HYPHEN BioMed
155 rue d'Eragny, 95000 Neuville-sur-Oise, France
Tél : +33 (0)1 34 40 65 10
Fax : +33 (0)1 34 48 72 36
www.hyphen-biomed.com
info@hyphen-biomed.com

CE

LIAPHEN™ Protein C

REF 120003

IVD R1 4 vials x 5 mL, R2 4 vials x 2.3 mL

English, revision: 03-2022

INTENDED USE:

Immuno-turbidimetric method for the *in vitro* quantitative determination of Protein C antigen in human citrated plasma, using an automated method. This method is for the detection of Protein C deficiencies in patients who are suspected of congenital or acquired deficiency.
This device of *in vitro* diagnostic use is intended for professional use in the laboratory.

SUMMARY AND EXPLANATION:

Technical: [1,2]
Protein C (PC) is a vitamin K dependent glycoprotein, which inhibits and regulates coagulation through specific cleavages of Factors Va and VIIIa, suppressing their procoagulant cofactor activity.
Clinical: [3-7]
Determination of PC Antigen (PC:Ag) in human plasma may help in the diagnosis of congenital or acquired PC deficiencies.
Acquired deficiencies are observed in hepatic diseases, during VKA therapy or in Disseminated Intravascular Coagulation (DIC).
Congenital deficiencies can be quantitative (Type I) or qualitative (Type II).
Congenital or acquired PC deficiency is a risk factor of venous thrombosis.

PRINCIPLE:

LIAPHEN™ Protein C is an immunoturbidimetric method, based on antigen-antibody reaction: PC:Ag of the sample reacts with latex particles sensitized with rabbit antibodies, leading to latex particles agglutination. This agglutination can be directly detected through the change of absorbance. The absorbance change is directly proportional to the amount of PC:Ag in the sample.

REAGENTS:

R1 **Reaction Buffer**, liquid form. Contains Disodium dihydrogen ethylenediaminetetraacetate, BSA, preservatives and stabilizers.
R2 **Latex,** anti-Protein C antibodies-coated latex particles at approximately 0.25%, liquid form. Contains BSA, preservatives and stabilizers.

The product is classified as non-hazardous and is not subject to labeling according to EC Regulation No. 1272/2008 [CLP].

WARNINGS AND PRECAUTIONS:

- This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.
- Use only the reagents from the same batch of kits.
- Waste should be disposed of in accordance with applicable local regulations.
- Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

REAGENT PREPARATION:

R1 R2 Reagent is ready to use; homogenize by gentle inversion, while avoiding formation of foam and load it directly on the analyzer following Application Guide instruction.

STORAGE AND STABILITY:

Unopened reagents should be stored at 2-8°C in their original packaging. Under these conditions, they can be used until the expiry date printed on the kit.

R1 R2 Reagent stability after opening, free from any contamination or evaporation, and stored closed, is of:

- **3 months** at 2-8°C.
- **Do not freeze**
- **Stability on board of the analyzer: see the specific Application Guide.**

Combination of storage are not recommended.

REAGENTS AND MATERIALS REQUIRED BUT NOT PROVIDED:

- Diluent: Imidazole Buffer (AR021B/AR021K/AR021L/AR021M/ AR021N).
- Specific calibrator and controls with known PC:Ag titration, such as:

Product Name	Reference
BIOPHEN™ Plasma Calibrator	222101
BIOPHEN™ Normal Control Plasma	223201
BIOPHEN™ Abnormal Control Plasma	223301

- Automatic analyzer for immuno-turbidimetric assays such as: CS-series, CN-series.
- Laboratory material.

SPECIMEN COLLECTION AND PREPARATION:

The blood (9 volumes) should be carefully collected onto the trisodium citrate anticoagulant (1 volume) (0.109 M, 3.2%) by clean venipuncture.
Samples should be collected, prepared and stored in accordance with applicable local guidelines (for the United States, see the CLSI H21-A5[8] guideline for further information concerning specimen collection, handling and storage).
For plasma storage, please refer to references[8,9].

PROCEDURE:

HYPHEN BioMed provides Application Guides for defined coagulation analyzer families. The Application Guides contain analyzer/assay specific handling and performance information and supersede the information in these Instructions for Use.

QUALITY CONTROL:

The use of quality controls serves to validate method compliance, along with between-test assay homogeneity for a given batch of reagents.
Include the quality controls with each series, as per good laboratory practice, in order to validate the test. A new calibration curve should be established, preferably for each test series, and at least for each new reagent batch, or after analyzer maintenance, or when the measured quality control values fall outside the acceptance range for the method.
Each laboratory must define its acceptance ranges and verify the expected performance in its analytical system.

RESULTS:

- The concentration of PC:Ag (%) in the test specimen is directly inferred from the calibration curve, when the standard dilution is used.
- If other dilutions are used, the level obtained should be multiplied by the additional dilution factor used.
- Lot to lot variability measured on 3 lots is: %CV ≤ 10%.
- The results should be interpreted according to the patient's clinical and biological condition.

LIMITATIONS:

- To ensure optimum test performance and to meet the specifications, the technical instructions validated by HYPHEN BioMed should be followed carefully.
- Any reagent presenting no limpid appearance or showing signs of contamination must be rejected.
- Any suspicious samples or those showing signs of activation must be rejected.
- User defined modifications are not supported by HYPHEN BioMed as they may affect performance of the system and assay results. It is the responsibility of the user to validate modifications to these

instructions or use of the reagents on analyzers other than those included in HYPHEN BioMed Application Guides or these Instructions for Use.
- An unexpected abnormal result should be confirmed by another method and/or another sample collected, and considered according to clinical context.
- Heterophilic antibodies may interfere in the assay by giving abnormally high PC:Ag values.

EXPECTED VALUES:

The reference interval established, in internal study, on healthy adult subjects on CS-series (n=123) and on CN-series (n=120), was measured between 70 and 127% and between 67 and 125% respectively (Central 90%, 95th percentile). However, each laboratory has to determine its own normal range.

PERFORMANCES:

Mathematical analyses are performed using a validated statistical software built in accordance with CLSI guidelines.
Performances studies were conducted as described in CLSI guidelines.
The following performance data represent typical results and are not to be regarded as specifications for LIAPHEN™ Protein C.

Analytical performances
Measuring Range
The measuring range is defined by the analyzer system used and is documented in the respective Application Guides of the analyzers.
Precision
Precision studies were assessed using laboratory controls and spiked pooled plasmas over a 20-days period, 2 series per day and 2 repetitions within each series for a sample level. Coefficient of variation (CV) for all samples is less than 5 % and is documented in the respective Application Guides of the instruments.
Interfering substances
Interferences are defined by the analyzer system used and are documented in the respective Application Guides of the analyzers.

Clinical performances

Agreement

	Sysmex CS5100 (n=173)		
Analyte	**Linear regression**	**r**	**Reference / comparison method**
Protein C	y = 3.52 + 0.88x	0,980	HemosIL® Protein C

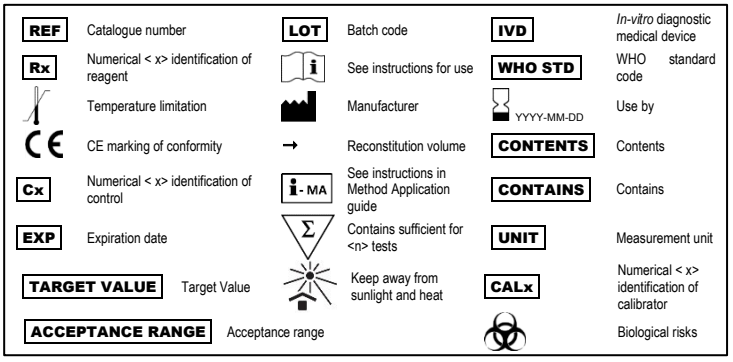
Sensitivity/Specificity

	Sysmex CS5100 (n=173)		
Analyte	**Sensitivity**	**Specificity**	**Area under the curve**
Protein C	0.970	1.000	1.000

REFERENCES:

1. Horellou M.H. Intérêt du dosage de la Protéine C dans les accidents thromboemboliques veineux. Feuil. Biol. 1985.
2. Stenflo J. Structure and Function of Protein C. Semin. Thromb. Haemostasis. 1984.
3. Manucci P.M. Deficiencies of Protein C, an inhibitor of blood coagulation. Lancet. 1982.
4. Esmon C.T. Protein C activation. Semin. Thromb. Haemostasis. 1984.
5. Exner T. Characterisation and some properties of the Protein C activator from Agkistrodom Concortrix venom. Thromb. Haemostasis.1988.
6. Pabinger I.. Clinical relevance of Protein C. Blut. 1986.
7. Cooper P.C. *et al.* Recommendations for clinical laboratory testing for protein C deficiency, for the subcommittee on plasma coagulation inhibitors of the ISTH. J. Thromb. Haemost. 2020.
8. CLSI Document H21-A5: "Collection, transport, and processing of blood specimens for testing plasma -based coagulation assays and molecular hemostasis assays; approved guideline". 2008.
9. Mauge L. and Alhenc-Gelas M. Stabilité pré-analytique des paramètres de la coagulation: revue des données disponibles. Ann Biol Clin. 2014.

The following symbols may appear on the product labeling:



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