Instructions for Use

EX Assay · REF 1081EU · UDI 59998629921081EU

Intended Purpose

The EX is a ready-to-use reagent for in-vitro diagnostic professional use, intended for examination of the extrinsic coagulation system in citrated blood during viscoelastometry analysis.

CE IVD
Notified Body 2265

CAUTION: Use outside the intended purpose may lead to test results being incorrectly interpreted by the user.

Indications for Use

Indicated when an alteration of the extrinsic coagulation system is suspected.

Contra-indications for Use

None identified.

Intended Users

- Trained healthcare professionals
- Trained laboratory professionals

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 EX assay, whole blood coagulation is activated by a combination of recombinant tissue factor (TF), calcium chloride and polybrene (heparin antagonist). Viscoelastometry detects CT, MCF/A20, and ML.

The coagulation activation can be prolonged when there are clotting factor deficiencies of the extrinsic pathway or non-heparin anticoagulants present.

The assay allows determination of coagulation activation, clot formation and clot stability/fibrinolysis in whole blood, supporting patient management during coagulopathy. Often used together with other viscoelastometry assays.

Materials Provided

10 sealed single-use pouches, each containing one pipet tip with dry chemistry reagent (recombinant tissue factor, polybrene, 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-second aspiration/dispensing cycles
- Blood collection tube (3.2% sodium citrate) for coagulation testing

Storage and Stability

Condition	Detail
Refrigerated (unopened)	Store at +2 to +8 °C. Stable until expiration date on pouch label.
Room temperature (unopened)	Unopened pouches may be stored at room temperature for up to 1 month.
After opening	For immediate use within 1 minute of 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 only.

CAUTION: Use outside intended purpose may lead to incorrectly interpreted results.

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

CAUTION: Single use only — do not reuse.

CAUTION: Any serious incident that has occurred as a result of the use of the device must 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.

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

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

NOTE: Dispose of waste according to local regulations.

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

Residual Risks, Undesirable Side-Effects, and Information for the Patient

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

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

Warnings related to residual risks are provided throughout this document. No undesirable side-effects were identified during 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 recommended procedures using a blood collection tube with 3.2% sodium citrate. Samples should be analysed within 3 hours from blood collection. Store 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. Use of an 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), allow the sample to warm up for 5 minutes on the heated position of the viscoelastometry analyzer.
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 reagents with the blood sample. Ensure sample pipetting is performed without interruption.
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 EX assay over time.

Result Interpretation and Expected Values

The CT detects coagulation activation. A5, A10, A20, MCF and ML detect clot formation and clot stability/fibrinolysis.

The reference range was determined in a clinical study including 121 healthy individuals (aged 19–79.3 years; 54.5% female, 45.5% male). Reference ranges were determined using the 95% central interval (2.5^{th} – 97.5^{th} percentile):

Parameter	Mean ± SD	2.5th – 97.5th Percentile
CT (sec)	48.3 ± 10.2	37 – 65
A5 (mm)	47.6 ± 4.7	40 – 57
A10 (mm)	55.2 ± 4.2	48 – 63
A20 (mm)	59.6 ± 3.7	53 – 66
MCF (mm)	60.2 ± 3.7	53 – 67
ML (%)	5.9 ± 2.6	2 – 12

Detection of Clotting Factor Deficiencies

EX CT cut-off >65 sec for INR ≥1.5. Study: 105 patients with suspected factor deficiencies + control group (n=104).

Measure	Value
Sensitivity	93%
Specificity	91%
Positive predictive value (PPV)	78%
Negative predictive value (NPV)	97%
Positive likelihood ratio (LR+)	10.25
Negative likelihood ratio (LR–)	0.08

Patients with INR >1.5 (n=54): EX CT mean 107.8 ± 28.4 sec (range 54–158 sec).

Accuracy of Clot Firmness

Comparison vs. EX-test by enicor demonstrated good agreement, with Spearman correlations ≥0.95.

Fibrinolysis Detection

Dose-response study using t-PA additions to citrated blood to assess fibrinolysis detection:

t-PA (ng/mL)	ML (%, mean±SD)	MCF (mm, mean±SD)
0	3.25 ± 0.5	56.8 ± 1
100	3.75 ± 0.5	56.5 ± 1
200	97 ± 0	48.8 ± 1.3
300	96 ± 0	39.8 ± 0.5
400	96 ± 0	34.3 ± 0.5
600	95 ± 0	28.8 ± 1

Precision

In a precision study, citrated blood with and without 50% haemodilution (HES) was tested in 3 runs, on 3 analyzers, 3 operators, including 3 EX assay lots (54 determinations per sample):

Sample	CT mean±SD (sec)	CT CV (%)	A20 mean±SD (mm)	A20 CV (%)
Citrated blood	51.9 ± 4.7	9.0%	58.3 ± 1.5	2.5%
50% haemodilution (HES)	114.5 ± 14.8	12.9%	34.9 ± 2.2	6.4%

Limitations and Interferences

Every in-vitro diagnostic method can deliver incorrect results under certain circumstances. Precautions should be taken to avoid misinterpretations.

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

In vitro additions tested include: aspirin, cangrelor, UFH, LMWH, apixaban, and haemodilution.

Interference Study — CT (sec):

Substances tested with in-vitro addition to citrated blood. Measurements performed in 6-fold determinations:

Substance / Condition	Mean (sec)	SD (sec)	Change vs. Control
Citrated blood (control)	69.5	3.3	n/a
+ Aspirin 0.1 mg/mL	63.7	3.5	–5.8
+ Cangrelor 100 ng/mL	64	3.3	–5.5
+ UFH 3 IU/mL	61	3.7	–8.5
+ UFH 5 IU/mL	80.8	3.7	+11.3
+ LMWH 1 IU/mL	64.7	8.5	–4.8
+ Apixaban 100 ng/mL	64.3	3.5	–5.2
+ Apixaban 300 ng/mL	96.2	19.8	+26.7
40% haemodilution	65.2	4.2	–4.3

NOTE: Apixaban at 300 ng/mL led to a marked prolongation of CT. Other substances resulted in minor changes only.

Interference Study — A20 (mm):

Substance / Condition	Mean (mm)	SD (mm)	Change vs. Control
Citrated blood (control)	54.3	0.8	n/a
+ Aspirin	54.3	1.2	0
+ Cangrelor	53.8	0.6	–0.5
+ UFH 3 IU/mL	54	0.6	–0.3
+ UFH 5 IU/mL	53.8	1	–0.5
+ LMWH 1 IU/mL	52.2	0.5	–2.1
+ Apixaban 100 ng/mL	53.8	0.9	–0.5
+ Apixaban 300 ng/mL	54	0.6	–0.3

Substance / Condition	Mean (mm)	SD (mm)	Change vs. Control
40% haemodilution	45.3	0.5	–9

NOTE: Haemodilution at 40% led to a marked decline in clot firmness (A20). All other tested substances resulted in minor or negligible changes.

Summary of Safety and Performance

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

Manufacturer

APIRO Diagnostics Kft.	Liget utca 3/2, HU-2040 Budaörs, Hungary
+36 30 203 3334	info@apiro.eu | www.apiro.eu
Distributed in Australia by:	Haemoview Diagnostics

Symbols

Symbol	Meaning	Symbol	Meaning
Manufacturer icon	Manufacturer	Hourglass icon	Use-by date
LOT	Batch code	REF	Catalogue number
Country of manufacture (HU)	Country of manufacture	Crossed box icon	Do not use if package is damaged
2°C – 8°C	Temperature limit	No-reuse icon	Do not re-use
IFU book icon	Consult instructions for use or eIFU	Σ n	Contains sufficient for <n> tests
Not for near-patient testing	Not intended for near-patient testing	■ Caution/Warning	Caution / Warning
UDI	Unique device identifier	CE 2265	CE marking of conformity (NB 2265)
IVD	In vitro diagnostic medical device	Biohazard icon	Biological risks

Version History

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

Disclaimer for Australian Healthcare Professionals
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