## STAT High Sensitive Troponin-I

Customer Service: Contact your local representative or find country specific contact information on www.abbottdiagnostics.com

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

### Key to symbols used

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
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<tr>
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</table>

**Control Number**: Control Number

**Reaction Vessels**: Reaction Vessels

**Reagent Lot**: Reagent Lot

**Replacement Caps**: Replacement Caps

**Sample Cups**: Sample Cups

**Septum**: Septum

**Warning: May cause an allergic reaction.**

**Warning: Causes serious eye irritation.**

See REAGENTS section for a full explanation of symbols used in reagent component naming.

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*Abbott*
NAME
ARCHITECT STAT High Sensitive Troponin-I

INTENDED USE
The ARCHITECT STAT High Sensitive Troponin-I assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of cardiac troponin I (cTnI) in human plasma and serum on the ARCHITECT i System with STAT protocol capability.

The cTnI values are used as an aid in the diagnosis of myocardial infarction (MI) and to aid in the assessment of 30-day and 90-day prognosis relative to all-cause mortality and major adverse cardiac events (MACE) including myocardial infarction, revascularization, and cardiac death in patients who present with symptoms suggestive of acute coronary syndrome (ACS).

SUMMARY AND EXPLANATION OF TEST
Cardiac troponin I is a regulatory subunit of the troponin complex associated with the actin thin filament within cardiac muscle cells.1 Troponin I, in conjunction with troponin C and troponin T, plays an integral role in the regulation of muscle contraction. Three distinct tissue-specific isoforms of troponin I have been identified from skeletal and cardiac muscles. The cardiac isoform exhibits only 60% similarity with the skeletal muscle isoform and contains additional amino acids at the N-terminus; cTnI has a molecular weight of approximately 24,000 daltons.2,3 Clinical studies have demonstrated the release of cTnI into the blood stream within hours following myocardial infarction (MI) or ischemic injury. High sensitivity assays can detect elevated levels of cTnI (above the 99th percentile of an apparently healthy reference population) within 3 hours after the onset of chest pain. Cardiac troponin I reaches peak concentrations in approximately 8 to 28 hours and remains elevated for 3 to 10 days following MI.2,4 Cardiac troponin I is the preferred biomarker for the detection of myocardial injury based on improved sensitivity and superior tissue-specificity compared to other available biomarkers of necrosis, including CK-MB, myoglobin, lactate dehydrogenase, and others.5,6 The high tissue specificity of cTnI measurements is beneficial for identifying cardiac injury in clinical conditions involving skeletal muscle injury resulting from surgery, trauma, extensive exercise, or muscular disease.2,4 High tissue specificity of cTnI, however, should not be confused with the specificity for the mechanism of injury (e.g., MI versus myocarditis). When an increased value for cTnI is encountered (e.g., exceeding the 99th percentile of a reference control population) in the absence of evidence of myocardial ischemia, a careful search of other possible etiologies for cardiac damage should be taken.1 Elevated troponin levels may be indicative of myocardial injury associated with heart failure, renal failure, chronic renal disease, myocarditis, arrhythmias, pulmonary embolism, or other clinical conditions.10,11

In 2012, the Global Task Force with joint leadership among the European Society of Cardiology (ESC), American College of Cardiology Foundation (ACCF), American Heart Association (AHA), and World Heart Federation (WHF) refined past criteria with the third universal definition of MI that also supports use (AHA), and World Heart Federation (WHF) refined past criteria with the third universal definition of MI that also supports use of cTnI as a preferred biomarker for myocardial injury. Their universal definition of MI is a typical rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile upper reference limit (URL) together with evidence of myocardial ischemia with at least one of the following: ischemic symptoms, pathological Q waves on electrocardiogram (ECG), ischemic ECG changes, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality, or identification of an intracoronary thrombus by angiography or autopsy.12,13 The recommended criteria are based on the principle that any reliable detectable amount of myocardial necrosis, if caused by myocardial ischemia, constitutes an MI. A gender difference in 99th percentile has been reported, indicating the benefit of using gender specific 99th percentile cutoff values.12 A single, elevated cTnI value may not be sufficient to make the diagnosis of myocardial infarction. Serial sampling to detect the temporal rise and fall of cTnI levels is recommended for the differentiation of acute cardiac events from chronic cardiac disease.12,13

The use of delta values (difference of cTnI levels between two test points) may have the potential to improve the clinical specificity for ACS.12,14 Several major studies have shown that cTnI is also useful as a predictor of cardiac risk in patients with unstable anagia.15 Additional studies have shown that during a 30-day follow-up, patients with acute coronary syndromes (including unstable angina) were at greater risk of progressing to MI if cTnI was elevated.15,16 Results from the PRISM trial showed that elevated cTnI levels could help to identify patients with unstable angina who had additional cardiac risk (especially within the first 72 hours after onset of symptoms) and who could benefit from treatment with a glycoprotein IIb/IIIa receptor antagonist.17 Thus, cTnI can play an important role in identifying patients with acute coronary syndromes who are at greater risk for cardiac events. The ESC, ACCF, AHA, and National Academy of Clinical Biochemistry (NACB) also recommend using cTnI results when making treatment decisions regarding unstable angina and non-ST segment elevation MI (NSTEMI).6,19

Studies employing sensitive troponin assays, capable of measuring troponin levels in the general population or in patients with stable cardiovascular disease, have shown that elevated troponin levels are associated with structural heart disease, risk of future cardiovascular events, and mortality.20,21 Other research has shown that elevated troponin is indicative of future risk in patients undergoing chemotherapy, following non-cardiac surgery, or with heart failure.22

BIOLGICAL PRINCIPLES OF THE PROCEDURE
The ARCHITECT STAT High Sensitive Troponin-I assay is a 2-step immunoassay to determine the presence of cTnI in human plasma and serum using CMIA technology with flexible assay protocols, referred to as Chemiluminescence Immunoassay (CMIA). In the first step, sample and anti-troponin I antibody-coated paramagnetic microparticles are combined. Cardiac troponin I present in the sample binds to the anti-troponin I coated microparticles. After incubation and wash, anti-troponin I acridinium-labeled conjugate is added in the second step. Following another incubation and wash, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of cTnI in the sample and the RLUs detected by the ARCHITECT i System optics. The concentration of cTnI is read relative to a standard curve established with calibrators of known cTnI concentrations. For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS
Reagent Kit, 100/500 Tests
Note: Some kit sizes are not available in all countries or for use on all ARCHITECT i Systems. Please contact your local distributor.

ARCHITECT STAT High Sensitive Troponin-I Reagent Kit (3P25)
- **MICROPARTICLES** 1 bottle (6.6 mL/29.0 mL) Anti-troponin I (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizer. Minimum concentration: 0.035% solids. Preservative: ProClin 300.
- **CONJUGATE** 1 bottle (5.9 mL/28.5 mL) Anti-troponin I (mouse, human chimeric, monoclonal) acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizer and human IgG. Minimum concentration: 0.1 mg/L. Preservative: ProClin 300.

Assay Diluent
ARCHITECT i Multi-Assay Manual Diluent (7D82-50)
- **MULTI-ASSAY MANUAL DILUENT** 1 Bottle (100 mL) ARCHITECT i Multi-Assay Manual Diluent containing phosphate buffered saline solution. Preservative: antimicrobial agent.

Other Reagents
ARCHITECT i Pre-Trigger Solution
- **PRE-TRIGGER SOLUTION** Pre-trigger solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT i Trigger Solution
- **TRIGGER SOLUTION** Trigger solution containing 0.35 N sodium hydroxide.

ARCHITECT i Wash Buffer
- **WASH BUFFER** Wash buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.
WANTINGS AND PRECAUTIONS

- For In Vitro Diagnostic Use.
- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

- **CAUTION:** This product contains human sourced and/or potentially infectious components. Refer to the REAGENTS section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. Therefore, all human sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens.27 Biosafety Level 228 or other appropriate biosafety practices29,30 should be used for materials that contain or are suspected of containing infectious agents.

- The following warnings and precautions apply to the Microparticles:

  **WARNING:** Contains methylisothiazolones.
  - May cause an allergic skin reaction.

  **Prevention**
  - P261 Avoid breathing mist / vapours / spray.
  - P272 Contaminated work clothing should not be allowed out of the workplace.
  - P280 Wear protective gloves / protective clothing / eye protection.

  **Response**
  - P302+P352 If ON SKIN: Wash with plenty of water.
  - P333+P313 IF skin irritation or rash occurs: Get medical advice / attention.
  - P363 Wash contaminated clothing before reuse.

  This material and its container must be disposed of in a safe way.

- The following warnings and precautions apply to the Conjugate:

  **WARNING:** Contains methylisothiazolones. Contains octoxynol.
  - May cause an allergic skin reaction.
  - Causes serious eye irritation.

  **Prevention**
  - P261 Avoid breathing mist / vapours / spray.
  - P264 Wash hands thoroughly after handling.
  - P272 Contaminated work clothing should not be allowed out of the workplace.
  - P280 Wear protective gloves / protective clothing / eye protection.

  **Response**
  - P305+P351 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
  - P337+P313 IF eye irritation persists: Get medical advice / attention.
  - P302+P352 IF ON SKIN: Wash with plenty of water.
  - P333+P313 IF skin irritation or rash occurs: Get medical advice / attention.
  - P363 Wash contaminated clothing before reuse.

  This material and its container must be disposed of in a safe way.

- Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

- For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

**Handling Precautions**

- Do not use reagents beyond the expiration date.
- Do not pool reagents within a kit or between reagent kits.
- Before loading the ARCHITECT STAT High Sensitive Troponin-I Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the PROCEDURE, Assay Procedure section of this package insert.
- Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.
- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
- Once a septum has been placed on the reagent bottle, do not invert the bottle as this will result in reagent leakage and may compromise assay results.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts, and have no effect on assay efficacy.

- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

**Storage Instructions**

- The ARCHITECT STAT High Sensitive Troponin-I Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, the reagents are stable until the expiration date.
- The ARCHITECT STAT High Sensitive Troponin-I Reagent Kit may be stored on board the ARCHITECT i System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT i System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded. For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

**Indications of Reagent Deterioration**

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

**INSTRUMENT PROCEDURE**

- The ARCHITECT STAT High Sensitive Troponin-I assay is designed for use with the ARCHITECT i System with STAT protocol capability.
- ARCHITECT System software version 8.10 or higher must be installed from an ARCHITECT i System CD-ROM.
- For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.
SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types
- The specimen collection tubes listed below can be used with the ARCHITECT STAT High Sensitive Troponin-I assay.
  - Lithium heparin with and without separator
  - K<sub>2</sub> EDTA, K<sub>3</sub> EDTA
  - Serum without separator
  - Serum with thrombin-based clot activator

Note: For limitations, refer to the Limitations bullets under the Preparation for Analysis and Storage subsections of the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS section.

When serial specimens are being evaluated, use the same specimen type throughout the evaluation.

The ARCHITECT i System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT STAT High Sensitive Troponin-I assay.

Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.

Specimen Conditions
- Performance has not been established for the use of the following specimen types:
  - heat-inactivated
  - pooled
  - obvious microbial contamination

Performance has not been established for the use of cadaveric specimens or body fluids other than human serum or plasma.

For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter, including cryoprecipitate.

- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation.

Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.

Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.

For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Preparation for Analysis
- Follow the tube manufacturer’s processing instructions for plasma and serum collection tubes. Gravity separation is not sufficient for specimen preparation.

- Limitations
  - For serum collection tubes, allow for proper clotting prior to analysis.

Note: Serum specimens from individuals on anticoagulant therapy may show inconsistent results due to incomplete clotting. Abbott recommends the use of plasma for rapid turnaround of results.

- Serum with thrombin-based clot activator showed acceptable results when centrifuged 30 minutes after blood draw. Other clotting times were not evaluated.

- If the specimens contain fibrin, red blood cells, or other particulate matter, including cryoprecipitate, or
  - have been stored at 2-8°C for more than 24 hours, centrifuge at a Relative Centrifugal Force (RCF) of 3,000 to 3,500 x g for 30 minutes before testing to ensure consistency in results.
  - Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.

- Process specimens as follows before testing:
  - Serum specimens:
    - centrifuge at an RCF of 3,000 to 3,500 x g for 30 minutes.
  - Plasma specimens:
    - centrifuge at an RCF of 13,000 to 13,500 x g for 30 minutes.
    - OR
    - centrifuge at an RCF of 3,000 to 3,500 x g for 10 minutes,
    - transfer the supernatant into a new centrifuge tube, taking care to avoid transfer of any pellet, and
    - spin again at an RCF of 3,000 to 3,500 x g for an additional 10 minutes.
  - Transfer the supernatant to a sample cup or secondary tube for testing. Care must be taken to avoid transfer of any pellet or lipid layer, if present.

Storage
- Specimens may be stored on or off the clot, red blood cells, or separator gel
  - at room temperature for up to 8 hours or
  - at 2-8°C for up to 72 hours.

- If testing will be delayed more than 72 hours, plasma or serum should be removed from the red blood cells, clot, or separator gel and stored at -10°C or colder for up to 30 days.

- Freeze specimens only once.

- Limitations
  - Serum with thrombin-based clot activator: after 24 hours at 2-8°C, serum should be stored at -10°C or colder.
  - Lithium heparin without separator: after freeze/thaw, results demonstrated a mean shift of +12.7%.

Shipping
- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- Specimens may be shipped on wet ice or dry ice. Do not exceed the storage time limitations listed above.
- When shipping specimens, package and label specimens in compliance with applicable regulations covering the transport of clinical specimens and infectious substances.
PROCEDURE

Materials Provided:
• 3P25 ARCHITECT STAT High Sensitive Troponin-I Reagent Kit
• Materials Required but not Provided
  • ARCHITECT / System with STAT protocol capability
  • ARCHITECT STAT High Sensitive Troponin-I assay file, may be obtained from:
    • ARCHITECT / System e-Assay CD-ROM found on www.abbottdiagnostics.com
    • ARCHITECT / System Assay CD-ROM
  • 3P25-10 ARCHITECT STAT High Sensitive Troponin-I Controls or other commercial controls
  • 7DB2-50 ARCHITECT Multi-Assay Manual Diluent
  • ARCHITECT / Trigger Solution
  • ARCHITECT / Wash Buffer
  • ARCHITECT / Reagent Kit
  • ARCHITECT / Sample Cups
  • ARCHITECT / Septum
  • ARCHITECT / Replacement Caps
  • Pipettes or pipette tips (optional) to deliver the specified volumes

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

Before loading the ARCHITECT STAT High Sensitive Troponin-I Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.

• Invert the microparticle bottle 30 times.
• Visualize inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
• If the microparticles do not resuspend, DO NOT USE. Contact your Abbott representative.

Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the Handling Precautions section of this package insert.

Load the ARCHITECT STAT High Sensitive Troponin-I Reagent Kit on the ARCHITECT / System with STAT protocol capability.
• Verify that all necessary reagents are present.
• Ensure that septums are present on all reagent bottles.

Order calibration, if necessary.
For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.

• Order tests.
  • For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.

The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 8 replicates can be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.

• Priority: 210 µL for the first test plus 160 µL for each additional test from the same sample cup.
• ≤ 3 hours on board: 210 µL for the first test plus 160 µL for each additional test from the same sample cup.
• > 3 hours on-board: replace with a fresh sample (patient specimens, controls, and calibrators).
• If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.

• Prepare calibrators and controls.
  • Mix ARCHITECT STAT High Sensitive Troponin-I Calibrators and Controls by gentle inversion before use.
  • To obtain the recommended volume requirements for the ARCHITECT STAT High Sensitive Troponin-I Calibrators and Controls, hold the bottles vertically and dispense 15 drops of each calibrator or 10 drops of each control into each respective sample cup.

• Load samples
  • For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
  • Press RUN.
  • For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
  • For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

• Specimens with a troponin I concentration exceeding 50,000.0 pg/mL are flagged with the code ">50,000.0 pg/mL" and may be diluted using the Automated Dilution Protocol or the Manual Dilution Procedure.

• Automated Dilution Protocol
  • If using the Automated Dilution Protocol, the system performs a 1:10 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.
  
  • Manual Dilution Procedure
    • The suggested dilution is 1:10.
    • For one test, add 25 µL of the patient specimen to 225 µL of ARCHITECT / Multi-Assay Manual Diluent.
    • The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution. This will be the reported result. The result should be greater than 10.0 pg/mL before the dilution factor is applied.

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

• To perform an ARCHITECT STAT High Sensitive Troponin-I calibration, test Calibrators A, B, C, D, E, and F in duplicate.
  • Calibrators should be priority loaded.
  • Calibration Range: 0.0 – 50,000.0 pg/mL.
  • A single sample of each control level must be tested to evaluate the assay calibration.
    • Ensure that assay control values are within the ranges specified in the control package insert.
    • Once an ARCHITECT STAT High Sensitive Troponin-I calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
      • A reagent kit with a new lot number is used.
      • Controls are out of range.

For detailed information on how to perform an assay calibration, refer to ARCHITECT System Operations Manual, Section 6.
QUALITY CONTROL PROCEDURES
The recommended control requirement for the ARCHITECT STAT High Sensitive Troponin-I assay is that a single sample of each control be tested once every 24 hours each day of use. If your laboratory quality control procedures require more frequent use of controls to verify test results, follow those procedures. Additional controls may be tested in conformance with applicable regulations or accreditation requirements and your laboratory’s quality control policy.

Each laboratory should establish control means and ranges to monitor the acceptable performance of the assay. If a control is out of its specified range, the associated test results are invalid and samples must be retested. Recalibration may be indicated.

Verification of Assay Claims
For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT STAT High Sensitive Troponin-I assay belongs to method group 1.

RESULTS
Calculations
- The ARCHITECT STAT High Sensitive Troponin-I assay utilizes a 4 Parameter Logistic Curve Fit data reduction method (4PLC, Y-weighted) to generate a calibration curve.

Alternate Result Units
- The default result unit for the ARCHITECT STAT High Sensitive Troponin-I assay is pg/mL. When one of the alternate result units, ng/mL, µg/L, or ng/L is selected, the following conversion factor is used by the system:
  - Conversion Formula: (Concentration in pg/mL) x (0.001) = ng/mL
  - Conversion Formula: (Concentration in pg/mL) x (0.001) = µg/L
  - Conversion Formula: (Concentration in pg/mL) x (1.0) = ng/L

Flags
Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

Measuring Interval
Measuring interval is defined as the range of values in pg/mL which meets the limits of acceptable performance for both imprecision and bias for an undiluted sample. For the verification studies described in this package insert, the range is 10 pg/mL (Limit of Quantitation - LoQ) to 50,000 pg/mL.

LIMITATIONS OF THE PROCEDURE
- A mean shift of +12.7% was observed for plasma that was removed from lithium heparin without separator tubes and stored at -10°C or colder. Refer to the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS section in this package insert for specimen limitations.
- Any condition resulting in myocardial injury can potentially increase cardiac troponin I levels.
- The ARCHITECT STAT High Sensitive Troponin-I assay results should be used in conjunction with other information such as ECG, clinical observations, and symptoms, etc.
- A single cTnI result may not be sufficient to evaluate MI. Serial blood draws are recommended for evaluation of acute coronary syndrome (ACS) patients.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as ARCHITECT STAT High Sensitive Troponin-I that employ mouse monoclonal antibodies. Additional clinical or diagnostic information may be required to determine patient status.
- Heterophilic antibodies and rheumatoid factor (RF) in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays. The presence of heterophilic antibodies or RF in a patient specimen may demonstrate anomalous values. Additional information may be required for diagnosis.
- Although the ARCHITECT STAT High Sensitive Troponin-I assay is specifically designed to minimize the effects of HAMA, heterophilic antibodies, and RF, assay results that are not consistent with other clinical observations may require additional information for diagnosis.
- Specimens from individuals with pathologically high total protein may demonstrate anomalous values. Additional information may be required for diagnosis.
- The ARCHITECT STAT High Sensitive Troponin-I assay cannot be used on the ARCHITECT i 2000 System.
- Refer to the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS section in this package insert for specimen limitations.

EXPECTED VALUES
Data in the EXPECTED VALUES section were generated using the ARCHITECT i 2000 System. Assay results obtained in individual laboratories may vary from data presented.

Any condition resulting in myocardial injury can potentially increase cardiac troponin I levels. A reference range study was conducted based on guidance from Clinical and Laboratory Standards Institute (CLSI) document C28-A3c. Specimens were collected in 3 tube types (serum separator, lithium heparin separator, K2 EDTA) from 1,531 apparently healthy individuals in a US population with normal levels of BNP, HbA1c, and estimated GFR values. Each specimen was frozen, thawed, and evaluated in replicates of one using the ARCHITECT STAT High Sensitive Troponin-I assay. The 4,593 results were used to establish the 99th percentiles below. The observed 99th percentiles described below for this population were determined using the robust statistical method described in CLSI document C28-A3c.

### Apparently Healthy Population

<table>
<thead>
<tr>
<th>Population</th>
<th>N</th>
<th>Age Range (years)</th>
<th>99th Percentile (pg/mL)</th>
<th>90% CI* (pg/mL)</th>
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<tbody>
<tr>
<td>Female</td>
<td>765</td>
<td>21 - 75</td>
<td>15.6</td>
<td>[13.8, 17.5]</td>
</tr>
<tr>
<td>Male</td>
<td>766</td>
<td>21 - 73</td>
<td>34.2</td>
<td>[28.9, 39.2]</td>
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<tr>
<td>Overall</td>
<td>1531</td>
<td>21 - 75</td>
<td>26.2</td>
<td>[23.3, 29.7]</td>
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</table>

* CI = Confidence Interval

It is recommended that each laboratory verify that the 99th percentile is transferable to its own population or establish its own 99th percentile.
SPECIFIC PERFORMANCE CHARACTERISTICS

Data in the SPECIFIC PERFORMANCE CHARACTERISTICS section were generated using the ARCHITECT i 2000sr System. Assay results obtained in individual laboratories may vary from data presented.

Precision

The ARCHITECT STAT High Sensitive Troponin-I assay is designed to have within-laboratory (total) imprecision of ≤ 10% CV with controls or panels across the range of 10 to 50,000 pg/mL. A study was performed for the ARCHITECT STAT High Sensitive Troponin-I assay with guidance from the National Committee for Clinical Laboratory Standards (NCCLS/CLSI) document EP6-A2. The ARCHITECT STAT High Sensitive Troponin-I Controls and 6 panels were assayed in replicates of 2 at 2 separate times per day for 20 days on 2 instruments using 3 reagent lots and 2 calibrator lots. Each reagent lot used a single calibration curve throughout the study. Results from this study are summarized in the following table.

## TABLE 1 - SPECIFIC PERFORMANCE CHARACTERISTICS

<table>
<thead>
<tr>
<th>Sample Level</th>
<th>Instrument</th>
<th>Reagent Lot</th>
<th>N (pg/mL)</th>
<th>Mean SD Within-Run %CV</th>
<th>Mean SD Within-Laboratory (Total) %CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Control</td>
<td>A 80</td>
<td>18.5</td>
<td>3.2</td>
<td>0.72</td>
<td>3.7</td>
</tr>
<tr>
<td></td>
<td>B 80</td>
<td>19.3</td>
<td>3.2</td>
<td>0.72</td>
<td>3.7</td>
</tr>
<tr>
<td></td>
<td>C 80</td>
<td>19.2</td>
<td>3.2</td>
<td>0.72</td>
<td>3.7</td>
</tr>
<tr>
<td>Medium Control</td>
<td>A 80</td>
<td>19.0</td>
<td>3.2</td>
<td>0.72</td>
<td>3.7</td>
</tr>
<tr>
<td></td>
<td>B 80</td>
<td>19.0</td>
<td>3.2</td>
<td>0.72</td>
<td>3.7</td>
</tr>
<tr>
<td></td>
<td>C 80</td>
<td>19.0</td>
<td>3.2</td>
<td>0.72</td>
<td>3.7</td>
</tr>
<tr>
<td>High Control</td>
<td>A 80</td>
<td>1469.1</td>
<td>268.17</td>
<td>1.8</td>
<td>4.13</td>
</tr>
<tr>
<td></td>
<td>B 80</td>
<td>15126.0</td>
<td>306.09</td>
<td>2.4</td>
<td>380.69</td>
</tr>
<tr>
<td></td>
<td>C 80</td>
<td>15159.9</td>
<td>336.55</td>
<td>2.2</td>
<td>364.08</td>
</tr>
<tr>
<td>Panel 1 (Native cTnI)</td>
<td>A 80</td>
<td>10.8</td>
<td>4.2</td>
<td>0.57</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>B 80</td>
<td>11.6</td>
<td>4.2</td>
<td>0.57</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>C 80</td>
<td>11.5</td>
<td>4.2</td>
<td>0.57</td>
<td>3.3</td>
</tr>
<tr>
<td>Panel 2 (Bio-Rad Level Low)</td>
<td>A 80</td>
<td>43.3</td>
<td>1.27</td>
<td>2.9</td>
<td>14.66</td>
</tr>
<tr>
<td></td>
<td>B 80</td>
<td>46.1</td>
<td>1.48</td>
<td>3.2</td>
<td>15.76</td>
</tr>
<tr>
<td></td>
<td>C 80</td>
<td>46.4</td>
<td>1.48</td>
<td>3.2</td>
<td>15.76</td>
</tr>
<tr>
<td>Panel 3 (Native cTnI)</td>
<td>A 80</td>
<td>195.4</td>
<td>4.73</td>
<td>2.4</td>
<td>6.52</td>
</tr>
<tr>
<td></td>
<td>B 80</td>
<td>197.3</td>
<td>4.46</td>
<td>2.3</td>
<td>5.21</td>
</tr>
<tr>
<td></td>
<td>C 80</td>
<td>196.8</td>
<td>5.12</td>
<td>2.6</td>
<td>5.76</td>
</tr>
<tr>
<td>Panel 4 (Bio-Rad Level 2)</td>
<td>A 80</td>
<td>1198.0</td>
<td>31.35</td>
<td>2.6</td>
<td>33.80</td>
</tr>
<tr>
<td></td>
<td>B 80</td>
<td>1281.3</td>
<td>33.38</td>
<td>2.6</td>
<td>40.95</td>
</tr>
<tr>
<td></td>
<td>C 80</td>
<td>1267.1</td>
<td>27.57</td>
<td>2.2</td>
<td>31.72</td>
</tr>
</tbody>
</table>
| Precision Profile

Data from the 20-day precision and limit of quantitation (LoQ) studies were evaluated together to estimate the following parameters:

### Precision Below LoQ

- 10% CV = 4.7 pg/mL
- 20% CV = 13 pg/mL

**Concentration is within the observed range of the Limit of Detection (LoD): 1.1 to 1.9 pg/mL**

### Precision at 99th Percentiles

- Female: 15.6 pg/mL = 5.3% CV
- Male: 34.2 pg/mL = 3.5% CV

### Linearity

The ARCHITECT STAT High Sensitive Troponin-I assay is designed to have a deviation from linearity of ± 10 pg/mL for samples ≤ 10 pg/mL and ± 10% for samples between 10 and 50,000 pg/mL. A linearity study based on guidance from NCCLS/CLSI document EP6-A2 was performed for the ARCHITECT STAT High Sensitive Troponin-I assay. Dilution sets with cTnI concentrations ranging from ≤ 10 pg/mL and ± 10% for samples between 10 and 50,000 pg/mL were evaluated. The observed deviation from linearity was ≤ 6.8% for samples > 50,000 pg/mL and ± 10% for samples between 10 and 50,000 pg/mL.

### Automated Dilution Procedure Verification

A study was performed to evaluate 36 samples prepared by spiking recombinant cTnI stock solution into human serum samples at concentrations between 40,000 and 500,000 pg/mL. Each specimen was tested with the automated dilution protocol and manual dilution procedure (dilution factor: 1:10). The mean difference in concentration (% Diff) was calculated for each level.* The mean difference in measured concentration was 1.6% for samples > 50,000 pg/mL and 0.4 pg/mL for samples < 10 pg/mL.

### Sensitivity (Detection Limits)

A study to determine Limit of Quantitation (LoQ), Limit of Blank (LoB), and Limit of Detection (LoD) was performed based on guidance from the NCCLS/CLSI document EP17-A. Testing was performed using 2 instruments and 2 reagent lots. The LoQ, LoB, and LoD were determined for each of the 4 reagent lot and instrument combinations.

### Limit of Quantitation

The ARCHITECT STAT High Sensitive Troponin-I assay is designed to have an LoQ of ≤ 10 pg/mL. The LoQ is defined as the lowest amount of analyte in a sample that can be accurately quantitated with bias ≤ 10% and imprecision ≤10% CV.

The observed LoQ for the ARCHITECT STAT High Sensitive Troponin-I assay ranged from 4.0 to 10.0 pg/mL across the 4 reagent lot/instrument combinations.

### Limit of Blank, Limit of Detection

The observed LoB ranged from 0.7 to 1.3 pg/mL, and the observed LoD ranged from 1.1 to 1.9 pg/mL across the 4 reagent lot/instrument combinations.
Analytical Specificity
The ARCHITECT STAT High Sensitive Troponin-I assay is designed to have analytical specificity of ≤ 0.1% cross-reactivity with skeletal troponin I and ≤ 1% cross-reactivity with cardiac troponin T and troponin C.

A study was performed for the ARCHITECT STAT High Sensitive Troponin-I assay. Specificity was determined by studying the cross-reactivity of 1000 ng/mL skeletal troponin I, 1000 ng/mL cardiac troponin T, and 1000 ng/mL troponin C in samples prepared with cTnI across the range of ≤ 10 to 45,000 pg/mL. The observed percent cross-reactivity for each potential cross-reactant at each cTnI concentration was ≤ 0.1%.

Interference
Evaluation of Potentially Interfering Drugs
In the ARCHITECT STAT High Sensitive Troponin-I assay, potential interference from various drugs is ≤ 10% at the levels tested. A study based on guidance from the CLSI document EP7-A29 was performed for the ARCHITECT STAT High Sensitive Troponin-I assay. The potentially interfering drugs listed below were tested in samples with cTnI concentrations of 15 pg/mL and 500 pg/mL. Each cTnI level was tested with potentially interfering drugs at therapeutic and high concentrations. The observed percent differences ranged from -3.1% to 4.3% at the therapeutic concentrations and -5.5% to 4.1% at the high concentrations.

<p>|</p>
<table>
<thead>
<tr>
<th>Potentially Interfering Drug</th>
<th>Therapeutic Conc.</th>
<th>High Conc.</th>
<th>Potentially Interfering Drug</th>
<th>Therapeutic Conc.</th>
<th>High Conc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylsalicylic Acid</td>
<td>200 µg/mL</td>
<td>1000 µg/mL</td>
<td>Acetylsalicylic Acid</td>
<td>200 µg/mL</td>
<td>1000 µg/mL</td>
</tr>
<tr>
<td>Adrenaline</td>
<td>60 ng/mL</td>
<td>0.37 µg/mL</td>
<td>Adrenaline</td>
<td>60 ng/mL</td>
<td>0.37 µg/mL</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>12 µg/mL</td>
<td>400 µg/mL</td>
<td>Allopurinol</td>
<td>12 µg/mL</td>
<td>400 µg/mL</td>
</tr>
<tr>
<td>Amiloride</td>
<td>0.1 µg/mL</td>
<td>40 µg/mL</td>
<td>Amiloride</td>
<td>0.1 µg/mL</td>
<td>40 µg/mL</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>10 µg/mL</td>
<td>1000 µg/mL</td>
<td>Amoxicillin</td>
<td>10 µg/mL</td>
<td>1000 µg/mL</td>
</tr>
<tr>
<td>Ascorbic Acid</td>
<td>12 µg/mL</td>
<td>300 µg/mL</td>
<td>Ascorbic Acid</td>
<td>12 µg/mL</td>
<td>300 µg/mL</td>
</tr>
<tr>
<td>Atalidione</td>
<td>1 µg/mL</td>
<td>10 µg/mL</td>
<td>Atalidione</td>
<td>1 µg/mL</td>
<td>10 µg/mL</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>11 µg/mL</td>
<td>42 µg/mL</td>
<td>Bivalirudin</td>
<td>11 µg/mL</td>
<td>42 µg/mL</td>
</tr>
<tr>
<td>Caffeine</td>
<td>12 µg/mL</td>
<td>100 µg/mL</td>
<td>Caffeine</td>
<td>12 µg/mL</td>
<td>100 µg/mL</td>
</tr>
<tr>
<td>Captopril</td>
<td>1.0 µg/mL</td>
<td>50 µg/mL</td>
<td>Captopril</td>
<td>1.0 µg/mL</td>
<td>50 µg/mL</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>5 µg/mL</td>
<td>150 µg/mL</td>
<td>Carvedilol</td>
<td>5 µg/mL</td>
<td>150 µg/mL</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>120 µg/mL</td>
<td>2500 µg/mL</td>
<td>Cefoxitin</td>
<td>120 µg/mL</td>
<td>2500 µg/mL</td>
</tr>
<tr>
<td>Cinnarizine</td>
<td>4 µg/mL</td>
<td>400 µg/mL</td>
<td>Cinnarizine</td>
<td>4 µg/mL</td>
<td>400 µg/mL</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>15 µg/mL</td>
<td>75 µg/mL</td>
<td>Clopidogrel</td>
<td>15 µg/mL</td>
<td>75 µg/mL</td>
</tr>
<tr>
<td>Cocaine</td>
<td>0.1 µg/mL</td>
<td>10 µg/mL</td>
<td>Cocaine</td>
<td>0.1 µg/mL</td>
<td>10 µg/mL</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>0.8 µg/mL</td>
<td>5 µg/mL</td>
<td>Cyclophosphamide</td>
<td>0.8 µg/mL</td>
<td>5 µg/mL</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>2.5 µg/mL</td>
<td>50 µg/mL</td>
<td>Diclofenac</td>
<td>2.5 µg/mL</td>
<td>50 µg/mL</td>
</tr>
<tr>
<td>Digoxin</td>
<td>1.0 µg/mL</td>
<td>7.5 µg/mL</td>
<td>Digoxin</td>
<td>1.0 µg/mL</td>
<td>7.5 µg/mL</td>
</tr>
<tr>
<td>Dopamine</td>
<td>0.3 µg/mL</td>
<td>900 µg/mL</td>
<td>Dopamine</td>
<td>0.3 µg/mL</td>
<td>900 µg/mL</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>10 µg/mL</td>
<td>50 µg/mL</td>
<td>Doxycycline</td>
<td>10 µg/mL</td>
<td>50 µg/mL</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>3 µg/mL</td>
<td>7 µg/mL</td>
<td>Epirubicin</td>
<td>3 µg/mL</td>
<td>7 µg/mL</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>11 µg/mL</td>
<td>250 µg/mL</td>
<td>Erythromycin</td>
<td>11 µg/mL</td>
<td>250 µg/mL</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>12 µg/mL</td>
<td>4 µg/mL</td>
<td>Fondaparinux</td>
<td>12 µg/mL</td>
<td>4 µg/mL</td>
</tr>
<tr>
<td>Furosemide</td>
<td>20 µg/mL</td>
<td>400 µg/mL</td>
<td>Furosemide</td>
<td>20 µg/mL</td>
<td>400 µg/mL</td>
</tr>
</tbody>
</table>

Conc. = Concentration
TPA = Tissue plasminogen activator

Evaluation of Potentially Interfering Endogenous Substances
In the ARCHITECT STAT High Sensitive Troponin-I assay, potential interference from endogenous substances is ≤ 10% at the levels tested. A study based on guidance from the CLSI document EP7-A29 was performed for the ARCHITECT STAT High Sensitive Troponin-I assay. Potentially interfering endogenous substances were evaluated to determine the impact on cTnI results. Samples with cTnI concentrations of 15 pg/mL and 500 pg/mL demonstrated interference within ± 10% for the potentially interfering substances listed below.

<table>
<thead>
<tr>
<th>Potentially Interfering Substance</th>
<th>Potentially Interfering Substance Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unconjugated Bilirubin</td>
<td>≤ 20.0 mg/dL</td>
</tr>
<tr>
<td>Conjugated Bilirubin</td>
<td>≤ 20.0 mg/dL</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>≤ 500.0 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≤ 3000 mg/dL</td>
</tr>
</tbody>
</table>

Total protein was evaluated using human serum albumin (HSA) and concentrated normal specimens. Samples supplemented with HSA to total protein ≤ 12 g/dL, demonstrated interference within ± 10%. Specimens were concentrated to produce elevated total protein concentrations. The concentrated specimens were supplemented with cTnI to target concentrations of 15 and 500 pg/mL. The results are presented in the following table.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Mean (Range)</th>
<th>Native cTnI Concentration Range (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAMA</td>
<td>-2.8% (-11.7% to 3.3%)</td>
<td>10.1 to 370.3</td>
</tr>
<tr>
<td>RF</td>
<td>-3.4% (-21.2% to 9.5%)</td>
<td>11.9 to 386.0</td>
</tr>
</tbody>
</table>
Clinical Results

Diagnosis

Serial sampling to detect the temporal rise and fall of cTnI levels is recommended for the differentiation of acute cardiac events from chronic cardiac disease. A prospective study was performed to assess diagnostic accuracy of the ARCHITECT STAT High Sensitive Troponin-I assay. Specimens were collected at 11 emergency departments from 1,101 subjects presenting to the emergency department with symptoms consistent with acute coronary syndrome (ACS). All subject diagnoses were adjudicated by three board certified cardiologists according to current standard of care. The observed MI prevalence in this study was 11.81%.

748 specimens with serial sampling from 130 MI subjects
7,488 specimens with serial sampling from 971 non-MI subjects

The specimens were collected in three tube types (lithium heparin separator, K₂ EDTA, serum separator) and frozen. The specimens were thawed and evaluated using the ARCHITECT STAT High Sensitive Troponin-I assay.

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

<table>
<thead>
<tr>
<th>Tube Type</th>
<th>Time Point</th>
<th>N</th>
<th>AUC</th>
<th>95% CI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>K₂ EDTA</td>
<td>Baseline</td>
<td>931</td>
<td>0.9326</td>
<td>[0.9048, 0.9604]</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours</td>
<td>942</td>
<td>0.9431</td>
<td>[0.9081, 0.9782]</td>
</tr>
<tr>
<td></td>
<td>4 - 9 Hours</td>
<td>862</td>
<td>0.9503</td>
<td>[0.9149, 0.9857]</td>
</tr>
<tr>
<td>Lithium Heparin</td>
<td>Baseline</td>
<td>951</td>
<td>0.9197</td>
<td>[0.8914, 0.9480]</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours</td>
<td>958</td>
<td>0.9349</td>
<td>[0.8996, 0.9712]</td>
</tr>
<tr>
<td>Serum Separator</td>
<td>Baseline</td>
<td>903</td>
<td>0.9498</td>
<td>[0.9190, 0.9805]</td>
</tr>
</tbody>
</table>

* CI = Confidence Interval

The results were further analyzed using the serial sampling time points collected during the emergency department visit. The results using the gender-specific 99th percentile cutoffs (female 15.6 pg/mL; male 34.2 pg/mL) are summarized in the table below.

<table>
<thead>
<tr>
<th>Tube Type</th>
<th>Time Point</th>
<th>N</th>
<th>Sensitivity (%)</th>
<th>95% CI*</th>
<th>Specificity (%)</th>
<th>95% CI*</th>
<th>Positive Predictive Value (%)</th>
<th>95% CI*</th>
<th>Negative Predictive Value (%)</th>
<th>95% CI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>K₂ EDTA</td>
<td>Baseline</td>
<td>931</td>
<td>84.44 (75.28, 91.23)</td>
<td>85.49 (82.93, 87.81)</td>
<td>38.38 (31.58, 45.54)</td>
<td>98.09 (96.82, 98.95)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours</td>
<td>942</td>
<td>90.91 (82.16, 96.27)</td>
<td>84.74 (82.17, 87.07)</td>
<td>34.65 (28.11, 41.66)</td>
<td>99.05 (98.06, 99.62)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 - 9 Hours</td>
<td>862</td>
<td>93.90 (86.34, 97.99)</td>
<td>83.33 (80.53, 85.86)</td>
<td>37.20 (30.60, 44.17)</td>
<td>99.24 (98.23, 99.78)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lithium Heparin</td>
<td>Baseline</td>
<td>951</td>
<td>81.05 (71.72, 88.37)</td>
<td>83.18 (80.50, 85.62)</td>
<td>34.84 (28.58, 41.52)</td>
<td>97.53 (96.13, 98.53)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours</td>
<td>958</td>
<td>90.70 (82.49, 95.90)</td>
<td>83.03 (80.37, 85.46)</td>
<td>34.51 (28.33, 41.10)</td>
<td>98.91 (97.86, 99.53)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Separator</td>
<td>Baseline</td>
<td>884</td>
<td>87.32 (77.30, 94.04)</td>
<td>85.85 (83.27, 88.18)</td>
<td>35.03 (28.02, 42.54)</td>
<td>97.83 (97.60, 99.42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours</td>
<td>942</td>
<td>90.67 (81.71, 96.16)</td>
<td>84.54 (81.96, 86.89)</td>
<td>33.66 (27.18, 40.63)</td>
<td>99.05 (98.06, 99.62)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 - 9 Hours</td>
<td>863</td>
<td>93.15 (84.74, 97.74)</td>
<td>82.03 (79.17, 84.64)</td>
<td>32.38 (26.10, 39.16)</td>
<td>99.23 (98.22, 99.75)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* CI = Confidence Interval

The results using the overall 99th percentile cutoff (26.2 pg/mL) are summarized in the table below.

<table>
<thead>
<tr>
<th>Tube Type</th>
<th>Time Point</th>
<th>N</th>
<th>Sensitivity (%)</th>
<th>95% CI*</th>
<th>Specificity (%)</th>
<th>95% CI*</th>
<th>Positive Predictive Value (%)</th>
<th>95% CI*</th>
<th>Negative Predictive Value (%)</th>
<th>95% CI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>K₂ EDTA</td>
<td>Baseline</td>
<td>931</td>
<td>84.44 (75.28, 91.23)</td>
<td>85.73 (83.18, 88.03)</td>
<td>38.78 (31.92, 45.98)</td>
<td>98.10 (96.82, 98.95)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours</td>
<td>942</td>
<td>92.21 (83.81, 97.09)</td>
<td>85.20 (82.66, 87.50)</td>
<td>35.68 (29.03, 42.76)</td>
<td>99.19 (98.25, 99.70)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 - 9 Hours</td>
<td>862</td>
<td>93.90 (86.34, 97.99)</td>
<td>82.82 (79.99, 85.40)</td>
<td>36.49 (29.99, 43.38)</td>
<td>99.23 (98.22, 99.75)</td>
<td></td>
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<tr>
<td>Lithium Heparin</td>
<td>Baseline</td>
<td>951</td>
<td>85.26 (76.51, 91.70)</td>
<td>83.76 (81.12, 86.17)</td>
<td>36.82 (30.43, 43.56)</td>
<td>98.08 (96.81, 98.95)</td>
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<tr>
<td></td>
<td>2 - 4 Hours</td>
<td>958</td>
<td>91.86 (83.95, 96.66)</td>
<td>83.72 (81.09, 86.11)</td>
<td>35.75 (29.43, 42.45)</td>
<td>99.05 (98.05, 99.62)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Separator</td>
<td>Baseline</td>
<td>864</td>
<td>87.32 (77.30, 94.04)</td>
<td>86.35 (83.79, 88.63)</td>
<td>35.84 (28.70, 43.47)</td>
<td>98.73 (97.61, 99.42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours</td>
<td>942</td>
<td>90.70 (83.40, 97.01)</td>
<td>85.81 (83.31, 88.07)</td>
<td>35.94 (29.16, 43.16)</td>
<td>99.20 (98.27, 99.71)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 - 9 Hours</td>
<td>863</td>
<td>93.15 (84.74, 97.74)</td>
<td>84.05 (81.31, 86.54)</td>
<td>35.05 (28.36, 42.21)</td>
<td>99.25 (98.26, 99.76)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* CI = Confidence Interval

a Sensitivity = 100 × A / (A + C)
b Specificity = 100 × D / (B + D)
c Positive Predictive Value = 100 × A / (A + B)
d Negative Predictive Value = 100 × D / (C + D)
The use of delta values (difference of cTnI levels between two test points) may have the potential to improve the clinical specificity for acute coronary syndrome (ACS). An analysis of delta values was performed based on analyses described in the literature. The absolute percent difference (delta value) was calculated between each of the three time points (Baseline, 2-4 Hours, 4-9 Hours) for each subject. The following two groups of subjects were compared:

- Subjects who had an absolute percent difference greater than the given cutoff and at least one value greater than the 99th percentile
- Subjects who had an absolute percent difference less than or equal to the given cutoff or did not have any value greater than the 99th percentile

The sensitivity, specificity, positive predictive value, and negative predictive value were calculated for the given cutoffs for each tube type. The absolute percent change for lithium heparin separator tubes using the gender-specific 99th percentile cutoffs (female 15.6 pg/mL; male 34.2 pg/mL) are summarized in the table below. The K2 EDTA and serum separator results were comparable.

<table>
<thead>
<tr>
<th>Cutoff (Absolute Percent Change)</th>
<th>Time Point</th>
<th>N</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>Baseline vs. 2 - 4 Hours</td>
<td>836</td>
<td>70.77</td>
<td>93.26</td>
<td>46.94</td>
<td>97.43</td>
</tr>
<tr>
<td></td>
<td>Baseline vs. 4 - 9 Hours</td>
<td>772</td>
<td>79.17</td>
<td>90.57</td>
<td>46.34</td>
<td>97.69</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours vs. 4 - 9 Hours</td>
<td>819</td>
<td>63.24</td>
<td>94.81</td>
<td>52.44</td>
<td>96.81</td>
</tr>
<tr>
<td>50%</td>
<td>Baseline vs. 2 - 4 Hours</td>
<td>836</td>
<td>56.92</td>
<td>95.20</td>
<td>50.00</td>
<td>96.33</td>
</tr>
<tr>
<td></td>
<td>Baseline vs. 4 - 9 Hours</td>
<td>772</td>
<td>73.61</td>
<td>93.29</td>
<td>53.00</td>
<td>97.17</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours vs. 4 - 9 Hours</td>
<td>819</td>
<td>50.00</td>
<td>97.34</td>
<td>62.96</td>
<td>95.56</td>
</tr>
<tr>
<td>100%</td>
<td>Baseline vs. 2 - 4 Hours</td>
<td>836</td>
<td>36.92</td>
<td>97.80</td>
<td>58.54</td>
<td>94.84</td>
</tr>
<tr>
<td></td>
<td>Baseline vs. 4 - 9 Hours</td>
<td>772</td>
<td>61.11</td>
<td>95.00</td>
<td>55.70</td>
<td>95.96</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours vs. 4 - 9 Hours</td>
<td>819</td>
<td>42.65</td>
<td>98.40</td>
<td>70.73</td>
<td>94.31</td>
</tr>
<tr>
<td>250%</td>
<td>Baseline vs. 2 - 4 Hours</td>
<td>836</td>
<td>29.23</td>
<td>98.83</td>
<td>67.86</td>
<td>94.31</td>
</tr>
<tr>
<td></td>
<td>Baseline vs. 4 - 9 Hours</td>
<td>772</td>
<td>55.56</td>
<td>96.86</td>
<td>64.52</td>
<td>95.49</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours vs. 4 - 9 Hours</td>
<td>819</td>
<td>19.12</td>
<td>98.80</td>
<td>59.09</td>
<td>93.10</td>
</tr>
</tbody>
</table>

The absolute percent change for the lithium heparin separator tubes using the overall 99th percentile cutoff (26.2 pg/mL) are summarized in the table below. The K2 EDTA and serum separator results were comparable.

<table>
<thead>
<tr>
<th>Cutoff (Absolute Percent Change)</th>
<th>Time Point</th>
<th>N</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>Baseline vs. 2 - 4 Hours</td>
<td>836</td>
<td>70.77</td>
<td>93.51</td>
<td>47.92</td>
<td>97.43</td>
</tr>
<tr>
<td></td>
<td>Baseline vs. 4 - 9 Hours</td>
<td>772</td>
<td>79.17</td>
<td>90.71</td>
<td>46.72</td>
<td>97.69</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours vs. 4 - 9 Hours</td>
<td>819</td>
<td>63.24</td>
<td>94.67</td>
<td>51.81</td>
<td>96.60</td>
</tr>
<tr>
<td>50%</td>
<td>Baseline vs. 2 - 4 Hours</td>
<td>836</td>
<td>56.92</td>
<td>95.46</td>
<td>51.39</td>
<td>96.34</td>
</tr>
<tr>
<td></td>
<td>Baseline vs. 4 - 9 Hours</td>
<td>772</td>
<td>73.61</td>
<td>93.71</td>
<td>54.64</td>
<td>97.19</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours vs. 4 - 9 Hours</td>
<td>819</td>
<td>50.00</td>
<td>97.90</td>
<td>61.82</td>
<td>95.55</td>
</tr>
<tr>
<td>100%</td>
<td>Baseline vs. 2 - 4 Hours</td>
<td>836</td>
<td>36.92</td>
<td>97.80</td>
<td>58.54</td>
<td>94.84</td>
</tr>
<tr>
<td></td>
<td>Baseline vs. 4 - 9 Hours</td>
<td>772</td>
<td>61.11</td>
<td>95.54</td>
<td>56.41</td>
<td>95.97</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours vs. 4 - 9 Hours</td>
<td>819</td>
<td>42.65</td>
<td>98.40</td>
<td>70.73</td>
<td>94.31</td>
</tr>
<tr>
<td>250%</td>
<td>Baseline vs. 2 - 4 Hours</td>
<td>836</td>
<td>29.23</td>
<td>98.83</td>
<td>67.86</td>
<td>94.31</td>
</tr>
<tr>
<td></td>
<td>Baseline vs. 4 - 9 Hours</td>
<td>772</td>
<td>55.56</td>
<td>96.86</td>
<td>64.52</td>
<td>95.49</td>
</tr>
<tr>
<td></td>
<td>2 - 4 Hours vs. 4 - 9 Hours</td>
<td>819</td>
<td>19.12</td>
<td>98.80</td>
<td>59.09</td>
<td>93.10</td>
</tr>
</tbody>
</table>

\[a = \frac{A}{A + C}\]
\[b = \frac{D}{B + D}\]
\[c = \frac{A}{A + B}\]
\[d = \frac{D}{C + D}\]
Prognosis

The ARCHITECT STAT High Sensitive Troponin-I assay was evaluated for use as an aid in the assessment of 30-day and 90-day prognosis relative to all-cause mortality (ACM) and major adverse cardiac events (MACE) consisting of myocardial infarction, urgent revascularization, and cardiac death in subjects who present with symptoms suggestive of acute coronary syndrome (ACS).

Subjects from the diagnostic study above were followed-up for subsequent events by medical record review and/or subject/caregiver contact.

The 30-day and 90-day prognosis (Kaplan-Meier analysis) and hazard ratios (Cox regression) for the gender-specific 99th percentiles (female, 15.6 pg/mL; male, 34.2 pg/mL) are summarized in the tables below.

### 30-Day and 90-Day Prognosis Results

<table>
<thead>
<tr>
<th>Tube Type</th>
<th>Follow-Up Time Point</th>
<th>N</th>
<th>Hazard Ratio [95% CI]</th>
<th>Likelihood Ratio P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>K2 EDTA</td>
<td>30 Days</td>
<td>1064</td>
<td>3.49 [1.79, 6.88]</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>90 Days</td>
<td>1064</td>
<td>4.17 [2.52, 6.34]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Lithium Heparin</td>
<td>30 Days</td>
<td>1085</td>
<td>3.53 [1.83, 6.86]</td>
<td>0.0030</td>
</tr>
<tr>
<td>Separator</td>
<td>90 Days</td>
<td>1085</td>
<td>2.91 [2.36, 6.44]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Serum</td>
<td>30 Days</td>
<td>1027</td>
<td>3.28 [1.58, 6.73]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Separation</td>
<td>90 Days</td>
<td>1027</td>
<td>3.98 [2.34, 6.79]</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

* CI = Confidence Interval
† Censored = subject has not experienced MACE at the indicated follow-up time point.

The 30-day and 90-day prognosis (Kaplan-Meier analysis) and hazard ratios (Cox regression) for the overall 99th percentile cutoff (26.2 pg/mL) are summarized in the tables below.

### 30-Day and 90-Day Hazard Ratios

<table>
<thead>
<tr>
<th>Tube Type</th>
<th>Follow-Up Time Point</th>
<th>N</th>
<th>Hazard Ratio [95% CI]</th>
<th>Likelihood Ratio P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>K2 EDTA</td>
<td>30 Days</td>
<td>1064</td>
<td>3.49 [1.79, 6.88]</td>
<td>0.0003</td>
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<tr>
<td></td>
<td>90 Days</td>
<td>1064</td>
<td>4.17 [2.52, 6.34]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Lithium Heparin</td>
<td>30 Days</td>
<td>1085</td>
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<td>0.0030</td>
</tr>
<tr>
<td>Separator</td>
<td>90 Days</td>
<td>1085</td>
<td>2.91 [2.36, 6.44]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Serum</td>
<td>30 Days</td>
<td>1027</td>
<td>3.28 [1.58, 6.73]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Separation</td>
<td>90 Days</td>
<td>1027</td>
<td>3.98 [2.34, 6.79]</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

* ACM = all cause mortality
† Censored = subject has not experienced MACE at the indicated follow-up time point.

### BIBLIOGRAPHY


The following U.S. Patents are relevant to the ARCHITECT System or its components. There are other such patents and patent applications in the United States and worldwide.

5 468 646
5 543 524
5 545 739
5 565 570
5 669 819
5 783 699

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