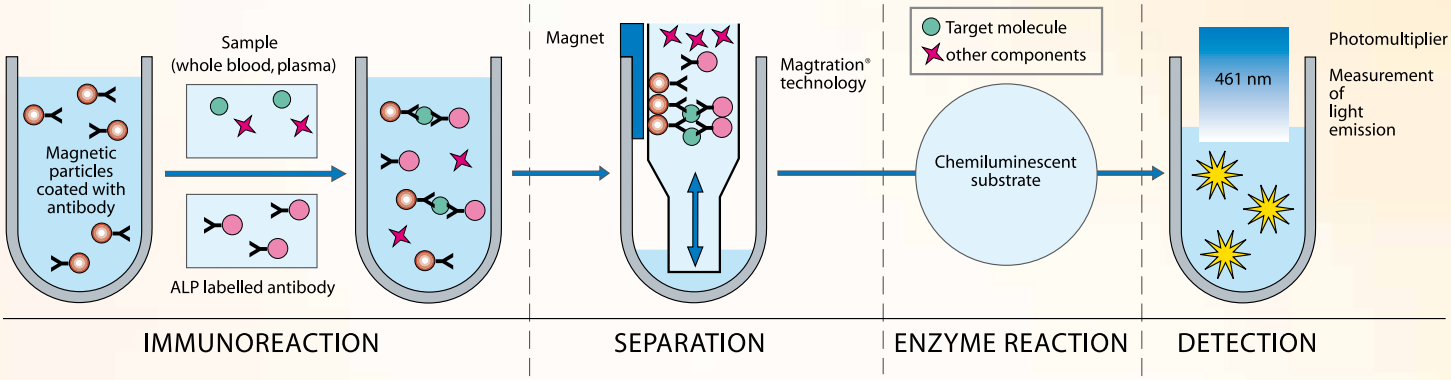
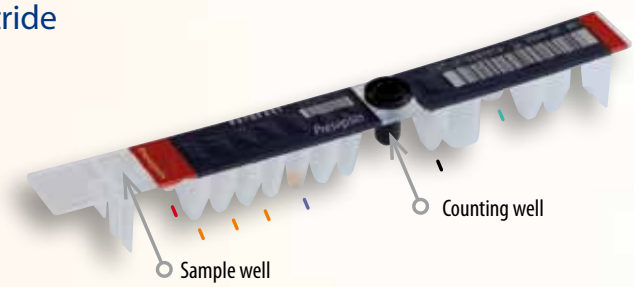
PATHFAST™ The highly precise, fast and compact chemiluminescence immunoassay analysis system

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:	15 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 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

Mitsubishi Chemical Europe GmbH
Willstätter Str. 30, 40549 Düsseldorf, Germany
Phone: +49 (0) 211 - 5 20 54 10
Facsimile: +49 (0) 211 - 59 12 72
email: Pathfast@mc-e.de

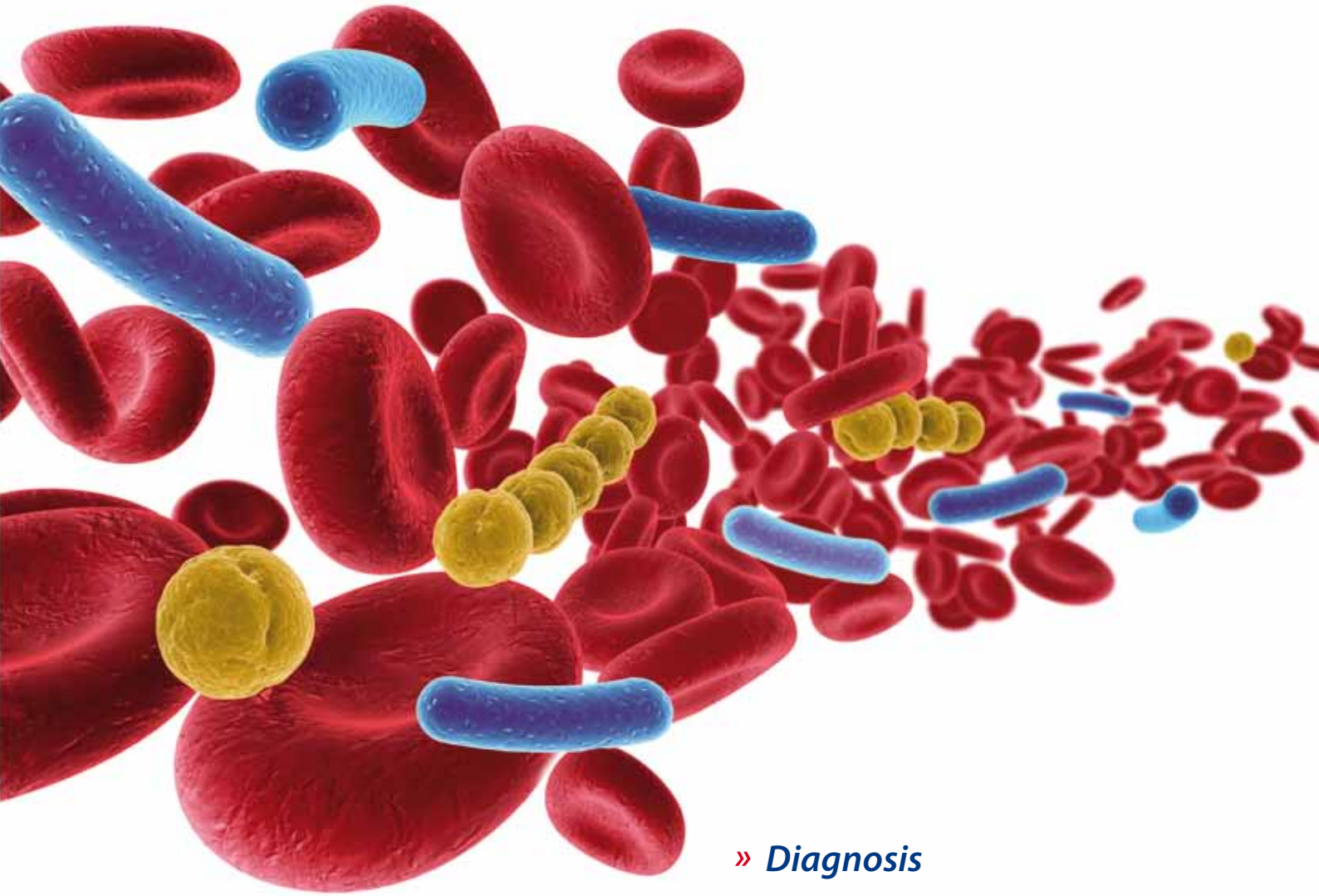
LSI Medience Corporation
13-4 Uchikanda 1-chome, Chiyoda-ku,
Tokyo 101 - 8517, Japan
Phone: +81 - 3 - 67 22 - 40 80
Facsimile: +81 - 3 - 67 22 - 40 81

www.PATHFAST.eu

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*

LSI Medience Corporation

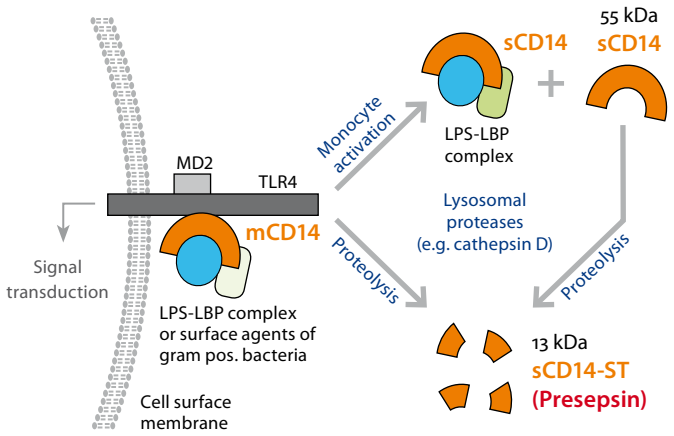
MITSUBISHI CHEMICAL EUROPE

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.[3,4,6]

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).[5]

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

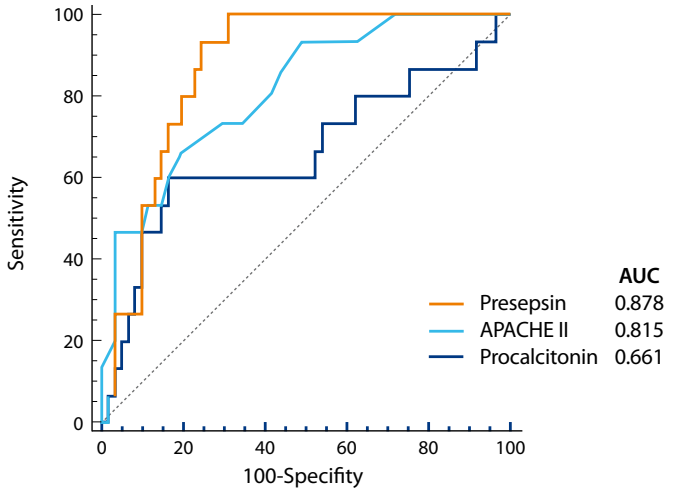
Quartiles of presepsin showed a strong association with the 30 day mortality: [5]

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.[5]

ROC analysis at presentation

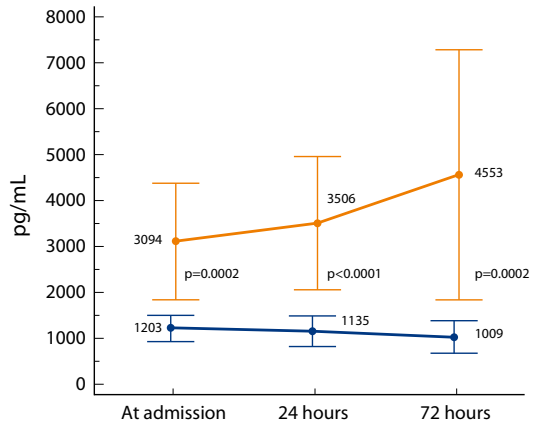


Presepsin showed superior prognostic accuracy!

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.

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 Sens.= 96.0%; Spec.=81.5%, PPV=69.4%; NPV = 98.0% (Prevalence 30%)
< 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:

		Presepsin (pg/ml)				
	Study Group	< 200	< 300	< 500	< 1000	≥ 1000
Sepsis grade	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Sepsis	85 (60.7)	3 (3.5)	12 (14.1)	30 (35.3)	59 (42.1)	26 (30.6)
Severe sepsis	40 (28.6)	0	0	5 (12.5)	16 (40.0)	24 (60.0)
Septic shock	15 (10.7)	0	0	0	4 (26.7)	11 (73.3)
All patients	140 (100)	3 (2.1)	12 (8.6)	35 (25)	79 (56.4)	61 (43.6)
Mortality prediction						
Death	23 (16.4)	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.

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 (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) 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 May; 11(5): Epub

2) 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

3) Kojika M, Takahashi G, Matsumoto N, Kikkawa T, Hoshikawa K, Shioya N, Shibata S, Suzuki Y, Aoki H, Shirakawa K, Endo S. Serum levels of soluble CD14 subtype reflect the APACHE II and SOFA Scores. Medical Postgraduates 2010 Jan; 48(1): 46-50

4) Takahashi G, Suzuki Y, Kojika M, Matsumoto N, Shozushima T, Makabe H, Yamada Y, Shioya N, Shibata S, Shirakawa K, Endo S. Evaluation of responses to IVIG therapy in patients with severe sepsis and septic shock by soluble CD14 subtype monitoring. Medical Postgraduates 2010 Jan; 48(1): 19-24

5) Spanuth E, Wilhelm J, Loppnow H, Ebelt H, Ivandic B, Werdan K. Diagnostic and Prognostic Value of Presepsin (Soluble CD14 Subtype) in Emergency Patients with Early Sepsis Using the New Assay PATHFAST Presepsin. IFCC World Lab/EuroMedLab P Proceedings 2011; 2.29: 128-133

6) 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 Dec;18(6):891-7. doi: 10.1007/s10156-012-0435-2. Epub 2012 Jun 13

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.