REF K6427

SIEMENS

Dimension Vista® System
Flex® reagent cartridge

TNIH

See shaded sections: Updated information from 2018-03 version.

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High-Sensitivity Troponin I

Intended Use: The Dimension Vista® High-Sensitivity Troponin I (TNIH) assay is for *in vitro* diagnostic use in the quantitative measurement of cardiac troponin I in human plasma using the Dimension Vista® system. The assay can be used to aid in the diagnosis of acute myocardial infarction (AMI).

Summary: Troponin I (TnI) exists in three 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.

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.[9-14]

The 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:[12]

- 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 subjects.

Principles of Procedure: The Dimension Vista® TNIH assay is a homogeneous, sandwich chemiluminescent immunoassay based on LOCI technology. The LOCI reagents include two synthetic bead reagents and two biotinylated anti-cardiac troponin I monoclonal antibody fragments. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with a third anti-cardiac troponin I monoclonal antibody and contains chemiluminescent dye. Sample is incubated with Chemibeads and biotinylated antibodies to form bead-cardiac troponin I-biotinylated antibody sandwiches. Sensibeads are added and bind to the biotin to form bead-pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads which diffuses into the Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is a direct function of the cardiac troponin I concentration in the sample.[15-17]

Reagents

Wells[a]	Form	Ingredient	Concentration[b,c]	Source
1–2	Liquid	Biotinylated Antibody[c]	5 µg/mL	Mouse monoclonal
		Biotinylated Antibody	2 µg/mL	Sheep monoclonal
3–4	Liquid	Troponin I Chemibeads[c]	30 µg/mL	Sheep monoclonal
5–6	Empty			
7–8	Liquid	Streptavidin Sensibead[c]	975 µg/mL	Recombinant *E. coli*
9–12	Liquid	Assay Buffer		

a. Wells are numbered consecutively from the wide end of the cartridge.
b. Nominal value per well in a cartridge.
c. Contain buffers, stabilizers and preservatives.

Risk and Safety:

H317
P280, P272, P302 + P352, P333 + P313, P363, P501

Warning!
May cause an allergic skin reaction.

Wear protective gloves/protective clothing/eye protection/face protection. Contaminated work clothing should not be allowed out of the workplace. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Wash contaminated clothing before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: 5-chloro-2-methyl-3(2h)-isothiazolone mixture with 2-methyl-3(2h)-isothiazolone

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

Precautions: Used LOCI reaction vessels contain human body fluids; handle with appropriate care to avoid skin contact or ingestion.

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

For *in vitro* diagnostic use.

For Professional Use.

Reagent Preparation: All reagents are liquid and ready to use.

Store at: 2–8°C

Expiration: Refer to carton for expiration date of individual unopened reagent cartridges. Sealed wells on the instrument are stable for 30 days.

Open Well Stability: 7 days for wells 1–12

Specimen Collection and Handling: Recommended specimen: lithium heparin plasma. Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[18]

Separated samples are stable for 8 hours at room temperature and for 24 hours when stored at 2–8°C. Samples can be frozen at or below -20°C for up to 40 days in a non-frost free freezer and at or below -70°C for up to 1 year. Do not store frozen samples in an automatic defrosting freezer (frost free freezer). 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. Samples containing precipitates must be centrifuged before performing the assay.

Samples and controls stabilized with sodium azide cannot be used.

Plasma samples can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[19] Follow the instructions provided with your specimen collection device for use and processing.[20]

Plasma should be physically separated from cells as soon as possible with a maximum limit of two hours from the time of collection.[21]

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. 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.

The purpose of specimen storage information is to provide guidance to users; however, users may validate their own procedures for storing patient samples.

Procedure

Materials Provided

TNIH Flex reagent cartridge, Cat. No. K6427

Materials Required But Not Provided

TNIH CAL, Cat. No. KC627
CTNI SDIL, Cat. No. KD692
LOCI Reaction Vessels, Cat. No. KS855
Quality Control Materials

Test Steps

Sampling, reagent delivery, mixing, and processing are automatically performed by the Dimension Vista system. For details of this processing, refer to your Dimension Vista Operator's Guide.

Test Conditions

Sample Volume (delivered to the LOCI reaction vessel)	10 µL
Chemibead Reagent Volume	20 µL
Biotinylated Antibody Reagent Volume	20 µL
Sensibead Volume	20 µL
Assay Buffer Volume	100 µL
Temperature	37°C
Reaction Time	10 minutes
Wavelength	Illumination (680 nm) Emission (612 nm)
Type of Measurement	Chemiluminescence

Calibration

Calibration Material	TNIH CAL, Cat. No. KC627
Calibration Scheme	5 Levels, Level A n=5, Levels B-E n=3
Units	pg/mL [ng/L][d] (pg/mL x 1) = [ng/L]
Typical Calibration Levels	Level A - 0 pg/mL [ng/L] Level B - 60 pg/mL [ng/L] Level C - 500 pg/mL [ng/L] Level D - 8000 pg/mL [ng/L] Level E - 27,000 pg/mL [ng/L]
Calibration Frequency	Every 30 days for any one lot Calibration interval may be extended based on acceptable verification of calibration.
A new calibration is required:	• For each new lot of Flex® reagent cartridges • After major maintenance or service, if indicated by quality control results • As indicated in laboratory quality control procedures • When required by government regulations

d. Système International d'Unités [SI Units] are in brackets.

Quality Control

Follow government regulations or accreditation requirements for quality control frequency. At least once each day of use, analyze two levels of a Quality Control (QC) material with known cardiac troponin I concentrations. Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.

Results: The instrument calculates the concentration of cardiac troponin I in pg/mL [ng/L] using the calculation scheme described in your Dimension Vista® Operator's Guide.

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

Analytical Measurement Range (AMR): 3.0 – 25,000.0 pg/mL [ng/L]

This is the range of analyte values that can be measured directly from the specimen without any dilution or pretreatment that is not part of the usual analytical process and is equivalent to the assay range.

• Samples with results in excess of 25,000.0 pg/mL [ng/L] should be repeated on dilution.

Autodilution (AD) requires onboard CTNI Sample Diluent (Cat. No. KD692). The autodilute sample volume is 20 µL (dilution factor = 5) for plasma to obtain results within the analytical measurement range. Refer to your Dimension Vista® Operator's Guide.

Manual Dilution: Dilute with CTNI Sample Diluent (Cat. No. KD692) to obtain results within reportable range. Enter dilution factor on the instrument, but no greater than 5. Reassay. Resulting readout is corrected for dilution.

• Samples with results less than 3.0 pg/mL [ng/L] will be reported as "less than 3.0 pg/mL [ng/L]" by the instrument.

Limitations of Procedure

Patient samples may contain cardiac troponin-specific autoantibodies that could react in immunoassays to give depressed results. A test result that is inconsistent with the clinical picture and patient history should be interpreted with caution.[22]

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. This assay has been designed to minimize interference from heterophilic antibodies. Nevertheless, complete elimination of this interference from all patient specimens cannot be guaranteed. A test result that is inconsistent with the clinical picture and patient history should be interpreted with caution.[23-25]

Specimens that contain biotin at a concentration of 300 ng/mL demonstrate a less than 10% change in results. Biotin concentrations greater than this may lead to falsely depressed results for patient samples. Testing specimens from renal dysfunction patients taking biotin may lead to false negative results. Therefore, do not use this device in patients with renal impairment (eGFR<60), unless it is confirmed that the patient is not taking biotin. Patients taking more than 20 mg/day of biotin may have falsely negative results, and should not use this test. There have been reports of multiple sclerosis patients taking biotin doses exceeding 20 mg/day. Therefore, do not use this device in patients with Multiple Sclerosis, unless it is confirmed that the patient is not taking more than 20 mg/day of biotin.

Dextran 40 at 60 g/L increases the troponin result in plasma at 35.1 pg/mL [ng/L] and 1337.4 pg/mL [ng/L] by 22% and 4% respectively. Dextran 40 at 15 g/L and 45 g/L demonstrates less than 10% change in results when testing plasma samples at the concentrations stated above.

Protein Gamma Globulin at 6 g/dL increases the troponin result in plasma samples at approximately 40 pg/mL [ng/L] and 1000 pg/mL [ng/L] of troponin. Protein Gamma Globulin at 2.5 g/dL demonstrates less than 10% change in results when testing plasma samples at the concentrations stated above.

The instrument reporting system contains flags and comments to provide the user with information regarding instrument processing errors, instrument status information and potential errors in cardiac troponin I results. Refer to your Dimension Vista® Operator's Guide for the meaning of report flags and comments. Any report containing flags and/or comments should be addressed according to your laboratory's procedure manual and not reported.

Maximum Observed Repeatability

The expected maximum observed standard deviations for repeatability (within-run precision) using n=5 replicates at the following TNIH concentrations are:

Concentration	Acceptable SD Maximum
50.0 pg/mL [ng/L]	4.8 pg/mL [ng/L]
500.0 pg/mL [ng/L]	31.4 pg/mL [ng/L]

A system malfunction may exist if the maximum 5-test SD precision is exceeded.

Expected Results

Lithium heparin plasma specimens were collected from apparently healthy individuals with no known diseases of the cardiovascular system or other serious acute or chronic diseases or infections 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 Guidance EP28-A3c.[26]

The combined gender was used to determine the overall observed 99th percentile of 58.9 pg/mL [ng/L]. The potential range of results for the 99th percentile is 42.2 to 82.3 pg/mL [ng/L] for the Dimension Vista® family of systems, dependent upon instrument and reagent lot. Two female subjects had troponin values of approximately 400 pg/mL and 4700 pg/mL, and were considered to be outliers. These results were not included in the 99th percentile determination.

n	Age (years)	99th Percentile pg/mL [ng/L]	90% CI[1] pg/mL [ng/L]
2021	22–91	58.9	42.2–82.3

[1] Confidence interval

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

Sample Type	Gender	n	99th Percentile[a] pg/mL [ng/L]	90% CI[b] pg/mL [ng/L]
Lithium Heparin Plasma	Female	1017	53.7	37.7–115.7
	Male	1004	78.5	41.4–114.5
	Combined	2021	58.9	42.2–82.3

[a] IFCC Task Force on Clinical Applications of Cardiac Bio-Markers recommends that troponin values be reported as whole numbers.[12]

[b] Confidence interval

The Dimension Vista® TNIH assay meets the IFCC Task Force on Clinical Applications of Cardiac Bio-Markers' definition of a high-sensitivity troponin assay.[12]

1. Total imprecision (CV) at the 99th percentile value should be at or below 10%.
   • The 10% CV (Within-Lab Imprecision) for the Dimension Vista® TNIH assay was measured to be 10.0 pg/mL [ng/L].
2. Measurable concentrations should be attainable at concentrations above the limit of detection (LoD) in at least 50% of healthy subjects.
   • Greater than 50% of the healthy patient population used to determine the 99th percentile produced a value above the LoD.

Clinical Performance

A prospective study was performed to assess diagnostic accuracy for 2498 subjects. Lithium heparin plasma 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 13.0%.

The results were analyzed using the serial sampling time points collected during the emergency department visit. A positive is defined as a sample exceeding the 99th percentile cutoff at the particular time point. The results are presented using serial timed intervals analyzed according to the 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 58.9 pg/mL [ng/mL], are summarized in Table 1. Gender-specific data are presented in Tables 2 and 3.

Elevated TnI Values in Patients Without AMI

There are conditions other than AMI that are known to cause myocardial injury and elevated TnI values.[9-14, 27-34]

The Dimension Vista® 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 Dimension Vista® TNIH test result above the 99th percentile (> 58.9 pg/mL [ng/L]) on one or more serial draws. 88% 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 valvar heart disease, tachycardia.

Non-cardiac conditions: Chronic lung disease, cardiac contusion related to a traumatic injury, renal failure, pneumonia, pulmonary embolism, shock, systemic sclerosis.

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

	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
Time Since Presentation (hours)	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Lithium Heparin Plasma												
0–<1.5	138	79.0	71.4–85.0	969	92.5	90.6–94.0	182	59.9	52.6–66.7	925	96.9	95.5–97.8
≥1.5– <2.5	238	89.9	85.4–93.1	1646	91.2	89.7–92.5	359	59.6	54.5–64.6	1525	98.4	97.7–98.9
≥2.5– <3.5	199	90.5	85.6–93.8	1377	90.6	89.0–92.1	309	58.3	52.7–63.6	1267	98.5	97.7–99.0
≥3.5– <4.5	146	93.2	87.9–96.2	1097	90.9	89.0–92.4	236	57.6	51.2–63.8	1007	99.0	98.2–99.5
≥4.5– <6	69	94.2	86.0–97.7	467	88.9	85.7–91.4	117	55.6	46.5–64.2	419	99.0	97.6–99.6
≥6– <9	191	92.7	88.1–95.6	913	87.4	85.1–89.4	292	60.6	54.9–66.0	812	98.3	97.1–99.0
≥9– <24	216	93.1	88.9–95.7	837	85.5	83.0–87.8	322	62.4	57.0–67.5	731	97.9	96.6–98.8
≥24	64	93.8	85.0–97.5	254	85.8	81.0–89.6	96	62.5	52.5–71.5	222	98.2	95.5–99.3

Results for females based on time of presentation to the emergency department, calculated using the female- specific 99th percentile of 53.7 pg/mL [ng/mL] is summarized in Table 2.

Using the lower female-specific 99th percentile instead of the overall 99th percentile of 58.9 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 (drawn at ≥4.5–<6 hours after presentation), up to 68% of positive test results for females may be non-MI.

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

	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
Time Since Presentation (hours)	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Lithium Heparin Plasma												
0– <1.5	42	83.3	69.4–91.7	409	94.4	91.7–96.2	58	60.3	47.5–71.9	393	98.2	96.4–99.1
≥1.5– <2.5	77	89.6	80.8–94.6	727	92.3	90.1–94.0	125	55.2	46.5–63.6	679	98.8	97.7–99.4
≥2.5– <3.5	71	94.4	86.4–97.8	624	92.6	90.3–94.4	113	59.3	50.1–67.9	582	99.3	98.2–99.7
≥3.5– <4.5	50	94.0	83.8–97.9	489	91.4	88.6–93.6	89	52.8	42.5–62.8	450	99.3	98.1–99.8
≥4.5– <6	27	96.3	81.7–99.3	243	86.0	81.1–89.8	60	43.3	31.6–55.9	210	99.5	97.4–99.9
≥6– <9	67	94.0	85.6–97.7	379	88.1	84.5–91.0	108	58.3	48.9–67.2	338	98.8	97.0–99.5
≥9– <24	72	93.1	84.8–97.0	345	89.0	85.2–91.9	105	63.8	54.3–72.4	312	98.4	96.3–99.3
≥24	28	96.4	82.3–99.4	111	83.8	75.8–89.5	45	60.0	45.5–73.0	94	98.9	94.2–99.8

Results for males based on time of presentation to the emergency department, calculated using the male-specific 99th percentile of 78.5 pg/mL [ng/mL] is summarized in Table 3.

Using the higher male-specific 99th percentile instead of the overall 99th percentile of 58.9 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 3.8%.

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

	Sensitivity			Specificity			Positive Predictive Value			Negative Predictive Value		
Time Since Presentation (hours)	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Lithium Heparin Plasma												
0– <1.5	96	74.0	64.4–81.7	560	92.5	90.0–94.4	113	62.8	53.6–71.2	543	95.4	93.3–96.9
≥1.5– <2.5	161	84.5	78.1–89.3	919	91.8	89.9–93.4	211	64.5	57.8–70.6	869	97.1	95.8–98.0
≥2.5– <3.5	128	85.2	78.0–90.3	753	90.4	88.1–92.3	181	60.2	52.9–67.1	700	97.3	95.8–98.3
≥3.5– <4.5	96	86.5	78.2–91.9	608	92.4	90.1–94.3	129	64.3	55.8–72.1	575	97.7	96.2–98.7
≥4.5– <6	42	88.1	75.0–94.8	224	92.0	87.7–94.9	55	67.3	54.1–78.2	211	97.6	94.6–99.0
≥6– <9	124	87.9	81.0–92.5	534	90.6	87.9–92.8	159	68.6	61.0–75.3	499	97.0	95.1–98.2
≥9– <24	144	90.3	84.3–94.1	492	87.2	84.0–89.9	193	67.4	60.5–73.6	443	96.8	94.8–98.1
≥24	36	88.9	74.7–95.6	143	91.6	85.9–95.1	44	72.7	58.2–83.7	135	97.0	92.6–98.8

Specific Performance Characteristics

The following data represent typical performance for the Dimension Vista® System.

Precision[a]

Specimen Type	n	Mean pg/mL [ng/L]	Repeatability SD[b] pg/mL [ng/L]	Repeatability %CV[c]	Within-Lab SD pg/mL [ng/L]	Within-Lab %CV
Plasma 1	80	12.4 (12.4)	0.69 (0.69)	5.6	0.71 (0.71)	5.7
Plasma 2	80	50.7 (50.7)	0.98 (0.98)	1.9	1.37 (1.37)	2.7
Plasma 3	80	76.4 (76.4)	1.44 (1.44)	1.9	1.77 (1.77)	2.3
Plasma 4	80	160.9 (160.9)	1.72 (1.72)	1.1	2.65 (2.65)	1.6
QC	80	8088.5 (8088.5)	99.54 (99.54)	1.2	200.36 (200.36)	2.5

a. CLSI EP05-A3[35] was used. During each day of testing, two separate runs with two test samples for each test material were analyzed for 20 days for a total of 80 replicates.
b. Standard Deviation.
c. Coefficient of Variation.

Hemolysis, Icterus, Lipemia (HIL) Interference

The TNIH assay was evaluated for interference according to CLSI EP07-A2.[36] Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Lithium heparin plasma test sample ranges were: 40±20 pg/mL [ng/L] and 1350 ± 650 pg/mL [ng/L]. Bias exceeding 10% is considered interference.

Substance Tested	Substance concentration	Bias (%)*
Hemoglobin hemolysate (monomer)	400 mg/dL [0.25 mmol/L]	≤10
Bilirubin (conjugated)	30 mg/dL [356 µmol/L]	≤10
Bilirubin (conjugated)	40 mg/dL [475 µmol/L]	-11
Bilirubin (unconjugated)	40 mg/dL [684 µmol/L]	≤10
Lipemia (Intralipid®)	3000 mg/dL [33.9 mmol/L]	≤10

Intralipid® is a registered trademark of Fresenius Kabi AD, Bad Homburg, Germany.

*Analyte results should not be corrected based on this bias.

Biotin Interference

The TNIH assay was evaluated for interference according to CLSI EP07-A2.[36] Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Lithium heparin plasma test sample ranges were: 40 ± 20 pg/mL [ng/L] and 1350 ± 650 pg/mL [ng/L]. Bias exceeding 10% is considered interference.

Interfering Substance	Substance Concentration	TNIH (pg/mL)	Bias, %
Biotin	300 ng/mL	36.1	-5
		1309.1	-1
	360 ng/mL	43	-13
		1423.1	-12
	480 ng/mL	43	-18
		1423.1	-18
	840 ng/mL	43	-85
		1423.1	-49
	1200 ng/mL	43	-91
		1423.1	-96

See limitations section for information regarding patients with either renal impairment or multiple sclerosis. Some studies have shown that serum concentrations of biotin can reach 355 ng/mL within the first hour after biotin ingestion for apparently healthy subjects consuming supplements of 20 mg biotin per day[37] and plasma concentrations of biotin can reach up to 1160 ng/mL for apparently healthy subjects after a single dose of 300 mg biotin.[38]

Non-Interfering Substances

The following substances have no significant effect (less than or equal to 10% or ± 5.0 pg/mL [ng/L] whichever is greater) in the TNIH assay when added to lithium heparin plasma pools with troponin levels of 40± 20 pg/mL [ng/L] and 1350 ± 650 pg/mL [ng/L] at the low/therapeutic and high/toxic concentrations indicated.

	Low or Therapeutic Concentration		High or Toxic Concentration	
Potential Interferent	Conventional Units	SI Units	Conventional Units	SI Units
Abciximab	0.4 mg/dL	NA	4.0 mg/dL	NA
Acetaminophen	2.0 mg/dL	133 µmol/L	20.0 mg/dL	1324 µmol/L
Acetylsalicylic Acid	26.1 mg/dL	1.45 mmol/L	65.2 mg/dL	3.62 mmol/L
Allopurinol	1.3 mg/dL	91.9 µmol/L	4.0 mg/dL	294 µmol/L
Amiodarone	0.2 mg/dL	2.6 µmol/L	0.6 mg/dL	8.92 µmol/L
Ampicillin	1.1 mg/dL	29.1 µmol/L	5.6 mg/dL	152 µmol/L
Ascorbic Acid	1.2 mg/dL	68.5 µmol/L	6.0 mg/dL	342 µmol/L
Atenolol	0.1 mg/dL	4.1 µmol/L	1.0 mg/dL	37.6 µmol/L
Caffeine	1.3 mg/dL	64.4 µmol/L	6.0 mg/dL	308 µmol/L
Captopril	0.1 mg/dL	4.6 µmol/L	0.5 mg/dL	23 µmol/L
Cefoxitin	12.63 mg/dL	281 µmol/L	69.5 mg/dL	1546 µmol/L
Cholesterol	NA[j]	NA[j]	300 mg/dL	7.8 mmol/L
Cinnarizine	0.0285 mg/dL	0.8 µmol/L	2.5 mg/dL	67.8 µmol/L
Clopidogrel	0.32 mg/dL	9.9 µmol/L	7.5 mg/dL	233 µmol/L
Cocaine	0.05 mg/dL	1.6 µmol/L	1.0 mg/dL	33 µmol/L
Dextran 40	15 g/L	375 µmol/L	45 g/L	1125 µmol/L
Digitoxin	17 ng/mL	22.2 nmol/L	60 ng/mL	78.4 nmol/L
Digoxin	1.4 ng/mL	1.8 nmol/L	6.1 ng/mL	7.8 nmol/L
Diltiazem	0.025 mg/dL	0.55 µmol/L	0.68 mg/dL	15 µmol/L
Disopyramide	0.45 mg/dL	10.4 µmol/L	1.3 mg/dL	29.5 µmol/L
Dopamine	0.04 mg/dL	1.96 µmol/L	0.11 mg/dL	5.87 µmol/L
Doxycycline	1.1 mg/dL	22.5 µmol/L	3.2 mg/dL	67.5 µmol/L
Erythromycin	1.1 mg/dL	15 µmol/L	6.0 mg/dL	81.6 µmol/L
Furosemide	2.0 mg/dL	60.4 µmol/L	6.0 mg/dL	181 µmol/L
Ibuprofen	4.0 mg/dL	194.3 µmol/L	50 mg/dL	2425 µmol/L
Isosorbide Dinitrate	50.1 ng/mL	212 nmol/L	150.2 ng/mL	636 nmol/L
Lisinopril	0.01 mg/dL	0.25 µmol/L	0.03 mg/dL	0.74 µmol/L
Low MW Heparin	0.85 U/mL	NA	2.0 U/mL	NA
Lovastatin	17.2 ng/mL	42.4 nmol/L	80 ng/mL	197.8 nmol/L
Methotrexate	50 mg/dL	1.1 mmol/L	91 mg/dL	2 mmol/L
Methyldopa	0.48 mg/dL	20.1 µmol/L	1.69 mg/dL	70.9 µmol/L
Methylprednisolone	1.65 mg/dL	44 µmol/L	4.0 mg/dL	106.8 µmol/L
Mexiletine	0.15 mg/dL	7 µmol/L	0.48 mg/dL	22.3 µmol/L
Nicotine	0.004 mg/dL	0.2 µmol/L	0.10 mg/dL	6.2 µmol/L
Nifedipine	0.013 mg/dL	361.3 nmol/L	0.04 mg/dL	1156.1 nmol/L
Nitrofurantoin	0.20 mg/dL	8.4 µmol/L	0.40 mg/dL	16.8 µmol/L
Nitroglycerine	7.5 ng/mL	33 nmol/L	160 ng/mL	704.5 nmol/L
Phenobarbital	2.5 mg/dL	107.8 µmol/L	10.0 mg/dL	431.5 µmol/L
Phenytoin	1.36 mg/dL	49.6 µmol/L	5.43 mg/dL	198 µmol/L
Primidone	1.1 mg/dL	48.2 µmol/L	4.0 mg/dL	183.5 µmol/L
Propranolol	0.06 mg/dL	1.93 µmol/L	0.23 mg/dL	7.71 µmol/L
Protein, Albumin	NA[j]	NA[j]	6 g/dL	60 g/L
Protein, Gamma Globulin	2.5g/dL	NA	NA	NA
Protein, Total	NA[j]	NA[j]	12 g/dL	NA
Quinidine	0.38 mg/dL	11.7 µmol/L	1.2 mg/dL	37 µmol/L
Rheumatoid Factor	750 IU/mL	NA	1500 IU/mL	NA
Simvastatin	0.004 ug/mL	0.01 µmol/L	32 ug/mL	76.5 µmol/L
Theophylline	1.25 mg/dL	69.4 µmol/L	4.0 mg/dL	222.2 µmol/L
Tissue Plasminogen Activator (TPA)	0.52 µg/mL	NA	2.3 µg/mL	NA
Thyroxine	0.023 mg/dL	0.3 µmol/L	0.06 mg/dL	0.8 µmol/L
Triglyceride	500 mg/dL	NA	1000 mg/dL	NA
Trimethoprim	1.25 mg/dL	43.1 µmol/L	4.0 mg/dL	138.3 µmol/L
Verapamil	0.035 mg/dL	0.8 µmol/L	0.22 mg/dL	4.4 µmol/L
Warfarin	0.20 mg/dL	6.6 µmol/L	1.0 mg/dL	32.5 µmol/L

j. Low level testing is not relevant for this endogenous substance.

Hook Effect

The Dimension Vista® TNIH assay shows no hook effect up to 1,000,000 pg/mL [ng/L].

Specificity

The TNIH assay shows high specificity for cTnI. The following compounds were added at the concentrations indicated to lithium heparin samples with cTnI concentrations of less than 4.0 pg/mL [ng/L] and 20–60 pg/mL [ng/L]. TNIH assay results from the spiked samples were compared with those of unspiked control samples. Percent cross-reactivity is calculated as:

$$\% \text{ Cross-reactivity} = \frac{[\text{measured analyte}] - [\text{control analyte}]}{[\text{cross-reactant}]} \times 100$$

Cross-reactant	Amount ng/mL [µg/L]	Cross-reactivity (%)
Cardiac Troponin T	1000	0.003
Skeletal Troponin I	1000	0.002
Tropomyosin	1000	ND
Actin	1000	ND
Troponin C	1000	ND
Myosin Light Chain	1000	ND
Myoglobin	1000	ND
CK-MB	1000	ND

*ND= Not detectable

Limit of Detection and Limit of Blank

The limit of blank (LoB) and limit of detection (LoD) were determined as described in CLSI Document EP17-A2.[39]

The limit of blank (LoB) is defined as the highest measurement result that is likely to be observed for a blank sample. The Dimension Vista® TNIH assay has an LoB of 1.0 pg/mL [ng/L].

The limit of detection (LoD) is defined as the lowest concentration of cTnI that can be detected with 95% probability. The observed LoD ranged from 0.7–1.9 pg/mL [ng/L] across three reagent lots. The Dimension Vista® TNIH assay has an LoD of 2.0 pg/mL [ng/L].

Limit of Quantitation

The limit of quantitation (LoQ) was determined as described in CLSI Document EP17-A2.[39]

The LoQ is defined as the lowest concentration of cTnI that can be detected at a total CV of 20%. The Dimension Vista® TNIH assay has an LoQ of 3.0 pg/mL [ng/L].

Linearity

The Dimension Vista® TNIH assay is linear from 3.0–25,000.0 pg/mL [ng/L].

Linearity was evaluated according to CLSI Document EP06-A.[40] Native lithium heparin plasma samples were used to create a dilution series for each sample type by mixing high and low level samples. The resulting sample mixtures were tested with the Dimension Vista® TNIH assay.

Bibliography: See adjacent panel.

Symbols Key: See adjacent panel.

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Symbols Key
Symbolschlüssel
Explication des Symboles
Interpretazione simboli
Clave de los Símbolos

2	Do not reuse / Nicht zur Wiederverwendung / Ne pas réutiliser / Non riutilizzare / No reutilizar
	Use By / Verwendbar bis / Utiliser jusque / Utilizzare entro / Fecha de caducidad
LOT	Batch Code / Chargenbezeichnung / Code du lot / Codice del lotto / Código de lote
REF	Catalogue Number / Bestellnummer / Référence du catalogue / Numero di catalogo / Número de catálogo
	Caution, consult accompanying documents / Achtung, Begleitdokumente beachten / Attention voir notice d'instructions / Attenzione, vedere le istruzioni per l'uso / Atención, ver instrucciones de uso
	Manufacturer / Hersteller / Fabricant / Fabbricante / Fabricante
EC REP	Authorized Representative in the European Community / Bevollmächtigter in der Europäischen Gemeinschaft / Mandataire dans la Communauté européenne / Mandatario nella Comunità Europea / Representante autorizado en la Comunidad Europea
Σ	Contains sufficient for <n> tests / Inhalt ausreichend für <n> Tests / Contenu suffisant pour "n" tests / Contenuto sufficiente per "n" saggi / Contenido suficiente para <n> ensayos
IVD	*In Vitro* Diagnostic Medical Device / *In-Vitro*-Diagnostikum / Dispositif médical de diagnostic *in vitro* / Dispositivo medico-diagnostico *in vitro* / Producto sanitario para diagnóstico *in vitro*
	Temperature Limitation / Temperaturbegrenzung / Limites de température / Limiti di temperatura / Límite de temperatura
	Consult Instructions for Use / Gebrauchsanweisung beachten / Consulter les instructions d'utilisation / Consultare le istruzioni per l'uso / Consulte las instrucciones de uso
NON STERILE	Non-sterile / Nicht steril / Non stérile / Non sterile / No estéril
CE	CE Mark / CE Zeichen / Marquage CE / Marchio CE / Marca CE
CONTENTS	Contents / Inhalt / Contenu / Contenuto / Contenido
→	Reconstitution Volume / Rekonstitutionsvolumen / Volume de reconstitution / Volume di ricostituzione / Volumen de reconstitución
LEVEL	Level / Konzentration / Niveau / Livello / Nivel
RxOnly	Prescription Device (US Only) / Verschreibungspflichtiges Medizinprodukt (nur USA) / Dispositif soumis à prescription (États-Unis uniquement) / Dispositivo su prescrizione (solo USA) / Dispositivo de prescripción médica (solo EE. UU.)

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