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Troponin T hs STAT

cobas®

REF	Σ	SYSTEM
		cobas e 411
05092728 190	100	**cobas e** 601
		cobas e 602

English

System information

For **cobas e** 411 analyzer: test number 090
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 107

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 **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "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. Cardiac troponin T increases rapidly after myocardial infarction (AMI) and may persist up to 2 weeks thereafter.[1,2,3] Early detectability of the troponin increase in blood depends on the analytical sensitivity of the specific troponin test used; cardiac troponin T-high sensitive (cTnT-hs) helped to reduce the observational time from 6 to 3 hours when compared to conventional troponin tests such as suggested by several studies[4,5,6] and recommended by the 2011 ESC and the 2014 NICE guidelines on non-ST elevation myocardial infarction (NSTEMI).[7,8] The 2015 ESC guidelines on NSTEMI propose to further shorten the observation time to 0h/1h. This accelerated approach to rule-in or rule-out AMI within 0h/1h has to be used with high-sensitive cardiac Troponin (hs-cTn) tests and using an algorithm validated for the specific hs-cTn assay.[9,10,11,12] The specific algorithm values for cTnT-hs were recommended in these guidelines and have been validated in 3 studies, APACE, APACE-2015 and TRAPID-AMI.[13,14,15] In contrast to ST-elevation myocardial infarction (STEMI), the diagnosis of NSTEMI heavily relies on measured cardiac troponin results. 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 optimally less than or equal to 10 %.[16]

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).[17,18,19,20]

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).[21,22,23,24,25]

The results of a sub-study of the PLATO trial, involving 9946 patients hospitalised for NSTE-ACS, also support the use of cTnT-hs testing to identify which NSTE-ACS patients will benefit most from an aggressive anti-platelet treatment strategy.[26]

Cardiac troponin has been reconfirmed as the preferred marker of myocardial injury in the new guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes.[9,27]

Troponins are released during the process of myocyte necrosis. While they are cardiac specific, they are not specific of MI only. To distinguish between acute and chronic cTn elevations, the Universal Definition of AMI requires the need for serial sampling to observe a rise and/or fall of cTn above the 99th percentile upper reference limit. Absolute changes in cTn appear to have a higher diagnostic accuracy for AMI compared to relative changes.[16,28] Results interpretation have to be analyzed integrating the clinical assessment, including ischemic symptoms and electrocardiographic changes.

The universal definition of AMI recognize that the improved analytical sensitivity of cTn assays used over the last years have allowed for detection of myocardial injury associated with other etiologies.[16] Chronic elevations of cTn can be detected in clinically stable patients such as patients with ischemic or non-ischemic heart failure,[29,30,31] in patients with different forms of cardiomyopathy,[32] renal failure,[33,34,35,36,37,38] sepsis[39] and diabetes.[40,41]

Elevated levels of troponin T correlate with the severity of coronary artery disease and to poor outcome independent of natriuretic peptide (NT-proBNP or BNP) levels.[42,43,44,45]

Low concentrations of troponin T are an independent predictor of cardiovascular events including occurrence and recurrence of atrial fibrillation[46]

Myocardial cell injury leading to elevated cTnT concentrations in the blood can also occur in other clinical conditions such as myocarditis,[47] heart contusion,[48] pulmonary embolism[49] and drug-induced cardiotoxicity.[50]

Other diagnostic tests such as myoglobin, CK-MB, NT-proBNP and CRP can complement the diagnostic and prognostic information of troponin T in different indications.[42,51,52,53,54]

The Elecsys Troponin T hs STAT assay employs two monoclonal antibodies specifically directed against human cardiac troponin T.[55,56] 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 STAT calibrators (Troponin T hs STAT 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.[57]

Test principle

Sandwich principle. Total duration of assay: 9 minutes.

cobas e 411 analyzer:

- 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.

cobas e 601 and **cobas e** 602 analyzers:

- During a 9 minute incubation, antigen in the sample (50 µL), a biotinylated monoclonal anti-cardiac troponin T-specific antibody, a monoclonal anti-cardiac troponin T-specific antibody labeled with a ruthenium complex and streptavidin-coated microparticles react to form a sandwich complex, which is bound to the solid phase.

All analyzers:

- 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 or e-barcode.

a) Tris(2,2-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The reagent rackpack is labeled as TNT-HSST.

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M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-troponin T-Ab~biotin (gray cap), 1 bottle, 8 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)$_3^{2+}$ (black cap), 1 bottle, 8 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.
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.

K_2-EDTA, K_3-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 05092736190, Troponin T hs STAT CalSet, for 4 x 1.0 mL
- REF 05095107190, PreciControl Troponin, for 4 x 2.0 mL
- REF 03609987190, Diluent MultiAssay, 2 x 16 mL sample diluent
- General laboratory equipment
- **cobas e** analyzer

Accessories for **cobas e** 411 analyzer:

- 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, AssayCup, 60 x 60 reaction cups
- REF 11706799001, AssayTip, 30 x 120 pipette tips
- REF 11800507001, Clean-Liner

Accessories for **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, 48 magazines x 84 reaction cups or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Accessories for all analyzers:

- REF 11298500316, ISE Cleaning Solution/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 prior to use and the reading in of the test-specific parameters via the reagent barcode take place automatically. No manual input is necessary. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers (except for the **cobas e** 602 analyzer).

cobas e 601 and **cobas e** 602 analyzers: PreClean M solution is necessary.

Bring the cooled reagents to approximately 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 STAT assay (REF 05092728190) has been standardized against the Troponin T STAT assay (REF 04660307190, 4th gen.). 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).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

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

If necessary, repeat the measurement of the samples concerned.

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 (**cobas e** 601 and **cobas e** 602 analyzers) or in pg/mL, ng/mL, µg/L (**cobas e** 411 analyzer).

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, Limit of Detection and Limit of Quantitation

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, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 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.

An internal study was performed based on guidance from the CLSI protocol EP17-A2. Limit of Blank and Limit of Detection were detected to be the following:

	cobas e 411 analyzer	**cobas e** 601 and **cobas e** 602 analyzers
Limit of Blank (ng/L = pg/mL)	2.57	2.26
Limit of Detection (ng/L = pg/mL)	4.88	2.85

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 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 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 (age range: 20-71 years), the upper reference limit (99th percentile) for troponin T was determined at 14 ng/L (pg/mL), 95 % confidence interval 12.7-24.9 ng/L (pg/mL).[58]

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

Based on the WHO criteria for the definition of AMI[59] 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.[60,61]

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.[62]

Due to the release kinetics of cardiac troponin T, an initially test result < 99th percentile within the first hour of the onset of symptoms does not rule out myocardial infarction in all patients. Therefore lower cutoffs have been proposed for immediate rule-out and also specific delta changes for 0h/1h algorithms.[9] Additional testing at appropriate time intervals is indicated if the first measurements are not conclusive and the clinical condition is still suggestive of ACS.[9] The troponin values should always be used in conjunction with full clinical assessment (including chest pain characteristics and ECG).

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.[9,16]

An electrocardiogram (ECG) is recorded for allowing differentiation of patients with or without ST-segment changes.

Laboratory assessment of patients with suspicion of ACS should include markers of myocardial damage, preferably cardiac troponin.[9] If concentrations of troponin or cardiac enzymes rise, irreversible myocyte cell damage will have occurred and these patients must be regarded as having had myocardial damage.

Factors associated with elevated values[16,47,63,64,65,66]

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.

Troponin T hs STAT

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The ESC and AHA/ACC guidelines and the Universal Definition of MI recommend serial sampling with a rise or fall in troponin to distinguish between acute and chronic cTn elevations. Results should be interpreted in conjunction with clinical presentation including medical history, signs and symptoms, ECG data and biomarker concentrations.[9,16,27]

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.

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 duplicate each for 21 days (n = 84). The following results were obtained:

cobas e 411 analyzer					
		Repeatability		**Intermediate precision**	
Sample	Mean ng/L (pg/mL)	SD ng/L (pg/mL)	CV %	SD ng/L (pg/mL)	CV %
Human serum 1	6.2	0.6	9.4	1.1	17.8
Human serum 2	12.7	0.4	3.2	0.8	6.2
Human serum 3	23.2	0.6	2.6	1.0	4.4
Human serum 4	312	3.1	1.0	4.3	1.4
Human serum 5	943	8.1	0.9	13.7	1.4
Human serum 6	2718	21.1	0.8	35.5	1.3
Human serum 7	8131	63.0	0.8	119	1.5
PreciControl TN1	25.6	0.5	2.1	0.9	3.6
PreciControl TN2	1819	27.2	1.5	39.4	2.2

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	10.2	0.38	3.7	0.41	4.0
Human serum 2	17.7	0.44	2.5	0.47	2.7
Human serum 3	42.5	0.76	1.8	0.90	2.1
Human serum 4	623	10.1	1.6	13.0	2.1
Human serum 5	4298	53.2	1.2	67.5	1.6
Human serum 6	9127	138	1.5	201	2.2
PreciControl TN1	27.2	0.41	1.5	0.50	1.9
PreciControl TN2	2278	20.1	0.9	33.6	1.5

Method comparison

A comparison of the Elecsys Troponin T hs STAT assay (Elecsys 2010 analyzer; y) with the Elecsys Troponin T STAT assay, REF 04660307190 (Elecsys 2010 analyzer; x), using clinical samples gave the following correlations (ng/L or pg/mL):

Number of samples measured: 155

Passing/Bablok[67]	Linear regression
y = 1.05x + 28	y = 1.0x + 38
τ = 0.867	r = 0.997

The sample concentrations were between approximately 13 and 7000 ng/L (pg/mL).

Analytical specificity

The Elecsys Troponin T hs STAT 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 criteria[68] 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.[69]

Sensitivity and specificity calculated with AMI defined according to WHO criteria

The optimal cut-off 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.[61] Sensitivity and specificity in peak troponin T values with the Elecsys Troponin T hs assay were calculated at this ROC optimized AMI cutoff 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

Troponin T hs pg/mL	Sensitivity %	LCI[b] %	UCI[c] %	Specificity %	LCI %	UCI %
50	95	88.8	97.5	98	96.1	99.0
70	84	76.0	89.6	99	98.2	99.9
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

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For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

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.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see https://usdiagnostics.roche.com for definition of symbols used):

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

CE

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

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