Instructions for Use

RVV Assay · REF 1071EU · UDI 59998629921071EU

Intended Purpose

The RVV Assay is a ready-to-use reagent for in-vitro diagnostic professional use, intended for detection of direct FXa antagonists 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 the presence of FXa antagonists in the patient's blood is suspected.

Contra-indications for Use

The assay shall not be used in patients treated with unfractionated heparin (UFH), as this can lead to false-positive results in the RVV assay.

Intended Users

- Trained healthcare professionals
- Trained laboratory professionals

Intended Patient Population

Adult patients suspected to be exposed to direct FXa antagonists.

Principle of the Assay

The RVV assay uses Russell's viper venom to directly activate coagulation factor X as the trigger for thrombin generation in whole blood on viscoelastometry analyzers.

Direct FXa inhibitors (apixaban, rivaroxaban, edoxaban) selectively and reversibly inhibit activated factor Xa. In the RVV assay, thrombin generation is mediated via coagulation factors X and V. The reagent contains Russell's viper venom and calcium chloride.

When no anticoagulants are present, the clotting time (CT) is short. In the presence of FXa antagonists, CT is prolonged. Due to its mode of action, the RVV assay is also sensitive to unfractionated heparin, dabigatran, and other anticoagulants — it is not specific to FXa antagonists alone.

The 50 ng/mL cut-off was defined according to published literature: "A DOAC level of less than 50 ng/mL may be considered a minimal, clinically insignificant anticoagulant effect."

Materials Provided

10 sealed single-use pouches, each containing one pipet tip with dry chemistry reagent (Russell's viper venom and calcium chloride). 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)

Reagent Preparation

The reagent is ready to use — no preparation required.

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; 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 the intended purpose may lead to incorrectly interpreted results.

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

CAUTION: Intended for 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: Wear gloves and minimise skin exposure when handling all materials.

CAUTION: Incorrect storage conditions may affect reagent stability.

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 bad 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 for this 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 an 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 automatically, or stop it 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 RVV assay over time.

Result Interpretation and Expected Values

The effect of FXa antagonists is detected by the clotting time (CT). A prolonged CT indicates the presence of FXa antagonists at clinically significant levels.

Reference Range for CT (Healthy Subjects)

The reference range was determined in a study of 122 healthy individuals (aged 18.9–79.2 years; 51.6% female, 48.4% male) using the 95% central interval (2.5^{th} – 97.5^{th} percentile):

Parameter	Mean	2.5th – 97.5th Percentile (sec)
RVV CT [sec]	Not stated	47 – 89

Clinical Study — FXa Antagonist Levels

102 samples from patients taking FXa antagonists; reference collective n=122.

Drug	N	Mean (ng/mL)	Min (ng/mL)	Max (ng/mL)	SD
Apixaban	58	205.5	0	488	131.2
Rivaroxaban	29	154.1	0	442	124.8
Edoxaban	15	220.5	36.7	453	134.3

RVV CT for Samples with FXa Antagonist >50 ng/mL (n=87)

Statistic	Value
Mean ± SD (sec)	238 ± 73.6
Range (sec)	110 – 430
2.5th – 97.5th Percentile (sec)	116.8 – 386.7

Diagnostic Performance at Cut-off 105 sec (Total N=224)

Measure	Value
Sensitivity	100%
Specificity	94%
Positive predictive value (PPV)	92%
Negative predictive value (NPV)	100%
Positive likelihood ratio (LR+)	17.13

Measure	Value
Negative likelihood ratio (LR–)	0

Precision

Precision was assessed in 3 runs, on 3 analyzers, by 3 operators, using 3 lots (54 determinations per sample). Results for RVV clotting time [sec]:

Sample	Mean CT (sec)	SD (sec)	CV (%)
Citrated blood	59.6	8.5	14.2%
CB + 200 ng/mL apixaban	272.2	31.2	11.5%

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. Clinical context must be considered when interpreting the RVV assay result.

The RVV assay is not specific to FXa antagonists. UFH, dabigatran, argatroban, and coagulation factor deficiencies can also prolong CT. More specific methods such as anti-FXa analysis or mass spectrometry are available but may have longer turnaround times.

Interference Testing Results (6-Fold, CT in seconds):

Substances were added in vitro to citrated blood. Measurements were performed in 6-fold determinations.

Substance / Condition	Mean CT (sec)	SD (sec)	Change vs. Control
Citrated blood (control)	73.7	5.9	n/a
UFH 0.5 IU/mL	212.5	22.3	+138.8
UFH 1 IU/mL	398.2	14.0	+324.5
LMWH 0.5 IU/mL	1599.0	121.4	+1525.3
LMWH 1 IU/mL	401.8	26.9	+328.1
Dabigatran 100 ng/mL	216.2	10.2	+142.5
Dabigatran 300 ng/mL	354.2	12.9	+280.5
20% Hemodilution	68.7	5.3	–5.0
40% Hemodilution	72.7	3.3	–1.0

NOTE: UFH, LMWH, and dabigatran markedly prolong the RVV assay CT. Hemodilution had little effect on the assay.

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

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Distribution (Australia)	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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