20-day precision study was based on the Clinical and Laboratory Standards Institute (CLSI) guideline EP05-A3: *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition*. The study was conducted using three (3) lots of *i-STAT hs-TnI* cartridges and multiple *i-STAT 1* analyzers at one (1) site. Testing was conducted over 20 non-consecutive days, two (2) runs per day, by two (2) operators for each cartridge lot. The results for the study are shown below in **Table 2**.

The within-laboratory precision of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System* demonstrated acceptable performance as the results are shown to be within the acceptance criteria for all levels.

Table 2: 20-Day Precision Results for the i-STAT hs-TnI cartridge with the i-STAT 1 System

Sample Level	N	Mean (ng/L)	Repeatability		Between-Run		Between-Day		Within-Laboratory[a]	
			SD (ng/L)	%CV	SD (ng/L)	%CV	SD (ng/L)	%CV	SD (ng/L)	%CV
1	240	11.70	1.780	15.22	0.448	3.83	0.297	2.54	1.859	15.89
1	239[b]	11.59	0.755	6.52	0.129	1.11	0.026	0.22	0.767	6.61
2	240	15.62	0.619	3.97	0.262	1.68	0.224	1.44	0.709	4.54
3	240	33.94	1.184	3.49	0.333	0.98	0.211	0.62	1.248	3.68
4	240	84.25	2.750	3.26	0.163	0.19	0.403	0.48	2.784	3.30
5	240	511.95	19.298	3.77	4.825	0.94	3.189	0.62	20.146	3.94
6	240	786.65	35.636	4.53	9.337	1.19	6.291	0.80	37.372	4.75

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

[b] One falsely elevated outlier was excluded. The observed outlier rate in this study was 0.07% (1/1440).

ii. Whole Blood and Plasma Precision

The precision performance of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* was evaluated in point of care settings at three (3) clinical sites following a modified design based on CLSI EP05-A3: *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition*. The precision performance was evaluated using native venous whole blood and plasma specimens prospectively collected in lithium heparin anticoagulant tubes assigned to six (6) cardiac troponin I levels spanning the reportable range of the i-STAT hs-TnI test.

At each site, a minimum of one (1) whole blood and one (1) plasma specimen was tested per level by one (1) operator using eight (8) *i-STAT hs-TnI* cartridges on eight (8) *i-STAT 1* analyzers across three (3) runs (1 replicate/analyzer/run) for a total of 24 replicates per specimen. Spiked specimens constituted 4.16% (1/24) of total whole blood specimens and 4.54% (1/22) of total plasma specimens used in precision analysis.

The within-site precision of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* was demonstrated to be acceptable as the results are within the acceptance criteria for all levels for each specimen type at each site. The precision estimates for the i-STAT hs-TnI test in whole blood are shown in **Table 3** and for plasma are shown in **Table 4**.

Table 3: Whole Blood Precision Results for the i-STAT hs-TnI cartridge with the i-STAT 1 System

Site	Cardiac Troponin Level	N	Min (ng/L)	Max (ng/L)	Mean (ng/L)	Repeatability		Between-Analyzer		Within-Site	
						SD	CV (%)	SD	CV (%)	SD	CV (%)
1	1	24	4.1	6.0	5.16	0.457	8.86	0.231	4.48	0.513	9.93
	2	24	17.4	20.5	19.13	0.681	3.56	0.277	1.45	0.735	3.84
	3	23	27.2	31.1	29.03	1.056	3.64	0.000	0.00	1.056	3.64
	4	24	205.4	263.0	244.50	13.525	5.53	0.000	0.00	13.525	5.53
	5	24	584.8	721.2	638.50	31.329	4.91	0.000	0.00	31.329	4.91
		23	693.8	792.7	744.37	26.291	3.53	18.803	2.53	32.323	4.34
	6	22	874.6	983.5	934.77	22.925	2.45	20.847	2.23	30.986	3.31
2	1	24	6.6	9.7	7.39	0.523	7.08	0.439	5.94	0.683	9.25
	2	23	18.9	22.4	20.32	1.034	5.09	0.000	0.00	1.034	5.09
	3	23	42.1	48.7	44.22	1.376	3.11	0.708	1.60	1.548	3.50
		23	37.2	42.7	39.97	1.408	3.52	0.000	0.00	1.408	3.52
	4	24	64.8	77.4	71.44	3.114	4.36	0.000	0.00	3.114	4.36
		23	432.4	523.8	478.95	18.569	3.88	10.212	2.13	21.192	4.42
	5	24	554.9	660.2	606.65	27.684	4.56	11.418	1.88	29.946	4.94
	6	24	724.1	844.9	795.93	33.125	4.16	15.175	1.91	36.436	4.58
		22	812.4	940.0	881.15	29.334	3.33	16.048	1.82	33.437	3.79
3	1	24	11.4	13.8	12.49	0.609	4.87	0.213	1.70	0.645	5.16
	2	24	15.9	19.0	17.39	0.772	4.44	0.000	0.00	0.772	4.44
	3	24	24.4	27.8	26.57	0.757	2.85	0.559	2.11	0.941	3.54
		24	43.7	52.1	47.28	2.161	4.57	0.000	0.00	2.161	4.57
	4	23	314.2	370.4	336.58	13.989	4.16	2.233	0.66	14.166	4.21
	5	23	628.0	763.3	681.89	30.929	4.54	0.000	0.00	30.929	4.54
		24	630.0	800.1	742.43	36.996	4.98	23.575	3.18	43.869	5.91
	6 [a]	24	825.9	946.2	869.70	26.891	3.09	0.000	0.00	26.891	3.09

[a] Specimen from one (1) subject was spiked with ≤ 5% v/v recombinant cardiac troponin I antigen.

Table 4: Plasma Precision Results for the i-STAT hs-TnI cartridge with the i-STAT 1 System											
Site	Cardiac Troponin Level	N	Min (ng/L)	Max (ng/L)	Mean (ng/L)	Repeatability		Between - Analyzer		Within-Site	
						SD	CV (%)	SD	CV (%)	SD	CV (%)
1	1	23	5.6	9.5	6.08	0.763	12.55	0.154	2.53	0.778	12.80
	2	23	18.3	22.1	20.58	0.999	4.86	0.000	0.00	0.999	4.86
	3	23	28.6	32.4	30.83	0.818	2.65	0.445	1.44	0.932	3.02
	4	24	225.3	259.2	243.97	10.688	4.38	1.153	0.47	10.750	4.41
	5	24	548.1	662.9	602.70	32.572	5.40	0.000	0.00	32.572	5.40
	6	23	679.6	900.1	764.50	51.255	6.70	7.652	1.00	51.823	6.78
2	1	24	7.4	8.6	8.03	0.306	3.81	0.092	1.14	0.320	3.98
	2	24	20.0	23.8	22.59	0.889	3.94	0.144	0.64	0.900	3.99
	3	24	40.6	48.9	44.19	1.572	3.56	1.247	2.82	2.007	4.54
	4	24	72.4	81.1	76.81	1.977	2.57	0.000	0.00	1.977	2.57
		24	464.4	531.2	499.76	16.575	3.32	9.727	1.95	19.219	3.85
	5	24	624.3	924.4	712.17	52.591	7.38	19.881	2.79	56.223	7.89
		24	591.7	759.7	680.01	40.429	5.95	0.000	0.00	40.429	5.95
	6	21	858.5	990.1	945.62	23.419	2.48	26.280	2.78	35.201	3.72
3	1	24	11.6	33.9	13.65	4.330	31.71	0.000	0.00	4.330	31.71
	1	23 [b]	11.6	13.4	12.77	0.378	2.96	0.130	1.02	0.400	3.13
	2	24	22.9	33.2	24.84	1.999	8.05	0.000	0.00	1.999	8.05
	2	23 [b]	22.9	26.3	24.48	0.930	3.80	0.000	0.00	0.930	3.80
		24	17.2	20.6	18.80	0.798	4.24	0.000	0.00	0.798	4.24
	3	24	43.1	49.9	47.00	1.705	3.63	0.597	1.27	1.807	3.84
	4	24	315.9	375.0	338.27	10.893	3.22	9.056	2.68	14.165	4.19
	5	24	631.8	737.9	672.29	24.813	3.69	0.000	0.00	24.813	3.69
		24	664.0	797.1	743.01	33.451	4.50	6.694	0.90	34.114	4.59
	6 [a]	24	768.8	915.8	847.93	34.701	4.09	0.000	0.00	34.701	4.09

[a] Specimen from one (1) subject was spiked with ≤ 5% v/v recombinant cardiac troponin I antigen.

[b] One falsely elevated outlier was excluded. The observed outlier rate in this study was 0.38% (2/521).

iii. Precision in Control Materials

The precision performance of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the i-STAT 1 System was evaluated using *i-STAT hs-TnI* control and calibration verification materials at a single site. The study was based on CLSI EP15-A3: *User Verification of Precision and Estimation of Bias; Approved Guideline – Third Edition*. The study was conducted using one (1) lot of *i-STAT hs-TnI* cartridges and five (5) unique levels of frozen *i-STAT hs-TnI* control materials tested in five (5) replicates over five (5) consecutive days. The precision of the i-STAT hs-TnI test was evaluated using one (1) lot each of *i-STAT hs-TnI* Controls Levels 1 and 2 (L1 and L2) and one (1) lot each of *i-STAT hs-TnI* Calibration Verification Set Levels 1, 2, and 3 (CV1, CV2, and CV3).

The mean, standard deviation (SD) and coefficient of variation (CV) are presented below in **Table 5**.

Table 5: Precision Results in Control Materials for the i-STAT hs-TnI cartridge with the i-STAT 1 System								
Fluid Level*	**Mean (ng/L)**	**N**	**Repeatability**		**Between-Day**		**Within-Laboratory**	
			SD (ng/L)	**%CV**	**SD (ng/L)**	**%CV**	**SD (ng/L)**	**%CV**
CV1	2.85	25	0.202	7.07	0.066	2.33	0.212	7.45
L1	20.43	25	0.640	3.13	0.178	0.87	0.664	3.25
L2	98.46	25	3.108	3.16	0.924	0.94	3.242	3.29
CV2 / L3	592.85	25	28.288	4.77	12.617	2.13	30.974	5.22
CV3	1174.29	25	55.117	4.69	15.296	1.30	57.200	4.87

* Since *i-STAT hs-TnI* Calibration Verification Level 2 (CV2) and *i-STAT hs-TnI* Control Level 3 (L3) share the same target and have identical formulations, the i-STAT hs-TnI test results from CV2 were used to assess the precision in L3.

iv. Multi-site Multi-Day Precision

The multiday precision performance of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* was evaluated using a panel of six (6) frozen plasma samples, which included six (6) cardiac troponin I levels which were tested in point of care settings at three (3) clinical sites. At each site, each of the six (6) test materials was tested once per day for five (5) days by two (2) different operators, with each operator using three (3) *i-STAT hs-TnI* cartridges on three (3) *i-STAT 1* analyzers. The study followed a 3x5x2x3 design based on CLSI EP05-A3: *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition*. The results of the multi-day precision testing of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System* are shown in **Table 6** for all sites combined.

Abbott

Table 6: Multi-Site Multi-Day Precision Results for the i-STAT hs-TnI cartridge with the i-STAT 1 System (ng/L)																
Level	N	Min	Max	Mean	Repeatability		Between-Day		Between-Operator		Within-Site		Between-Site		Reproducibility	
					SD (95% CI)	%CV	SD (95% CI)	%CV	SD (95% CI)	%CV	SD (95% CI)	%CV	SD (95% CI)	%CV	SD (95% CI)	%CV
1	90	11.5	15.1	13.03	0.599 (0.554, 0.653)	4.60	0.135 (0.097, 0.223)	1.04	0.000 (0.000, 0.000)	0.00	0.614 (0.568, 0.669)	4.71	0.000 (0.000, 0.000)	0.00	0.614 (0.568, 0.668)	4.71
2	90	16.1	19.2	17.68	0.564 (0.521, 0.614)	3.19	0.225 (0.162, 0.372)	1.28	0.200 (0.151, 0.296)	1.13	0.639 (0.582, 0.710)	3.62	0.000 (0.000, 0.000)	0.00	0.639 (0.582, 0.710)	3.62
3	90	35.2	41.3	38.49	1.306 (1.206, 1.423)	3.39	0.192 (0.138, 0.317)	0.50	0.329 (0.249, 0.487)	0.86	1.360 (1.257, 1.482)	3.54	0.000 (0.000, 0.000)	0.00	1.360 (1.258, 1.481)	3.54
4	90	81.6	100.3	90.33	3.300 (3.048, 3.596)	3.65	0.917 (0.658, 1.515)	1.02	1.114 (0.842, 1.648)	1.23	3.602 (3.307, 3.955)	3.99	1.179 (0.614, 7.407)	1.31	3.789 (3.308, 4.437)	4.20
5	90	482.5	590.3	543.24	19.253 (17.786, 20.985)	3.54	4.407 (3.160, 7.275)	0.81	9.074 (6.856, 13.419)	1.67	21.735 (19.785, 24.116)	4.00	0.000 (0.000, 0.000)	0.00	21.735 (19.798, 24.096)	4.00
6	90	714.3	874.4	791.67	26.656 (24.626, 29.054)	3.37	5.316 (3.812, 8.776)	0.67	0.000 (0.000, 0.000)	0.00	27.181 (25.154, 29.567)	3.43	17.311 (9.013, 108.794)	2.19	32.225 (24.793, 46.052)	4.07

b. Linearity/assay reportable range:

i. Linearity

The linearity of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System* was established by testing venous whole blood and plasma samples of varying levels of cardiac troponin I. The study was designed based on CLSI EP06-Ed2: *Evaluation of the Linearity of Quantitative Measurement Procedures, 2nd Edition*. The study was conducted using whole blood samples of varying cardiac troponin I levels prepared by combining an unaltered whole blood sample and a whole blood sample spiked with a human sourced previously frozen plasma sample containing a high level of native cardiac troponin I in specific ratios to span the reportable range. Plasma samples of varying cardiac troponin I levels were prepared by combining plasma obtained via centrifugation from an unaltered whole blood sample and a plasma sample spiked with human sourced previously frozen plasma sample containing a high level of native cardiac troponin I in specific ratios to span the reportable range. The expected values for cardiac troponin I were determined for the lowest and highest levels as measured by the *i-STAT hs-TnI* cartridge on the *i-STAT 1* analyzer and mathematically calculated for intermediate levels using admixture ratios.

The regression summary of the results obtained in the *i-STAT hs-TnI* cartridge (y-axis) versus the expected values (x-axis) is provided in **Table 7** below. The results of the linearity study for the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System* met the acceptance criteria and demonstrated linearity over the reportable range of the test for both whole blood and plasma.

Table 7: Linearity Study Results for the i-STAT hs-TnI cartridge with the i-STAT 1 System

Assay	Sample Type	Test Sample Range (ng/L)	Reportable Range (ng/L)	Slope	Intercept (ng/L)	R^2
hs-TnI	Whole Blood	1.1 – 1070.0	2.9 – 1000.0	1.025	0.183	0.9990
	Plasma	1.4 – 1050.8	2.9 – 1000.0	1.043	-0.171	0.9993

ii. Sample Type Comparison

Comparison studies were performed based on CLSI EP35: *Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures, 1st ed.* using fresh lithium heparin whole blood (WB) and plasma samples with the *i-STAT hs-TnI* cartridge on i-STAT 1 analyzers. The relationship between the two sample types is summarized in **Table 8** below using a Passing-Bablok regression.

Table 8: Comparison of Whole Blood vs. Plasma Sample Type for the i-STAT hs-TnI cartridge with the i-STAT 1 System

Sample Type Comparison	Slope	Intercept	r
WB vs. Plasma	1.01	0.603	0.99

iii. High Dose Hook Effect

The i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1* System was evaluated for high dose hook effect. The testing was conducted using venous whole blood and plasma samples collected with lithium heparin and altered via spiking with recombinant human cardiac troponin ITC-complex and serial dilution to obtain cardiac troponin I levels up to 500,000 ng/L. The whole blood and plasma samples were tested alongside the highest level calibrator, MWC7, which cardiac troponin I level exceeds the upper limit of the reportable range of 1000.0 ng/L. The high dosage hook effect was evaluated by verifying that the measured *i-STAT hs-TnI* results of the test samples was greater than that of the MWC7 calibrator.

Hook effect was not observed for the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* using whole blood and plasma samples with cardiac troponin I concentrations up to 500,000 ng/L.

c. Traceability, Calibration and Reference Interval

i. Traceability and Calibration

The i-STAT hs-TnI test for cardiac troponin-I measures the amount of substance concentration in plasma or the plasma fraction of whole blood for *in vitro* diagnostic use. Cardiac troponin-I values assigned to i-STAT controls and calibration verification materials are traceable to i-STAT's working calibrator prepared from human cardiac troponin-ITC complex (NIST SRM2921).

i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods.

ii. Reference Interval / Reference Range

A reference range study was conducted with a United States (US) based general population. Venous whole blood specimens were collected from 895 apparently healthy subjects between the ages of 18 and 87 years at point-of-care settings in eight (8) clinical sites. Subjects included met the following biomarker criteria: N-terminal pro-B-type natriuretic peptide (NT-proBNP) <125 pg/mL (for subjects younger than 75 years) or < 450 pg/mL (for subjects 75 years or older), glomerular filtration rate (eGFR) values ≥ 60 mL/min, and Hemoglobin A1c (HbA1c) ≤ 6.5%.

Subjects were excluded based on the following criteria: BMI < 16.0 or > 35.0 kg/m^2, Type 1 or Type 2 diabetes, hospitalization within the previous 3 months, personal history of heart disease or vascular conditions (e.g. high blood pressure requiring medication, heart attack (acute myocardial infarction), angina), stent procedure or percutaneous cardiac intervention, angioplasty or balloon angioplasty, coronary artery bypass graft, surgery for a circulation problem (e.g., leg), statin use within the last 6 months, or known pregnancy or within 6 weeks postpartum.

The venous whole blood and plasma specimens were tested with the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* to determine the 99th percentile upper reference limit (URL) and associated 90% confidence intervals for the female, male, and overall population.

Based on the test results from whole blood specimen testing, the 99th percentile URL of an apparently healthy population for the i-STAT hs-TnI test was determined as presented in **Table 9**.

Table 9: 99th Percentile URL and 90% Confidence Intervals for the Female, Male and Overall Population for the i-STAT hs-TnI cartridge with the i-STAT 1 System			
Sex	**N**	**99th Percentile Upper Reference Limit (ng/L)**	**90% CI (ng/L)**
Female	490	13	(10, 17)
Male	404	28	(19, 58)
Overall	895	21	(14, 30)

Note: The overall and female 99th percentile URL values were determined using all data. The male 99th percentile URL value was determined using data with one outlier excluded.

d. Detection Limit

i. Limit of Blank and Detection (LoB/LoD)

The study was based on CLSI EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition*.

The LoB and LoD of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge was evaluated on the *i-STAT 1* analyzer using four (4) *i-STAT hs-TnI* cartridge lots for LoB testing and three (3) *i-STAT hs-TnI* cartridge lots for LoD testing. Whole blood and plasma samples from four (4) healthy donors were altered to blank cardiac troponin I levels for LoB testing. Whole blood and plasma samples from four (4) healthy donors with low level cardiac troponin I levels were used for LoD testing.

The LoB and LoD were determined based on the maximal LoB and LoD value obtained for each lot tested.

The determined LoB and LoD for i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System* are shown in **Table 10**.

Table 10: LoB and LoD Results for the i-STAT hs-TnI cartridge with the i-STAT 1 System		
Sample Type	**LoB (ng/L)**	**LoD (ng/L)**
Whole Blood	0.78	1.61
Plasma	0.57	1.05

ii. Limit of Quantitation (LoQ)

The study was based on the CLSI EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition*.

The LoQ of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge was evaluated on the *i-STAT 1* analyzer using four (4) *i-STAT hs-TnI* cartridge lots and whole blood and plasma samples containing a low-level of cardiac troponin I. The LoQ for the i-STAT hs-TnI test in the i-STAT *hs-TnI cartridge* with the *i-STAT 1 System* was determined for whole blood and plasma, as shown in **Table 11**.

The lower limit of the reportable range was set to be the greater of the LoQ values for whole blood and plasma.

Table 11: LoQ Results for the i-STAT hs-TnI cartridge with the i-STAT 1 System		
Sample Type	**LoQ* (ng/L)**	**Lower Limit of the Reportable Range (ng/L)**
Whole Blood	2.90	2.9
Plasma	1.18	

* LoQ determined as 20 %CV concentration using a precision profile method.

The 10 %CV concentration was determined to be 6.88 ng/L for whole blood and 3.70 ng/L for plasma.

e. Analytical Specificity

i. Interference

The performance of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge when tested in the presence of potentially interfering endogenous and exogenous substances was evaluated using whole blood and plasma samples. The study design was based on CLSI EP07-ED3: *Interference Testing in Clinical Chemistry, 3rd ed*. Each potentially interfering substance was tested at the concentration recommended in CLSI EP37: *Supplemental Tables for Interference Testing in Clinical Chemistry, 1st* ed., as applicable.

The effect of each potentially interfering substance was evaluated at two cardiac troponin I levels (approximately 20 ng/L and 600 ng/L) by comparing the test results from a control sample, spiked with blank solvent, with the results from a test sample spiked with the potentially interfering substance.

A substance was identified as an interferent if the difference between the control and test samples was outside of a pre-determined acceptable range for the assay. **Table 12** below contains the list of potentially interfering substances tested for the *i-STAT hs-TnI* test in the *i-STAT hs-TnI* cartridge and the interference results.

Table 12: Evaluation of Potentially Interfering Endogenous and Exogenous Substances for the i-STAT hs-TnI cartridge						
Substance	**Test Concentration[1]**		**Interference (Yes/No)**			**Comment**
	µmol/L	**mg/dL, unless specified[2]**	**Whole Blood**	**Plasma**	**Overall**	
Acetaminophen	1030	15.6	No	No	No	
Acetylsalicylic Acid	167	3.01	No	No	No	
Alkaline Phosphatase (ALP)	3060 (U/L)		No	No	No	
Allopurinol	441	6.00	No	No	No	

[1] Test concentrations were as recommended in CLSI EP37, *Supplemental Tables for Interference Testing in Clinical Chemistry, 1st Edition*, or from literature.

[2] For substances with recommended test concentrations listed in CLSI EP37 ED01, the concentration in mg/dL was calculated using the molecular weight of the form of the substance tested listed by the supplier and not CLSI. For substances without CLSI recommended test concentrations, the concentration in µmol/L was calculated using the molecular weight of the form of the substance.

Table 12: Evaluation of Potentially Interfering Endogenous and Exogenous Substances for the i-STAT hs-TnI cartridge						
Substance	**Test Concentration[1]**		**Interference (Yes/No)**			**Comment**
	µmol/L	**mg/dL, unless specified[2]**	**Whole Blood**	**Plasma**	**Overall**	
Ambroxol[a]	965	40	No	No	No	
Ampicillin	215	7.51	No	No	No	
Ascorbic Acid	298	5.25	No	No	No	
Atenolol	33.8	0.900	No	No	No	
Bilirubin (Conjugated)	475	40.0	No	No	No	
Bilirubin (Unconjugated)	684	40.0	Yes	Yes	Yes	Decreased results > 85.5 µmol/L (5 mg/dL). The reference range per CLSI EP37 for Bilirubin (Unconjugated) is 0-34 µmol/L (0.0-2.0 mg/dL).
Biotin	14.3	0.349	No	No	No	
Bivalirudin[a]	18.3	3.99	No	No	No	
Caffeine	556	10.8	No	No	No	
Carvedilol[a]	370	15	No	No	No	
Cefoxitin	15500	697	No	Yes	Yes	Decreased results > 6564 µmol/L (295 mg/dL)
Cholesterol	10300	398	No	No	No	
Clopidogrel[a]	180	7.5	No	No	No	
Cocaine[a]	11.406	0.346	No	No	No	
Cyclosporine	1.50	0.180	No	No	No	
Diclofenac	81.0	2.58	No	No	No	
Digoxin	0.0499	0.00390	No	No	No	
Dopamine	4.06	0.0770	No	No	No	
Doxycycline	40.5	2.08	No	No	No	
Enalaprilat	2.35	0.0903	No	No	No	
Enoxaparin[a]	500 IU/dL	5	No	No	No	
Epinephrine[a]	1.7	0.037	No	No	No	
Eptifibatide[a]	11	0.90	No	No	No	
Erythromycin	188	13.8	No	No	No	
Ethanol	130000	599	No	No	No	
Fibrinogen[a]	N/A	1 g/dL	No	Yes	Yes	Decreased results > 0.4 g/dL. The reference range per literature for Fibrinogen is 0.2-0.4 g/dL[3].
Fondaparinux[a]	2.3	0.40	No	No	No	
Furosemide	48.1	1.59	No	No	No	

[3] B.E. Statland, Clinical Decision Levels for Lab Tests, 2nd Edition (1987), Medical Economics Books.

Table 12: Evaluation of Potentially Interfering Endogenous and Exogenous Substances for the i-STAT hs-TnI cartridge						
Substance	**Test Concentration[1]**		**Interference (Yes/No)**			**Comment**
	µmol/L	**mg/dL, unless specified[2]**	**Whole Blood**	**Plasma**	**Overall**	
Hemoglobin	N/A	1000	No	No	No	
Human Anti-Mouse Antibody (HAMA)[a]	3000 (ng/mL)		No	No	No	
Ibuprofen	1060	21.9	No	No	No	
Intralipid (Intralipid 20%)[a]	N/A	3144	No	No	No	
Isosorbide Dinitrate	25.1	0.593	No	No	No	
Levodopa	38.0	0.749	No	No	No	
Lithium Heparin[a]	~3160 IU/dL		No	No	No	
Methyldopa	107	2.55	No	No	No	
Methylprednisolone	20.9	0.783	No	No	No	
Metronidazole	719	12.3	No	No	No	
Nicotine	5.97	0.0969	No	No	No	
Nifedipine	1.70	0.0589	No	No	No	
Nitrofurantoin	8.94	0.213	No	No	No	
Nystatin[a]	181.4	16.80	No	No	No	
Oxytetracycline[a]	24	1.2	No	No	No	
Phenobarbital	2970	69.0	No	No	No	
Phenylbutazone	1040	32.1	No	No	No	
Phenytoin	238	6.00	No	No	No	
Pravastatin	0.488	0.0218	No	No	No	
Primidone	261	5.70	No	No	No	
Rheumatoid Factor (RF)[a]	500 IU/mL		No	Yes	Yes	Decreased results >350 IU/mL
Rifampicin	58.3	4.80	No	No	No	
Salicylic Acid	207	3.31	No	No	No	
Simvastatin	0.199	0.00833	No	No	No	
Sodium Heparin	330 IU/dL		No	No	No	
Theophylline	333	6.00	No	No	No	
Tissue Plasminogen Activator (TPA)[a]	N/A	0.23	No	No	No	
Total Protein (Human Serum Albumin)	N/A	15 g/dL	No	Yes	Yes	Decreased results ≥ 8.5 g/dL. The reference range per CLSI EP37 for Total Protein is 6.4-8.3 g/dL.
Triglyceride	16940	1500	No	No	No	
Trimethoprim	145	4.21	No	No	No	
Verapamil	3.51	0.172	No	No	No	
Warfarin	243	7.49	No	No	No	

[a] The test concentration for this substance is not included in CLSI guideline EP37 1st edition.

ii. Cross-reactivity

The i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1* System was evaluated in the presence of potentially cross-reactive endogenous substances in whole blood and plasma samples based on CLSI guidance EP07-ED3: *Interference Testing in Clinical Chemistry, 3rd edition*. The effect of each potentially interfering substance listed below in **Table 13** was evaluated at three (3) cardiac troponin I concentrations (approximately <5.0 ng/L, 20 ng/L, and 600 ng/L) by comparing the performance of a test sample spiked with a potentially cross-reactive substance and a control sample spiked with an equal volume of blank plasma diluent as per CLSI EP07 ED3.

None (0) of the nine (9) substances tested were found to cross-react with the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* when tested in whole blood and plasma.

Table 13: Cross-Reactivity Testing for the i-STAT hs-TnI cartridge with the i-STAT 1 System

Substance	Substance Test Concentration (ng/L)	Outcome (Cross-Reactivity/ No Cross-Reactivity)
Actin	1,000,000	No Cross-Reactivity
Human Cardiac Troponin T (cTnT)	1,000,000	No Cross-Reactivity
Human Creatine Kinase Myocardial Band (CK-MB)	1,000,000	No Cross-Reactivity
Human Myoglobin	1,000,000	No Cross-Reactivity
Human Myosin LC (Light Chain)	1,000,000	No Cross-Reactivity
Human Skeletal Troponin I (sTnI)	1,000,000	No Cross-Reactivity
Human Skeletal Troponin T (sTnT)	1,000,000	No Cross-Reactivity
Human Troponin C (TnC)	1,000,000	No Cross-Reactivity
Tropomyosin	1,000,000	No Cross-Reactivity

iii. *Other sensitivity studies*

1) Hematocrit Sensitivity

The effect of hematocrit on the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT System* was assessed across a hematocrit range of 15-60% packed cell volume (PCV). The study was conducted using three (3) lots of *i-STAT hs-TnI* cartridges, *i-STAT 1* analyzers and whole blood samples tested at two (2) cardiac troponin I levels (approximately 20 ng/L and 600 ng/L). Each cardiac troponin I level was evaluated at seven (7) hematocrit levels, with the nominal hematocrit level as control condition and the higher and lower hematocrit levels as test conditions.

The results of the study for the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT System* demonstrated increased imprecision exceeding 10% for whole blood samples with hematocrit values above 57 %PCV and increased bias exceeding ±10% for whole blood samples with hematocrit values above 55 %PCV.

2) Altitude

The performance of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System* at two altitude conditions, approximately 7,500 and 10,000 feet above sea level, was evaluated in two separate test events using whole blood and plasma samples at relevant cardiac troponin I levels across the reportable range for the i-STAT hs-TnI test.

At each test event, the i-STAT hs-TnI results obtained from the *i-STAT hs-TnI* cartridges on the *i-STAT 1* analyzer within a hypobaric chamber simulating approximately 7,500 feet (at test event 1) and 10,000 feet (at test event 2) above sea level (test conditions) were compared to the i-STAT hs-TnI results from testing outside of the chamber at sea level (comparator condition). A Passing-Bablok regression analysis comparing the test conditions to the comparator condition was performed based on the CLSI guidance EP09c: *Measurement Procedure Comparison and Bias Estimation using Patient Samples, 3rd ed.*

The results of the study demonstrated equivalent performance between the *i-STAT hs-TnI* cartridges tested at both a simulated altitude of 7,500 and 10,000 feet above sea level (test conditions) and the *i-STAT hs-TnI* cartridges tested at sea level (comparator condition) when evaluated with the *i-STAT 1 System* using both whole blood and plasma samples. The results are summarized in **Table 14** below.

Table 14: Altitude Study Results for the i-STAT hs-TnI cartridge with the i-STAT 1 System

Altitude Condition	Sample Type	Correlation Coefficient (r)		Slope	
		r	95% CI	Slope	95% CI
7,500 ft.	Whole Blood	1.00	(0.997, 0.998)	0.99	(0.983, 1.005)
	Plasma	1.00	(0.998, 0.999)	1.00	(0.994, 1.013)
10,000 ft	Whole Blood	1.00	(0.994, 0.997)	1.02	(1.003, 1.042)
	Plasma	1.00	(0.995, 0.998)	1.04	(1.012, 1.050)

f. Assay Cut-Off

Refer to the Reference Range Section.

B. Comparison Studies

a. Matrix Equivalence - Non-Anticoagulated Whole Blood

A matrix equivalence study was conducted to evaluate the performance of the i-STAT hs-TnI test on the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System* using venous whole blood specimens collected in syringes without anticoagulant and specimens collected in lithium heparin tubes. The study was conducted using venous whole blood specimens prospectively collected from patients in point of care settings at two (2) clinical sites.

The study design and analysis method were based on recommendations from CLSI guideline EP35: *Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures, 1st ed.*

The matrix equivalence of the i-STAT hs-TnI test on the *i-STAT hs-TnI* cartridge using the *i-STAT 1* analyzer between venous whole blood specimens collected in syringes without anticoagulant (candidate) and specimens collected in a lithium heparin tube (primary) was assessed using regression analyses comparing the candidate specimen type to the primary specimen type.

Each specimen was tested in duplicate using two (2) *i-STAT hs-TnI* cartridges with two (2) *i-STAT 1* analyzers. A Passing-Bablok linear regression analysis was performed using the first replicate result from the candidate (y-axis) versus the first replicate result from the primary specimen (x-axis). The regression analysis results are summarized in **Table 15**. In the table, N is the number of paired specimens in the data set, and r is the correlation coefficient.

The performance of the venous whole blood specimens collected in syringes without anticoagulant (candidate) and whole blood specimens collected in a lithium heparin tube (primary) was demonstrated to be equivalent when tested using the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System*.

Table 15: i-STAT hs-TnI Cartridge Matrix Equivalence Results – Non-anticoagulated Whole Blood vs. Lithium Heparinized Whole Blood

N*	Candidate Specimen Range (ng/L)	Primary Specimen Range (ng/L)	r	Slope	Intercept
88	3.1 - 952.5	3.0 - 989.6	1.00	1.04	-0.01

* Includes 8 contrived whole blood specimens spiked with ≤ 5% v/v recombinant cardiac troponin I antigen tested internally at Abbott Point of Care.

b. Matrix Equivalence - Lithium Heparin Tube with Separator Gel (Whole Blood and Plasma)

A matrix equivalence study was conducted to evaluate the performance of the i-STAT hs-TnI test on the *i-STAT hs-TnI* cartridge on the *i-STAT 1 System* using venous whole blood and plasma specimens collected in a lithium heparin tube with a gel separator and specimens collected in lithium heparin tubes. The study was conducted using venous whole blood and plasma specimens prospectively collected from patients in point of care settings at two (2) clinical sites.

The study design and analysis method were based on recommendations from the Clinical and Laboratory Standards Institute (CLSI) guideline EP35: *Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures, 1st ed*.

The matrix equivalence was assessed by comparing whole blood and plasma specimens collected in lithium heparin tube with separator gel (candidate) to the specimens collected in a lithium heparin tube (primary) using regression analyses comparing the candidate specimen type to the primary specimen type.

Each specimen was tested in duplicate using two (2) *i-STAT hs-TnI* cartridges with two (2) *i-STAT 1* analyzers. A Passing-Bablok linear regression analysis was performed using the first replicate result from the candidate (y-axis) versus the first replicate result from the primary specimen (x-axis). The regression analysis results are summarized in **Table 16**. In the table, N is the number of paired specimens in the data set, and r is the correlation coefficient.

The performance of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge on the *i-STAT 1* analyzer when tested using the candidate and primary specimens for both whole blood and plasma was demonstrated to be equivalent.

Table 16: i-STAT hs-TnI Cartridge Matrix Equivalence Results – Lithium Heparin Tube with Separator Gel vs. Lithium Heparin Tube (Whole Blood and Plasma)

Sample Type	N*	Candidate Specimen Range (ng/L)	Primary Specimen Range (ng/L)	r	Slope	Intercept
Whole Blood	87	2.9 – 935.1	3.0 – 930.5	1.00	1.01	-0.15

Table 16: i-STAT hs-TnI Cartridge Matrix Equivalence Results – Lithium Heparin Tube with Separator Gel vs. Lithium Heparin Tube (Whole Blood and Plasma)						
Sample Type	**N***	**Candidate Specimen Range (ng/L)**	**Primary Specimen Range (ng/L)**	**r**	**Slope**	**Intercept**
Plasma	87	3.4 – 942.9	3.4 – 930.9	1.00	1.01	0.04

* Includes 8 contrived whole blood and plasma specimens spiked with ≤ 5% v/v recombinant cardiac troponin I antigen tested internally at Abbott Point of Care.

C. Clinical Sensitivity and Specificity

A pivotal study using prospectively collected venous whole blood and plasma specimens was conducted at 28 clinical sites to assess diagnostic accuracy of the i-STAT hs-TnI test in the i-STAT *hs-TnI* cartridge with the i-STAT 1 System. The facilities used and the study staff that performed the testing were representative of point of care end-users.

Venous whole blood specimens collected into lithium heparin tubes from 3585 subjects presenting to the Emergency Department (ED) with chest discomfort or equivalent ischemic symptoms consistent with Acute Coronary Syndrome (ACS) were included in the clinical performance evaluation.

The study sites represented geographically diverse EDs associated acute care hospitals, medical centers, tertiary care facilities, and primary care clinics with patient populations representing regional, urban, and rural areas of the United States. Subjects were adjudicated by board-certified cardiologists and/or emergency medicine physicians based on the fourth universal definition of MI. The adjudicators were blinded to the i-STAT hs-TnI test results. The observed MI prevalence in this study was 6.8% for females and 11.6% for males, as shown in **Table 17** below.

Table 17: MI prevalence in the i-STAT hs-TnI cartridge Pivotal Study				
Sex	**MIs**	**Non-MIs**	**Total Subjects**	**% MI Prevalence**
Female subjects	157	2138	2295	6.8
Male subjects	150	1140	1290	11.6

An analysis for both females and males was performed using overall (21 ng/L) and sex-specific (female 13 ng/L, male 28 ng/L) 99th percentile URL to demonstrate the clinical performance (clinical sensitivity, clinical specificity, positive predictive value (PPV) and negative predictive value (NPV)) of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* to aid in the diagnosis of MI. The results are summarized in **Table 18** through **Table 21** below.

NOTE: Of the specimens collected at greater than or equal to 6 hours, specimens were collected within 9 hours from presentation to the ED, except for 6 specimens from 3 female subjects collected within 10 hours from presentation to the ED, and 4 specimens from a male subject collected within 23 and 25 hours.

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Table 18: Clinical performance for the i-STAT hs-TnI cartridge with the i-STAT 1 System in whole blood using the overall 99th percentile URL (21 ng/L)													
Sex	Time Point (hours)	N	MI	Non-MI	Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
					Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI
Female	0 to 1	1870	129	1741	86.05	79.02	89.37	87.84	37.50	32.18	98.86	98.20
	>1 to 3	1799	119	1680	92.44	86.25	89.70	88.16	38.87	33.38	99.41	98.88
	>3 to 6	724	70	654	95.71	88.14	85.78	82.89	41.88	34.51	99.47	98.45
	>6	60	16	44	93.75	71.67	65.91	51.14	50.00	33.15	96.67	83.33
Male	0 to 1	1090	130	960	83.08	75.70	78.33	75.62	34.18	29.17	97.16	95.73
	>1 to 3	1025	118	907	92.37	86.14	77.95	75.14	35.28	30.16	98.74	97.63
	>3 to 6	439	69	370	95.65	87.98	74.32	69.64	40.99	33.69	98.92	96.88
	>6	47	12	35	91.67	64.61	54.29	38.19	40.74	24.51	95.00	76.39

Table 19: Clinical performance for the i-STAT hs-TnI cartridge with the i-STAT 1 System in whole blood using the sex-specific 99th percentile URL (female 13 ng/L, male 28 ng/L)												
Sex	Time Point (hours)	N	MI	Non-MI	Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
					Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI
Female	0 to 1	1870	129	1741	91.47	85.38	83.23	81.40	28.78	24.61	99.25	98.66
	>1 to 3	1799	119	1680	96.64	91.68	82.14	80.24	27.71	23.62	99.71	99.26
	>3 to 6	724	70	654	97.14	90.17	77.83	74.49	31.92	26.03	99.61	98.58
	>6	60	16	44	100.00	80.64	54.55	40.07	44.44	29.54	100.00	86.20
Male	0 to 1	1090	130	960	79.23	71.47	84.17	81.72	40.39	34.56	96.77	95.34
	>1 to 3	1025	118	907	90.68	84.08	83.90	81.37	42.29	36.36	98.58	97.47
	>3 to 6	439	69	370	94.20	86.02	82.97	78.81	50.78	42.22	98.71	96.74
	>6	47	12	35	91.67	64.61	57.14	40.86	42.31	25.54	95.24	77.33

Table 20: Clinical performance for the i-STAT hs-TnI cartridge with i-STAT 1 System in plasma using the overall 99th percentile URL (21 ng/L)												
Sex	Time Point (hours)	N	MI	Non-MI	Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
					Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI
Female	0 to 1	1865	128	1737	86.72	79.76	89.23	87.69	37.25	31.95	98.92	98.27
	>1 to 3	1799	118	1681	92.37	86.14	89.65	88.10	38.52	33.04	99.41	98.88
	>3 to 6	723	70	653	94.29	86.21	85.76	82.87	41.51	34.14	99.29	98.19
	>6	60	16	44	93.75	71.67	68.18	53.44	51.72	34.43	96.77	83.81
Male	0 to 1	1092	130	962	83.08	75.70	78.17	75.45	33.96	28.98	97.16	95.73
	>1 to 3	1021	117	904	92.31	86.02	77.10	74.25	34.29	29.26	98.73	97.60
	>3 to 6	439	69	370	95.65	87.98	73.24	68.51	40.00	32.83	98.91	96.83
	>6	47	12	35	91.67	64.61	54.29	38.19	40.74	24.51	95.00	76.39

Table 21: Clinical performance for the i-STAT hs-TnI cartridge with i-STAT 1 System in plasma using the sex-specific 99th percentile URL (female 13 ng/L, male 28 ng/L)												
Sex	Time Point (hours)	N	MI	Non-MI	Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
					Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI	Estimate	Lower Limit of One Sided 97.5% CI
Female	0 to 1	1865	128	1737	92.19	86.22	82.27	80.40	27.70	23.66	99.31	98.73
	>1 to 3	1799	118	1681	96.61	91.61	81.68	79.76	27.01	23.00	99.71	99.26
	>3 to 6	723	70	653	97.14	90.17	77.18	73.81	31.34	25.53	99.60	98.57
	>6	60	16	44	100.00	80.64	54.55	40.07	44.44	29.54	100.00	86.20
Male	0 to 1	1092	130	962	79.23	71.47	83.26	80.77	39.02	33.33	96.74	95.30
	>1 to 3	1021	117	904	90.60	83.95	82.74	80.14	40.46	34.69	98.55	97.42
	>3 to 6	439	69	370	94.20	86.02	80.27	75.91	47.10	38.96	98.67	96.63
	>6	47	12	35	91.67	64.61	54.29	38.19	40.74	24.51	95.00	76.39

8. Conclusion

The results of the studies demonstrate that the analytical and clinical performance of the candidate device, i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* is acceptable, and therefore safe and effective for the intended use of the device.

The results of these studies demonstrate that performance of the i-STAT hs-TnI test in the *i-STAT hs-TnI* cartridge with the *i-STAT 1 System* is substantially equivalent to the predicate device.