PATHFAST™
hs-cTnl
high sensitivity troponin I

IFCC & ESC compliant
0/1 h NSTEMI rule-out/rule-in algorithm
Results in < 17 minutes

POCT – whole blood/plasma

<17 min

LSI Medience Corporation
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

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).
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 |
|---------------------|------------------|------------------|
| Gender specific 99th percentile (ng/L) | % measurable concentrations | N |
| Overall | 27.9 | n= 487 (66.3%) | 734 |
| Males | 29.7 | n= 301 (78.8%) | 382 |
| Females | 20.3 | n= 186 (52.8%) | 352 |

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.

The ROC analyses of PATHFAST™ hs-cTnI and of a guidelines recommended well established laboratory-based high sensitivity troponin assay (LB hs-cTnI) revealed comparable discriminatory ability for the diagnosis of NSTEMI. The ROC analysis showed the AUC at 0 h (n=1,244) was 0.91 (95% CI, 0.89–0.93) for PATHFAST™ hs-cTnI, and 0.90 (95% CI, 0.87–0.92) for the LB hs-cTnI. After 1 h (n=1,251), AUC values increased to 0.94 (95% CI, 0.93–0.96) for PATHFAST™ hs-cTnI and 0.94 (95% CI, 0.92–0.96) for the LB hs-cTnI assay (Fig. 2A and 2B) (7).

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

### Diagnostic algorithms for PATHFAST™ hs-cTnI

The ESC guidelines recommended rule-in and rule-out algorithms using hs-cTn assays in patients admitted with suspected NSTEMI to the ED (2).

#### 0 h / 1 h Rule-out algorithm of NSTEMI for PATHFAST™ hs-cTnI

A rule-out of NSTEMI is possible by the combination of a baseline concentration below a cut-off level B and the delta from 0 h to 1 h < C (Fig. 3). 2015 ESC Guidelines recommend that in large validation cohorts the NPVs for rule-out of NSTEMI should exceed 98% (2). A diagnostic algorithm for a high-sensitive troponin I point of care assay was developed in a derivation dataset with 669 patients and validated in additional 610 patients. For PATHFAST™ hs-cTnI wide range of the combination was tested for 1,221 patients with suspected NSTEMI to achieve a NPV of above 99.5% with the highest number of patients ruled-out and the following cut off values have been identified (7-8, Table 2).

### Tab. 2: Rule-out of NSTEMI with serial sampling for PATHFAST™ hs-cTnI within one hour (7,8)

<table>
<thead>
<tr>
<th>0 h ≤ B (cTnI, ng/L)</th>
<th>Δ 0-1 h ≤ C (cTnI, ng/L)</th>
<th>NPV, % (95% CI)</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>3</td>
<td>99.7 (98.3, 100.0)</td>
<td>99.1 (96.9, 99.9)</td>
<td>58.1 (54.9, 61.2)</td>
</tr>
</tbody>
</table>

#### 0 h / 1 h Rule-in algorithm of NSTEMI for PATHFAST™ hs-cTnI

A rule-in for the likelihood of NSTEMI is possible if the hs-cTn value at admission (0 h) is measured above of a cut off level ≥ D or the hs-cTn concentration shows a rise within the first hour above the delta cut off level ≥ E (Table 3).

2015 ESC Guidelines recommend that the PPVs for validation cohorts should meet the rule-in criteria of 75-80% (2). For PATHFAST™ hs-cTnI the clinical study with 1,221 patients with suspected NSTEMI showed PPVs above 75% with specificities above 95%. The following cut off values have been identified (7-8, Table 3). Regarding the clinical situation of the individual patient the user may decide which cut off values may be applicable for optimal rule-out or rule-in.

### Tab. 3: Rule-in of NSTEMI with serial sampling for PATHFAST™ hs-cTnI within one hour (7,8)

<table>
<thead>
<tr>
<th>0 h ≥ D (cTnI, ng/L)</th>
<th>Δ 0-1 h ≥ E (cTnI, ng/L)</th>
<th>PPV, % (95% CI)</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>20</td>
<td>80.1 (73.7, 85.5)</td>
<td>65.7 (59.2, 71.7)</td>
<td>96.2 (94.8, 97.3)</td>
</tr>
</tbody>
</table>

#### Rule-out of NSTEMI at admission for PATHFAST™ hs-cTnI (0 h)

According to the ESC guideline rule-out is possible already at admission (0 h) if the value is below a cut off level A and if onset of chest pain > 3 h. Regarding the LoD of 2.3 ng/L (6) recent study data of PATHFAST™ hs-cTnI using a cut off level A of 3 ng/L with targeted NPV of 100% revealed the following results (7):

<table>
<thead>
<tr>
<th>NPV, % (95% CI)</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>% ruled-out (95% CI)</th>
<th>Total N</th>
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<tbody>
<tr>
<td>100.0 (98.8, 100.0)</td>
<td>100.0 (97.7, 100.0)</td>
<td>46.5 (42.6, 50.5)</td>
<td>37.2</td>
<td>792</td>
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</table>

For 0 h rule-out only individuals with a symptoms onset over 3 h before presentation were used.

### Conclusions from clinical studies

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

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

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

**Magnet**
- Magtration® technology

**Chemiluminescent substrate**

**Detection**
- Photon multiplier
- Measurement of light emission

**IMMUNOREACTION**
**SEPARATION**
**ENZYME REACTION**

**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™ Presespin
- **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

**PATHFAST™ Dimensions**

- Height: 475 mm
- Width: 569 mm
- Depth: 343 mm

**References**

<table>
<thead>
<tr>
<th>Product List</th>
<th>Item number</th>
<th>Pack size</th>
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<tbody>
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<td>1 x 1</td>
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<td>PATHFAST™ Immunoanalyser</td>
<td>300936</td>
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<tr>
<td>PATHFAST™ Presepsin control set PF0201-C</td>
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</table>

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**PATHFAST™ for critical care and sepsis diagnostics**

**SYSTEM**

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

**CONSUMABLES AND ACCESSORIES**

PATHFAST™ pipette tips
PATHFAST™ waste box

**REAGENT KITS FOR CRITICAL CARE DIAGNOSTICS**

PATHFAST™ hs-cTnI
PATHFAST™ Myoglobin
PATHFAST™ CK-MB
PATHFAST™ D-Dimer
PATHFAST™ NTproBNP
PATHFAST™ hsCRP

**REAGENT KITS FOR SEPSIS DIAGNOSTICS**

PATHFAST™ B·R·A·H·M·S PCT
PATHFAST™ B·R·A·H·M·S PCT control set
PATHFAST™ Presepsin
PATHFAST™ Presepsin control set

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