VITROS Products Immunodiagnostic

# INSTRUCTIONS FOR USE hsTnI

## VITROS Immunodiagnostic Products hs Troponin I Reagent Pack

REF 684 4436

## VITROS Immunodiagnostic Products hs Troponin I Calibrators

REF 684 4437

## Intended Use

For *in vitro* diagnostic use only.

### VITROS Immunodiagnostic Products hs Troponin I Reagent Pack

For the quantitative measurement of cardiac troponin I (cTnI) in human serum and plasma (heparin) using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems.

Cardiac troponin I elevations are associated with myocardial damage, and in patients with acute coronary syndrome (ACS), troponin values are used to aid in the diagnosis of myocardial infarction (MI). The test is further indicated for risk stratification of mortality, myocardial infarction or coronary revascularization in patients with acute coronary syndrome.

### VITROS Immunodiagnostic Products hs Troponin I Calibrators

For use in the calibration of the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems for the quantitative measurement of cardiac troponin I in human serum and plasma (heparin).

## Summary and Explanation of the Test

Troponin I, troponin T, and troponin C are components of the contractile apparatus in cardiac and skeletal muscle. Troponin I (TnI) in conjunction with troponin T and troponin C, regulates the calcium dependent interaction of actin and myosin. [1]

**Specificity of cTnI for myocardium:** Two of the three isoforms of TnI identified are expressed in the skeletal muscle, while the third one is selectively expressed in the cardiac muscle (myocardium). [2, 3] This cardiac TnI isoform (cTnI) has an additional 31 amino acid residues at the N terminus, not found in skeletal troponin. [4] Consequently, increases in cTnI values have not been reported to occur following injury to non-cardiac tissues and are considered specific for myocardial damage. [5, 6] Other biomarkers, e.g. creatine kinase MB isoform (CKMB), are less sensitive and less specific. [7] The VITROS hs Troponin I (hsTnI) test uses monoclonal antibodies specifically directed against human cTnI.

**cTnI and Myocardial Injury:** Elevated cardiac troponin (cTn) values above the 99$^{th}$ percentile Upper Limit of Normal (URL) indicate the presence of myocardial injury, which can be acute, with dynamic changes in cTn levels, or chronic, with persistently elevated cTn levels. [5] Conditions resulting in acute or chronic myocardial injury and elevated cTnI levels include but are not limited to heart failure, myocarditis, cardiomyopathy, critical illness, cardiotoxic chemotherapy, pulmonary embolism, pulmonary hypertension, stroke, sepsis and chronic kidney disease. [5] These cardiac and systemic conditions should also be considered when interpreting results from any cTnI test method.

cTnI values provide important prognostic information about the short and long term risk of cardiovascular death. [8-11] The assessment of the prognosis can be useful in identifying patients most likely to benefit from specific therapeutic interventions.

**cTnI and Myocardial Infarction (MI):** An acute MI is defined by an acute myocardial injury associated with a rising and/or falling pattern of cTn values with at least one value above the 99$^{th}$ percentile URL in the clinical context of myocardial ischaemia (i.e. characteristic symptoms, ECG changes, imaging evidence). [5] Clinical studies have demonstrated that cTnI is detectable in the bloodstream 4-6 hours after an acute MI and remains elevated for several days thereafter. [12]

**Importance of cTnI Serial Measurement:** Guidelines state that serial cTnI measurement is needed to differentiate an acute MI from other conditions resulting in cTnI elevations. [5, 13] cTnI release depends on blood flow, therefore, patient to patient variability is expected in the time to peak value, the time when cTnI exceeds the 99$^{th}$ percentile, or when changing pattern of values can be observed. Around peak levels (late presenters) and on the downslope curve (very late presenters), the change in cTnI values might not be as significant as on the upslope (early presenters). [5]

**Algorithms incorporating cTnI to Rule-in or Rule-out MI** vary by region and clinical guidelines. However, they should be used in conjunction with all available clinical information (i.e. detailed assessment of chest pain, ECG, imaging). In patients presenting very early a second cardiac troponin level should be obtained later, due to the time dependency of troponin release; also, additional serial cardiac troponin testing should be pursued if the clinical suspicion remains high or whenever the patient develops recurrent chest pain. [13]

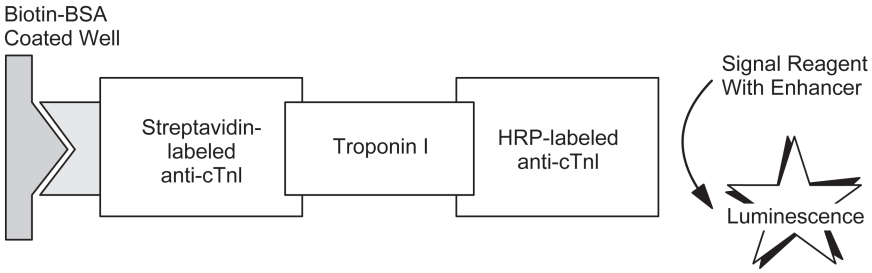
## Principles of the Procedure

An immunometric immunoassay technique is used. Cardiac troponin I present in the sample reacts simultaneously with streptavidin-conjugated antibody (mouse monoclonal anti-cTnI), bound by biotin-BSA on the wells, and a horseradish peroxidase (HRP)-labeled antibody conjugate (mouse monoclonal anti-cTnI). The antigen-antibody complex is captured by the antibody on the wells. Unbound materials are removed by washing. The bound HRP conjugate is measured by a luminescent reaction. [14] A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs its emission. The light signals are read by the system. The amount of HRP conjugate bound is directly proportional to the concentration of cardiac troponin I present.

| Test Type | System * | Incubation Time | Time to first result | Test Temperature | Reaction Sample Volume |
|---|---|---|---|---|---|
| Immunometric | ECi/ECiQ, 3600, 5600, XT 7600 | 8 minutes | 15 minutes | 37 °C | 60 µL |

* Not all products and systems are available in all countries.

### *Reaction Scheme*




## Warnings and Precautions

**WARNING:** ***Potentially Infectious Material***

***Human blood products provided as components of the VITROS hs Troponin I Calibrators have been obtained from donors who were tested individually and who were found to be negative for hepatitis B surface antigen, and for antibodies to human immunodeficiency virus (HIV 1+2) and hepatitis C virus (HCV), using approved methods (enzyme immunoassay). Treat as if capable of transmitting infection.***

***Use caution when handling material of human origin. Consider all samples potentially infectious. No test method can offer complete assurance that hepatitis B virus, HCV, HIV 1+2 or other infectious agents are absent. Handle, use, store and dispose of solid and liquid waste from samples and test components, in accordance with procedures defined by appropriate national biohazard safety guideline or regulation (e.g. CLSI document M29).*** [15]

**WARNING:** ***Contains ProClin 950 (CAS 2682-20-4)***

***The VITROS hs Troponin I assay reagent contains 1.0% ProClin 950. The VITROS hs Troponin I HRP conjugate reagent contains 0.5% ProClin 950. H315: Causes skin irritation. H317: May cause an allergic skin reaction. H319: Causes serious eye irritation. 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. P337 + P313: If eye irritation persists: Get medical advice/attention. P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P333 + P313: If skin***

*irritation or rash occurs: Get medical advice/attention. P363: Wash contaminated clothing before reuse.*

*Refer to www.orthoclinical.com for the Safety Data Sheets and for Ortho contact information.*

**WARNING**

# Reagents

## Reagent Pack Contents

1 reagent pack containing:

- 100 coated wells (biotin-BSA; streptavidin-mouse monoclonal anti-cTnI, 4 µg/mL).
- 8.2 mL assay reagent (buffer with horse serum, bovine gamma globulin, bovine serum albumin, and antimicrobial agent).
- 7.0 mL conjugate reagent (HRP-mouse monoclonal anti-cTnI, 5 µg/mL, in buffer with bovine serum albumin and antimicrobial agent).

## Reagent Pack Handling

- The reagent pack is supplied ready for use.
- The reagent pack contains homogeneous liquid reagents that do not require shaking or mixing prior to loading on the system.
- As with all immunoassay protein-based solutions, inappropriate handling of the reagent pack can cause foam to occur on the surface of the reagent. Avoid agitation, which may cause foaming or the formation of bubbles.
  - If reagent packs are dropped or agitated, small levels of fine foam could be generated that may not be detected by the system.
  - Reagent packs containing fine foam that is not detected by the system, may show a negative bias.
- If you must use a dropped or agitated reagent pack before it has been allowed to settle, you should verify performance by running high and low quality control samples in duplicate after loading the pack on the system.

## Reagent Pack Storage and Preparation

| Reagent | Storage Condition | | Stability |
|---|---|---|---|
| Unopened | Refrigerated | 2–8 °C (36–46 °F) | expiration date |
| Opened | On system | System turned on | ≤4 weeks |
| Opened | Refrigerated | 2–8 °C (36–46 °F) | ≤4 weeks |

- The VITROS hs Troponin I Reagent Pack is suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- Do not freeze unopened reagent packs.
- Load reagent packs directly from refrigerated storage to minimize condensation.
- Opened reagent packs are moisture/humidity sensitive. Store opened refrigerated reagent packs in a sealed VITROS Immunodiagnostic Products Reagent Pack Storage Box with desiccant.

## Calibrator Contents

- 1 set of VITROS hs Troponin I Calibrators 1, 2 and 3 (2 mL, human cTnI in human serum/buffer matrix containing EDTA with antimicrobial agents); nominal values 0; 40 and 27,000 ng/L (pg/mL)
- Lot calibration card
- Protocol card
- 24 calibrator bar code labels (8 for each calibrator)

## Calibrator Handling

- Use only with reagent packs of the same lot number. Mix thoroughly by inversion and bring to 15–30 °C (59–86 °F) before use. Each pack contains sufficient volume for a minimum of 8 determinations of each calibrator.

- Handle calibrators in stoppered containers to avoid contamination and evaporation. To avoid evaporation, limit the amount of time calibrators are on the system. Refer to the operating instructions for your system. Return to 2–8 °C (36–46 °F) as soon as possible after use, or load only sufficient volume for a single determination.

### Calibrator Storage and Preparation

| Calibrator | Storage Condition | | Stability |
|---|---|---|---|
| Unopened | Frozen | ≤-20 °C (-4 °F) | expiration date |
| Opened | Refrigerated | 2–8 °C (36–46 °F) | ≤2 Days |
| Opened | Frozen | ≤-20 °C (-4 °F) | ≤13 Weeks |

- VITROS hs Troponin I Calibrators are supplied frozen.
- VITROS hs Troponin I Calibrators are suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- Allow vials to stand upright at room temperature, for a minimum of 30 minutes to thaw. Thoroughly mix calibrators by inversion before use. Do not shake.
- Once thawed and opened calibrators may be stored at 2–8 °C (36–46 °F) for up to 2 days or frozen (with no more than 1 freeze-thaw cycle) for up to 13 weeks.
- The VITROS hs Troponin I test uses 60 µL of calibrator for each determination. Transfer an aliquot of each calibrator into a sample container (taking account of the minimum fill volume of the container), which may be bar coded with the labels provided. For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.

## Specimen Collection, Preparation and Storage

### Patient Preparation

No special patient preparation is necessary.

### Specimens Recommended

- Serum
- Plasma (Lithium Heparin)

### Specimens Not Recommended

- Do not use turbid specimens. Turbidity in specimens may affect test results.
- Do not use hemolysed samples as hemolysis may affect test results.

### Special Precautions

**IMPORTANT:** *Certain collection devices have been reported to affect other analytes and tests.* [16] *Owing to the variety of specimen collection devices available, Ortho Clinical Diagnostics is unable to provide a definitive statement on the performance of its products with these devices. Confirm that your collection devices are compatible with this test.*

### Specimen Collection and Preparation

- Collect specimens using standard procedures. [17]
- Follow the instructions provided with your collection device for use and processing of the sample. [18]
- Samples should be thoroughly separated from all cellular material. Failure to do so may lead to an erroneous result.
- Serum and plasma (lithium heparin) are the recommended sample types. **Serum and lithium heparin samples should not be used interchangeably when collecting serial samples from the same patient.**
- The VITROS hs Troponin I test uses 60 µL of sample for each determination. This does not take account of the minimum fill volume of the chosen sample container. For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.

### Handling and Storage Conditions

- Handle samples in stoppered containers to avoid contamination and evaporation.
- Follow procedures within your laboratory to avoid cross contamination of patient specimens.
- The amount of time samples are on the system prior to analysis should be limited to avoid evaporation. Refer to the operating instructions for your system.
- Return to 2–8 °C (36–46 °F) as soon as possible after use, or load sufficient volume for a single determination.

- Serum and plasma samples may be stored for up to 8 hours at room temperature 15–30 °C (59–86 °F). Serum and plasma samples may be stored for up to 2 days at 2–8 °C (36–46 °F). Thoroughly mix samples by inversion and bring to 15–30 °C (59–86 °F) before use.
- Samples that will not be tested within the time frames outlined above should be stored frozen at -20 °C (-4 °F). Serum and plasma samples tested initially and up to 13 weeks storage at -20 °C (-4 °F) showed no differences in clinical performance. Serum and plasma samples may be subjected to up to two freeze-thaw cycles.
- After thawing, frozen samples must be mixed thoroughly by inversion and centrifuged before performing the assay. After centrifuging transfer the supernatant to a sample cup or secondary tube for testing to avoid any precipitate.

# Testing Procedure

## Materials Provided

- VITROS Immunodiagnostic Products hs Troponin I Reagent Pack
- VITROS Immunodiagnostic Products hs Troponin I Calibrators

## Materials Required but Not Provided

- VITROS Immunodiagnostic Products Signal Reagent
- VITROS Immunodiagnostic Products Universal Wash Reagent
- VITROS Immunodiagnostic Products High Sample Diluent B
- VITROS Immunodiagnostic Products hs Troponin I Low Control
- VITROS Immunodiagnostic Products Reagent Pack Storage Box with desiccant
- Other quality control materials

## Operating Instructions

Check the inventory regularly to aid the management of reagents and ensure that sufficient VITROS Signal Reagent, VITROS Universal Wash Reagent and calibrated reagent lots are available for the work planned. When performing panels of tests on a single sample, ensure that the sample volume is sufficient for the tests ordered. Ensure sufficient VITROS High Sample Diluent B Reagent Pack is loaded onto the system before processing samples. Refer to the VITROS High Sample Diluent B Reagent Pack instructions for use.

For detailed information refer to the operating instructions for your system.

| | |
|---|---|
| **Note:** | Do not use visibly damaged product. |

## Sample Dilution

Samples with concentrations greater than the measuring range may be automatically diluted on the system up to 5-fold (1 part sample with 4 parts diluent) by the VITROS Immunodiagnostic and VITROS Integrated Systems with the VITROS Immunodiagnostic Products High Sample Diluent B Reagent Pack prior to testing. Refer to the VITROS High Sample Diluent B Reagent Pack Instructions for Use.

## Default Test Name

The default test name which will appear on patient reports is hs Troponin I. The default short name that will appear on the test selection menus and laboratory reports is hsTnI. These defaults may be reconfigured, if required. For detailed information refer to the operating instructions for your system.

# Calibration

## Calibration Procedure

- Calibration is lot specific; reagent packs and calibrators are linked by lot number. Reagent packs from the same lot may use the same calibration.
- A Master Calibration (a dose response curve covering the full calibration range) is established for each new reagent lot. Concentrations for the linked lot of calibrators are determined from the Master Calibration.
- Ensure that the Master Calibration for each new reagent lot is available on your system.
- Process calibrators in the same manner as samples. Calibration need not be programmed if bar code labels are used; load the calibrators in any order, calibration will be initiated automatically.
- When the calibrators are processed the signal expected for each calibrator is compared against the actual signal obtained. The Master Calibration is then rescaled to reflect the differences between the actual and expected signals. The validity of this calibration curve is assessed against a range of quality parameters, and if acceptable, it is stored for use with any reagent pack of that lot.

- The quality of calibration cannot be completely described by a single parameter. The calibration report should be used in conjunction with acceptable control values to determine the validity of the calibration.
- Recalibration is required after a pre-determined calibration interval, or when a different reagent lot is loaded.
- Calibration results are assessed against a range of quality parameters. Failure to meet any of the defined quality parameter ranges will be coded in the calibration report. For actions to be taken following a failed calibration refer to the operating instructions for your system.

Refer to the operating instructions for your system for detailed instructions on the calibration process.

### When to Calibrate

- Calibrate when the reagent pack and calibrator lot changes.
- Calibrate every 28 days.
- After specified service procedures have been performed.
- If quality control results are consistently outside of your acceptable range.

For additional information on when to calibrate, refer to the operating instructions for your system.

### Traceability of Calibration

Calibration of the VITROS hs Troponin I test is traceable to in-house reference calibrators, which have been value assigned to correlate to another commercially available test.

### Calibration Model

A modified four-parameter logistic curve fit function is used to construct the Master Calibration. The calibration process rescales the Master Calibration to establish a valid stored curve for the VITROS Immunodiagnostic System and VITROS Integrated Systems.

### Measuring (Reportable) Range

| VITROS System | Measuring (Reportable) Range |
|---|---|
| ECi/ECiQ, 3600, 5600, XT 7600 | 1.50–30,000 ng/L (1.50–30,000 pg/mL) |

## Quality Control

### Quality Control Material Selection

VITROS hs Troponin I Low Control and other controls containing suitable levels of cardiac troponin I are recommended for use with the VITROS Immunodiagnostic and VITROS Integrated Systems. The VITROS hs Troponin I Low Control contains 1 level troponin I (targeted near 99$^{th}$ percentile). The performance of commercial control fluids should be evaluated for compatibility with this test before they are used for quality control.

Control materials may show a difference when compared with other cardiac troponin I methods if they contain high concentrations of preservatives, stabilizers, or other nonphysiological additives, or otherwise depart from a true human sample matrix.

Appropriate quality control value ranges must be established for all quality control materials used with the VITROS hs Troponin I test.

### Quality Control Procedure Recommendations

- Good laboratory practice requires that controls be processed to verify the performance of the test.
- Choose control levels that check the clinically relevant concentrations.
- To verify system performance, analyze control materials:
  - After calibration
  - If the system is turned off for more than 2 hours
  - After reloading reagent packs that have been removed from the MicroWell Supply and stored for later use
  - According to local regulations or at least once each day that the test is being performed
  - After specified service procedures are performed

If quality control procedures within your laboratory require more frequent use of controls, follow those procedures.

- Analyze quality control materials in the same manner as patient specimens.
- If control results fall outside your acceptable range, investigate the cause before deciding whether to report patient results.
- Refer to published guidelines for general quality control recommendations. [19]

For more detailed information, refer to the operating instructions for your system.

### Quality Control Material Preparation and Storage

Refer to the manufacturer's product literature for preparation, storage, and stability information.

# Results

Results are automatically calculated by the VITROS Immunodiagnostic and VITROS Integrated Systems.

## Reporting Units and Unit Conversion

Analyte results are quoted in units of ng/L or pg/mL. To configure the units, refer to the operating instructions for your system.

| Conventional | Alternate |
|---|---|
| ng/L (pg/mL× 1) | pg/mL (ng/L × 1) |

# Limitations of the Procedure

## Known Interferences

The VITROS hs Troponin I test was evaluated for interference consistent with CLSI document EP07 [20]. Commonly encountered substances were tested on three lots of reagents. The following compounds, when tested, caused the bias shown at the concentrations indicated.

Refer to “Specificity” for a list of compounds tested that did not show interference.

| Interferent | Interferent Concentration | | Analyte Conc* ng/L | % Bias** |
|---|---|---|---|---|
| Acetylcysteine | 15.0 mg/dL | 920 µmol/L | 14.83 | 17.2 |
| | | | 348.4 | 11.7 |
| | 6.83 mg/dL | 419 µmol/L | 13.98 | 10.0 |
| | 9.95 mg/dL | 610 µmol/L | 326.8 | 10.0 |
| Bilirubin, unconjugated | 40 mg/dL | 684 µmol/L | 9.22 | -25.8 |
| | 10.4 mg/dL | 178 µmol/L | 9.53 | -10.0 |
| Cholesterol | 400 mg/dL | 10.3 mmol/L | 8.40 | -31.8 |
| | 315 mg/dL | 8.15 mmol/L | 9.43 | -10.0 |
| Dextran | 2400 mg/dL | 600 µmol/L | 18.27 | 89.5 |
| | | | 320.4 | 34.7 |
| | 433 mg/dL | 108 µmol/L | 13.39 | 10.0 |
| | 1332 mg/dL | 333 µmol/L | 351.4 | 10.0 |
| Fibrinogen | 1000 mg/dL | 29.4 µmol/L | 8.32 | -26.6 |
| | 490 mg/dL | 14.4 µmol/L | 9.13 | -10.0 |
| Hemoglobin | 1000 mg/dL | 10.0 g/L | 213.4 | -15.3 |
| | 608 mg/dL | 6.08 g/L | 259.6 | -10.0 |
| Sodium Azide | 100 mg/dL | 15,382 µmol/L | 9.78 | -19.1 |
| | 33.9 mg/dL | 5215 µmol/L | 11.43 | -10.0 |
| Streptokinase | 150,000 U/dL | | 8.56 | -34.0 |
| | | | 18.56 | -94.1 |
| | 11,111 U/dL | | 11.38 | -10.0 |
| | 4167 U/dL | | 226.4 | -10.0 |
| Total Protein | 15.0 g/dL | | 9.74 | -28.1 |
| | | | 274.2 | -16.2 |
| | 11.2 g/dL | | 8.93 | -10.0 |
| | 14.5 g/dL | | 249.9 | -10.0 |

* Average test concentration of replicate determinations using 3 different lots of reagent.

** Estimate of the maximum difference observed as a percentage.

**Note:** These results are representative. The degree of interference at concentrations other than those listed might not be predictable from these results. Other interfering substances may be encountered in the patient population.

### Other Limitations

- The VITROS hs Troponin I test has no high dose hook effect up to a concentration of 100,000 ng/L (100,000 pg/mL).
- Heterophilic antibodies in serum or plasma samples may cause interference in immunoassays.[21] These antibodies may be present in blood samples from individuals regularly exposed to animals or who have been treated with animal serum products. Results that are inconsistent with clinical observations indicate the need for additional testing.

## Expected Values and Interpretation of Results

The ESC/ACC/AHA/WHF Expert Consensus Document established that acute myocardial injury with clinical, ECG and/or imaging evidence of acute myocardial ischemia and rise and/or fall of cardiac troponin (cTn) with at least one value above the 99$^{th}$ percentile Upper Reference Limits (URLs) are criteria for defining acute myocardial infarction (AMI).[5]

### Expected Values:

It is recommended that each laboratory establish its own upper reference limits and confirm the validity of the diagnostic cutoff for the population it serves.

The VITROS hs Troponin I 99$^{th}$ percentile URLs were established from matched serum and lithium heparin plasma of nine hundred fifty-two (952) apparently healthy adults, including 486 female and 466 male subjects. The results included variation from reagent lots, systems, operators, and reagent age. The subjects ranged in age from 22 to 91 years old, with fifty-nine percent of the subjects ≥ 50 years of age.

Subjects were excluded if they met any of the following exclusion criteria:

- History of kidney disease, diabetes, heart disease, cancer, lung disease, thyroid disease, or stroke
- High blood pressure, cholesterol or triglycerides
- Muscle or skeletal injury or surgery in the last 3 months
- Current smoker
- Pregnancy
- Additional exclusion criteria:
  - Hemoglobin A1c ≥ 6.5%
  - NT-proBNP > 125 pg/mL for subjects < 75 years of age or > 450 pg/mL for subjects ≥ 75 years of age
  - eGFR < 60 mL/min

The overall observed 99$^{th}$ percentile URL from the 952 lithium heparin plasma samples is 11 ng/L (90% CI of 8.4–14.8 ng/L). The overall observed 99$^{th}$ percentile from the 952 serum samples is 11 ng/L (90% CI of 7.8–16.3 ng/L). The 99$^{th}$ percentile URL values and respective 90% Confidence Intervals (CI), determined for lithium heparin plasma (females, males, and overall) and serum (females, males, and overall) using the non-parametric statistical method, are shown in the table below.

| Sample Type | Gender | Number of Samples | 99$^{th}$ Percentile URL ng/L (pg/mL) | 90% CI* ng/L (pg/mL) |
|---|---|---|---|---|
| Lithium Heparin Plasma | Female | 486 | 9 | 4.8–19.0 |
| | Male | 466 | 13 | 9.7–22.9 |
| | Overall | 952 | 11 | 8.4–14.8 |
| Serum | Female | 486 | 9 | 4.4–21.4 |
| | Male | 466 | 12 | 8.8–23.7 |
| | Overall | 952 | 11 | 7.8–16.3 |

* CI = Confidence Interval

Alternate units: 1.00 ng/L = 1.00 pg/mL

For a troponin test to be labelled as high sensitivity it has to fulfil the two IFCC TF-CB established criteria[22]:

- The test should have analytical imprecision (% CV) at the 99$^{th}$ percentile ≤ 10% and
- The test should measure troponin concentrations above the Limit of Detection (LoD) in ≥ 50% of healthy subjects

The VITROS hs Troponin I test met these criteria. The 10% CV Limit of Quantitation (LoQ) was measured to be 1.99 ng/L (1.99 pg/mL). Greater than 50% of the healthy subjects used to establish the 99$^{th}$ percentile had cTnI results above the claimed LoDs on the VITROS Immunodiagnostic and VITROS Integrated Systems.

### Interpretation of Results:

Myocardial injury is defined by elevated cTn values above the 99$^{th}$ percentile and can occur in various cardiac and/or systemic conditions not associated with AMI. Conditions such as heart failure, myocarditis, structural heart disease, sepsis, kidney disease, pulmonary embolism, pulmonary hypertension, stroke, chemotherapeutic agents, critically ill patients, and strenuous exercise can result in acute or chronic myocardial injury. While in acute myocardial injury cTn levels are expected to rise and/or fall, in chronic myocardial injury such as structural heart disease and chronic kidney disease, the cTn levels are stable.

Due to the multitude of conditions associated with troponin elevations, serial measurements of cTn are recommended and detection of a rise and/or fall of cardiac troponin (cTn) values in the setting of acute myocardial ischemia is considered essential for AMI diagnosis. [5]

Results of this test should be used in conjunction with clinical presentation, other diagnostic tests, and in accordance with the appropriate clinical guidelines.

# Performance Characteristics

## Clinical Sensitivity and Specificity

A subset of serial serum samples obtained from the Advantageous Predictors of Acute Coronary Syndromes Evaluation (APACE) study, a well-characterized, ongoing prospective, international, multicenter sample collection in 12 sites in five European countries, was used in the clinical validation. See Trial Registration No: NCT00470587 at clinicaltrials.gov for more details. The enrolled subjects presented to the emergency department with symptoms of chest pain and angina pectoris. Peak symptoms had to have occurred within the last 12 hours. Subjects with kidney failure requiring dialysis were excluded. Information from subjects in the study was adjudicated by at least two independent cardiologists and a consensus diagnosis was obtained. Diagnosis of MI was conducted using the diagnostic criteria described in the ACC/ECS/AHA guidelines. [23, 24] Once the subjects were discharged they were contacted by telephone at 30 days, 6 months, and 12 months to determine major adverse cardiac events (cardiac-related mortality and myocardial infarction) and all-cause mortality.

The 1231 subjects in the study ranged in age from 18 years to 93 years (females 18-92 years, males 19-93 years). The population consisted of 420/1231 (34.12%) females and 811/1231 (65.88%) males. A final adjudicated diagnosis of MI was assigned to 158/1231 (12.84%) subjects and a final adjudicated diagnosis of no MI was assigned to 1073/1231 (87.16%) subjects. Of the 158 MI subjects, 41 (25.95%) were female and 117 (74.05%) were male, and of the 1073 no MI subjects, 379 (35.32%) were female and 694 (64.68%) were male. The prevalence of MI in females was 9.76% (41/420) and in males was 14.43% (117/811).

Serial serum samples were tested and analyzed for each time point within and across gender. Receiver Operating Characteristic (ROC) curves [25] were generated. The diagnostic accuracy measurements of the VITROS hs Troponin I test, as quantified by areas under the ROC curves (AUC), [26] for each time point within and across gender ranged from 0.94 to 0.97.

The clinical performance [clinical sensitivity, clinical specificity, negative predictive value (NPV), positive predictive value (PPV), negative likelihood ratio (LR-) and positive likelihood ratio (LR+)] and the two-tailed 95% exact confidence intervals (CI) of the VITROS hs Troponin I test versus adjudicated diagnosis was determined using the overall and gender-specific 99$^{th}$ percentile cutoffs and are summarized in the following tables:

**All Subjects using 11 ng/L Cutoff (Overall 99$^{th}$ Percentile - Serum)**

| Time Point | N | Sensitivity (%) (n/N) | 95% CI (%) | Specificity (%) (n/N) | 95% CI (%) | NPV (%) (n/N) | 95% CI (%) | PPV (%) (n/N) | 95% CI (%) |
|---|---|---|---|---|---|---|---|---|---|
| Baseline | 1231 | 81.65 (129/158) | 74.72–87.35 | 91.99 (987/1073) | 90.20–93.54 | 97.15 (987/1016) | 95.93–98.08 | 60.00 (129/215) | 53.12–66.60 |
| 1 hour | 1039 | 93.75 (120/128) | 88.06–97.26 | 90.67 (826/911) | 88.59–92.48 | 99.04 (826/834) | 98.12–99.58 | 58.54 (120/205) | 51.47–65.36 |
| 2 hours | 869 | 95.79 (91/95) | 89.57–98.84 | 89.53 (693/774) | 87.16–91.60 | 99.43 (693/697) | 98.54–99.84 | 52.91 (91/172) | 45.16–60.55 |
| 3 hours | 442 | 94.44 (51/54) | 84.61–98.84 | 87.63 (340/388) | 83.93–90.74 | 99.13 (340/343) | 97.47–99.82 | 51.52 (51/99) | 41.25–61.68 |

| Time Point | N | LR- | 95% CI | LR+ | 95% CI |
|---|---|---|---|---|---|
| Baseline | 1231 | 0.20 | 0.14–0.28 | 10.19 | 8.21–12.64 |
| 1 hour | 1039 | 0.07 | 0.04–0.13 | 10.05 | 8.17–12.36 |
| 2 hours | 869 | 0.05 | 0.02–0.12 | 9.15 | 7.42–11.30 |
| 3 hours | 442 | 0.06 | 0.02–0.19 | 7.63 | 5.81–10.03 |

### All Subjects using 9 ng/L Cutoff for Females and 12 ng/L for Males (Gender-Specific 99th Percentiles - Serum)

| Time Point | N | Sensitivity (%) (n/N) | 95% CI (%) | Specificity (%) (n/N) | 95% CI (%) | NPV (%) (n/N) | 95% CI (%) | PPV (%) (n/N) | 95% CI (%) |
|---|---|---|---|---|---|---|---|---|---|
| Baseline | 1231 | 82.28 (130/158) | 75.42–87.89 | 91.71 (984/1073) | 89.89–93.29 | 97.23 (984/1012) | 96.03–98.15 | 59.36 (130/219) | 52.54–65.93 |
| 1 hour | 1039 | 93.75 (120/128) | 88.06–97.26 | 90.67 (826/911) | 88.59–92.48 | 99.04 (826/834) | 98.12–99.58 | 58.54 (120/205) | 51.47–65.36 |
| 2 hours | 869 | 93.68 (89/95) | 86.76–97.65 | 89.66 (694/774) | 87.30–91.72 | 99.14 (694/700) | 98.14–99.68 | 52.66 (89/169) | 44.85–60.38 |
| 3 hours | 442 | 92.59 (50/54) | 82.11–97.94 | 87.89 (341/388) | 84.22–90.96 | 98.84 (341/345) | 97.06–99.68 | 51.55 (50/97) | 41.18–61.82 |

| Time Point | N | LR- | 95% CI | LR+ | 95% CI |
|---|---|---|---|---|---|
| Baseline | 1231 | 0.19 | 0.14–0.27 | 9.92 | 8.03–12.26 |
| 1 hour | 1039 | 0.07 | 0.04–0.13 | 10.05 | 8.17–12.36 |
| 2 hours | 869 | 0.07 | 0.03–0.15 | 9.06 | 7.32–11.23 |
| 3 hours | 442 | 0.08 | 0.03–0.22 | 7.64 | 5.79–10.10 |

### Females using 9 ng/L Cutoff (Female 99th Percentile Cutoff-Serum)

| Time Point | N | Sensitivity (%) (n/N) | 95% CI (%) | Specificity (%) (n/N) | 95% CI (%) | NPV (%) (n/N) | 95% CI (%) | PPV (%) (n/N) | 95% CI (%) |
|---|---|---|---|---|---|---|---|---|---|
| Baseline | 420 | 85.37 (35/41) | 70.83–94.43 | 92.88 (352/379) | 89.80–95.25 | 98.32 (352/358) | 96.39–99.38 | 56.45 (35/62) | 43.26–69.01 |
| 1 hour | 346 | 94.12 (32/34) | 80.32–99.28 | 91.99 (287/312) | 88.40–94.75 | 99.31 (287/289) | 97.52–99.92 | 56.14 (32/57) | 42.36–69.26 |
| 2 hours | 291 | 91.67 (22/24) | 73.00–98.97 | 91.01 (243/267) | 86.92–94.16 | 99.18 (243/245) | 97.08–99.90 | 47.83 (22/46) | 32.89–63.05 |
| 3 hours | 133 | 92.86 (13/14) | 66.13–99.82 | 88.24 (105/119) | 81.05–93.42 | 99.06 (105/106) | 94.86–99.98 | 48.15 (13/27) | 28.67–68.05 |

| Time Point | N | LR- | 95% CI | LR+ | 95% CI |
|---|---|---|---|---|---|
| Baseline | 420 | 0.16 | 0.08–0.33 | 11.98 | 8.15–17.61 |
| 1 hour | 346 | 0.06 | 0.02–0.25 | 11.75 | 7.99–17.27 |
| 2 hours | 291 | 0.09 | 0.02–0.35 | 10.20 | 6.83–15.22 |
| 3 hours | 133 | 0.08 | 0.01–0.54 | 7.89 | 4.73–13.18 |

### Males using 12 ng/L Cutoff (Male 99th Percentile Cutoff-Serum)

| Time Point | N | Sensitivity (%) (n/N) | 95% CI (%) | Specificity (%) (n/N) | 95% CI (%) | NPV (%) (n/N) | 95% CI (%) | PPV (%) (n/N) | 95% CI (%) |
|---|---|---|---|---|---|---|---|---|---|
| Baseline | 811 | 81.20 (95/117) | 72.93–87.82 | 91.07 (632/694) | 88.69–93.08 | 96.64 (632/654) | 94.95–97.88 | 60.51 (95/157) | 52.41–68.21 |
| 1 hour | 693 | 93.62 (88/94) | 86.62–97.62 | 89.98 (539/599) | 87.29–92.27 | 98.90 (539/545) | 97.62–99.59 | 59.46 (88/148) | 51.09–67.44 |
| 2 hours | 578 | 94.37 (67/71) | 86.20–98.44 | 88.95 (451/507) | 85.90–91.55 | 99.12 (451/455) | 97.76–99.76 | 54.47 (67/123) | 45.25–63.47 |
| 3 hours | 309 | 92.50 (37/40) | 79.61–98.43 | 87.73 (236/269) | 83.20–91.40 | 98.74 (236/239) | 96.38–99.74 | 52.86 (37/70) | 40.55–64.91 |

| Time Point | N | LR- | 95% CI | LR+ | 95% CI |
|---|---|---|---|---|---|
| Baseline | 811 | 0.21 | 0.14–0.30 | 9.09 | 7.06–11.71 |
| 1 hour | 693 | 0.07 | 0.03–0.15 | 9.35 | 7.31–11.95 |
| 2 hours | 578 | 0.06 | 0.02–0.16 | 8.54 | 6.63–11.01 |
| 3 hours | 309 | 0.09 | 0.03–0.25 | 7.54 | 5.41–10.50 |

The cutoffs and clinical performance information above should only be used as a guide. It is recommended that each laboratory establish its own upper reference limits and confirm the validity of the diagnostic cutoff for the population it serves.

Results of this test should be used in conjunction with clinical presentation, other diagnostic tests, and in accordance with the appropriate clinical guidelines.

## Risk Stratification

The VITROS hs Troponin I test was evaluated for its prognostic value as an aid in the assessment of cardiac-related mortality/MI and all-cause mortality over 30 days (d), 6 months (m) and 12 months. Of the 1231 subjects enrolled in the study, 1226 were followed up. The cumulative event free rates (CEFR) (Kaplan-Meier analysis) over 30 days, 6 months and 12 months for subjects classified according to the overall and gender-specific 99$^{th}$ percentile cutoffs are summarized in the following tables:

### Prognosis for Cardiac-Related Mortality and MI

| VITROS hs Troponin I Test | Follow up period | ≤ Cutoff | | | | > Cutoff | | | | Log Rank p-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Subjects at Risk (N) | Events (N) | Censored (N) | CEFR (%) | Subjects at Risk (N) | Events (N) | Censored (N) | CEFR (%) | |
| Overall 99$^{th}$ Percentile 11 ng/L | 30 d | 966 | 3 | 963 | 99.69 | 260 | 5 | 255 | 98.08 | 0.0041 |
| | 6 m | 966 | 9 | 957 | 99.07 | 260 | 11 | 249 | 95.77 | 0.0002 |
| | 12 m | 966 | 14 | 952 | 98.55 | 260 | 14 | 246 | 94.62 | 0.0002 |
| Gender-Specific 99$^{th}$ Percentile 9 ng/L female 12 ng/L male | 30 d | 968 | 4 | 964 | 99.59 | 258 | 4 | 254 | 98.45 | 0.0439 |
| | 6 m | 968 | 10 | 958 | 98.97 | 258 | 10 | 248 | 96.12 | 0.0014 |
| | 12 m | 968 | 15 | 953 | 98.45 | 258 | 13 | 245 | 94.96 | 0.0010 |

### Prognosis for All-Cause Mortality

| VITROS hs Troponin I Test | Follow up period | ≤ Cutoff | | | | > Cutoff | | | | Log Rank p-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Subjects at Risk (N) | Deaths (N) | Censored (N) | CEFR (%) | Subjects at Risk (N) | Deaths (N) | Censored (N) | CEFR (%) | |
| Overall 99$^{th}$ Percentile 11 ng/L | 30 d | 966 | 1 | 965 | 99.90 | 260 | 4 | 256 | 98.46 | 0.0013 |
| | 6 m | 966 | 9 | 957 | 99.07 | 260 | 8 | 252 | 96.92 | 0.0083 |
| | 12 m | 966 | 15 | 951 | 98.45 | 260 | 12 | 248 | 95.38 | 0.0030 |
| Gender-Specific 99$^{th}$ Percentile 9 ng/L female 12 ng/L male | 30 d | 968 | 1 | 967 | 99.90 | 258 | 4 | 254 | 98.45 | 0.0012 |
| | 6 m | 968 | 9 | 959 | 99.07 | 258 | 8 | 250 | 96.90 | 0.0079 |
| | 12 m | 968 | 14 | 954 | 98.55 | 258 | 13 | 245 | 94.96 | 0.0006 |

The cohort of subjects with at least one VITROS hs Troponin I test value above the overall and gender-specific cutoffs had significantly lower cumulative event free rates for cardiac-related mortality/MI and all-cause mortality at 30 days, 6 months and 12 months than the cohort of subjects with all VITROS hs Troponin I test values less than or equal to the overall and gender-specific cutoffs.

Results of this test should be used in conjunction with clinical presentation, other diagnostic tests, and in accordance with the appropriate clinical guidelines.

## Limit of Detection

The Limit of Detection (LoD) for the VITROS hs Troponin I test was designed to be < 3.00 ng/L in accordance with CLSI document EP17 [27]. The LoD for the VITROS hs Troponin I test is between 0.39 and 0.86 ng/L, based on 500 determinations with five low-level samples. The Limit of Blank (LoB) is between 0.14 and 0.51 ng/L, based on 400 determinations of four blank samples. Representative performance data are shown below.

### Limit of Blank and Limit of Detection

| System | LoB | | LoD | |
|---|---|---|---|---|
| | ng/L | pg/mL | ng/L | pg/mL |
| ECi/ECiQ | 0.51 | 0.51 | 0.86 | 0.86 |
| 3600 | 0.19 | 0.19 | 0.39 | 0.39 |
| 5600 | 0.23 | 0.23 | 0.43 | 0.43 |
| XT 7600 | 0.14 | 0.14 | 0.42 | 0.42 |

## Limit of Quantitation

The Limit of Quantitation (LoQ) for the VITROS hs Troponin I test is 1.23 ng/L, as determined based on CLSI document EP17 [27], from 75 determinations with five LoQ pools and a precision goal of 20% CV. The LoQ was determined to be the lowest concentration at which precision and accuracy design requirements are still met and within the linear range of the test for the VITROS ECi/ECiQ and 3600 Immunodiagnostic Systems and the VITROS 5600 and XT 7600 Integrated Systems.

### Limit of Quantitation

| LoQ (20% CV) | |
|---|---|
| ng/L | pg/mL |
| 1.23 | 1.23 |

## Accuracy

Accuracy was evaluated consistent with CLSI document EP09. [28] The table shows the results of endogenous serum samples analyzed on the VITROS ECi/ECiQ Immunodiagnostic System compared with those analyzed using the VITROS 3600 Immunodiagnostic System, the VITROS 5600 Integrated System, and the VITROS XT 7600 Integrated System. The relationship between the VITROS systems was determined by Weighted Deming regression and Pearson correlation.

| VITROS System | n | Slope | Correlation Coefficient | Conventional Units (ng/L)* | |
|---|---|---|---|---|---|
| | | | | Range of Samples | Intercept |
| 3600 vs. ECi/ECiQ | 112 | 1.01 | 1.00 | 1.20–26340 | -0.09 |
| 5600 vs. ECi/ECiQ | 112 | 0.99 | 1.00 | 1.20–26340 | -0.17 |
| XT 7600 vs. ECi/ECiQ | 112 | 1.03 | 1.00 | 1.11–26890 | -0.24 |
| 5600 vs. 3600 | 112 | 0.98 | 1.00 | 1.20–26170 | -0.08 |
| XT 7600 vs. 3600 | 112 | 1.02 | 1.00 | 1.11–26890 | -0.15 |
| XT 7600 vs. 5600 | 112 | 1.04 | 1.00 | 1.11–26890 | -0.07 |

* Alternate units: 1.00 ng/L = 1.00 pg/mL

## Precision

Precision was evaluated consistent with CLSI document EP05. [29] Two replicates each of eight patient pools (four human serum and four human plasma) and two controls were tested on two separate occasions per day on at least 20 different test days. The experiment was performed using three reagent lots on one VITROS ECi/ECiQ Immunodiagnostic System, one VITROS 3600 Immunodiagnostic System, one VITROS 5600 Integrated System, and one VITROS XT 7600 Integrated System. The test was designed to have within-laboratory precision of ≤ 20% at or near the LoQ, ≤ 10% at the 99$^{th}$ percentile, and < 7% between the 99$^{th}$ percentile and 30,000 ng/L. Representative performance data are shown below.

| VITROS System | Conc. Units - ng/L | | | | | | | No. Observ. | No. Days |
|---|---|---|---|---|---|---|---|---|---|
| | Mean hs Troponin I Conc. | Within-run* | | Within-calibration** | | Within-lab*** | | | |
| | | SD | CV (%) | SD | CV (%) | SD | CV (%) | | |
| ECi/ECiQ | 2.97 | 0.217 | 7.1 | 0.286 | 9.4 | 0.403 | 13.9 | 80 | 20 |
| | 10.75 | 0.359 | 3.3 | 0.612 | 5.6 | 0.785 | 7.4 | 80 | 20 |
| | 63.22 | 1.299 | 2.1 | 2.768 | 4.4 | 3.074 | 4.9 | 80 | 20 |
| | 303.7 | 5.73 | 1.9 | 8.57 | 2.8 | 8.82 | 2.9 | 80 | 20 |
| | 12000 | 316.1 | 2.7 | 454.7 | 3.9 | 540.7 | 4.4 | 80 | 20 |
| | 16380 | 461.3 | 2.9 | 794.7 | 5.0 | 854.5 | 5.0 | 80 | 20 |
| | 2.19 | 0.202 | 9.0 | 0.284 | 12.7 | 0.382 | 17.9 | 80 | 20 |
| | 6.68 | 0.276 | 4.1 | 0.487 | 7.2 | 0.612 | 9.3 | 80 | 20 |
| | 56.86 | 1.759 | 3.1 | 2.739 | 4.8 | 2.951 | 5.2 | 80 | 20 |
| | 298.0 | 6.71 | 2.3 | 10.62 | 3.6 | 11.25 | 3.7 | 80 | 20 |

| VITROS System | Conc. Units - ng/L | | | | | | | No. Observ. | No. Days |
|---|---|---|---|---|---|---|---|---|---|
| | Mean hs Troponin I Conc. | Within-run* | | Within-calibration** | | Within-lab*** | | | |
| | | SD | CV (%) | SD | CV (%) | SD | CV (%) | | |
| 3600 | 2.53 | 0.055 | 2.3 | 0.167 | 6.9 | 0.258 | 9.8 | 80 | 20 |
| | 10.24 | 0.239 | 2.4 | 0.528 | 5.3 | 0.702 | 6.7 | 80 | 20 |
| | 67.55 | 0.779 | 1.2 | 2.558 | 3.8 | 3.097 | 4.5 | 80 | 20 |
| | 325.5 | 4.28 | 1.3 | 10.02 | 3.1 | 12.79 | 3.9 | 80 | 20 |
| | 14220 | 407.8 | 2.9 | 548.7 | 3.9 | 659.6 | 4.6 | 80 | 20 |
| | 18860 | 343.5 | 1.8 | 794.4 | 4.2 | 992.0 | 5.3 | 80 | 20 |
| | 1.84 | 0.064 | 3.7 | 0.116 | 6.6 | 0.192 | 9.9 | 80 | 20 |
| | 5.59 | 0.092 | 1.7 | 0.317 | 5.8 | 0.436 | 7.6 | 80 | 20 |
| | 65.60 | 0.810 | 1.3 | 2.518 | 3.9 | 3.300 | 5.0 | 80 | 20 |
| | 323.2 | 6.15 | 1.9 | 12.9 | 4.0 | 15.56 | 4.8 | 80 | 20 |
| 5600 | 2.44 | 0.076 | 3.3 | 0.152 | 6.6 | 0.229 | 8.9 | 80 | 20 |
| | 10.13 | 0.191 | 2.0 | 0.395 | 4.1 | 0.640 | 6.1 | 80 | 20 |
| | 66.46 | 1.142 | 1.8 | 2.625 | 4.0 | 3.051 | 4.5 | 80 | 20 |
| | 308.5 | 4.72 | 1.6 | 9.00 | 3.0 | 9.02 | 2.9 | 80 | 20 |
| | 14090 | 262.7 | 1.9 | 415.8 | 3.0 | 764.8 | 5.4 | 80 | 20 |
| | 18460 | 236.3 | 1.3 | 565.0 | 3.1 | 544.8 | 2.9 | 80 | 20 |
| | 1.71 | 0.119 | 7.4 | 0.151 | 9.4 | 0.206 | 11.3 | 80 | 20 |
| | 5.48 | 0.141 | 2.7 | 0.254 | 4.9 | 0.422 | 7.4 | 80 | 20 |
| | 65.27 | 1.143 | 1.8 | 1.907 | 3.0 | 2.602 | 3.9 | 80 | 20 |
| | 309.2 | 3.42 | 1.1 | 9.15 | 3.0 | 9.56 | 3.0 | 80 | 20 |
| XT 7600 | 2.55 | 0.070 | 2.9 | 0.125 | 5.2 | 0.248 | 9.3 | 80 | 20 |
| | 10.30 | 0.271 | 2.8 | 0.464 | 4.7 | 0.920 | 8.5 | 80 | 20 |
| | 66.92 | 1.267 | 2.0 | 2.567 | 4.0 | 4.306 | 6.2 | 80 | 20 |
| | 310.2 | 4.02 | 1.3 | 10.60 | 3.5 | 14.59 | 4.6 | 80 | 20 |
| | 13750 | 260.8 | 1.9 | 552.7 | 4.1 | 616.8 | 4.4 | 80 | 20 |
| | 18360 | 461.1 | 2.5 | 776.2 | 4.3 | 844.6 | 4.5 | 80 | 20 |
| | 1.82 | 0.090 | 5.2 | 0.119 | 6.9 | 0.174 | 9.1 | 80 | 20 |
| | 5.57 | 0.114 | 2.2 | 0.267 | 5.1 | 0.531 | 9.1 | 80 | 20 |
| | 65.50 | 0.914 | 1.4 | 2.407 | 3.8 | 4.064 | 6.0 | 80 | 20 |
| | 307.7 | 3.97 | 1.3 | 10.60 | 3.5 | 14.71 | 4.7 | 80 | 20 |

* Within-run (repeatability). Between Duplicate precision averaged over all runs

** Within-calibration. Total precision with weighted components of within-run, between-run, and between-day variation.

*** Within-lab. A measure of the effect of recalibration on total precision, calculated within reagent lot, using data from at least 5 calibrations

## Specificity

### *Substances that Do Not Interfere*

The VITROS hs Troponin I test was evaluated for interference consistent with CLSI document EP07 [20]. Of the compounds tested, none was found to cause a bias of >10% with the test at the concentrations indicated at nominal troponin I concentrations of 10.00 ng/L and 300.0 ng/L.

| Compound | Concentration | |
|---|---|---|
| Acetaminophen | 156 µg/mL | 1030 µmol/L |
| Adrenaline (epinephrine) | 20 µg/dL | 1.09 µmol/L |
| Allopurinol | 6.0 mg/dL | 441 µmol/L |
| Alprazolam | 0.0258 mg/dL | 0.835 µmol/L |
| Ambroxol | 63 µg/dL | 1.52 µmol/L |
| Amlodipine besylate | 0.0104 mg/dL | 0.183 µmol/L |
| Amoxicillin | 5.40 mg/dL | 148 µmol/L |
| Ascorbic acid | 5.25 mg/dL | 298 µmol/L |
| Atorvastatin calcium | 0.162 mg/dL | 1.34 µmol/L |
| Benazepril HCl | 0.044 mg/dL | 0.954 µmol/L |

| Compound | Concentration | |
|---|---|---|
| Bilirubin, conjugated | 40 mg/dL | 475 µmol/L |
| Biotin | 3510 ng/mL | 14,300 nmol/L |
| Bivalirudin | 2.18 mg/dL | 10.0 µmol/L |
| Caffeine | 10.8 mg/dL | 556 µmol/L |
| Carvedilol | 43.2 µg/dL | 1.06 µmol/L |
| Cefoxitin sodium | 697 mg/dL | 15,500 µmol/L |
| Ceftriaxone disodium hemi (heptahydrate) | 100 mg/dL | 1510 µmol/L |
| Cephalexin sodium | 13.4 mg/dL | 363 µmol/L |
| Cinnarizine | 108 µg/dL | 2.93 µmol/L |
| Clopidogrel | 2.4 µg/dL | 0.057 µmol/L |
| Cocaine | 0.6 mg/dL | 17.7 µmol/L |
| Cotinine | 0.24 mg/dL | 4.89 µmol/L |
| Cyclosporin A | 0.18 mg/dL | 1.50 µmol/L |
| Digoxin | 0.0039 mg/dL | 0.0499 µmol/L |
| Diphenhydramine | 0.0774 mg/dL | 3.03 µmol/L |
| Dopamine | 0.0621 mg/dL | 4.06 µmol/L |
| Enalaprilat | 0.0819 mg/dL | 2.35 µmol/L |
| Enoxaparin (LMWH) | 360 U/dL | N/A |
| Eptifibatide | 1.44 mg/dL | 17.3 µmol/L |
| Erythromycin | 13.8 mg/dL | 188 µmol/L |
| Ethanol | 600 mg/dL | 130,000 µmol/L |
| Fondaparinux | 0.39 mg/dL | 2.26 µmol/L |
| Furosemide | 1.59 mg/dL | 48.1 µmol/L |
| HAMA (human anti-mouse antibodies) | 800 µg/L | 0.005 µmol/L |
| Heparin (Sodium), UFH | 330 U/dL | N/A |
| Ibuprofen | 21.9 mg/dL | 1060 µmol/L |
| Insulin | 3.12 µg/dL | 0.005 µmol/L |
| L-dopa (Levodopa) | 0.75 mg/dL | 38.0 µmol/L |
| Levothyroxine | 0.0429 mg/dL | 0.552 µmol/L |
| Lidocaine | 1.5 mg/dL | 64.0 µmol/L |
| Methylprednisolone | 0.783 mg/dL | 20.9 µmol/L |
| Metronidazole | 12.3 mg/dL | 719 µmol/L |
| Naproxen sodium | 39.3 mg/dL | 1560 µmol/L |
| Nifedipine | 0.0588 mg/dL | 1.70 µmol/L |
| Nitrofurantoin | 0.213 mg/dL | 8.94 µmol/L |
| Nitroglycerin (Nitrostat) | 1.2 µg/dL | 0.053 µmol/L |
| Omeprazole | 0.84 mg/dL | 24.3 µmol/L |
| Oxycodone | 0.0324 mg/dL | 1.03 µmol/L |
| Oxytetracycline | 1.2 mg/dL | 24.2 µmol/L |
| Phenytoin | 6.0 mg/dL | 238 µmol/L |
| Propranolol HCl | 0.115 mg/dL | 3.88 µmol/L |
| Pseudoephedrine | 0.330 mg/dL | 20.0 µmol/L |
| Quinidine | 1.5 mg/dL | 46.2 µmol/L |
| Rheumatoid Factor | 900 IU/mL | N/A |
| Rifampicin (Rifampin) | 4.8 mg/dL | 58.3 µmol/L |
| Rivaroxaban | 0.270 mg/dL | 6.19 µmol/L |
| Salicylic acid | 2.86 mg/dL | 207 µmol/L |
| Spironolactone | 0.0555 mg/dL | 1.33 µmol/L |
| Theophylline | 6.0 mg/dL | 333 µmol/L |
| TPA (Alteplase) | 1.2 mg/dL | 0.171 µmol/L |

| Compound | Concentration | |
|---|---|---|
| Triglyceride | 1500 mg/dL | 16.9 mmol/L |
| Vancomycin hydrochloride | 12.3 mg/dL | 82.8 µmol/L |
| Verapamil | 0.16 mg/dL | 3.51 µmol/L |
| Vorapaxar | 36 µg/dL | 0.731 µmol/L |
| Warfarin sodium | 8.0 mg/dL | 259 µmol/L |

### *Cross-Reactivity*

The cross-reactivity of the VITROS hs Troponin I test was evaluated by adding the following substances to one human serum sample pool containing no Troponin I.

| Cross-Reactant | Cross Reactant Concentration | | Mean Result of Control Pool | Mean Result of Cross-Reactant Pool | % Cross-Reactivity |
|---|---|---|---|---|---|
| | ng/mL | ng/L | ng/L | ng/L | |
| Actin (from Rabbit Muscle) | 100 | 100,000 | * | * | * |
| Cardiac Troponin C (Recombinant) | 100 | 100,000 | * | * | * |
| Cardiac Troponin T (Recombinant) | 100 | 100,000 | * | * | * |
| CK-MB (Recombinant) | 100 | 100,000 | * | * | * |
| Myoglobin (Recombinant) | 1000 | 1000,000 | * | * | * |
| Myosin (Recombinant) | 100 | 100,000 | * | * | * |
| Skeletal Troponin I | 100 | 100,000 | * | * | * |
| Tropomyosin (from porcine muscle) | 200 | 200,000 | * | * | * |

* Not Detectable. Concentration was below the measuring range of the test, 1.50–30,000 ng/L.

The cross-reactivity of the VITROS hs Troponin I test was evaluated by adding the following substances to one human serum sample pool containing Troponin I at a concentration of 10.00 ng/L.

| Cross-Reactant | Cross Reactant Concentration | | Mean Result of Control Pool | Mean Result of Cross-Reactant Pool | % Cross-Reactivity |
|---|---|---|---|---|---|
| | ng/mL | ng/L | ng/L | ng/L | |
| Actin (from Rabbit Muscle) | 100 | 100,000 | 16.98 | 12.23 | 0.0 |
| Cardiac Troponin C (Recombinant) | 100 | 100,000 | 16.98 | 13.57 | 0.0 |
| Cardiac Troponin T (Recombinant) | 100 | 100,000 | 16.98 | 12.16 | 0.0 |
| CK-MB (Recombinant) | 100 | 100,000 | 16.98 | 16.94 | 0.0 |
| Myoglobin (Recombinant) | 1000 | 1000,000 | 16.98 | 17.07 | 0.0 |
| Myosin (Recombinant) | 100 | 100,000 | 16.98 | 12.59 | 0.0 |
| Skeletal Troponin I | 100 | 100,000 | 16.98 | 12.66 | 0.0 |
| Tropomyosin (from porcine muscle) | 200 | 200,000 | 16.98 | 16.78 | 0.0 |

Cross-reactivity was expressed as the mean result obtained for the cross-reactant pool minus the mean result obtained for the control sample divided by the cross-reactant concentration in percentage term.

$$\% \text{ Cross-reactivity} = \frac{(\text{Mean Troponin I Result Cross-reactant Pool}) - (\text{Mean Troponin I Result Control Sample})}{\text{Concentration of Cross-reactant}} \times 100$$

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## Glossary of Symbols

The following symbols may have been used in the labeling of this product.

| | | |
|---|---|---|
| Do Not Reuse | Upper Limit of Temperature | Range |
| Use by or Expiration Date (Year-Month-Day) | Lower Limit of Temperature | Range of Means |
| LOT Batch Code or Lot Number | Temperature Limitation | Midpoint |
| SN Serial Number | Consult Instructions for Use | Revised |
| REF Catalog Number or Product Code | Attention: The Instructions for Use (IFU) has been updated | Supersedes |
| Caution | S1 For use in Slide Supply 1 | Σ Contains Sufficient for "n" Tests |
| Keep Dry (Protect from Moisture/Humidity) | S2 For use in Slide Supply 2 | IVD *in vitro* Diagnostic Medical Device |
| Manufacturer | SI SI Units | Der Grüne Punkt (the Green Dot). Manufacturer follows certain packaging material waste disposal management regulations |
| Date of Manufacture | CONV Conventional Units | σ Estimated within-lab SD |
| EC REP Authorized Representative in the European Community | Value | |
| Corrosive | Flammable | Serious Health Hazards |
| Health Hazards | Acute Toxicity | Environmental or Aquatic Toxicity |

## Revision History

| Date of Revision | Version | Description of Technical Changes* |
|---|---|---|
| 2020-04-22 | 3.0 | Calibrator Storage and Preparation: changed -20 °C to ≤-20 °C |

The change bars indicate the position of a technical amendment to the text with respect to the previous version of the document.

When this Instructions For Use is replaced, sign and date below and retain as specified by local regulations or laboratory policies, as appropriate.

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Obsolete Date

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