Coagulation Factor VII Deficient Plasma

FACTOR VII DEFICIENT

Revision bar indicates update to previous version.

CE 0197

Intended Use

FACTOR VII DEFICIENT is an in vitro diagnostic reagent for the quantitative, WHO-standardized determination for use in assays of coagulation factor VII (FVII) activity as aid to diagnosis of congenital or acquired FVII deficiencies in patients with bleeding disorders or at risk for FVII deficiency in human sodium citrated plasma by means of automated, semi-automated and/or manual coagulometric methods.

Summary and Explanation

Coagulation factor VII (FVII) is involved in the extrinsic pathway of the coagulation system; consequently a prolongation of prothrombin time (PT) is seen in case of a FVII deficiency. Patients with FVII deficiency can experience bleeding. FVII and other coagulation factors of the vitamin K-dependent prothrombin complex are reduced under anticoagulant therapy with vitamin K antagonists[1–3].

The PT-based one-stage clotting assay using **FACTOR VII DEFICIENT** is applied for determination of FVII activity.

The determination of FVII in plasma is indicated in the following cases:

- clarifying the cause of a prolonged PT,
- diagnosing congenital or acquired factor deficiency states,
- monitoring therapy with prothrombin complex concentrate[4]
- detailed monitoring of anticoagulant therapy with vitamin K antagonists[5]
- testing the protein synthesis function in liver diseases[6]

Principles of the Procedure

A plasma deficient in any of the factors comprising the extrinsic pathway will result in a prolonged thromboplastin time (PT). Coagulation factor deficient plasma can be used to confirm a factor deficiency, in general, and to identify and quantify factor deficiency in patient plasma. A mixture of the respective coagulation factor deficient plasma and the patient plasma is tested in the PT assay, and the result is interpreted using a reference curve obtained with dilutions of **STANDARD PLASMA** or a normal plasma pool mixed with the deficient plasma. A patient plasma deficient in a specific factor will not be able to compensate for the absence of the factor in the corresponding coagulation factor deficient plasma and therefore result in a prolonged PT.

Reagents

Note: **FACTOR VII DEFICIENT** can be used manually or on automated coagulation analyzers. Sysmex provides Reference Guides (Application Sheets) for several coagulation analyzers. The Reference Guides (Application Sheets) contain analyzer/assay specific handling and performance information which may differ from that provided in these Instructions for Use. In this case, the information contained in the Reference Guides (Application Sheets) supersedes the information in

these Instructions for Use. Please also consult the instruction manual of the instrument manufacturer!

Reagent	Description	Storage	Stability
Coagulation Factor VII Deficient Plasma FACTOR VII DEFICIENT	Lyophilized reagent containing: • human plasma[a], FVII activity ≤1 % • Stabilizer: • D-Mannitol (reconstituted: 20 g/L)	2–8 °C May be used up to the expiry date indicated on the label if stored unopened.	15–25 °C: reconstituted, 8 hours[b]; ≤ –20 °C: reconstituted, 4 weeks[b]

[a] from pooled plasma collected from selected healthy blood donor
[b] closed original vial

FACTOR VII DEFICIENT is manufactured by immunoadsorption from normal plasma and is free from the antigen of the respective factor. Fibrinogen is present in a quantity of at least 1 g/L, and the remaining coagulation factors are present in an activity greater than 40 % of Norm.

FACTOR VII DEFICIENT can be frozen and thawed once after reconstitution without a loss of coagulation activity. The plasma must be well sealed and frozen as quickly as possible. Thawing should be accomplished at 37 °C within 10 minutes. Thawed plasma should be used within 2 hours when held at 15 to 25 °C.

On-board stability
Information regarding on-board stability is specified in the Reference Guides (Application Sheets) for the different coagulation analyzers.

Warnings and Precautions

For *in-vitro* diagnostic use only.

For laboratory professional use.

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State through your local distribution representative in which the user and/or patient is established.

Safety data sheets (MSDS/SDS) available upon request.

CAUTION! POTENTIAL BIOHAZARD
Each donor or donor unit was tested and found to be negative for human immunodeficiency virus (HIV) 1 and 2, hepatitis B virus (HBV) and hepatitis C virus (HCV) using either tests that are CE marked or FDA approved for this purpose. Because no known test can offer complete assurance of the absence of infectious agents, all human derived products should be handled with appropriate caution.

Caution
This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with all government requirements.

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). In case Eudamed is not available, SSP can be delivered by the manufacturer on request.

Preparing Reagents

FACTOR VII DEFICIENT: Dissolve the contents of a vial with 1 mL of distilled or deionized water. Before use, let stand at least 15 minutes at 15 to 25 °C, then shake carefully to mix (without foam formation). Mix carefully once more before using.

PT reagent: Use according to the respective Instructions for Use.

Specimen Collection and Handling

Collecting the Specimen

To obtain the plasma, carefully mix 1 part sodium citrate solution 0.11 mol/L (3.2 %) with 9 parts venous blood, avoiding the formation of foam.

Centrifuge the blood specimen at 1 500 × g for no less than 15 minutes at room temperature[7].

Storing the Specimen

Stability of the samples:

15 to 25 °C	3 hours
≤ −20 °C	4 weeks

Plasma stored at ≤ −20 °C is to be thawed in a water bath within 10 minutes at 37 °C, mixed gently and then tested immediately. If testing cannot be performed immediately, the specimen may be held for a maximum of two hours at 4 °C until tested[7].

Procedure

Materials Provided

REF	Contents	
OTXV13	Coagulation Factor VII Deficient Plasma FACTOR VII DEFICIENT	3 × → 1 mL

Materials Required but not Provided

Item	Description
REF OUHP29, OUHP49 REF B4212-40, B4212-50, B4212-100	Thromborel® S, or Dade® Innovin®
REF ORKE41	CONTROL N, Control Plasma N
REF OUPZ17	CONTROL P, Control Plasma P
REF OQAA33 REF B4234-25 REF B4265-35, B4265-37 –	IMIDAZOLE BUFFER, Imidazole Buffer Solution, or OV BUFFER, Dade® Owren's Veronal Buffer, or CA SYSTEM BUFFER, Dade® CA System Buffer, or Physiological Saline Solution
REF ORKL17	STANDARD PLASMA, Standard Human Plasma
Coagulation analyzers[c], such as:	• Automated Blood Coagulation Analyzer CA-600 series (CA-600 series) • AUTOMATED BLOOD COAGULATION ANALYZER CS-2500 (CS-2500 System) • AUTOMATED BLOOD COAGULATION ANALYZER CS-5100 (CS-5100 System)

[c] Availability of analyzers may vary by country.

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 and performance are not modified.

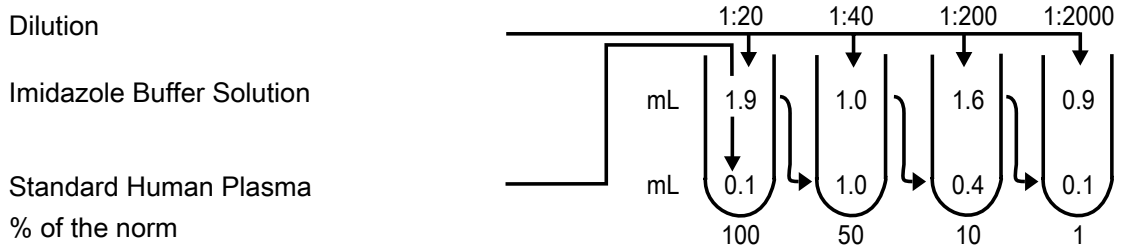
Manual Testing

Dilute the plasma sample 1:20 in IMIDAZOLE BUFFER (bring to room temperature (15–25 °C)). Pipette into a test tube pre-warmed to 37 °C:	
FACTOR VII DEFICIENT	100 µL
Sample dilution	100 µL
	Incubate at 37 °C for exactly 60 seconds

PT reagent (pre-warmed to 37 °C)	200 µL
	On addition of PT reagent start stop-watch or timer on the coagulation analyzer and determine the coagulation time.

Establishment of the Reference Curve

Use either STANDARD PLASMA or fresh citrated pooled plasma from no less than 10 healthy donors. Using IMIDAZOLE BUFFER, prepare dilutions as shown in the following scheme and determine the coagulation times as described under "Manual Testing", page 3. The reference curve must be re-generated if there is a change in the instrument or in the lot of reagent used, or if there is any change in the experimental conditions.



Additional dilutions can be prepared if necessary. Plot the measured coagulation times (ordinate) on log graph paper against the corresponding percentage factor activities (abscissa). The coagulation times are dependent on the measurement principle and thus also on the coagulation analyzer used. Therefore, each laboratory must establish its own reference curve.

Internal Quality Control

Normal range: CONTROL N
Pathological range: CONTROL P

Two levels of quality control material (normal and pathologic range) have to be measured at start of the test run, with each calibration, upon reagent vial changes and at least every eight hours on each day of testing.The controls should be processed just like the samples. Each laboratory should establish its own quality control range, either by means of the target values and ranges provided by the manufacturer of the controls or by means of its own confidence ranges established in the laboratory. If the control values lie outside the confidence range determined beforehand, then the reagent, calibration curve and coagulation analyzer should be checked. Patient results must not be released until the cause of the deviation is identified and corrected.

Results

Read the coagulation factor content from the reference curve in % of Norm. If the given nominal value of the STANDARD PLASMA is not 100 % of Norm, but e.g. only 95 %, multiply the result read from the curve by 0.95. In the case of coagulation times which correspond to a coagulation factor content of more than 100 % of Norm, further determinations will be required using higher dilutions of specimen (e.g. 1:40). The percent of norm value read from the reference curve for such a higher dilutions must be multiplied by a correction factor corresponding to the dilution; e.g. for a dilution of 1:40 by a correction factor of 2.

Limitations

Therapeutic doses of hirudin or other direct thrombin inhibitors lead to an erroneously lower factor activity[8,9].

Specific inhibitors against plasmatic coagulation factors may also modify the real factor activity[10]. Partial activation of the coagulation factors due to incorrect sample handling can lead to falsely elevated single factor results. Lupus anticoagulants can influence the PT and thus also affect coagulation factor determinations[11].

The manufacturer has validated use of these reagents on various analyzers to optimize product performance and meet product specifications. 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 and

performance are not modified. User defined modifications are not supported by the manufacturer 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 Application Sheets or these Instructions for Use.

Results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation and other findings.

Expected Values[12]

Factor VII 70 to 120 % of Norm

Reference intervals vary from laboratory to laboratory depending on the population served and the technique, method, equipment and reagent lot used. Therefore, each laboratory must establish its own reference intervals or verify them whenever one or more of the aforementioned variables are changed.

Performance Characteristics

Measuring Range

The measuring range depends on the individual application of the assay due to instrument related conditions. Application specific performance data is listed in the respective Reference Guides of the instruments.

For manual methods the measuring range for the determination of coagulation FVII extends from 1 to approximately 100 % of Norm, and can be increased to approximately 200 % of Norm by using a higher dilution of sample (see above).

Precision

The precision depends on the individual application of the assay due to instrument related conditions. Application specific performance data is listed in the respective Reference Guides of the instruments. Applications of the assay showed a precision of lower than or equal to 9.3 % CV on fully automated instruments and lower than or equal to 14.3 % CV on semi-automated instruments.

The reproducibility was assessed by the manufacturer for coagulation factor VII based on publicly available proficiency testing information in 2019/2020. The overall reproducibility median CV% was found to be <9 % (samples >15 % of Norm) including PT reagent used, lot, instrument, laboratory and operator variability factors.

Method Comparison

In a study, the determination of FVII on the BFA System was compared to another coagulation analyzer.

The correlations resulted in the following:

	n	Slope	Intercept [% of Norm]	Correlation Coefficient
Factor VII	69	1.1	−1.2	0.98

Technical Assistance

For customer support, contact your local technical support provider or distributor.

Current Version of Application Sheets

FACTOR VII DEFICIENT can be used in combination with various automated coagulation analyzers. Sysmex provides Reference Guides/Application Sheets for the coagulation analyzers listed in section "Materials Required but not Provided", page 3 under the dedicated link below:

sysmex-ifu.com/ag

As the manufacturer continuously monitors the product performance and safety, the users are required to ensure that they work with the correct revision of the instructions for the product lots in use. Please periodically review the availability of new electronic labeling revisions to ensure safe use of the product.

The IFU version number is visible on each product box label. Sysmex ensures that all products lots bearing the same IFU version number are compatible with the electronic labeling provided via sysmex-ifu.com.

References

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Definition of Symbols

The following symbols may appear on the product labeling:

	Do not reuse		Use By
LOT	Batch Code	REF	Catalogue Number
	Caution		Manufacturer
EC REP	Authorized representative in the European Community	CH REP	Authorized representative in Switzerland
	Contains sufficient for <n> tests		Biological Risks
IVD	*In Vitro* Diagnostic Medical Device		Temperature Limitation
	Consult instruction for Use		Non-sterile
CE	CE marking of conformity	CE 0197	CE marking of conformity with notified body ID number. Notified body ID number can vary.
CONTENTS	Contents	→	Reconstitution volume
LEVEL	Level		Keep away from sunlight and heat
WARNING	Warning	DANGER	Danger
RxOnly	Prescription device (US only)	UDI	Device Identification (UDI) barcode
REACH xx/xx/xx	REACH Authorization Number		

Legal Information

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