PATHFAST™ hs-cTnI: early and immediate diagnosis of MI in the emergency department (ED)

PATHFAST™ hs-cTnI is a chemiluminescent enzyme immunoassay (CLEIA) for quantitative measurement of cardiac troponin I (cTnI) concentration in whole blood or plasma at the point of care (POC).

Low concentrations of cTnI can be analysed by using high sensitivity cardiac troponin (hs-cTnI) assays which meet the criteria defined by IFCC and ESC (1,2). PATHFAST™ provides high accuracy and precision of test results similar to central lab analyser, combined with the flexibility of a POCT assay within 17 minutes out of whole blood and plasma by all in one cartridge solution. The new PATHFAST™ hs-cTnI assay fits for the recommendations on the IFCC and ESC guidelines for the early detection of AMI (1-3,9).

Clinical benefits of hs-cTn assays

hs-cTnI assays detect troponin levels at low concentrations with high accuracy and precision at the earliest point of time. They measure low levels of troponin released by ischemia/micro-necrosis (Fig. 1) and allow even detection and quantification of troponin levels of healthy individuals (4).

The European Society of Cardiology (ESC) recommend the use of hs-cTn assays (2, 3) for early rule-in and rule-out of Acute Myocardial Infarction (AMI) and differentiation from patients with non-coronary artery cardiac diseases. High-sensitivity troponins can detect small changes for a short time accurately even at the early phase of the disease and differentiate acute disease from chronic state (Fig.1, 9).

In addition to the diagnosis of AMI, detection of low cardiac troponin levels may make it possible to predict information (risk stratification) in terms of short- and long term mortality of patients (5).

**Fig. 1: cTnI kinetics after acute myocardial injury including acute myocardial infarction**

- **Very early sampling**
  - Rising cTn values from below to >99th percentile
  - Delta is detectable
- **Early sampling**
  - cTn values >99th percentile
  - Delta may not be seen over a short period
- **Later sampling**
  - cTn values >99th percentile
  - Declining delta
- **Very late sampling**
  - Acute myocardial infarction
  - Chronic myocardial injury
  - 99th percentile URL

In clinical studies PATHFAST™ hs-cTnI has been evaluated for a 99th percentile upper reference limit of 29.0 ng/L at an imprecision of 6.1%, which is less than 10% and fits for the criteria of hs-cTnI, declared by IFCC (1).
Criteria for a high sensitivity cTN assays

**Recommendation from IFCC (1)**

- 99th percentile of hs-assays should be measured with an analytical imprecision of <10% CV
- hs-cTn assays should measure cTn above the limit of detection (LOD) in 50% of healthy individuals
- Gender specific 99th percentile values should be established for men and women

**Recommendation from ESC guideline (2,3)**

New ESC guidelines of 2015 advises to use 0 h /3 h rule-out or a 0 h /1 h rule-in/rule-out algorithm by using high sensitivity troponin assays as an alternative to the established 0 h /3 h /6 h procedere (2).

For PATHFAST™ hs-cTnI assay the 99th percentiles values were determined in 734 healthy individuals and are listed in Table 1. Gender specific 99th percentile cut offs for overall, females and males are 27.9 ng/L (this value is not significantly different from the FDA cleared overall 99th percentile of 29.0 ng/L before exclusion of individuals with abnormal NT-proBNP, HbA1c and eGFR), 20.3 ng/L, and 29.7 ng/L respectively (6).

**Tab. 1: Gender specific 99th percentile by PATHFAST™ hs-cTnI assay**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Gender specific 99th percentile (ng/L)</th>
<th>% measurable concentrations &gt; LoD</th>
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<tbody>
<tr>
<td>Overall</td>
<td>734</td>
<td>27.9</td>
<td>n= 487 (66.3%)</td>
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<tr>
<td>Males</td>
<td>382</td>
<td>29.7</td>
<td>n= 301 (78.8%)</td>
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<tr>
<td>Females</td>
<td>352</td>
<td>20.3</td>
<td>n= 186 (52.8%)</td>
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</tbody>
</table>

For PATHFAST™ hs-cTnI assay the 99th percentiles values were determined in 734 healthy individuals and are listed in Table 1. Gender specific 99th percentile cut offs for overall, females and males are 27.9 ng/L (this value is not significantly different from the FDA cleared overall 99th percentile of 29.0 ng/L before exclusion of individuals with abnormal NT-proBNP, HbA1c and eGFR), 20.3 ng/L, and 29.7 ng/L respectively (6).

Troponin concentrations were measured with the PATHFAST™ hs-cTnI assay in EDTA plasma.

Samples from 993 patients obtained at 0 hour, 1 hour and 3 hours after admission to the Chest Pain Unit (CPU) with suspicion of acute coronary syndrome, were used. 219 AMI patients were identified (23.5%) by two independent cardiologists with blinded cTnI values.

The ROC analysis for the discrimination between AMI and non-AMI patients including the clinical sensitivity and specificity, as well as the Positive and Negative Predictive Values (PPV and NPV) based on the 99th percentile value are explained in Table 2 for PATHFAST™ hs-cTnI assay. Comparison with one established central laboratory methods (troponin I) showed comparable diagnostic validity for AMI (NSTEMI and STEMI) (Fig. 2A) and NSTEMI patients (Fig. 2B) (7).

PATHFAST™ hs-cTnI assay offers the opportunity for chest pain units and emergency units to test hs-cTnI in less than 17 minutes.
The ESC guidelines recommended rule-in and rule-out algorithms using hs-cTn assays in patients admitted with suspected NSTEMI to the ED (2).

### The clinical application of a 0/1 h diagnostic algorithm based on a novel PATHFAST™ POC hs-cTnI assay is safe (7,8).

The diagnostic performance of PATHFAST™ hs-cTnI assay is comparable to a guideline–recommended established laboratory hs-cTn assay (7,8).
**PATHFAST™ Test Principle**

**IMMUNOREACTION**

- Sample (whole blood, plasma)
- Magnetic particles coated with antibody
- ALP labelled antibody

**SEPARATION**

- Magnet
- Magtration® technology
- Chemiluminescent substrate

**ENZYME REACTION**

- Target molecule
- Other components

**DETECTION**

- Photomultiplier
- Measurement of light emission

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**PATHFAST™ Technical Specifications**

- **Instrument type**: Desktop Immunoassay Analyzer
- **Throughput**: Up to 6 samples or parameters per run
- **Measuring time**: <17 minutes for 6 samples using emergency markers or PATHFAST™ Presepsin
- **Sampling material**: Whole blood, plasma, serum
- **Measuring principle**: Chemiluminescence enzyme immunoassay technology (CLEIA) and Magtration® technology.
- **Reaction temperature**: 37 °C
- **Sample volume**: 100 µl
- **Data storage**: Patient data: 1000, QC data: 1800, CAL data: 300
- **Datatransfer**: ASTM and Fixed standard
- **Weight**: 28 kg
- **El. requirements**: 100 - 240 V AC (50/60 Hz)
- **Power consumption**: 360 VA
- **Monitor/keyboard**: LCD touch-screen
- **Printer**: Integrated
- **PC**: Integrated, Handheld Barcodereader included
- **Interface**: RS-232C and Ethernet Port
- **Calibration**: Factory calibration, 2-point calibration every 4 weeks
- **24-h operation (stand-by)**: Recommended

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**PATHFAST™ Dimensions**

- **Dimensions**: 343 mm x 569 mm x 475 mm

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**References**

   IFCC educational materials on selected analytical and clinical applications of high sensitivity cardiac troponin assays. Clin Biochem 2015; 48: 201-203
   Third Universal Definition of Myocardial Infarction. Eur Heart J 2012; 33: 2551-256
   Cardiac biomarkers of acute coronary syndrome: from history to high-sensitivity cardiac troponin. Intern Emerg Med 2017;12: 147-155
   Troponin I and cardiovascular risk prediction in the general population: the BiomarCaRE consortium. Eur Heart J 2016; 37: 2428-2437
   Validation of high-sensitivity performance for a United States Food and Drug Administration cleared cardiac troponin I assay. Clin Biochem. 2018 Jun; 56:4-10
   Rule-out and rule-in of non-ST-elevation myocardial infarction using a novel high-sensitivity troponin I point of care assay. ESC Congress Paris 2019, P2675
# Product List
**PATHFAST™** for critical care and sepsis diagnostics

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<thead>
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<th>Item number</th>
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## SYSTEM

**PATHFAST™ Immunoanalyser**
Analyzer for the detection of cardiac and other emergency parameters and sepsis

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## CONSUMABLES AND ACCESSORIES

**PATHFAST™ pipette tips**

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**PATHFAST™ waste box**

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## REAGENT KITS FOR CRITICAL CARE DIAGNOSTICS

**PATHFAST™ hs-cTnI**

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**PATHFAST™ Myoglobin**

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**PATHFAST™ CK-MB**

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**PATHFAST™ D-Dimer**

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**PATHFAST™ NTproBNP**

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**PATHFAST™ hsCRP**

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## REAGENT KITS FOR SEPSIS DIAGNOSTICS

**PATHFAST™ Presepsin**

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**PATHFAST™ Presepsin control set**

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