Haematex Research
Bleeding Matters

DOAC-TEST™

DOAC-Test Reagent X9211

RUO - RESEARCH / INVESTIGATIONAL USE ONLY

INTENDED USE
DOAC Test reagent can be used to detect all known DOACs (including dabigatran, apixaban, rivaroxaban and edoxaban) in plasma by a simple clotting time method.

INTRODUCTION
New or direct oral anticoagulants (DOACs) include inhibitors of thrombin (eg. dabigatran) and factor Xa (eg. rivaroxaban, apixaban and edoxaban). The latter group are difficult to quantitate using current clotting methods (1) and expensive chromogenic assays for the individual agents are in use.

The lupus anticoagulant-resistant dilute Russells viper venom test (dRVT-LR or "Confirm") has been suggested as a possible test method for all the DOACs since it is very sensitive to both classes of these inhibitors in vitro (2) and in vivo (3) and is less affected by extraneous variables such as heparins or low factor VIII levels than other clotting tests (2).

DOAC-test reagent is a modified phospholipid-rich Russells viper venom reagent with enhanced sensitivity to DOACs. It is a “ready for use” slightly cloudy orange solution. It is resistant to most lupus inhibitors and heparins (up to 1u/ml) but is sensitive to warfarin and defects in the common coagulation pathway.

CONTENTS OF PRODUCT

Product Code	Pack size
X9211	10ml vials

PRECAUTIONS
DOAC Test is intended for use on citrated test plasmas containing DOACs. If the test result is longer than 300 sec, test dilutions of the sample in pooled normal plasma as described in reference 3 and multiply the result by the dilution factor. If this does not help and DOACs are still suspected to be present, apply appropriate chromogenic or antithrombin assays to obtain specific DOAC results. Contact your distributor or manufacturer for technical support.

Do not use after the expiry date indicated on the label. The reagent is stable for approximately 1 year if stored at 2-8°C. Mix briefly before use. Treat all clinical material as potentially infectious and dispose of in accordance with local operating regulations. For further information, please refer to safety Data Sheet and Product details available from Haematex.

INSTRUCTIONS FOR USE
Sample preparation:
Blood samples should be collected by clean venipuncture 9:1 into 0.109M sodium citrate. Plasma should be tested soon after centrifugation at 1500g for 10 minutes in general accordance with principles of CLSI (4).

Method:
For manual tests, mix 0.2ml pre-warmed test sample in a clotting tube with 0.2ml DOAC-Test reagent (also at 37°C) and time to a clotting endpoint. Smaller volumes can be used but should remain in 1:1 ratio.

For automated tests, use thrombin time mode preferably with extended acquisition time (up to 200 sec).

APPLICATION
A test plasma should be tested with the DOAC-test reagent as described above. If the clotting time result is abnormal a 1:1 mix with normal plasma should be prepared and tested. The normal plasma for mixing should be carefully selected to provide results 30-40sec.

The clotting time result (sec) can be applied to the vertical axis of the calibration curve and interpolated horizontally onto the calibration curve defined previously for the relevant DOAC (Fig. 1). Then a concentration (ng/ml) can be derived from the horizontal axis.

If this procedure is followed for the 1:1 mix the apparent DOAC concentration should be multiplied by 2 to allow for dilution. If the results from the neat plasma and the mix correspond (+/- 10%) then there is probably no underlying defect affecting the common pathway. However, if the result from the neat plasma is significantly higher than that given by the diluted sample then an underlying defect co-exists with the DOAC. An APTT test may be helpful for further interpretation. Also, DOAC Stop can eliminate DOACs and reveal a baseline clotting result (7).

LIMITATIONS:
Quantitation is more reliable when carried out on mixes of test and normal plasma but is then less sensitive than results from neat plasma. All the usual precautions for turbid, icteric and haemolysed samples should be observed, especially if testing on a photoelectric coagulometer.

PERFORMANCE CHARACTERISTICS:
As with all clotting tests, the local normal range (+/- 2SD) and mean result should be determined according to CLSI guidelines (5). The normal range depends on partly on instrumentation, reagent and the category of subjects being studied (eg. age, pregnancy, etc) but is approximately 30-40sec on normal healthy donors.

Calibration curves (as shown in Fig. 1) can be prepared by using DOAC standards diluted in normal plasma as described previously (2). DOAC-containing calibrators are available from various commercial suppliers.

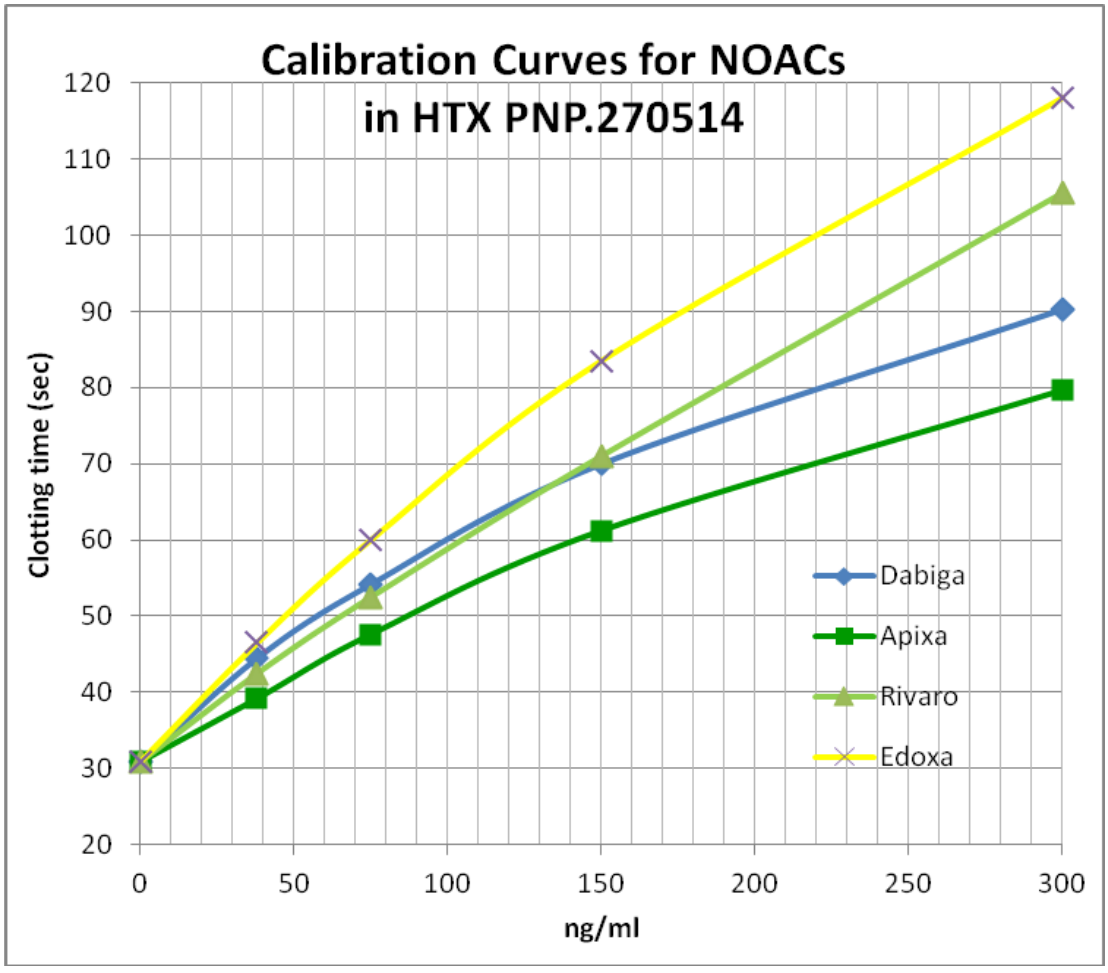
INDEMNITY NOTICE

DOAC Test is intended for use on plasma samples containing DOACs. Follow procedures and refer to precautions that may affect the stated or implied claims and performance of this product. Haematex or its distributors are not liable for damages.

REFERENCES

1. Ten Cate H. Monitoring new oral anticoagulants, managing thrombosis or both? Thromb. Haemost. 2012; 107; 803-805.
2. Exner T, Ellwood L, Rubie J, Barancewicz. Testing for new oral anticoagulants with LA resistant Russell's viper venom reagents. An in vitro study. Thromb. Haemost. 2013; 109; 762-5.
3. Altman R, Gonzalez CD. Simple and rapid assay for effect of the new oral anticoagulant (NOAC) rivaroxaban: preliminary results support further tests with all NOACs. Thromb. J. 2014; 12; 7.
4. CLSI; blood sample collection guidelines.
5. CLSI; normal ranges etc.
6. Sennesael AL, Exner T, Chatelain B, et al, An optimized dRVVT-based assay to estimate the intensity of anticoagulation in patients treated with direct oral anticoagulants. Thromb Res. 2017; 157: 29-37.
7. Exner T, Michalopoulos N, Pearce J. et al. Simple method for removing DOACs from plasma samples. Thromb. Res. 2018; 16: 1028-39.

FIG.1.



HTX.190519