CE XXXX IVD

Precision in Hemostasis

Behnk Elektronik

BE Factor VII Deficient Plasma FVII

Auxiliary reagent (human citrated plasma) for the quantitative determination of Factor VII activity in human citrated plasma

REF 771607: DP (6 x 1 mL)

| INTENDED USE

Freeze dried citrated human plasma from which Factor VII has been removed by selective immuno-adsorption.
Suitable for use with manual procedure on semi-automated coagulometer, or on automated coagulation analyzer, it is an auxiliary reagent for the *in vitro* quantitative determination of Factor VII in human citrated plasma using BEHNK reagents for Prothrombin Time (PT) measurements as follows:
REF 775100: BE Cal Ref (Reference plasma for calibration)
REF 771100, REF 771101: BE PT LI Thromboplastin low ISI
REF 771150, REF 771151: BE PT HI Thromboplastin high ISI
REF 771700: BE Owren Buffer (Plasma dilution buffer)
The assay is intended as an aid in the laboratory investigation of coagulation abnormalities and for characterization of coagulation factor activity. Results must be interpreted in conjunction with clinical findings and other laboratory tests. For clinical laboratory use by healthcare professionals.

| PRINCIPLE [1] [2]

The test is based on the measurement of clotting time in the presence of thromboplastin and calcium with a method in which all factors are present in excess (supplied by Factor VII Deficient Plasma) except Factor VII, which is derived from the sample to be tested.

| GENERALITIES [2] [4] [5] [7] [8] [10]

FVII (proconvertin) is a Vitamin K-dependent glycoprotein composed of a single polypeptide chain. It forms with Tissular Factor (TF) an equimolar complex in the presence of Ca^{2+}. Within this complex, FVII can be activated into FVIIa by Factors Xa, IXa, XIIa, and thrombin and by TF/FVIIa complex itself.
The TFPI (Tissue Factor Pathway Inhibitor) inactivates the complex TF/FVIIa.
TF/FVIIa complex could be inhibited by antithrombin in the presence of heparin.

Deficiencies in FVII may be observed in following cases:

- Isolated deficiency:
  - Congenital deficiency and dysprothrombinemias
  - Acquired deficiency associated with factor VII inhibitors
- Acquired deficiency of FVII associated with deficiency of other coagulation factors:
  - Deficiency of vitamin K intake, absorption, or metabolism disorders (hemorrhagic disease of the newborn, bile retention, antibiotic therapy)
  - Treatments with Vitamin K antagonists
  - Hepatic disorders
  - Fibrinolysis
  - Disseminated intravascular coagulation (DIC)

Increased levels of FVII appear to be associated with an increased risk of cardiovascular disease.

REAGENTS

DP **FVII** Deficient Plasma FVII

Freeze dried human citrated plasma

According to (EC) 1272/2008 regulation, this reagent is not classified as dangerous.

SAFETY CAUTIONS

- Refer to current Safety Data Sheet (SDS) available on request or on www.behnk.de
- Each donor unit used to manufacture this product was tested and found non-reactive for HbsAg, antibody to Hepatitis C and antibody to HIV-1/HIV-2.
- However, no test method can offer complete assurance that infectious agents are absent. All specimens or reagents from biological origin should be handled as potentially infectious, in accordance with good laboratory practices using appropriate precautions.
- Waste disposal: Respect legislation in force in the country.

Any serious incident that has occurred in connection with the device is notified to the manufacturer and the competent authority of the Member State in which the user and/or patient is based.

PREPARATION OF REAGENTS

Open the vial carefully.
Add exactly the volume of demineralized water stated on the label.
Cap the vial and let stand for 15 minutes at room temperature.
Mix gently by swirling and inverting before use, to homogenize the content.

STABILITY AND STORAGE

Unopened vials, stored away from light at 2-8 °C are stable until the expiry date stated on the label.
Stability after reconstitution:

- 18-25°C 4 hours
- On board Stability (OBS)* 4 hours

* 16-22 °C
Do not use any reagent after expiry date.

SAMPLES COLLECTION AND HANDLING [9] [11] [13] [14]

Plasma from careful venipuncture with anticoagulant ratio of 1/10 (trisodium citrate solution 0.109 M, *i.e.* 3,2%). Mix immediately the blood with anticoagulant.
Avoid drawing with a syringe that could result in the formation of micro-clots.
Centrifuge for 15 minutes at 2000-2500 g and extract supernatant.
Storage in plastic tube: 4 h at 15-25°C, 15 days at -20°C*, 1 month at -80°C*.
*If quickly frozen; thaw plasmas at 37°C until complete thawing.

Do not store at 2-8 °C, because the Factor VII may be activated by the kallikrein system in this temperature range.

LIMITS [3]

Thrombin inhibitors (hirudin, argatroban, …) present in the specimen may decrease Factor VII activity in the specimen.
For a more comprehensive review of factors affecting this assay, refer to the publication of Young D.S.

MATERIAL REQUIRED BUT NOT PROVIDED

Basic medical analysis laboratory equipment.
Automated or semi-automated coagulation analyzer.
Demineralized water.

| REFERENCE RANGE [6]

Plasma (adult): Usually between 55% and 170 %

Each laboratory should establish its own normal ranges for the population that it serves.

QUALITY CONTROL

REF 773100: BE Trol 1; REF 773101: BE Trol 2
Controls are required for checking the accuracy and reproducibility of the results.
The control intervals should be adapted to each laboratory's individual requirements.
Values obtained should fall within the defined limits.
Follow the applicable government regulations and local guidelines for quality control.

PROCEDURE

Manual method on semi-automated systems
Pre-incubate PT reagent (Thromboplastin) 15 min to reach a temperature of 37 °C and mix gently before use.
Dilute samples and controls: 1/10 in BE Owren Buffer.
Calibrators: prepare dilutions as indicated in § Calibration.

- Diluted Plasma (calibrators, controls, plasmas): 100 µL
- Deficient Plasma: 100 µl

Incubate for 120 sec at 37 °C

- Thromboplastin (37 °C): 200 µL

The automatic countdown timer will start immediately after Thromboplastin addition and stop when the clot is formed.
Automated method on Behnk Thrombolyzer series
Refer to the full detailed application specific to the automated system.

Note:

- Performances and stability data have been validated on Thrombolyzer Compact X (available on request).
- With manual procedure and on other automated coagulation analyzer, performances and stability data must be validated by user.

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CALIBRATION [12]

Use REF 775100: BE Cal Ref

Reference plasma traceable to SSCLOT5, non WHO SSC/ISTH Secondary Coagulation Standard from NIBSC.

Manual method on semi-automated analyzer: Prepare a calibration curve with dilution 1/10, 1/20, 1/40 and 1/80 in BE Owren Buffer. Measure in triplicate the clotting time of each level.

Automated method on Behnk Thrombolyzer series: Perform a calibration with BE Cal Ref using automatic dilutions indicated in the specific application.

CALCULATION

Results are expressed in % of Deficient Factor according to the calibration curve.

PERFORMANCES

The studies were performed on Thrombolyzer Compact X.

Precision; Repeatability (Within run) and Reproducibility (Between run)

Within run N = 20	Level 1	Level 2
Mean (%)	99	39
S.D. (%)	3.0	1.0
C.V. (%)	2.8	2.6

Between run N = 20	Level 1	Level 2
Mean (%)	113	59
S.D. (%)	5.8	3.7
C.V. (%)	5.1	6.2

Detection limit: equivalent to 6 % of Factor VII

Measuring Range: from 10 % (QL) to 200 %

Interferences (PT LI, sec):

Turbidity	No interference up to 450 mg/dL of Triglycerides
Low Molecular weight heparin	No interference up to 0.114 IU anti Xa
Unfractionated heparin	No interference up to 0.038 IU anti Xa
Total Bilirubin	Negative interference from 228 µmol/L
Hemoglobin	No interference up to 258 µmol/L

Other substances may interfere with the results (see § Limits)

Calibration Stability: Make a new calibration when changing reagent batch, if quality control results are found out of the established range and after maintenance operations.

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(12) *Secondary Coagulation Standard Lot #5 NIBSC code: SSCLOT5 Instructions for use (Version 3.0, Dated 03/08/2020)*

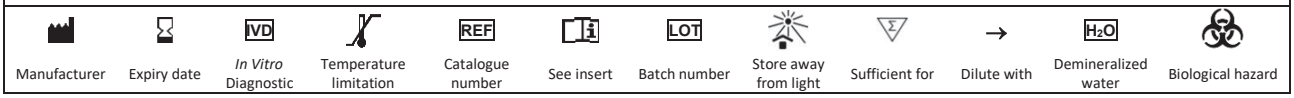
(13) *CLSI Document H03-A6: "Procedures for the collection of diagnostic blood specimens by venipuncture; approved standard". Sixth Edition, 26, 27, 2007.*

(14) *CLSI Document H21-A5: "Collection, transport, and processing of blood specimens for coagulation test and general performance of coagulation assays; approved guideline". Fifth Edition, 20, 5, 2008.*

| = Significant modifications

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Table of symbols



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