SIEMENS Healthineers

High-Sensitivity Troponin I (TnIH)

Current Revision and Date[a]	Rev. 07, 2022-09	
Product Name	Atellica IM High-Sensitivity Troponin I (TnIH)	REF 10997840 (100 tests) REF 10997841 (500 tests)
Abbreviated Product Name	Atellica IM TnIH	
Test Name/ID	TnIH	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM APW3	REF 10998580
Optional Materials	Atellica IM Multi-Diluent 11	REF 10995642 (2-pack)
	Atellica IM TnIH MCM	REF 10997842
Specimen Types	Serum, lithium-heparin plasma	
Sample Volume	100 µL	
Measuring Interval	2.50–25,000.00 pg/mL (ng/L)	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

Intended Use

The Atellica® IM High-Sensitivity Troponin I (TnIH) assay is for *in vitro* diagnostic use in the quantitative measurement of cardiac troponin I in human serum or plasma (lithium heparin) using the Atellica® IM Analyzer. The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI).

Summary and Explanation

Troponin I (TnI) exists in 3 distinct isoforms: cardiac muscle, slow-twitch skeletal muscle, and fast-twitch skeletal muscle.[1] Each isoform is encoded by a distinct gene, each with a unique amino acid sequence, leading to a 40% dissimilarity among isoforms.[1–4]

Cardiac troponin I (cTnI) is an inhibitory protein of the troponin-tropomyosin complex. cTnI is the only TnI isotype present in the myocardium and is not expressed during any developmental stage in skeletal muscle.[2,5,6] cTnI has a molecular weight of 24,000 daltons.[7]

The cardiac form of TnI is further unique in that it has 31 additional amino acid residues on its N-terminal, not present in the skeletal forms, which allows for specific monoclonal antibody development.[7] The cardiac specificity of this isoform improves the accuracy of detection of cardiac muscle ischemia in patients with acute or chronic skeletal muscle injury and possible concomitant myocardial injury, and is the basis for its selection as a cardiac marker in the diagnosis of AMI.[1,3–5,7,8]

The Global MI Task Force's third version of the universal definition of myocardial infarction defined AMI as evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia.[9] Under these circumstances, the following criterion meets the diagnosis of AMI:

Detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin) with at least 1 value above the 99th percentile upper reference limit (URL) and with at least 1 of the following conditions:

- Symptoms of ischemia.
- New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBB).
- Development of pathological Q waves in the electrocardiogram (EKG).
- Imaging evidence of new loss of viable myocardium, or new regional wall motion abnormality.
- Identification of an intracoronary thrombus by angiography or autopsy.

Definition of a High-Sensitivity Assay

The International Federation of Clinical Chemistry (IFCC) Task Force on Clinical Applications of Cardiac Bio-Markers defines a troponin assay as a high-sensitivity assay if it meets the following criteria:[10]

- Total imprecision (CV) at the 99th percentile value should be at or below 10%.
- Measurable concentrations should be attainable at concentrations above the limit of detection (LoD) in at least 50% of healthy individuals.

Troponin values must be used in the context of the patient clinical presentation. Serial sampling is recommended to detect the temporal rise and fall of troponin levels characteristic of AMI. The demonstration of a temporal rise and fall in troponin is needed to distinguish AMI from troponin elevations associated with non-AMI conditions, such as renal failure, arrhythmias, pulmonary embolism, chronic renal disease, myocarditis, and cardiotoxicity.[9,11–14]

Principles of the Procedure

The Atellica IM TnIH is a 3-site sandwich immunoassay using direct chemiluminescent technology. The Solid Phase reagent consists of magnetic latex particles conjugated with streptavidin with 2 bound biotinylated capture monoclonal antibodies, each recognizing a unique cTnI epitope.

The Lite Reagent comprises a conjugate with an architecture consisting of a proprietary acridinium ester and a recombinant anti-human cTnI sheep Fab covalently attached to bovine serum albumin (BSA) for chemiluminescent detection.

A direct relationship exists between the amount of troponin I present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Reagents

Material Description	Storage	Stability[a]
Atellica IM TnIH ReadyPack® primary reagent pack **Lite Reagent** 8.0 mL/reagent pack Bovine serum albumin (BSA) conjugated to a recombinant monoclonal (sheep) Fab anti-human cTnI (~0.2–0.4 µg/mL) labeled with acridinium ester in HEPES buffer; stabilizers; preservatives **Solid Phase** 13.0 mL/reagent pack Streptavidin-coated magnetic latex particles (0.45 mg/mL) with 2 biotinylated (mouse and sheep) monoclonal anti-troponin I antibodies in buffer; stabilizers; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
Atellica IM TnIH CAL L 1.0 mL/vial HEPES buffer; bovine serum albumin (BSA); surfactants; preservatives	Unopened at 2–8°C Opened at 2–8°C Opened at ≤ -20°C Onboard at room temperature Atellica® Sample Handler[b]	Until expiration date on product 4 hours 30 days; thaw 1 time 4 hours
Atellica IM TnIH CAL H 1.0 mL/vial; lyophilized After reconstitution, human serum; human cTnI; preservatives	Lyophilized at 2–8°C Reconstituted at 2–8°C Reconstituted at ≤ -20°C Onboard at room temperature Atellica Sample Handler[b]	Until expiration date on product 4 hours 30 days; thaw 1 time 4 hours
Atellica IM APW3 ReadyPack ancillary reagent pack[c] 25.0 mL/pack Phosphate-buffered saline; sodium azide (< 0.1%); surfactant	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
Atellica IM Multi-Diluent 11 ReadyPack ancillary reagent pack[d] 5.0 mL/pack Tris buffer; goat serum; protein stabilizers; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 28 days

[a] Refer to *Storage and Stability*.

[b] Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

[c] Refer to *Materials Required but Not Provided*.

[d] Refer to *Optional Materials*.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens.com/healthineers.

CAUTION POTENTIAL BIOHAZARD

Contains human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2), as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions.[15–17]

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Note For information about reagent preparation, refer to *Preparing the Reagents* in the *Procedure* section.

Note For information about calibrator preparation, refer to *Preparing the Calibrators*.

Storage and Stability

Store reagents in an upright position. Protect the product from heat and light sources. Unopened reagents are stable until the expiration date on the product when stored at 2–8°C.

Store Atellica IM TnIH CAL L in an upright position. Unopened calibrator is stable until the expiration date on the product when stored at 2–8°C. Opened calibrator is stable for 4 hours at 2–8°C. Freeze opened product at ≤ -20°C for up to 30 days; thaw 1 time. Calibrators are stable for 4 hours at room temperature.

Store Atellica IM TnIH CAL H in an upright position. Lyophilized calibrator is stable until the expiration date on the product when stored at 2–8°C. Reconstituted calibrator is stable for 4 hours at 2–8°C. Freeze reconstituted product at ≤ -20°C for up to 30 days; thaw 1 time. Reconstituted calibrators are stable for 4 hours at room temperature.

Store Atellica IM APW3 in an upright position. Unopened Atellica IM APW3 is stable until the expiration date on the product when stored at 2–8°C.

Store Atellica IM Multi-Diluent 11 in an upright position. Unopened Atellica IM Multi-Diluent 11 is stable until the expiration date on the product when stored at 2–8°C.

Do not use products beyond the expiration date printed on the product labeling.

Onboard Stability

Reagents are stable onboard the system for 28 days. Discard reagents at the end of the onboard stability interval.

Note Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

Atellica IM APW3 is stable onboard the system for 28 days.

Atellica IM Multi-Diluent 11 is stable onboard the system for 28 days.

Do not use products beyond the expiration date printed on the product labeling.

Specimen Collection and Handling

Serum and plasma (lithium heparin) are the recommended sample types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[17]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[18]
- Follow the instructions provided with your specimen collection device for use and processing.[19]
- Allow blood specimens to clot completely before centrifugation.[16]
- Keep tubes capped at all times.[16]
- The use of a single sample type (either lithium-heparin plasma or serum) is recommended for troponin analysis when collecting serial samples from the same patient.
- For serum specimens, complete clot formation should take place before centrifugation. Serum should be physically separated from cells as soon as possible from the time of collection.[16]
- Samples must be free of fibrin or other particulate matter. The presence of fibrin, red blood cells, or suspended particles may lead to inaccurate results. Serum samples that contain suspended fibrin particles or erythrocyte stroma must be re-centrifuged before testing.
- If clotting time is increased due to thrombolytic or anticoagulant therapy, the use of plasma specimens will allow for faster sample processing and reduce the risk of micro-clots, fibrin, or particulate matter.
- For plasma specimens, avoid transferring white blood cells or platelets from the layer located just above the red blood cells.
- If a fixed angle rotor is used for centrifugation, care should be taken to avoid re-suspending cellular material (platelets) upon removal from the centrifuge.

Storing the Specimen

- Samples are stable up to 8 hours when tightly capped and stored at room temperature.
- Samples are stable up to 24 hours when tightly capped and stored at 2–8°C.
- Samples can be frozen at ≤ -20°C for up to 40 days. Do not store in a frost-free freezer.
- Samples can be frozen at ≤ -70°C for up to 1 year.
- Freeze samples only once and mix thoroughly after thawing.

CAUTION

Thoroughly mix thawed samples and centrifuge them before using.[16] Collect the supernatant into a clean vial.

The handling and storage information provided here is based on data or references maintained by the manufacturer. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Transporting the Specimen

Ship samples frozen.

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

Preparing the Samples

This assay requires 100 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For information about determining the minimum required volume, refer to the online help.

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to *Dilutions*.

Note Do not use specimens with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[16]

Note For a complete list of appropriate sample containers, refer to the online help.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10997840	1 ReadyPack primary reagent pack containing Atellica IM TnIH Lite Reagent and Solid Phase Atellica IM TnIH master curve and test definition MC TDEF 1 vial Atellica IM TnIH CAL low calibrator CAL L 1 vial Atellica IM TnIH CAL high calibrator CAL H Atellica IM TnIH CAL calibrator lot-specific value sheet CAL LOT VAL	100
10997841	5 ReadyPack primary reagent packs containing Atellica IM TnIH Lite Reagent and Solid Phase Atellica IM TnIH master curve and test definition MC TDEF 2 vials Atellica IM TnIH CAL low calibrator CAL L 2 vials Atellica IM TnIH CAL high calibrator CAL H Atellica IM TnIH CAL calibrator lot-specific value sheet CAL LOT VAL	500

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

REF	Description	
	Atellica IM Analyzer[a]	
10998580	Atellica IM APW3 (probe wash)	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack WASH

[a] Additional system fluids are required to operate the system: Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner. For system fluid instructions for use, refer to the Document Library.

Optional Materials

The following materials may be used to perform this assay, but are not provided:

REF	Description	
10995642	Atellica IM Multi-Diluent 11 (diluent)	2 ReadyPack ancillary reagent packs containing 5.0 mL/pack DIL
10997842	Atellica IM TnIH MCM (master curve material)	5 x 1.0 mL levels of master curve material MCM

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 100 µL of sample into a cuvette.
2. Dispenses 130 µL of Solid Phase and 80 µL of Lite Reagent, then incubates for 8 minutes at 37°C.
3. Separates, aspirates, then washes the cuvette with Atellica IM Wash.
4. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
5. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading primary reagent packs onto the system, mix them by hand and visually inspect the bottom of the reagent pack to ensure that all particles are resuspended. For information about preparing the reagents for use, refer to the online help.

Preparing the System

Ensure that the system has sufficient reagent packs loaded in the reagent compartment. The system automatically mixes reagent packs to maintain homogeneous suspension of the reagents. For information about loading reagent packs, refer to the online help.

For automated dilutions, ensure that Atellica IM Multi-Diluent 11 is loaded on the system.

Master Curve Definition

Before initiating calibration on each new lot of reagent, load the assay master curve and test definition values by scanning the MC TDEF 2D barcodes. For loading instructions, refer to the online help.

Performing Calibration

For calibration of the Atellica IM TnIH assay, use the calibrators provided with each kit.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

At the end of the onboard stability interval, replace the reagent pack on the system with a new reagent pack. Recalibration is not required, unless the lot calibration interval is exceeded.

Stability Interval	Days
Lot Calibration	47
Pack Calibration	31
Reagent Onboard Stability	28

For information about lot calibration and pack calibration intervals, refer to the online help.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Preparing the Calibrators

Low Calibrator

The Atellica IM TnIH CAL L is liquid and ready to use. Gently mix and invert the vials to ensure homogeneity of the material.

DO NOT ADD WATER TO THE LOW CALIBRATOR.

High Calibrator

Prepare the Atellica IM TnIH CAL H using the following steps:

1. Add 1.00 mL of special reagent water into the vial using a class A volumetric pipet or an equivalent pipet. Replace cap.

   Note For information about special reagent water requirements, refer to the online help.

2. Let the vial stand for 15–20 minutes at room temperature to allow the lyophilized material to dissolve.
3. Gently mix and invert the vial to ensure homogeneity of the material.

Note For extended storage, aliquot the low and high calibrators into cryovials and seal tightly. Store material according to stability limits specified in *Storage and Stability*. Do not store in a frost-free freezer.

Before using frozen calibrators, allow the material to completely thaw. Gently mix and invert the vials to ensure homogeneity of the material. Use immediately and discard any remaining material.

Note Use calibrators within the stability limits specified in *Storage and Stability* and discard any remaining material.

Calibration Procedure

The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the online help.

Use the following lot-specific materials to perform calibration:

- For the master curve and assay test definitions, refer to the lot-specific master curve and test definition sheet MC TDEF provided with the assay reagents.
- Calibrators provided in an assay kit must only be used with reagents from that assay kit lot. Do not use calibrators from one assay kit with reagents from a different assay kit lot.
- For the calibrator definitions, refer to the lot-specific value sheet CAL LOT VAL provided with the calibrator materials.
- Generate lot-specific barcode labels to use with the calibrator samples.

For instructions about how to perform the calibration procedure, refer to the online help.

Performing Quality Control

For quality control of the Atellica IM TnIH assay, use an appropriate quality control material of known analyte concentration with at least 2 levels at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use.

A satisfactory level of performance is achieved when the analyte values obtained are within the expected control interval for the system or within your interval, as determined by an appropriate internal laboratory quality control scheme. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the online help.

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Test quality control samples after a successful calibration.

Taking Corrective Action

If the quality control results do not fall within the assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

Results

Calculation of Results

The system determines the result using the calculation scheme described in the online help. The system reports results in pg/mL (common units) or ng/L (SI units), depending on the units defined when setting up the assay.

Conversion formula: 1.0 pg/mL (common units) = 1.0 ng/L (SI units)

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Dilutions

The measuring interval for serum and plasma is 2.50–25,000.00 pg/mL (ng/L). For information about dilution options, refer to the online help.

Patient samples with cTnI levels > 25,000.00 pg/mL (ng/L) can be diluted and retested to obtain quantitative results. Patient samples with cTnI levels ≤ 25,000.00 pg/mL (ng/L) should not be diluted.

For automated dilutions, ensure that Atellica IM Multi-Diluent 11 is loaded in the reagent compartment. Ensure that sufficient sample volume is available to perform the dilution and that the appropriate dilution factor is selected when scheduling the test, as indicated in the table below.

For automatic dilutions, enter a dilution setpoint ≤ 25,000.00 pg/mL (ng/L).

Sample	Dilution	Sample Volume (µL)
Serum and plasma	1:2	100
Serum and plasma	1:5	60

Interpretation of Results

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

An unknown interference was observed in analytical spiking and dilution studies causing negative bias that may affect interpretation of patient results. The unknown interference may be due to the presence of troponin autoantibodies, which have been reported in up to 10% of patients with or without AMI and up to 20% of patients positive for rheumatoid factor.[20] **If the cTnI result is below the 99th percentile value at the first blood draw, at least two additional blood samples should be drawn before results are interpreted as negative for AMI.**

Limitations

The following information pertains to limitations of the assay:

- The use of a single sample type (either lithium heparin or serum) is recommended for troponin analysis when collecting serial samples from the same patient.
- If clotting time is increased due to thrombolytic or anticoagulant therapy, using serum samples may increase the risk of micro-clots, fibrin, or particulate matter. Lithium-heparin plasma is the preferred sample type for patients undergoing anticoagulant therapy.
- Samples from patients receiving preparations of mouse monoclonal antibodies for therapy or diagnosis may contain human anti-mouse antibodies (HAMA). Such samples may show either falsely elevated or falsely depressed values when tested with this method.[21]
- Specimens from some individuals with pathologically high gamma globulin levels may demonstrate depressed troponin values. Additional information may be required for diagnosis.
- Heterophilic antibodies and rheumatoid factor in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.[22]
- An unknown interference was observed in analytical spiking and dilution studies causing negative bias that may affect interpretation of patient results. The unknown interference may be due to the presence of troponin autoantibodies, which have been reported in up to 10% of patients with or without AMI and up to 20% of patients positive for rheumatoid factor.[20] **If the cTnI result is below the 99th percentile value at the first blood draw, at least two additional blood samples should be drawn before results are interpreted as negative for AMI.**

Expected Values

A reference interval for apparently healthy adults was established in accordance with CLSI Document EP28-A3c[23] on the Atellica IM Analyzer.

Serum and lithium-heparin plasma specimens were collected from 2007 apparently healthy individuals from the United States who ranged in age from 22–91 years of age. Each specimen was frozen, thawed, and assayed once. The 99th percentile values were determined using the non-parametric statistical method described in CLSI Document EP28-A3c.[23] Two female subjects had troponin values of approximately 300 pg/mL (ng/L) and 5000 pg/mL (ng/L), and were considered to be outliers. These results were not included in the 99th percentile determination.

The 99th percentile values determined for lithium-heparin plasma (female, male, and combined), and for serum (female, male, and combined) are shown in the following table. The 90% confidence intervals demonstrate that there is no statistical basis for using separate 99th percentile values based on gender or sample type.

The combined gender and the more commonly used sample type of lithium-heparin plasma were used to determine the overall observed 99th percentile of 45.20 pg/mL (ng/L). In the IFCC-recommended reporting format (whole numbers), the 99th percentile is 45 pg/mL (ng/L).

Sample Type	Gender	N	99th Percentile[a] (pg/mL; ng/L)	90% CI[b] (pg/mL; ng/L)
Lithium heparin	Female	1007	34.11	27.36–66.23
	Male	1000	53.48	38.73–80.22
	Combined	2007	45.20	33.21–64.30
Serum	Female	1007	38.64	28.58–72.36
	Male	994	53.53	33.77–78.03
	Combined	2001	45.43	35.47–63.63

[a] IFCC Task Force on Clinical Applications of Cardiac Bio-Markers recommends that troponin values be reported as whole numbers.[10]

[b] Confidence interval.

Performance Characteristics

Measuring Interval

The Atellica IM TnIH assay provides results from 2.50–25,000.00 pg/mL (ng/L). The lower end of the measuring interval is defined by the LoQ. Report patient results below the measuring interval as < 2.50 pg/mL (ng/L). When sample results exceed the measuring interval, refer to *Dilutions*.

Specificity

The Atellica IM TnIH assay shows high specificity for cTnI. The following compounds were added at the concentrations indicated to a serum or lithium-heparin plasma sample with a known cTnI concentration. Atellica IM TnIH assay results from the spiked samples were compared with those of unspiked control samples. Percent cross-reactivity was determined in accordance with CLSI Document EP07-A2[24] and is calculated as:

$$\% \text{ cross-reactivity} = \frac{(\text{concentration of spiked sample} - \text{concentration of unspiked sample})}{\text{concentration of compound}} \times 100$$

Cross-reactant	Amount (ng/mL)	Cross-reactivity (%)
Cardiac troponin T[a]	1000	ND[b]
Skeletal troponin I	1000	ND
Tropomyosin	1000	ND
Actin	1000	ND
Troponin C	1000	ND
Myosin light chain	1000	ND
Myoglobin	1000	ND
CK-MB	1000	ND

[a] Human recombinant.
[b] Not detectable (< 0.01%).

Assay results obtained at individual laboratories may vary from the data presented.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[25] The assay is designed to have a limit of detection (LoD) ≤ 1.6 pg/mL (ng/L), and a limit of quantitation (LoQ) ≤ 3.0 pg/mL (ng/L).

Representative detection capability data are shown below. Assay results obtained at individual laboratories may vary from the data presented.

The LoB corresponds to the highest measurement result that is likely to be observed for a blank sample. The LoB of the Atellica IM TnIH assay is 0.50 pg/mL (ng/L).

The LoD corresponds to the lowest concentration of cTnI that can be detected with a probability of 95%. The LoD for the Atellica IM TnIH assay is 1.60 pg/mL (ng/L).

The LoQ corresponds to the lowest amount of analyte in a sample at which the within-laboratory precision is 20%. The LoQ of the Atellica IM TnIH assay is 2.50 pg/mL (ng/L).

Report results below the LoQ as < 2.50 pg/mL (ng/L).

Actual results will vary depending on the study design and on the samples used. Assay results obtained at individual laboratories may vary from the data presented.

High-Sensitivity Determination

The Atellica IM TnIH assay meets the IFCC Task Force on Clinical Applications of Cardiac Bio-Markers' definition of a high-sensitivity troponin assay.[10]

1. Total imprecision (CV) at the 99th percentile value of 45.20 pg/mL (ng/L) is below 10%.
2. Greater than 50% of measurements from individuals in the healthy patient population used to determine the 99th percentile value were above the LoD of 1.60 pg/mL (ng/L).

Clinical Performance

A prospective study was performed to assess diagnostic accuracy for subjects in both serum and lithium-heparin plasma sample types. Specimens were collected at 29 emergency departments across the United States, from subjects presenting with symptoms consistent with acute coronary syndrome (ACS).

All subject diagnoses were adjudicated by panels of certified cardiologists and emergency physicians according to the Third Universal Definition Of Myocardial Infarction - consensus guideline[9] endorsed by the European Society of Cardiology (ESC), the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), and the World Heart Federation (WHF). The observed AMI prevalence in this study was 13%.

The results from the study are presented using serial time intervals analyzed according to the time of presentation to the emergency department.

Time of Presentation to the Emergency Department

The pooled gender results based on time of presentation to the emergency department, calculated using the overall 99th percentile of 45.20 pg/mL (ng/L), are summarized in table 1. Gender-specific data are presented in tables 2 and 3.

Table 1: Pooled gender results based on time of presentation to the emergency department

Time since presentation (hours)	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
	N[a]	%	95% CI[b]	N	%	95% CI	N	%	95% CI	N	%	95% CI
Lithium-heparin plasma												
0– < 1.5	145	77.2	69.8–83.3	964	91.8	89.9–93.4	190	58.9	51.8–65.7	919	96.4	95.0–97.4
≥ 1.5– < 2.5	240	90.0	85.6–93.2	1625	90.6	89.1–91.9	368	58.7	53.6–63.6	1497	98.4	97.6–98.9
≥ 2.5– < 3.5	201	92.0	87.5–95.0	1369	90.6	88.9–92.0	314	58.9	53.4–64.2	1256	98.7	97.9–99.2
≥ 3.5– < 4.5	149	92.6	87.3–95.8	1080	90.9	89.1–92.5	237	58.2	51.9–64.3	992	98.9	98.0–99.4
≥ 4.5– < 6	66	97.0	89.6–99.2	461	89.2	86.0–91.7	114	56.1	47.0–64.9	413	99.5	98.3–99.9
≥ 6– < 9	193	92.7	88.2–95.6	905	87.6	85.3–89.6	291	61.5	55.8–66.9	807	98.3	97.1–99.0
≥ 9– < 24	215	94.0	89.9–96.4	835	86.6	84.1–88.7	314	64.3	58.9–69.4	736	98.2	97.0–99.0
≥ 24	62	93.5	84.6–97.5	253	83.4	78.3–87.5	100	58.0	48.2–67.2	215	98.1	95.3–99.3
Serum												
0– < 1.5	140	78.6	71.1–84.6	980	92.1	90.3–93.7	186	59.1	52.0–65.9	934	96.8	95.4–97.7
≥ 1.5– < 2.5	239	87.9	83.1–91.4	1646	90.9	89.5–92.2	358	58.7	53.5–63.6	1527	98.1	97.3–98.7
≥ 2.5– < 3.5	195	90.8	85.9–94.1	1384	90.8	89.1–92.2	305	58.0	52.4–63.4	1274	98.6	97.8–99.1
≥ 3.5– < 4.5	147	91.2	85.5–94.8	1083	91.0	89.2–92.6	232	57.8	51.3–63.9	998	98.7	97.8–99.2
≥ 4.5– < 6	64	96.9	89.3–99.1	454	89.6	86.5–92.1	109	56.9	47.5–65.8	409	99.5	98.2–99.9
≥ 6– < 9	185	93.5	89.0–96.3	904	88.7	86.5–90.6	275	62.9	57.1–68.4	814	98.5	97.4–99.2
≥ 9– < 24	213	93.9	89.8–96.4	841	86.7	84.2–88.8	312	64.1	58.6–69.2	742	98.2	97.0–99.0
≥ 24	63	90.5	80.7–95.6	255	85.5	80.6–89.3	94	60.6	50.5–69.9	224	97.3	94.3–98.8

[a] Number of samples.

[b] Confidence interval.

Results for females based on time of presentation to the emergency department, calculated using the female-specific 99th percentile of 34.11 pg/mL (ng/L) for plasma and 38.64 pg/mL (ng/L) for serum, are summarized in table 2.

Using the lower female-specific 99th percentiles instead of the overall 99th percentile of 45.20 pg/mL (ng/L) may result in a higher proportion of positive test results for females that are non-MI. Taking into consideration the lower bound of the 95% confidence interval, in the worst-case scenario (lithium-heparin plasma drawn at ≥ 4.5–< 6 hours after presentation), up to 68% of positive test results for females may be non-MI.

Table 2: Results for females based on time of presentation to the emergency department

Time since presentation (hours)	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
	N[a]	%	95% CI[b]	N	%	95% CI	N	%	95% CI	N	%	95% CI
Lithium-heparin plasma												
0– < 1.5	45	84.4	71.2–92.3	401	93.3	90.4–95.3	64	59.4	47.1–70.5	382	98.2	96.3–99.1
≥ 1.5– < 2.5	79	89.9	81.3–94.8	720	91.7	89.4–93.5	130	54.6	46.0–62.9	669	98.8	97.7–99.4
≥ 2.5– < 3.5	73	94.5	86.7–97.8	621	91.6	89.2–93.6	121	57.0	48.1–65.5	573	99.3	98.2–99.7
≥ 3.5– < 4.5	50	94.0	83.8–97.9	487	89.5	86.5–91.9	98	48.0	38.3–57.7	439	99.3	98.0–99.8
≥ 4.5– < 6	26	96.2	81.1–99.3	238	87.0	82.1–90.7	56	44.6	32.4–57.6	208	99.5	97.3–99.9
≥ 6– < 9	69	94.2	86.0–97.7	374	88.0	84.3–90.9	110	59.1	49.7–67.8	333	98.8	97.0–99.5
≥ 9– < 24	74	94.6	86.9–97.9	342	87.4	83.5–90.5	113	61.9	52.7–70.4	303	98.7	96.7–99.5
≥ 24	27	96.3	81.7–99.3	110	80.9	72.6–87.2	47	55.3	41.2–68.6	90	98.9	94.0–99.8
Serum												
0– < 1.5	42	81.0	66.7–90.0	407	93.4	90.5–95.4	60	56.7	44.1–68.4	389	97.9	96.0–99.0
≥ 1.5– < 2.5	77	89.6	80.8–94.6	721	91.8	89.6–93.6	127	54.3	45.7–62.7	671	98.8	97.7–99.4
≥ 2.5– < 3.5	67	92.5	83.7–96.8	619	92.4	90.0–94.2	109	56.9	47.5–65.8	577	99.1	98.0–99.6
≥ 3.5– < 4.5	48	93.8	83.2–97.9	484	90.3	87.3–92.6	92	48.9	38.9–59.0	440	99.3	98.0–99.8
≥ 4.5– < 6	26	96.2	81.1–99.3	236	87.7	82.9–91.3	54	46.3	33.7–59.4	208	99.5	97.3–99.9
≥ 6– < 9	63	95.2	86.9–98.4	378	88.6	85.0–91.4	103	58.3	48.6–67.3	338	99.1	97.4–99.7
≥ 9– < 24	73	94.5	86.7–97.8	342	89.5	85.8–92.3	105	65.7	56.2–74.1	310	98.7	96.7–99.5
≥ 24	26	96.2	81.1–99.3	111	82.9	74.8–88.8	44	56.8	42.2–70.3	93	98.9	94.2–99.8

[a] Number of samples.

[b] Confidence interval.

Results for males based on time of presentation to the emergency department, calculated using the male-specific 99th percentile of 53.48 pg/mL (ng/L) for plasma and 53.53 pg/mL (ng/L) for serum, are summarized in table 3.

Using the higher male-specific 99th percentiles instead of the overall 99th percentile of 45.20 pg/mL (ng/L) may result in a higher proportion of negative test results for males that are MI. For males that are MI, data analyzed using the male-specific cutoff versus the overall cutoff increased the false-negative rate by up to 0.9%.

Table 3: Results for males based on time of presentation to the emergency department

Time since presentation (hours)	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
	N[a]	%	95% CI[b]	N	%	95% CI	N	%	95% CI	N	%	95% CI
Lithium-heparin plasma												
0– < 1.5	100	75.0	65.7–82.5	563	91.5	88.9–93.5	123	61.0	52.1–69.1	540	95.4	93.3–96.8
≥ 1.5– < 2.5	161	87.6	81.6–91.8	905	91.2	89.1–92.8	221	63.8	57.3–69.9	845	97.6	96.4–98.5
≥ 2.5– < 3.5	128	89.8	83.4–94.0	748	90.0	87.6–91.9	190	60.5	53.4–67.2	686	98.1	96.8–98.9
≥ 3.5– < 4.5	99	90.9	83.6–95.1	593	92.4	90.0–94.3	136	66.2	57.9–73.6	556	98.4	97.0–99.1
≥ 4.5– < 6	40	92.5	80.1–97.4	223	90.6	86.0–93.8	58	63.8	50.9–74.9	205	98.5	95.8–99.5
≥ 6– < 9	124	91.1	84.8–95.0	531	88.5	85.5–91.0	174	64.9	57.6–71.6	481	97.7	96.0–98.7
≥ 9– < 24	141	93.6	88.3–96.6	493	85.6	82.2–88.4	203	65.0	58.2–71.3	431	97.9	96.1–98.9
≥ 24	35	91.4	77.6–97.0	143	88.1	81.8–92.4	49	65.3	51.3–77.1	129	97.7	93.4–99.2
Serum												
0– < 1.5	98	77.6	68.3–84.7	573	91.6	89.1–93.6	124	61.3	52.5–69.4	547	96.0	94.0–97.3
≥ 1.5– < 2.5	162	86.4	80.3–90.9	925	91.5	89.5–93.1	219	63.9	57.4–70.0	868	97.5	96.2–98.3
≥ 2.5– < 3.5	128	87.5	80.7–92.2	765	89.9	87.6–91.9	189	59.3	52.1–66.0	704	97.7	96.3–98.6
≥ 3.5– < 4.5	99	88.9	81.2–93.7	599	92.7	90.3–94.5	133	66.2	57.8–73.7	565	98.1	96.6–98.9
≥ 4.5– < 6	38	94.7	82.7–98.5	218	90.8	86.3–94.0	56	64.3	51.2–75.5	200	99.0	96.4–99.7
≥ 6– < 9	122	91.0	84.6–94.9	526	89.9	87.1–92.2	164	67.7	60.2–74.4	484	97.7	96.0–98.7
≥ 9– < 24	140	93.6	88.2–96.6	499	85.6	82.2–88.4	203	64.5	57.7–70.8	436	97.9	96.1–98.9
≥ 24	37	86.5	72.0–94.1	144	88.9	82.7–93.0	48	66.7	52.5–78.3	133	96.2	91.5–98.4

[a] Number of samples.
[b] Confidence interval.

Elevated TnI Values in Patients Without AMI

There are conditions other than AMI that are known to cause myocardial injury and elevated TnI values.[9,11–14,26–33]

The Atellica IM TnIH clinical trial enrolled all patients presenting to the emergency department with symptoms consistent with ACS. Some of these patients had an acute or chronic condition other than AMI.

In the clinical trial, 11% of patients without an AMI diagnosis had at least one Atellica IM TnIH test result above the 99th percentile (> 45.20 pg/mL (ng/L) on 1 or more serial draws. 88% of these patients were found to have 1 or more of the following conditions:

Cardiac conditions

- Angina
- Atrial fibrillation
- Cardiomyopathy
- Coronary artery disease
- Heart failure

- Hypertensive urgency
- Pericarditis
- Recent cardiac intervention
- Severe valvular heart disease
- Tachycardia

Non-cardiac conditions

- Chronic lung disease
- Cardiac contusion related to a traumatic injury
- Renal failure
- Pneumonia
- Pulmonary embolism
- Shock
- Systemic sclerosis

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[34] Samples were assayed on an Atellica IM Analyzer in duplicate in 2 runs per day for 20 days. The following representative results were obtained:

			Repeatability		Within-Laboratory Precision	
Sample Type	N[a]	Mean (pg/mL; ng/L)	SD[b] (pg/mL; ng/L)	CV[c] (%)	SD (pg/mL; ng/L)	CV (%)
Serum 1	80	12.72	0.55	4.3	0.59	4.7
Serum 2	80	127.93	2.30	1.8	3.09	2.4
Serum 3	80	1334.97	22.28	1.7	27.48	2.1
Serum 4	80	13,815.89	192.05	1.4	266.91	1.9
Plasma 1	80	12.03	0.49	4.1	0.64	5.3
Plasma 2	80	131.21	2.23	1.7	2.75	2.1
Plasma 3	80	1363.38	27.11	2.0	32.00	2.3
Plasma 4	80	12,862.97	212.91	1.7	291.00	2.3

[a] Number of samples tested.
[b] Standard deviation.
[c] Coefficient of variation.

Assay results obtained at individual laboratories may vary from the data presented.

Interferences

Interference testing was performed in accordance with CLSI Document EP07-A2.[24]

Testing was performed with both human serum and lithium-heparin plasma samples, with troponin concentrations in the ranges of 20–60 pg/mL (ng/L) and 1000–2000 pg/mL (ng/L). The following drugs were added to the samples at the concentrations indicated, and were evaluated for potential interference using the Atellica IM TnIH assay. The results demonstrated a ≤ 10% interference from each drug.

	Low or Therapeutic Concentration		High or Toxic Concentration	
Potential Interferents	**Common units**	**SI units**	**Common units**	**SI units**
Abciximab	5 µg/mL	N/A[a]	40 µg/mL	N/A
Acetaminophen	20 µg/mL	133 µmol/L	200 µg/mL	1324 µmol/L
Acetylsalicylic acid	261 µg/mL	1.45 mmol/L	652 µg/mL	3.62 mmol/L
Allopurinol	13 µg/mL	92 µmol/L	40 µg/mL	294 µmol/L
Amiodarone	1.8 µg/mL	2.6 µmol/L	6.1 µg/mL	8.92 µmol/L
Ampicilin	10 µg/mL	29.1 µmol/L	53 µg/mL	152 µmol/L
Ascorbic acid	12 µg/mL	68.5 µmol/L	60 µg/mL	342 µmol/L
Atenolol	1.1 µg/mL	4.14 µmol/L	10 µg/mL	37.6 µmol/L
Caffeine	12 µg/mL	64.4 µmol/L	60 µg/mL	308 µmol/L
Captropril	1.0 µg/mL	4.6 µmol/L	5.0 µg/mL	23 µmol/L
Cefoxitin	120 µg/mL	281 µmol/L	660 µg/mL	1546 µmol/L
Cinnarizine	200 ng/mL	542 nmol/L	400 ng/mL	1084 nmol/L
Clopidogrel	37.5 µg/mL	116 µmol/L	75 µg/mL	233 µmol/L
Cocaine	0.1 µg/mL	0.33 µmol/L	10 µg/mL	33 µmol/L
Digoxin	1.4 ng/mL	1.8 nmol/L	6.1 ng/mL	7.8 nmol/L
Digitoxin	30 ng/mL	39 nmol/L	60 ng/mL	78 nmol/L
Diltiazem	0.2 µg/mL	0.55 µmol/L	6.2 µg/mL	15 µmol/L
Disopyramide	3.5 µg/mL	10.4 µmol/L	10 µg/mL	29.5 µmol/L
Dopamine	0.3 µg/mL	1.96 µmol/L	0.9 µg/mL	5.87 µmol/L
Doxycycline	10.0 µg/mL	22.5 µmol/L	30 µg/mL	67.5 µmol/L
Erythromycin	11 µg/mL	14.96 µmol/L	60 µg/mL	81.6 µmol/L
Furosemide	20 µg/mL	60.4 µmol/L	60 µg/mL	181 µmol/L
Ibuprofen	40 µg/mL	194.3 µmol/L	500 µg/mL	2425 µmol/L
Isosorbide dinitrate	50 ng/mL	212 nmol/L	150 ng/mL	636 nmol/L
Lisinopril	0.10 µg/mL	0.25 µmol/L	0.30 µg/mL	0.74 µmol/L
Lovastatin	40 ng/mL	95 nmol/L	80 ng/mL	191 nmol/L
Low MW heparin	6.75 U/mL	N/A	30 U/mL	N/A
Methotrexate	546 µg/mL	1.2 mmol/L	910 µg/mL	2.0 mmol/L
Methyldopa	4.2 µg/mL	20.12 µmol/L	15 µg/mL	71 µmol/L

	Low or Therapeutic Concentration		High or Toxic Concentration	
Potential Interferents	**Common units**	**SI units**	**Common units**	**SI units**
Methylprednisolone	N/A	N/A	40 µg/mL	107 µmol/L
Mexiletine	1.3 µg/mL	7 µmol/L	4.0 µg/mL	22.3 µmol/L
Nicotine	37 ng/mL	0.23 µmol/L	1000 ng/mL	6.2 µmol/L
Nifedipine	125 ng/mL	362 nmol/L	400 ng/mL	1156 nmol/L
Nitrofurantoin	2.0 µg/mL	8.4 µmol/L	4.0 µg/mL	16.8 µmol/L
Nitroglycerine	7.5 ng/mL	33 nmol/L	160 ng/mL	704 nmol/L
Phenobarbital	24 µg/mL	107.6 µmol/L	97 µg/mL	431 µmol/L
Phenytoin	12 µg/mL	49.5 µmol/L	50 µg/mL	198 µmol/L
Primidone	10.5 µg/mL	48.2 µmol/L	40 µg/mL	183 µmol/L
Propranolol	0.50 µg/mL	1.94 µmol/L	2.0 µg/mL	7.71 µmol/L
Quinidine	3.7 µg/mL	11.56 µmol/L	12 µg/mL	37 µmol/L
Simvastatin	16 µg/mL	38 µmol/L	32 µg/mL	76 µmol/L
Theophylline	12 µg/mL	69.4 µmol/L	40 µg/mL	222 µmol/L
Thyroxine	0.08 µg/mL	0.11 µmol/L	1.01 µg/mL	1.30 µmol/L
Tissue plasminogen activator (TPA)	1.15 µg/mL	N/A	2.3 µg/mL	N/A
Trimethoprim	12 µg/mL	43 µmol/L	40 µg/mL	138 µmol/L
Verapamil	0.33 µg/mL	0.72 µmol/L	2.0 µg/mL	4.4 µmol/L
Warfarin	2.0 µg/mL	6.6 µmol/L	10 µg/mL	32.5 µmol/L

[a] Not applicable.

Assay results obtained at individual laboratories may vary from the data presented.

Hemolysis, Icterus, Lipemia (HIL), and Other Interferences

Potential interference in the Atellica IM TnIH assay from the compounds listed below is designed to be ≤ 10%.

Specimens that are...	Demonstrate ≤ 10% change in results up to...
Hemolyzed	500 mg/dL of hemoglobin
Lipemic	2000 mg/dL of triglycerides
Icteric	40 mg/dL of conjugated bilirubin
Icteric	60 mg/dL of unconjugated bilirubin

Specimens that contain...	Demonstrate ≤ 10% change in results up to...
Biotin	3500 ng/mL
Cholesterol	500 mg/dL
Protein Albumin	6 g/dL

Specimens that contain...	Demonstrate ≤ 10% change in results up to...
Protein Gamma Globulin	2.5 g/dL
Total Protein	12 g/dL

Assay results obtained at individual laboratories may vary from the data presented.

Linearity

The Atellica IM TnIH assay is linear from 2.50–25,000.00 pg/mL (ng/L). Linearity was evaluated according to the CLSI Document EP06-A.[35] Serum and lithium-heparin plasma samples were used to make pools at 3 different cTNI ranges. The dilution series were made by mixing high- and low-dose samples. The resulting sample mixtures were tested with the Atellica IM TnIH assay.

High-Dose Hook Effect

High cTnI concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with cTnI concentrations as high as 500,000 pg/mL (ng/L) will report > 25,000.00 pg/mL (ng/L).

Standardization

The Atellica IM TnIH assay standardization is traceable to an internal standard manufactured using human heart homogenate. Assigned values for calibrators are traceable to this standardization.

Technical Assistance

For customer support, contact your local technical support provider or distributor.

siemens.com/healthineers

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Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
	Version of instructions for use
	Internet URL address to access the electronic instructions for use
	Revision

Symbol	Symbol Title and Description
	Caution Consult instructions for use or accompanying documents for cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device.
	Biological risks Potential biological risks are associated with the medical device.
	Corrosive
	Dangerous to environment
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable
	Oxidizing
	Explosive
	Toxic
	Compressed gas
	Keep away from sunlight Prevent exposure to sunlight and heat.
	Up Store in an upright position.
	Do not freeze
	Temperature limit Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines.
	Handheld barcode scanner

Symbol	Symbol Title and Description
IVD	*In vitro* diagnostic medical device
Σ (n)	Contains sufficient for <n> tests Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol.
RxOnly	Prescription device (US only) Applies only to United States-registered IVD assays. CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.
	Mixing of substances Mix product before use.
	Reconstitute and mix lyophilized product before use.
	Target
	Interval
	Legal Manufacturer
EC REP	Authorized Representative in the European Community
	Use-by date Use by the designated date.
LOT	Batch code
REF	Catalog number
	Recycle
PRINTED WITH SOY INK	Printed with soy ink
CE	CE Mark
CE 0088	CE Mark with notified body ID number Notified body ID number can vary.
YYYY-MM-DD	Date format (year-month-day)
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
UNITS C	Common Units
UNITS SI	International System of Units

Symbol	Symbol Title and Description
MATERIAL	Material
MATERIAL ID	Unique material identification number
CONTROL NAME	Name of control
CONTROL TYPE	Type of control

Legal Information

US Pats 7,309,615; 7,785,904

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