Elecsys Troponin T hs Gen 6

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REF		Σ	SYSTEM
09374337190	09374337500	300	**cobas e** 402 **cobas e** 801

English

System information

Short name	ACN (application code number)	Application
TNT6ST	10253	9 minutes (STAT = Short Turn Around Time)

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 (AMI).

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **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 kDa) differs from skeletal muscle TnT. Due to its high tissue specificity, cTnT is a highly sensitive marker for myocardial damage. Cardiac troponin T increases rapidly after acute myocardial infarction (AMI) and may persist up to 2 weeks thereafter.[1,2,3] Early detectability of the cTn increase in blood depends on the analytical sensitivity of the specific troponin test used. High-sensitivity cardiac troponin assays are the preferred markers for myocardial injury in the guidelines for the management of acute coronary syndrome (ACS) and in the Universal Definition of myocardial infarction (MI).[4,5,6] The Universal Definition of MI states that in patients with suspected ACS, a rise and/or fall in cTN concentration above the 99th percentile upper reference limit (URL) of a healthy population, combined with evidence of myocardial ischemia (e.g., symptoms, electrocardiogram (ECG) changes, or imaging results), support the diagnosis of MI. The International Federation of Clinical Chemistry (IFCC) definition of "high-sensitivity cTn (hs-cTn) assay" specifies two requirements: a cTn assay with an imprecision (coefficient of variation) at the 99th percentile URL ≤ 10 % and the ability to detect cTn concentrations above the assay's Limit of Detection (LoD) in at least 50 % of healthy male and female individuals.[7]

Hs-cTn assays have enabled the detection of very low concentrations, improving diagnostic accuracy and allowing more rapid triage of patients with suspected acute myocardial injury. Compared to conventional cardiac troponin (cTn), hs-cTn tests help to reduce the observational time from 6 to 3 hours, as suggested by the Universal Definition of MI and recommended by the 2011 ESC and the 2014 NICE guidelines on non-ST-elevation myocardial infarction (NSTEMI).[4,8,9]

Furthermore, as of 2020, the ESC guidelines on NSTEMI and the 2023 ESC guidelines for the management of ACS recommend the ESC 0 h / 1 h and 0 h / 2 h algorithms to rule in and rule out NSTEMI.[6,10] Similarly, the NICE 2020 guidance for the early rule-out of NSTEMI, the AHA/ACC 2021 recommendations for the evaluation and diagnosis of acute chest pain, and the AHA/ACC 2025 guideline for the management of patients with ACS, support the use of hs-cTn accelerated diagnostic pathways (ADPs).[5,11,12] These ADPs to rule in or rule out AMI require the use of high-sensitivity cardiac troponin (hs cTn) tests in conjunction with the clinical picture (e.g. information from medical history, findings from clinical examination, ECG, additional laboratory and imaging results).[4,5,6,11,12]

In addition to their complementary use in the diagnosis and in the risk stratification for the diagnosis of MI, high-sensitivity cardiac troponins provide prognostic information to predict risk of short- and long-term major adverse cardiovascular events (MACE) in patients presenting with suspected ACS.[4] The Universal Definition of MI acknowledges that the improved analytical sensitivity of cTn assays used in recent years has allowed for detection of myocardial injury associated with other etiologies.[4] Although hs-cTn elevations are cardiac-specific, they are not specific of MI only; myocardial injury can be acute or chronic, or it can be of cardiac or non-cardiac origin. Some of the causes of myocardial injury are cardiac arrhythmias, heart failure, hypertensive emergencies, critical illness (e.g. sepsis), myocarditis, Takotsubo syndrome, valvular heart disease, aortic dissection, pulmonary embolism or hypertension, renal dysfunction, and acute neurological events (e.g. stroke). Serial sampling to detect a rise or fall in hs-cTn concentrations is recommended to distinguish between acute and chronic cardiac and non-cardiac conditions. For the above reasons, results must be analyzed in conjunction with the clinical assessment, including ischemic symptoms and electrocardiographic changes.[6]

The 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure and the fourth definition of myocardial infarction recognize the role of cTn in risk stratification and decision-making in patients with acute heart failure (AHF). In addition to measuring B-type natriuretic peptides, the guidelines recommend measuring cTn in patients presenting with acute dyspnea and suspected AHF. These measurements are intended to help in the differentiation of AHF from non-cardiac causes of acute dyspnea or to exclude myocardial injury or type-1 AMI.[4,13]

The 2022 ESC guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery (NCS) recommend pre- and post-operative measurements of hs-cTn for the diagnosis of myocardial injury after non-cardiac surgery (MINS) and perioperative myocardial injury/infarction (PMI). In addition, perioperative hs-cTn measurements are recommended for prediction of MACE, such as cardiovascular death and myocardial infarction. Cardiac troponin changes during surgery and cTn peak elevations within the first 3 days after surgery can be used to diagnose MINS or PMI and to predict MACE.[4,14,15,16,17]

The 2022 ESC guidelines on cardio-oncology recommend the use of cardiac biomarkers (cTn and B-type natriuretic peptide) in the risk prediction, monitoring, and diagnosis of cardiotoxicity in selected patients receiving cardiotoxic cancer treatments (e.g. anthracylines and/or immune-checkpoint inhibitors).[18]

The Elecsys Troponin T hs Gen 6 assay employs 2 monoclonal antibodies specifically directed against human cTnT.[19,20] The antibodies recognize 2 epitopes (amino acid positions 125-131 and 136-147) located in the central part of the cTnT protein, which consists of 288 amino acids.

The calibrators for the Elecsys Troponin T hs Gen 6 assay (CalSet Troponin T hs Gen 6) 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 cTnT 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.[21]

Test principle

Sandwich principle. Total duration of assay: 9 minutes.

- During a 9-minute incubation, antigen in the sample (30 µL), a biotinylated monoclonal cardiac troponin T-specific antibody, a monoclonal 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.
- 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 II 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 **cobas** link.

Reagents - working solutions

The **cobas e** pack is labeled as TNT6.

M Streptavidin-coated microparticles, 1 bottle, 12.4 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.

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R1 Anti-cardiac troponin T-Ab~biotin, 1 bottle, 15.8 mL:
Biotinylated monoclonal anti-cardiac troponin T antibody (mouse) 0.7 mg/L; phosphate buffer 100 mmol/L, pH 6.0; preservative; inhibitors.

R2 Anti-cardiac troponin T-Ab~ruthenium, 1 bottle, 15.8 mL:
Monoclonal anti-cardiac troponin T antibody (mouse/human chimeric) 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 for laboratory professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing mist or vapours.

P272 Contaminated work clothing should not be allowed out of the workplace.

P280 Wear protective gloves.

Response:

P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Hazardous components:

- 2-methyl-2H-isothiazol-3-one hydrochloride

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

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 available via the **cobas** link.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the **cobas e** pack **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
on the analyzers	16 weeks

Specimen collection and preparation

Serum and Li-heparin plasma are the validated sample types for this assay.

Samples must be collected in standard sampling tubes or tubes containing separating gel.

Serum and Li-heparin plasma samples must not be used interchangeably.

Criterion: Slope 0.90-1.10 + coefficient of correlation ≥ 0.95.

Stability: 4 hours at 20-25 °C, 24 hours at 2-8 °C, 12 months at -20 °C (± 5 °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 and calibrators are at 20-25 °C prior to measurement.

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

Sample preparation

- Do not use specimens with apparent contamination. Before placing samples on the system, make sure that samples are free from bubbles or foam, fibrin, particulate matter, and any kind of films.
- For plasma samples, avoid transferring material from the white blood cell / platelet layer located just above the red blood cells.
- For serum samples, make sure that the clot formation is complete before centrifugation; fibrin still present may lead to erroneous results.
- Never centrifuge a primary tube with separation gel more than once. Tubes must be stored in an upright position at all times after phlebotomy.
- Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[22]

Aliquot preparation

Transfer the supernatant into a secondary tube, avoiding the use of the very top of the sample and of the area just above the gel / blood cell pellet.

Follow the blood collection tube manufacturer's recommendations for centrifugation.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- REF 09374400190, CalSet Troponin T hs Gen 6, for 4 x 1.0 mL
- REF 09374418190, PreciControl Troponin T hs Gen 6, for 6 x 2.0 mL
- REF 07299010190, Diluent MultiAssay, 36 mL sample diluent
- General laboratory equipment
- **cobas e** analyzer

Additional materials for **cobas e** 402 and **cobas e** 801 analyzers:

- REF 06908799190, ProCell II M, 2 x 2 L system solution
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
- REF 06908853190, PreClean II M, 2 x 2 L wash solution
- REF 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- REF 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit

Elecsys Troponin T hs Gen 6

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- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- 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 takes place automatically prior to use.

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the **cobas e** pack.

Calibration

Traceability: The Elecsys Troponin T hs Gen 6 assay (REF 09374337190) has been standardized against recombinant human cardiac troponin T (cTnT) full-length protein that was quantified by amino acid analysis (AAA). For calibration of this method, an amino acid mix solution was used that is traceable to NIST SRM 350b and NIST SRM 84, an independent reference material of the National Institute of Standards and Technology.

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 **cobas e** pack 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:

- every 12 weeks when using the same reagent lot
- every 28 days when using the same **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

Use PreciControl Troponin T hs Gen 6 or other suitable controls for routine quality control procedures.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per **cobas e** pack, 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 ng/L, in pg/mL, or in ng/mL).

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 856 µmol/L or ≤ 50 mg/dL
Hemoglobin	≤ 0.62 mmol/L or ≤ 1000 mg/dL
Intralipid	≤ 1500 mg/dL
Biotin	≤ 4.92 µmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1200 IU/mL
Albumin	≤ 7 g/dL

Criterion: Recovery of ± 2.40 ng/L of initial value for samples ≤ 24.0 ng/L and ± 10 % of initial value for samples > 24 ng/L.

When using samples with hemoglobin concentrations > 1000 mg/dL, falsely depressed results are obtained.

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

Pharmaceutical substances
In vitro tests were performed on 17 commonly used pharmaceuticals. No interference with the assay was found.

In addition, the following special cardiac drugs were tested. No interference with the assay was found.

Special cardiac drugs

Drug	Concentration tested mg/L
Clopidogrel	75
Methylprednisolon	7.5
Phenprocoumon (Marcumar)	3.00
Simvastatin	30.0
Spironolactone	75.0
Tolbutamide	1500
Torasemide	15.0
Valsartan	205.6
Sacubitril	194.4
Dabigatran etexilate (Pradaxa)	300.0
Ezetimibe	10
Rivaroxaban	40
Propafenone	300
Carvedilol	37.5
Digoxin	0.25
Nifedipine	30.0
Verapamil	240
Empagliflozin (Jardiance)	17.5
Epinephrine (adrenaline)	0.50
Insulin (human)	1.60
Lidocaine	80.0
Lisinopril	10.0
Metoprolol tartrate	150
Tenecteplase	40
Evolocumab (Repatha)	290
Liraglutide (Victoza)	1.2

Criterion: Recovery of ± 2.40 ng/L of initial value for samples ≤ 24.0 ng/L and ± 10 % of initial value for samples > 24 ng/L.

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

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

1.5-9500 ng/L (defined by the Limit of Quantitation (intermediate precision CV: 20 %) and the maximum of the master curve). Values below the Limit of Quantitation (intermediate precision CV: 20 %) are reported as

Elecsys Troponin T hs Gen 6

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< 1.5 ng/L. Values above the measuring range are reported as > 9500 ng/L (or up to 95000 ng/L for 10-fold diluted samples).

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 1.0 ng/L

Limit of Detection = 1.5 ng/L

Limit of Quantitation (intermediate precision CV: 20 %) = 1.5 ng/L

Limit of Quantitation (intermediate precision CV: 10 %) = 3.0 ng/L

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 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 % or ≤ 20 %.

An internal study was performed based on guidance from the CLSI protocol EP17 A2. Representative results for Limit of Blank, Limit of Detection, and Limit of Quantitation, obtained with Li-heparin plasma samples on the **cobas e** 801 analyzer were determined to be the following:

	Representative result (ng/L)
Limit of Blank	0.686
Limit of Detection	1.37
Limit of Quantitation Intermediate CV 10 %	2.30
Limit of Quantitation Intermediate CV 20 %	0.97

Imprecision at the established 99th percentile URL value

The expected imprecision at the 99th percentile value was estimated using Li-heparin plasma samples. Representative data generated with the **cobas e** 801 analyzer in Li-heparin plasma samples are presented in the table below.

Population	99th percentile URL (ng/L)	CV (%) based on imprecision profile
Female	18	3.26
Male	32	2.92
Overall	27	2.99

Dilution

Samples with cTnT concentrations above the measuring range can be diluted with Diluent MultiAssay. The recommended dilution is 1:10 (either automatically by the analyzer or manually). The concentration of the diluted sample must be ≥ 700 ng/L.

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

A multicenter prospective observational study was performed with the Elecsys Troponin T hs Gen 6 assay to establish the reference range in healthy individuals and the 99th percentile URL; serum and Li-heparin plasma were evaluated using the **cobas e** 801 analyzer. The study involved a total of 4147 apparently healthy individuals (age range: 20-88 years) from 34 study sites from diverse locations over the world, including the United States, Europe, China, and Japan. Subjects were screened following the 2022 IFCC-recommended criteria. The universal (male and female combined) and the sex-specific 99th percentile URL were calculated using the non-parametric method. The URLs apply to both sample types.

Population	N	99th percentile[a),23] (ng/L)	95 % CI[b)]
Female[c)]	2176	18	16-23
Male[c)]	1971	32	28-35
Overall[c)]	4147	27	24-31

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

b) CI = confidence interval

c) Combined (serum and Li-heparin plasma)

As required by the criteria set by the IFCC for hs-cTn, more than 50 % of the healthy population had an Elecsys Troponin T hs Gen 6 assay level above the 1.5 ng/L Limit of Detection (LoD). From the total of the 8294 samples measured (4147 Li-heparin plasma and 4147 serum samples combined), 89.7 % had values > LoD, with 99.2 % in the male population and 81.0 % in the female population.[7]

Samples	Sex	Healthy persons with values > LoD (1.5 ng/L) in % (combined serum and Li-heparin plasma)
4352	Female	81.0
3942	Male	99.2
8294	Overall	89.7

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 (EP05-A3) 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:

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		Repeatability		**Intermediate precision**	
Sample	Mean ng/L	SD ng/L	CV %	SD ng/L	CV %
Human Li-heparin plasma 1	2.50	0.182	7.3	0.225	9.0
Human Li-heparin plasma 2	4.30	0.165	3.8	0.262	6.1
Human Li-heparin plasma 3	7.91	0.246	3.1	0.344	4.3
Human Li-heparin plasma 4	20.1	0.320	1.6	0.584	2.9
Human Li-heparin plasma 5	21.7	0.326	1.5	0.658	3.0
Human Li-heparin plasma 6	30.3	0.305	1.0	0.781	2.6
Human Li-heparin plasma 7	86.9	0.648	0.7	2.29	2.6
Human Li-heparin plasma 8	142	1.01	0.7	3.46	2.4
Human Li-heparin plasma 9	355	2.28	0.6	7.86	2.2
Human Li-heparin plasma 10	3997	30.8	0.8	156	3.9

Elecsys Troponin T hs Gen 6

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		Repeatability		**Intermediate precision**	
Sample	Mean ng/L	SD ng/L	CV %	SD ng/L	CV %
Human Li-heparin plasma 11	9082	72.8	0.8	272	3.0
Human Li-heparin plasma 12	9149	178	1.9	307	3.4
PC TNT6 L1[d)]	4.64	0.161	3.5	0.258	5.6
PC TNT6 L2[d)]	35.5	0.313	0.9	1.22	3.4
PC TNT6 L3[d)]	222	1.52	0.7	7.58	3.4

d) PreciControl Troponin T hs Gen 6 (level 1-3)

Method comparison

A comparison of the Elecsys Troponin T hs Gen 6 assay, REF 09374337190 (**cobas e** 402 analyzer; 9-min. application; y), with the Elecsys Troponin T hs Gen 6 assay, REF 09374337190 (**cobas e** 801 analyzer; 9-min. application; x), using Li-heparin plasma samples gave the following correlations (ng/L):

Number of samples measured: 154

Passing/Bablok[24]	Linear regression
y = 0.986x - 0.324	y = 0.985x + 2.09
τ = 0.989	r = 1.000

The sample concentrations were between 2.47 and 9356 ng/L.

Analytical specificity

Representative results for analytical specificity were determined with the following cross-reacting substances on the **cobas e** 801 analyzer using Li-heparin plasma samples:

Compound	Concentration tested (ng/mL)
Fast-skeletal muscle troponin T	10
Slow-skeletal muscle troponin T	500
Fast-skeletal muscle troponin I	1000
Slow-skeletal muscle troponin I	1000
Human cardiac troponin I	1000
Fast-skeletal muscle troponin C	1000
Slow-skeletal muscle troponin C	1000

Recovery of ≤ ± 1.97 ng/L of the initial value was obtained for a sample close to the lower end of the measuring range (approximately 5 ng/L cTnT). For samples with elevated analyte concentrations (approximately 40 ng/L, 110 ng/L, 2800 ng/L, and 8000 ng/L cTnT), recovery was ≤ ± 8 % of the initial values.

Clinical performance for the diagnosis of AMI

50 clinical centers from the United States, Europe, China, and Japan participated in the international prospective PERFORM-TSIX study, enrolling patients presenting with signs and symptoms of ACS in the emergency department (ED). 4306 patients (age: ≥ 20 years) were included to evaluate the clinical performance of the assay for the diagnosis of AMI. The patients were selected by the following criteria: subjects with symptoms suggestive of acute coronary syndrome and/or myocardial ischemia as well as subjects with non-cardiac symptoms in whom myocardial infarction was suspected or troponin or other cardiac marker determination was planned as part of suspected ACS routine care.

No exclusion criteria were applied.

1-5 serial blood draws per patient were collected. The adjudicated diagnosis of MI was based on the diagnostic criteria defined by the fourth definition of MI.[4]

The diagnostic sensitivity, diagnostic specificity, negative predictive value (NPV), and positive predictive value (PPV) at the 99th percentile of the Elecsys Troponin T hs Gen 6 assay were calculated for different time intervals from admission to the hospital.

Clinical performance of the Elecsys Troponin T hs Gen 6 assay applying the universal (male and female combined) 99th percentile URL cutoffs at multiple time intervals after admission to the emergency department in the overall (male and female combined) and sex-specific subcohorts in Li-heparin plasma samples

Time	Population	N e)	Sensitivity estimate in % (95 % CI f))	Specificity estimate in % (95 % CI f))	NPV estimate in % (95 % CI f))	PPV estimate in % (95 % CI f))
0-1 h	Overall	3737	88.95 (85.21-92.02)	70.86 (69.30-72.39)	98.40 (97.82-98.86)	24.15 (21.85-26.58)
	Female	1469	89.77 (81.47-95.22)	81.32 (79.16-83.34)	99.20 (98.50-99.64)	23.44 (19.02-28.34)
	Male	2268	88.68 (84.23-92.23)	63.65 (61.50-65.76)	97.70 (96.73-98.44)	24.40 (21.72-27.24)
1-2 h	Overall	3920	92.75 (89.40-95.30)	70.66 (69.14-72.15)	99.06 (98.61-99.40)	22.57 (20.38-24.89)
	Female	1556	81.29 (79.20-83.26)	81.29 (79.20-83.26)	99.58 (99.03-99.86)	22.75 (18.50-27.47)
	Male	2364	92.24 (88.15-95.27)	63.28 (61.19-65.34)	98.60 (97.83-99.16)	22.51 (19.96-25.22)
2-4 h	Overall	3852	93.00 (89.77-95.47)	69.99 (68.44-71.50)	99.03 (98.56-99.38)	23.25 (21.04-25.58)
	Female	1530	96.59 (90.36-99.29)	79.89 (77.73-81.93)	99.74 (99.24-99.95)	22.67 (18.53-27.24)
	Male	2322	91.76 (87.69-94.83)	63.09 (60.96-65.17)	98.42 (97.59-99.02)	23.47 (20.87-26.23)
4-6 h	Overall	1527	93.68 (88.97-96.80)	65.41 (62.81-67.95)	98.77 (97.81-99.39)	25.83 (22.46-29.43)
	Female	582	97.67 (87.71-99.94)	74.03 (70.11-77.68)	99.75 (98.62-99.99)	23.08 (17.17-29.89)
	Male	945	92.37 (86.41-96.28)	59.71 (56.24-63.10)	97.98 (96.32-99.03)	26.95 (22.90-31.31)
> 6 h	Overall	167	94.12 (80.32-99.28)	56.39 (47.53-64.97)	97.40 (90.93-99.68)	35.56 (25.74-46.35)
	Female	69	100.00 (71.51-100.00)	72.41 (59.10-83.34)	100.00 (91.59-100.00)	40.74 (22.39-61.20)
	Male	98	91.30 (71.96-98.93)	44.00 (32.55-55.94)	94.29 (80.84-99.30)	33.33 (21.95-46.34)

e) N = number of patients

f) CI = confidence interval

No quantitative differences in results were observed between serum and Li-heparin plasma samples.

Note: The Elecsys Troponin T hs Gen 6 assay is not intended to be used in isolation. Results must be interpreted in conjunction with other diagnostic tests and clinical information.

Laboratory assessment of patients with suspicion of ACS must include markers of myocardial damage, preferably cTn.[6] Elevation of cTn values with at least 1 value above the 99th percentile URL characterizes myocardial injury.[4,6]

Besides an elevation of cTn values above the URL and a rise or fall pattern, clinical evidence of myocardial ischemia is required for the diagnosis of AMI. As recommended in the ESC guidelines, it is important to obtain a careful history and a precise description of the symptoms. An ECG is recorded for differentiation of patients with or without ST-segment changes.

Due to the release kinetics of cTnT, an initial test result < 99th percentile within the first hours of the onset of symptoms does not rule out MI in all patients.

Caution is advised when interpreting cTn results in patient populations such as elderly, critically ill individuals (e.g. with sepsis or end-stage renal

disease), those who present with non-cardiac symptoms, and those who present very early after the onset of symptoms.

Factors associated with elevated values

Published clinical studies have shown that elevations of cTn values in patients with myocardial injury may arise secondary to many cardiac and non-cardiac conditions and can be acute or chronic, such as critical illness (e.g. sepsis, respiratory failure, burns, shock), myocarditis, Takotsubo syndrome, heart failure, cardiomyopathies, aortic dissection or valve disease, heart transplants, pulmonary embolism or hypertension, renal disfunction, acute neurological disease (stroke and subarachnoid haemorrhage), cardiac contusions, among others.[4,5,6,25,26] Elevations have also been seen in patients with rhabdomyolysis and polymyositis.[27,28]

The ESC and AHA/ACC guidelines and the Universal Definition of MI recommend serial sampling with a rise or fall in cTn values to distinguish between acute and chronic cTn elevations. Results must be interpreted in conjunction with clinical presentation, including medical history, signs and symptoms, ECG data, and biomarker concentrations.[4,5,6]

References

1 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(12):1349-1353.

2 Liebetrau C, Mollmann H, Nef H, et al. Release kinetics of biomarkers in patients undergoing transcoronary ablation of septal hypertrophy. Clin Chem 2012;58(6):1049-1054.

3 Katus HA, Scheffold T, Remppis A, et al. Proteins of the troponin complex. Laboratory Medicine 1992;23(5):311-317.

4 Thygesen K, Alpert JS, Jaffe AS, et al. Fourth definition of myocardial infarction. J Am Coll Cardiol 2018;30:72(18):2231-2264.

5 Gulati M , Levy P, Mukherjee D, et al 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021;144:e368–e454.

6 Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndrome. Eur Heart J. 2023;44(38):3720-3826.

7 Aakre K, Saenger A, Body R et al. Analytical considerations in deriving the 99th percentile upper reference limits for high-sensitivity cardiac troponin assays: Educational recommendations from the IFCC committee on Clinical application of cardiac biomarkers. Clin . Chem 2022; 68(8): 1022-1030.

8 Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for the management of acute coronary syndrome in patients presenting without persistent ST-segment elevation. The Task Force for the management of acute coronary syndrome (ACS) in patient presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2011;32(23):2999-3054.

9 NICE (2014) Myocardial infarction (acute): Early rule out using high-sensitivity troponin tests (Elecsys Troponin T high-sensitive, ARCHITECT STAT High Sensitive Troponin-I and AccuTnI+3 assays). NICE diagnostics guidance DG15. Available at www.nice.org.uk/dg15 [NICE guideline].

10 Collet JP, Thiele H, Barbato E, et al.; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021 Apr 7;42(14):1289-1367.

11 NICE (2020), High-sensitivity troponin tests for the early rule out of NSTEMI Diagnostics guidance DG40, Available at https://www.nice.org.uk/guidance/dg40.

12 Rao Sunil V, O'Donoghue Michelle L, Ruel M, et al. "2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines." J Am Coll Cardiol 2025; S0735-1097(24):10424-X.

13 McDonagh T, Metra M, Adamo M et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.Eur Heart J 2021;42(36):3599-3726.

14 Kristensen SD, Knuuti J, Saraste A, et al.2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J 2014; 35(35):2383-431.

15 Duceppe E, Parlow J, MacDonald P, et al. Canadian cardiovascular society guidelines on perioperative cardiac risk assessment and management for patients undergoing noncardiac surgery. Canadian Journal of Cardiology Can J Cardiol. 2017;33(1):17-32.

16 Menosi Gualandro DM, Savoy Fornari S, Caramelli B et al. Guideline for Perioperative Cardiovascular Evaluation of the Brazilian Society of Cardiology – 2024. Arq Bras Cardiol. 2024;121(9):e20240590.

17 Halvorsen S, Mehilli J . Cassese S et al. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery Eur Heart J 2022; 43(39):3826-3924.

18 Lyon AR, López-Fernández T, Couch LS, et al. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). Eur Heart J 2022;43(41):4229-4361.

19 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(4):782-783.

20 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.

21 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.

22 Clinical and Laboratory Standards Institute. Procedures for the handling and Processing of Blood specimens for common laboratory tests: Approved Guideline - Fourth Edition. Wayne, PA: Clinical and laboratory Standards Institute; 2010. CLSI Document -GP44-A4.

23 Wu AHB, Christenson RH, Greene DN et al. Clinical laboratory practice recommendations for the use of cardiac troponin in acute coronary syndrome: expert opinion from the Academy of the American Association for Clinical Chemistry and the Task Force on Clinical Applications of Cardiac Bio-Markers of the International Federation of Clinical Chemistry and Laboratory Medicine. Clin Chem 2018; 64(4):645-655.

24 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.

25 Huis M, Craft C, Hood R Blunt cardiac trauma review. Cardiol Clinics 2018; 36(1): 183-191.

26 Erbel C, Taskin R, Doesch A, et al. High-sensitive troponin T measurements early after heart transplantation predict short- and long-term survival. Transpl Int 2013;26(3):267-272.

27 Lavallaz JD, Zehnter T, Puelacher C, et al. Rhabdomyolysis: A Noncardiac Source of Increased Circulating Concentrations of Cardiac Troponin T? . J Am Coll. Cardiol. 2018,72 Pt A, 2936-2937.

28 Zhang L, Wang GC, Ma L, et al. Cardiac involvement in adult polymyositis or dermatomyositis: a systematic review Clin Cardiol 2012;35(11):686-691.

For further information, please refer to the appropriate user guide or operator's manual for the analyzer concerned, the respective application sheets 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.

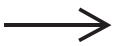
Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Elecsys Troponin T hs Gen 6

The Summary of Safety & Performance Report can be found here:
https://ec.europa.eu/tools/eudamed

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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