ARCHITECT

SYSTEM

en

*STAT* Troponin-I

REF 2K41

840653/R08

**Read Highlighted Changes**
**Revised March, 2010**

# *STAT* 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

| | | | |
|---|---|---|---|
| REF | List Number | SN | Serial Number |
| IVD | *In Vitro* Diagnostic Medical Device | REACTION VESSELS | Reaction Vessels |
| LOT | Lot Number | SAMPLE CUPS | Sample Cups |
| | Expiration Date | SEPTUM | Septum |
| 2°C 8°C | Store at 2-8°C | REPLACEMENT CAPS | Replacement Caps |
| | Consult instructions for use | REAGENT LOT | Reagent Lot |
| EC REP | Authorized Representative | ASSAY CD-ROM | Assay CD-ROM |
| | Manufacturer | CONTROL NO. | Control Number |

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

## 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 *i* System with *STAT* protocol capability. Troponin-I values are used to assist in the diagnosis of myocardial infarction (MI) and in the risk stratification of patients with acute coronary syndromes (including unstable angina and non-ST elevation) with respect to relative risk of mortality, myocardial infarction, or increased probability of ischemic events.

## SUMMARY AND EXPLANATION OF 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 99$^{th}$ 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 99$^{th}$ 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 to determine the presence of cTnI in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

In the first step, sample, assay diluent and anti-troponin-I antibody-coated paramagnetic microparticles are combined. 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 then added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of troponin-I in the sample and the RLUs detected by the ARCHITECT *i** System 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.

* *i* = immunoassay

## REAGENTS

**Reagent Kit, 100 Tests/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* Troponin-I Reagent Kit (2K41)

- **MICROPARTICLES** 1 or 4 Bottles (6.6 mL/27.0 mL) Anti-troponin-I (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine and goat) stabilizers. Preservatives: antimicrobial agents.
- **CONJUGATE** 1 or 4 Bottles (5.9 mL/26.3 mL) Anti-troponin-I (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizer. Preservative: ProClin 300.
- **ASSAY DILUENT** 1 or 4 Bottles (10.0 mL/50.9 mL) Troponin-I Assay Diluent, containing protein (bovine and goat) stabilizers in phosphate buffer. Preservative: ProClin 300.

**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.

## WARNINGS AND PRECAUTIONS

- **IVD**
- **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 requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens[19]. Biosafety Level 2[20] or other appropriate biosafety practices[21,22] should be used for materials that contain or are suspected of containing infectious agents.
- The ARCHITECT *STAT* Troponin-I Assay Diluent and Conjugate contain methylisothiazolones, which are components of ProClin, and are classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.

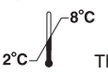
R43 May cause sensitization by skin contact.
S24 Avoid skin contact.
S35 This material and its container must be disposed of in a safe way.
S37 Wear suitable gloves.
S46 If swallowed, seek medical advice immediately and show this container or label.

- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.
- For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

### Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between reagent kits.**
- Prior to loading the ARCHITECT *STAT* Troponin-I Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that 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 which 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* 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, reagents are stable until the expiration date.
- The ARCHITECT *STAT* 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 on-board 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 may be invalid and may require retesting. 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 *i* System with *STAT* protocol capability from the ARCHITECT *i* Assay CD-ROM Addition B prior to performing the assay. For detailed information on assay file installation and on 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.
- The default result unit for the ARCHITECT *STAT* Troponin-I assay is ng/mL. For information regarding alternate result units, see the **RESULTS** section of this package insert.

## SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

**Specimen Types**

- Heparinized plasma, EDTA plasma and serum specimens may be used for the ARCHITECT *STAT* Troponin-I assay.
- 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 plasma specimens for the ARCHITECT *STAT* Troponin-I assay.**

- Studies were performed comparing EDTA plasma and serum specimens to heparinized plasma specimens. The results from these studies are summarized below.*

  EDTA plasma compared to heparinized plasma correlation:
  $y = 0.941x - 0.005$, $r = 0.9996$

  Serum compared to heparinized plasma correlation:
  $y = 1.144x - 0.018$, $r = 0.9948$
- 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 the correct specimen type is used in the ARCHITECT *STAT* Troponin-I assay.

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

**Specimen Conditions**

- Do not use heat-inactivated specimens.
- Do not use samples with obvious microbial contamination.
- Performance has not been established using cadaver specimens or body fluids other than human heparinized plasma, EDTA plasma, or serum.
- Ensure specimens are free of fibrin, red blood cells, and other particulate matter.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- Inspect all samples for bubbles. Remove bubbles prior to analysis.

**Preparation for Analysis**

- Refer to the specimen collection tube manufacturer's instructions as well as these package insert instructions for specimen collection and preparation for analysis. Each laboratory should follow the tube manufacturer's processing instructions for 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.

**Storage**

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

Heparinized Plasma and Serum

- 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.

EDTA Plasma

- If testing will be delayed more than 6 hours, remove the plasma from the cells or gel. Specimens removed from cells 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.

**Shipping**

- When shipping specimens, 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 specimens frozen on dry ice.

## PROCEDURE

**Materials Provided**

- 2K41 ARCHITECT *STAT* Troponin-I Reagent Kit

**Materials Required but not Provided**

- ARCHITECT *i* System with *STAT* protocol capability
- 3K51 ARCHITECT *i* **ASSAY CD-ROM** - US - Addition B
- 3K53 ARCHITECT *i* **ASSAY CD-ROM** - WW (excluding US) - Addition B
- 2K41-01 ARCHITECT *STAT* Troponin-I Calibrators
- 2K41-10 ARCHITECT *STAT* Troponin-I Controls

- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

**Assay Procedure**

- Before loading the ARCHITECT *STAT* Troponin-I Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment:
  - **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 Laboratories representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions on placing septums on bottles, refer to the **Handling Precautions** section of this package insert.
- 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, refer to the ARCHITECT System Operations Manual, Section 5.
- Load the ARCHITECT *STAT* Troponin-I Reagent Kit on the ARCHITECT *i* System with *STAT* protocol capability.
  - Verify that all necessary assay reagents are present. Ensure that septums are present on all reagent bottles.
- The minimum sample volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.
  - Priority: 165 µL for the first ARCHITECT *STAT* Troponin-I test plus 115 µL for each additional ARCHITECT *STAT* Troponin-I test from the same sample cup.
  - ≤ 3 hours on board: 165 µL for the first ARCHITECT *STAT* Troponin-I test plus 115 µL for each additional ARCHITECT *STAT* Troponin-I test from the same sample cup.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrators and controls.
  - ARCHITECT *STAT* Troponin-I Calibrators and Controls should be mixed according to instructions in their respective package inserts.
  - To obtain the recommended volume requirements for the ARCHITECT *STAT* Troponin-I Calibrators, hold the bottles **vertically** and dispense 9 drops of each calibrator into each respective sample cup. Dispense 165 µL 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 Operations Manual, Section 3.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9. If your laboratory requires more frequent maintenance, follow those 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 with the Automated Dilution Procedure or the Manual Dilution Procedure.

Automated Dilution Protocol

- If using the 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

- Manual dilutions should be performed as follows:
  - The suggested dilution for a troponin-I test is 1:20.
  - 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.
  - Add 10 µL of the patient specimen to 190 µL of ARCHITECT *STAT* Troponin-I Calibrator A.
  - 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 concentration of the specimen diluted (before dilution factor is applied) should be 2.5 ng/mL (2.5 µg/L) or greater.
  - For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

**Calibration**

- To perform an ARCHITECT *STAT* Troponin-I calibration, test the Calibrators A, B, C, D, E, and F in duplicate. A single sample of each ARCHITECT *STAT* Troponin-I Control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the control package insert. Calibrators should be priority loaded.
- 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.
  - 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 a single sample of each control level to 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. Use ARCHITECT *STAT* Troponin-I Calibrators in place of MasterCheck as described in the ARCHITECT System Operations Manual, Appendix B.

## RESULTS

**Calculation**

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

**Alternate Result Units**

- The default result unit for the ARCHITECT *STAT* Troponin-I assay is ng/mL. When the alternate result unit, µg/L, is selected, the conversion factor used by the system is 1.0. When the alternate result unit, ng/L, is selected, the conversion factor used by the system is 1000.0.
- Conversion Formula: (Concentration in ng/mL) x (1.0) = µg/L
- Conversion Formula: (Concentration in ng/mL) x (1000.0) = 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.

## 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).[23] Such specimens may show either falsely elevated or depressed values when tested with assay kits that employ mouse monoclonal antibodies.[24] Additional clinical or diagnostic information may be required to determine patient status.
- 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.[26] The presence of heterophilic antibodies in a patient specimen may cause anomalous values to be observed. Additional information may be required for diagnosis.
- 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 *i* 2000 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 non-cardiac 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 99$^{th}$ percentile was determined to be statistically equivalent for heparinized plasma, EDTA plasma and serum specimens based on the total population tested.

**Apparently Healthy Population**

| Population | n | Age Range | 99$^{th}$ 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 |

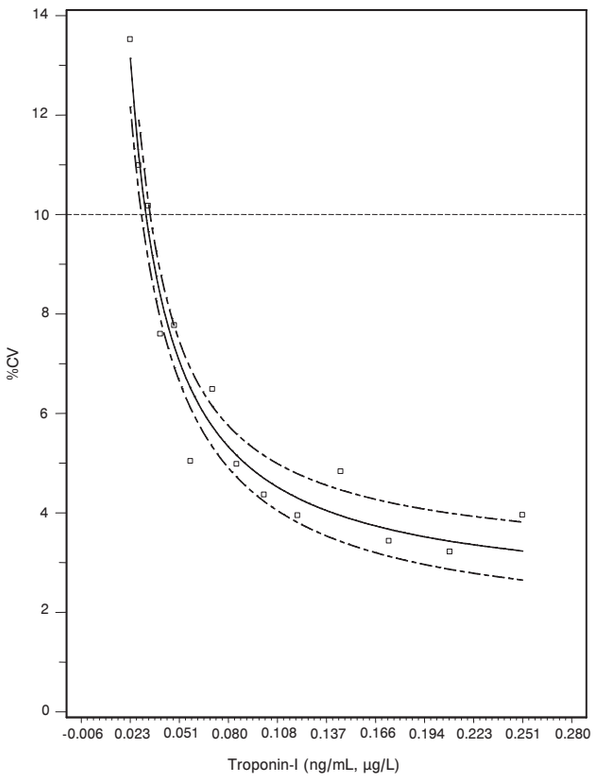
* Representative data; results in individual laboratories may vary from these data.

### 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.

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

Autodilution Verification

A study was performed evaluating the recovery of 29 serum, 27 heparinized plasma, and 30 EDTA plasma specimens using the ARCHITECT Troponin-I autodilution method resulting in a mean % Recovery** of 108.3% for serum specimens, 109.4% for heparinized plasma specimens, and 113.2% for EDTA plasma specimens.*

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

* 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% cross-reactivity 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 |

| Drug | Drug Concentration | Drug | Drug Concentration |
|---|---|---|---|
| Cinnarizine | 400 µg/mL | Sodium Heparin | 8 U/mL |
| Cocaine | 10 µg/mL | Streptokinase* | 31.3 U/mL |
| 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 ($t_{1/2}$).[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 |

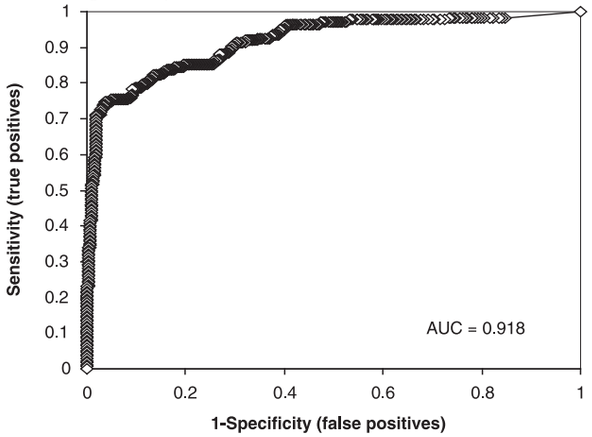
* Representative data; results in individual laboratories may vary from these data.

**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.

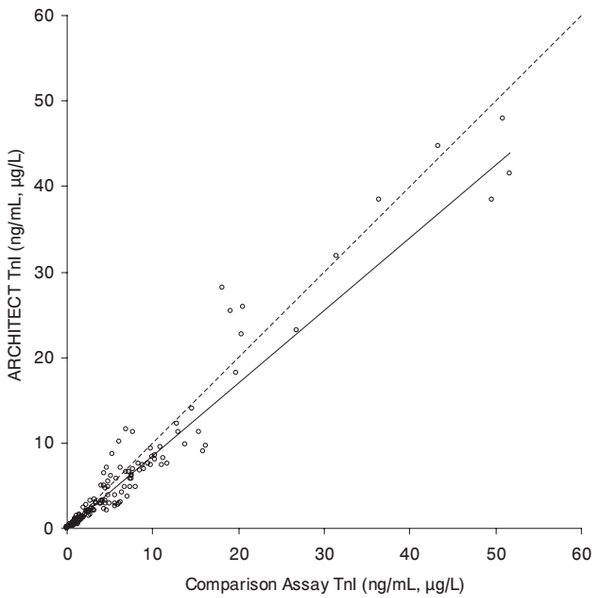
As with all diagnostic tests, each laboratory should establish its own diagnostic cutoff to assure proper representation of specific populations and to reflect current practice and criteria for MI diagnosis at their institution.

**Method Comparison**

The ARCHITECT *STAT* Troponin-I assay is designed to have a correlation coefficient (r) of ≥ 0.90. A study was performed where lithium heparin plasma specimens were tested in replicates of one using the ARCHITECT *STAT* Troponin-I assay with two reagent lots on two 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** | 147 | 0.85 (0.81 to 0.91) | -0.09 (-0.20 to 0.01) | 0.97 |




Sample Range (ARCHITECT *STAT* Troponin-I):
0.04 – 47.94 ng/mL (0.04 – 47.94 µg/L)
Sample Range (Comparison Assay):
0.02 – 51.58 ng/mL (0.02 – 51.58 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.

## BIBLIOGRAPHY


1. Perry SV. The regulation of contractile activity in muscle. *Biochem Soc Trans* 1979;7:593-617.
2. Mair J, Wagner I, Puschendorf B, *et al*. Cardiac troponin I to diagnose myocardial injury. *Lancet* 1993;341:838-9.
3. Leszyk J, Dumaswala R, Potter JD, *et al*. Amino acid sequence of bovine cardiac troponin I. *Biochemistry* 1988;27:2821-7.
4. Mair J, Morandell D, Genser N, *et al*. Equivalent early sensitivities of myoglobin, creatine kinase MB mass, creatine kinase isoform ratios, and cardiac troponins I and T for acute myocardial infarction. *Clin Chem* 1995;41:1266-72.
5. Bertinchant JP, Larue C, Pernel I, *et al*. Release kinetics of serum cardiac troponin I in ischemic myocardial injury. *Clin Biochemistry* 1996;29:587-94.
6. National Academy of Clinical Biochemistry Committee. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: Clinical Characteristics and Utilization of Biochemical Markers in Acute Coronary Syndromes. *Clin Chem* 2007;53:552-574.
7. Mair J, Larue C, Mair P, *et al*. Use of cardiac troponin I to diagnose perioperative myocardial infarction in coronary artery bypass grafting. *Clin Chem* 1994;40:2066-70.
8. Adams JE, Sicard GA, Allen BT, *et al*. Diagnosis of perioperative myocardial infarction with measurement of cardiac troponin I. *N Eng J Med* 1994;330:670-4.
9. Mair J, Genser N, Morandell D, *et al*. Cardiac troponin I in the diagnosis of myocardial injury and infarction. *Clin Chim Acta* 1996;245:19-38.
10. The Joint International Society and Federation of Cardiology/World Health Organization Task Force on Standardization of Clinical Nomenclature. Nomenclature and criteria for diagnosis of ischemic heart disease. *Circulation* 1979;59:607-9.
11. Thygesen K, Alpert JS, White HD. Universal Definition of Myocardial Infarction. *Circulation* 2007;116:2634-2653.
12. The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined—a consensus document of the Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36:959-69.
13. Keffer JH. The cardiac profile and proposed practice guideline for acute ischemic heart disease. *Am J Clin Pathol* 1997;107:398-409.
14. Hamm CW, Braunwald E. A classification of unstable angina revisited. *Circulation* 2000;102:118-22.
15. Heeschen C, Hamm CW, Goldmann B, *et al*. Troponin concentrations for stratification of patients with acute coronary syndromes in relation to therapeutic efficacy of tirofiban. *Lancet* 1999;354:1757-62.
16. Ottani F, Galvani M, Nicolini FA, *et al*. Elevated cardiac troponin levels predict the risk of adverse outcome in patients with acute coronary syndromes. *Am Heart J* 2000;140:917-27.
17. Olatidoye AG, Wu AHB, Feng YJ, *et al*. Prognostic role of troponin T versus troponin I in unstable angina pectoris for cardiac events with meta-analysis comparing published studies. *Am J Cardiol* 1998;81:1405-10.
18. The American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). ACC/AHA guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction-2002: Summary Article. *Circulation* 2002;106: 1893-1900.
19. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
20. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories.* 5th ed. Washington, DC: US Government Printing Office; January 2007.
21. World Health Organization. *Laboratory Biosafety Manual.* 3rd ed. Geneva: World Health Organization; 2004.
22. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections: Approved Guideline-Third Edition.* CLSI Document M29-A3. Wayne, PA: Clinical and Laboratory Standards Institute, 2005.
23. Schroff RW, Foon KA, Beatty SM, *et al*. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45:879-85.
24. Primus FJ, Kelley EA, Hansen HJ, *et al*. "Sandwich"-type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy. *Clin Chem* 1988;34:261-4.
25. The Task Force on the Management of Acute Coronary Syndromes of the European Society of Cardiology. Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-segment Elevation. *Eur Heart J* 2002;23:1809-1840.
26. Boscato LM and Stuart MC. Heterophilic antibodies; a problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.
27. Bodor GS. Cardiac troponin-I: a highly specific biochemical marker for myocardial infarction. *J Clin Immunoassay* 1994;17:40-4.
28. Antman EM, Tanasijevic MJ, Thompson B, *et al*. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. *N Eng J Med.* 1996;335:1342-9.
29. Galvani M, Ottani F, Ferrini D, *et al*. Prognostic influence of elevated values of cardiac troponin I in patients with unstable angina. *Circulation* 1997;95:2053-9.
30. Jaffe, AS. Elevations in cardiac troponin measurements: false false-positives. *Cardio Tox* 2001;1:87-92.
31. National Committee for Clinical Laboratory Standards. *How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline-Second Edition.* NCCLS Document C28-A2. Wayne, PA: NCCLS, 2000.
32. National Committee for Clinical Laboratory Standards. *Evaluation of Precision Performance of Clinical Chemistry Devices - Approved Guideline.* NCCLS document EP5-A. Wayne, PA: NCCLS, 1999.
33. M. Panteghini *et al*. Evaluation of Imprecision for Cardiac Troponin Assays at Low-Range Concentrations. *Clin Chem* 2004;50(2):327-332.
34. National Committee for Clinical Laboratory Standards. *Interference Testing in Clinical Chemistry: Approved Guideline.* NCCLS document EP7-A. Villanova, PA:NCCLS, 2002.
35. Activase. *Physicians' Desk Reference.* 58th ed. Montvale, NJ: Thomson PDR; 2004:1349-1353.
36. Streptase. *Physicians' Desk Reference.* 58th ed. Montvale, NJ: Thomson PDR; 2004:782-784.
37. National Committee for Clinical Laboratory Standards. *Assessment of the Clinical Accuracy of Laboratory Tests Using Receiver Operating Characteristic (ROC) Plots; Approved Guideline.* NCCLS Document GP10-A. Wayne, PA: NCCLS, 1995.
38. Passing H, Bablok W. A new biometrical procedure for testing the equality of measurements from two different analytical methods. *J Clin Chem Clin Biochem* 1983;21:709-20.





Abbott Laboratories
Diagnostics Division
Abbott Park, IL 60064 USA

EC REP ABBOTT
Max-Planck-Ring 2
65205 Wiesbaden
Germany
+49-6122-580



Produced by Fisher Diagnostics
a division of Fisher Scientific Company, LLC
a part of Thermo Fisher Scientific Inc.
8365 Valley Pike, Middletown, VA 22645-1905 USA
for Abbott

Distributed by Abbott Laboratories, Abbott Park, IL 60064 USA

March 2010



Abbott