

Instructions for use – FIB

REF 1061EU – FIB

UDI 59998629921061EU_1V4

Intended purpose



The FIB is a ready to use reagent for in-vitro diagnostic professional use, intended for qualitative examination of the fibrinogen level in citrated blood during viscoelastometry analysis.



CAUTION: A use of the device outside of its intended purpose, may lead to the test results being incorrectly interpreted by the user.

Indications for use

Indicated to be used when a diminished fibrinogen level in the patient's blood is suspected.

Contra-indications for use

None identified.

Intended users



- trained healthcare professionals,
- trained laboratory professionals.

Environment of use

Indoors in a typical setting of a laboratory, equipped and designed to ensure standard electrical connections, adequate lighting as well as standard environment settings regarding temperature, humidity and pressure to ensure the functionality of typical electrical devices like electrical medical devices and personal computers.

Intended patient population

Adult patients where an examination of coagulation activation, clot formation and/or clot stability is desired.

Principle of the assay



In the FIB assay coagulation is activated by a combination of recombinant tissue factor, calcium chloride and polybrene as a heparin antagonist. Concurrently platelet function is blocked using a combination of cytochalasin D (actin polymerization inhibitor) and eptifibatide (fibrinogen receptor antagonist) [1].

The clot formation is then detected using viscoelastometry [2-3]. Viscoelastometry allows for the detection of whole blood formation in whole blood and thus detects coagulation initiation (by the clotting time, CT), blood clot firmness (by the maximum clot firmness, MCF, or related parameters, such as the A20, amplitude 20 minutes after CT) and clot stability or fibrinolysis (by the maximum lysis, ML). In viscoelastometry the clot formation depends on the fibrinogen and platelet content of the sample, as well as the process of blood clot polymerization.

By the platelet inhibition, the clot firmness measurement in the FIB assay represents a functional assessment of the fibrinogen level in the sample. Higher fibrinogen levels result in higher clot firmness, and lower fibrinogen levels, results in weaker clots. The clot firmness in viscoelastometry-based fibrinogen assays is also influenced by the fibrin polymerization process. Substances interfering with the clot polymerization (such as hydroxyethyl starch, HES) can therefore impair the clot firmness in viscoelastometry-based fibrinogen assays [4-5].

The use of a combination of recombinant tissue factor, calcium chloride, polybrene and one or two platelet inhibitors is commonly used in viscoelastometry tests such as the fib-tem® or FIB-test assays [2-3] (tem® is a registered trademark by CA Casyso, Switzerland).

Materials provided

10 sealed single-use pouches containing one pipet tip with reagent each, providing a dry chemistry reagent composed of recombinant tissue factor, cytochalasin D, eptifibatide, polybrene (a heparin antagonist), calcium chloride, buffer and stabilizers. Each pouch contains one desiccant bag.

Additional materials and devices required

- Viscoelastometry analyzer and receptacles (Cups & Pins),
- Electronic pipette for 340 µL with 3 sec aspiration / dispensing cycles,
- Blood collection tube (3.2% sodium citrate) for coagulation testing.

Reagent preparation

The reagent is ready to use.

Storage and stability



Store at +2 to +8 °C. The unopened reagent tips are stable until the expiration date stated on the pouch label. Unopened pouches may be stored at room temperature for up to 1 month. Opened pouches are for immediate use within 1 minute after opening the pouch.



CAUTION: Incorrect storage conditions may affect reagent stability and lead to wrong test results.

Warnings and precautions

For professional use by trained personnel.



CAUTION: Do not use tips from defective pouches or from pouches missing the desiccant pack.



CAUTION: Intended for single use - do not reuse.



CAUTION: Any serious incident that has occurred as a result of the use of the device has to be reported to the manufacturer and the competent authority of the Member State in which the user and/or patient is established.

CAUTION: Failure to comply with these instructions for use may result in device handling errors leading to wrong test results.



CAUTION: Human blood samples should be handled with care, following general precautions recommended for bio-hazardous materials [6].

CAUTION: General precautions (e.g., wear gloves and minimize skin exposure to specimens and reagents) should be followed when handling all materials.

NOTE: Dispose of waste according to local regulations.

NOTE: A material safety data sheet is available upon request.

Residual risks, undesirable side-effects, and information for the patient

The following residual risks were identified during the risk management activities for the device:

- In case of an off-label use of the product, test results may be incorrectly interpreted by the user.
- In case of device handling errors, patient's coagulation may be incorrectly reflected.
- In case of the use of the expired product, patient's coagulation may be incorrectly reflected.
- In case of unacceptable transport and storage conditions, patient's coagulation may be incorrectly reflected.

Warnings related to the residual risks are provided throughout the document.

No undesirable side-effects were identified during the post-market activities for the device.

No information for the patient is required to be provided for the device.

Sample collection



CAUTION: Collect a venous blood sample according to the recommended procedures [7-8] using a blood collection tube with 3.2% sodium citrate. Samples should be analyzed within 3 hours from blood collection. Store the blood at room temperature. Always ensure blood collection tubes are filled to the indicated fill volume to avoid excessive citrate levels.

Test procedure

1. Check the expiry date of the device. The expiry date format is yyyy-mm-dd.



CAUTION: Do not use the expired product. The use of the expired product may lead to wrong test results.

2. Allow the reagent tip pouch to reach room temperature.
3. If the sample is cold (< 22°C) it is advised to allow the sample to warm up for 5 min on the heated position of the viscoelastometry analyzer. In evaluations on the effect of pre-warming blood tubes which had room temperature little to no effect was observed vs. tubes which were not pre-warmed.
4. Create the test in the software of the viscoelastometry analyzer according to the analyzer manual.
5. Place the Cup and Pin into the analyzer according to the analyzer manual.
6. Tear open the reagent tip pouch, attach the reagent tip to the electronic pipette and aspirate 340 µL sample from the blood tube.
7. Dispense the blood sample into the Cup.
8. Aspirate and dispense the sample once again to facilitate thorough mixing of the reagents with the blood sample. Ensure sample pipetting is performed without interruption of the process.
9. Start the test as described in the analyzer manual.
10. The test will stop, or you can stop the test as described in the analyzer manual.
11. Remove the Cup & Pin and dispose according to local regulations.

Quality control

Plasma-based quality control materials can be used to confirm the stability of test results determined with the FIB assay over time.

Result interpretation and expected values

The clot formation is detected via the A5 (amplitude 5 minutes after clotting time - CT), A10 (amplitude 10 minutes after CT), A20 (amplitude 20 minutes after CT) and MCF parameters.

Reference range

The reference range for the FIB assay was determined in a clinical study including 121 healthy individuals, aged 19 - 79.3 years, 54.5% female and 45.5% male, and calculated by the 95% central interval:

	A5 (mm)	A10 (mm)	A20 (mm)	MCF (mm)
2.5 th – 97.5 th percentile	6 – 20	7 – 22	8 – 24	9 – 25
Mean±SD	12.2 ± 3.6	13.4 ± 3.9	14.3 ± 4.1	15.6 ± 4.5

Viscoelastometry also provides the CT parameter (in sec), which can be used as a process marker:

2.5 th – 97.5 th percentile	Mean±SD
31 - 56	41.6 ± 9.4

Accuracy

To confirm the accuracy of the FIB assay, its results were compared with a reference test, the FIB-test assay by enicor [3].

The study included 103 samples from intensive care patients and healthy individuals.

The slope, bias and correlation were calculated for the FIB assay parameters (A5, A10, A20, MCF) vs. the reference test (FIB-test by enicor). According to CLSI EP09 (EP09c) the Deming regression slope and bias (intercept) were calculated. As a descriptive method in addition the Spearman correlation was calculated. FIBa: FIB assay (Apiro), FIBe: FIB-test (Enicor)

Parameter	N	Slope	Bias	Spearman
FIBa-A5 vs FIBe-A5	102	1.04	-0.56	0.91
FIBa-A10 vs FIBe-A10	102	1.06	-1.08	0.90
FIBa-A20 vs FIBe-A20	102	1.04	-1.04	0.91
FIBa-MCF vs FIBe-MCF	102	1.05	-1.13	0.89

The determined agreement of the FIB assay to the reference method compares very well with recent literature comparing different generations of viscoelastometry assays [9-10].

In the study group 12 samples had high fibrinogen level (> 4 g/L). One can see that in this group the clot firmness parameters of the FIB assay provided on average higher results than the reference range:

		A5 (mm)	A10 (mm)	A20 (mm)	MCF (mm)
reference range	2.5 th – 97.5 th percentile	6 – 20	7 – 22	8 – 24	9 – 25
	Mean±SD	12.2 ± 3.6	13.4 ± 3.9	14.3 ± 4.1	15.6 ± 4.5
high fibrinogen	2.5 th – 97.5 th percentile	17.6 – 33.5	18.8 – 35.5	19.8 – 37.5	21.8 – 39.5
	Mean±SD	26.1 ± 5.6	28.1 ± 5.9	29.50 ± 6.26	31.4 ± 6.3

Precision

In a precision study citrated blood with and without hemodilution (40% using 0.9% saline with 3.2% citrate) was tested in 3 runs, on three analyzers, three operations and including 3 FIB reagent lots (54 determinations per sample). The resulting mean and standard deviation (SD) were as follows:

	A20 [mm]	
	mean	SD
citrated blood (CB)	15	1.7
hemodilution (40%)	12	1.9

Limitations and interferences

Every in vitro diagnostic method can deliver wrong results under certain circumstances. It is therefore advisable to use certain precautions to avoid misinterpretations.

Measurements with noisy curves or irregular shapes should be discarded and repeated. The clinical context and other laboratory values (when available) should be considered when interpreting the FIB assay. Generally, consider repeating a measurement that gives a very surprising or otherwise implausible result.

Interference by the following substances was tested using citrated blood with the in vitro addition of unfractionated heparin (UFH), low molecular weight heparin (LMWH) and apixaban (Eliquis®, direct FXa antagonist). In addition, hemodilution was tested using 20% and 40% of saline 0.9%, sodium citrate 3.2%. Means, standard deviations (SD) and the change vs. the control for the A20 parameter is shown (6-fold determinations):

	A20 (mm)		
	mean	SD	Change
Citrated blood (control)	9	0.6	n.a.
+ UFH 3 IU/mL	8.2	1.5	-0.8
+ UFH 5 IU/mL	8	0.6	-1
+ LMWH 1 IU/mL	9	0.9	0
+ Apixaban 100 ng/mL	8	0	-1
+ Apixaban 300 ng/mL	9.3	0.5	0.3
20% hemodilution (saline)	8	0	-1
40% hemodilution (saline)	7.2	0.8	-1.8

One can see that the clot firmness detection in the FIB assay showed only minor variations in the presence of UFH, LMWH or apixaban. 40% hemodilution decreased the clot firmness by 1.8 mm.

Summary of safety and performance



Summary of safety and performance is provided in electronic format and is available for download on www.apiro.eu/eIFU

Manufacturer



APIRO Diagnostics Kft.

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Symbols

Symbol	Meaning
	Manufacturer
	Batch code
	Country of manufacture
	Temperature limit
	Consult instructions for use or electronic instructions for use
	Contains human blood or plasma derivatives
	Not intended for near-patient testing
	Unique device identifier
	In vitro diagnostic medical device

Symbol	Meaning
	Use-by date
	Catalogue number
	Do not use if package is damaged and consult instructions for use
	Do not re-use
	Contains sufficient for <n> tests
	Caution / Warning
	CE marking of conformity
	Biological risks

References

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- [7] CLSI/NCCLS H03-A6; Procedures for the collection of diagnostic blood specimens by venipuncture.
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Version history of these instructions for use

Date	Version	Change description
2025-10-29	1	Initial version