IB10 sphingotest®
product catalog

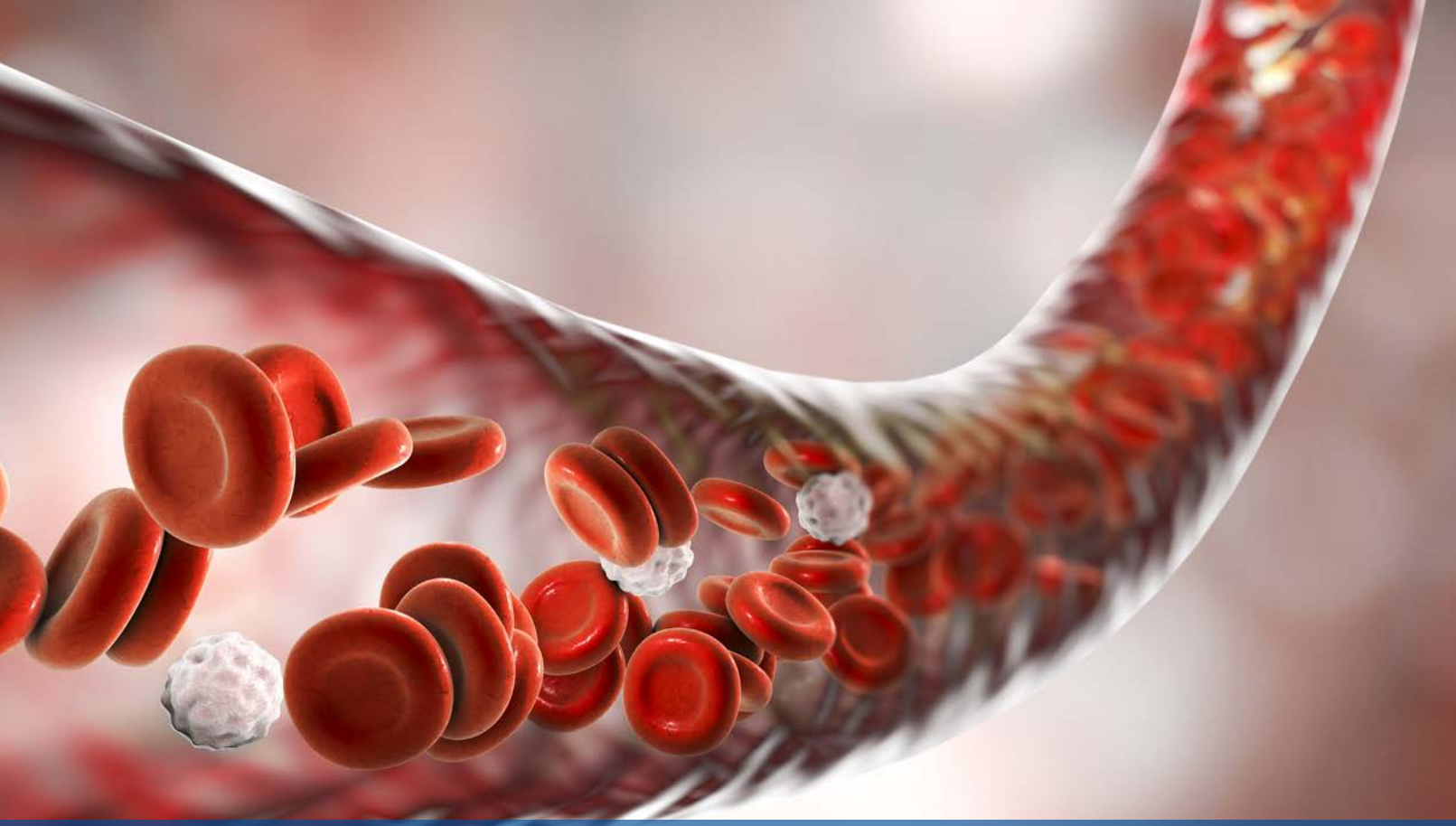
sphingotec
The Biomarker Company

Our Mission

To improve patient outcomes with innovative diagnostic solutions for acute care in real-time.

SphingoTec develops and markets innovative in vitro diagnostic (IVD) tests for novel and proprietary blood-based protein biomarkers for the diagnosis, outcome prediction and monitoring of acute medical conditions, such as acute heart failure, circulatory failure and acute kidney injury.

SphingoTec's first-in-class biomarker tests are made available on its proprietary whole-blood point-of-care Nexus IB10 platform for convenient and rapid testing in near-patient and laboratory settings alongside a broad standard-of-care test portfolio for acute care.



IB10 sphingotest® bio-ADM®

The assay for the endothelial function biomarker bioactive Adrenomedullin

IB10 sphingotest® bio-ADM® is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of bioactive Adrenomedullin (bio-ADM®) in human EDTA whole blood or plasma. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

The relevance of endothelial function in critical care

In critical care settings, one of the main causes of organ failure and ultimately mortality is loss of endothelial function, which is associated with leakage of blood vessels. Although the symptoms of loss of endothelial functions are well-known, there are currently no simple, blood-based detection methods established for monitoring the worsening and improvement of endothelial function.

bio-ADM® can easily be measured in the blood enabling the assessment of the endothelial function up to 48 hours before the symptoms become visible. Regular assessment of the bio-ADM® levels allows for the monitoring of critically ill patients. Elevated bio-ADM® blood levels predict both blood pressure drop resulting in shock as well as leaky vessels leading to the formation of edema (1a).

Decreasing levels of bio-ADM® reflect an improvement of the endothelial function, which is closely associated with the patient's clincal condition (1b).

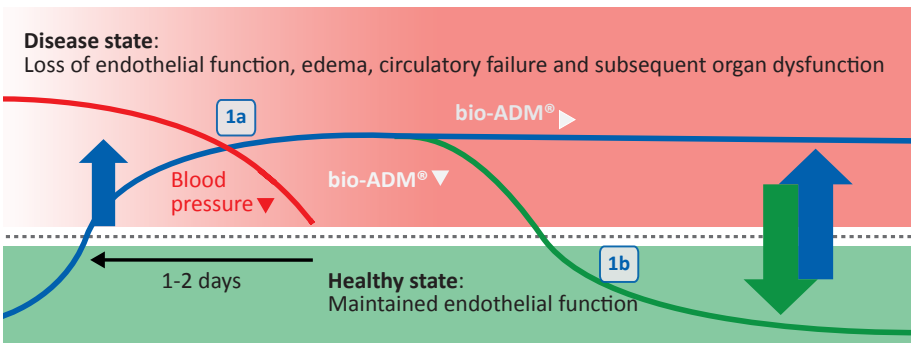
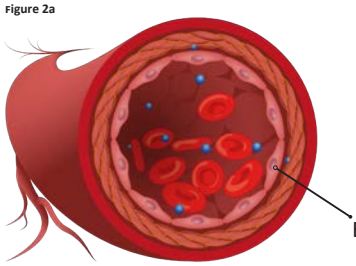


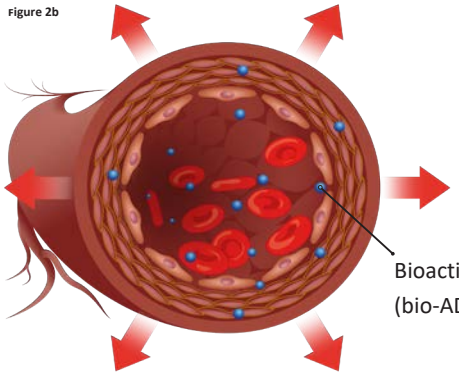
Figure 2a



Healthy State

Research has identified bioactive Adrenomedullin as a controlling hormone of the endothelial barrier, the interior wall protecting the blood vessels (2a). The median bio-ADM® concentration of 200 healthy subjects was 20.7 pg/mL; the 99th percentile was 43 pg/mL.[1]

Figure 2b



Disease State

In certain conditions such as septic shock[2], cardiogenic shock[3] or acute heart failure[4], the endothelial barrier becomes leaky, and additional bio-ADM® is produced to re-seal the barrier. However, bio-ADM® has a second function. It also expands the blood vessels, resulting in a dangerous blood pressure drop, which leads to shock and may ultimately escalate into multiple organ failure (2b).

bio-ADM®

- is a blood-based parameter for quantifying the blood levels of bioactive Adrenomedullin
- aids in the early prediction of vasopressor demand in critically ill patients
- allows monitoring of the endothelial function
- is independent from inflammation or any other comorbidities
- aids in the diagnosis of residual congestion
- has been validated in more than 22,000 patients

Whole Blood vs. Plasma Comparison

Passing-Bablok regression analysis comparing the whole blood concentrations vs. the corresponding plasma concentrations from the same subject samples:

Slope	1.03 (95% C.I. = [0.96 – 1.10])
y-intercept	7.0 pg/mL

Key Features

Reproducibility

Sample	Test Lot	Mean Level (pg/mL)	Total Precision CV (%)
1	A	58.8	15.0%
	B	53.5	16.8%
2	A	149.4	8.0%
	B	150.6	10.7%

Easy Handling

Sample Type	EDTA whole blood or plasma samples
Time to Result	20 minutes
Measuring Range	45 - 500 pg/mL
Limit of Detection	45 pg/mL
No High Dose Hook Effect	up to 100,000 pg/mL

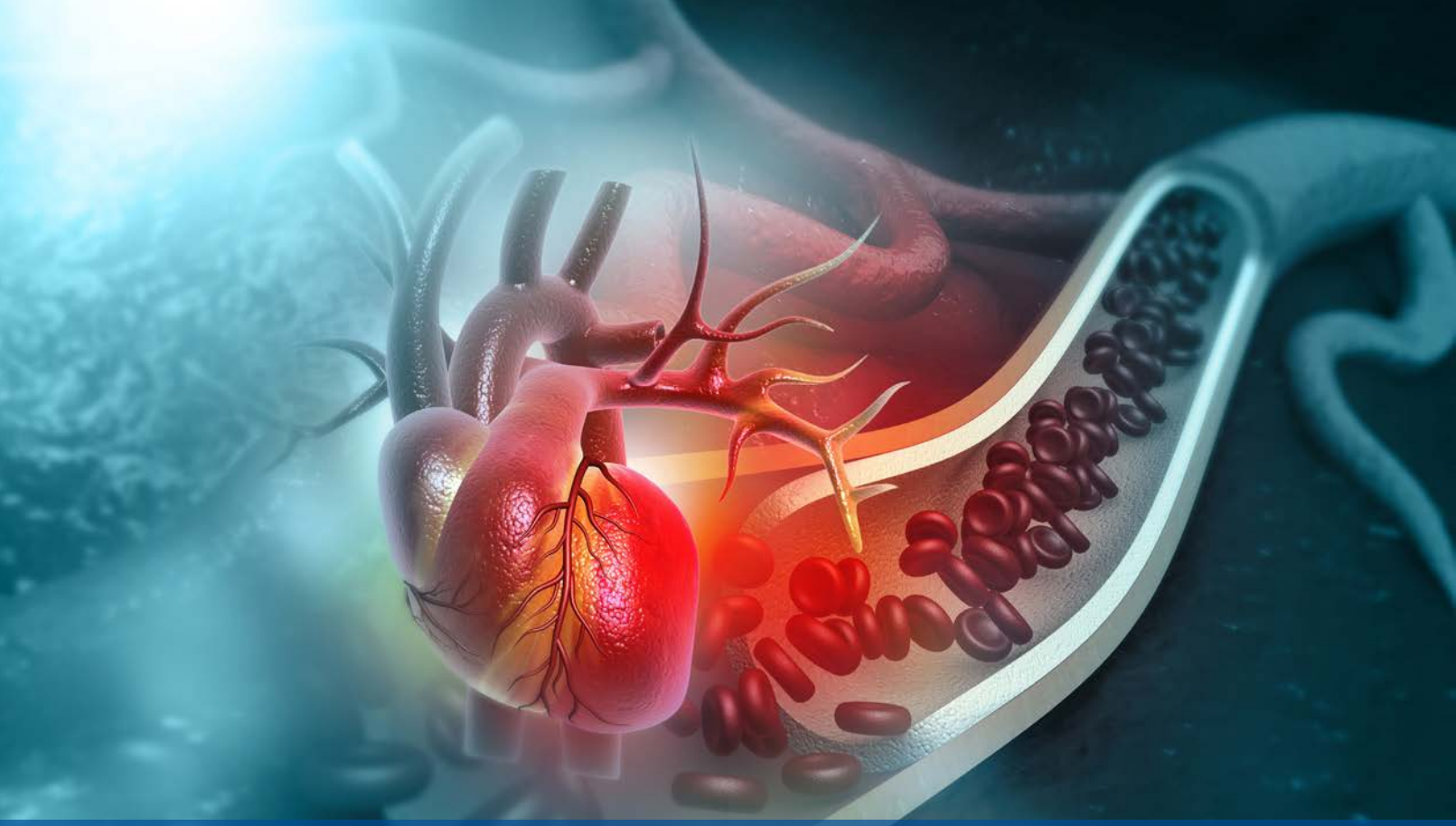
References

[1] Marino et al. (2014), Plasma adrenomedullin is associated with short-term mortality and vasopressor requirement in patients admitted with sepsis, Crit. Care, DOI: 10.1186/cc13731

[2] Geven et al. (2018), Vascular effects of adrenomedullin and the anti-adrenomedullin antibody adrecizumab in sepsis, Shock, DOI: 10.1097/SHK.0000000000001103

[3] Tolpannen et al. (2017), Adrenomedullin - a marker of impaired hemodynamics, organ dysfunction, and poor prognosis in cardiogenic shock, Ann Intensive Care, DOI: 10.1186/s13613-016-0229-2

[4] Ter Maaten et al. (2019), Bio-adrenomedullin as a marker of congestion in patients with new-onset and worsening heart failure, Eur J Heart Fail, DOI: 10.1002/ejhf.1437



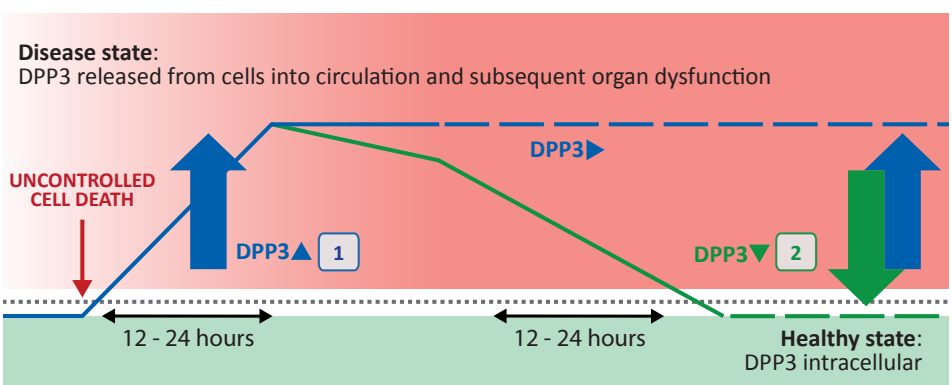
IB10 sphingotest® DPP3

The assay for measuring DPP3-release, a cause of cardiac depression

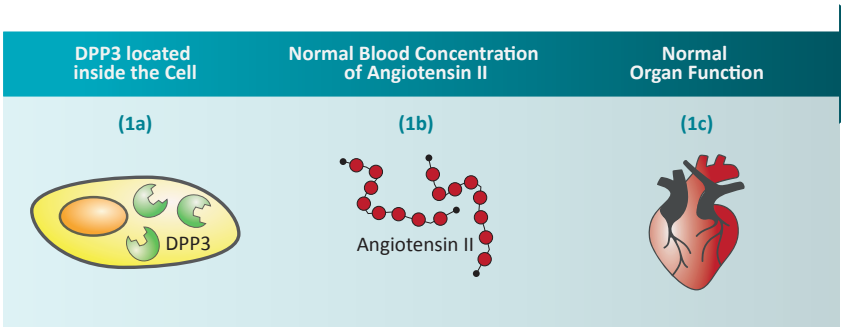
IB10 sphingotest® DPP3 is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of Dipeptidyl Peptidase 3 (DPP3) in human EDTA whole blood and plasma. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

The pathomechanism behind DPP3-release

Recently, a so far unknown disease mechanism leading to short-term organ failure was identified. According to the new findings, the release of the cardiac depressant factor DPP3 into the bloodstream plays a major role in sudden loss of heart function.[1,2] DPP3 is a natural enzyme that plays a vital role in the recycling of cellular proteins. When massive, uncontrolled cell death occurs, for example, in major surgeries, cardiogenic shock[1,4], sepsis, or burns[3], DPP3 is released into the bloodstream, having a toxic-like effect on the human biology. This is because in the bloodstream, DPP3 inactivates angiotensin II, a hormone that is important for the heart function. This inactivation is leading to hemodynamic instability and consequently cardiac depression.

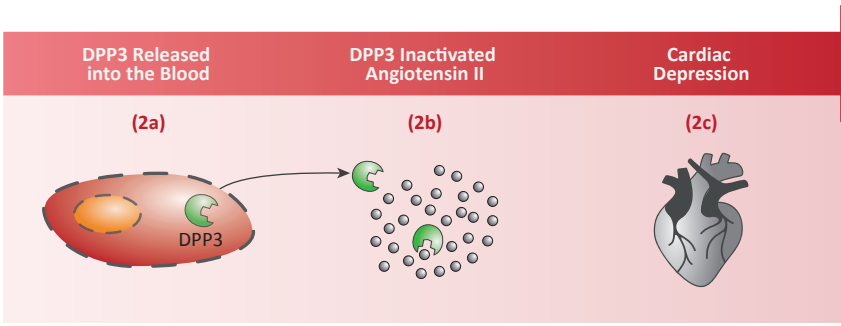


High or rising DPP3 blood levels **(1)**, determined with the IB10 sphingotest® DPP3 indicate worsening of the patient's status that can lead to short term organ failure and death. On the other hand, decreasing DPP3 levels **(2)** indicate a substantially reduced mortality risk.[1]



Healthy State

In healthy state, DPP3 is located intracellularly (1a) and active angiotensin II (1b) contributes to maintaining a normal heart function (1c). The median DPP3 concentration of 5,021 healthy subjects was 15 ng/mL; the upper normal range (97.5th percentile) was 40 ng/mL.



Disease State

In a disease state, uncontrolled cell death leads to the release of DPP3 **(2a)**. Angiotensin II is inactivated by DPP3 **(2b)**, which leads to haemodynamic instability and cardiac depression **(2c)**.

DPP3

- is a blood-based parameter for quantifying the DPP3 release into the blood stream
- aids in the guidance for induction or escalation of therapy
- aids in the stratification of patients at high risk to develop short-term organ dysfunction
- aids in the monitoring of treatment success

Whole Blood vs. Plasma Comparison

Passing-Bablok regression analysis comparing the whole blood concentrations vs. the corresponding plasma concentrations from the same subject samples:

Slope	1.09 (95% C.I. = [1.02 – 1.16])
y-intercept	-0.77 ng/mL

Key Features

Reproducibility

Sample	Test Lot	Mean Level (ng/mL)	Total Precision CV %
1	A	14.1	11.8
	B	14.1	8.2
2	A	31.9	7.2
	B	31.9	7.0
3	A	92.9	9.6
	B	93.5	8.3

Easy Handling

Sample Type	EDTA whole blood or plasma samples
Time to Result	20 minutes
Measuring Range	5 - 150 ng/mL
Limit of Detection	5 ng/mL
No High Dose Hook Effect	up to 6,000 ng/mL

References

[1] Deniau et al. (2019), Circulating dipeptidyl peptidase 3 is a myocardial depressant factor - dipeptidyl peptidase 3 inhibition rapidly and sustainably improves haemodynamics, Eur J Heart Fail, DOI: 10.1002/ejhf.1601.

[2] Magliocca et al. (2019), Dipeptidyl peptidase 3, a biomarker in cardiogenic shock and hopefully much more, Eur J Heart Fail, DOI: 10.1002/ejhf.1649

[3] Dépret et al. (2020), Circulating dipeptidyl peptidase-3 at admission is associated with circulatory failure, acute kidney injury and death in severely ill burn patients, Crit. Care,. DOI: 10.1186/s13054-020-02888-5.

[4] Takagi et al. (2019), Circulating dipeptidyl-peptidase 3 and alteration in hemodynamics in cardiogenic shock: Results from the OptimaCC Trial, Eur J Heart Fail., DOI: 10.1002/ejhf.1600

IB10 sphingotest® penKid®

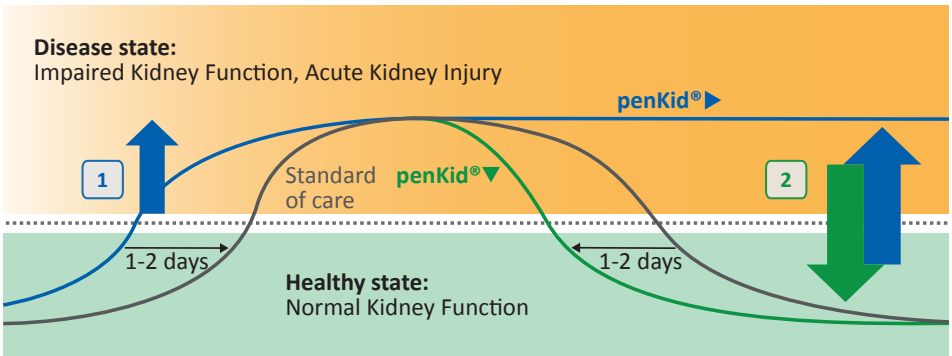
The assay for the kidney function biomarker Proenkephalin

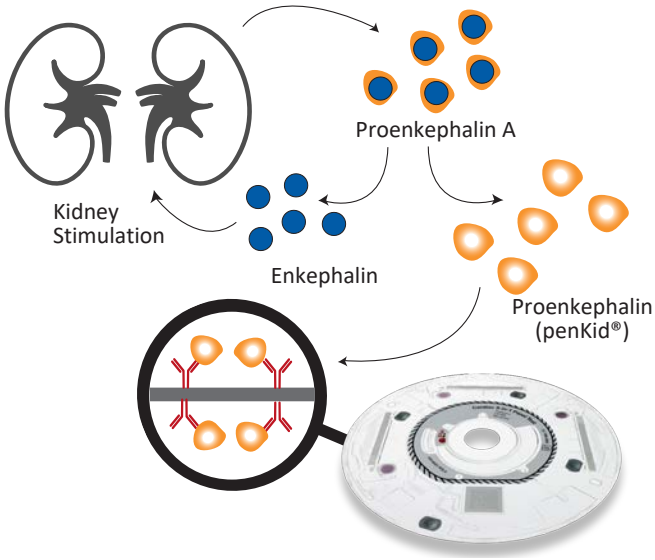
IB10 sphingotest® penKid® is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of Proenkephalin (penKid®) in human EDTA whole blood and plasma. The test is designed for professional use only and may be used on sites where near-patient testing is practiced.

Kidney function diagnostics with penKid®

Acute kidney injury affects 1 in 3 patients in intensive care units (ICU). Timely information on kidney function is therefore of high importance to early initiate nephron-protective strategies. Existing creatinine-based estimations of the glomerular filtration rate (eGFR) routinely used in critical care settings are unspecific, error-prone and have a substantial time delay. An emerging body of evidence demonstrates that the biomarker proenkephalin, detectable with the IB10 sphingotest® penKid® overcomes these limitations by indirectly measuring the levels of the kidney stimulating hormone enkephalin which reflects the true glomerular filtration rate (true GFR).[1,2]

Measuring penKid® levels reveals kidney function in real-time and offers a blood-based alternative for the in vivo measurement of true GFR. Independent of co-morbidities and the frequently occurring inflamation in critically ill patients, rising penKid® blood levels (1) predict acute kidney injury up to 48 hours earlier than today's standard of care and decreasing levels (2) show the normalization of kidney function.[3]





Diagnostic Principle

Kidney function is stimulated by the hormone enkephalin which remained hard to detect. penKid® overcomes this limitation by measuring a stable fragment that results out of enkephalin processing. The median penKid® concentration of 4,643 healthy subjects was 45 pmol/L; the 99th percentile was 80 pmol/L.[4]

penKid®

- is a blood-based parameter that correlates with true GFR
- admission levels provide direct information about kidney function
- relative changes in blood concentration promptly show the improvement or deterioration of kidney function
- can be used without restriction in all patients on ICU
- predicts acute kidney injury up to 48 hours before the standard of care
- was validated in more than 40,000 patients

Whole Blood vs. Plasma Comparison

Passing-Bablok regression analysis comparing the whole blood concentrations vs. the corresponding plasma concentrations from the same subject samples:

Slope	1.06 (95% C.I. = [0.83 – 1.17])
y-Intercept	-9.30 pmol/L

Key Features

Reproducibility

Sample	Test Lot	Mean Level (pmol/L)	Total Precision CV %
1	A	99	10.5
	B	97	9.8
2	A	227	9.4
	B	228	11.2

Easy Handling

Sample Type	EDTA whole blood or plasma samples
Time to Result	20 minutes
Measuring Range	50 - 500 pmol/L
Limit of Detection	50 pmol/L
No High Dose Hook Effect	up to 250,000 pmol/L

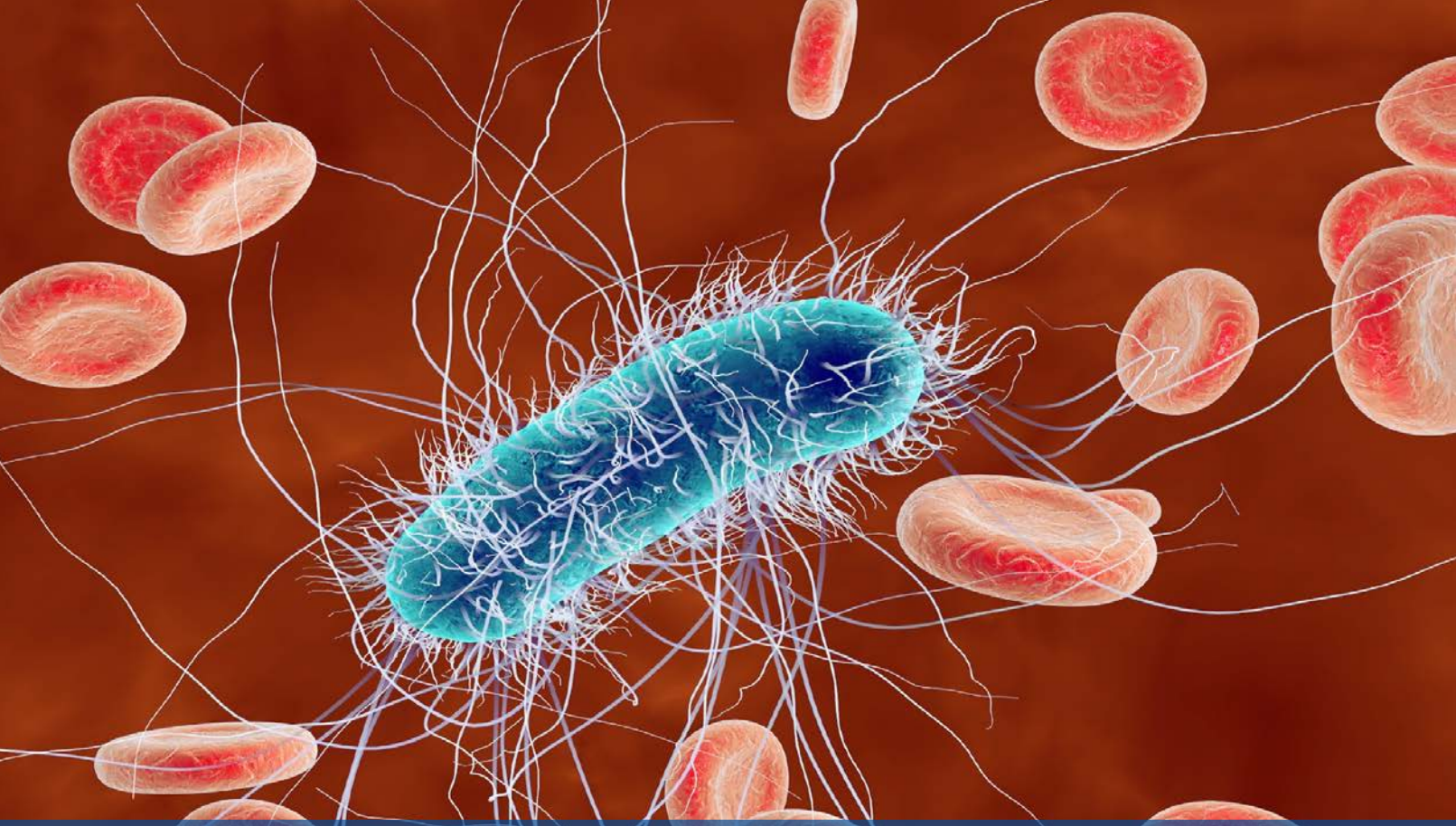
References

[1] Beunders et al. (2017), Proenkephalin (PENK) as a novel biomarker for kidney function, JALM, DOI: 10.1373/jalm.2017.023598

[2] Beunders et al. (2020), Proenkephalin compared to conventional methods to assess kidney function in critically ill sepsis patients, Shock, DOI: 10.1097/SHK.0000000000001510

[3] Hollinger et al. (2018), Proenkephalin A 119-159 (Penkid) is an early biomarker of septic acute kidney injury - the kidney in sepsis and septic shock (Kid-SSS) study, Kidney Int Rep, DOI: 10.1016/j.ekir.2018.08.006

[4] Marino et al. (2015), Diagnostic and short-term prognostic utility of plasma proenkephalin (pro-ENK) for acute kidney injury in patients admitted with sepsis in the emergency department , J Nephrol, DOI 10.1007/s40620-014-0163-z



IB10 sphingotest® PCT

The assay for the in vitro quantitative determination of Procalcitonin

IB10 sphingotest® PCT is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of Procalcitonin (PCT) in the concentration range of 0.3 µg/L to 10 µg/L in human EDTA whole blood or plasma. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

Clinical Significance

Sepsis is the most common cause of death in intensive care units (ICU) with a mortality rate up to 50% depending on severity. The earlier sepsis is identified and treated, the better the prognosis.[1] PCT levels in sepsis are often greater than 1 µg/L and reach values of 10 µg/L or even higher with severe sepsis and septic shock. As the septic infection resolves, the PCT levels also return to ranges < 0.5 µg/L, with a half-life of 24 hours. **The IB10 sphingotest® PCT** is only intended for the diagnosis of sepsis, the assessment of the degree of severity, and monitoring of the change of sepsis severity.[2] This assay is neither suitable nor intended for other applications and/or uses.

Expected Values

All measurements with EDTA whole blood samples collected from 100 apparently healthy individuals were found as < 0.3 µg/L for the IB10 sphingotest® PCT.

Diagnosis of Sepsis[3]

PCT (µg/L)	Analysis
< 0.5	Local bacterial infection is possible. Systemic infection (sepsis) is not likely. Low risk for progression to severe systemic infection (severe sepsis).
	Levels below 0.5 µg/L do not exclude an infection, because localized infections (without systemic signs) may be associated with such low levels.
> 0.5 and < 2	Systemic infection (sepsis) is possible, but various conditions are known to induce PCT as well.
	Moderate risk for progression to severe systemic infection (severe sepsis). The patient should be closely monitored both clinically and by re-assessing PCT within 6-24 hours.
> 2 and < 10	Systemic infection (sepsis) is likely, unless other causes are known.
	High risk for progression to severe systemic infection (severe sepsis).
> 10	Important systemic inflammatory response, almost exclusively due to severe bacterial sepsis or septic shock.
	High likelihood of severe sepsis or septic shock.

Key Features

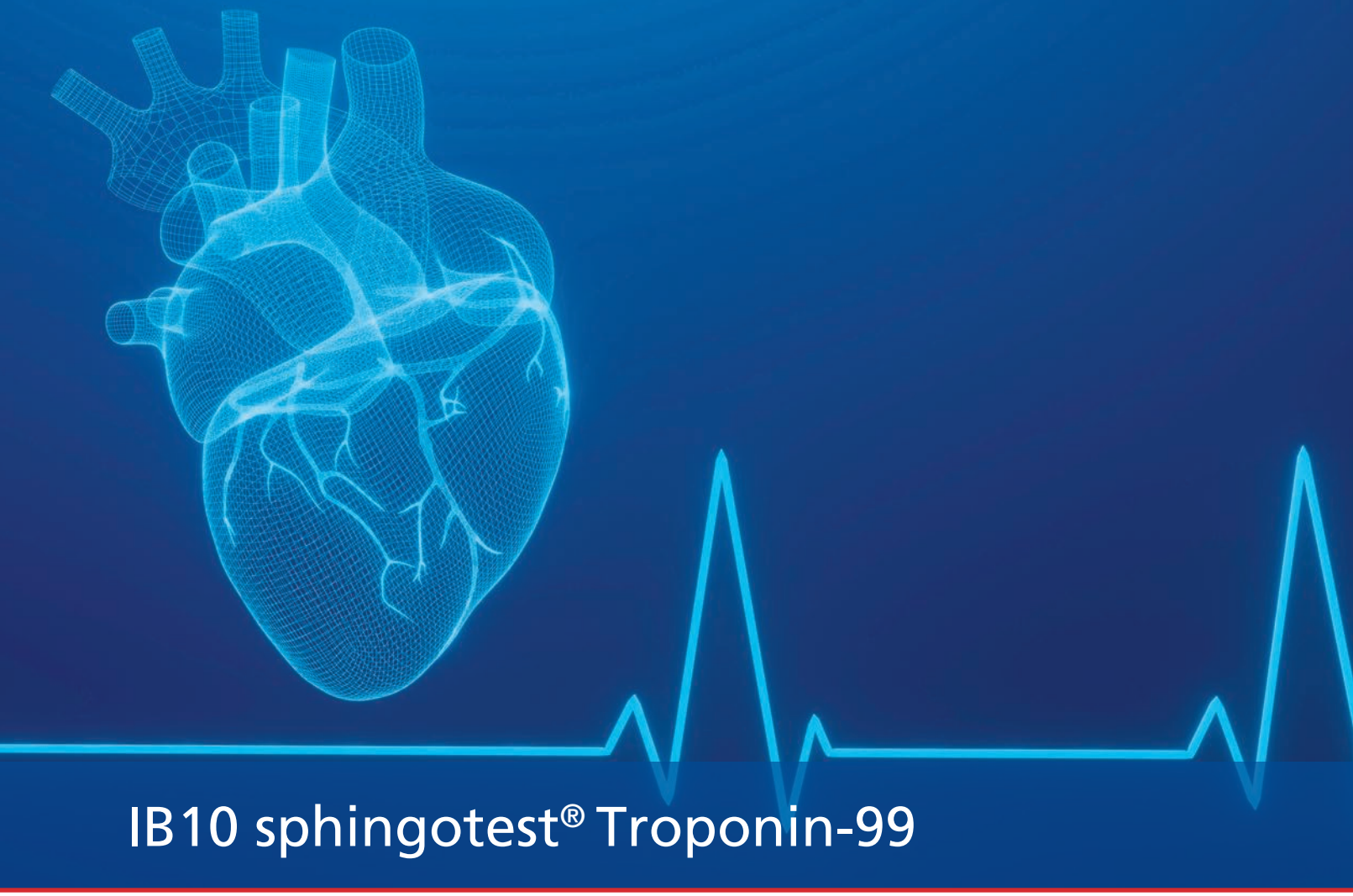
Easy Handling	
Sample Type	EDTA whole blood or plasma samples
Time to Result	20 minutes
Measuring Range	0.3 - 10 µg/L
Limit of Detection	0.3 µg/L
No High Dose Hook Effect	up to 10,000 µg/L

References

[1] Russell (2006), Management of sepsis; N Engl J Med, DOI: 10.1056/nejmra043632

[2] Harbarth et al. (2001), Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis, Am J Respir Crit Care Med, DOI: 10.1164/ajrccm.164.3.2009052

[3] Meisner (2010), Procalcitonin (PCT) - biochemistry and clinical diagnosis, First Edition Uni-med, ISBN: 978-3-8374-1241-3



IB10 sphingotest® Troponin-99

The assay for the in vitro quantitative determination of Cardiac Troponin I

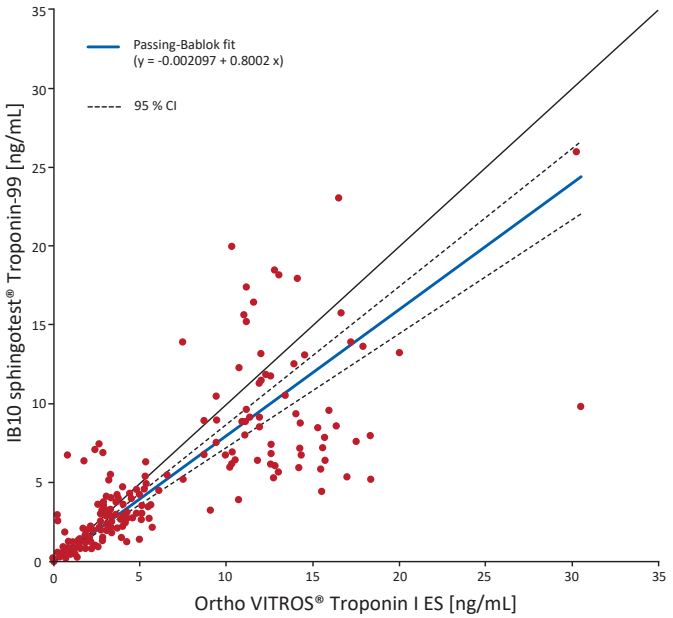
IB10 sphingotest® Troponin-99 is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of Cardiac Troponin I (cTnI) in human Lithium-Heparin whole blood and plasma. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

Clinical Significance

cTnI determination aids in the diagnosis of myocardial infarction (MI) and patients with non-ST-segment elevation (NSTEMI) acute coronary syndrome (ACS).[1,2] Elevated cTnI levels in the NSTEMI ACS sub-population correlate with the relative risk of mortality, MI or increased probability of ischemic events requiring urgent revascularization procedures. For patients with chronic or acute decompensated heart failure (HF), measurements of cTnI provide complementary information to assist in patient evaluation and management.

Method Comparison

Correlation between IB10 sphingotest® Troponin-99 and Ortho VITROS® Troponin I ES.



Expected Values

From a population of 224 individuals, the IB10 sphingotest® Troponin-99 Test was used to determine the concentration upper reference limits of cTnI. This population included apparently healthy individuals.

Upper Reference Limit

The 99th percentile upper reference limit is 0.10 ng/mL. Each laboratory should establish a reference range that represents the patient population that is to be evaluated at their facility.

Whole Blood vs. Plasma Comparison

Passing-Bablok regression analysis comparing the whole blood concentrations vs. the corresponding plasma concentrations from the same subject samples:

Slope	1.0 (95% C.I. = [0.93 – 1.07])
y-intercept	0.01 ng/mL

Key Features

Reproducibility

Sample/Marker	Mean Level (ng/mL)	Total Precision CV (%)
1	0.46	12.6
2	4.43	10.1

Easy Handling

Sample Type	Lithium-Heparin whole blood or plasma samples
Time to Result	20 minutes
Measuring Range	0.05 - 30 ng/mL
Limit of Detection	0.05 ng/mL
No High Dose Hook Effect	up to 500 ng/mL

References

[1] Thygesen et al. (2007), Joint ESC/ACCF/AHA/WHF Task force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction, Eur Heart J DOI: 10.1093/eurheartj/ehm355, Circulation DOI: 10.1161/CIRCULATIONAHA.107.187397, J Am Coll Cardiol DOI: 10.1016/j.jacc.2007.09.011

[2] Larue et al. (1993), Cardiac specific immunoenzymatic assay of Troponin-99 in the early phase of acute myocardial infarction, Clin Chem, 39:972-9.

IB10 sphingotest® NT-proBNP

The assay for the in vitro quantitative determination of N-terminal pro-brain natriuretic peptide

IB10 sphingotest® NT-proBNP is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of N-terminal pro-brain natriuretic peptide (NT-proBNP) in human whole blood or plasma using EDTA or Lithium-Heparin as the anticoagulant. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

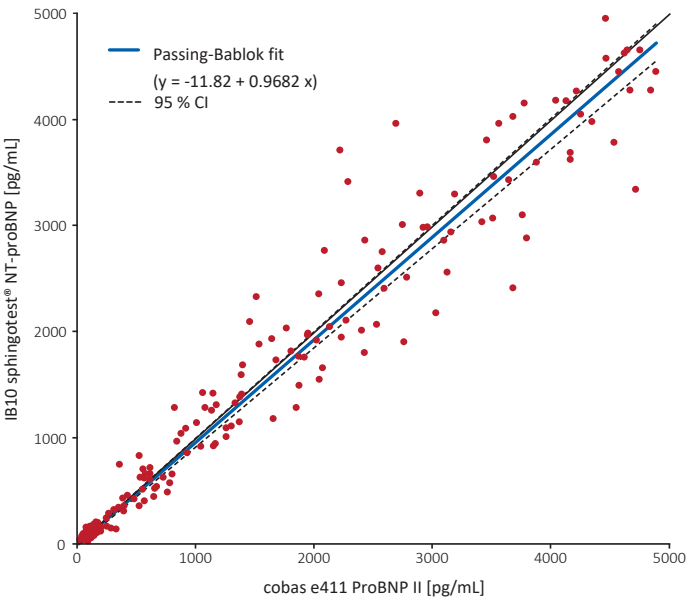
Clinical Significance

NT-proBNP is a valuable diagnostic and prognostic marker for cardio-vascular diseases, especially in patients with a New York Heart Association (NYHA) Class I-IV Congestive Heart Failure (CHF).[1,2]

The measurement of NT-proBNP is an important tool for aiding in the diagnosis and the assessment of the severity of patients with CHF.[3,4]

Method Comparison

Correlation between IB10 sphingotest® NT-proBNP and Roche Elecsys® ProBNP II (cobas e411)



Expected Values

Recommended Decision Threshold Values:

- Patients under 75 years of age: 125 pg/mL
- Patients 75 years of age and older: 450 pg/mL

Each laboratory should establish a reference range that represents the patient population that is to be evaluated.

Whole Blood vs. Plasma Comparison

Passing-Bablok regression analysis comparing the whole blood concentrations vs. the corresponding plasma concentrations from the same subject samples:

Slope	1.01 (95% C.I. = [0.97 – 1.06])
y-Intercept	2.72 pg/mL

Key Features

Reproducibility

Sample	Mean Level (pg/mL)	Total Precision CV (%)
1	130.1	13.8
2	1615.8	11.6

Easy Handling

Sample Type	EDTA or Lithium-Heparin whole blood or plasma samples
Time to Result	20 minutes
Measuring Range	30 - 5,000 pg/mL
Limit of Detection	30 pg/mL
No High Dose Hook Effect	up to 300,000 pg/mL

References

[1] Costello-Boerrigter et al. (2005), The prognostic value of N-terminal proB-type natriuretic peptide, Nat Clin Pract Cardiovasc Med, DOI: 10.1038/ncpcardio0156

[2] Cowie et al. (2003), Clinical applications of B-type natriuretic peptide (BNP) testing, Eur Heart J, DOI: 10.1016/s0195-668x(03)00476-7

[3] Mair et al. (2001), The Impact of cardiac natriuretic peptide determination on the diagnosis and management of heart failure, Clin Chem Lab Med, DOI: 10.1515/CCLM.2001.093

[4] McDonagh et al. (2004), NT-proBNP and the diagnosis of heart failure: a pooled analysis of three European epidemiological studies, Eur J Heart Fail, DOI: 10.1016/j.ejheart.2004.01.010

IB10 sphingotest® D-Dimer

The assay for the in vitro quantitative determination of D-Dimer

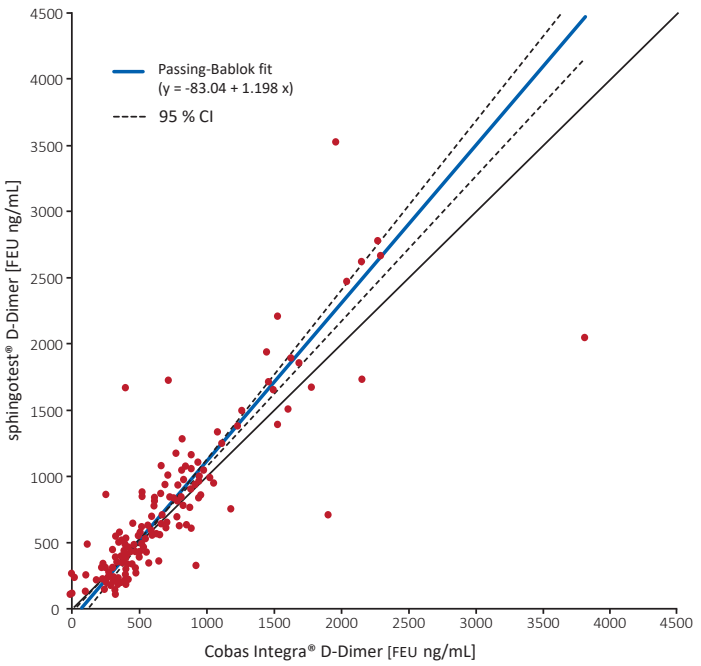
IB10 sphingotest® D-Dimer is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of cross-linked fibrin degradation products containing D-Dimer in Lithium-Heparin or Citrate whole blood or plasma. The IB10 sphingotest® D-Dimer reports results in Fibrinogen Equivalent Units (FEU) ng/mL. It is commonly accepted that 1 D-Dimer Unit (D-DU) is equal to 2 FEU. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

Clinical Significance

D-Dimer determinations aid in the quantitative assessment and evaluation of patients presenting with clinical symptoms of Venous Thromboembolism (VTE) including severely evolving disseminated intravascular coagulation, pulmonary embolism and deep vein thrombosis. Values at or below the upper limit of a healthy reference population are highly predictive of exclusion of VTE as a cause of symptoms.[1,2,3]

Method Comparison

Equivalence study between IB10 sphingotest® D-Dimer and Roche Cobas Integra® system.



Expected Values

From a population of 244 individuals, the IB10 sphingotest® D-Dimer test was used to determine the concentration upper reference limit of D-Dimer. This population included apparently healthy individuals. The 95th percentile upper reference limit, using lithium heparin as anticoagulant, is 446.8 FEU ng/mL. The IB10 sphingotest® D-Dimer reports results in FEU ng/mL. It is comonly accepted that 1 D-DU is equal to 2 FEU.

Each laboratory should establish a reference range that represents the patient population that is to be evaluated at their facility.

Whole Blood vs. Plasma Comparison

Comparison studies were performed using whole blood and plasma samples using either Lithium-Heparin or Citrate as anticoagulant. When performing a Passing-Bablok regression analysis comparing the whole blood concentrations vs. the corresponding plasma concentrations from the same subject samples, the results were:

Lithium-Heparin = 1.03 (Lithium-Heparin plasma) - 9.1 ng/mL
Citrate = 1.04 (Citrate plasma) - 4.85 ng/mL

Key Features

Reproducibility

Sample	Mean level (FEU ng/mL)	Total precision CV (%)
1	452.6	6.7
2	843.9	9.0

Easy Handling

Sample Type	Lithium-Heparin or Citrate whole blood and plasma samples
Time to Result	20 minutes
Measuring Range	100 - 4,000 FEU ng/mL
Limit of Detection	100 FEU ng/mL
No High Dose Hook Effect	up to 40,000 FEU ng/mL

References

[1] Anderson et al. (1991), A population-based perspective of the hospital incidence and case-fatalities of deep vein thrombosis and pulmonary embolism, Arch Intern Med, DOI: 10.1001/archinte.1991.00400050081016

[2] Kyrle et al. (2005) Deep vein thrombosis. Lancet, DOI: 10.1016/S0140-6736(05)71880-8

[3] Carson et al. (1992) The clinical course of pulmonary embolism, N Engl J Med, DOI: 10.1056/NEJM199205073261902

IB10 sphingotest® Shortness of Breath

The panel assay for the in vitro quantitative determination of Cardiac Troponin I, N-terminal pro-brain natriuretic peptide and D-Dimer

IB10 sphingotest® Shortness of Breath is a rapid point-of-care (POC) immunoassay for the in vitro quantitative determination of Cardiac Troponin I (cTnI), N-terminal pro-brain natriuretic peptide (NT-proBNP) and D-Dimer in human Lithium-Heparin whole blood and plasma. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

Clinical Significance

IB10 sphingotest® Shortness of Breath is intended as an aid in the differential diagnosis and prognostic assessment of patients with symptoms of chest pain, typically accompanied by respiratory distress. Individually or in conjunction with each other, these markers: aid in the diagnosis of myocardial infarction (MI), aid in the risk stratification of patients with acute coronary syndrome (ACS) including prediction of the likelihood of developing heart failure (HF), aid in the diagnosis, assessment of severity and likelihood of survival in HF[1-3], and aid in determining the probability of rule-out of patients presenting with clinical symptoms of venous thromboembolism (VTE) including pulmonary embolism (PE) and deep vein thrombosis.[4]

Expected Values

Upper Reference Limit - cTnI

From a population of 224 individuals, IB10 sphingotest® Shortness of Breath was used to determine the concentration upper reference limit of cTnI. This population included apparently healthy individuals. The 99th percentile upper reference limit is 0.10 ng/mL.

Recommended Decision Threshold Values - NT-proBNP

From calibration based on the reference Roche Elecsys® proBNP assay as measured on both the Roche Elecsys® and the Ortho VITROS® Immunodiagnostic Systems, the recommended Decision Threshold Values for the IB10 sphingotest® Shortness of Breath (NT-proBNP) are:

Patients under 75 years of age	125 pg/mL
Patients 75 years of age and older	450 pg/mL

Upper Reference Limit - D-Dimer

From a population of 244 individuals, the IB10 sphingotest® Shortness of Breath was used to determine the concentration upper reference limit of D-Dimer. The 95th percentile upper reference limit, using lithium heparin as anti-coagulant, is 446.8 Fibrinogen Equivalent Units (FEU) ng/mL. It is comonly accepted that 1 D-DU is equal to 2 FEU.

Key Features

Reproducibility

Marker/Sample		Mean Level	Total Precision CV (%)
cTnI	1	0.46 ng/mL	12.6
	2	4.43 ng/mL	10.1
NT-proBNP	1	130.07 pg/mL	13.8
	2	1615.8 pg/mL	11.6
D-Dimer	1	452.6 FEU ng/mL	6.7
	2	843.9 FEU ng/mL	9.0

Method Comparison

Correlation between IB10 sphingotest® Shortness of Breath and Ortho VITROS® Troponin I ES, Roche Cobas e411 NT-proNTP and Cobas Integra D-Dimer.

cTnI	IB10 = 0.80 (95% C.I. = [0.72-0.87]) VITROS® - 0.002 ng/mL
NT-proBNP	IB10 = 0.97 (95% C.I. = [0.93-1.00]) Cobas e411 - 11.82 pg/mL
D-Dimer	IB10 (FEU ng/mL) = 1.20 (95% C.I. = [1.10-1.28]) Cobas Integra - 83.04 ng/mL

Whole Blood vs. Plasma Comparison

A comparison study was performed using whole blood and plasma samples. Using a Passing-Bablok regression analysis comparing the whole blood concentrations (WB) vs. the corresponding plasma concentrations (PL) from the same subject samples, the following relationships were determined:

cTnI	WB = 1.00 (95% C.I. = [0.93-1.07]) PL + 0.01 ng/mL
NT-proBNP	WB = 1.107 (95% C.I. = [0.94-1.31]) PL + 5.20 pg/mL
D-Dimer	WB = 1.03 (95% C.I. = [0.979-1.087]) PL - 9.1 ng/mL

Easy Handling

Sample Type	Lithium-Heparin whole blood and plasma samples
Time to Result	20 minutes
Measuring Range	
cTnI	0.05 – 30 ng/mL
NT-proBNP	30 – 5,000 pg/mL
D-Dimer	100 – 4,000 FEU ng/mL
Limit of Detection	
cTnI	0.05 ng/mL
NT-proBNP	30 pg/mL
D-Dimer	100 FEU ng/mL
No High Dose Hook Effect	
cTnI	up to 500 ng/mL
NT-proBNP	up to 300,000 pg/mL
D-Dimer	up to 40,000 FEU ng/mL

References

[1] DeLemos et al. (2001), The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes, N Engl J Med, DOI: 10.1056/NEJMoa011053

[2] Peacock et al. (2008), Cardiac troponin and outcome in acute heart failure, N Engl J Med, DOI: 10.1056/NEJMoa0706824

[3] Sakhuja et al. (2007) Amino-terminal pro-brain natriuretic peptide, brain natriuretic peptide, and troponin T for prediction of mortality in acute heart failure, Clin Chem, DOI: 10.1373/clinchem.2006.074047

[4] Kyrle et al. (2005), Deep vein thrombosis, Lancet, DOI: 10.1016/S0140-6736(05)71880-8

IB10 sphingotest® 3-in-1 Cardiac

The panel assay for the in vitro quantitative determination of Cardiac Troponin I, CK-MB and Myoglobin

IB10 sphingotest® 3-in-1 Cardiac is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of Cardiac Troponin I (cTnI), Creatine kinase-MB (CK-MB) and Myoglobin, in human Lithium-Heparin whole blood and plasma. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

Clinical Significance

This panel of three cardiac markers enhances the reliability of earlier identification and risk stratification of patients presenting with chest pain compared to a single marker.[1,2] Measurements of cardiac protein markers are essential for the accurate diagnosis of Acute Coronary Syndrome (ACS) in the absence of well-defined electrocardiographic ST-segment elevations.[3]

Method Comparison

Correlation between IB10 sphingotest® 3-in-1 Cardiac and Ortho VITROS® Troponin I ES, Myoglobin and CK-MB Tests.

cTnI	IB10 = 0.80 (95% C.I. = [0.72-0.87]) VITROS - 0.002 ng/mL
CK-MB	IB10 = 1.29 (95% C.I. = [1.11-1.48]) VITROS - 0.53 ng/mL
Myoglobin	IB10 = 1.00 (95% C.I. = [0.87-1.15]) VITROS - 5.11 ng/mL

Whole Blood vs. Plasma Comparison

A comparison study was performed using whole blood and plasma samples. Using a Passing-Bablok regression analysis comparing the whole blood (WB) concentrations vs. the corresponding plasma concentrations (PL) from the same subject samples, the following relationships were determined:

cTnI	WB = 1.00 (95% C.I.= [0.93-1.07]) PL + 0.01 ng/mL
CK-MB	WB = 1.17 (95% C.I.= [1.09-1.29]) PL - 0.19 ng/mL
Myoglobin	WB = 0.92 (95% C.I.= [0.83-1.04]) PL + 0.00 ng/mL

Key Features

Reproducibility

Marker/Sample		Mean Level (ng/mL)	Total Precision CV (%)
cTnI	1	0.46	12.6
	2	4.43	10.1
CK-MB	1	7.13	10.3
	2	13.33	11.5
Myoglobin	1	106.1	12.1
	2	202.7	12.7

Expected Values

From a population of 224 individuals, the IB10 sphingotest® 3-in-1 Cardiac was used to determine the concentration upper reference limits of cTnI, CK-MB and Myoglobin. This population included apparently healthy individuals.

cTnI	0.10 ng/mL (99th reference percentile)
CK-MB	8.58 ng/mL (95th reference percentile)
Myoglobin	99.84 ng/mL (95th reference percentile)

Each laboratory should establish a reference range that represents the patient population that is to be evaluated at their facility.

Easy Handling

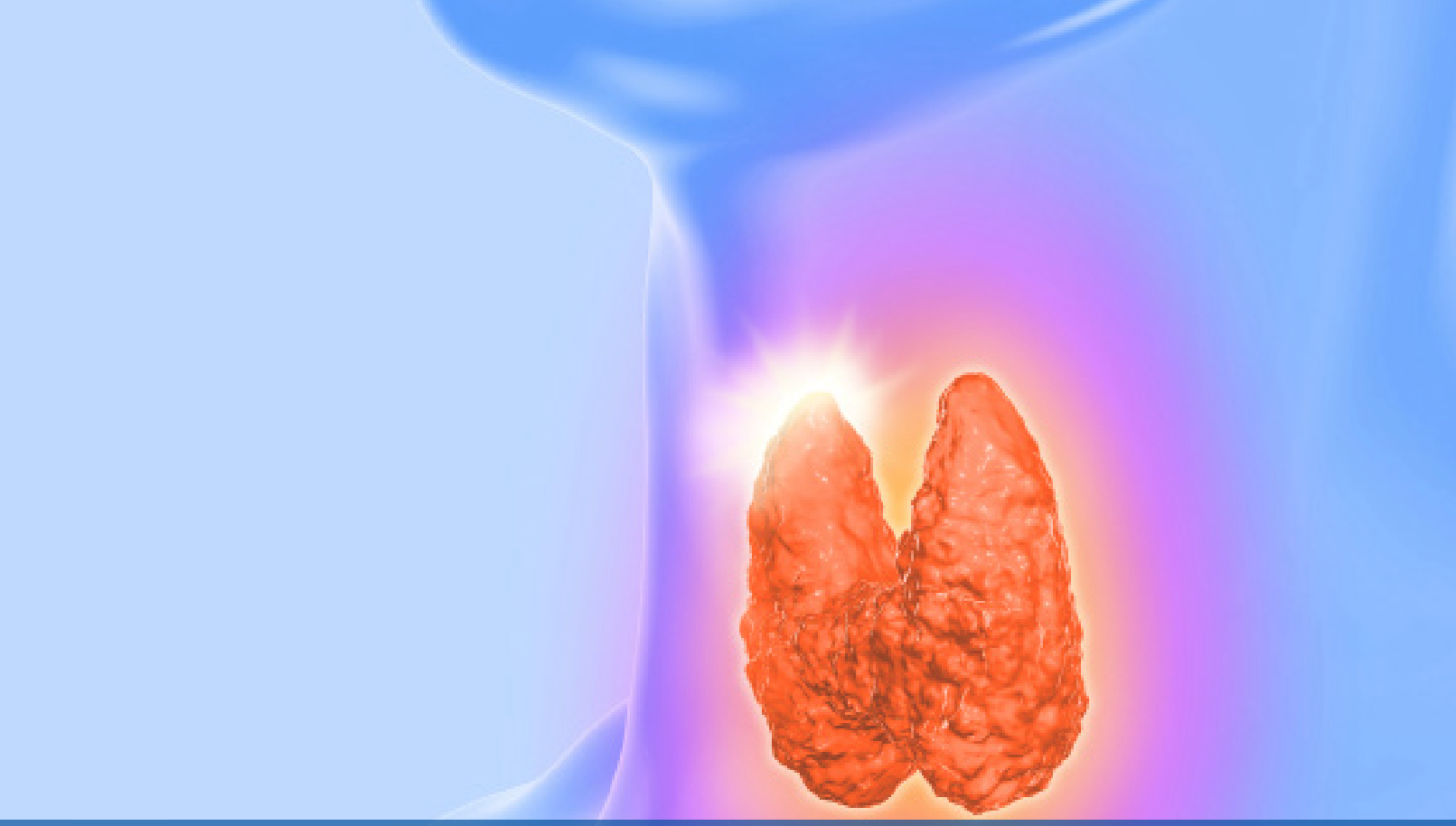
Sample Type	Lithium-Heparin whole blood and plasma samples
Time to Result	20 minutes
Measuring Range	
cTnI	0.05 - 30 ng/mL
CK-MB	2.0 - 60 ng/mL
Myoglobin	30.0 - 500 ng/mL
Limit of Detection	
cTnI	0.05 ng/mL
CK-MB	2.0 ng/mL
Myoglobin	30.0 ng/mL
No High Dose Hook Effect	
cTnI	up to 500 ng/mL
CK-MB	up to 200 ng/mL
Myoglobin	up to 4,000 ng/mL

References

[1] Newby et al. (2001), Bedside multimarker testing for risk stratification in chest pain patients – the chest pain evaluation by creatine kinase-MB, myoglobin and troponin I (CHECKMATE) study, Circulation, DOI: 10.1161/01.cir.103.14.1832

[2] Apple et al. (1995), Cardiac troponin, CK-MB and myoglobin for the early detection of acute myocardial infarction and monitoring of reperfusion following thrombolytic therapy, Clin Chim Acta, DOI: 10.1016/0009-8981(95)06064-k

[3] Thygesen et al. (2007), Universal definition of myocardial infarction, Eur Heart J, DOI: 10.1093/eurheartj/ehm355



IB10 sphingotest® TSH

The assay for the in vitro quantitative determination of thyroid-stimulating hormone

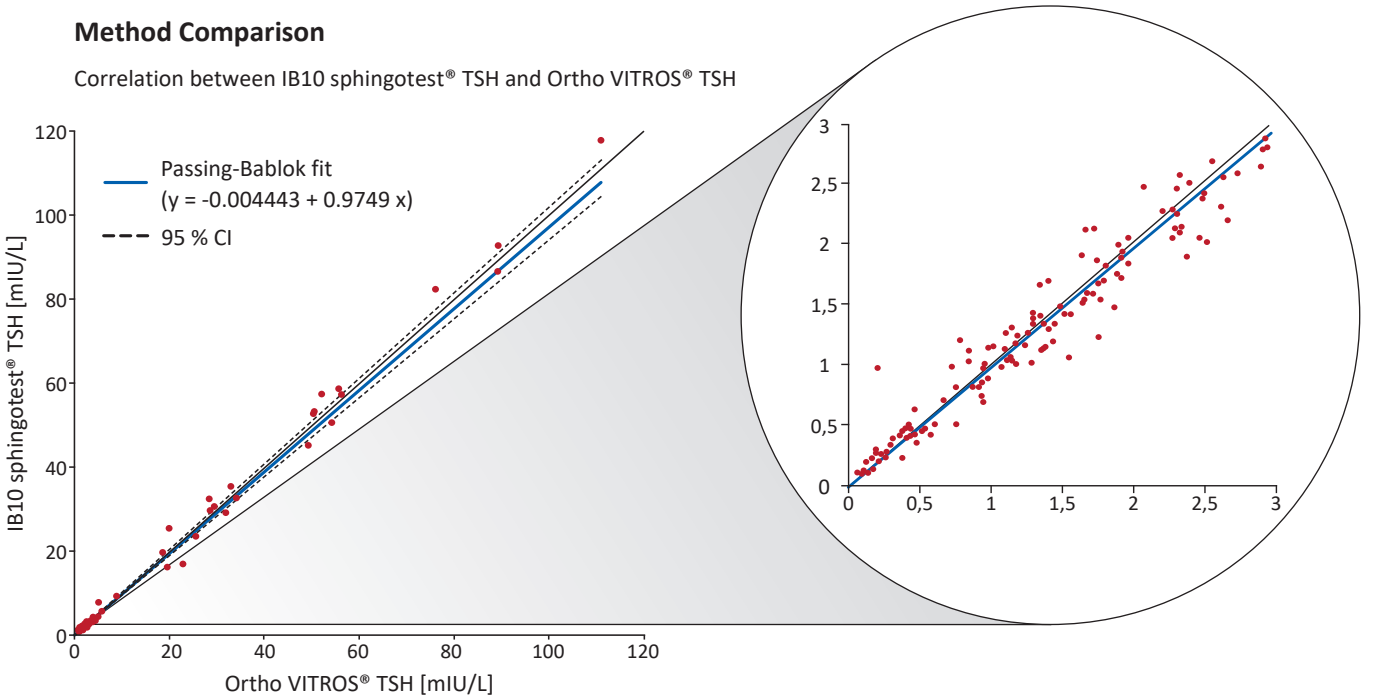
The **IB10 sphingotest® TSH** is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of thyroid stimulating hormone (TSH) in human Lithium-Heparin whole blood and plasma. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

Clinical Significance

TSH is recognized as a sensitive indicator of thyroid status and thus the TSH assay has been widely adopted as the front-line thyroid function test.[1-3] A normal TSH result excludes suspected thyroid disease in ambulatory patients with intact hypothalamic and pituitary function. Whereas elevated and suppressed TSH results are diagnostic of hypo- and hyperthyroidism.[4] Functional sensitivity of 0.11 mIU/L and as such can be classified as a 2nd generation assay. It is able to differentiate between hyperthyroid and euthyroid conditions.

Method Comparison

Correlation between IB10 sphingotest® TSH and Ortho VITROS® TSH



Expected Values

Reference Range(s)		
Premature Infants (28-36 weeks)		0.7 - 27.0 mIU/L
Term Infants (>37 weeks)	1-4 days	1.00 - 39.00 mIU/L
	2-20 weeks	1.70 - 9.10 mIU/L
	5 months - 20 years	0.70 - 6.40 mIU/L
Adults	21-54 years	0.40 - 4.20 mIU/L
	55-87 years	0.50 - 8.90 mIU/L
Pregnancy	First Trimester	0.30 - 4.50 mIU/L
	Second Trimester	0.50 - 4.60 mIU/L
	Third Trimester	0.80 - 5.20 mIU/L

As a guide, the following ranges were determined. The euthyroid reference interval for IB10 sphingotest® TSH was determined as the central 95% of the measurements with human plasma samples collected from 265 apparently healthy individuals.

2.5th percentile (mIU/L)	97.5th percentile (mIU/L)	Median (mIU/L)
0.25	3.85	1.43

Whole Blood vs. Plasma Comparison

Passing-Bablok regression analysis comparing the whole blood concentrations vs. the corresponding plasma concentrations from the same subject samples:

Slope	0.99 (95% C.I. = [0.96 – 1.02])
y-Intercept	-0.03 mIU/L

Key Features

Reproducibility

Sample / Marker		Mean Level (mIU/L)	Total Precision CV %
1	A	3.91	6.1
	B	3.98	6.3
2	A	44.72	7.8
	B	47.87	8.4

Easy Handling

Sample Type	Lithium-Heparin whole blood or plasma samples
Time to Result	20 minutes
Measuring Range	0.11 - 120 mIU/L
Limit of Detection	0.11 mIU/L
No High Dose Hook Effect	up to 8,000 mIU/L

References

[1] Surks et al. (1990), American Thyroid Association Guidelines for the use of laboratory tests in thyroid disorders, JAMA, DOI: 10.1001/jama.1990.03440110095035

[2] Keffer (1996), Preanalytical considerations in testing thyroid function, Clin Chem, DOI: 10.1093/clinchem/42.1.125.

[3] John et al. (1988), Evaluation of a new strategy for detection of thyroid dysfunction in the routine laboratory, Clin Chem, DOI: 10.1093/clinchem/34.6.1110

[4] Nicoloff et al. (1990), The use and misuse of the sensitive thyrotropin assays, J Clin Endocrinol Metab, DOI: 10.1210/jcem-71-3-553

IB10 sphingotest® beta-hCG

The assay for the in vitro quantitative determination of human chorionic gonadotropin

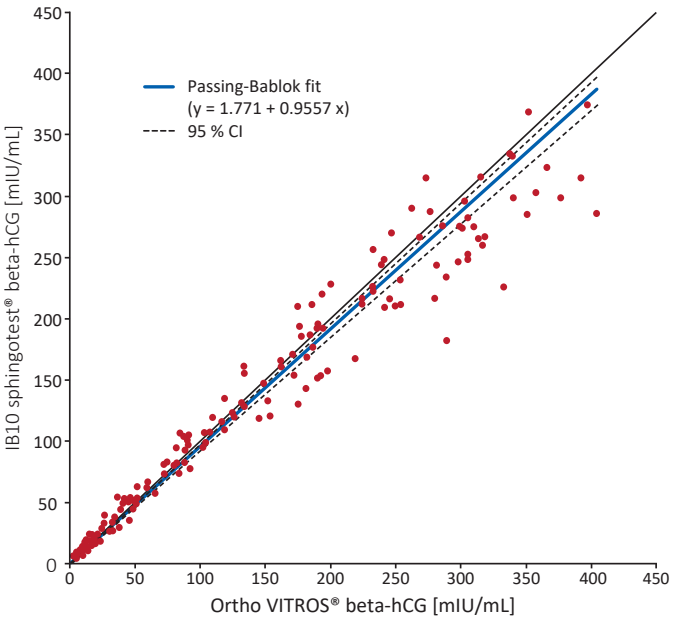
IB10 sphingotest® beta-hCG is a rapid point-of-care (POC) immunoassay for the quantitative in vitro determination of human chorionic gonadotropin (hCG) in human Lithium-Heparin whole blood and plasma. The assay detects total hCG, measuring both the intact hCG molecule and its free beta subunit. The quantitative measurement of hCG aids in the early detection of pregnancy. The test is designed for professional use only and may be used on sites where near patient testing is practiced.

Clinical Significance

hCG is the primary analyte used for pregnancy confirmation and monitoring due to its rapid rise in both blood and urine soon after conception. The detection of hCG within 3 - 4 weeks of the last menstrual period is the most reliable indicator for the confirmation of pregnancy. During a normal pregnancy, levels of hCG in the blood vary but are approximately 25 - 50 mIU/mL in the week after conception and rise exponentially doubling every 1.5 - 3 days during the first six weeks.[1] hCG levels continue to rise through the end of the first trimester, followed by a slow decline as the pregnancy reaches full-term (~ 40 weeks).

Method Comparison

Equivalence study between IB10 sphingotest® beta-hCG and Ortho VITROS® Total β-hCG II.



Whole Blood vs. Plasma Comparison

Passing-Bablok regression analysis comparing the whole blood concentrations vs. the corresponding plasma concentrations from the same subject samples:

Slope	1.05 (95% C.I. = [1.00 – 1.09])
y-Intercept	-0.51 mIU/mL

Expected Values

Each laboratory should establish its own expected values that represents the population that is to be evaluated at their facility. As a guide, the following ranges were determined. The IB10 sphingotest® beta-hCG Test was used to determine the concentration upper reference limit of hCG in human plasma samples collected from apparently healthy, non-pregnant individuals. The 95th percentile upper reference limit as determined with the samples is 5.42 mIU/mL hCG.

Reference Group	N	Median (mIU/mL)	95th percentile (mIU/mL)
Non-preg. female	248	1.56	5.75
Female age <50	150	0.43	4.15
Female age >50	98	3.26	7.91

Representative hCG ranges during normal pregnancy based on Last Menstrual Period (LMP) are summarized below. Other clinical reference citations may show different values.

After LMP (weeks)	hCG Range (mIU/mL)[2]
4	5 - 100
5	200 - 3,000
6	10,000 - 80,000
7-14	90,000 - 500,000
15-26	5,000 - 8,000
27-40	3,000 - 15,000

Key Features

Reproducibility

Sample	Mean level (mIU/mL)	Total precision CV (%)
1	97.0	13.8
2	24.31	12.7

Easy Handling

Sample Type	Lithium-Heparin whole blood or plasma samples
Time to Result	20 minutes
Measuring Range	4.0 - 400 mIU/mL
Limit of Detection	4.0 mIU/mL
No High Dose Hook Effect	up to 700,000 mIU/mL

References

[1] Vaitukaitis et al. (1976), Gonadotropins and their subunits - basic and clinical studies, Recent Prog Horm Res, DOI: 10.1016/b978-0-12-571132-6.50019-1

[2] Wu (2006), Tietz clinical guide to laboratory tests, 4th Ed. Philadelphia - Saunders-Elsevier - pp. 252-259

The IB10 sphingotest® PCT is a rapid point-of-care (POC) immunoassay for the in vitro quantitative determination of Procalcitonin (PCT) in the concentration range of 0.3 µg/L to 10 µg/L in EDTA whole blood and plasma. This assay is only intended for the diagnosis of sepsis, the assessment of the degree of severity, and monitoring of the change of sepsis severity. This assay is neither suitable nor intended for other applications and/or uses.

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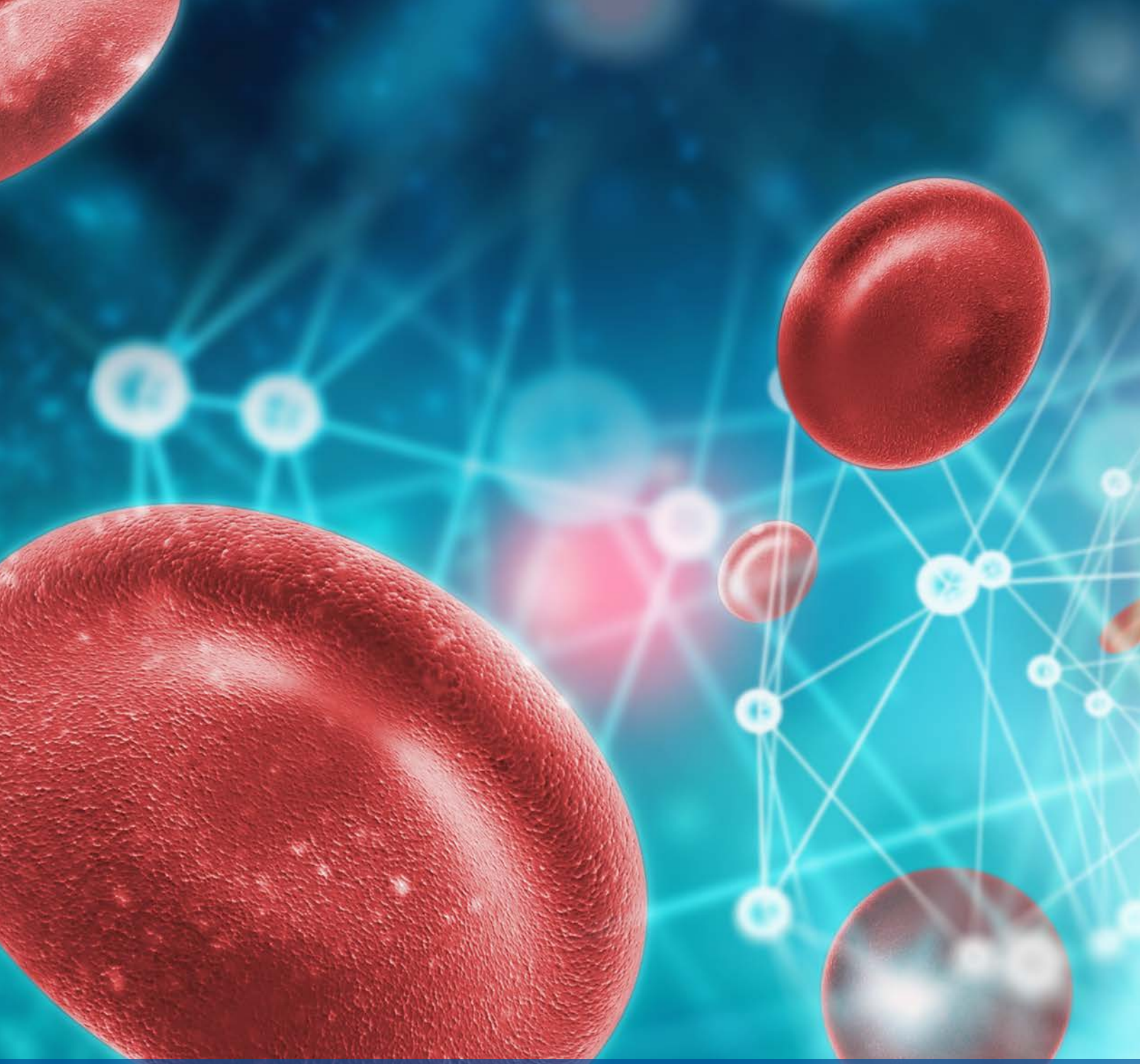

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