SIEMENS

**ADVIA Centaur® XP**
**ADVIA Centaur® XPT**
Immunoassay Systems

# High-Sensitivity Troponin I (TNIH)

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| **Current Revision and Date**[a] | Rev. F, 2020-03 | | |
| **Product Name** | ADVIA Centaur® High-Sensitivity Troponin I (TNIH) assay (100 tests) | REF | 10994774 |
| | ADVIA Centaur High-Sensitivity Troponin I (TNIH) assay (500 tests) | REF | 10994775 |
| **Systems** | ADVIA Centaur XP system<br>ADVIA Centaur XPT system | | |
| **Materials Required but Not Provided** | ADVIA Centaur Wash 1 (2 x 1500 mL) | REF | 01137199 (112351) |
| | ADVIA Centaur Wash 1 (2 x 2500 mL) | REF | 03773025 |
| **Specimen Types** | Human serum, plasma (lithium heparin) | | |
| **Measuring Interval** | 2.50–25,000.00 pg/mL (ng/L) | | |
| **Reagent Storage** | 2–8°C | | |
| **Reagent On-System Stability** | 28 days | | |

[a] In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

## Intended Use

The ADVIA Centaur® 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 ADVIA Centaur XP and ADVIA Centaur XPT systems. 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 one value above the 99th percentile upper reference limit (URL) and with at least one 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 ADVIA Centaur TNIH is a 3-site sandwich immunoassay using direct chemiluminescent technology. The Solid Phase reagent consists of magnetic latex particles conjugated with streptavidin with two 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. The accumulated light signal is directly related to the sample cTnI concentration.

# Reagents

| Reagent | Description | Storage | Reagent Stability |
|---|---|---|---|
| ADVIA Centaur TNIH ReadyPack® primary reagent pack; Lite Reagent | 8.0 mL/reagent pack<br>bovine serum albumin (BSA) conjugated to a recombinant monoclonal Fab anti-human cTnI (~0.2–0.4 µg/mL) labeled with acridinium ester in HEPES buffer with stabilizers and preservatives | 2–8°C | **Unopened:** Stable until the expiration date on the product<br>**On-system:** 28 days |
| ADVIA Centaur TNIH ReadyPack primary reagent pack; Solid Phase Reagent | 13.0 mL/reagent pack<br>0.45 mg/mL streptavidin-coated magnetic latex particles with 2 biotinylated (mouse and sheep) monoclonal anti-troponin I antibodies in buffer with stabilizers and preservatives | 2–8°C | **Unopened:** Stable until the expiration date on the product<br>**On-system:** 28 days |

| Reagent | Description | Storage | Reagent Stability |
|---|---|---|---|
| ADVIA Centaur TNIH High Calibrator CAL H | 1.0 mL/vial after reconstitution human serum with human cTnI and preservatives (lyophilized) | 2–8°C | **Unopened:** Stable until the expiration date on the product |
| | | 2–8°C | **Reconstituted:** 4 hours |
| | | ≤ -20°C | **Reconstituted:** 30 days |
| | | | **On-system:** 4 hours |
| ADVIA Centaur TNIH Low Calibrator CAL L | 1.0 mL/vial HEPES buffer with bovine serum albumin (BSA), surfactants, and preservatives (liquid) | 2–8°C | **Unopened:** Stable until the expiration date on the product |
| | | 2–8°C | **Opened:** 4 hours |
| | | ≤ -20°C | **Opened:** 30 days |
| | | | **On-system:** 4 hours |
| ADVIA Centaur Wash 1[a] WASH 1 | 1500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant | 2–25°C | **Unopened:** Stable until the expiration date on the product |
| | | | **On-system:** 1 month |
| ADVIA Centaur Wash 1[a] WASH 1 | 2500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant | 2–25°C | **Unopened:** Stable until the expiration date on the product |
| | | | **On-system:** 1 month |
| ADVIA Centaur ReadyPack ancillary reagent pack; Multi-Diluent 11[b] M-DIL 11 | 5.0 mL/pack tris buffer and goat serum with protein stabilizers and preservatives | 2–8°C | **Unopened:** Stable until the expiration date on the product |
| | | | **On-system:** 28 consecutive days after the ancillary pack is pierced |

[a] Refer to *Materials Required but Not Provided*
[b] Refer to *Optional Materials*

## Warnings and Precautions

Safety data sheets (MSDS/SDS) are available on siemens.com/healthcare.

**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.

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

For professional use.

For *in vitro* diagnostic use.

## Preparing Reagents

All ADVIA Centaur TNIH ReadyPack reagents are liquid and ready to use. Remove all of the reagents from the refrigerator, and mix all primary reagent packs by hand. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended before loading it onto the system. For detailed information about preparing the reagents for use, refer to the system operating instructions.

**Note**

- Discard the primary reagent packs at the end of the on-system stability interval.
- Do not use reagents beyond the expiration date.

## Storing and Stability

Store the reagents upright at 2–8°C. Protect reagent packs from heat and light sources. Reagent packs loaded on the system are protected from light.

Reagents are stable at 2–8°C until the expiration date on the product.

# Specimen Collection and Handling

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

The following recommendations for handling and storing blood samples include guidelines furnished by the Clinical and Laboratory Standards Institute (CLSI).[18–20]

## Collecting the Specimen

- Serum and plasma can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[18]
- 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.
- Follow the instructions provided with your specimen collection device for use and processing.[19]
- Allow blood specimens to clot completely before centrifugation.[20]
- Keep tubes stoppered and upright at all times.
- 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 or below -20°C for up to 40 days in non-frost-free freezer.

- Samples can be frozen at or below -70°C for up to 1 year.
- Freeze samples only once and mix thoroughly after thawing. Frozen samples must be centrifuged at 2200 x g for 10 minutes after thawing, before analysis.

The purpose of handling and storage information is to provide guidance to users. 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 samples for shipment in compliance with applicable federal and international regulations covering the transport of clinical samples and etiological agents.

## Procedure

### Materials Provided

The following materials are provided:

| REF | Contents | Number of Tests |
|---|---|---|
| 10994774 | 1 ReadyPack primary reagent pack containing ADVIA Centaur TNIH Lite Reagent and Solid Phase reagents | 100 |
| | 1 vial of ADVIA Centaur TNIH Low Calibrator CAL L | |
| | 1 vial of ADVIA Centaur TNIH High Calibrator CAL H | |
| | ADVIA Centaur TNIH Master Curve card | |
| | ADVIA Centaur TNIH Calibrator Assigned Value Card and barcode labels | |
| 10994775 | 5 ReadyPack primary reagent packs containing ADVIA Centaur TNIH Lite Reagent and Solid Phase reagents | 500 |
| | 2 vials of ADVIA Centaur TNIH Low Calibrator CAL L | |
| | 2 vials of ADVIA Centaur TNIH High Calibrator CAL H | |
| | ADVIA Centaur TNIH Master Curve card | |
| | ADVIA Centaur TNIH Calibrator Assigned Value Card and barcode labels | |

### Materials Required but Not Provided

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

| Item | | Description | |
|---|---|---|---|
| REF | 01137199 (112351) | ADVIA Centaur Wash 1 WASH 1 | 2 x 1500 mL/pack |
| REF | 03773025 | ADVIA Centaur Wash 1 WASH 1 | 2 x 2500 mL/pack |

### Optional Materials

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

| Item | | Description | |
|---|---|---|---|
| REF | 10994776 | ADVIA Centaur TNIH Master Curve Material MCM | 5 x 1.0 mL |
| | | ADVIA Centaur TNIH MCM lot-specific value sheet | |
| REF | 05699280 (117228) | ADVIA Centaur Multi-Diluent 11 M-DIL 11 | 2 ReadyPack ancillary reagent packs that contain 5.0 mL/pack |

## Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following actions:

1. Dispenses 100 µL of sample into a cuvette.
2. Dispenses 130 µL of Solid Phase Reagent and 80 µL of Lite Reagent, and incubates for 8.25 minutes at 37°C.
3. Separates, aspirates, and washes the cuvettes with ADVIA Centaur Wash 1.
4. Dispenses 300 µL of ADVIA Centaur Acid Reagent and 300 µL of ADVIA Centaur Base Reagent to initiate the chemiluminescent reaction.
5. Reports results according to the selected option, as described in the system operating instructions.

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.

## Preparing the System

Ensure that the system has sufficient primary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Load the ReadyPack primary reagent packs in the primary reagent compartment using the arrows on the packs as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about loading reagents, refer to the system operating instructions.

If automatic dilution of a sample is required, load ADVIA Centaur Multi-Diluent 11 in the ancillary reagent entry.

## 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 detailed information about determining the minimum required volume, refer to the system operating instructions.

**Note** The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. For detailed information, refer to *Dilutions*.

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples must be free of fibrin or other particulate matter.
- Samples should be free of bubbles.

**Note** Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[20]

## On-System Stability

The ADVIA Centaur TNIH assay reagents are stable onboard the system for 28 days and are stable unopened until the expiration date on the product. Discard reagent packs at the end of the 28-day onboard stability interval. Do not use reagents beyond the expiration date.

Reagent packs loaded on the system are protected from light.

ADVIA Centaur TNIH Calibrators are stable on the system for 4 hours. Dispose of any calibrator that remains in the sample cups after 4 hours.

## Defining Master Curve Values

Assay calibration is required before you use a new reagent lot. For each new lot number of ReadyPack primary reagent, enter master curve values on the system. The Master Curve card contains the master curve values. Enter the values using the barcode reader or keyboard.

For detailed information about entering master curve values, refer to the system operating instructions.

# Performing Calibration

For calibration of the ADVIA Centaur TNIH assay, use the ADVIA Centaur TNIH Calibrators provided.

**Note** The low and high calibrators provided in this kit are matched to the ReadyPack primary reagent pack. Do not mix calibrator lots with different lots of reagent packs.

Each lot of calibrators is packaged with a lot-specific Calibrator Assigned Value Card to facilitate entering the calibration values on the system. Enter the values using the barcode reader or keyboard. For detailed information about entering calibration values, refer to the system operating instructions.

### Preparing the Calibrators

The ADVIA Centaur TNIH Low Calibrator is liquid and ready to use. DO NOT ADD WATER TO THE LOW CALIBRATOR.

Prepare the ADVIA Centaur TNIH High Calibrator using the following steps:

1. Add 1.00 mL of reagent water into the high calibrator vial using a class A volumetric pipet. Replace cap.

**Note** For information about reagent water, refer to the system operating instructions.

2. Let the high calibrator stand undisturbed for 15–20 minutes at room temperature to allow the lyophilized material to dissolve.
3. Gently swirl and invert the high calibrator until homogeneous.

**Note** The low and high calibrators can be aliquoted into tightly sealed cryovials and frozen at or below -20°C for up to 30 days in a non-frost-free freezer and thawed only once. To ensure complete homogeneity, the thawed calibrators must be gently mixed and inverted.

### Calibration Procedure

For detailed information about processing calibrators, refer to the system operating instructions.

Perform the calibration procedure using the following steps:

1. Ensure that the appropriate master curve values are entered on the system. Refer to *Defining Master Curve Values*.
2. Enter the calibrator assigned values located on the ADVIA Centaur TNIH Calibrator Assigned Value Card into the system.
3. Schedule the calibrators to the worklist.
4. Prepare 2 sample cups with ADVIA Centaur TNIH Calibrator barcode labels: 1 cup for the low calibrator and 1 cup for the high calibrator. Place the barcode label on the sample cup with the readable characters oriented vertically.

**Note** Calibrator barcode labels are lot-number specific. Do not use barcode labels from one calibrator lot with any other lot of calibrators.

5. Gently mix the low and high calibrators until homogeneous.

6. Dispense a sufficient volume of each calibrator into the appropriate sample cups. Avoid bubbles.

**Note** Refer to the system operator's guide for sample volume requirements.

7. Load the calibrator sample cups in the rack.
8. Place the rack in the sample entry queue.
9. Load the reagents and other materials required to perform the assay.
10. Start the entry queue, if required.

**Note** Dispose of any calibrator that remains in the sample cups after 4 hours. Do not return any calibrators back into the vials after calibration because evaporation can occur, which may affect performance. Do not refill sample cups when the contents are depleted; if required, dispense fresh calibrators.

### Calibration Frequency

Calibrate the assay at the end of the 28-day calibration interval.

Additionally, the ADVIA Centaur TNIH assay requires a two-point calibration:

- When changing lot numbers of primary reagent packs.
- After major maintenance or service.
- When indicated by quality control results.

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

## Performing Quality Control

For quality control of the ADVIA Centaur TNIH assay, use quality control material with at least 2 levels of controls with known troponin I concentrations. Perform the quality control procedure according to the quality control instructions for use.

Quality control samples should be assayed at least once on each day that samples are analyzed to monitor system performance and chart trends. Quality control samples should also be assayed when performing a 2-point calibration.

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

For detailed information about entering quality control values, refer to the system operating instructions.

A satisfactory level of performance is achieved when the analyte values obtained are within the Acceptable Control range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme.

### Taking Corrective Action

If the quality control results do not fall within the expected values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- Repeat testing of patient samples before reporting results.

Perform corrective actions in accordance with established laboratory protocol. If necessary, contact your local technical support provider or distributor for assistance.

# Results

## Calculation of Results

The instrument reports troponin I 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 = 1.0 ng/L.

For detailed information about how the system calculates results, refer to the system operating instructions. For information about reporting results of diluted samples, refer to *Dilutions*.

## Dilutions

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to the following information for the sample volume required to perform onboard dilutions:

| Dilution | Sample Volume (µL) |
|---|---|
| 1:2 | 150 |
| 1:5 | 60 |

Patient samples with cTnI levels > 25,000 pg/mL (ng/L) can be diluted and retested to obtain quantitative results. Patient samples with cTnI levels ≤ 25,000 pg/mL (ng/L) should not be diluted.

- Patient samples can be automatically diluted by the system.
- For automatic dilutions, ensure that ADVIA Centaur Multi-Diluent 11 is loaded and set the system parameters as follows:

  Dilution point: 25,000 pg/mL (ng/L)

  Dilution factor: 2, 5

For detailed information about automatic dilutions, refer to the system operating instructions.

## Interpretation of Results

Results of this assay should always be interpreted in conjunction with 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.[21]
**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.
- Do not pour the calibrators back into the vials after calibration because evaporation could occur, which may affect performance.
- Dispose of any calibrator remaining in the sample cups after 4 hours.

- Do not refill calibrator sample cups when the contents are depleted. If required, dispense fresh calibrators.
- 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.[22] 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.
- 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.[23]
- 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.[21] **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 study was conducted using the ADVIA Centaur TNIH assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) Guideline Protocol EP28-A3c.[24]

Serum and lithium-heparin plasma specimens were collected from 2010 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.[24] Two female subjects had troponin values of approximately 400 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 47.34 pg/mL (ng/L). In the IFCC-recommended reporting format (whole numbers), the 99th percentile is 47 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 | 1012 | 36.99 | 30.22–72.63 |
| | Male | 998 | 57.27 | 38.58–90.15 |
| | Combined | 2010 | 47.34 | 36.39–64.27 |
| Serum | Female | 1006 | 39.59 | 29.62–74.64 |
| | Male | 984 | 58.05 | 37.50–80.35 |
| | Combined | 1990 | 46.47 | 36.99–65.20 |

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

# Performance Characteristics

## 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 47.34 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 | % | 95% CI[a] | n | % | 95% CI[a] | n | % | 95% CI[a] | n | % | 95% CI[a] |
| **Lithium Heparin Plasma** | | | | | | | | | | | | |
| 0– < 1.5 | 141 | 78.0 | 70.5–84.1 | 957 | 92.8 | 91.0–94.3 | 179 | 61.5 | 54.2–68.3 | 919 | 96.6 | 95.3–97.6 |
| ≥ 1.5– < 2.5 | 238 | 89.5 | 85.0–92.8 | 1623 | 90.7 | 89.2–92.0 | 364 | 58.5 | 53.4–63.5 | 1497 | 98.3 | 97.5–98.9 |
| ≥ 2.5– < 3.5 | 198 | 92.9 | 88.5–95.7 | 1345 | 90.4 | 88.7–91.9 | 313 | 58.8 | 53.3–64.1 | 1230 | 98.9 | 98.1–99.3 |
| ≥ 3.5– < 4.5 | 149 | 91.3 | 85.6–94.8 | 1078 | 90.9 | 89.0–92.5 | 234 | 58.1 | 51.7–64.3 | 993 | 98.7 | 97.8–99.2 |
| ≥ 4.5– < 6 | 63 | 95.2 | 86.9–98.4 | 457 | 89.5 | 86.3–92.0 | 108 | 55.6 | 46.2–64.6 | 412 | 99.3 | 97.9–99.8 |
| ≥ 6– < 9 | 194 | 92.8 | 88.3–95.7 | 890 | 88.1 | 85.8–90.1 | 286 | 62.9 | 57.2–68.3 | 798 | 98.2 | 97.1–99.0 |
| ≥ 9– < 24 | 212 | 92.9 | 88.7–95.7 | 838 | 85.9 | 83.4–88.1 | 315 | 62.5 | 57.1–67.7 | 735 | 98.0 | 96.7–98.8 |
| ≥ 24 | 62 | 93.5 | 84.6–97.5 | 246 | 86.2 | 81.3–89.9 | 92 | 63.0 | 52.8–72.2 | 216 | 98.1 | 95.3–99.3 |
| **Serum** | | | | | | | | | | | | |
| 0– < 1.5 | 142 | 78.9 | 71.4–84.8 | 978 | 93.1 | 91.4–94.6 | 179 | 62.6 | 55.3–69.3 | 941 | 96.8 | 95.5–97.8 |
| ≥ 1.5– < 2.5 | 236 | 88.6 | 83.9–92.0 | 1630 | 91.4 | 90.0–92.7 | 349 | 59.9 | 54.7–64.9 | 1517 | 98.2 | 97.4–98.8 |
| ≥ 2.5– < 3.5 | 190 | 92.1 | 87.4–95.2 | 1371 | 91.2 | 89.6–92.6 | 296 | 59.1 | 53.4–64.6 | 1265 | 98.8 | 98.1–99.3 |
| ≥ 3.5– < 4.5 | 145 | 90.3 | 84.4–94.2 | 1089 | 91.5 | 89.7–93.0 | 224 | 58.5 | 51.9–64.7 | 1010 | 98.6 | 97.7–99.2 |
| ≥ 4.5– < 6 | 62 | 96.8 | 89.0–99.1 | 459 | 89.1 | 85.9–91.6 | 110 | 54.5 | 45.2–63.5 | 411 | 99.5 | 98.2–99.9 |
| ≥ 6– < 9 | 190 | 91.6 | 86.8–94.8 | 905 | 88.5 | 86.3–90.4 | 278 | 62.6 | 56.8–68.1 | 817 | 98.0 | 96.8–98.8 |
| ≥ 9– < 24 | 214 | 93.0 | 88.8–95.7 | 849 | 86.7 | 84.2–88.8 | 312 | 63.8 | 58.3–68.9 | 751 | 98.0 | 96.7–98.8 |
| ≥ 24 | 65 | 92.3 | 83.2–96.7 | 255 | 86.3 | 81.5–90.0 | 95 | 63.2 | 53.1–72.2 | 225 | 97.8 | 94.9–99.0 |

[a] CI = Confidence interval

Results for females based on time of presentation to the emergency department, calculated using the female-specific 99th percentile of 36.99 pg/mL (ng/L) for plasma and 39.59 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 47.34 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 71% 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 | % | 95% CI[a] | n | % | 95% CI[a] | n | % | 95% CI[a] | n | % | 95% CI[a] |
| **Lithium Heparin Plasma** | | | | | | | | | | | | |
| 0– < 1.5 | 41 | 82.9 | 68.7–91.5 | 396 | 93.9 | 91.1–95.9 | 58 | 58.6 | 45.8–70.4 | 379 | 98.2 | 96.2–99.1 |
| ≥ 1.5– < 2.5 | 76 | 89.5 | 80.6–94.6 | 710 | 91.8 | 89.6–93.6 | 126 | 54.0 | 45.3–62.4 | 660 | 98.8 | 97.6–99.4 |
| ≥ 2.5– < 3.5 | 72 | 95.8 | 88.5–98.6 | 605 | 91.9 | 89.5–93.8 | 118 | 58.5 | 49.5–67.0 | 559 | 99.5 | 98.4–99.8 |
| ≥ 3.5– < 4.5 | 52 | 94.2 | 84.4–98.0 | 481 | 89.4 | 86.3–91.8 | 100 | 49.0 | 39.4–58.7 | 433 | 99.3 | 98.0–99.8 |
| ≥ 4.5– < 6 | 24 | 95.8 | 79.8–99.3 | 239 | 86.2 | 81.2–90.0 | 56 | 41.1 | 29.2–54.1 | 207 | 99.5 | 97.3–99.9 |
| ≥ 6– < 9 | 70 | 95.7 | 88.1–98.5 | 370 | 87.8 | 84.1–90.8 | 112 | 59.8 | 50.6–68.4 | 328 | 99.1 | 97.3–99.7 |
| ≥ 9– < 24 | 71 | 94.4 | 86.4–97.8 | 347 | 88.8 | 85.0–91.7 | 106 | 63.2 | 53.7–71.8 | 312 | 98.7 | 96.8–99.5 |
| ≥ 24 | 25 | 100.0 | 86.7–100.0 | 106 | 82.1 | 73.7–88.2 | 44 | 56.8 | 42.2–70.3 | 87 | 100.0 | 95.8–100.0 |
| **Serum** | | | | | | | | | | | | |
| 0– < 1.5 | 41 | 80.5 | 66.0–89.8 | 405 | 94.8 | 92.2–96.6 | 54 | 61.1 | 47.8–73.0 | 392 | 98.0 | 96.0–99.0 |
| ≥ 1.5– < 2.5 | 77 | 88.3 | 79.3–93.7 | 708 | 91.9 | 89.7–93.7 | 125 | 54.4 | 45.7–62.9 | 660 | 98.6 | 97.4–99.3 |
| ≥ 2.5– < 3.5 | 67 | 95.5 | 87.6–98.5 | 615 | 92.8 | 90.5–94.6 | 108 | 59.3 | 49.8–68.1 | 574 | 99.5 | 98.5–99.8 |
| ≥ 3.5– < 4.5 | 47 | 93.6 | 82.8–97.8 | 484 | 90.3 | 87.3–92.6 | 91 | 48.4 | 38.4–58.5 | 440 | 99.3 | 98.0–99.8 |
| ≥ 4.5– < 6 | 24 | 95.8 | 79.8–99.3 | 239 | 87.0 | 82.2–90.7 | 54 | 42.6 | 30.3–55.8 | 209 | 99.5 | 97.3–99.9 |
| ≥ 6– < 9 | 68 | 95.6 | 87.8–98.5 | 379 | 88.7 | 85.1–91.5 | 108 | 60.2 | 50.8–68.9 | 339 | 99.1 | 97.4–99.7 |
| ≥ 9– < 24 | 71 | 94.4 | 86.4–97.8 | 353 | 89.8 | 86.2–92.5 | 103 | 65.0 | 55.5–73.6 | 321 | 98.8 | 96.8–99.5 |
| ≥ 24 | 28 | 96.4 | 82.3–99.4 | 107 | 84.1 | 76.0–89.8 | 44 | 61.4 | 46.6–74.3 | 91 | 98.9 | 94.0–99.8 |

[a] CI = Confidence interval

Results for males based on time of presentation to the emergency department, calculated using the male-specific 99th percentile of 57.27 pg/mL (ng/L) for plasma and 58.05 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 47.34 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 2.9%.

**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 | % | 95% CI[a] | n | % | 95% CI[a] | n | % | 95% CI[a] | n | % | 95% CI[a] |
| **Lithium Heparin Plasma** | | | | | | | | | | | | |
| 0– < 1.5 | 100 | 74.0 | 64.6–81.6 | 561 | 92.0 | 89.4- 94.0 | 119 | 62.2 | 53.2- 70.4 | 542 | 95.2 | 93.1- 96.7 |
| ≥ 1.5– < 2.5 | 162 | 87.7 | 81.7–91.9 | 913 | 90.7 | 88.6- 92.4 | 227 | 62.6 | 56.1- 68.6 | 848 | 97.6 | 96.4- 98.5 |
| ≥ 2.5– < 3.5 | 126 | 89.7 | 83.1–93.9 | 740 | 90.1 | 87.8- 92.1 | 186 | 60.8 | 53.6- 67.5 | 680 | 98.1 | 96.8- 98.9 |
| ≥ 3.5– < 4.5 | 97 | 86.6 | 78.4–92.0 | 597 | 92.5 | 90.1–94.3 | 129 | 65.1 | 56.6–72.8 | 565 | 97.7 | 96.1–98.7 |
| ≥ 4.5– < 6 | 39 | 92.3 | 79.7–97.3 | 218 | 92.2 | 87.9–95.1 | 53 | 67.9 | 54.5–78.9 | 204 | 98.5 | 95.8–99.5 |
| ≥ 6– < 9 | 124 | 87.9 | 81.0–92.5 | 520 | 88.8 | 85.9–91.3 | 167 | 65.3 | 57.8–72.1 | 477 | 96.9 | 94.9–98.1 |

**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 | % | 95% CI[a] | n | % | 95% CI[a] | n | % | 95% CI[a] | n | % | 95% CI[a] |
| ≥ 9– < 24 | 141 | 91.5 | 85.7–95.1 | 491 | 84.7 | 81.3–87.6 | 204 | 63.2 | 56.4–69.6 | 428 | 97.2 | 95.2–98.4 |
| ≥ 24 | 37 | 86.5 | 72.0–94.1 | 140 | 89.3 | 83.1–93.4 | 47 | 68.1 | 53.8–79.6 | 130 | 96.2 | 91.3–98.3 |
| **Serum** | | | | | | | | | | | | |
| 0– < 1.5 | 101 | 75.2 | 66.0–82.6 | 573 | 92.8 | 90.4–94.7 | 117 | 65.0 | 56.0–73.0 | 557 | 95.5 | 93.5–96.9 |
| ≥ 1.5– < 2.5 | 159 | 85.5 | 79.2–90.2 | 922 | 91.5 | 89.6–93.2 | 214 | 63.6 | 56.9–69.7 | 867 | 97.3 | 96.1–98.2 |
| ≥ 2.5– < 3.5 | 123 | 86.2 | 79.0–91.2 | 756 | 91.1 | 88.9–93.0 | 173 | 61.3 | 53.8–68.2 | 706 | 97.6 | 96.2–98.5 |
| ≥ 3.5– < 4.5 | 98 | 84.7 | 76.3–90.5 | 605 | 93.1 | 90.7–94.8 | 125 | 66.4 | 57.7–74.1 | 578 | 97.4 | 95.8–98.4 |
| ≥ 4.5– < 6 | 38 | 94.7 | 82.7–98.5 | 220 | 90.9 | 86.4–94.0 | 56 | 64.3 | 51.2–75.5 | 202 | 99.0 | 96.5–99.7 |
| ≥ 6– < 9 | 122 | 87.7 | 80.7–92.4 | 526 | 90.5 | 87.7–92.7 | 157 | 68.2 | 60.5–74.9 | 491 | 96.9 | 95.0–98.1 |
| ≥ 9– < 24 | 143 | 91.6 | 85.9–95.1 | 496 | 86.1 | 82.8–88.9 | 200 | 65.5 | 58.7–71.7 | 439 | 97.3 | 95.3–98.4 |
| ≥ 24 | 37 | 89.2 | 75.3–95.7 | 148 | 89.9 | 84.0–93.8 | 48 | 68.8 | 54.7–80.1 | 137 | 97.1 | 92.7–98.9 |

[a] CI = 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.[9,11–14,25–32]

The ADVIA Centaur 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 ADVIA Centaur TNIH test result above the 99th percentile (> 47.34 pg/mL (ng/L)) on one or more serial draws. 89% of these patients were found to have one 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

## Measuring Interval

The ADVIA Centaur TNIH assay measures cTnI concentrations from 2.50–25,000.00 pg/mL (ng/L). The low end of the assay range is defined by the limit of quantitation (LoQ).

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

## Specificity

The ADVIA Centaur TNIH assay shows high specificity for cTnI. The following compounds were added at the concentrations indicated to a serum or lithium heparin sample with a known cTnI concentration. ADVIA Centaur 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[33] 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] ND = Not Detectable (< 0.01%)

## Detection Capability

The limit of blank (LoB), limit of detection (LoD), and the limit of quantitation (LoQ) were determined as described in CLSI Document EP17-A2.[34] The assay is designed to have an LoD of ≤ 1.6 pg/mL (ng/L), and an LoQ of ≤ 3.0 pg/mL (ng/L).

The LoB is defined as the highest measurement result that is likely to be observed for a blank sample. The ADVIA Centaur TNIH assay has an LoB of 0.50 pg/mL (ng/L).

The LoD is defined as the lowest concentration of cTnI that can be detected with 95% probability. The ADVIA Centaur TNIH assay has an LoD of 1.60 pg/mL (ng/L).

The LoQ is defined as the lowest concentration of cTnI that can be detected at a total CV of 20%. The ADVIA Centaur TNIH assay has an LoQ of 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. Results obtained at individual laboratories may vary from the data provided.

## High-Sensitivity Determination

The ADVIA Centaur 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 47.34 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).

### Precision

Precision was evaluated according to the CLSI Document EP05-A3.[35] Serum and lithium-heparin plasma samples were assayed twice a day in replicates of 2, for 20 days (n = 80 replicates per sample) using the ADVIA Centaur TNIH assay. The following representative results were obtained:

| | Mean | Repeatability (Within-Run) | | Within-Lab (Total Precision) | |
|---|---|---|---|---|---|
| **Sample Types** | **(pg/mL; ng/L)** | **SD (pg/mL; ng/L)** | **%CV** | **SD (pg/mL; ng/L)** | **%CV** |
| Serum 1 | 13.11 | 0.63 | 4.8 | 0.70 | 5.4 |
| Serum 2 | 138.62 | 1.81 | 1.3 | 2.68 | 1.9 |
| Serum 3 | 1461.96 | 12.47 | 0.9 | 17.52 | 1.2 |
| Serum 4 | 14,099.79 | 102.77 | 0.7 | 133.95 | 0.9 |
| Plasma 1 | 12.68 | 0.45 | 3.6 | 0.62 | 4.9 |
| Plasma 2 | 145.93 | 1.84 | 1.3 | 2.28 | 1.6 |
| Plasma 3 | 1522.05 | 13.56 | 0.9 | 21.32 | 1.4 |
| Plasma 4 | 13,436.79 | 104.88 | 0.8 | 148.73 | 1.1 |

## Interferences

Potential interference in the ADVIA Centaur TNIH assay from the compounds listed below is designed to be ≤ 10%. Interfering substances at the levels indicated were tested as described in CLSI Document EP07-A2[33] using the ADVIA Centaur TNIH assay.

| **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 |
| Protein Gamma Globulin | 2.5 g/dL |
| Total Protein | 12 g/dL |

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 in the ADVIA Centaur 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 | NA[a] | 40 µg/mL | NA |
| 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 | NA | 30 U/mL | NA |
| 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 |
| Methylprednisolone | NA | NA | 40 µg/mL | 107 µmol/L |

| | Low or Therapeutic Concentration | | High or Toxic Concentration | |
|---|---|---|---|---|
| **Potential Interferents** | **Common units** | **SI units** | **Common units** | **SI units** |
| 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 | NA | 2.3 µg/mL | NA |
| 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] NA = not applicable

### Linearity

The ADVIA Centaur TNIH assay is linear from 2.50–25,000.00 pg/mL (ng/L).

Linearity was evaluated according to the CLSI Document EP06-A.[36] 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 ADVIA Centaur TNIH assay.

### High-Dose Hook Effect

No hook effect has been observed in patient samples with cTnI levels as high as 500,000 pg/mL (ng/L).

### Standardization

The ADVIA Centaur TNIH assay is standardized to an internal standard manufactured using human heart homogenate. Assigned values for calibrators are traceable to this standardization.

## Technical Assistance

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

siemens.com/healthcare

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## Definition of Symbols

The following symbols may appear on the product labeling:

| Symbol | Definition | Symbol | Definition |
|---|---|---|---|
| IVD | *In vitro* diagnostic medical device | REF | Catalog number |
| | Legal manufacturer | EC REP | Authorized Representative in the European Community |
| CE | CE Mark | CE 0088 | CE Mark with identification number of notified body |
| | Consult instructions for use | | Biological risk |
| | Do not freeze (> 0°C) | | Temperature limitation |
| | Lower limit of temperature | | Upper limit of temperature |
| | Keep away from sunlight and heat | | Up |
| | Use by | Σ (n) | Contains sufficient for (n) tests |
| LOT | Batch code |  | Shake the reagent pack vigorously. Refer to *Preparing Reagents* in the assay-specific ADVIA Centaur product instructions for detailed information. |
| YYYY-MM-DD | Date format (year-month-day) | Rev. | Revision |
| MC DEF | Master Curve Definition | CHECKSUM | Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid. |
| LOT DTL | Lot Details | DER GRÜNE PUNKT | Green dot |
| | Recycle | PRINTED WITH SOY INK | Printed with soy ink |
| RxOnly | Prescription device (US only) | | |

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Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591 USA

**Global Siemens Headquarters**
Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

**Siemens Healthcare Headquarters**
Siemens Healthcare GmbH
Henkestr. 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
siemens.com/healthcare

**Global Division**
Siemens Healthcare
Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens.com/healthcare