# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
ASSAY AND INSTRUMENT

## I Background Information:

### A 510(k) Number

K253051

### B Applicant

Abbott Point of Care

### C Proprietary and Established Names

i-STAT hs-TnI cartridge with the i-STAT Alinity System

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| MMI | Class II | 21 CFR 862.1215 - Creatine Phosphokinase/Creatine Kinase or Isoenzymes Test System | CH - Clinical Chemistry |
| JJE | Class I | 21 CFR 862.2160 – Discrete Photometric Chemistry Analyzer for Clinical Use | CH-Clinical Chemistry |

## II Submission/Device Overview:

### A Purpose for Submission:

Adding previously cleared i-STAT hs-TnI cartridge onto a new instrument

### B Measurand:

Cardiac troponin I (cTnI)

**C Type of Test:**

Quantitative Immunoassay

## III Intended Use/Indications for Use:

**A Intended Use(s):**
See Indications for Use below.

**B Indication(s) for Use:**
The i-STAT hs-TnI cartridge with the i-STAT Alinity System is intended for use in the in vitro quantification of cardiac troponin (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 Alinity System is intended to be used as an aid in the diagnosis of myocardial infarction (MI).

**C Special Conditions for Use Statement(s):**

Rx-For Prescription Use Only

**D Special Instrument Requirements:**

i-STAT Alinity Instrument

## IV Device/System Characteristics:

**A Device Description:**

The i-STAT hs-TnI cartridge is a single-use disposable unit. The cartridge contains electrochemical sensors and the following test reagents:

| Reactive Ingredient | Biological Source | Minimum Quantity |
|---|---|---|
| Antibody/Alkaline Phosphatase Conjugate | Murine IgG: Caprine IgG/Bovine Intestine | 0.004 µg |
| IgG | Caprine IgG | 11.2 µg |
| IgG | Murine IgG | 17.3 µg |
| Sodium Aminophenyl Phosphate | N/A | 2.8 mg |
| IgM | Murine IgM | 2.7 µg |
| Heparin | Porcine Intestine | 0.3 IU |

The analysis time of the i-STAT hs-TnI cartridge is approximately 15 minutes. The sample volume required for the i-STAT hs-TnI cartridge is approximately 22 µL.

Other components of the i-STAT Alinity System are the i-STAT Alinity instrument, i-STAT Alinity base station, i-STAT Alinity battery, i-STAT Alinity electronic simulator and i-STAT Alinity printer.

The i-STAT Alinity instrument is a handheld, in vitro diagnostic analytical device designed to run only i-STAT test cartridges.

The i-STAT Alinity instrument is the main user interface of the i-STAT Alinity System and functions as the electro-mechanical interface to the test cartridge. All fluid movements within the i-STAT hs-TnI cartridge (test sample or reagent) are automatically controlled by the i-STAT Alinity instrument by electro-mechanical interaction with the cartridge. No additional reagents or steps are required to run the cartridge.

The i-STAT Alinity's Lithium-ion (Li-ion) cells and fuel gauge have been replaced with functionally equivalent new Li-ion cells and fuel gauge since its last clearance in K234143.

Additionally, liquid quality control materials are sold separately as an optional quality control methodology. The liquid controls available for use with the i-STAT *hs-TnI* cartridge 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.

## B Principle of Operation:

The i-STAT hs-TnI cartridge with the i-STAT Alinity System is an immunoassay for cardiac troponin I. 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.

The i-STAT hs-TnI cartridge with the i-STAT Alinity System uses anti-cTnI antibodies for labeling and capture. The capture antibodies are coated on paramagnetic microparticles. Both label and capture antibodies are contained within the cartridge on a biosensor chip. All the steps of the ELISA are automated and conducted within the test cartridge. 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.

## C Instrument Description Information:

1. Instrument Name:

   i-STAT Alinity Instrument

2. Specimen Identification:

   The specimen identification may be manually entered or automatically scanned by the device.

3. Specimen Sampling and Handling:

   The sample type must be selected using the device touchscreen. After the sample is selected the on-screen help appears and the help graphics on the device screen vary based on the sample type selected. The reagent cartridge contains a sample chamber that includes the sample well and the channel leading from the well up to the fill mark. The cartridge label is intended to help the operator fill the cartridge correctly. When filled, the sample chamber contains sufficient sample for testing. Sample volume and placement are monitored by the instrument and an error message will be generated if filled incorrectly. Sample should be remixed thoroughly before testing.

4. Calibration:

   The i-STAT cartridges include an on-board calibration that is performed with each cartridge use. The calibration solution is automatically released from its foil pack and is positioned over the sensors. The signals produced by the sensors' responses to the calibrant solution are measured. This one-point calibration adjusts the offset of the stored calibration curve.

5. Quality Control:

   The sponsor recommends i-STAT Controls and i-STAT Calibration Verification solutions for use with the i-STAT cartridges with the i-STAT Alinity system.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):

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

### B Predicate 510(k) Number(s):

K240984

### C Comparison with Predicate(s):

| **Device & Predicate Device(s):** | K253051 | K240984 |
|---|---|---|
| Device Trade Name | i-STAT hs-TnI cartridge with the i-STAT Alinity System | i-STAT hs-TnI cartridge with the i-STAT 1 System |
| **General Device Characteristic Similarities** | | |

| Device & Predicate Device(s): | K253051 | K240984 |
|---|---|---|
| Intended Use/Indications For Use | Intended for use in the in vitro quantification of cardiac troponin. Intended to be used as an aid in the diagnosis of myocardial infarction. | Same |
| **General Device Characteristic Differences** | | |
| Instrument Platform | i-STAT Alinity Instrument | i-STAT 1 Analyzer |

## VI Standards/Guidance Documents Referenced:

Clinical & Laboratory Standards Institute (CLSI) EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – 3rd Edition.

CLSI EP06: Evaluation of the Linearity of Quantitative Measurement Procedures; 2nd Edition.

CLSI EP07: Interference Testing in Clinical Chemistry; 3rd Edition.

CLSI EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; 3rd Edition.

CLSI EP12: Evaluation of Qualitative Binary Output Examination Performance; 3rd Edition.

CLSI EP17: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; 2nd Edition.

CLSI EP28-A3c: Defining Establishing and Verifying Reference Intervals in the Clinical Laboratory.

CLSI EP35: Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures.

CLSI EP37: Supplemental Tables for Interference Testing in Clinical Chemistry.

IEC 61326-1: Electrical equipment for measurement control and laboratory use – EMC requirements- Part I: General requirements; 3rd Edition.

IEC 61326-2-6: Electrical equipment for measurement control and laboratory use- EMC requirements- Part 2-6: Particular requirements- in vitro diagnostic (IVD) medical equipment.

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

*Internal within-site 20-day precision*

A single-site precision study for the i-STAT hs-TnI cartridge with the i-STAT Alinity System was conducted following the recommendations in CLSI EP05-A3.

A panel of six (6) plasma samples with troponin concentrations spanning the assay reportable range were assayed in two runs per day over at least 20 non-consecutive days using three reagent lots. For each sample, two replicates were measured in each run. The results of the study with the three lots combined are shown in the table below. The within-laboratory imprecision includes within-run (repeatability), between-run and between-day variability components. Overall precision includes repeatability, between-run, between-day and between-lot components of variability.

| Sample | N | Mean (ng/L) | Repeatability | | Between-Run | | Between-Day | | Within-Laboratory | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV |
| 1 | 240 | 11.35 | 0.407 | 3.58 | 0.105 | 0.92 | 0.093 | 0.82 | 0.430 | 3.79 |
| 2 | 240 | 15.15 | 1.350 | 8.91 | 0.367 | 2.42 | 0.371 | 2.45 | 1.447 | 9.55 |
| | 239* | 15.07 | 0.515 | 3.42 | 0.154 | 1.02 | 0.271 | 1.80 | 0.602 | 4.00 |
| 3 | 240 | 33.01 | 0.873 | 2.64 | 0.323 | 0.98 | 0.182 | 0.55 | 0.948 | 2.87 |
| 4 | 240 | 83.46 | 2.073 | 2.48 | 0.918 | 1.10 | 0.341 | 0.41 | 2.293 | 2.75 |
| 5 | 240 | 505.50 | 13.050 | 2.58 | 5.121 | 1.01 | 2.598 | 0.51 | 14.258 | 2.82 |
| 6 | 240 | 763.85 | 24.222 | 3.17 | 5.398 | 0.71 | 4.375 | 0.57 | 25.199 | 3.30 |

| Sample | N | Mean (ng/L) | Between-lot | | Overall | |
|---|---|---|---|---|---|---|
| | | | SD (ng/L) | %CV | SD (ng/L) | %CV |
| 1 | 240 | 11.35 | 0.878 | 7.73 | 0.984 | 8.67 |
| 2 | 240 | 15.15 | 1.081 | 7.13 | 1.826 | 12.05 |
| | 239* | 15.07 | 1.114 | 7.40 | 1.270 | 8.43 |
| 3 | 240 | 33.01 | 2.056 | 6.23 | 2.276 | 6.90 |
| 4 | 240 | 83.46 | 2.733 | 3.27 | 3.626 | 4.34 |
| 5 | 240 | 505.50 | 13.020 | 2.58 | 19.566 | 3.87 |
| 6 | 240 | 763.85 | 8.363 | 1.09 | 27.032 | 3.54 |

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

*Between Instrument Precision*

An internal between-instrument precision study for the i-STAT hs-TnI cartridge with the i-STAT Alinity System was conducted using a panel of six plasma samples. Each sample was tested using three i-STAT Alinity instruments with one lot of i-STAT *hs-TnI* cartridges, in five replicates over five (5) non-consecutive days, The results are provided below:

| Sample | N | Mean (ng/L) | Repeatability | | Between-Instrument | | Between-Day | | Within-Laboratory | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV |
| 1 | 75 | 13.89 | 9.069 | 65.30 | 1.470 | 10.59 | 1.639 | 11.80 | 9.332 | 67.19 |
| | 74* | 12.81 | 0.409 | 3.20 | 0.064 | 0.50 | 0.103 | 0.80 | 0.427 | 3.33 |
| 2 | 75 | 17.10 | 0.593 | 3.47 | 0.088 | 0.51 | 0.148 | 0.86 | 0.617 | 3.61 |
| 3 | 75 | 36.34 | 1.309 | 3.60 | 0.263 | 0.72 | 0.415 | 1.14 | 1.398 | 3.85 |
| 4 | 75 | 87.13 | 2.536 | 2.91 | 0.525 | 0.60 | 0.665 | 0.76 | 2.674 | 3.07 |
| 5 | 75 | 519.61 | 19.609 | 3.77 | 4.353 | 0.84 | 6.465 | 1.24 | 21.101 | 4.06 |
| 6 | 75 | 759.32 | 21.803 | 2.87 | 3.522 | 0.46 | 3.726 | 0.49 | 22.397 | 2.95 |

*One falsely elevated outlier was excluded. The observed outlier rate in this study was 0.22% (1/450)

*Control material precision*

A within-laboratory precision study for the i-STAT hs-TnI cartridge with the I STAT Alinity System was performed using two levels of i-STAT hs-TnI control materials (L1 and L2) and three levels of calibration verification materials (CV1, CV2, and CV3) at an internal site. Each sample was tested in five replicates over 5 consecutive days using one lot of i-STAT hs-TnI cartridges. The results are provided below:

| Sample | N | Mean (ng/L) | Repeatability | | Between-Day | | Within-Laboratory | |
|---|---|---|---|---|---|---|---|---|
| | | | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV |
| CV1 | 25 | 2.81** | 0.121 | 4.30 | 0.036 | 1.28 | 0.126 | 4.49 |
| L1 | 25 | 19.36 | 0.573 | 2.96 | 0.158 | 0.82 | 0.594 | 3.07 |
| L2 | 25 | 90.61 | 3.186 | 3.52 | 0.926 | 1.02 | 3.317 | 3.66 |
| CV2/L3* | 25 | 548.44 | 33.108 | 6.04 | 10.579 | 1.93 | 34.757 | 6.34 |
| CV3 | 25 | 1109.25** | 92.048 | 8.30 | 28.244 | 2.55 | 96.284 | 8.68 |

*i-STAT hs-TnI Calibration Verification Level 2(CV2) and i-STAT hs-TnI Control Level 3 (L3) share the same target value.

** Results outside of the reportable range may be displayed when running Calibration Verification material.

*Point-of-Care Reproducibility Study*

A multi-day precision study was conducted at three point-of-care (POC) sites following the recommendations in CLSI EP05-A3 by point of care operators using plasma samples.

A panel of six (6) plasma samples with troponin concentrations spanning the assay reportable range were assayed in one run per day for five days by two different operators at each site. For each sample, three replicates were measured in each run by each operator. The combined results for this study are shown in table below. The within-site imprecision includes within-run(repeatability), between-day and between-operator variability components. Reproducibility includes within-site and between site variability components.

| Sample | N | Mean (ng/L) | Repeatability | | Between-Day | | Between-Operator | | Within-Site | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV |
| 1 | 90 | 13.02 | 0.471 | 3.61 | 0.080 | 0.61 | 0.000 | 0.00 | 0.477 | 3.66 |
| 2 | 90 | 17.67 | 0.546 | 3.09 | 0.184 | 1.04 | 0.064 | 0.36 | 0.580 | 3.28 |
| 3 | 90 | 36.95 | 1.363 | 3.69 | 0.323 | 0.87 | 0.482 | 1.30 | 1.481 | 4.01 |
| 4 | 90 | 88.95 | 2.683 | 3.02 | 1.187 | 1.34 | 0.505 | 0.57 | 2.977 | 3.35 |
| 5 | 90 | 529.10 | 16.334 | 3.09 | 7.161 | 1.35 | 5.591 | 1.06 | 18.691 | 3.53 |
| 6 | 90 | 765.71 | 25.507 | 3.33 | 7.653 | 1.00 | 6.978 | 0.91 | 27.529 | 3.60 |

| Sample | N | Mean (ng/L) | Between-Site | | Reproducibility | |
|---|---|---|---|---|---|---|
| | | | SD (ng/L) | %CV | SD (ng/L) | %CV |
| 1 | 90 | 13.02 | 0.137 | 1.05 | 0.497 | 3.81 |
| 2 | 90 | 17.67 | 0.215 | 1.22 | 0.619 | 3.50 |
| 3 | 90 | 36.95 | 0.290 | 0.79 | 1.509 | 4.08 |
| 4 | 90 | 88.95 | 1.585 | 1.78 | 3.373 | 3.79 |
| 5 | 90 | 529.10 | 0.000 | 0.00 | 18.691 | 3.53 |
| 6 | 90 | 765.71 | 6.613 | 0.86 | 28.313 | 3.70 |

*Point of Care (Multi-Site) Whole blood and Plasma Precision*

A multi-site precision study was conducted using native lithium heparin venous whole blood and lithium heparin plasma specimens with one lot of i-STAT hs-TnI cartridge. At each site, each sample was measured using 8 i-STAT hs-TnI cartridges on 8 i-STAT Alinity instruments in a run across three runs per day for a total of 24 replicates per sample. The result for each site is shown below.

Whole Blood

| Site | Level | N | Mean (ng/L) | Repeatability | | Between-Analyzer | | Within-Site | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV |
| 1 | 1 | 24 | 4.92 | 0.437 | 8.89 | 0.000 | 0.00 | 0.437 | 8.89 |
| | 2 | 24 | 18.87 | 0.655 | 3.47 | 0.000 | 0.00 | 0.655 | 3.47 |
| | 3 | 24 | 28.33 | 1.050 | 3.71 | 0.000 | 0.00 | 1.050 | 3.71 |
| | 4 | 24 | 244.90 | 8.198 | 3.35 | 3.932 | 1.61 | 9.092 | 3.71 |
| | 5-1 | 24 | 630.14 | 24.562 | 3.90 | 0.000 | 0.00 | 24.562 | 3.90 |
| | 5-2 | 24 | 730.91 | 46.557 | 6.37 | 0.000 | 0.00 | 46.557 | 6.37 |
| | 6 | 22 | 915.10 | 33.286 | 3.64 | 0.000 | 0.00 | 33.286 | 3.64 |
| 2 | 1 | 24 | 7.19 | 0.407 | 5.67 | 0.000 | 0.00 | 0.407 | 5.67 |
| | 2 | 24 | 21.09 | 0.898 | 4.26 | 0.000 | 0.00 | 0.898 | 4.26 |
| | 3-1 | 24 | 43.49 | 1.304 | 3.00 | 0.000 | 0.00 | 1.304 | 3.00 |
| | 3-2 | 23 | 40.02 | 2.009 | 5.02 | 1.374 | 3.43 | 2.434 | 6.08 |
| | 4-1 | 23 | 70.86 | 2.655 | 3.75 | 0.000 | 0.00 | 2.655 | 3.75 |
| | 4-2 | 24 | 479.75 | 17.223 | 3.59 | 0.000 | 0.00 | 17.223 | 3.59 |
| | 5 | 24 | 638.64 | 29.038 | 4.55 | 0.000 | 0.00 | 29.038 | 4.55 |
| | 6-1 | 23 | 751.79 | 25.722 | 3.42 | 6.640 | 0.88 | 26.565 | 3.53 |
| | 6-2 | 24 | 862.09 | 26.952 | 3.13 | 0.000 | 0.00 | 26.952 | 3.13 |
| 3 | 1 | 24 | 12.40 | 0.597 | 4.82 | 0.000 | 0.00 | 0.597 | 4.82 |
| | 2 | 24 | 17.16 | 0.330 | 1.92 | 0.000 | 0.00 | 0.330 | 1.92 |
| | 3-1 | 24 | 25.25 | 0.831 | 3.29 | 0.000 | 0.00 | 0.831 | 3.29 |
| | 3-2 | 24 | 46.21 | 1.676 | 3.63 | 1.097 | 2.37 | 2.003 | 4.33 |
| | 4 | 23 | 315.73 | 8.102 | 2.57 | 0.000 | 0.00 | 8.102 | 2.57 |
| | 5-1 | 24 | 676.15 | 22.246 | 3.29 | 9.886 | 1.46 | 24.344 | 3.60 |
| | 5-2 | 24 | 748.03 | 28.362 | 3.79 | 8.141 | 1.09 | 29.507 | 3.94 |
| | 6* | 24 | 847.32 | 25.854 | 3.05 | 13.790 | 1.63 | 29.302 | 3.46 |

*contrived sample

Plasma

| Site | Level | N | Mean (ng/L) | Repeatability | | Between-Analyzer | | Within-Site | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV |
| 1 | 1 | 24 | 6.05 | 0.411 | 6.79 | 0.000 | 0.00 | 0.411 | 6.79 |
| | 2 | 24 | 20.17 | 0.991 | 4.91 | 0.000 | 0.00 | 0.991 | 4.91 |
| | 3 | 24 | 30.30 | 0.948 | 3.13 | 0.000 | 0.00 | 0.948 | 3.13 |
| | 4 | 24 | 239.30 | 16.214 | 6.78 | 0.000 | 0.00 | 16.214 | 6.78 |
| | 5-1 | 24 | 580.67 | 32.616 | 5.62 | 18.231 | 3.14 | 37.365 | 6.43 |
| | 5-2 | 24 | 711.62 | 41.302 | 5.80 | 0.000 | 0.00 | 41.302 | 5.80 |
| | 6 | 24 | 873.40 | 44.751 | 5.12 | 0.000 | 0.00 | 44.751 | 5.12 |

| Site | Level | N | Mean (ng/L) | Repeatability | | Between-Analyzer | | Within-Site | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | SD (ng/L) | %CV | SD (ng/L) | %CV | SD (ng/L) | %CV |
| 2 | 1 | 24 | 8.14 | 0.257 | 3.16 | 0.176 | 2.17 | 0.312 | 3.83 |
| | 2 | 24 | 21.99 | 0.588 | 2.68 | 0.144 | 0.65 | 0.606 | 2.75 |
| | 3 | 24 | 43.02 | 1.142 | 2.65 | 0.000 | 0.00 | 1.142 | 2.65 |
| | 4-1 | 24 | 71.93 | 2.295 | 3.19 | 0.988 | 1.37 | 2.498 | 3.47 |
| | 4-2 | 24 | 484.88 | 12.535 | 2.59 | 4.983 | 1.03 | 13.489 | 2.78 |
| | 5-1 | 24 | 669.80 | 39.092 | 5.84 | 9.308 | 1.39 | 40.184 | 6.00 |
| | 5-2 | 23 | 655.06 | 21.216 | 3.24 | 5.349 | 0.82 | 21.880 | 3.34 |
| | 6 | 23 | 881.93 | 54.165 | 6.14 | 0.000 | 0.00 | 54.165 | 6.14 |
| 3 | 1 | 24 | 12.17 | 0.476 | 3.91 | 0.000 | 0.00 | 0.476 | 3.91 |
| | 2-1 | 24 | 23.99 | 1.001 | 4.17 | 0.000 | 0.00 | 1.001 | 4.17 |
| | 2-2 | 24 | 18.14 | 0.915 | 5.05 | 0.498 | 2.75 | 1.042 | 5.75 |
| | 3 | 24 | 46.11 | 1.754 | 3.80 | 0.589 | 1.28 | 1.851 | 4.01 |
| | 4 | 24 | 318.03 | 10.465 | 3.29 | 0.000 | 0.00 | 10.465 | 3.29 |
| | 5-1 | 24 | 642.10 | 21.442 | 3.34 | 3.497 | 0.54 | 21.725 | 3.38 |
| | 5-2 | 24 | 723.90 | 34.315 | 4.74 | 2.151 | 0.30 | 34.382 | 4.75 |
| | 6* | 24 | 802.39 | 29.241 | 3.64 | 6.039 | 0.75 | 29.858 | 3.72 |

*contrived sample

2. Linearity:

Linearity of the i-STAT hs-TnI cartridge with the i-STAT Alinity System was evaluated following the recommendations in the CLSI EP06 2nd Edition guideline.

Linearity was evaluated using 11 whole blood samples and 11 lithium heparin plasma samples ranging in concentrations from < 2.90 ng/L (LoQ) to > 1000.0 ng/L. The whole high blood sample (B1) was a native whole blood sample spiked with a native plasma sample with a high concentration of cardiac troponin I and the low whole blood sample (B11) was an unaltered native whole blood sample. The high plasma sample (P1) and the low plasma sample (P11) were prepared by separating plasma portion of the whole blood. The intermediate whole blood samples (B2 to B10) and the intermediate plasma samples (P2 to P11) were prepared by mixing high and low concentration samples in specific ratios to span the reportable range.

Each sample was tested in replicates of 3 per cartridge lot and a total of 9 replicates per sample were obtained using three cartridge lots. The mean of the 9 replicates was used to calculate the reported results. Data were analyzed using weighted least squares linear regression.

Deviation from linearity were never observed to be greater than 8.58% within the claimed measuring range from 2.90 to 1000.0 ng/L for the whole blood sample.

Deviation from linearity were never observed to be greater than – 14.82% within the claimed measuring range from 2.9 to 1000 ng/L for the plasma sample.

The sponsor also provided information to support the use of surrogate samples in the linearity study. Additionally, the sponsor provided a sub-range linearity study results obtained with fresh native samples and the results were found to be similar to the full range studies.

*Hook Effect*
A study was performed to support the claim that there was no hook effect with troponin samples with concentrations up to 500,000 ng/L.

3. Analytical Specificity/Interference:

*Endogenous and Exogenous Interference*

The analytical specificity of the i-STAT hs-TnI cartridge with the i-STAT Alinity System was evaluated following the recommendations from the CLSI EP07-3rd ed guideline.

Each substance was tested at 2 levels of the analyte (approximately between 15-25 ng/L and between 500-750 ng/L) using lithium heparin venous whole blood and lithium heparin plasma samples.

The samples with high and low analyte levels were further divided into two groups: i.e., test sample (with added interferent) and control sample (without interferent). Each sample level was tested in multiple replicates (n>15) using two i-STAT hs-TnI cartridge lots on multiple i-STAT Alinity instruments. Test results from sample spiked with the potential interferent were compared to test results from the control samples lacking the potential interferent.

Interference was considered non-significant if the bias between the test and control sample was within ± 10% of the control sample. The following table lists the concentrations of each substance at which no significant interference was found

| Substance | Highest Concentration Tested without Significant Interference | |
|---|---|---|
| | Whole Blood | Plasma |
| **Endogenous Substances** | | |
| Bilirubin (conjugated) | 40 mg/dL | 40 mg/dL |
| Bilirubin (unconjugated) | 5 mg/dL | 5 mg/dL |
| Cholesterol | 398 mg/dL | 398 mg/dL |
| Fibrinogen | 1g/dL | 0.45 g/dL |
| Hemoglobin | 1000 mg/dL | 1000 mg/dL |
| Total Protein (Human Serum Albumin) | 15 g/dL | 8.9 g/dL |
| Triglyceride | 1500 mg/dL | 1500 mg/dL |

| Substance | Highest Concentration Tested without Significant Interference | |
|---|---|---|
| | Whole Blood | Plasma |
| Intralipid | 3144 mg/dL | 3144 mg/dL |
| **Exogenous Substances** | | |
| Acetaminophen | 15.6 mg/dL | 15.6 mg/dL |
| Acetylsalicylic Acid | 3.01 mg/dL | 3.01 mg/dL |
| Alkaline Phosphatase | 3060 U/L | 3060 U/L |
| Allopurinol | 6.00 mg/dL | 6.00 mg/dL |
| Ambroxol | 40 mg/dL | 40 mg/dL |
| Ampicillin | 7.51 mg/dL | 7.51 mg/dL |
| Ascorbic Acid | 5.25 mg/dL | 5.25 mg/dL |
| Atenolol | 0.90 mg/dL | 0.90 mg/dL |
| Biotin | 0.349 mg/dL | 0.349 mg/dL |
| Bivalirudin | 3.99 mg/dL | 3.99 mg/dL |
| Caffeine | 10.8 mg/dL | 10.8 mg/dL |
| Carvedilol | 15 mg/dL | 15 mg/dL |
| Cefoxitin | 697 mg/dL | 295 mg/dL |
| Clopidogrel | 7.5 mg/dL | 7.5 mg/dL |
| Cocaine | 0.346 mg/dL | 0.346 mg/dL |
| Cyclosporine | 0.180 mg/dL | 0.180 mg/dL |
| Diclofenac | 2.58 mg/dL | 2.58 mg/dL |
| Digoxin | 0.0039 mg/dL | 0.0039 mg/dL |
| Dopamine | 0.077 mg/dL | 0.077 mg/dL |
| Doxycycline | 2.08 mg/dL | 2.08 mg/dL |
| Enalaprilat | 0.0903 mg/dL | 0.0903 mg/dL |
| Enoxaparin | 5 mg/dL | 5 mg/dL |
| Epinephrine | 0.037 mg/dL | 0.037 mg/dL |
| Eptifibatide | 0.90 mg/dL | 0.90 mg/dL |
| Erythromycin | 13.8 mg/dL | 13.8 mg/dL |
| Ethanol | 599 mg/dL | 599 mg/dL |
| Fondaparinux | 0.40 mg/dL | 0.40 mg/dL |
| Furosemide | 1.59 mg/dL | 1.59 mg/dL |
| Ibuprofen | 21.9 mg/dL | 21.9 mg/dL |
| Isosorbide Dinitrate | 0.593 mg/dL | 0.593 mg/dL |
| Levodopa | 0.749 mg/dL | 0.749 mg/dL |
| Lithium Heparin | 3160 IU/dL | 3160 IU/dL |
| Methyldopa | 2.55 mg/dL | 2.01 mg/dL |
| Methylprednisolone | 0.783 mg/dL | 0.783 mg/dL |
| Metronidazole | 12.3 mg/dL | 12.3 mg/dL |
| Nicotine | 0.0969 mg/dL | 0.0969 mg/dL |
| Nifedipine | 0.0589 mg/dL | 0.0589 mg/dL |
| Nitrofurantoin | 0.213 mg/dL | 0.213 mg/dL |
| Nystatin | 16.80 mg/dL | 16.80 mg/dL |
| Oxytetracycline | 1.2 mg/dL | 1.2 mg/dL |
| Phenobarbital | 69.0 mg/dL | 69.0 mg/dL |
| Phenylbutazone | 32.1 mg/dL | 32.1 mg/dL |

| Substance | Highest Concentration Tested without Significant Interference | |
|---|---|---|
| | Whole Blood | Plasma |
| Phenytoin | 6.00 mg/dL | 6.00 mg/dL |
| Pravastatin | 0.0218 mg/dL | 0.0218 mg/dL |
| Primidone | 5.70 mg/dL | 5.70 mg/dL |
| Rifampicin | 4.80 mg/dL | 4.80 mg/dL |
| Salicylic Acid | 3.31 mg/dL | 3.31 mg/dL |
| Simvastatin | 0.00833 mg/dL | 0.00833 mg/dL |
| Sodium Heparin | 330 IU/dL | 330 IU/dL |
| Theophylline | 6.00 mg/dL | 6.00 mg/dL |
| Tissue Plasminogen Activator (TPA) | 0.23 mg/dL | 0.23 mg/dL |
| Trimethoprim | 4.21 mg/dL | 4.21 mg/dL |
| Verapamil | 0.172 mg/dL | 0.172 mg/dL |
| Warfarin | 7.49 mg/dL | 7.49 mg/dL |

Interference beyond ±10% of the control sample was observed at the concentrations shown below for the following compounds in plasma.

| Substance | Interferent level | Analyte Level (ng/L) | % Interference |
|---|---|---|---|
| Bilirubin (unconjugated) | 6 mg/dL | 14.77 | -12.3% |
| | 6 mg/dL | 537.84 | -11.7% |
| Fibrinogen | 0.9 g/dL | 19.71 | -11.5% |
| | 0.5 g/dL | 595.35 | -10.6% |
| Total Protein | 12.84 g/dL | 21.55 | -10.1% |
| | 9 g/dL | 573.68 | -11.3% |
| Cefoxitin | 400 mg/dL | 20.15 | -11.6% |
| | 400 mg/dL | 660.41 | -11.8% |
| Methyldopa | 2.25 mg/dL | 18.10 | 12.4% |

Interference beyond ±10% of the control sample was observed at the concentrations shown below for the following compounds in whole blood.

| Substance | Interferent level | Analyte Level (ng/L) | % Interference |
|---|---|---|---|
| Bilirubin (unconjugated) | 8 mg/dL | 16.59 | -14.2% |
| | 6 mg/dL | 642.45 | -11.5% |

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

Lithium heparin venous whole blood and lithium heparin plasma samples with 3 concentration levels (normal (< 5 ng/L), low (15 -25 ng/L) and high (500 – 750 ng/L)) were divided into two groups: i.e., test sample (with added interferent) and control sample (without interferent). Each sample was tested in replicates of 30 using one i-STAT hs-TnI cartridge lot on multiple i-STAT Alinity instruments. Test results from sample spiked with the potential interferent were compared to test results from the control samples lacking the potential interferent.

Interference was considered non-significant if the bias between the test and control sample were within ± 10% of the control sample. The following table lists the concentrations of each substance at which no significant interference was found:

| Substance | Highest Concentration Tested without Significant Interference | |
|---|---|---|
| | Whole Blood | Plasma |
| Human Anti-Mouse Antibody (HAMA) | 3000 ng/mL | 3000 ng/mL |
| Rheumatoid Factor Antibody (RF) | 450 IU/mL | 300 IU/mL |

Interference beyond ±10% of the control sample was observed at the concentration shown below for the following compound in whole blood:

| Compound | Interferent level | Analyte Level (ng/L) | % Interference |
|---|---|---|---|
| Rheumatoid Factor Antibody (RF) | 475 IU/mL | 654.84 | -10.1% |

Interference beyond ±10% of the control sample was observed at the concentration shown below for the following compound in plasma:

| Compound | Interferent level | Analyte Level (ng/L) | % Interference |
|---|---|---|---|
| Rheumatoid Factor Antibody (RF) | 325 IU/mL | 21.85 | -10.8% |

*Cross-reactivity*

A study was performed to evaluate potential interference due to cross-reacting substances following the recommendations in the CLSI EP07, 3rd Edition guideline. The interferents (listed in the table below) were added to lithium heparin plasma or whole blood samples targeting cTnI at normal (< 5 ng/L), low (15-25 ng/L) and high concentrations (500-750 ng/L). The low samples were unaltered native samples, the medium range samples were spiked with native troponin and the high range samples were spiked with recombinant troponin. Each sample was tested in multiple replicates using one lot of i-STAT *hs-TnI* cartridges on the i-STAT Alinity instruments. The difference in results between test and control sample was calculated for each of the three cTnI level and analyzed for % cross-reactivity using the below equation..

$$\%\ \text{Cross} - \text{reactivity} = \frac{(\text{Mean cTnI with cross reactant} - \text{Mean cTnI control})}{\text{Concentration of cross} - \text{reactant}} \text{x } 100\%$$

The sponsor defined no significant cross-reactivity as the %cross-reactive was ≤1%. The following table lists the concentrations of each substance at which the %cross-reactive was ≤1%.

| Potential Cross-Reacting Substance | Highest Concentration Tested (ng/L) |
|---|---|
| Actin | 1,000, 000 |
| Human Cardiac Troponin T (recombinant cTnT) | 1,000, 000 |
| Human Creatine Kinase Myocardial Band (Ck-MB) | 1,000,000 |
| Human Myoglobin | 1,000,000 |
| Human Myosin LC (Light Chain) | 1,000, 000 |
| Human Skeletal Troponin I (recombinant sTnI) | 1,000, 000 |
| Human Skeletal Troponin T (recombinant sTnT) | 1,000, 000 |
| Human Troponin C (TnC) | 1,000, 000 |
| Tropomyosin | 1,000, 000 |

Although the human troponin C (TnC) testing showed the %cross-reactive ≤1%. at 1,000,000 ng/L, the results indicate that TnC had an impact on the troponin results including at medical decision levels. Therefore, an additional dose-response study was conducted. The effect of human TnC was evaluated by comparing the test results from a control sample to the results from a test sample spiked with human TnC at different concentrations. Interference was considered non-significant if the bias between the test and control sample was within ± 10% of the control sample. The following table lists the concentrations at which no significant interference was found.

| Sample Type | Cardiac Troponin I level | Highest Troponin C Tested Without Interference (ng/L) | Control Sample cTnI Level (ng/L) | Test Sample cTnI Level (ng/L) | Difference (%) |
|---|---|---|---|---|---|
| Whole blood | Low | 350,000 | 14.87 | 15.62 | 5.08 |
| | High | 350,000 | 540.05 | 559.57 | 3.61 |
| Plasma | Low | 105,000 | 15.30 | 16.73 | 8.69 |
| | High | 63,000 | 594.97 | 633.95 | 6.55 |

The results of these tests demonstrate that the performance of the i-STAT hs-TnI cartridge on the i-STAT Alinity System is not affected by the presence of human TnC at 350,000 ng/L for whole blood sample and at 63,000 ng/L for plasma.

The following information is provided in the labeling:

- Elevated levels of conjugated bilirubin >30 mg/dL in plasma may result in an increased rate of star-outs (***). The reference range per CLSI EP37 for Bilirubin (Conjugated) is 0.0-2.4 µmol/L (0.0-0.2 mg/dL).

The sponsor describes that decreased results can be expected from unconjugated bilirubin concentrations > 85.5 µmol/L (5 mg/dL). The sponsor explains that the reference range per CLSI EP37 for Bilirubin (Unconjugated) is 0-34 µmol/L (0.0-2.0 mg/dL). Elevated levels of unconjugated bilirubin may be observed in patients with hemolytic disorders (i.e., hemolytic anemia), cholestatis, and disorders of impaired bilirubin conjugation and secretion, such as

Gilbert's syndrome, Crigler-Najjar syndrome, chronic viral hepatitis, or chronic alcohol cirrhosis.

The following limitations are included in the labeling:

- Samples from patients who have been exposed to animals or who have received therapeutic or diagnostic procedures employing immunoglobulins or reagents derived from immunoglobulins may contain antibodies, e.g., HAMA or other heterophile antibodies, which may interfere with immunoassays and produce erroneous results. The generation of potentially interfering antibodies in response to bacterial infections has been reported. While this product contains reagents that minimize the effect of these interferents and QC algorithms designed to detect their effects, the possibility of interference causing erroneous results should be evaluated carefully in cases where there are inconsistencies in the clinical information.

- 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.

4. Detection Limit and Assay Reportable Range:
   *Reportable Range*
   2.9 – 1000.0 ng/L

   *Detection limit*

   Limit of blank (LoB), limit of detection (LoD), and limit of quantification (LoQ) studies for the i-STAT hs-TnI cartridge with the i-STAT Alinity System were conducted following the recommendations in the CLSI EP17-A2 guideline.

   *Limit of Blank (LoB)*

   The LoB was evaluated using fresh lithium heparin whole blood samples and plasma samples from four (4) apparently healthy donors altered to achieve blank cardiac troponin I level samples. The samples were tested using four (4) lots of the i-STAT hs-TnI cartridges. A total of 80 measurements were obtained for each lot by testing samples across 3 days. The LoB was calculated following EP17-A2 guideline for each lot. The highest LoB values obtained across all lots was 0.79 ng/L for whole blood and 0.96 ng/L for plasma.

   *Limit of Detection (LoD)*

   The LoD was evaluated using fresh lithium heparin whole blood and lithium heparin plasma samples from four (4) individual healthy donors. The study was performed using three (3) lots of the i-STAT hs-TnI cartridges. For each sample, a total of 60 measurements were obtained from each of the three cartridge lots over three (3) days. The LoD was calculated non-parametrically for each lot. The highest LoD values obtained across all lots was 1.53 ng/L for whole blood and 1.42 ng/L for plasma.

*Limit of Quantification (LoQ)*

The LoQ was evaluated using fresh lithium heparin whole blood and lithium heparin plasma samples. For each sample type, 13 independent fresh low-analyte samples from individual healthy donors were tested using 4 lots of the i-STAT hs-TnI cartridges. Each sample was measured in 10 replicates per lot. The LoQ was determined independently for each cartridge lot using a precision profile approach as the concentration where the %CV was less than or equal to 20%. The highest LoQ values obtained across all lots was 2.29 ng/L for whole blood and 2.89 ng/L for plasma.

The above studies support the following detection limits claims for the i-STAT hs-TnI cartridge with the i-STAT Alinity System:

| Sample Type | LoB | LoD | LoQ |
|---|---|---|---|
| Whole Blood | 0.79 | 1.53 | 2.29* |
| Plasma | 0.96 | 1.42 | 2.89 |

*8 outliers were observed in this study and all were included in the analysis.

The following limitation is included in the labeling:

- A small proportion of cartridges that reported falsely elevated or falsely low results that would not reflect a patient's true physiological troponin concentration were observed in analytical studies. The rate of these results is designed and observed to be <1%. Due to possibility of a falsely elevated or falsely low result being reported by the system, troponin results should always be used by health care professionals in conjunction with the patient's clinical data, signs, and symptoms in accordance with the fourth universal definition of MI requiring 1) acute myocardial injury with clinical evidence of acute myocardial ischemia, 2) detection of a rise and/or fall of cTn values and 3) serial sampling.

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

*Traceability*

The i-STAT hs-TnI cartridge with the i-STAT Alinity System is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material SRM2921.

*Stability*

The sponsor has provided information to support the following sample stability claims in their labeling:

- Lithium heparin whole blood and lithium heparin plasma: 4 hours at room temperature (18-30ºC)
- Non-anticoagulant whole blood: 3 minutes at room temperature (18-30ºC).

6. Assay Cut-Off:

See Clinical Cut-off Section below.

## B Comparison Studies:

1. Method Comparison with Predicate Device:

Not applicable.

2. Matrix Comparison:

*Lithium Heparin Tube Type Equivalence (Lithium Heparin with Separator Gel vs Lithium Heparin)*

The matrix equivalence between whole blood and plasma samples collected in lithium heparin tubes (primary tube) and lithium heparin tubes with separator gel (candidate tube) was evaluated for the i-STAT hs-TnI cartridge with the i-STAT Alinity System following the recommendations in the CLSI EP35, 1st Edition guideline.

Matched whole blood samples collected from the clinical study sites were tested. Plasma samples were prepared from the whole blood samples. Each sample was tested in duplicate. A Passing-Bablok regression analysis was performed using the first result from the candidate specimen type (Y: lithium heparin tube with separator gel) versus the first result from the primary specimen (X: lithium heparin tube). The regression analysis results are summarized below:

Whole blood

| Samples | Candidate (Lithium Heparin Tube with Separator Gel ) hs-TnI Range (ng/L) | Primary (Lithium Heparin Tube) hs-TnI Range (ng/L) | N | Slope (95% CI) | Intercept (95%CI) | R (95%CI) |
|---|---|---|---|---|---|---|
| All samples | 3.0-863.4 | 3.1-874.4 | 86 | 0.99 (0.97,1.00) | 0.09 (-0.34, 0.38) | 1.00 (1.00, 1.00) |

Plasma

| Samples | Candidate (Lithium Heparin Tube with Separator Gel ) hs-TnI Range (ng/L) | Primary (Lithium Heparin Tube) hs-TnI Range (ng/L) | N | Slope (95% CI) | Intercept (95%CI) | R (95%CI) |
|---|---|---|---|---|---|---|
| All samples | 3.1-999.4 | 3.7-979.6 | 88 | 1.01 (1.00,1.02) | -0.12 (-0.5, 0.25) | 1.00 (1.00, 1.00) |

Non anticoagulant equivalence

A study assessing the matrix equivalency between non-anticoagulated venous whole blood specimens (candidate specimen type) to specimens collected into a lithium heparin tube (primary specimen type) was performed. For a given subject, the pair of specimens were collected in one syringe without anticoagulant and in one lithium heparin tube.

A total of 86 matched whole blood samples (7 contrived samples) collected from the clinical study sites were tested. Each sample was tested in duplicate. A Passing-Bablok regression analysis was performed using the first result from the candidate specimen types (Y: non anticoagulated whole blood) versus the first result from the primary specimen (X: lithium heparin whole blood). The regression analysis results are summarized below:

| Candidate (non-anticoagulant WB) hs-TnI Range (ng/L) | Primary (LiHep WB) hs-TnI Range (ng/L) | N | Slope (95% CI) | Intercept (95%CI) | R (95%CI) |
|---|---|---|---|---|---|
| 2.9-863.3 | 3.1-874.4 | 86 | 1.02 (1.01,1.03) | 0.17 (-0.15, 0.49) | 1.00 (0.99, 1.00) |

The following limitations are included in the labeling:

- Do not test non-anticoagulated samples beyond 3 minutes. Partially clotted samples will impact i-STAT hs-TnI results.
- If performing i-STAT hs-TnI testing using both a specimen collected without anticoagulant and a specimen collected with lithium heparin anticoagulant from a single patient, the i-STAT hs-TnI test results observed for the specimen collected without anticoagulant may be 3.1% - 4.4% higher at the 99$^{th}$ percentile URLs compared to the specimen collected with lithium heparin.

## C Clinical Studies:

1. Clinical Sensitivity:

A multi-center pivotal study using prospectively collected venous whole blood and plasma specimens was conducted at 28 sites to assess the diagnostic accuracy of the i-STAT hs-TnI cartridge with the i-STAT Alinity System. The sites represented geographically diverse Emergency Department (ED) associated with acute care hospitals, medical centers, tertiary care facilities, and primary care clinics with patient populations reflecting regional, urban, and rural areas in the US.

Venous whole blood specimens collected into lithium heparin tubes from 3586 subjects presenting to the ED with signs and symptoms suggestive of acute coronary syndrome (ACS) were included in the clinical performance evaluation. Plasma was obtained from whole blood by centrifugation. Each whole blood and plasma specimen was evaluated using the candidate test system. All subjects were adjudicated by a panel of board-certified cardiologists and emergency medicine physicians, who reviewed the subject's clinical presentation, medical history, relevant clinical data, and locally measured standard of care (SOC) troponin test. The adjudication outcome (MI or non-MI) was based on the Fourth Universal Definition of MI. The adjudicators were blinded to the i-STAT High Sensitivity Troponin I assay results. Adjudicators were also blinded to site diagnoses. The observed MI prevalence in this study was 6.8% (157/2296) for females and 11.6% (150/1290) for males.

The results were analyzed using the serial sampling time points collected as part of the ED visit. The clinical performance (clinical sensitivity, clinical specificity, positive predictive value (PPV), and negative predictive value (NPV)) of the i-STAT hs-TnI cartridge with the i-STAT Alinity System results in the diagnosis of MI in this trial is shown below. The results are summarized in the following tables.

An analysis of device performance was performed separately for males and females using the sex-specific 99$^{th}$ percentile cutoffs (female 13 ng/L, male 28 ng/L). The sensitivity and specificity results are summarized in the following tables. *****All time points are relative to ED presentation.

**Whole Blood**

| Sex Dependent Cutoff (Female 13 ng/L, Male 28 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours)* | n | MI | Non-MI | Sensitivity | | Specificity | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Female | 0 to < 1 | 1870 | 128 | 1742 | 92.19 | 86.22 | 83.12 | 81.29 |
| | > 1 to 3 | 1801 | 119 | 1682 | 96.64 | 91.68 | 82.82 | 80.94 |
| | >3 to 6 | 726 | 70 | 656 | 97.14 | 90.17 | 77.90 | 74.56 |
| | >6 | 60 | 16 | 44 | 100.00 | 80.64 | 54.55 | 40.07 |
| Male | 0 to <1 | 1092 | 130 | 962 | 79.23 | 71.47 | 84.30 | 81.87 |
| | >1 to 3 | 1023 | 118 | 905 | 90.68 | 84.08 | 84.09 | 81.56 |
| | >3 to 6 | 439 | 69 | 370 | 94.20 | 86.02 | 82.16 | 77.94 |
| | >6 | 47 | 12 | 35 | 91.67 | 64.61 | 57.14 | 40.86 |

**Plasma**

| Sex Dependent Cutoff (Female 13 ng/L, Male 28 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours)* | n | MI | Non-MI | Sensitivity | | Specificity | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Female | 0 to < 1 | 1870 | 128 | 1742 | 92.19 | 86.22 | 82.43 | 80.58 |
| | > 1 to 3 | 1800 | 118 | 1682 | 96.61 | 91.61 | 81.39 | 79.46 |
| | >3 to 6 | 725 | 70 | 655 | 97.14 | 90.17 | 77.40 | 74.05 |
| | >6 | 60 | 16 | 44 | 100.00 | 80.64 | 54.55 | 40.07 |
| Male | 0 to <1 | 1091 | 130 | 961 | 79.23 | 71.47 | 83.56 | 81.08 |
| | >1 to 3 | 1024 | 117 | 906 | 90.68 | 84.08 | 83.33 | 80.77 |
| | >3 to 6 | 438 | 69 | 369 | 94.20 | 86.02 | 81.30 | 77.01 |
| | >6 | 47 | 12 | 35 | 91.67 | 64.61 | 57.14 | 40.86 |

The positive predictive value (PPV) and negative predictive value (NPV) results using the sex-specific 99$^{th}$ percentile cutoffs (female 13ng/L and male 28 ng/L) are summarized in the following tables.

**Whole Blood**

| Sex Dependent Cutoff (Female 13 ng/L, Male 28 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours)* | n | MI | Non-MI | PPV | | NPV | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Female | 0 to < 1 | 1870 | 128 | 1742 | 28.64 | 24.49 | 99.31 | 98.74 |
| | > 1 to 3 | 1801 | 119 | 1682 | 28.47 | 24.28 | 99.71 | 99.27 |
| | >3 to 6 | 726 | 70 | 656 | 31.92 | 26.03 | 99.61 | 98.59 |
| | >6 | 60 | 16 | 44 | 44.44 | 29.54 | 100.00 | 86.20 |

| Sex Dependent Cutoff (Female 13 ng/L, Male 28 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours)* | n | MI | Non-MI | PPV | | NPV | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Male | 0 to <1 | 1092 | 130 | 962 | 40.55 | 34.70 | 96.78 | 95.35 |
| | >1 to 3 | 1023 | 118 | 905 | 42.63 | 36.67 | 98.58 | 97.47 |
| | >3 to 6 | 439 | 69 | 370 | 49.62 | 41.19 | 98.70 | 96.71 |
| | >6 | 47 | 12 | 35 | 42.31 | 25.54 | 95.24 | 77.33 |

**Plasma**

| Sex Dependent Cutoff (Female 13 ng/L, Male 28 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours) * | n | MI | Non-MI | PPV | | NPV | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Female | 0 to < 1 | 1870 | 128 | 1742 | 27.83 | 23.78 | 99.31 | 98.73 |
| | > 1 to 3 | 1800 | 118 | 1682 | 26.70 | 22.72 | 99.71 | 99.25 |
| | >3 to 6 | 725 | 70 | 655 | 31.48 | 25.66 | 99.61 | 98.58 |
| | >6 | 60 | 16 | 44 | 44.44 | 29.54 | 100.00 | 86.20 |
| Male | 0 to <1 | 1091 | 130 | 961 | 39.46 | 33.73 | 96.75 | 95.31 |
| | >1 to 3 | 1024 | 118 | 906 | 41.47 | 35.63 | 98.56 | 97.45 |
| | >3 to 6 | 438 | 69 | 369 | 48.51 | 40.21 | 98.68 | 96.67 |
| | >6 | 47 | 12 | 35 | 42.31 | 25.54 | 95.24 | 77.33 |

An analysis of device performance was performed separately for males and females using the overall 99$^{th}$ percentile cutoffs (21 ng/L). The sensitivity and specificity results are summarized in the following table.

**Whole Blood**

| Overall Cutoff (21 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours)* | n | MI | Non-MI | Sensitivity | | Specificity | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Female | 0 to 1 | 1870 | 128 | 1742 | 86.72 | 79.76 | 89.37 | 87.72 |
| | > 1 to 3 | 1801 | 119 | 1682 | 91.60 | 85.22 | 90.01 | 88.49 |
| | >3 to 6 | 726 | 70 | 656 | 94.29 | 86.21 | 85.98 | 83.11 |
| | >6 | 60 | 16 | 44 | 93.75 | 71.67 | 68.18 | 53.44 |
| Male | 0 to <1 | 1092 | 130 | 962 | 81.54 | 74.00 | 78.69 | 75.99 |
| | >1 to 3 | 1023 | 118 | 905 | 92.37 | 86.14 | 78.45 | 75.66 |
| | >3 to 6 | 439 | 69 | 370 | 95.65 | 87.98 | 74.59 | 69.92 |
| | >6 | 47 | 12 | 35 | 91.67 | 64.61 | 54.29 | 38.19 |

**Plasma**

| Overall Cutoff (21 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours)* | n | MI | Non-MI | Sensitivity | | Specificity | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Female | 0 to 1 | 1870 | 128 | 1742 | 86.72 | 79.76 | 89.44 | 87.91 |
| | > 1 to 3 | 1800 | 118 | 1682 | 92.37 | 86.14 | 89.71 | 88.17 |
| | >3 to 6 | 725 | 70 | 655 | 94.29 | 86.21 | 85.80 | 82.92 |
| | >6 | 60 | 16 | 44 | 93.75 | 71.67 | 70.45 | 55.78 |
| Male | 0 to <1 | 1091 | 130 | 961 | 83.08 | 75.70 | 78.46 | 75.75 |
| | >1 to 3 | 1024 | 118 | 906 | 92.37 | 86.14 | 77.48 | 74.65 |
| | >3 to 6 | 438 | 69 | 369 | 95.65 | 87.98 | 73.44 | 68.71 |
| | >6 | 47 | 12 | 35 | 91.67 | 64.61 | 54.29 | 38.19 |

The positive predictive value (PPV) and negative predictive value (NPV) results using the overall 99$^{th}$ percentile cutoff (21 ng/L) are summarized in the following tables.

**Whole blood**

| Overall Cutoff (21 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours)* | n | MI | Non-MI | PPV | | NPV | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Female | 0 to 1 | 1870 | 128 | 1742 | 37.25 | 31.95 | 98.92 | 98.27 |
| | > 1 to 3 | 1801 | 119 | 1682 | 39.35 | 33.78 | 99.34 | 98.80 |
| | >3 to 6 | 726 | 70 | 656 | 41.77 | 34.37 | 99.30 | 98.20 |
| | >6 | 60 | 16 | 44 | 51.72 | 34.43 | 96.77 | 83.81 |
| Male | 0 to <1 | 1092 | 130 | 962 | 34.08 | 29.04 | 96.93 | 95.47 |
| | >1 to 3 | 1023 | 118 | 905 | 35.86 | 30.67 | 98.75 | 97.64 |
| | >3 to 6 | 439 | 69 | 370 | 41.25 | 33.91 | 98.92 | 96.89 |
| | >6 | 47 | 12 | 35 | 40.74 | 24.51 | 95.00 | 76.39 |

Plasma

| Overall Cutoff (21 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours) * | n | MI | Non-MI | PPV | | NPV | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Female | 0 to 1 | 1870 | 128 | 1742 | 37.63 | 32.29 | 98.92 | 98.28 |
| | > 1 to 3 | 1800 | 118 | 1682 | 38.65 | 33.16 | 99.41 | 98.88 |
| | >3 to 6 | 725 | 70 | 655 | 41.51 | 34.14 | 99.29 | 98.20 |
| | >6 | 60 | 16 | 44 | 53.57 | 35.81 | 96.88 | 84.26 |

| Overall Cutoff (21 ng/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Time Point (hours) * | n | MI | Non-MI | PPV | | NPV | |
| | | | | | % | Lower limit of one sided 97.5%CI | % | Lower limit of one sided 97.5%CI |
| Male | 0 to 1 | 1091 | 130 | 961 | 34.29 | 29.26 | 97.16 | 95.74 |
| | >1 to 3 | 1024 | 118 | 906 | 34.82 | 29.76 | 98.73 | 97.61 |
| | >3 to 6 | 438 | 69 | 369 | 40.24 | 33.04 | 98.91 | 96.83 |
| | >6 | 47 | 12 | 35 | 40.74 | 24.51 | 95.00 | 76.39 |

In the study there were 1,290 male patients; among them there were 150 patients with MI and 1140 patients without MI. In the study, there were 2296 female patients, among them there were 157 patients with MI and 2139 patients without MI.

The sponsor provided the following information in their labeling:

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

- The analyte results should be assessed in conjunction with the patient's medical history, clinical examination, and other findings.

- Due to the release kinetics of cardiac troponin I, an initial test result may not be definitive in diagnosing MI. Serial troponin measurements are suggested. The patient's clinical presentation (history, risk factors, physical exam, and ECG findings), a rise/fall pattern in results, and noninvasive modalities should be considered in conjunction with troponin in the diagnostic evaluation of suspected myocardial infarction in accordance with the fourth universal definition of MI to help guide the choice of therapeutic options.

<u>The sponsor included the following information regarding performance observed using whole blood samples in the study.</u>

- In the i-STAT hs-TnI clinical study, the percent of false negatives for females using the sex-specific cutoff (13 ng/L) was up to 3.82% lower when compared to the false negative rate for females using the overall cutoff of 21 ng/L. When using the female cutoff of 13 ng/L, 2.55% of females with MI had non-elevated i-STAT hs-TnI test results. When using the overall cutoff of 21 ng/L, 6.37% of females with MI had non-elevated i-STAT hs-TnI test results.

  When using the female cutoff (13 ng/L), there were 4 false negative female subjects (out of 157 female subjects adjudicated with MI). In these subjects, no result above the cutoff was obtained with the i-STAT hs-TnI test. Among the 4 false negative female subjects

based on the female cutoff, all had at least one standard of care (SOC) troponin test with a concentration above the cutoff of the tests used by the sites.

When using the overall cutoff (21 ng/L), there were 10 false negative female subjects (out of 157 female subjects adjudicated with MI). In these subjects, no result above the cutoff was obtained with the i-STAT hs-TnI test. Among the 10 false negative female subjects based on the female cutoff, 9 subjects had at least one standard of care (SOC) troponin test with a concentration above the cutoff of the tests used by the sites.

- In the i-STAT hs-TnI clinical study, the percent of false negatives for males using the sex-specific cutoff (28 ng/L) was up to 2.00% higher when compared to the false negative rate for males using the overall cutoff of 21 ng/L. When using the male cutoff of 28 ng/L, 9.33% of males with MI had non-elevated i-STAT hs-TnI test results. When using the overall cutoff of 21 ng/L, 7.33% of males with MI had non-elevated i-STAT hs-TnI test results.

  When using the male cutoff (28 ng/L), there were 14 false negative male subjects (out of 150 male subjects adjudicated with MI). In these subjects, no result above the cutoff was obtained with the i-STAT hs-TnI test. Among the 14 false negative male subjects based on the male specific cutoff, 2 were early presenters and had no blood draw tested with the i-STAT hs-TnI test when the SOC troponin test detected troponin concentration above the SOC cutoff. The remaining 12 subjects had at least one SOC troponin test with a concentration above the cutoff of the tests used by the sites.

  When using the overall cutoff (21 ng/L), there were 11 false negative male subjects (out of 150 male subjects adjudicated with MI). In these subjects, no result above the cutoff was obtained with the i-STAT hs-TnI test. Among the 11 false negative male subjects based on the male specific cutoff, 2 were early presenters and had no blood draw tested with the i-STAT hs-TnI test when the SOC troponin test detected troponin concentration above the SOC cutoff. The remaining 9 subjects had at least one SOC troponin test with a concentration above the cutoff of the tests used by the sites.

- When using the female cutoff (13 ng/L), the lower bound of the one-sided 97.5% CI for the PPV was as low as 24.28% (at > 1 to 3 hours). Taking into consideration the lower bound of the one-sided 97.5% CI, up to 75.51% (at 0 to 1 hour), 75.72% (at > 1 to 3 hours), 73.97% (at > 3 to 6 hours), and 70.46% (at > 6 hours) of positive troponin results could come from females who are not having an MI. When using the overall cutoff (21 ng/L), the lower bound of the one-sided 97.5% CI for the PPV was as low as 31.95% (at 0 to 1 hour). Taking into consideration the lower bound of the one-sided 97.5% CI, up to 68.05% (at 0 to 1 hour), 66.22% (at > 1 to 3 hours), 65.63% (at > 3 to 6 hours), and 65.57% (at > 6 hours) of positive troponin results could come from females who are not having an MI.
- When using the male cutoff (28 ng/L), the lower bound of the one-sided 97.5% CI for the PPV was as low as 25.54% (at > 6 hours). Taking into consideration the lower bound of the one-sided 97.5% CI, up to 65.30% (at 0 to 1 hour), 63.33% (at > 1 to 3 hours), 58.81% (at > 3 to 6 hours), and 74.46% (at > 6 hours) of positive troponin results could come from males who are not having an MI. When using the overall cutoff (21 ng/L), the

lower bound of the one-sided 97.5% CI for the PPV was as low as 24.51% (at > 6 hours). Taking into consideration the lower bound of the one-sided 97.5% CI, up to 70.96% (at 0 to 1 hour), 69.33% (at > 1 to 3 hours), 66.09% (at > 3 to 6 hours), and 75.49% (at > 6 hours) of positive troponin results could come from males who are not having an MI.

The sponsor included similar information for the results observed using plasma samples.

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

- When an increased cardiac troponin I value is encountered (e.g. exceeding the 99$^{th}$ percentile URL) in the absence of myocardial ischemia, other etiologies of cardiac damage should be considered. Elevated troponin levels may be indicative of myocardial injury associated with heart failure, acute renal failure, chronic kidney disease, sepsis, myocarditis, arrhythmias, pulmonary embolism, or other clinical conditions. Additionally, as documented in literature, in certain samples, a high molecular weight complex comprised of immunoglobulin and cTnI (macrotroponin) can be present and may result in elevated cTnI measurements. The patient's clinical presentation (history, risk factors, physical exam, and ECG findings), a rise/fall pattern in results, and noninvasive modalities should be considered in conjunction with troponin in the diagnostic evaluation of suspected myocardial infarction to help guide the choice of therapeutic options.

- False negative rates using the overall cutoff for females and sex-specific cutoff for males were higher compared to the false negative rates using the sex-specific cutoff for females and overall cutoff for males. False positive rates using the overall cutoff for males and sex-specific cutoff for females were higher compared to the false positive rates using the sex-specific cutoff for males and overall cutoff for females. Refer to the Clinical Performance section above.

- Cardiac troponin may not appear in circulation for 4-6 hours following the onset of symptoms of MI. Consequently, a single negative result may not be sufficient to rule out MI. Per the fourth universal definition of MI, myocardial injury is considered acute when there is evidence of elevated cardiac troponin (cTn) values with at least 1 value above the 99$^{th}$ percentile upper reference limit (URL) and there is a rise and/or fall of cTn values.

- The results of different cTnI assays are not comparable. Additionally, as cTnI and cTnT are distinct molecules the results are not interchangeable, nor comparable. In addition, significant variation in absolute troponin values may be observed for a given patient specimen with different analytic methods.

- The test results should be assessed in conjunction with the patient's symptoms, clinical examination, and other findings.

2. Clinical Specificity:

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

3. Clinical Cut-Off

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

4. Other Clinical Supportive Data (When 1. And 2. Are Not Applicable):

## D Expected Values/Reference Range:

A reference range study was conducted based on guidance from CLSI EP 28-A3c. Specimens were collected from 896 apparently healthy adults in a US population with the following levels of biomarkers:

| Biomarker | All subjects |
|---|---|
| Cardiac NT-proBNP | < 125 pg/mL for subjects younger than 75 years or < 450 pg/mL for subjects 75 years or older |
| HbA1c(%) | ≤ 6.5% |
| GFR (mL/min/1.73m$^2$) | ≥ 60 |

The exclusion criteria used were:

- BMI > 35.0 or < 16.0 kg/m$^2$
- Diagnosed with Type 1 or Type 2 diabetes
- Hospitalized within the last three (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 of a circulation problem (e.g., leg).
- Statin use within the last 6 months.
- Known pregnancy or within 6 weeks postpartum.

Venous whole blood samples were collected into lithium heparin collection tubes. Corresponding plasma from whole blood specimens were obtained by centrifugation. Each specimen was tested in replicate of one using the candidate test system. The 99th percentiles described in the following table for this population were determined using the nonparametric method as described in EP28-A3c.

The female, male, and overall 99th percentile URL values in the labeling for the i-STAT hs-TnI cartridge with the i-STAT Alinity System are summarized in the table below:

| Sex | N | 99th Percentile (ng/L) | 90%CI (ng/L) |
|---|---|---|---|
| Female | 490 | 12 | (10, 17) |
| Male* | 404 | 29 | (20, 61) |
| Overall | 895 | 21 | (15, 29) |

The 99th percentile URL values were previously determined for the i-STAT hs-TnI cartridge with the i-STAT 1 System (K240984). The 99th percentile URL values for both test systems are similar. Therefore, the same female, male, and overall 99th percentile URL values will be used for the i-STAT hs-TnI cartridge on both i-STAT systems (both i-STAT 1 System and i-STAT Alinity System) as shown in the table below:

| Sex | N | 99th Percentile (ng/L) | 90%CI (ng/L) |
|---|---|---|---|
| Female | 490 | 13 | (10, 17) |
| Male* | 404 | 28 | (19, 58) |
| Overall | 895 | 21 | (14, 30) |

*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.

## E Other Supportive Instrument Performance Characteristics Data:

1. Hematocrit study

   The effect of hematocrit on the i-STAT hs-TnI cartridge with the i-STAT Alinity System was assessed across a hematocrit (HCT) range of 15 – 60% packed cell volume (PCV). The study was conducted using three (3) lots of i-STAT *hs-TnI* cartridges on i-STAT Alinity instrument. Lithium heparin venous whole blood samples from 5 donors were altered to target two cardiac troponin I levels (low: 15 – 25 ng/L and high: 500 – 700 ng/L). Each sample was evaluated at 8 HCT levels, with the nominal HCT levels at 45% PCV and low and high PCV as test conditions. Each sample was measured in replicates of 5 from each of three (3) cartridge lots (15 replicates per HcT level per donor per cardiac troponin I level).

   The HCT sensitivity at each troponin I level was assessed by comparing the results at the low and high HCT levels (test conditions) to the nominal HCT level (control condition). Results showed the accuracy is insensitive to HCT levels between 15 – 55%. Increased imprecision (>10% CV%) and increased bias was observed for samples with hematocrit levels ≥ 55%.

   Limitations

   The following limitation is provided in the labeling:

   The i-STAT hs-TnI test has been characterized between 15 – 60% PCV. Increased imprecision exceeding 10% has been observed for whole blood samples with hematocrit values ≥ 55% PCV.

   For patients with hematocrit over 55% PCV, the i-STAT hs-TnI result in whole blood may not be accurate as a bias up to ±10% has been observed.

   Patients with known hematocrit above 55% should only be tested using plasma samples.

   If the hematocrit is unknown and suspected to be elevated*, and the i-STAT hs-TnI whole blood result is within ±10% of the i-STAT hs-TnI 99th percentile URL (overall 21 ng/L,

female 13 ng/L, male 28 ng/L), obtain a hematocrit measurement and if > 55% PCV, test the sample with plasma or an alternative method.

*Note: female hematocrit reference range is 38 – 46%PCV and male hematocrit reference range is 43 – 51%PCV. An elevated hematocrit can be due to but not limited to, loss of fluids, such as in dehydration, diuretic therapy, and burns, or an increase in red blood cells, such as in cardiovascular and renal disorders, polycythemia vera, and impaired ventilation.

2. Altitude Effect

The performance of the i-STAT hs-TnI cartridge with the i-STAT Alinity System at an altitude of approximately 10,000 feet (ft) above sea level using whole blood and plasma specimen was evaluated across the assay reportable range. A barometric chamber was used to simulate an altitude of approximately 10,000 (ft) above sea level (target altitude as the test condition) and outside the chamber was used for sea level (Dallas, Texas) (as the control condition). The results of the study demonstrate that the test yields accurate results up to approximately 10,000 feet above sea level.

Limitations

The following limitations are provided in the labeling:

- The frequency of suppressed results is affected by atmospheric pressure. Suppressed result rate may increase with higher elevations (decreased barometric pressure) and may become persistent if testing is performed at more than 7500 feet (2286 meters) above sea level. Where unavailability of results is unacceptable, Abbott Point of Care recommends having an alternate method.

- The i-STAT hs-TnI test has not been evaluated at altitude >10,000 feet. No impact on performance was found up to 10,000 feet of altitude.

3. Operating Range Study

The performance of the i-STAT hs-TnI cartridge with the i-STAT Alinity System across its operating temperature (16-30°C) and operating relative humidity (%RH of 10-90%) were evaluated. The protocol and results were reviewed and found acceptable to support the test yields accurate results across the operating temperature range of 16-30°C and % RH between 10-90%.

4. Tilting Study

A study was performed to evaluate the robustness of the i-STAT hs-TnI cartridge with the i-STAT Alinity System when the instrument is placed at a non-level angle during a cartridge test cycle. The study was conducted using on lot of i-STAT hs-TnI cartridges using whole blood samples. Each sample was evaluated at nine tilt angles, with a level of surface 0° as control condition 15°, 20°, 25°, 30°, -15°, -20°, -25°, and -30° as test conditions. Each test condition was tested along with its corresponding control condition using 10 i-STAT hs-TnI cartridges on 10 i-STAT Alinity instruments respectively. The impact of instrument tilt angle during testing was assessed by comparing the i-STAT hs-TnI test results collected at the tilt

angles (test conditions) to the test results collected on a level surface (control condition). The results demonstrated that the candidate device was not impacted by tilt angles ranging from +30° incline to -15° decline for all cardiac troponin I levels.

Limitations

The following limitations are provided in the labeling:

- The analyzer must remain on a flat surface with the display facing up during testing. Movement of the analyzer during testing may increase the frequency of suppressed results or quality check codes. A level surface includes running the analyzer in the downloader/recharger.

- The i-STAT hs-TnI test was characterized for tilt angle between -20° (display angled down) and +30° (displayed angled up) versus a level surface. Increased bias was observed for a tilt angle more than -15° (display angled down).

5. Vibration

   A study was performed to evaluate the robustness of the i-STAT hs-TnI cartridge with the i-STAT Alinity System when the instrument is exposed to vibration during a cartridge test cycle. The study was conducted using one lot of i-STAT hs-TnI cartridges and 13 i-STAT Alinity instruments. Each sample was evaluated at three vibration levels, with no vibration as a control condition and 4.8 mm/s, 10 mm/s, and 15 mm/s as test conditions. The impact of vibration during testing was assessed by comparing i-STAT hs-TnI results collected in the presence of vibration (test conditions) to the results collected with no vibration (control condition). The results of the study demonstrated that the i-STAT hs-TnI test in the i-STAT hs-TnI cartridge when tested on the i-STAT Alinity instrument is insensitive to vibration up to 15 mm/s across the range of cTnI levels tested.

6. EMC and Electrical Safety

   The sponsor provided documentation demonstrating that acceptable electrical safety EMC testing has been performed.

7. Software and Cybersecurity

   The sponsor provided software and cybersecurity documentation that was reviewed and found to be acceptable.

## VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

## IX Conclusion:

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