ARCHITECT STAT Troponin-I

REF 2K41-27
REF 2K41-37

en

STAT Troponin-I
2K41
G1-0467/R11
B2K4Y0

Read Highlighted Changes: Revised June 2015.

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.

NAME

ARCHITECT STAT Troponin-I

INTENDED USE

ARCHITECT STAT Troponin-I is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of cardiac troponin-I in human serum and plasma on the ARCHITECT iSystem with STAT protocol capability. Troponin-I values are used to assist in the diagnosis of myocardial infarction (MI).

SUMMARY AND EXPLANATION OF THE TEST

Troponin-I (TnI) is a regulatory subunit of the troponin complex associated with the actin thin filament within muscle cells.[1] TnI, in conjunction with troponin-C and troponin-T, plays an integral role in the regulation of muscle contraction. Three distinct tissue specific isoforms of TnI 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; cardiac troponin-I (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 damage. Elevated levels of cTnI (above the values established for non-MI specimens) are detectable in serum within 4 to 6 hours after the onset of chest pain, reach peak concentrations in approximately 8 to 28 hours, and remain elevated for 3 to 10 days following MI.[2, 4, 5] Cardiac troponin 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.[6] The high specificity of cTnI measurements is beneficial in identifying cardiac injury for clinical conditions involving skeletal muscle injury resulting from surgery, trauma, extensive exercise, or muscular disease.[7-9] High tissue specificity of cardiac troponin, however, should not be confused with the specificity for the mechanism of injury (e.g., MI vs. myocarditis). When an increased value for cardiac troponin 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.[6]

The World Health Organization (WHO) criteria for defining MI are the presence of two of the following three elements: ECG changes, serum cardiac enzyme changes, and prolonged chest pain.[10] More recently, a Global Task Force with joint leadership among the European Society of Cardiology (ESC), the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), and the World Heart Federation (WHF) refined past criteria with a universal definition of myocardial infarction that also supports use of cTnI as a preferred biomarker for myocardial injury. Their universal definition of MI is a typical rise and gradual fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the 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, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.[11] The recommended criteria are based on the principle that any reliable detectable amount of myocardial necrosis, if caused by myocardial ischemia, constitutes an MI.[6] An elevated troponin value alone is not sufficient to make the diagnosis of myocardial infarction. Serial sampling is recommended to detect the temporal rise and fall of troponin levels characteristic of MI.[12, 13] In addition, other markers such as CK-MB can be used in conjunction with troponin-I results in aiding the diagnosis of MI.

Several major studies have shown that cTnI is also useful as a predictor of cardiac risk in patients with unstable angina.[14] Previous studies showed 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 is 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.[15, 17] Thus, cTnI can play an important role in identifying patients with acute coronary syndromes who are at greater risk for cardiac events. The ACCF, AHA, and the National Academy of Clinical Biochemistry (NACB) also recommend using troponin results when making treatment decisions regarding unstable angina and non-ST segment elevation MI (NSTEMI).[6, 18]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT STAT Troponin-I assay is a two-step immunoassay for the quantitative determination of cTnI in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample, assay diluent, and anti-troponin-I antibody-coated paramagnetic microparticles are combined. The Troponin-I present in the sample binds to the anti-troponin-I coated microparticles.
2. After incubation and wash, anti-troponin-I acridinium-labeled conjugate is added to create a reaction mixture.
3. Following another incubation and wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of troponin-I in the sample and the RLUs detected by the ARCHITECT iSystem optics.

   The concentration of troponin-I is read relative to a standard curve established with calibrators of known troponin-I concentrations.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Kit Contents

ARCHITECT STAT Troponin-I 2K41

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT iSystems. Please contact your local distributor.

REF	2K41-27	2K41-37
Σ	100	500
MICROPARTICLES	1 x 6.6 mL	1 x 27.0 mL
CONJUGATE	1 x 5.9 mL	1 x 26.3 mL
ASSAY DILUENT	1 x 10.0 mL	1 x 50.9 mL

MICROPARTICLES Anti-troponin-I (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine and goat) stabilizers. Minimum concentration: 0.075% solids. Preservatives: antimicrobial agents.

CONJUGATE Anti-troponin-I (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 320.0 ng/mL. Preservative: ProClin 300.

ASSAY DILUENT Troponin-I Assay Diluent, containing protein (bovine and goat) stabilizers in phosphate buffer. Preservative: ProClin 300.

Other Reagents

PRE-TRIGGER SOLUTION ARCHITECT Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

WASH BUFFER ARCHITECT Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

Warnings and Precautions

- **IVD**
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[19-22]

The following warnings and precautions apply to: **ASSAY DILUENT** and **CONJUGATE**	
	
WARNING	Contains methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / 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.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the 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 an open 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.

Reagent Storage

When stored and handled as directed, reagents are stable until the expiration date.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8°C	Until expiration date	May be used immediately after removal from 2-8°C storage. Store in upright position.
On board	System temperature	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 iSystem. 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 Troponin-I assay file must be installed on the ARCHITECT iSystem with STAT protocol capability prior to performing the assay.

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.

Alternate Result Units

The default result unit for the ARCHITECT STAT Troponin-I assay is ng/mL.

Edit assay parameter "Result concentration units" to select an alternate unit.

Conversion formula(s):

(Concentration in ng/mL) x (1.0) = (Concentration in µg/L)

(Concentration in ng/mL) x (1000.0) = (Concentration in ng/L)

Default result unit	Conversion factor	Alternate result unit
ng/mL	1.0	µg/L
ng/mL	1000.0	ng/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Verified specimen types to be used with this assay:

Specimen Types	Collection Tubes
Serum	Serum
Plasma	Heparin

- For serum specimens, ensure that complete clot formation has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting times. If the specimen is centrifuged before complete clot formation, the presence of fibrin may cause erroneous results.

Abbott Laboratories recommends the use of heparinized plasma specimens for the ARCHITECT STAT Troponin-I assay.

- When serial specimens are being evaluated, use the same specimen type throughout the evaluation.
- The instrument 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 assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - obvious microbial contamination
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human heparinized plasma or serum.
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Each laboratory should follow the tube manufacturer's processing instructions for heparinized plasma and serum collection tubes and ensure it is compatible with the ARCHITECT STAT Troponin-I assay.
- Inadequate centrifugation of the specimen may cause an erroneous result.
- Thaw frozen specimens and mix thoroughly by LOW speed vortexing or by gently inverting, then centrifuge at 2,500-3,000 x g for 10 minutes prior to use to remove particulate matter and to ensure consistency in the results. **Thaw specimens only once.**
- If a lipid layer forms on the specimen surface, avoid the lipid layer when withdrawing the specimen.
- To ensure consistency in results, centrifuge specimens before testing if
  - they contain fibrin, red blood cells, or other particulate matter or
  - they were frozen and thawed.
- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.
- 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.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	Room temperature	8 hours
	2-8°C	≤ 72 hours
	-10°C or colder	≤ 30 days

Test all samples (patient specimens, controls, and calibrators) within 3 hours of being placed on board the ARCHITECT iSystem. Refer to the ARCHITECT System Operations Manual, Section 5, for a more detailed discussion of on-board sample storage constraints.

If testing will be delayed more than 8 hours, remove the plasma or serum from the cells, clot, or gel.

Specimens removed from the cells, clot, or gel may be stored up to 72 hours at 2-8°C or stored frozen (-10°C or colder) prior to being tested.

Specimens can be stored up to 30 days frozen at -10°C or colder.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Prior to shipping, remove the plasma or serum specimen from the cells, clot, or gel.
- Ship frozen on dry ice.
- Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

2K41 ARCHITECT STAT Troponin-I Reagent Kit

Materials Required but not Provided

- ARCHITECT STAT Troponin-I Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 2K41-01 ARCHITECT STAT Troponin-I Calibrators
- 2K41-10 ARCHITECT STAT Troponin-I Controls
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

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

Assay Procedure

- Before loading the 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.**
  - Visually 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 local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Reagent Handling** section of this package insert.
- Load the reagent kit on the ARCHITECT iSystem.

- 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.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 10
  - Priority:

    Sample volume for first test: 165 µL

    Sample volume for each additional test from same sample cup: 115 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 165 µL

    Sample volume for each additional test from same sample cup: 115 µL
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT STAT Troponin-I Calibrators and Controls.
  - ARCHITECT STAT Troponin-I Calibrators and Controls should be mixed according to instructions in their respective package inserts.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 9 drops

    for each control: 165 µL
- 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 value exceeding 50.00 ng/mL (50.00 µg/L) are flagged with the code "> 50.00" and may be diluted using either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a 1:9 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.

Specimens with a troponin-I value exceeding 440.00 ng/mL (440.00 µg/L) are flagged with the code ">440.00" when run using the Automated Dilution Protocol. These specimens may be diluted by the following Manual Dilution Procedure.

Manual Dilution Procedure

1. Suggested dilution: 1:20
2. Prior to diluting the specimen, dispense several drops of ARCHITECT STAT Troponin-I Calibrator A into a clean test tube for use in the next step.
3. Add 10 µL of the patient specimen to 190 µL of ARCHITECT STAT Troponin-I Calibrator A.
4. 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 and report the result. The result should be > 2.5 ng/mL (2.5 µg/L) before the dilution factor is applied.

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

Calibration

- Test Calibrators A-F in duplicate. The calibrators should be priority loaded.

  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 respective control package insert.
- Calibration Range: 0.00 - 50.00 ng/mL (0.00 - 50.00 µg/L).
- Once an ARCHITECT STAT 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 or
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Quality Control Procedures

The recommended control requirement for the ARCHITECT STAT Troponin-I assay is that a single sample of each control level be tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

The ARCHITECT STAT Troponin-I Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and must be retested. Recalibration may be indicated.

For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

The ARCHITECT STAT Troponin-I assay belongs to method group 1.

RESULTS

Calculation

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

For information on alternate result units, refer to the **INSTRUMENT PROCEDURE, Alternate Result Units** section of this package insert.

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.

LIMITATIONS OF THE PROCEDURE

- Cardiac troponin-I levels can be increased in any condition resulting in cardiac cell damage. For MI diagnostic purposes, the ARCHITECT STAT Troponin-I results should be used in conjunction with other information such as cardiac marker results (e.g., CK-MB and/or myoglobin), ECG, clinical observations and symptoms, etc.
- 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 that employ mouse monoclonal antibodies. Additional clinical or diagnostic information may be required to determine patient status.[23, 24]
- A single negative troponin-I result is not sufficient to declare that a patient has not had a heart attack or cardiac damage. Serial negative blood draws over time are recommended before patients are classified as negative for a heart attack.[6, 25]

- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. The presence of heterophilic antibodies in a patient specimen may cause anomalous values to be observed. Additional information may be required for diagnosis.[26]
- Although the ARCHITECT STAT Troponin-I assay is specifically designed to minimize the effects of HAMA and heterophilic antibodies, assay results that are not consistent with other clinical observations may require additional information for diagnosis.
- Refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section in this package insert for specimen limitations.
- *In vitro* studies suggest the measured level of cardiac troponin-I in serum and plasma specimens may be decreased in the presence of streptokinase or tissue-type plasminogen activator.
- ARCHITECT STAT Troponin-I is not intended to be used on the ARCHITECT i2000 System.

EXPECTED VALUES

It is recommended that each laboratory establish its own reference range, which may be unique to the population it serves depending upon geographical, patient, dietary, or environmental factors.

Any condition resulting in myocardial cell damage can potentially increase cardiac troponin-I levels. Published studies have documented that these conditions include, but are not limited to, angina, unstable angina, congestive heart failure, myocarditis, cardiac surgery, or invasive testing and noncardiac related causes such as pulmonary embolism, renal failure, and sepsis.[27-30]

Serial sampling is recommended to detect the temporal rise and fall of troponin levels characteristic of MI.[12, 13]

For diagnostic cutoff and additional information, refer to the SPECIFIC PERFORMANCE CHARACTERISTICS, Clinical Performance section in this package insert.

A reference range study was conducted based on guidance from Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) Protocol C28-A2.[31] Apparently healthy individuals were evaluated in replicates of one using the ARCHITECT STAT Troponin-I assay. Heparinized plasma specimens were used to establish the normal ranges below.* The observed 99th percentile was determined to be statistically equivalent for heparinized plasma and serum specimens based on the total population tested.

Apparently Healthy Population			
Population	n	Age Range	99th Percentile (ng/mL, µg/L)
Female	225	18-62	0.013
Male	224	18-63	0.033
TOTAL	449	18-63	0.028

* Representative data; results in individual laboratories may vary from these data.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT STAT Troponin-I assay precision is ≤ 10% total CV for samples ≥ 0.20 ng/mL (≥ 0.20 µg/L). A study was performed for the ARCHITECT STAT Troponin-I assay with guidance from the CLSI (formerly NCCLS) Protocol EP5-A.[32] ARCHITECT STAT Troponin-I Controls, Cardiac Multiconstituent Controls (MCC) and two human panels were assayed using three lots of reagents, in replicates of two at two separate times per day for 20 days on two instruments. Each reagent lot used a single calibration curve throughout the study. Data from this study are summarized in the following table.*

Sample	Instrument	Reagent Lot	n	Mean Conc. Value (ng/mL, µg/L)	Within Run SD	Within Run %CV	Total Run SD	Total Run %CV
Low Control	1	A	80	0.117	0.006	5.3	0.007	5.6
		B	80	0.116	0.005	4.5	0.006	5.3
		C	80	0.118	0.006	4.9	0.007	5.8
	2	A	80	0.103	0.005	5.1	0.006	5.8
		B	80	0.113	0.005	4.1	0.005	4.5
		C	80	0.121	0.006	5.2	0.007	5.7
Medium Control	1	A	80	0.498	0.020	3.9	0.024	4.9
		B	80	0.478	0.015	3.1	0.019	4.0
		C	80	0.478	0.013	2.7	0.018	3.8
	2	A	80	0.470	0.017	3.7	0.025	5.3
		B	80	0.483	0.015	3.2	0.021	4.4
		C	80	0.499	0.018	3.6	0.021	4.2
High Control	1	A	80	13.126	0.379	2.9	0.450	3.4
		B	80	12.472	0.337	2.7	0.469	3.8
		C	80	12.444	0.337	2.7	0.379	3.0
	2	A	80	13.695	0.398	2.9	0.465	3.4
		B	80	12.697	0.360	2.8	0.508	4.0
		C	80	12.717	0.453	3.6	0.456	3.6
Low MCC	1	A	80	0.474	0.017	3.6	0.017	3.7
		B	80	0.481	0.015	3.2	0.018	3.8
		C	80	0.496	0.015	3.0	0.016	3.2
	2	A	80	0.446	0.017	3.8	0.018	4.0
		B	80	0.488	0.019	3.9	0.020	4.1
		C	80	0.517	0.021	4.0	0.022	4.3
Medium MCC	1	A	80	3.278	0.093	2.8	0.104	3.2
		B	80	3.313	0.107	3.2	0.111	3.3
		C	80	3.392	0.104	3.1	0.116	3.4
	2	A	80	3.265	0.120	3.7	0.126	3.9
		B	80	3.330	0.127	3.8	0.132	4.0
		C	80	3.466	0.125	3.6	0.126	3.6
High MCC	1	A	80	10.876	0.306	2.8	0.364	3.3
		B	80	10.864	0.245	2.3	0.249	2.3
		C	80	11.352	0.298	2.6	0.298	2.6
	2	A	80	11.091	0.329	3.0	0.337	3.0
		B	80	11.140	0.347	3.1	0.364	3.3
		C	80	11.473	0.359	3.1	0.364	3.2
Panel 1	1	A	80	0.327	0.008	2.4	0.010	3.0
		B	80	0.349	0.010	2.8	0.010	2.8
		C	80	0.359	0.010	2.9	0.010	2.9
	2	A	80	0.299	0.011	3.6	0.011	3.6
		B	80	0.348	0.010	2.8	0.011	3.1
		C	80	0.375	0.011	3.1	0.012	3.1
Panel 2	1	A	80	1.928	0.063	3.3	0.065	3.4
		B	80	1.953	0.060	3.1	0.063	3.2
		C	80	2.003	0.074	3.7	0.079	3.9
	2	A	80	1.903	0.051	2.7	0.063	3.3
		B	80	1.998	0.062	3.1	0.065	3.2
		C	80	2.100	0.070	3.3	0.076	3.6

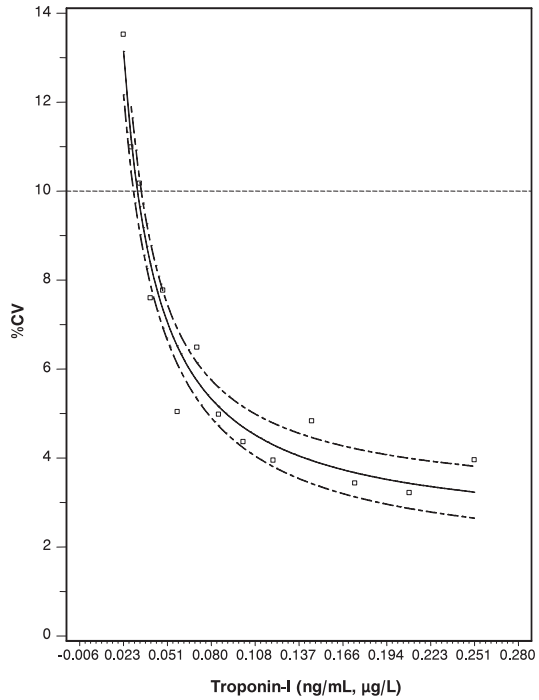
* Representative data; results in individual laboratories may vary from these data.

Precision Profile

The ARCHITECT STAT Troponin-I assay concentration at 10% CV is ≤ 0.10 ng/mL (≤ 0.10 µg/L). In a study, human panels (n = 14) were prepared to concentrations ranging from 0.02 ng/mL to 0.25 ng/mL (0.02 µg/L to 0.25 µg/L). Testing was performed with guidance from the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Protocol.[33] Panels were tested in replicates of 2 over 10 days on one instrument using two reagent lots and three calibrations for a total of 40 replicates per panel. The total %CVs (combining variance components for replicate, run, day, and reagent lot) were calculated and plotted against the mean concentration.

A reciprocal curve was fitted through the data and the 10% CV value was estimated as the concentration corresponding to the 10% CV level of the fitted curve. In this study, the lowest ARCHITECT STAT Troponin-I assay value exhibiting a 10% CV was 0.032 ng/mL (0.032 µg/L). Individual laboratory results may vary from this study due to differences in the testing protocol, and variation between instruments, calibrations, reagents, and replicates. Data from this study are summarized in the following graph*.

Precision Profile



* Representative data; results in individual laboratories may vary from these data.

Dilution Linearity

The ARCHITECT STAT Troponin-I assay recovers diluted specimens within 20% of the expected result. A dilution linearity study was performed evaluating ARCHITECT STAT Troponin-I with specimens, which had undiluted values that ranged between 10.0 and 50.4 ng/mL (10.0 and 50.4 µg/L). These specimens were diluted manually using normal human serum at various dilution factors and % recovery results are summarized in the following table.*

Sample ID	Dilution Factor	Mean Expected Value (ng/mL, µg/L)	Mean Observed Value (ng/mL, µg/L)	% Recovery**
1	Undiluted	9.969	9.969	---
	1:2	4.984	4.860	98
	1:20	0.498	0.463	93
	1:50	0.199	0.205	103
2	Undiluted	25.222	25.222	---
	1:2	12.611	12.414	98
	1:20	1.261	1.261	100
	1:50	0.504	0.491	97
3	Undiluted	39.023	39.023	---
	1:2	19.511	19.206	98
	1:20	1.951	1.971	101
	1:50	0.780	0.762	98
4	Undiluted	42.589	42.589	---
	1:2	21.294	20.320	95
	1:20	2.129	2.108	99
	1:50	0.852	0.801	94
5	Undiluted	43.740	43.740	---
	1:2	21.870	20.581	94
	1:20	2.187	2.149	98
	1:50	0.875	0.866	99
6	Undiluted	50.354	50.354	---
	1:2	25.177	24.815	99
	1:20	2.518	2.087	83
	1:50	1.007	0.842	84

* Representative data; results in individual laboratories may vary from these data.

$$\text{** \% Recovery} = \frac{\text{Mean Observed Value (ng/mL, µg/L)}}{\text{Mean Expected Value (ng/mL, µg/L)}} \times 100$$

Autodilution Verification

Recovery performance was evaluated for the autodilution method. A study was performed evaluating the recovery of 29 serum and 27 heparinized plasma specimens using the ARCHITECT Troponin-I autodilution method resulting in a mean % Recovery** of 108.3% for serum specimens and 109.4% for heparinized plasma specimens.*

$$\text{** \% Recovery} = \frac{\text{Mean Observed Value (ng/mL)}}{\text{Mean Undiluted Value (ng/mL)}} \times 100$$

* Representative data; results in individual laboratories may vary from these data.

Analytical Sensitivity

The ARCHITECT STAT Troponin-I assay analytical sensitivity is ≤ 0.01 ng/mL (≤ 0.01 µg/L) at the 95% level of confidence (n = 36 runs, 10 replicates of Calibrator A and 4 replicates of Calibrator B per run). Analytical sensitivity is defined as the concentration at two standard deviations above the ARCHITECT STAT Troponin-I Calibrator A (0.00 ng/mL, 0.00 µg/L) grand mean and represents the lowest concentration of troponin that can be distinguished from zero.

Analytical Specificity

The ARCHITECT STAT Troponin-I assay analytical specificity is ≤ 0.1% crossreactivity with skeletal troponin-I and ≤ 1% with cardiac troponin-C and cardiac troponin-T. A study based on guidance from CLSI (formerly NCCLS) Protocol EP7-A[34] was performed for the ARCHITECT STAT Troponin-I assay. Specificity of the assay was determined by studying the cross-reactivity of the following compounds in normal human serum.*

Cross-reactant	Cross-reactant Concentration (ng/mL, µg/L)	% Cross Reactivity
Skeletal troponin-I	100	0.07
Cardiac troponin-C	1000	0.00
Cardiac troponin-T	1000	0.32

* Representative data; results in individual laboratories may vary from these data.

Interference

Potential interference from various drugs and elevated levels of bilirubin, hemoglobin, triglycerides, and total protein in the ARCHITECT STAT Troponin-I assay is ≤ 15% at the levels indicated. A study based on guidance from the CLSI (formerly NCCLS) Protocol EP7-A[34] was performed for the ARCHITECT STAT Troponin-I assay. Troponin-I negative specimens and specimens with troponin-I levels between 0.5 and 3.0 ng/mL (0.5 and 3.0 µg/L) were tested with the following potentially interfering compounds.

Drug	Drug Concentration	Drug	Drug Concentration
Abciximab	20 µg/mL	Ibuprofen	500 µg/mL
Acetaminophen	250 µg/mL	Low MW Heparin	5 U/mL
Acetylsalicylic Acid	600 µg/mL	Methyldopa	25 µg/mL
Allopurinol	400 µg/mL	Nifedipine	60 µg/mL
Ambroxol	400 µg/mL	Nitrofurantoin	64 µg/mL
Ampicillin	50 µg/mL	Nystatin	7.5 µg/mL
Ascorbic Acid	40 µg/mL	Oxytetracycline	5 µg/mL
Atenolol	10 µg/mL	Phenytoin	100 µg/mL
Caffeine	100 µg/mL	Propranolol	5 µg/mL
Captopril	50 µg/mL	Quinidine	20 µg/mL
Cinnarizine	400 µg/mL	Sodium Heparin	8 U/mL
Cocaine	10 µg/mL	Streptokinase*	31.3 U/mL

Drug	Drug Concentration	Drug	Drug Concentration
Diclofenac	50 µg/mL	Theophylline	75 µg/mL
Digoxin	7.5 µg/mL	t-PA*	2.3 µg/mL
Dopamine	900 µg/mL	Trimethoprim	75 µg/mL
Eptifibatide	7 µg/mL	Verapamil	160 µg/mL
Erythromycin	200 µg/mL	Warfarin	30 µg/mL
Furosemide	400 µg/mL		

* *In vitro* concentrations of streptokinase and t-PA would be below interfering concentrations within 2 hours of administration based on each drug's expected half-life (t½).[35, 36]

Potentially Interfering Substance	Potentially Interfering Substance Concentration
Bilirubin	20 mg/dL
Hemoglobin	500 mg/dL
Total Protein (Low)	4 g/dL
Total Protein (High)	10 g/dL
Triglycerides	1000 mg/dL

Evaluation of Potentially Interfering Clinical Conditions

The ARCHITECT STAT Troponin-I assay was evaluated using specimens with HAMA and Rheumatoid Factor (RF) to further assess the clinical specificity. Eleven specimens positive for HAMA and ten specimens positive for RF were evaluated for % interference with troponin-I levels spiked between 0.5 and 1.0 ng/mL (0.5 and 1.0 µg/L); % interference results are summarized in the following table.*

Clinical Condition	Number of Specimens	% Interference
HAMA	11	-4.5
RF	10	-3.5

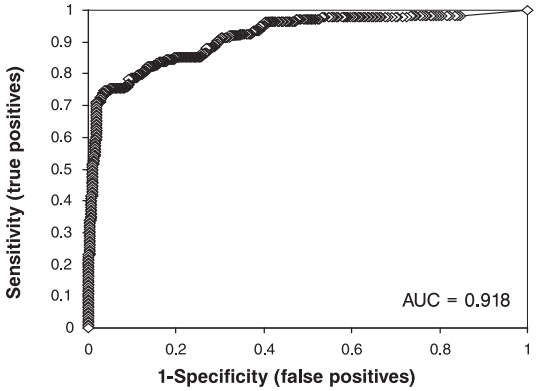
* Representative data; results in individual laboratories may vary from these data.

Clinical Performance

The ARCHITECT STAT Troponin-I assay diagnostic cutoff is 0.30 ng/mL (0.30 µg/L). A study based on guidance from CLSI (formerly NCCLS) Protocol GP10-A[37] was performed for the ARCHITECT STAT Troponin-I assay. Specimens from the following populations were collected from four clinical sites and evaluated using the ARCHITECT STAT Troponin-I assay:

- 174 specimens from 77 MI patients as diagnosed according to WHO criteria.
- 778 specimens from 366 non-MI patients as diagnosed according to WHO criteria.

All troponin-I values were used to determine the diagnostic cutoff by receiver operator characteristics (ROC) curve analysis and to determine the optimum clinical sensitivity and specificity.[37] The following graph depicts the ROC curve using these specimens.*



These data were further analyzed using time stratification from time of admission to the medical center and compared to another commercially available cTnI diagnostic assay (using the manufacturer's recommended MI cutoff). The data are summarized in the following table.*

		Hours Post Admission		
		0-6	6-12	12-24
ARCHITECT STAT Troponin-I	% Sensitivity	60.0	78.6	91.7
(cutoff = 0.30 ng/mL, 0.30 µg/L)	% Specificity	95.4	94.6	96.5
Another Commercially Available cTnI Assay	% Sensitivity	50.0	67.9	72.9
(cutoff = 0.50 ng/mL, 0.50 µg/L)	% Specificity	98.3	98.5	98.8
WHO MI Positive (n)		70	56	48
WHO MI Negative (n)		346	259	173
Total Specimens (n)		416	315	221

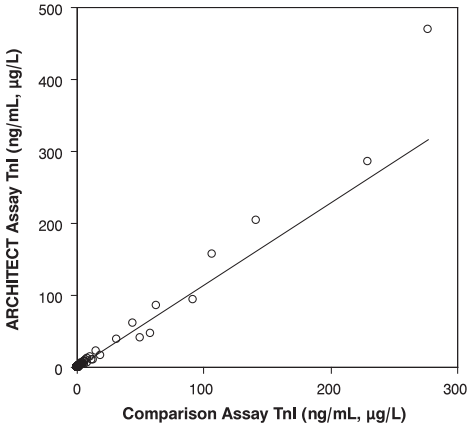
* Representative data; results in individual laboratories may vary from these data.

As with all diagnostic tests, each laboratory should establish its own diagnostic cutoff to assure proper representation of specific populations and to reflect current practice and criteria for MI diagnosis at their institution.

Method Comparison

The ARCHITECT STAT Troponin-I assay method comparison correlation coefficient (r) is ≥ 0.90. A study was performed where specimens were tested in replicates of one using ARCHITECT STAT Troponin-I over a period of three calibration cycles with three reagent lots on three instruments and compared to a commercially available diagnostic kit (Comparison Assay). Data from this study were analyzed using the Passing-Bablok[38] regression method and are summarized in the following table and scatter plot.*

ARCHITECT STAT Troponin-I vs. Comparison Assay				
Regression Method	n	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)
Passing-Bablok**	460	1.14 (1.09 to 1.19)	-0.003 (-0.004 to -0.002)	0.98



Sample Range (ARCHITECT STAT Troponin-I):
0-469 ng/mL (0-469 µg/L)

Sample Range (Comparison Assay): 0-277 ng/mL (0-277 µg/L)

* Representative data; results in individual laboratories may vary from these data.

** A linear regression method with no special assumptions regarding the distribution of the samples and measurement errors.

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Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
ASSAY DILUENT	Assay Diluent
CONJUGATE	Conjugate
CONTROL NO.	Control Number
EC REP	Authorized Representative in the European Community
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCED FOR ABBOTT BY	Produced for Abbott by
PRODUCT OF USA	Product of USA
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WARNING: SENSITIZER	Warning: May cause an allergic reaction.
WASH BUFFER	Wash Buffer

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