IVD

VIDAS® High sensitive Troponin I (TNHS)

VIDAS® High sensitive Troponin I is an automated quantitative test for use on the instruments of the VIDAS® family for the determination of human cardiac troponin I in human serum or plasma, using the ELFA technique (Enzyme Linked Fluorescent Assay).

The VIDAS® High sensitive Troponin I assay is intended to be used as an aid in the diagnosis of myocardial infarction (MI) and for the risk stratification of patients with symptoms suggestive of acute coronary syndrome (ACS) with respect to relative risk of all-cause mortality and major adverse cardiac events (MACE) consisting of myocardial infarction and revascularization, at 30 days. This assay is intended for use in clinical laboratories (centralized or decentralized) by qualified laboratory professionals.

SUMMARY AND EXPLANATION

The troponin complex, consisting of subunits I, T and C, is bound to the myofibrillar thin filaments of striated muscle where it plays a role in the calcium-mediated regulation of muscle contraction (1). Distinct isoforms of troponin I and T exist in cardiac myocytes and can be specifically measured by immunoassays when released in blood (2). Because of its high myocardial tissue specificity, cardiac troponin (I or T) is the preferred marker for the detection of myocardial injury, and has become the standard as an aid in the diagnosis of myocardial infarction (MI) in the clinical setting of cardiac ischemia (3).

Cardiac troponin I (cTnI) levels rise rapidly after the onset of myocardial injury and fall to normal levels within 7 days (4). In view of this rising and falling pattern, serial measurements of cTnI are recommended with blood samples drawn at presentation and after 6-9 hours; occasionally a third sample may be required after 12-24 hours (5). With high-sensitivity cTnI assays, the second sample is recommended to be drawn after 3 hours (6).

The decision limit for MI diagnosis is defined as the 99th percentile of the distribution of cTnI in a healthy reference population (3). The 99th percentile value differs according to gender (7). The coefficient of variation (CV) at the decision limit should be $\leq$10%, although a CV between 10% and 20% is still clinically acceptable (3, 5). The diagnosis of MI requires serial testing with at least one cTnI value above the 99th percentile (3).

Although cTnI is specific for cardiac injury, it is not specific for cardiac damage due to ischemic heart disease. Consequently, cTnI can also be elevated in conditions other than MI such as pulmonary embolism, heart failure, myocarditis, renal failure, severe infections and trauma (3). It is recommended to do serial cTnI measurements in order to distinguish acute MI, characterized by a rising or falling pattern, from chronic elevations due to other conditions (3).

Using the difference in cTnI concentrations between two samples (delta values) has allowed to improve the specificity of cTnI assays for the diagnosis of MI (8).

To rule-in or rule-out MI, an algorithm can be used based on various decision thresholds and delta values for cTnI, taking the clinical context of each patient into account (9).

For patients with acute coronary syndrome (ACS), cTnI also predicts the risk of death or recurrent ischemic events (4). Clinical studies have shown that ACS-patients with increased levels of cTnI have a higher risk of having MI within 30 days of follow-up (10, 11). Risk stratification of ACS patients is the basis for therapeutic decision making (9, 12). In this process, measurement of cTnI is a key distinguishing factor to decide on selection of the site of care and the timing and aggressiveness of intervention (9, 12).

Other studies using cTnI assays have shown that elevated levels of troponin are associated with structural heart diseases, a future risk of cardiovascular events and death in the general population or in patients with stable cardiovascular disease (13, 14).

The VIDAS® High sensitive Troponin I assay is an aid in the diagnosis of myocardial infarction and for the risk stratification of patients with acute coronary syndrome.

PRINCIPLE

The assay principle combines a one-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA).

The Solid Phase Receptacle (SPR®) serves as the solid phase as well as the pipetting device. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips.

All of the assay steps are performed automatically by the instrument. The sample is transferred into the wells containing alkaline phosphatase-labeled anti-cardiac troponin antibodies (conjugate). The sample/conjugate mixture is cycled in and out of the SPR® several times. This operation enables the troponin I to bind with the immunoglobulins, fixed to the interior wall of the SPR®, and the conjugate, to form a sandwich. Unbound components are eliminated during washing steps.

Two detection steps are then performed successively. During each step, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR®. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone), the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is proportional to the concentration of antigen present in the sample. At the end of the assay, the results are automatically calculated by the instrument in relation to two calibration curves stored in memory corresponding to the two detection steps. A fluorescence threshold value determines the calibration curve to be used for each sample. The results are then printed out.

CONTENT OF THE KIT - RECONSTITUTION OF REAGENTS (60 TESTS):

60 TNHS Strips	STR	Ready-to-use.
60 TNHS SPR®s 2 x 30	SPR®	Ready-to-use. Interior of SPR®s coated with mouse monoclonal anti-cardiac troponin I immunoglobulins.
TNHS Controls C1 Control 1 x 2 mL C2 Control 1 x 2 mL	C1 C2	Reconstitute with 2 mL of distilled water. Leave for at least 10 minutes at 18-25°C and then mix using a vortex-type mixer. After reconstitution, the control is stable for 8 hours at 2-8°C or until the expiration date of the kit when stored at -25 ± 6°C. 9 freeze/thaw cycles are possible. Human serum* + troponin I + preservative. MLE data indicate the acceptable range in ng/L ("Control C1 Dose Value Range" or "Control C2 Dose Value Range").
TNHS Calibrators S1 Calibrator 2 x 2 mL S2 Calibrator 2 x 2 mL	S1 S2	Reconstitute with 2 mL of distilled water. Leave for at least 10 minutes at 18-25°C and then mix using a vortex-type mixer. After reconstitution, the calibrator is stable for 8 hours at 2-8°C or until the expiration date of the kit when stored at -25 ± 6°C. 4 freeze/thaw cycles are possible. Human serum* + troponin I + preservative. MLE data indicate the concentration in ng/L ("Calibrator (S1) Dose Value" or "Calibrator (S2) Dose Value") and the acceptable range in "Relative Fluorescence Value ("Calibrator (S1) RFV Range" or "Calibrator (S2) RFV Range").
TNHS Diluent 1 x 2 mL (liquid)	R1	Ready-to-use. Protein stabilizer of animal origin + preservatives.
Specifications for the factory master data required to calibrate the test: • MLE bar codes printed on the box label.		
1 package insert provided in the kit or downloadable from www.biomerieux.com/techlib.		

* This product has been tested and shown to be negative for HBs antigen, and antibodies to HIV1, HIV2 and HCV. However, since no existing test method can totally guarantee their absence, this product must be treated as potentially infectious. Therefore, usual safety procedures should be observed when handling.

The SPR®

The interior of the SPR® is coated during production with mouse monoclonal anti-cardiac troponin I immunoglobulin. Each SPR® is identified by the code "TNHS". Only remove the required number of SPR®s from the pouch and **carefully reseal the pouch after opening**.

The Reagent Strip

The strip consists of 10 wells covered with a labeled foil seal. The label comprises a barcode which mainly indicates the assay code, kit lot number and expiration date. The foil of the first well is perforated to facilitate the introduction of the sample. The last well of each strip is a cuvette in which the fluorometric reading is performed. The wells in the center section of the strip contain the various reagents required for the assay.

Description of the TNHS strip

Well	Reagents
1	Sample well.
2 - 3 - 4	Empty wells.
5	Conjugate: alkaline phosphatase-labeled monoclonal anti-Troponin antibodies.
6 -7 - 8	Wash Buffer.
9	Empty well.
10	Reading cuvette with substrate: 4-Methyl-umbelliferyl-phosphate (0.6 mmol/L) + diethanolamine* (DEA) (0.62 mol/L or 6.6%) pH 9.2 + 1 g/L sodium azide (300 µL).

***** Signal word: **DANGER**

Hazard statement

H318: Causes serious eye damage.

Precautionary statement

P280: Wear protective gloves/protective clothing/eye protection/face protection.
P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
For further information, please refer to the Material Safety Data Sheet.

MATERIALS AND DISPOSABLES REQUIRED BUT NOT PROVIDED

- Pipette with disposable tips to dispense 2 mL and 200 µL.
- Powderless, disposable gloves.
- For other specific materials and disposables, please refer to the Instrument User's Manual.
- Instruments of the VIDAS® family: VIDAS®, mini-VIDAS® or VIDAS® 3.

WARNINGS AND PRECAUTIONS

- **For *in vitro* diagnostic use only.**
- **For professional use only by qualified laboratory professionals.**
- **The kit contains products of human origin. No known analysis method can totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious and handled observing the usual safety precautions (see Laboratory Biosafety Manual - WHO - Geneva - latest edition).**
- The kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious, and handled observing the usual safety precautions (do not ingest; do not inhale).
- Do not use the SPR®s if the pouch is pierced or if the dot sealing a SPR® has come unstuck.
- Do not use visibly deteriorated STRs (damaged foil or plastic).
- Do not use reagents after the expiration date indicated on the kit label.
- Do not mix reagents (or disposables) from different lots.
- Use **powderless** gloves, as powder has been reported to cause false results for certain enzyme immunoassay tests.
- Kit reagents contain sodium azide which can react with lead or copper plumbing to form explosive metal azides. If any liquid containing sodium azide is disposed of in the plumbing system, drains should be flushed with water to avoid build-up.
- The substrate in well 10 contains an irritant agent (6.6% diethanolamine). Refer to the hazard statements "H" and the precautionary statements "P" indicated above.
- Spills should be wiped up thoroughly after treatment with liquid detergent or a solution of household bleach containing at least 0.5% sodium hypochlorite. See the User's Manual for cleaning spills on or in the instrument. Do not autoclave solutions containing bleach.
- The instrument should be regularly cleaned and decontaminated (see the User's Manual).

STORAGE CONDITIONS

- Store the VIDAS® High sensitive Troponin I kit at 2-8°C.
- **Store all unused reagents at 2-8°C.**
- After opening the kit, check that the SPR® pouch is correctly sealed and undamaged. If not, do not use the SPR®s.
- **Carefully reseal the pouch with the desiccant inside after use to maintain stability of the SPR®s and return the complete kit to 2-8°C.**
- If stored according to the recommended conditions, all components are stable until the expiration date indicated on the label. Refer to the kit composition table for special storage conditions.

SPECIMENS

Specimen type and collection

Human serum or plasma (lithium heparin).

Since EDTA causes a decrease in the values measured, **plasma collected on EDTA should not be used**.

For a given patient, serial troponin testing must be performed using the same type of sample tube.

Types of tubes validated:

- Plastic tube with clot activator,
- Plastic tube with clot activator and separation gel,
- Plastic tube with lithium heparin,
- Plastic tube with lithium heparin and separation gel.

It is recommended to validate collection tubes before use as some contain substances which interfere with test results.

Note: Blood sampling tube results may vary from one manufacturer to another depending on the materials and additives used.
It is the responsibility of each laboratory to validate the type of sample tube used and to follow the manufacturer's recommendations for use.

Sample preparation

Follow the tube manufacturer's recommendations for use.
The pre-analytical step, including the preparation of blood samples, is an essential first step when performing medical analyses. In accordance with Good Laboratory Practice, this step is performed under the responsibility of the laboratory manager.
Insufficient clot time can result in the formation of fibrin with micro-clots that are invisible to the naked eye. The presence of fibrin, red blood cells, or suspended particles can lead to erroneous results.

Samples containing suspended fibrin particles or erythrocyte stroma should be centrifuged before testing.

For serum specimens, ensure that complete clot formation has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting times.

SPECIAL CASE OF FROZEN SAMPLES

Preparation of frozen-stored samples: after thawing, these samples must be thoroughly mixed before testing. Mix using a vortex-type mixer. **Clarify samples by centrifugation before testing.**
Frozen sera: centrifuge for 10 minutes at 3 900 x *g*.
Frozen plasma:
- centrifuge for 10 minutes at 13 000 x *g*

OR

- centrifuge for 10 minutes at 3 000 to 3 900 x *g*, then transfer the supernatant into a new tube, taking care not to transfer any pellet material, and centrifuge again for 10 minutes at 3 000 to 3 900 x *g*.

Sample stability

Samples (serum and plasma) can be stored in primary tubes at +18/+25°C for 4 hours, or at +2/+8°C for 48 hours; if longer storage is required, store the sera or plasma in aliquotes at -25 ± 6°C for 1 month, or at < -60°C for 4 months, with up to 3 freeze/thaw cycles.

Sample-related interferences

It is recommended not to use samples that are hemolyzed, lipemic or icteric and, if possible, to collect a new sample.
Refer to the section **PERFORMANCE - Study of drugs and other potentially interfering substances"** for the components or substances tested.

INSTRUCTIONS FOR USE

For complete instructions, see the Instrument User's Manual.

Reading VIDAS® Protocol Test Change (PTC) data and MLE data

When using the assay for the first time:

With the external instrument barcode reader,

1. Scan the PTC barcode(s) at the end of the package insert. This reading allows VIDAS® PTC protocol data to be transferred to the instrument software for its update.
2. Scan the MLE data on the box label.

Note: If the MLE data have been read before the VIDAS® PTC protocol, read the MLE data again.

When opening a new lot of reagents:

Enter the specifications (or factory master data) into the instrument using the master lot entry (MLE) data.
If this operation is not performed **before initiating the tests**, the instrument will not be able to print results.
Note: the master lot data need only be entered once for each lot.
It is possible to enter MLE data **manually or automatically** depending on the instrument (refer to the User's Manual).

Calibration

Calibration, using the **two calibrators** provided in the kit, must be performed each time a new lot of reagents is opened, after the master lot data have been entered, and then **every 28 days**. This operation provides instrument-specific calibration curves and compensates for possible minor variations in assay signal throughout the shelf-life of the kit.
The calibrators identified by S1 and S2, must be tested **in duplicate** (see User's Manual) in the same run. The calibration values must be within the set RFV (Relative Fluorescence Value). If this is not the case, **recalibrate using S1 and S2.**

Controls

Two controls are included in each VIDAS® High sensitive Troponin I kit. These controls must be performed immediately after opening a new kit to ensure that reagents have not deteriorated. Each calibration must also be checked using these controls. The instrument will only be able to check the control values if they are identified by C1 and C2.
Results cannot be validated if the control values deviate from the expected values.

Procedure

1. **Remove the required reagents from the refrigerator. They can be used immediately.**
2. Use one "TNHS" strip and one "TNHS" SPR® for each sample, control or calibrator to be tested. **Make sure the storage pouch has been carefully resealed after the required SPR®s have been removed.**
3. The test is identified by the "TNHS" code on the instrument. The calibrators must be identified by "S1" and "S2", and tested **in duplicate**. The controls should be identified by "C1" and "C2" and tested singly.
4. Mix the calibrators and/or controls and/or samples using a vortex-type mixer (for serum or plasma separated from the pellet).
5. Before pipetting, ensure that the samples, calibrators, controls and diluent are free of bubbles.
6. **For this test, the test portion of the calibrators, controls and samples is 200 µL.**
7. Insert the "TNHS" SPR®s and "TNHS" strips into the instrument. Check to make sure the color labels with the assay code on the SPR®s and the Reagent Strips match.
8. **Initiate the assay immediately.** All the assay steps are performed automatically by the instrument.
9. Reclose the vials and return them to the required temperature after pipetting.
10. The assay will be completed within approximately **20 minutes**. After the assay is completed, remove the SPR®s and strips from the instrument.
11. Dispose of the used SPR®s and strips into an appropriate recipient.

QUALITY CONTROL

Additional quality controls can be performed in accordance with local regulations or requirements related to accreditation, as well as requirements defined within the scope of the laboratory's quality control policy.

RESULTS AND INTERPRETATION

The results are automatically calculated by the instrument using two calibration curves which are stored by the instrument, and are expressed in ng/L (or pg/mL).

The VIDAS® High sensitive Troponin I assay is standardized against a competitor's method.

The VIDAS® High sensitive Troponin I assay results are displayed by the instrument from 1.5 to 40 000 ng/L.

Samples with cardiac troponin I concentrations greater than 40 000 ng/L must be retested after being diluted 1/4 in the VIDAS® High sensitive Troponin I kit diluent (1 volume of sample + 3 volumes of diluent).

If the dilution factor has not been entered when the Work List was created (see User's Manual), multiply the result by the dilution factor to obtain the sample concentration.

Interpretation of test results should be made taking into consideration the patient's clinical history.

LIMITATIONS OF THE METHOD

Interference may be encountered with certain samples containing antibodies directed against reagent components. For this reason, assay results should be interpreted taking into consideration the patient's clinical history, and the results of any other tests performed.

REFERENCE VALUES

These results are given as a guide; it is recommended that each laboratory establish its own reference values from a rigorously selected population.

The 99th percentile values were obtained using plasma samples from 815 apparently healthy individuals from a European population (447 men and 368 women between 41 and 80 years of age), with no history of cardiovascular disease, no cardiac medication, normal NT-proBNP and HbA1c levels, a normal glomerular filtration rate, and no severe hypertension. The 99th percentile values obtained are reported below:

Population	99th percentile (ng/L)	90% CI * (ng/L)
Global	19	[15 – 38]
Male	25	[17 – 50]
Female	11	[8 – 29]

***** CI = Confidence Interval

ANALYTICAL PERFORMANCE

Measurement range

The measurement range is the range of values corresponding to the acceptable performance limits (precision and linearity).
The VIDAS® High sensitive Troponin I assay measurement range extends from 4.9 to 40 000 ng/L.

Limits of detection and quantitation

The study was performed using several reagent lots and instruments of the VIDAS® family according to CLSI® EP17-A2 recommendations.
The observed Limits of Blank (LoB) are between 0 and 1.9 ng/L and the observed Limits of Detection (LoD) are between 1.3 and 3.2 ng/L.
The Limit of Quantitation (LoQ) is the lowest concentration that can be measured with an acceptable within-laboratory precision level of 20% CV. The observed LoQs are between 2.9 and 4.9 ng/L.

Linearity

The study was performed according to CLSI® EP06-A recommendations. The VIDAS® High sensitive Troponin I assay is linear over the claimed measurement range.

Hook effect

No hook effect was found up to cardiac troponin I concentrations of 1 200 000 ng/L.

Precision

The VIDAS® High sensitive Troponin I assay has been designed to report a within-lot within -laboratory CV ≤ 10% for samples with a concentration between 19 and 40 000 ng/L.

A precision study was performed according to CLSI® EP05-A3 recommendations. A panel of human samples representing 7 concentration levels in the measurement range was analyzed on several instruments of the VIDAS® family so as to include the following main sources of variability: repeatability, run, day, calibration and lot.

Repeatability (within-run precision), within-lot precision and within-laboratory precision (between-lot within-instrument) were estimated for each level of concentration studied and are reported in the following table as an example:

Samples	Mean Concentration (ng/L)	Within-run CV (%)	Within-lot Within-laboratory CV (%)	Between-lot Within-laboratory CV (%)
1	13.1	8.2	9.4	10.1
2	16.7	6.0	7.5	8.0
3	23.1	4.7	6.0	6.4
4	38.4	3.4	5.0	5.7
5	286.0	1.8	3.8	4.6
6	2 797.8	2.9	4.5	5.0
7	28 384.1	3.6	6.0	6.8

Based on these data, the within-lot within-laboratory CV at the 99th percentile value defined on the global healthy population was estimated using a precision profile. A 7.0% CV was obtained at 19 ng/L.

Analytical specificity

The analytical specificity of the VIDAS® High sensitive Troponin I assay was established by testing cross-reactive compounds according to CLSI® EP07-A2 recommendations.

The results of this study are reported in the following table:

Tested compounds	Tested concentrations (ng/L)	Cross-reactivity %
Skeletal Troponin I	1 000 000	≤ 0.04%
Cardiac Troponin C	1 000 000	≤ 0.09%
Cardiac Troponin T	1 000 000	≤ 0.09%
Skeletal Troponin T	1 000 000	≤ 0.02%

Study of drugs and other potentially interfering substances

Potential interference by commonly used drugs and other substances was determined according to CLSI® EP07-A2 recommendations. No significant interference was detected up to the maximum concentrations indicated below.

Tested drugs	Maximum concentrations	Tested drugs	Maximum concentrations
Abciximab	12 mg/L	L-Nicotine	6.2 µmol/L
Acetylsalicylic Acid	3.62 mmol/L	Nitroglycerin	120 µg/L
Amoxicillin	206 µmol/L	Paracetamol	1 324 µmol/L
Atenolol	37.6 µmol/L	Propranolol	7.71 µmol/L
Caffeine	308 µmol/L	Theophylline	222 µmol/L
Clopidogrel	45 mg/L	Warfarin	32.5 µmol/L
Eptifibatide	8.1 mg/L	Prasugrel	36 mg/L
Ethanol	86.8 mmol/L	Ticagrelor	108 mg/L
Fondaparinux	4.5 mg/L	Ibuprofen	2 425 µmol/L
Low molecular weight heparin	5 000 IU/L	Codeine	5.34 µmol/L
Sodium heparin	3 000 IU/L		

Tested Substances	Maximum concentrations
Hemoglobin	4.85 g/L
Lipids	30 g/L
Bilirubin	120 mg/L
Albumin	48 g/L
HAMA	2 000 ng/mL
Biotin	2 mg/L
Rheumatoid factor	800 IU/mL

CLINICAL PERFORMANCE

For diagnostic purposes

The diagnostic performance of the VIDAS® High sensitive Troponin I assay (sensitivity, specificity, negative predictive value, and positive predictive value) was evaluated during a multicenter clinical study:

- using the 99th percentile defined on the global healthy population as the decision cut-off value,
- or using the 99th percentile defined on the global healthy population as the decision cut-off value, as well as the difference in cTnI concentrations between admission and the following hours (delta values),
- or using a two-hour algorithm for MI rule-in and rule-out.

The study was performed using 682 patients (validation cohort) presenting to the emergency department with symptoms suggestive of ACS. The diagnosis of all the patients was independently established by certified cardiologists, according to the current recommendations (3). The MI prevalence observed during this study is 15.7%. The patient samples were collected on admission, and then at different times during the 3 hours following their admission.

Diagnostic performance obtained using the decision cut-off value

The results obtained within the scope of this study are presented in the following table:

Collection time (hours)**	Number of patients	Sensitivity (%) [95% CI*]	Specificity (%) [95% CI*]	Negative predictive value (%) [95% CI*]	Positive predictive value (%) [95% CI*]
Initial value (T0)	682	74.8 [65.8 ; 82.0]	90.6 [87.9 ; 92.7]	95.1 [92.9 ; 96.7]	59.7 [51.2 ; 67.6]
1 hour (T1h)	630	87.1 [78.8 ; 92.5]	90.7 [87.9 ; 92.9]	97.6 [95.8 ; 98.8]	61.8 [53.3 ; 69.7]
2 hours (T2h)	597	89.1 [81.1 ; 94.0]	89.5 [86.5 ; 91.9]	97.8 [96.1 ; 99.0]	60.7 [52.3 ; 68.6]
3 hours (T3h)	682	90.7 [83.6 ; 94.8]	87.3 [84.3 ; 89.8]	98.0 [96.4 ; 99.1]	57.1 [49.5 ; 64.3]

* CI = Confidence Interval

** An interval of ± 30 minutes is associated to the reported time points.

Interpretation of test results should be made taking into consideration the patient's clinical history.

Diagnostic performance obtained using the decision cut-off value and the delta values

To improve the clinical specificity of the test for MI, cTni delta values between 10 and 25 ng/L were used in addition to the 99th percentile (19 ng/L) to evaluate the diagnostic performance.

The two groups of patients taken into account for this analysis are the following:

- Positive interpretation: patients who show differences in absolute value greater than or equal to the studied delta value with at least one cTnI concentration greater than or equal to the 99th percentile at the two collection times.
- Negative interpretation: patients who show differences in absolute value below the studied delta value or who did not show a cTnI concentration greater than or equal to the 99th percentile at the two collection times.

The results obtained within the scope of this study are presented in the following table:

Collection time	Delta value used (ng/L)	Sensitivity (%) [95% CI*]	Specificity (%) [95% CI*]	Negative predictive value (%) [95% CI*]	Positive predictive value (%) [95% CI*]
T2h vs T0	10	78.3 [68.8 ; 85.5]	95.6 [93.5 ; 97.3]	96.0 [93.9 ; 97.6]	76.6 [67.1 ; 84.0]
	15	75.0 [65.3 ; 82.7]	96.4 [94.4 ; 97.9]	95.5 [93.3 ; 97.1]	79.3 [69.6 ; 86.5]
	20	72.8 [63.0 ; 80.9]	97.0 [95.1 ; 98.3]	95.1 [92.9 ; 96.8]	81.7 [72.0 ; 88.6]
	25	69.6 [59.5 ; 78.0]	97.8 [96.1 ; 98.9]	94.6 [92.4 ; 96.3]	85.3 [75.6 ; 91.6]
T3h vs T0	10	82.2 [73.9 ; 88.3]	95.0 [92.9 ; 96.5]	96.6 [94.8 ; 98.0]	75.2 [66.7 ; 82.2]
	15	80.4 [71.9 ; 86.8]	96.3 [94.5 ; 97.7]	96.3 [94.5 ; 97.7]	80.4 [71.9 ; 86.8]
	20	76.6 [67.8 ; 83.6]	96.7 [94.9 ; 98.0]	95.7 [93.7 ; 97.2]	81.2 [72.5 ; 87.6]
	25	74.8 [65.8 ; 82.0]	97.4 [95.7 ; 98.5]	95.4 [93.4 ; 96.9]	84.2 [75.6 ; 90.2]

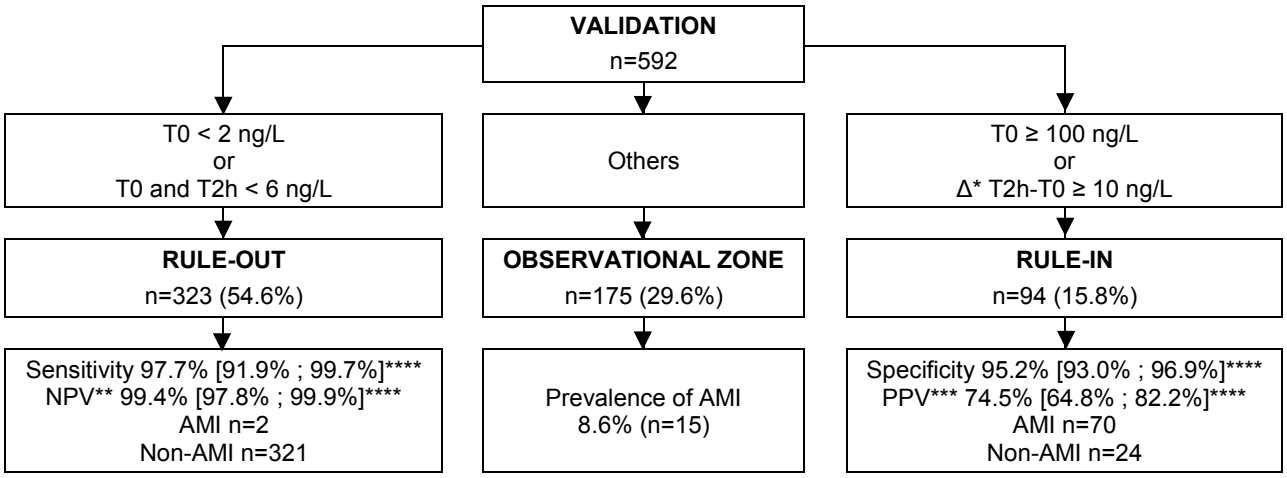
* CI = Confidence Interval

Interpretation of test results should be made taking into consideration the patient's clinical history.

Diagnostic performance obtained with a two-hour algorithm for MI rule-in and rule-out

This analysis takes into account individuals presenting to the emergency department with symptoms suggestive of ACS but without ST-segment elevation MI.
To aid in more rapid management of patients, an algorithm based on the levels of cTnI measured on admission (T0) and at 2 hours ± 30 minutes after admission (T2h) was first established in a cohort of 605 individuals and subsequently validated in an independent cohort of 592 individuals (from the validation cohort).

The algorithm is based on rule-out criteria for MI (cTnI concentration at T0 is less than 2 ng/L or cTnI concentrations at T0 and T2h are less than 6 ng/L) and rule-in criteria for MI (cTnI concentration at T0 is greater than or equal to 100 ng/L or the difference in cTnI concentration between T2h and T0 is greater than or equal to 10 ng/L).
The results obtained in the validation study are presented below:



* Δ = difference in concentration between T0 and T2h
** NPV = negative predictive value
*** PPV = positive predictive value
**** 95% Confidence Interval

This algorithm rules out the diagnosis of MI in 54.6% of patients with an NPV of 99.4%. Likewise, the diagnosis of MI is established for 15.8% of patients with a PPV of 74.5%. No conclusion can be made for the 29.6% of patients remaining in the observational zone.
The clinical context must also be considered in the interpretation of the results of this algorithm.

For risk stratification purposes

Use of the VIDAS® High sensitive Troponin I assay was evaluated within the scope of risk stratification of patients with symptoms suggestive of acute coronary syndrome (ACS) with respect to relative risk of all-cause mortality (ACM) and major adverse cardiac events (MACE) consisting of MI and revascularization, at 30 days.
A Kaplan-Meier analysis (Logrank test) and Cox regression (hazard ratio) were performed using the VIDAS® High sensitive Troponin I assay values obtained on admission (T0) and the clinical data for the events that occurred within 30 days for each patient. The assay values are those described in the section "**For diagnostic purposes**".
The analyses were evaluated using the 99th percentile defined on the global healthy population (19 ng/L) as the decision cut-off value.

The results obtained within the scope of these studies are presented in the following tables:

Risk stratification at 30 days: Logrank test

VIDAS® High sensitive Troponin I assay < Decision cut-off			VIDAS® High sensitive Troponin I assay ≥ Decision cut-off			Logrank test probability value**
Patients			Patients			
With MACE/ACM* event	Without MACE/ACM* event	Proportion with MACE/ACM* event	With MACE/ACM* event	Without MACE/ACM* event	Proportion with MACE/ACM* event	
36	512	6.6%	43	91	32.1%	< 0.0001

*ACM = All-Cause Mortality

** Probability Value < 0.05: the risk of occurrence of an MACE or ACM event within 30 days is not the same for a VIDAS® High sensitive Troponin I assay value above or below the decision cut-off value.

Risk stratification at 30 days: Hazard ratio

Number of patients	Hazard Ratio [95% CI*]	Hazard Ratio Probability Value**
682	1.35 [1.12 – 1.63]	0.0020

* CI = Confidence Interval
** Probability Value < 0.05: the risk of occurrence of an MACE or ACM event within 30 days is 35% higher if the VIDAS® High sensitive Troponin I assay value is above the decision cut-off value.

WASTE DISPOSAL

Dispose of used or unused reagents as well as any other contaminated disposable materials following procedures for infectious or potentially infectious products.
It is the responsibility of each laboratory to handle waste and effluents produced according to their nature and degree of hazardousness and to treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations.

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INDEX OF SYMBOLS

Symbol	Meaning
	Catalog number
	*In Vitro* Diagnostic Medical Device
	Manufacturer
	Temperature limit
	Use by date
	Batch code
	Consult Instructions for Use
	Contains sufficient for <n> tests
	Date of manufacture

REVISION HISTORY

Change type categories:

N/A	Not applicable (First publication)
Correction	Correction of documentation anomalies
Technical change	Addition, revision and/or removal of information related to the product
Administrative	Implementation of non-technical changes noticeable to the user
Note:	*Minor typographical, grammar, and formatting changes are not included in the revision history*

Release date	Part Number	Change Type	Change Summary
2015/10	9309099A	Administrative	FIRST PUBLICATION
		Technical change	FIRST PUBLICATION

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