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IVD

FIBRIPHEN™ LRT

REF CK585K

R 6 vials x 5 mL

English, revision:07-2024

INTENDED USE:

Clotting method based on Clauss method for the *in vitro* quantitative determination of Fibrinogen in human citrated plasma, using an automated method. This method is an aid to diagnosis of Fibrinogen abnormalities in patients who are suspected of congenital or acquired disorders.
This device of *in vitro* diagnostic use is intended for professional use in the laboratory.

SUMMARY AND EXPLANATION:

Technical:[1-3]
Fibrinogen is a 340 Kd soluble plasma glycoprotein, synthesized in the liver, containing 6 peptidic chains, with a 2 to 2 symmetry, and linked by disulfide bridges (2 Aα, 2 Bβ and 2γ chains). Thrombin clots fibrinogen and forms fibrin, which is then stabilized by activated Factor XIII in presence of calcium. Fibrinogen is lysed by plasmin to fragments X and Y, first, then D and E.
Clinical:[2-14]
Congenital or acquired Fibrinogen disorders may affect its level or function. Clauss method is for the quantification of functional Fibrinogen.
Hypofibrinogenemia is mainly associated with severe liver disease, or excessive consumption of fibrinogen (DIC, hyperfibrinolysis) and certain others treatments.
Numerous variants (eg afibrinogenemia, hypofibrinogenemia, dysfibrinogenemia) of fibrinogen have been described, associated to asymptomatic cases, or to cases with bleeding and/or thrombosis.
Fibrinogen is an acute phase reactant. Increased concentrations are observed in various clinical situations associated with inflammation, cancers and have also been considered as a risk factor for cardiovascular disease events and thrombosis, nonvascular mortality.

PRINCIPLE:

In the presence of a constant and in excess amount of bovine thrombin, the clotting time (CT) obtained for diluted citrated plasma is inversely proportional to the plasma fibrinogen concentration.

REAGENTS:

R **Calcium Thrombin** (bovine origin), at approximately 80 NIH/mL, liquid form. Contains BSA, a heparin neutralizing substance, 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.
- 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 European Member State in which the user and/or the patient is established.
- Summary of Safety and Performance (SSP) is available in the European database on medical devices (see Eudamed public website: https://ec.europa.eu/tools/eudamed or on request to HYPHEN BioMed).

REAGENT PREPARATION:

R Reagent is ready to use; homogenize 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.

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

- **90 days** at 2-8°C.
- **Stability on board of the analyzer: see the specific Application Guide.**

REAGENTS AND MATERIALS REQUIRED BUT NOT PROVIDED:

Reagents:

- Imidazole buffer (AR021B/AR021K/AR021L/AR021M/AR021N) or Hemostasis Hepes Buffer (AR033K/AR033L/AR033M/AR033N) . Use the same buffer for all dilutions performed.
- Specific calibrators and controls:

Product Name	Reference
BIOPHEN™ Plasma Calibrator	222101
BIOPHEN™ Normal Control Plasma	223201
BIOPHEN™ Abnormal Control Plasma	223301
EASYPLASMA™ Control Set	225601
EASYPLASMA™ Calibrator	226601
CI TROL 1*	291070 (SMN : 10873821)
CONTROL PLASMA N*	ORKE415 (SMN : 10873873)
CONTROL PLASMA P*	OUPZ175 (SMN : 10873890)

*Target assigned value available for Sysmex branded control on CS-series and CN-series

- Automatic analyzer for clotting assays such as: CS-series, STA-R® family, ACL-TOP® family, CN-series.
- Laboratory material.

Please note that the applications on other analyzers can be validated by the instrument manufacturer in accordance with the requirements of the REGULATION (EU) 2017/746 under their responsibility as long as the intended purpose is not modified.

TRACEABILITY:

Certificates of traceability and Instructions for Use of above calibrators and controls are available on the HYPHEN BioMed website. For more information refer to Instructions for Use of above calibrators and controls.

SPECIMEN COLLECTION AND PREPARATION:

Collection, preparation and storage of Platelet Poor Plasma (PPP) should be made according to laboratory or other validated methods [3,15-16].
The blood (9 volumes) should be carefully collected onto the trisodium citrate anticoagulant (1 volume) (0.109 M, 3.2%) by clean venipuncture.
According to CLSI H21-A5[15] and studies[16]:

- Plasma should remain at room temperature for no longer than 4 hours.
- If assays will not be completed within 4 hours, plasma should be frozen at −20 °C or below.
- Plasma samples should be thawed at 37°C, only once.

PROCEDURE:

HYPHEN BioMed provides Application Guides for defined coagulation analyzer families. The Application Guides contain analyzer/assay specific handling and performance information and complement 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 Fibrinogen (reported in g/L) in the test specimen is directly inferred from the calibration curve, when the standard dilution is used.
- Lot to lot variability measured on 3 lots is: %CV = 4%
- The results should be interpreted according to the patient's clinical and biological condition and other findings.

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.
- Clauss method and fibrinogen antigenic assay (such as LIAPHEN™ Fibrinogen (120102)) have to be performed for dysfibrinogenemia. Recovery of therapeutic fibrinogen concentrates can be impacted by the type of reagent (weaker with bovine thrombin)[9]. Anti-thrombin drugs may interfere in Fibrinogen Clauss assays.[3]

- 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.

EXPECTED VALUES:

The reference interval established on healthy adult subjects (n=135) on instrument CS-series, (n=133) on CN-series, (n=131) on STA-R® family, (n=135) on ACL-TOP® family, was measured respectively between 2.2 and 3.8g/L, 2.2 and 3.8 g/L, 2.2 and 3.8 g/L, 2.3 and 3.9 (Central 90%, 95th percentile). However, each laboratory has to determine its own normal range.
A normal range study was performed on each analyzer and is documented in the respective Application Guides of the analyzers.

PERFORMANCES:

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 FIBRIPHEN™ LRT.
Mathematical analyses are performed using a validated statistical software built in accordance with CLSI guidelines.
All performances are documented in the respective Application Guides of the analyzers.

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.
Accuracy
Accuracy studies were assessed using laboratory controls and pooled plasmas.
Trueness: bias is less than 9% for all samples.
Precision: coefficient of variation (CV) for all samples is less than 6% for repeatability, less than 9% for reproducibility and less than 9% for within laboratory. Precision 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

	ACL TOP® family			
Analyte	**n**	**Linear regression**	**r**	**Reference / comparison method**
Fibrinogen	110	y = 0.97x+0.04	0.989	HemosIL® Fibrinogen-C

Sensitivity/Specificity

Range [0.0-4.0] g/L:

	ACL TOP® family				
Analyte	**n**	**Sensitivity**	**Specificity**	**Area under the curve (ROC)**	
Fibrinogen	53	0.93	1.00	1.000	
Analyte	**n**	**PPV**	**NPV**	**LR+**	**LR-**
Fibrinogen	53	100%	87%	+∞	0.15

Range ≥1.5 g/L:

	ACL TOP® family				
Analyte	**n**	**Sensitivity**	**Specificity**	**Area under the curve (ROC)**	
Fibrinogen	50	0.92	0.92	0.983	
Analyte	**n**	**PPV**	**NPV**	**LR+**	**LR-**
Fibrinogen	50	89%	91%	7.39	0.09

PPV: Predictive value of a positive result
NPV: Predictive value of a negative result
LR+ : Likelihood Ratio +
LR- : Likelihood Ratio –

REFERENCES:

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4. Clauss A. Gerinnungsphysiologische Schnellmethode zur Bestimmung des Fibrinogens. 1957.
5. VanDeWater L. *et al.* Analysis of elevated fibrin(ogen) degradation product levels in patients with liver disease. Blood. 2019.
6. Lowe G.D.O. *et al.* Epidemiology of coagulation factors, inhibitors and activation markers: The Third Glasgow MONICA Survey I. Illustrative reference ranges by age, sex and hormone use. Bristish Journal of Haematology. 1997.
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11. De Moerloose.P *et al.* Rare coagulation disorders: fibrinogen, factor VII and factor XIII. 2016.
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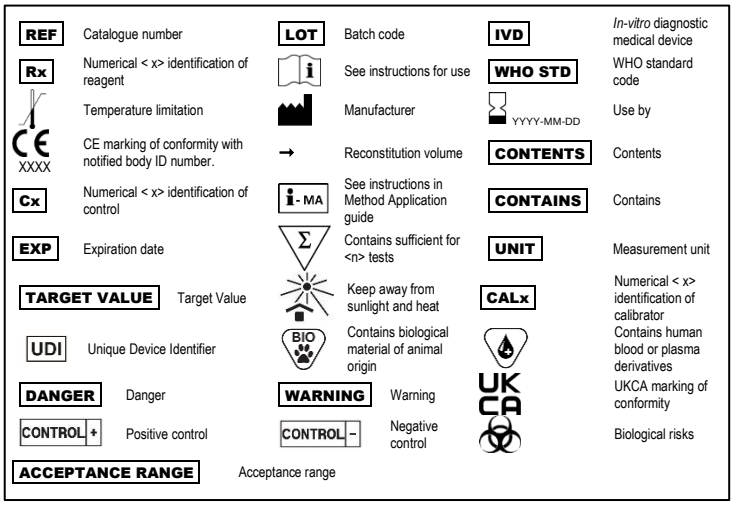
13. Besser.W.M. Acquired hypofibrinogenemia: current perspectives. Journal of Blood Medecine. 2016.
14. Danesh.J. Plasma Fibrinogen Level and the Risk of Major Cardiovascular Diseases and Nonvascular Mortality, An Individual Participant Meta-analysis. 2005.
15. CLSI Document H21-A5: "Collection, transport, and processing of blood specimens for testing plasma-based coagulation assays and molecular hemostasis assays; approved guideline". 2008
16. Ieko M. *et al.* Expert consensus regarding standardization of sample preparation for clotting time assays. Int J Hematol. 2020.

e-IFU (other languages) are available on www.hyphen-biomed.com.
For customer support and Application Guides, please contact your local provider or distributor (see www.hyphen-biomed.com).

Changes compared to the previous version.

The following symbols may appear on the product labeling:



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