PATHFAST™

B·R·A·H·M·S **PCT**

Master the challenge in sepsis diagnostic

> up to 6 samples in parallel
> in less than 17 minutes
> out of whole blood, plasma or serum
> in high-sensitive central lab quality
> for guided antibiotic stewardship

PCT on WHO Essential In-vitro Diagnostics List

PCT in sepsis patients

Sepsis with acute organ dysfunction (severe sepsis) is the number one cause of death in the non-coronary intensive care unit and one of the most significant challenges in critical care. [1]

The early recognition and diagnosis of sepsis is a crucial factor for improving patient outcomes. To address such challenges, a well-known and guideline-established biomarker for sepsis is useful. With its widely accepted usage and clinically proven usability, PCT becomes a viable option when it comes to answer- ing the question "which biomarker can be used for diagnosis of septic patients?"

PCT is the 116 amino-acid precursor of the peptide hormone calcitonin. In healthy individuals, PCT is expressed by neuro-endocrine C cells of the thyroid, pulmonary and pancreatic tissues. Upon formation, PCT is successively cleaved into calci- tonin, katacalcin, and an N-terminal fragment [2]. Procalcitonin is expressed by different types of cells from numerous organs in response to pro-inflammatory stimulation, particularly systemic bacterial infection and sepsis [2-4]. PCT is used as an aid in the diagnosis of sepsis, severe sepsis and septic shock in systemic inflammatory response to bacterial infection, as well as in the assessment of the degree of sepsis severity [3]. PCT has shown to be useful in decision making to initiate, to monitor and to stop

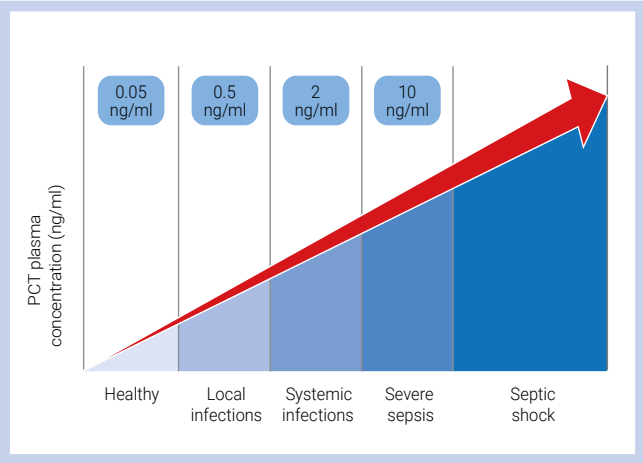


Fig. 1: PCT increase reflects the likelihood to develop from a healthy condition to the most severe states of disease (severe sepsis and septic shock)

antibiotic treatment in randomized controlled clinical studies in patients with acute respiratory tract infections and sepsis [4-7]. PCT levels in sepsis are generally higher than 1-2 ng/ml and can reach values between 10 and 100 ng/ml, or considerably higher in individual cases, thus enabling the

diagnostic differentiation between various clinical conditions and a severe bacterial in- fection (sepsis) (Fig. 1).

In healthy people, plasma PCT concentrations are found to be below 0.05 ng/ml, but PCT concentrations can increase up to 1000 ng/ml in patients with sepsis, severe sepsis or septic shock. PCT levels are low in viral infections, chronic inflammatory dis- orders or autoimmune processes [8].

These cut-off definitions were made in accordance with the results of the consensus conference of the American College of Chest Physicians/Society of Critical Care Medicine (sepsis-1) and the SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference (sepsis-2) where severe sepsis was still a distin- guishing criterion [10,12]. Since 2016, a new sepsis definition (sepsis-3) came into force. Since according to the new definition every form of sepsis is associated with organ dysfunction, the term “severe sepsis” should no longer be used [11].

Antibiotic stewardship with the help of B·R·A·H·M·S PCT

In many cases the prescription of antibiotics is not indicated. Especially in lower respiratory tract infections (LRTI) the infection is predominantly of viral origin. However 75% of the patients are treated with antibiotics. In critically ill patients with sepsis, severe sepsis, or severe bacterial infections, like pneumonia, the duration of the antibiotic therapy is often

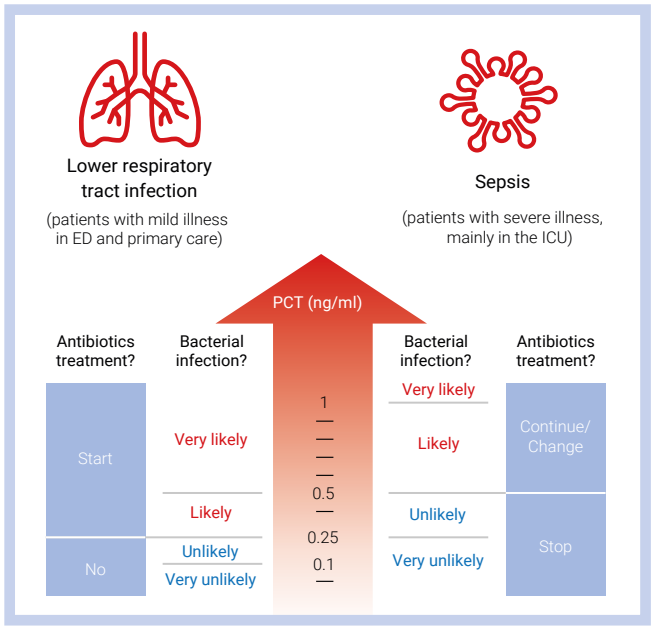
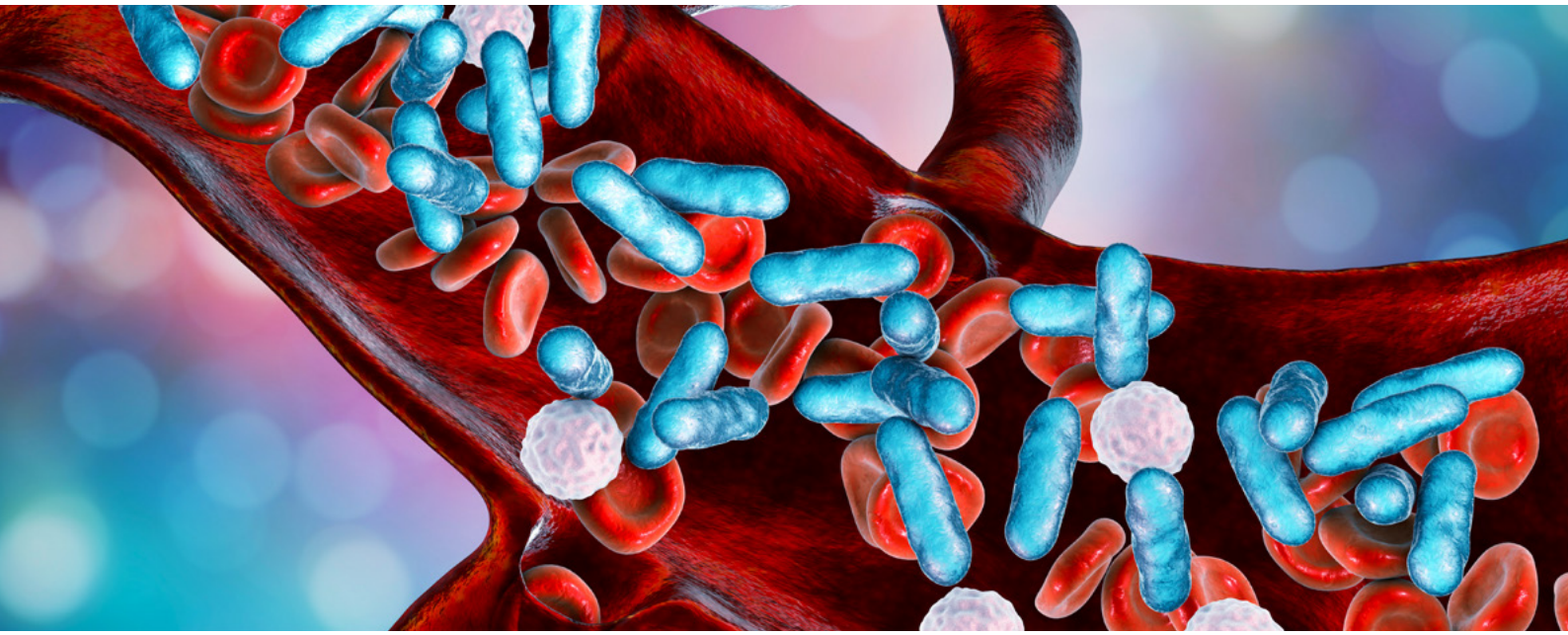


Fig. 2: Cut-off levels of clinical algorithms adapted to patients’ severity

longer than indicated and could be stopped earlier without any adverse impact on the patient. This antibiotic overuse contributes to increasing anti- microbial resistance, increased risk of drug-related adverse events and higher medical costs. The use of a sensitive B·R·A·H·M·S PCT assay, like PATHFAST™ B·R·A·H·M·S PCT, for determining the necessary and optimal duration of antibiotic therapy is shown in Figure 2 [9]. The sensitivity PATHFAST™ B·R·A·H·M·S PCT assay allows to measure low concentrations (<0.1 ng/ml) of PCT thus allowing to detect LRTI.



PATHFAST™ B·R·A·H·M·S PCT

The test principle of PATHFAST™ B.R.A.H.M.S PCT is based on non-competitive CLEIA combined with MAGTRATION® technology and is standardised against the B·R·A·H·M·S PCT sensitive KRYPTOR assay. During incubation of the sample with alkaline phosphatase labelled anti-PCT monoclonal antibody and anti- PCT monoclonal antibody coated magnetic particles, the PCT of the sample binds to the anti-PCT antibodies forming an immune complex with enzyme labelled antibody and antibody coated magnetic particles. After removing the unbound substances by MAGTRATION® technology, a chemiluminescent substrate is added. After a short incubation, the luminescence intensity generated by the enzyme reaction is measured. The luminescence intensity is related to the PCT concentration of the sample which is calculated by means of a standard curve.
The data obtained with PATHFAST™ B·R·A·H·M·S PCT demonstrated correlation to the B·R·A·H·M·S PCT sensitive Kryptor assay and Elecsys B·R·A·H·M·S PCT (Fig. 3 and Fig. 4).

Assay standardization: Against the B·R·A·H·M·S PCT sensitive KRYPTOR assay

Sample stability (Plasma and Serum)	
+15 to +25 °C	6 hours
+2 to +8 °C	1 day
-20°C or lower	2 months
Measuring range	0.02 - 100 ng/ml
Correlation vs Elecsys B·R·A·H·M·S PCT	y = 1.05x - 0.015, r = 0.996, n = 156 (serum samples)
Correlation vs B·R·A·H·M·S PCT sensitive KRYPTOR	y = 1.02x - 0.012, r = 0.985, n = 180 (EDTA plasma samples)

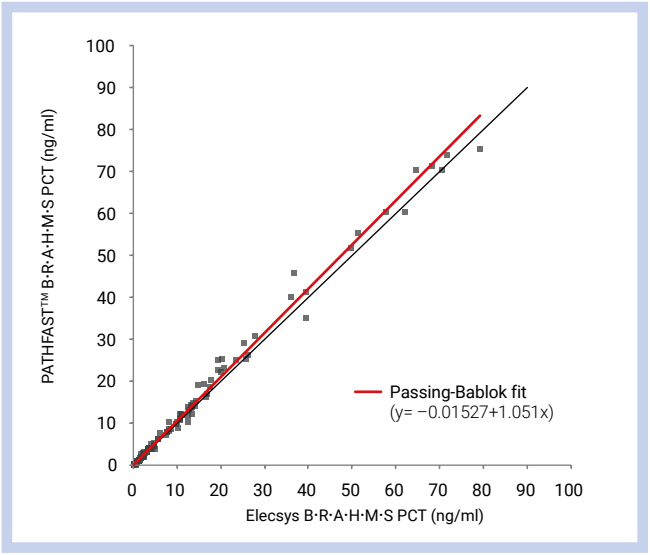


Fig. 3: Comparison PATHFAST™ B·R·A·H·M·S PCT with Elecsys B·R·A·H·M·S PCT

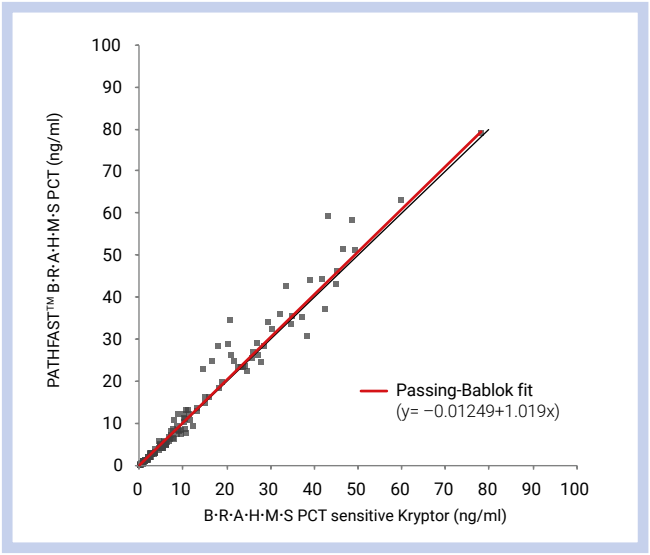


Fig. 4: Comparison PATHFAST™ B·R·A·H·M·S PCT with B·R·A·H·M·S PCT sensitive KRYPTOR

The Advantage of using a quality PATHFAST™ B·R·A·H·M·S PCT

In order to optimize the process of ED patient flow, a fast decision on a broad spectrum of diseases and injuries helps contribute to a shorter average length of stay in the ED.
A reliable, stable and clinically proven diagnostic solution supports the clinical-based decision, lowering patient risk and reducing treatment costs.

The application of the B·R·A·H·M·S PCT on the PATHFAST™ system will comply with the highest testing standard possible, and will support the sepsis diagnostic for the future. The clinical reliability of B·R·A·H·M·S PCT has been evaluated in over 5,700 clinical studies until now and owns the biggest market share in sepsis diagnostic.

- **accelerate your clinical decision making (assay time <17 min)**
- **well validated biomarker with over 5,700 publications**
- **save overall treatment costs**
- **useable at the POC or ED/ICU**
- **guideline accepted**
- **usage of whole blood, plasma or serum**
- **results in central lab quality**
- **high flexibility**
- **antibiotic stewardship**
- **low patient volume needed (100 µl)**

Specific performance data

1. Imprecision

Imprecision was determined using plasma samples. The within-run and total standards deviations (S.D.) and coefficient of variations (C.V.) were calculated according to the CLSI document EP5-A2.

		Within-run precision		Total precision	
Sample	**Mean (ng/ml)**	**S.D. (ng/ml)**	**C.V. (ng/ml)**	**S.D.**	**C.V.**
QC-L	0.097	0.004	4.4%	0.007	6.9%
QC-M	2.02	0.105	5.2%	0.113	5.6%
QC-H	36.1	1.83	5.1%	2.08	5.8%
QC-HH	80.5	4.30	5.3%	4.75	5.9%

2. Sensitivity

Limit of blank (LoB)	0.004 ng/ml
Limit of Detection (LoD)	0.007 ng/ml
Limit of Quantification (LoQ) at 20% CV	0.009 ng/ml

3. Expected values

PCT (ng/ml)	Interpretation
<0.5	Low risk for systemic bacterial infection, but local infection possible
≥0.5 – <2.0	Moderate risk for the development of severe systemic infection (severe sepsis or septic shock)
≥2.0 – ≤10	High risk for the development of severe systemicinfection (severe sepsis or septic shock)
>10	Important systemic inflammatory response with very high risk of severe sepsis and septic shock

Application and benefit of PATHFAST™ B·R·A·H·M·S PCT

With its easy and intuitive design, PATHFASTTM offers an easy way to analyse your patient samples by performing only 3 simple steps.

1

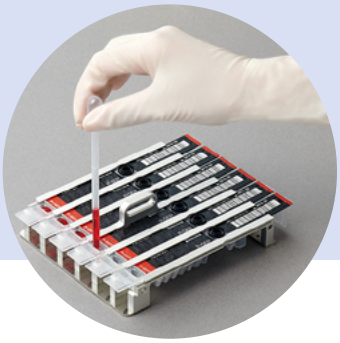
Collect

whole blood, serum or plasma samples, using heparin-NA, heparin-Li or EDTA collection tubes.

2

Transfer

100 µL sample into each sample well of the reagent cartridges.



3

Place

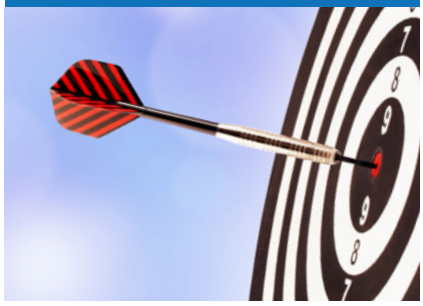
the loaded reagent rack into the instrument and start the assay. Get **results in <17 minutes.**

Due to its reagent design and reagent throughput, PATHFAST™ is designed as an optimal companion combining the quality of results of a central lab analyser with the flexibility of a point of care testing device in one instrument. The PATHFAST™ B·R·A·H·M·S PCT assay can either complement the central lab patient testing or simply can be placed into the ED/ICU in order to perform rapid and reliable patient assessment at the point of care. The ability to use whole blood samples provides multiple options to enhance the diagnostic power for sepsis patients.

B·R·A·H·M·S PCT on PATHFAST™

- **> Rapid & fast results**
- **> In less than 17 minutes**
- **> Out of whole blood, serum or plasma**

- **> Precise & accurate**
- **> High quality results**
- **> CLEIA assay**



- **> High flexibility**
- **> Usable for NPT**
- **> Usable in central lab**
- **> Comparable results with other B·R·A·H·M·S assays**

Product List

PATHFAST™ for critical care and sepsis diagnostics

	Item number	Pack size
SYSTEM		
PATHFAST™ Immunoanalyser Analyzer for the detection of cardiac and other emergency parameters and sepsis	300929	1 x 1
CONSUMABLES AND ACCESSORIES		
PATHFAST™ pipette tips	300936	5 x 42 units
PATHFAST™ waste box	300950	10 units
REAGENT KITS FOR CRITICAL CARE DIAGNOSTICS		
PATHFAST™ hs-cTnI	PF1241-K	60 tests
PATHFAST™ Myoglobin	PF1021-K	60 tests
PATHFAST™ CK-MB	PF1031-K	60 tests
PATHFAST™ D-Dimer	PF1051-K	60 tests
PATHFAST™ NTproBNP	PF1061-K	60 tests
PATHFAST™ hsCRP	PF1071-K	60 tests
REAGENT KITS FOR SEPSIS DIAGNOSTICS		
PATHFAST™ B·R·A·H·M·S PCT	PF1221-K	60 tests
PATHFAST™ B·R·A·H·M·S PCT control set	PF0221C	4 x 1 ml
PATHFAST™ Presepsin	PF1201-K	60 tests
PATHFAST™ Presepsin control set	PF0201-C	4 x 1 ml

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www.pathfast.eu

PHC Europe
A Member of PHC Group

Eikdonk 1 | 4825 AZ Breda | Netherlands
T: +31 (0) 76 543 3833
www.phchd.com/eu/biomedical