SIEMENS

ADVIA Centaur® CP
Immunoassay System

High-Sensitivity Troponin I (TNIH)

Current Revision and Date[a]	Rev. B, 2021-06	
Product Name	ADVIA Centaur High-Sensitivity Troponin I (TNIH)	REF 10994774 (100 tests)
		REF 10994775 (500 tests)
Abbreviated Product Name	ADVIA Centaur TNIH	
Test Name/ID	TNIH	
Systems	ADVIA Centaur CP System	
Materials Required but Not Provided	ADVIA Centaur Ancillary Probe Wash 3	REF 10699211
	ADVIA Centaur Wash 1 (2 x 1500 mL)	REF 01137199 (112351)
	ADVIA Centaur Wash 1 (2 x 2500 mL)	REF 03773025
Optional Materials	ADVIA Centaur TNIH MCM	REF 10994776
	ADVIA Centaur Multi-Diluent 11	REF 05699280
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.

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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® CP system. 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 ADVIA Centaur TNIH is a 3-site sandwich immunoassay using direct chemiluminometric technology. The Solid Phase reagent is 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 whose architecture consists 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
ADVIA Centaur TNIH ReadyPack® primary reagent pack[a, b] **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
ADVIA Centaur TNIH CAL L[a] 1.0 mL/vial, liquid HEPES buffer; bovine serum albumin (BSA); surfactants; preservatives	Unopened at 2–8°C Opened at 2–8°C Opened at ≤ -20°C At room temperature	Until expiration date on product 4 hours 30 days; thaw 1 time 4 hours
ADVIA Centaur TNIH CAL H[a] 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 At room temperature	Until expiration date on product 4 hours 30 days; thaw 1 time 4 hours
ADVIA Centaur Multi-Diluent 11 ReadyPack ancillary reagent pack[a, c] 5.0 mL/pack Tris buffer; goat serum; protein stabilizers; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
ADVIA Centaur ReadyPack ancillary reagent; Ancillary Probe Wash 3[a, d] 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
ADVIA Centaur Wash 1[a, d] 1500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%); surfactant	Unopened at 2–25°C Onboard	Until expiration date on product 1 month
ADVIA Centaur Wash 1[a, d] 2500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%); surfactant	Unopened at 2–25°C Onboard	Until expiration date on product 1 month

[a] Store in an upright position.
[b] Prevent exposure to sunlight and heat.
[c] Refer to *Optional Materials*.
[d] Refer to *Materials Required but Not Provided*.

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 (MSDS/SDS) 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.

Storage and Stability

Store all reagents in an upright position, away from light and heat. Do not use products beyond the expiration date printed on the product labeling.

For information about product storage and stability, refer to *Reagents*.

Onboard Stability

Discard products at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

For information about product onboard stability, refer to *Reagents*.

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]

- 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. Samples can be frozen at ≤ -70°C for up to 1 year. Do not store in a frost-free freezer.
- Freeze samples only once. Thawed samples used in troponin testing must be thoroughly mixed and centrifuged prior to analysis to remove particulate matter.

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 a complete list of appropriate sample containers and information about determining the minimum required volume, refer to the system online help.

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

Do not use samples with apparent contamination.

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

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

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

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 1 vial ADVIA Centaur TNIH CAL low calibrator CAL L 1 vial ADVIA Centaur TNIH CAL high calibrator CAL H ADVIA Centaur TNIH master curve card ADVIA Centaur TNIH CAL calibrator assigned value sheet and barcode labels	100
10994775	5 ReadyPack primary reagent packs containing ADVIA Centaur TNIH Lite Reagent and Solid Phase 2 vials ADVIA Centaur TNIH CAL low calibrator CAL L 2 vials ADVIA Centaur TNIH CAL high calibrator CAL H ADVIA Centaur TNIH master curve card ADVIA Centaur TNIH CAL calibrator assigned value sheet and barcode labels	500

Materials Required but Not Provided

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

REF	Description	
	ADVIA Centaur CP system[a]	
10699211	ADVIA Centaur Ancillary PW3 (probe wash)	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack APW 3
01137199 (112351)	ADVIA Centaur Wash 1 (wash)	2 x 1500 mL/pack WASH 1
03773025	ADVIA Centaur Wash 1 (wash)	2 x 2500 mL/pack WASH 1

[a] Additional system fluids are required to operate the system: ADVIA Centaur Acid Reagent, ADVIA Centaur Base Reagent, and ADVIA Centaur Cleaning Solution.

Optional Materials

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

REF	Description	
10994776	ADVIA Centaur TNIH MCM (master curve material)	5 x 1.0 mL levels of master curve material MCM
05699280	ADVIA Centaur Multi-Diluent 11 (diluent)	2 ReadyPack ancillary reagent packs containing 5.0 mL/pack DIL

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 10 minutes at 37°C.
3. Performs a wash sequence using ADVIA Centaur Wash 1.
4. Dispenses 300 µL each of ADVIA Centaur Acid Reagent and ADVIA Centaur Base Reagent to initiate the chemiluminescent reaction.
5. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading the packs onto the system, reagents require mixing. For information about mixing the reagents, refer to the system online help.

Preparing the System

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided* and *Materials Required but Not Provided* for guidance about required reagents.

For information about loading products, refer to the system online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, enter the assay master curve values by scanning the master curve card. For information about defining the master curve, refer to the system online help.

Performing Calibration

For calibration of the ADVIA Centaur TNIH assay, use the calibrators provided with each kit.

Note Calibrators provided in an assay kit must only be used with the reagent lot provided in the same kit.

Calibration Frequency

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

- At the end of the 28-day calibration interval.
- When changing lot numbers of primary reagent packs.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

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 ADVIA Centaur 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 ADVIA Centaur TNIH CAL H using the following steps:

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

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

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

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

Before using frozen calibrators, allow the material to thaw completely. 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 *Reagents* and discard any remaining material.

Calibration Procedure

Perform the calibration procedure using the following steps:

1. Ensure that the appropriate master curve and calibrator assigned values are entered on the system. For information about defining the master curve and entering calibrator values, refer to the system online help.
2. Load the required reagents for the assay.
3. Schedule the calibrators.
4. Label 2 sample containers with barcode labels: 1 container for the low calibrator and 1 container for the high calibrator. Place the barcode labels on the sample cups with the readable characters oriented vertically.

   Note Barcode labels are lot-specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.

5. Gently mix the product and dispense a sufficient volume of each calibrator into the appropriate sample containers. Avoid bubbles.

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

6. Load the samples according to the system online help.

Note Dispose of any calibrator that remains in the sample containers after 4 hours. Do not refill or reuse sample containers. Do not return any calibrator material back into the original container.

Performing Quality Control

For quality control of the ADVIA Centaur TNIH assay, use an appropriate quality control material of known analyte concentration with a minimum of two levels (low and high) 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 procedure. 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 system 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 expected control interval, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the system online help.

Results

Calculation of Results

The system determines the result using the calculation procedure described in the system 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 system online help.

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

For automated dilutions, perform the following activities:

- Load ADVIA Centaur Multi-Diluent 11.
- Ensure that sufficient sample volume is available. Refer to the table below.
- Select the appropriate dilution factor.

For automatic dilutions, enter a dilution setpoint of 25,000 pg/mL (ng/L).

Sample	Dilution	Sample Volume (µL)
Serum and plasma	1:2	100
Serum and plasma	1:5	40

Interpretation of Results

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

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.
- Specimens from some individuals with pathologically high gamma globulin levels may demonstrate depressed troponin values. This may be due to the presence of cardiac troponin-specific autoantibodies.[20] Additional information may be required for diagnosis.
- 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.
- Heterophilic antibodies and rheumatoid factor in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[21] 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.[22]

Expected Values

A reference interval for apparently healthy adults was established in accordance with CLSI Document EP28-A3c[23] on the ADVIA Centaur XP system.

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.[23] 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

Sample Type	Gender	N	99th Percentile[a] (pg/mL; ng/L)	90% CI[b] (pg/mL; ng/L)
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] Confidence interval.

As with all *in vitro* diagnostic assays, each laboratory should establish its own diagnostic cutoff value, which reflects criteria for AMI diagnosis at their institution and is representative of specific populations.

Performance Characteristics

The reagent formulations used on the ADVIA Centaur CP system are the same as those used on all ADVIA Centaur systems. Some performance characteristics were established using the ADVIA Centaur XP system.

Assay performance characteristics are representative data. Results obtained at individual laboratories may vary from the data presented.

Measuring Interval

The ADVIA Centaur TNIH assay measures cTnI concentrations from 2.50–25,000.00 pg/mL (ng/L). The lower end of the measuring interval is defined by the Limit of Quantitation (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 ADVIA Centaur 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. 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[24] and is calculated as:

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

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

Cross-reactant	Amount (ng/mL)	Cross-reactivity (%)
Myoglobin	1000	ND
CK-MB	1000	ND

[a] Human recombinant.

[b] Not detectable (< 0.01%).

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. 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 ADVIA Centaur 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 ADVIA Centaur 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 CV is 20%. The LoQ of the ADVIA Centaur 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. 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 (coefficient of variation) 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).

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 from baseline blood draw
- the time of presentation to the emergency department

The cutoff value, and sensitivity and specificity information should only be used as a guide when determining the appropriate cutoff value for your institution. Because sensitivity and specificity are influenced by the cutoff value, laboratories should select a cutoff value based on their specific sensitivity and specificity requirements.

Analysis 1: Time from baseline blood draw

The results were analyzed using serial time intervals subsequent to a baseline blood draw collected for the study during the emergency department visit. The baseline blood draw for the study was collected 45 minutes (median) after the emergency department blood draw.

Note The initial emergency department blood draw occurred at a median of 44 minutes (interquartile range of 26–70 minutes) following patient admission.

The pooled gender results that are summarized in table 1 are based on time from the study baseline blood draw, calculated using the overall 99th percentile of 47.34 pg/mL (ng/L). Gender-specific data are presented in tables 2 and 3:

Table 1: Pooled gender results based on time from study baseline blood draw

Time-Point (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												
Baseline	296	84.5	79.9–88.1	1975	90.9	89.5–92.1	430	58.1	53.4–62.7	1841.0	97.5	96.7–98.1
≥ 0.75– < 1.5	255	89.8	85.5–92.9	1858	91.0	89.6–92.2	397	57.7	52.8–62.4	1716.0	98.5	97.8–99.0
≥ 1.5– < 2.5	137	92.0	86.2–95.5	1032	90.2	88.2–91.9	227	55.5	49.0–61.8	942.0	98.8	97.9–99.3
≥ 2.5– < 3.5	114	92.1	85.7–95.8	679	90.0	87.5–92.0	173	60.7	53.3–67.7	620.0	98.5	97.3–99.2
≥ 3.5– < 9	248	94.0	90.3–96.3	1110	87.3	85.2–89.1	374	62.3	57.3–67.1	984.0	98.5	97.5–99.1
≥ 9–24	227	91.2	86.8–94.2	883	86.9	84.5–88.9	323	64.1	58.7–69.1	787.0	97.5	96.1–98.3
Serum												
Baseline	296	85.5	81.0–89.0	2022	91.6	90.4–92.8	422	60.0	55.2–64.5	1896.0	97.7	97.0–98.3
≥ 0.75– < 1.5	246	88.2	83.6–91.7	1866	91.5	90.1–92.7	376	57.7	52.7–62.6	1736.0	98.3	97.6–98.8
≥ 1.5– < 2.5	129	91.5	85.4–95.2	1049	90.6	88.6–92.2	217	54.4	47.7–60.9	961.0	98.9	98.0–99.4
≥ 2.5– < 3.5	113	91.2	84.5–95.1	689	90.4	88.0–92.4	169	60.9	53.4–68.0	633.0	98.4	97.1–99.1
≥ 3.5– < 9	248	93.1	89.3–95.7	1120	87.6	85.5–89.4	370	62.4	57.4–67.2	998.0	98.3	97.3–98.9
≥ 9–24	230	90.9	86.4–94.0	900	87.4	85.1–89.4	322	64.9	59.5–69.9	808.0	97.4	96.1–98.3

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

Results for females based on time from study baseline blood draw, calculated using the female-specific 99th percentile values of 36.99 pg/mL (ng/L) for plasma and 39.59 pg/mL (ng/L) for serum are summarized in table 2.

Table 2: Results for females based on time from study baseline blood draw

Time-Point (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												
Baseline	102	87.3	79.4–92.4	887	91.4	89.4–93.1	165	53.9	46.3–61.4	824.0	98.4	97.3–99.1
≥ 0.75– < 1.5	89	89.9	81.9–94.6	820	91.6	89.5–93.3	149	53.7	45.7–61.5	760.0	98.8	97.8–99.4
≥ 1.5– < 2.5	44	97.7	88.2–99.6	427	92.3	89.3–94.4	76	56.6	45.4–67.1	395.0	99.7	98.6–100.0
≥ 2.5– < 3.5	40	95.0	83.5–98.6	317	87.4	83.3–90.6	78	48.7	37.9–59.6	279.0	99.3	97.4–99.8
≥ 3.5– < 9	89	95.5	89.0–98.2	467	88.4	85.2–91.0	139	61.2	52.9–68.8	417.0	99.0	97.6–99.6
≥ 9–24	74	94.6	86.9–97.9	362	87.3	83.5–90.3	116	60.3	51.2–68.8	320.0	98.8	96.8–99.5
Serum												
Baseline	105	86.7	78.9–91.9	904	92.1	90.2–93.7	162	56.2	48.5–63.6	847.0	98.3	97.2–99.0
≥ 0.75– < 1.5	81	87.7	78.7–93.2	817	91.9	89.9–93.6	137	51.8	43.5–60.0	761.0	98.7	97.6–99.3
≥ 1.5– < 2.5	39	97.4	86.8–99.5	433	92.4	89.5–94.5	71	53.5	42.0–64.6	401.0	99.8	98.6–100.0
≥ 2.5– < 3.5	39	94.9	83.1–98.6	324	89.2	85.3–92.1	72	51.4	40.1–62.6	291.0	99.3	97.5–99.8
≥ 3.5– < 9	88	95.5	88.9–98.2	474	89.2	86.1–91.7	135	62.2	53.8–70.0	427.0	99.1	97.6–99.6
≥ 9–24	78	93.6	85.9–97.2	366	88.5	84.9–91.4	115	63.5	54.4–71.7	329.0	98.5	96.5–99.3

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

Results for males based on time from study baseline blood draw, calculated using the male-specific 99th percentile values of 57.27 pg/mL (ng/L) for plasma and 58.05 pg/mL (ng/L) for serum are summarized in table 3.

Table 3: Results for males based on time from study baseline blood draw

Time-Point (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												
Baseline	194	81.4	75.4–86.3	1088	90.9	89.0–92.5	257	61.5	55.4–67.2	1025	96.5	95.2–97.5
≥ 0.75– < 1.5	166	86.7	80.7–91.1	1038	90.9	89.0–92.5	238	60.5	54.2–66.5	966	97.7	96.6–98.5
≥ 1.5– < 2.5	93	86.0	77.5–91.6	605	90.6	88.0–92.7	137	58.4	50.0–66.3	561	97.7	96.1–98.6
≥ 2.5– < 3.5	74	89.2	80.1–94.4	362	91.4	88.1–93.9	97	68.0	58.2–76.5	339	97.6	95.4–98.8
≥ 3.5– < 9	159	89.9	84.3–93.7	643	87.1	84.3–89.5	226	63.3	56.8–69.3	576	97.2	95.5–98.3
≥ 9–24	153	88.9	82.9–92.9	521	86.9	83.8–89.6	204	66.7	59.9–72.8	470	96.4	94.3–97.7

Time-Point (hours)	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
	N[a]	%	95% CI[b]	N	%	95% CI	N	%	95% CI	N	%	95% CI
Serum												
Baseline	191	81.7	75.6–86.5	1118	91.9	90.2–93.4	246	63.4	57.2–69.2	1063	96.7	95.5–97.6
≥ 0.75– < 1.5	165	83.0	76.6–88.0	1049	91.8	90.0–93.3	223	61.4	54.9–67.6	991	97.2	95.9–98.0
≥ 1.5– < 2.5	90	83.3	74.3–89.6	616	90.9	88.4–92.9	131	57.3	48.7–65.4	575	97.4	95.7–98.4
≥ 2.5– < 3.5	74	89.2	80.1–94.4	365	91.5	88.2–94.0	97	68.0	58.2–76.5	342	97.7	95.5–98.8
≥ 3.5– < 9	160	90.0	84.4–93.8	646	88.9	86.2–91.1	216	66.7	60.1–72.6	590	97.3	95.6–98.3
≥ 9–24	152	89.5	83.6–93.4	534	88.2	85.2–90.7	199	68.3	61.6–74.4	487	96.7	94.7–98.0

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

Analysis 2: 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 4. Gender-specific data are presented in tables 5 and 6.

Table 4: Pooled gender results based on time from presentation to the emergency department

Time-Point (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	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

Time-Point (hours)	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
	N[a]	%	95% CI[b]	N	%	95% CI	N	%	95% CI	N	%	95% CI
≥ 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] 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 36.99 pg/mL (ng/L) for plasma and 39.59 pg/mL (ng/L) for serum are summarized in table 5.

Table 5: Results for females based on time of presentation to the emergency department

Time-Point (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	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] 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 57.27 pg/mL (ng/L) for plasma and 58.05 pg/mL (ng/L) for serum are summarized in table 6.

Table 6: Results for males based on time of presentation to the emergency department

Time-Point (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	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
≥ 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] 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 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 1 ADVIA Centaur TNIH test result above the 99th percentile (> 47.34 pg/mL (ng/L)) on 1 or more serial draws. 89% 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] using the ADVIA Centaur CP system. Samples were assayed in duplicate in 2 runs per day for 20 days. The assay was designed to have within-laboratory precision of ≤ 12% coefficient of variation (CV) for samples from 9–20 pg/mL (ng/L) and ≤ 10% CV for samples > 20 pg/mL (ng/L). The following 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	15.29	0.62	4.0	0.77	5.1
Serum 2	80	46.00	1.18	2.6	1.73	3.8
Serum 3	80	154.11	4.27	2.8	5.21	3.4
Serum 4	80	1544.35	33.46	2.2	43.68	2.8
Serum 5	80	14,862.43	380.27	2.6	491.22	3.3
Serum 6	80	23,361.97	1046.77	4.5	1094.75	4.7
Plasma 1	80	14.28	0.73	5.1	0.95	6.7
Plasma 2	80	51.24	1.46	2.9	2.04	4.0
Plasma 3	80	155.84	3.73	2.4	5.60	3.6
Plasma 4	80	1571.38	35.43	2.3	47.84	3.0
Plasma 5	80	13,736.22	415.39	3.0	561.37	4.1
Plasma 6	80	20,934.78	648.28	3.1	736.74	3.5

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

Results obtained at individual laboratories may vary from the data presented.

Assay Comparison

Assay comparison was determined by comparing the ADVIA Centaur TNIH assay using the ADVIA Centaur CP system and and the ADVIA Centaur XP system. The Passing-Bablok regression model was used in accordance with CLSI Document EP09-A3.[35]

Specimen Type	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Lithium heparin plasma	ADVIA Centaur XP TNIH assay	y = 0.95x + 2.93 pg/mL (ng/L)	12.46–20,283.76 pg/mL (ng/L)	160	0.999

[a] Number of samples tested.

[b] Pearson correlation coefficient.

Agreement of the assays may vary depending on the study design, comparative assay, and sample population used. 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 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	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

	Low or Therapeutic Concentration		High or Toxic Concentration	
Potential Interferents	**Common units**	**SI units**	**Common units**	**SI units**
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
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.

Results obtained at individual laboratories may vary from the data presented.

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

Potential interference in the ADVIA Centaur 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 of biotin
Cholesterol	500 mg/dL of cholesterol
Protein Albumin	6 g/dL
Protein Gamma Globulin	2.5 g/dL
Total Protein	12 g/dL

Results obtained at individual laboratories may vary from the data presented.

Linearity

Linearity was evaluated according to the CLSI Document EP06-A.[36] The ADVIA Centaur TNIH assay is linear from 2.50–25,000.00 pg/mL (ng/L). 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

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 ADVIA Centaur 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/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 Mark	CE XXXX	CE Mark with notified body ID number Notified body ID number can vary.
	Consult instructions for use		Biological risks Potential biological risks are associated with the medical device.
	Do not freeze		Temperature limit
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight Prevent exposure to sunlight and heat.		Up Store in an upright position.
	Use-by date Use by the designated date.	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.
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	PRINTED WITH SOY INK	Printed with soy ink
	Recycle	RxOnly	Prescription device (US only)

Legal Information

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