

Troponin T hs

Troponin T hs (high sensitive)

cobas®

REF		SYSTEM
05092744 190	200	Elecsys 2010 MODULAR ANALYTICS E170 cobas e 411 cobas e 601 cobas e 602

English

Intended use

Immunoassay for the in vitro quantitative determination of cardiac troponin T in human serum and plasma. This assay can be used as an aid in the differential diagnosis of acute coronary syndrome to identify necrosis, e.g. acute myocardial infarction. The test is further indicated for the risk stratification of patients presenting with acute coronary syndrome and for cardiac risk in patients with chronic renal failure. The test may also be useful for the selection of more intensive therapy and intervention in patients with elevated levels of cardiac troponin T.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and **cobas e** immunoassay analyzers.

Summary

Troponin T (TnT) is a component of the contractile apparatus of the striated musculature. Although the function of TnT is the same in all striated muscles, TnT originating exclusively from the myocardium (cardiac TnT, molecular weight 39.7 kD) clearly differs from skeletal muscle TnT. As a result of its high tissue-specificity, cardiac troponin T (cTnT) is a cardio-specific, highly sensitive marker for myocardial damage.¹ Cardiac troponin T increases approximately 3-4 hours after myocardial infarction (AMI) and may persist up to 2 weeks thereafter.^{2,3} In contrast to ST-elevation myocardial infarction (STEMI), the diagnosis of non-ST elevation myocardial infarction (NSTEMI) heavily relies on cardiac troponin result. According to the new universal definition of myocardial infarction, MI is diagnosed when blood levels of cardiac troponin are above the 99th percentile of the reference limit (of a healthy population) together with evidence of myocardial ischemia (symptoms, ECG changes or imaging results). The definition requires a troponin assay with an imprecision (coefficient of variation) at the 99th percentile less than or equal to 10 %.⁴ Cardiac troponin T (cTnT) is an independent prognostic marker which can predict the near-, mid- and even long-term outcome of patients with acute coronary syndrome (ACS).^{5,6,7,8,9}

In addition, 4 multicenter trials involving more than 7000 patients have shown that cardiac troponin T is also useful to identify patients that benefit from anti-thrombotic therapy (GPIIb/IIIa inhibitors, low molecular weight heparin).^{10,11,12,13,14}

Cardiac troponin is also the preferred marker of myocardial injury in the new guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes.^{15,16}

Low concentrations of troponin T can be detected in clinically stable patients such as patients with ischemic or non-ischemic heart failure,^{17,18,19,20} patients with different forms of cardiomyopathy,²¹ renal failure,^{22,23,24,25,26,27,28} sepsis²⁹ and diabetes.³⁰

Elevated levels of troponin T correlate with the severity of coronary artery disease and to poor outcome independent of natriuretic peptide (BNP or NT-proBNP) levels.^{17,18,31,32}

Low concentrations of troponin T are an independent predictor of cardiovascular events including occurrence and recurrence of atrial fibrillation.³³

Myocardial cell injury leading to elevated cTnT concentrations in the blood can also occur in other clinical conditions such as myocarditis,³⁴ heart contusion,³⁵ pulmonary embolism³⁶ and drug-induced cardiotoxicity.³⁷

Other diagnostic tests such as myoglobin, CK-MB, NT-proBNP, PIGF and CRP can complement the diagnostic and prognostic information of troponin T in different indications.^{31,38,39}

The Elecsys Troponin T hs assay employs two monoclonal antibodies specifically directed against human cardiac troponin T.^{40,41} The antibodies recognize two epitopes (amino acid position 125-131 and 136-147) located in the central part of the cardiac troponin T protein, which consists of 288 amino acids.

The Troponin T hs calibrators (Troponin T hs CalSet) contain recombinant human cardiac troponin T (rec. hcTnT). The rec. hcTnT is isolated from cell culture of *E. coli* BL21 containing a pET vector with human cardiac troponin T isoform 3 gene. After fermentation, the cells are disrupted by sonication and rec. hcTnT is purified by ion exchange chromatography. Purified rec. hcTnT is further characterized by SDS PAGE, Western blotting, immunological activity, and protein content.⁴²

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 50 µL of sample, a biotinylated monoclonal cardiac troponin T-specific antibody, and a monoclonal cardiac troponin T-specific antibody labeled with a ruthenium complex^{a)} react to form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex (Ru(bpy)₃²⁺)

Reagents - working solutions

The reagent rackpack is labeled as TNT-HS.

- M Streptavidin-coated microparticles (transparent cap), 1 bottle, 12 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Anti-troponin T-Ab~biotin (gray cap), 1 bottle, 14 mL: Biotinylated monoclonal anti-cardiac troponin T-antibody (mouse) 2.5 mg/L; phosphate buffer 100 mmol/L, pH 6.0; preservative; inhibitors.
- R2 Anti-troponin T-Ab~Ru(bpy)₃²⁺ (black cap), 1 bottle, 14 mL: Monoclonal anti-cardiac troponin T-antibody (mouse) labeled with ruthenium complex 2.5 mg/L; phosphate buffer 100 mmol/L, pH 6.0; preservative.

Precautions and warnings

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory reagents.



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Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.

All information required for correct operation is read in from the respective reagent barcodes.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	12 weeks
on the analyzers	4 weeks

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

K₂-EDTA, K₃-EDTA, Li-heparin and Na-heparin plasma.

Plasma (EDTA, heparin) and serum samples should not be used interchangeably.

Criterion: Slope 0.8-1.2 + coefficient of correlation ≥ 0.95 .

Stable for 24 hours at 2-8 °C, 12 months at -20 °C. Freeze only once.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Do not use samples and controls stabilized with azide.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- [REF] 05092752190, Troponin T hs CalSet, for 4 x 1 mL
- [REF] 05095107190, PreciControl Troponin, for 2 x 2 mL each of PreciControl Troponin 1 and 2
- [REF] 03609987190, Diluent MultiAssay, 2 x 16 mL sample diluent
- General laboratory equipment
- Elecsys 2010, MODULAR ANALYTICS E170 or **cobas e** analyzer

Accessories for Elecsys 2010 and **cobas e** 411 analyzers:

- [REF] 11662988122, ProCell, 6 x 380 mL system buffer
- [REF] 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- [REF] 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- [REF] 11933159001, Adapter for SysClean

- [REF] 11706802001, Elecsys 2010 AssayCup, 60 x 60 reaction vessels
- [REF] 11706799001, Elecsys 2010 AssayTip, 30 x 120 pipette tips

Accessories for MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers:

- [REF] 04880340190, ProCell M, 2 x 2 L system buffer
- [REF] 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- [REF] 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- [REF] 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- [REF] 03004899190, PreClean M, 5 x 600 mL detection cleaning solution
- [REF] 12102137001, AssayTip/AssayCup Combimagazine M, 48 magazines x 84 reaction vessels or pipette tips, waste bags
- [REF] 03023150001, WasteLiner, waste bags
- [REF] 03027651001, SysClean Adapter M

Accessories for all analyzers:

- [REF] 11298500316, Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers: PreClean M solution is necessary.

Bring the cooled reagents to approx. 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Calibration

Traceability: The Troponin T hs assay ([REF] 05092744) has been standardized against the Troponin T hs STAT assay ([REF] 05092728). This in turn was originally standardized against the Enzymun-Test Troponin T (CARDIAC T) method.

Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer). Renewed calibration is recommended as follows:

- after 1 month (28 days) when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Troponin.

In addition, other suitable control material can be used.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined



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limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

The analyzer automatically calculates the analyte concentration of each sample either in pg/mL, ng/L, ng/mL, µg/L (MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers) or in pg/mL, ng/mL, µg/L (Elecys 2010 and **cobas e** 411 analyzers).

Limitations - interference

The assay is unaffected by icterus (bilirubin < 428 µmol/L or < 25 mg/dL), hemolysis (Hb < 0.062 mmol/L or < 0.1 g/dL; samples showing visible signs of hemolysis may cause interference), lipemia (Intralipid < 1500 mg/dL) and biotin (< 82 nmol/L or < 20 ng/mL).

Falsely depressed results are obtained when using samples with hemoglobin concentrations > 0.1 g/dL.

Criterion: Recovery within ± 20 % of initial value at troponin T concentrations < 100 ng/L or pg/mL (± 10 % at troponin T concentrations ≥ 100 ng/L or pg/mL).

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

No interference was observed from rheumatoid factors up to a concentration of 1500 IU/mL.

There is no high-dose hook effect at troponin T concentrations up to 100000 ng/L (pg/mL).

In vitro tests were performed on 52 commonly used pharmaceuticals. No interference with the assay was found.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Limits and ranges

Measuring range

3-10000 ng/L or pg/mL (defined by the Limit of Blank and the maximum of the master curve). Values below the Limit of Blank are reported as < 3 ng/L or pg/mL. Values above the measuring range are reported as > 10000 ng/L or pg/mL (or up to 100000 ng/L or pg/mL for 10-fold diluted samples).

Lower limits of measurement

Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ)

Limit of Blank = 3 ng/L (pg/mL)

Limit of Detection = 5 ng/L (pg/mL)

Limit of Quantitation = 13 ng/L (pg/mL)

The Limit of Blank and Limit of Detection were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A requirements.

The Limit of Quantitation was determined using the result of functional sensitivity testing.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation (functional sensitivity) is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ≤ 10 % (10 independent runs; 1 run per day). It has been determined using low concentration troponin T samples.

Dilution

Samples with cardiac troponin T concentrations above the measuring range can be diluted with Diluent MultiAssay. The recommended dilution is 1:10 (either automatically by the MODULAR ANALYTICS E170, Elecsys 2010 or **cobas e** analyzers or manually). The concentration of the diluted sample must be > 1000 ng/L (pg/mL).

After manual dilution, multiply the result by the dilution factor.

After dilution by the analyzers, the MODULAR ANALYTICS E170, Elecsys 2010 and **cobas e** software automatically takes the dilution into account when calculating the sample concentration.

Expected values

In studies performed with the Elecsys Troponin T hs assay involving 533 healthy volunteers, the upper reference limit (99th percentile) for troponin T was 14 ng/L (pg/mL), 95 % confidence interval 12.7-24.9 ng/L (pg/mL).

The lowest concentration with a CV less than or equal to 10 % (LoQ) with the Elecsys Troponin T hs assay was 13 ng/L (pg/mL).

Based on the WHO criteria for the definition of AMI⁴³ from the 1970's, the cutoff (clinical discriminator) value for troponin T is 0.1 µg/L (ng/mL) or 100 ng/L (pg/mL) as determined from ROC analysis in results with an earlier test generation of the Elecsys Troponin T assay.^{44,45}

The WHO definition of AMI has been recently updated and takes into consideration the ESC/ACCF/AHA/WHF definition recommending the detection of a rise and/or fall of cardiac troponin in the clinical setting of myocardial ischemia using the 99th percentile troponin cutoff value.⁴⁶

Due to the release kinetics of cardiac troponin T, an initially test result < 99th percentile within the first hours of the onset of symptoms does not rule out myocardial infarction with certainty. If myocardial infarction is still suspected, repeat the test at appropriate intervals (6-12 hours after initial assessment).^{16,47}

It is important to obtain a careful history and a precise description of the symptoms. A physical examination with particular attention to the possible presence of cardiac contusion, acute and chronic heart failure, aortic dissection, aortic valve disease, hypertrophic cardiomyopathy, tachy- or bradyarrhythmias, apical ballooning syndrome, rhabdomyolysis with cardiac injury, pulmonary embolism, severe pulmonary hypertension, acute neurological disease, infiltrative diseases, drug toxicity, respiratory failure, sepsis, burns is required.¹⁶

An electrocardiogram is recorded for allowing differentiation of patients with suspicion of ACS (ST-segment elevation or ST-segment changes but without persistent ST-segment elevation or normal ECG).

Laboratory assessment should include markers of myocardial damage, preferably cardiac troponin. If concentrations of troponin or cardiac enzymes rise, irreversible cell damage will have occurred and these patients must be regarded as having had myocardial infarction as defined by the consensus conference. Finally a second cardiac troponin measurement should be obtained after 6 to 12 hours.^{16,47}

Factors associated with elevated values^{48,49,50,51,52,53,54}

Published clinical studies have shown elevations of cardiac troponin T in patients with myocardial injury, as seen in unstable angina pectoris, cardiac contusions, and heart transplants. Elevations have also been seen in patients with rhabdomyolysis and polymyositis.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.



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Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP5-A2) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplication each for 21 days (n = 84). The following results were obtained:

Elecsys 2010 and cobas e 411 analyzers					
		Repeatability		Intermediate precision	
Sample	Mean ng/L (pg/mL)	SD ng/L (pg/mL)	CV %	SD ng/L (pg/mL)	CV %
Human serum 1	7.5	0.4	5.6	1.1	15.0
Human serum 2	13.5	0.4	3.0	0.7	5.2
Human serum 3	24.0	0.6	2.4	0.8	3.1
Human serum 4	300	2.7	0.9	3.8	1.3
Human serum 5	894	7.4	0.8	13.5	1.5
Human serum 6	2665	24.1	0.9	37.5	1.4
Human serum 7	9044	63.5	0.7	115	1.3
PreciControl TN1	27.9	0.7	2.6	1.0	3.4
PreciControl TN2	2049	33.9	1.7	40.7	2.0

MODULAR ANALYTICS E170, cobas e 601 and cobas e 602 analyzers					
		Repeatability		Intermediate precision	
Sample	Mean ng/L (pg/mL)	SD ng/L (pg/mL)	CV %	SD ng/L (pg/mL)	CV %
Human serum 1	6.5	0.5	7.8	0.6	8.6
Human serum 2	11.0	0.5	4.8	0.6	5.2
Human serum 3	23.4	0.3	1.4	0.5	2.2
Human serum 4	293	2.3	0.8	4.5	1.5
Human serum 5	886	6.5	0.7	14.5	1.6
Human serum 6	2647	19.8	0.7	41.9	1.6
Human serum 7	8723	80.8	0.9	117	1.3
PreciControl TN1	29.0	0.4	1.3	0.5	1.9
PreciControl TN2	2106	18.8	0.9	33.9	1.6

Method comparison

A comparison of the Elecsys Troponin T hs assay (MODULAR ANALYTICS E170 analyzer; y) with the Elecsys Troponin T hs STAT assay (Elecsys 2010 analyzer; x) using clinical samples gave the following correlations (ng/L or pg/mL):

Number of samples measured: 142

Passing/Bablok⁵⁵ Linear regression

$$y = 0.99x + 0.47$$

$$y = 1.02x - 14$$

$$r = 0.951$$

$$r = 0.999$$

The sample concentrations were between approximately 3 and 8100 ng/L (pg/mL).

Analytical specificity

The Elecsys Troponin T hs assay does not show any significant cross-reaction with the following substances (tested with TnT concentrations of approximately 18 ng/L (pg/mL) and 38 ng/L (pg/mL); concentration of cross-reacting substances 500 ng/mL):

h-skeletal muscle troponin T 0.003 %, h-cardiac troponin I 0.2 %, h-skeletal muscle troponin I 0.003 %, human troponin C < 0.001 %.

Diagnostic sensitivity and specificity

One clinical center in Germany, one center in India, one center in Switzerland, and two centers in the US participated in prospective studies in patients presenting with chest pain in the emergency department. 507 patients were ruled in for calculation of sensitivity and specificity as selected by the following criteria: Chest pain for > 20 minutes, assessment by 12-lead ECG, age > 20 years, no pregnancy, no previous MI within 3 weeks before admission and a minimum of two blood draws. The patients were diagnosed for acute MI by application of:

1. WHO criteria⁴³ including ECG changes, symptoms characteristic for ACS and elevation of cardiac troponin, and
2. Criteria defined by the Joint ESC/ACCF/AHA/WHF task force.¹⁵

Sensitivity and specificity calculated with AMI defined according to WHO criteria

The optimal cutoff for the assessment of acute myocardial infarction by troponin T was previously calculated by ROC analysis at 0.1 µg/L (ng/mL) or 100 ng/L (pg/mL) in a study with an earlier test generation of the Elecsys Troponin T assay.^{45,47} Sensitivity and specificity in peak troponin T values with the Elecsys Troponin T hs assay were calculated at this ROC optimized AMI cut-off at 0.1 µg/L (ng/mL) or 100 ng/L (pg/mL).

Sensitivity %	N	95 % confidence interval (%)	Specificity %	N	95 % confidence interval (%)
99	78/79	93-100	98	420/428	96-99

The sensitivity and specificity at 0.1 ng/mL (100 pg/mL) were in addition calculated for the Elecsys Troponin T hs assay at different time intervals from admission to the hospital:

Time from admission (hours)	Sensitivity %	N	95 % confidence interval (%)	Specificity %	N	95 % confidence interval (%)
0	64	23/36	46-79	98	160/163	95-100
0-3	83	54/65	72-91	100	385/387	98-100
3-6	90	37/41	77-97	99	320/324	97-100
6-9	97	32/33	84-100	100	218/219	98-100
9-12	100	11/11	72-100	100	50/50	93-100
> 12	100	21/21	84-100	100	66/66	95-100

Sensitivity and specificity calculated with AMI defined according to the ESC/ACCF/AHA/WHF guidelines

Patients with AMI were defined by routine cardiac troponin values above the 99th percentile/10 % CV criteria, and presence of chest pain or ECG changes. Sensitivity and specificity at peak troponin T, high sensitive values were calculated at the 99th percentile of 14 ng/L (pg/mL).

Sensitivity %	N	95 % confidence interval (%)	Specificity %	N	95 % confidence interval (%)
100	112/112	97-100	75	297/395	71-79

Sensitivity and specificity of the Elecsys Troponin T hs assay was calculated at different troponin T levels.

Troponin T hs pg/mL	Sensitivity %	LCI ^(b) %	UCI ^(c) %	Specificity %	LCI %	UCI %
30	98	93.7	99.5	93	90.0	95.1
50	95	88.8	97.5	98	96.1	99.0
70	84	76.0	89.6	99	98.2	99.9



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Troponin T hs pg/mL	Sensitivity %	LCI ^{b)} %	UCI ^{c)} %	Specificity %	LCI %	UCI %
100	75	66.2	82.1	99	98.2	99.9

b) LCI = lower confidence interval

c) UCI = upper confidence interval

The sensitivity and specificity at the 99th percentile (Elecsys Troponin T hs assay)/10 % CV (Elecsys Troponin T assay, 4th gen.; 0.03 ng/mL) criteria were in addition calculated for different time intervals from admission to the hospital:

Time from admission (hours)	Test generation Troponin T	Sensitivity %	N	95 % confidence interval (%)	Specificity %	N	95 % confidence interval (%)
0	4th gen.	71	40/56	58-83	99	142/143	96-100
	Troponin T hs	93	52/56	83-98	76	109/143	68-83
0-3	4th gen.	81	75/93	71-88	99	356/359	98-100
	Troponin T hs	98	91/93	93-100	79	282/359	74-83
3-6	4th gen.	83	53/64	71-91	100	300/301	98-100
	Troponin T hs	100	64/64	94-100	77	232/301	72-82
6-9	4th gen.	86	42/49	73-94	99	201/203	97-100
	Troponin T hs	98	48/49	89-100	76	155/203	70-82
9-12	4th gen.	83	15/18	59-96	100	43/43	92-100
	Troponin T hs	94	17/18	73-100	72	31/43	56-85
> 12	4th gen.	83	25/30	65-94	98	56/57	91-100
	Troponin T hs	100	30/30	88-100	60	34/57	46-72

References

- European patent 394816 and US patent 6376206 by Roche Diagnostics GmbH. Specific antibodies to Troponin T, their production and use in a reagent for the determination of myocardial necrosis.
- Katus HA, Remppis A, Looser S, et al. Enzyme linked immunoassay of cardiac troponin T for the detection of acute myocardial infarction in patients. *Mol Cell Cardiol* 1989;21(7):1349-1353.
- Katus HA, Scheffold T, Remppis A, et al. Proteins of the troponin complex. *Laboratory Medicine* 1992;23(5):311-317.
- Alpert JS, Thygesen K, Jaffe A, et al. The universal definition of myocardial infarction: a consensus document: Ischaemic heart disease. *Heart* 2008;94:1335-1341.
- Hamm CW, Ravkilde J, Gerhardt W, et al. The prognostic value of serum troponin T in unstable angina. *N Engl J Med* 1992;327(3):146-150.
- Ohmann EM, Armstrong PW, Christenson RH, et al. Cardiac troponin T levels for risk stratification with admission cardiac troponin T levels in acute myocardial ischemia. GUSTO IIA Investigators. *N Engl J Med* 1996;335:1333-1334.
- Christenson RH, Duh SH, Newby LK, et al. Cardiac troponin T and cardiac troponin I: relative values in short-term risk stratification of patients with acute coronary syndromes. *Clin Chem* 1998;44(3):494-501.
- Lindahl B, Diderholm E, Lagerqvist B, et al. Mechanisms behind the prognostic value of Troponin T in unstable coronary artery disease: a FRISC II substudy. *J Am Coll Cardiol* 2001;38:979-986.
- Aviles RJ, Askari AT, Lindahl B, et al. Troponin T levels in patients with acute coronary syndromes, with or without renal dysfunction. *N Engl J Med* 2002;346:2047-2052.
- Lindahl B, Venge P, Wallentin L. Troponin T Identifies Patients With Unstable Coronary Artery Disease Who Benefit From Long-Term Antithrombotic Protection. *J Am Coll Cardiol* 1997;29(1):43-48.
- Hamm CW, Heeschen C, Goldmann B, et al. Benefit of abciximab in patients with refractory unstable angina in relation to serum troponin T levels. *N Engl J Med* 1999;340(21):1623-1629.
- Heeschen C, Hamm CW, Goldmann BU, et al. for PRISM study investigators. Troponin concentrations for stratification of patients with acute coronary syndromes in relation to therapeutic efficacy of tirofiban. *Lancet* 1999;354:1757-1762.
- Lindahl B, Diderholm E, Lagerqvist B, et al. Effects on mortality of long-term treatment with l.m.w. heparin in relation to troponin T level and ECG findings - a FRISC 2 substudy. *Eur Heart J* 2000;21(Suppl.):521.
- Newby LK, Ohman EM, Christenson RH, et al. Benefit of Glycoprotein IIb/IIIa Inhibition in Patients With Acute Coronary Syndromes and Troponin T-Positive Status: The PARAGON-B Troponin T Substudy. *Circulation* 2001;103:2891-2896.
- The Task Force for the diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology. Guidelines for the diagnosis and treatment of non-ST elevation acute coronary syndromes. *European Heart Journal* 2007;28:1598-1660.
- Thygesen K, Alpert JS, White HD on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for Redefinition of Myocardial Infarction. *JACC* 2007;50:2173-95.
- Latini R, Masson S, Anand IS, et al. Prognostic Value of Very Low Plasma Concentrations of Troponin T in Patients with Stable Chronic Heart Failure. *Circulation* 2007;116:1242-1249.
- Omland T, De Lemos JA, Christophi C, et al. Distribution and determinants of very low levels of cardiac troponin T in patients with stable coronary artery disease: The PEACE trial. *Eur Heart J* 2008;9(202):1342.
- Omland T, De Lemos JA, Christophi C, et al. Very low cardiac troponin T concentrations and cardiovascular events in patients with stable coronary artery disease: The PEACE trial. *Eur Heart J* 2008;29(202):1644.
- Allen J, Kleiman NS, Nassif D, et al. Prevalence and prognostic Significance of preprocedural cardiac troponin elevation among patients with stable coronary artery disease undergoing percutaneous coronary intervention. *Circulation* 2008;118:632-638.
- Sato Y, Kataoka K, Matsumori A, et al. Measuring serum aminoterminal type III procollagen peptide, 7S domain of type IV collagen, and cardiac troponin T in patients with idiopathic dilated cardiomyopathy and secondary cardiomyopathy. *Heart* 1997;78:505-508.
- Dierkes J, Domrose U, Westphal S, et al. Cardiac troponin T predicts mortality in patients with renal disease. *Circulation* 2000;102:1964-1969.
- Ooi DS, Zimmerman D, Graham J, et al. Cardiac troponin T predicts long-term outcomes in hemodialysis patients. *Clin Chem* 2001;47:412-417.
- Apple FS, Wu AHB. Myocardial infarction redefined: Role of cardiac troponin Testing. *Clin Chem* 2001;47:377-379.
- deFilippi C, Wasserman S, Rosanio S, et al. Cardiac Troponin T and C-reactive protein for predicting prognosis, coronary atherosclerosis, and cardiomyopathy in patients undergoing long term hemodialysis. *JAMA* 2003;290:353-359.
- Iliou MC, Fumeron C, Benoit MO, et al. Prognostic value of cardiac Markers in ESRD: Chronic Hemodialysis and New Cardiac markers Evaluation (CHANCE) study. *Am J Kidney Dis* 2003;42:513-523.
- Scott B, Deman A, Peeters P, et al. Cardiac troponin T and malondialdehyde modified plasma lipids in haemodialysis patients. *Neprhol Dial Transplant* 2003;18:737-742.



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- 28 Madsen LH, Ladefoged S, Hildebrandt P, et al. Comparison of four different cardiac troponin assays in patients with end-stage renal disease on chronic haemodialysis. *Acute Card Care* 2008;10(3):173-180.
- 29 ver Elst KM, Spapen HD, Nguyen DN, et al. Cardiac troponin I and T are biological markers of left ventricular dysfunction in septic shock. *Clin Chem* 2000;46:650-657.
- 30 Rossing P, Jorsal A, Tarnow L, et al. Plasma hs-Troponin T predicts cardiovascular and all cause mortality as well as deterioration in kidney function in type 1 diabetic patients with nephropathy. Abstract EASD 2008.
- 31 European patent application 890154 by F. Hoffmann-La Roche AG and Roche Diagnostics GmbH. Cardiac Troponin as an indicator of advanced coronary artery disease.
- 32 European patent application 1837659 by F. Hoffmann-La Roche AG and Roche Diagnostics GmbH. Means and methods for the differentiation of acute and chronic myocardial necrosis in symptomatic patients.
- 33 Masson S, Pirelli S, Pulitano G, et al. Circulating Markers of myocyte injury predict first recurrence of atrial fibrillation. *AHA* 2008 November 8-12. New Orleans.
- 34 Lauer B, Niederau C, Kühl U, et al. Cardiac troponin T in patients with clinically suspected myocarditis. *JACC* 1997;30:1354-1359.
- 35 Swaanenburg JCJM, Klaase JM, DeJongste MJL, et al. Troponin I, troponin T, CK-MB-activity and CK-MB mass as markers for the detection of myocardial contusion in patients who experienced blunt trauma. *Clin Chim Acta* 1998;272:171-181.
- 36 Giannitsis E, Müller-Bardorff M, Kurowski V, et al. Independent prognostic value of cardiac troponin T in patients with confirmed pulmonary embolism. *Circulation* 2000;102:211-217.
- 37 Herman EH, Lipshultz SE, Rifai N, et al. Use of cardiac troponin T levels as an indicator of doxorubicin-induced cardiotoxicity. *Cancer Res* 1998;58:195-197.
- 38 European patent 1363128 by F Hoffmann-La Roche AG and Roche Diagnostics GmbH. Diagnosis of myocardial infarction and acute coronary syndrome by combination of markers.
- 39 European patent application 1925943 by F. Hoffmann-La Roche AG and Roche Diagnostics GmbH. Means and methods for optimization of diagnostic and therapeutic approaches in chronic artery disease based on the detection of Troponin T and NT-pro BNP.
- 40 Davis GK, Labugger R, Van Eyk JE, et al. Cardiac troponin T is not detected in western blots of diseased renal tissue. *Clin Chem* 2001;47:782-783.
- 41 Ricchiuti V, Voss EM, Ney A, et al. Cardiac Troponin T isoforms expressed in renal diseased skeletal muscle will not cause false positive results by the second generation cTnT assay by Boehringer Mannheim; *Clin Chem* 1998;44(9):1919-1924.
- 42 Hallermayer K, Klenner D, Vogel R. Use of recombinant human cardiac troponin T for standardization of third generation troponin T methods. *Scand J Clin Invest* 1999;59(Suppl 230):128-131.
- 43 World Health Organization. Report of the Joint International Society and Federation of Cardiology/World Health Organization Task Force on Standardization of Clinical Nomenclature. Nomenclature and criteria for diagnosis of ischemic heart disease. *Circulation* 1979;59:607-609.
- 44 Müller-Bardorff M, Hallermayer K, Schröder A, et al. Improved troponin T ELISA specific for cardiac troponin T isoform: assay development and analytical validation. *Clin Chem* 1997;43(3):458-466.
- 45 Kampmann M, Rauscher T, Müller-Bardorff M, et al. Clinical Evaluation of Troponin T and CK-MB Mass on the Elecsys 2010 analyzer. Poster presented at Medlab 97, 12th IFCC European Congress of Clinical Chemistry, August 17-22, 1997, Basel, Switzerland.
- 46 Mendis S, Thygesen K, Kuulasmaa K, et al. World Health Organization definition of myocardial infarction: 2008-09 revision. *Int J Epidemiol* 2011;40(1):139-146.
- 47 Antmann E, Bassand J-P, Klein W, et al. Myocardial infarction redefined - a consensus document of the Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction: The Joint European Society of Cardiology/American College of Cardiology Committee. *Am Coll Cardiol* 2000;36:959-969.
- 48 Kobayashii S, Tanaka M, Tamura N, et al. Serum cardiac troponin T in polymyositis/dermatomyositis. *Lancet* 1992;340(8821):726.
- 49 Mair J, Dienstl F, Puschendorf B. Cardiac Troponin T in the Diagnosis of Myocardial Injury. *Critical Reviews in Clin Lab Sci* 1992;29(1):31-57.
- 50 Carrier M, Solymoss BC, Raymond C, et al. Cardiac Troponin T and Creatine Kinase MB Isoenzyme as Biochemical Markers of Ischemia after Heart Preservation and Transplantation. *J Heart Lung Transplant* 1994;13(4):696-700.
- 51 Löfberg M, Tähtelä R, Härkönen M, et al. Myosin Heavy-Chain Fragments and Cardiac Troponins in the Serum in Rhabdomyolysis. Diagnostic Specificity of New Biochemical Markers. *Arch Neurol* 1995;52:1210-1214.
- 52 Anderson JR, Hossein-Nia M, Brown P, et al. Donor Cardiac Troponin T Predicts Subsequent Inotrope Requirements Following Cardiac Transplantation. *Brief Communications in Transplant* 1994;58(9):1056-1057.
- 53 Franz WM, Remppis A, Kandolf R, et al. Serum Troponin T: Diagnostic Marker for Acute Myocarditis. Letter to the Editor in *Clin Chem* 1996;42(2):340-341.
- 54 Mair P, Mair J, Koller J, et al. Cardiac troponin T in the diagnosis of heart contusion. *Lancet* 1991;338:693.
- 55 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. *J Clin Chem Clin Biochem* 1988 Nov;26(11):783-790.

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

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CONTENT	Contents of kit
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