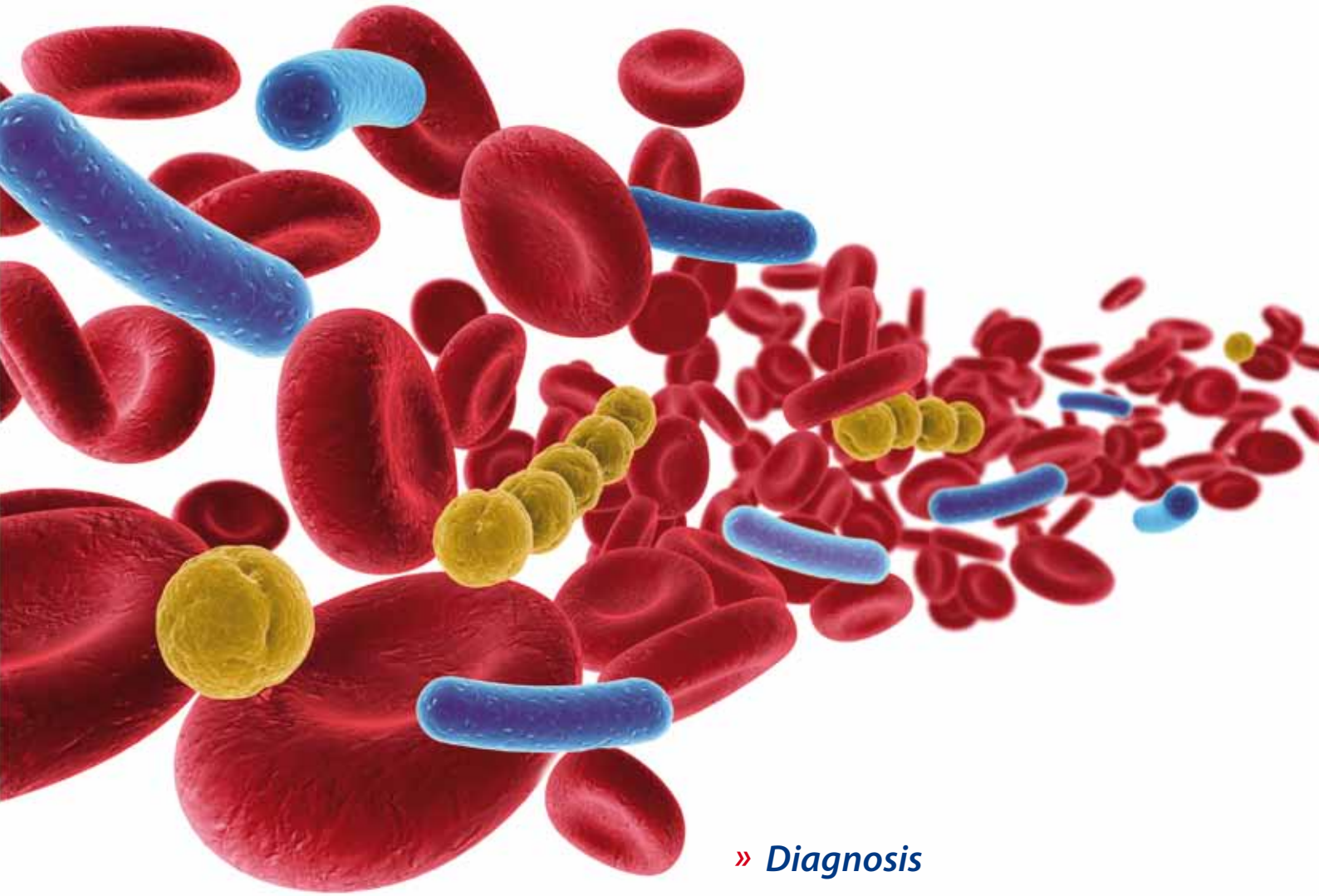
Fast and quantitative results out of whole blood in 15 minutes
For routine laboratory and point of care use

# NEW SEPSIS MARKER

# PATHFAST® *PRESEPSIN*



» *Diagnosis*

» *Prognosis at first presentation*

» *Disease monitoring*

MITSUBISHI CHEMICAL MEDIENCE CORPORATION

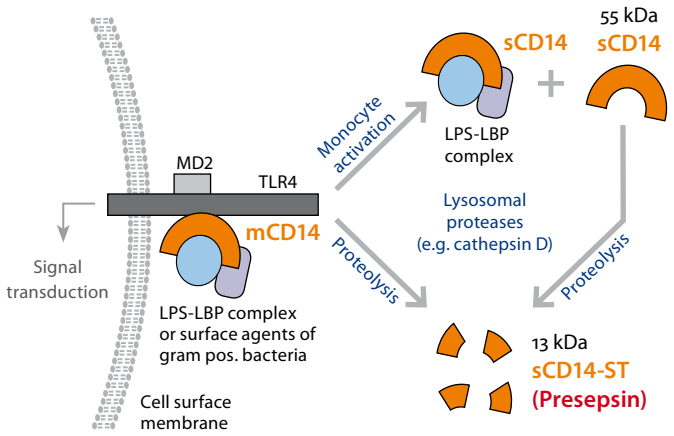
MITSUBISHI CHEMICAL

# New Sepsis marker
# PATHFAST® Presepsin

**PATHFAST® Presepsin is a chemiluminescent enzyme immunoassay for the quantitative measurement of presepsin concentration in whole blood or plasma. PATHFAST® Presepsin can be used as an aid in the diagnosis and prognosis of sepsis, in the assessment of the degree of septic severity, and in the risk stratification of critically ill septic patients.**

## Introduction

**Tentative mechanism of presepsin secretion**




mCD14: membrane CD14; sCD14: soluble CD14; sCD14-ST: soluble CD14 subtype (=Presepsin); LPS: lipopolysaccharide; PG: polyglycan, LBP: lipopolysaccharide binding protein, TLR4: toll-like receptor 4; MD2: Co-Protein of TLR4.

CD14 is a glycoprotein expressed on the membrane surface of monocytes/macrophages and serves as a receptor for complexes of lipopolysaccharides (LPS) and LPS binding protein (LPB), activating the toll-like receptor 4 (TLR4) specific pro-inflammatory signaling cascade on contact with infectious agents. Simultaneously, CD14 is shed from the cell membrane into the circulation forming soluble CD14 (sCD14). However, plasma protease activity generates also another sCD14 molecule called sCD14 subtype (sCD14-ST) or presepsin.[1] The levels of presepsin were significantly higher in septic patients than in patients with SIRS or appearently healthy individuals.[2] Presepsin levels were elevated earlier than IL-6 and D-dimer along with occurrence of blood bacteria in animal model. The determination of the presepsin concentration can be used for diagnosis and prognosis of sepsis and also to monitor the course of the disease.[3]

## Clinical use of PATHFAST® Presepsin

- **Early diagnosis and prognosis of sepsis**
- **Prognosis at first presentation**
- **For emergency and intensive care use**

## Early diagnosis and prognosis

In a reference range study presepsin concentrations were determined in EDTA plasma samples from 119 healthy individuals (age: 21 – 69 years; 60 females and 59 males).

Arithmetic mean: 160 pg/ml (95% CI: 48 – 171 pg/ml).[4]

The presepsin values were determined at presentation in the emergency department in patients with sepsis.

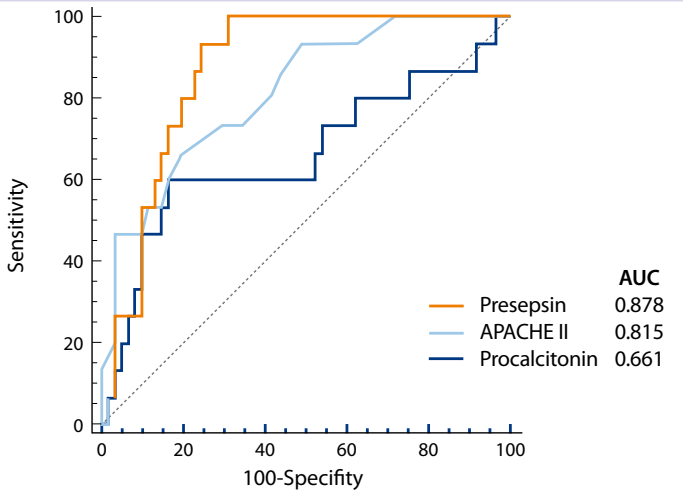
Quartiles of presepsin showed a strong association with the 30 day mortality:[4]

| **Quartile** | **1st** (n=37) | **2nd** (n=35) | **3rd** (n=35) | **4th** (n=33) |
|---|---|---|---|---|
| **Presepsin** (pg/ml) | 177 – 512 | 524 – 927 | 950 – 1810 | 1850 – 15757 |
| **Mortality** (p<0.0001) | 2.7% | 8.6% | 17.1% | 39.4% |

# Prognostic value of presepsin in emergency patients using the new assay PATHFAST® Presepsin

ROC analysis comparing the accuracy for the prediction of 30-day mortality revealed areas under the receiver operating characteristics curve (AUC) for presepsin, APACHE II score and procalcitonin of **0.878**, **0.815** and **0.661**, respectively.[4]

**ROC analysis at presentation**

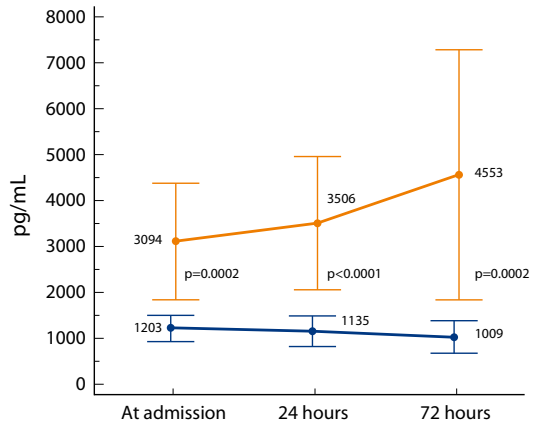



**Presepsin showed superior prognostic accuracy!**

## Disease monitoring

Presepsin was measured at presentation, at 24 hours and at 72 hours after admission. In patients with favorable outcome within 30 days after admission (n=104) presepsin levels decreased from baseline to 72 hours. In the patient group who experienced adverse outcome (n=36), presepsin levels showed an increasing tendency.[4]

**Correlation of presepsin values and patient outcome**




Course of mean values of presepsin (error bars 95% CI) in patients with worse outcome (orange line) and favourable outcome (blue line).

## Decision thresholds

| Presepsin (pg/ml) | Diagnosis |
|---|---|
| < 200 | Exclusion of sepsis |
| < 300 | Systemic infection not likely |
| < 500 | Systemic infection (sepsis) possible |
| < 1000 | Moderate risk of progression of systemic infection (severe sepsis), Increasing risk of unfavourable outcome |
| ≥ 1000 | High risk of progression of systemic infection (severe sepsis/septic shock), **High risk for 30 day mortality comparable to APACHE score ≥ 25** |

Presepsin determination at admission to the emergency department in 140 septic patients enrolled in a clinical outcome study revealed the following values:[5]

| Presepsin (pg/ml) | < 200 | 200–300 | 300–500 | 500–1000 | ≥ 1000 |
|---|---|---|---|---|---|
| Sepsis progression and mortality risk | Very low | Low | Moderate | High | Very high |
| **Sepsis, n (%)** | 3 (3.5) | 9 (10.6) | 18 (21.1) | 29 (34.1) | 26 (30.6) |
| **Severe sepsis, n (%)** | 0 | 0 | 5 (12.5) | 11 (27.5) | 24 (60.0) |
| **Septic shock, n (%)** | 0 | 0 | 0 | 4 (26.7) | 11 (73.3) |
| **30-day death, n (%)** | 0 | 0 | 0 | 5 (21.7) | 18 (78.3) |

## For emergency and intensive care use

PATHFAST Presepsin can be measured out of whole blood and is due to the fast turn around time and high prognostic power already at admission suitable for the use in emergency and intensive care units.

- **Sample material:** anticoagulated (EDTA/heparin) whole blood or plasma
- **Turn around time:** 15 min

# PATHFAST® Presepsin

## Early prognosis of sepsis is key for improved clinical outcome

### Analytical performance data

Analytical performance was evaluated on PATHFAST system with whole blood and plasma.[6,7]

| | |
|---|---|
| Assay range | 20 – 20000 pg/mL |
| Correlation between whole blood and plasma on PATHFAST | y = 1.04 x - 10.8 ; r = 0.986 ; n = 104<br>(y: EDTA whole blood, x: EDTA plasma) |
| Total % CV in plasma | QC-LL = 4.4%, QC-L = 4.0%, QC-M = 3.8%, QC-H = 5.0% |


**References**

1) Endo S, Takahashi G, Shozushima T, Matsumoto N, Kojika M, Suzuki Y, Inoue Y. Usefulness of Presepsin (soluble CD14 subtype) as a Diagnostic Marker for Sepsis, JJAAM. 2012; 23:27-28

2) Shozushima T, Takahashi G, Matsumoto N, Kojika M, Okamura Y, Endo S. Usefulness of presepsin (sCD14-ST) measurements as a marker for the diagnosis and severity of sepsis that satisfied diagnostic criteria of systemic inflammatory response syndrome. J Infect Chemother. 2011; 17(6):764-769.

3) Endo S, Suzuki Y, Takahashi G, Shozushima T, Ishikura H, Murai A, Nishida T, Irie Y, Miura M, Iguchi H, Fukui Y, Tanaka K, Nojima T, Okamura Y. Uselfulness of Presepsin in the diagnosis of sepsis in a multicenter prospective study. J Infect Chemother. 2012; 18(6):891-897.

4) Spanuth E, Wilhelm J, Loppnow H, Ebelt H, Ivandic B, Werdan K. (2012). Diagnostic and Prognostic Value of Presepsin (Soluble CD14 Subtype) in Emergency Patients with Early Sepsis Using the New Assay PATHFAST Presepsin. In Renz. H & Tauber. R (Ed.) Advances in Clinical Chemistry and Laboratory Medicine (pp.128-133). Berlin/Boston: De Gruyter

5) Spanuth E, Ebelt H, Ivandic B, Werdan K. The new Sepsis Marker Presepsin is Superior for Prognosis and Disease Monitoring compared to Procalcitonin. Poster presented at the 20th IFCC-EFLM European Congress of Clinical Chemistry and Laboratory Medicine, Milan (Italy), May 19th – 22nd 2013

6) Okamura Y, Yokoi H. Development of a point-of-care assay system for measurement of presepsin (sCD14-ST). Clinica Chimica Acta. 2011; 412:2157-2161

7) internal data


### The PATHFAST® System

**The PATHFAST analysis system combines the accuracy of a full-scale lab with the flexibility of a mobile solution. Best prerequisites for fast differential diagnosis at the point of care. Easy to operate, install and network. Highest precision make this device an adequate „outpost" of a full-scale lab on intensive care or emergency ward. Parallel processing enables the examination of six samples in only 15 minutes.**

Six parallel channels. Six quantitative analysis simultaneously. Six results in 15 minutes. This gives PATHFAST its unique speed.

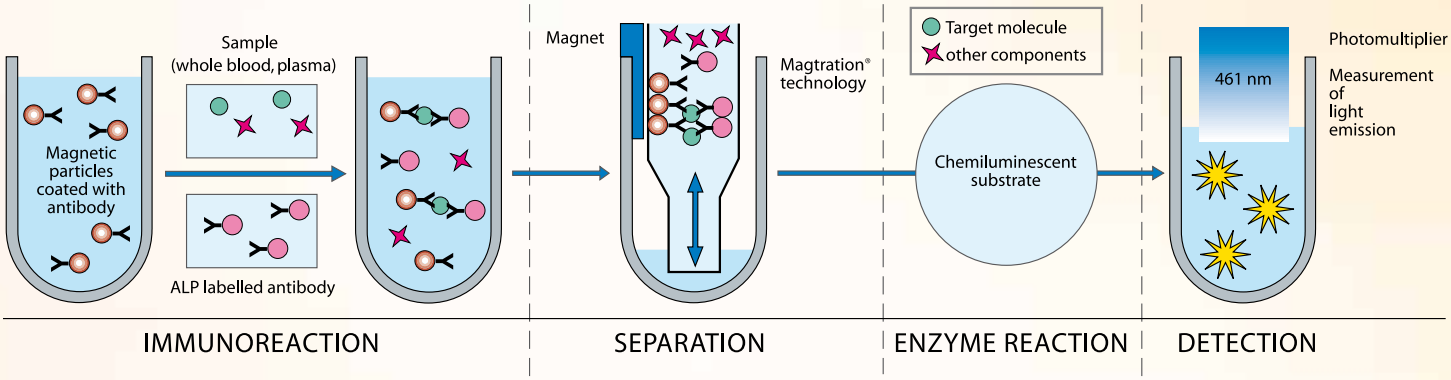
Its compact design and low weight make PATHFAST the ideal analysis system in emergency labs, hospitals and medical offices. Applied wherever fast quantitative results with full-scale lab quality provide decisive diagnostic advantages. Directly at the point of care.

PATHFAST is a fully automatic immunoassay analyzer, which combines the progressive chemiluminescence technology with the patented Magtration® technology. Small sample volumes can be detected with high accuracy and precision.

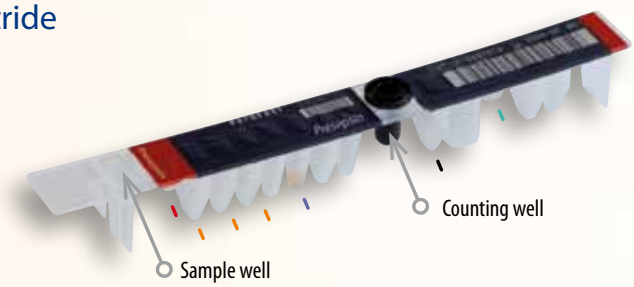
Insert the reagent cartridge, apply the samples and press the „Start" button. PATHFAST takes care of everything else fully automatic. A simple 3-step method provides results in lab quality.

# PATHFAST® The highly precise, fast and compact chemiluminescence immunoassay analysis system

## PATHFAST® Test Principle




## Reagent cartride




- Magnetic particles
- ALP-conjugated antibody
- Chemiluminescent substrate (CDP-Star with Sapphire II)
- Sample diluent
- Washing buffer

## PATHFAST® Technical Specifications


| | |
|---|---|
| Instrument type: | Desktop Immunoassay Analyzer |
| Throughput: | Up to 6 samples or parameters per run |
| Measuring time: | Less than 16 min for 6 samples using PATHFAST® Presepsin |
| Sampling material: | Whole blood, plasma |
| Measuring principle: | Analysis takes place with the help of the chemiluminescence enzyme immunoassay technology (CLEIA) and Magtration® technology. |
| Reaction temperature: | 37,5 °C |
| Sample volume: | 100 µl |
| Wavelength: | 300 - 650 nm |
| Data storage: | Patient data: 1000, QC data: 1800, CAL data: 300 |
| Datatransfer: | ASTM standard |
| Dimensions: | 375 (w) x 570 (d) x 510 (h) mm |
| Weight: | 33 kg |
| El. requirements: | 100 - 240 V AC (50/60 Hz) |
| Power consumption: | 360 VA |
| Monitor/keyboard: | LCD touch-screen |
| Printer: | Integrated |
| PC: | Integrated |
| Interface: | RS-232C |
| Calibration: | Factory calibration, 2-point calibration every 4 weeks |
| 24-h operation (stand-by): | recommended |

| Product List | Item number | Pack size |
|---|---|---|
| **SYSTEM** | | |
| PATHFAST® Immunoanalyser<br>Analyzer for the detection of sepsis, fertility, cardiac and other emergency parameters | 1114-0000 | 1 x 1 |
| **CONSUMABLES AND ACCESSORIES** | | |
| PATHFAST® pipette tips | 1114-1000 | 5 x 42 units |
| PATHFAST® waste box | 1114-1001 | 10 units |
| **REAGENT KITS FOR SEPSIS DIAGNOSTICS** | | |
| PATHFAST® Presepsin | 1110-4000 | 60 tests |
| PATHFAST® Presepsin control set | 1110-4001 | 4 x 1 ml |
| **REAGENT KITS FOR CRITICAL CARE DIAGNOSTICS** | | |
| PATHFAST® cTnI | 1110-2000 | 60 tests |
| PATHFAST® Myoglobin | 1110-2001 | 60 tests |
| PATHFAST® CK-MB | 1110-2002 | 60 tests |
| PATHFAST® D-Dimer | 1110-2003 | 60 tests |
| PATHFAST® NTproBNP | 1110-2004 | 60 tests |
| PATHFAST® hsCRP | 1110-2005 | 60 tests |
| PATHFAST® HCG | 1110-2009 | 60 tests |

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