Calibration

Each **BIOPHEN Rivaroxaban Plasma Calibrator kit** contains 4 sets of 3 vials with increasing concentrations of Rivaroxaban.

Calibrator	Indicative Rivaroxaban concentration (µg/ml)	Intra assay SD (n=10)	Inter assay SD (n=6)
CAL1	0,00*	0,003	0,008
CAL2	0,25*	0,008	0,010
CAL3	0,50*	0,014	0,021

Controls

Each **BIOPHEN Rivaroxaban Control Plasma kit** contains 2 sets of 6 vials with 2 different concentrations of Rivaroxaban. The Rivaroxaban concentrations and the acceptance ranges are indicated for each lot on the flyer provided with the kit. The following example shows the Rivaroxaban concentrations for one lot of Rivaroxaban Control Plasma:

Rivaroxaban Control	Rivaroxaban conc. (µg/ml)	Acceptance Range (µg/ml)	Intra assay SD (n=10)	Inter assay SD (n=6)
Level 1	0,10*	0,05 - 0,15	0,007	0,007
Level 2	0,30*	0,22 - 0,38	0,013	0,012

**These values are an example only : the exact concentration is provided for each lot on a batch specific flyer.*

Available Products

These products are CE marked.

In US: For Research Use Only. Not for Use in Diagnostic Procedures.

Product	Reference	Package
BIOPHEN DiXal	A221030	3 x 2.5 ml (3 x 50 tests)
BIOPHEN Heparin LRT	A221011	4 x 7.5 ml (4 x 100 tests)
BIOPHEN Rivaroxaban Plasma Calibrator	A222701	4 sets of 3 x 1 ml
BIOPHEN Rivaroxaban Plasma Control	A224501	6 sets of 2 x 1 ml

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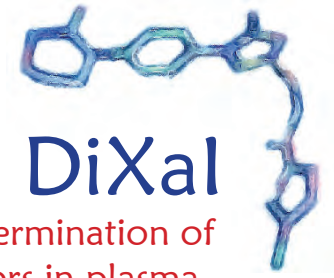
Manufactured By: HYPHEN BioMed



BIOPHEN® DiXal

For the quantitative determination of Direct Factor Xa Inhibitors in plasma

simple robust assay
insensitive to heparins
fully automatable
reliable laboratory method for measuring Rivaroxaban

Form AH162
02-2012

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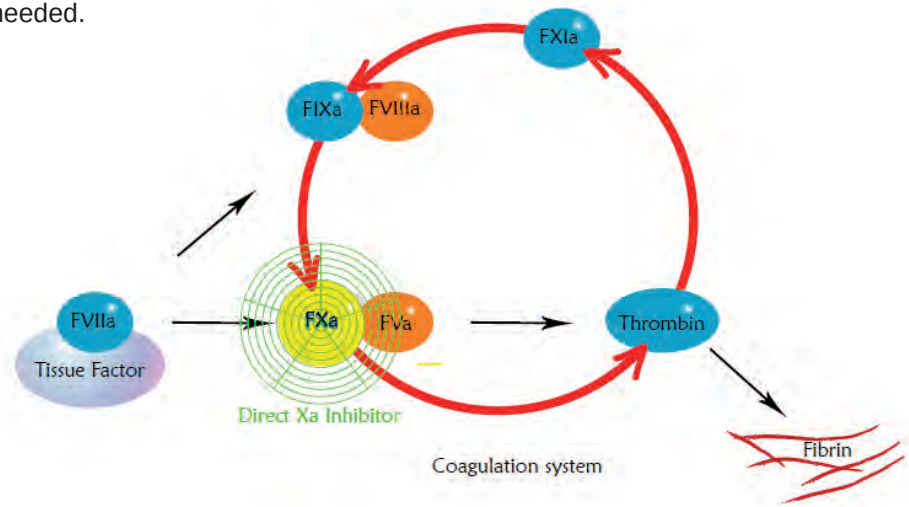
Introduction

Direct factor Xa Inhibitors (DiXaI) have increased prophylactic or curative applications in anticoagulant therapy. New oral DiXaI, like Rivaroxaban, are being introduced as a safe alternative for the treatment with vitamin K antagonists or with low molecular weight heparin. No routine monitoring is needed.



Rivaroxaban is a small-molecule that binds directly to factor Xa. It does not require antithrombin to exert its anticoagulant effect. Rivaroxaban competitively inhibits both free, Prothrombinase-bound, and clot-bound factor Xa.

In specific situations a good laboratory method for the determination of the kinetics of the drug in the human body is useful. This method has to be free of interference by plasmatic factors or by indirect inhibitors of factor Xa, and should have an optimised sensitivity in the therapeutic range.

The majority of the routine coagulation assays will be disturbed by DiXaI. A prolonged PT might give an indication for the presence of DiXaI, but it can not be applied for the quantitative determination.

Current Anti-Xa heparin assays, like **BIOPHEN Heparin LRT** (Ref. A221011), can be used along with Rivaroxaban plasma calibrators and controls at an adjusted sample dilution. These assays however are not optimised for DiXaI as these are designed for indirect, antithrombin dependent, factor Xa inhibitors. The mechanisms and kinetics of DiXaI are completely different.

BIOPHEN DiXaI is a chromogenic assay for in vitro quantitative measurement of Direct factor Xa Inhibitors, such as Rivaroxaban, in human citrated plasma or purified milieu.

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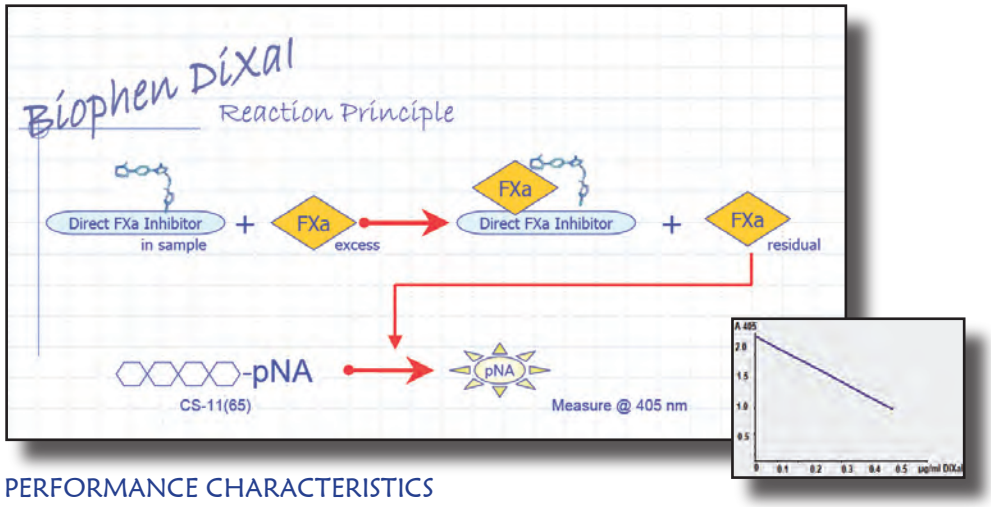
Assay Principle

Biophen DiXaI is a two stage method based on the inhibition of a constant and excess amount of exogenous factor Xa by the tested DiXaI. Rivaroxaban inhibits human Factor Xa in a mole to mole ratio. The factor Xa added to the test mixture will partially be blocked by the DiXaI while the residual factor Xa will hydrolyse a factor Xa specific chromogenic substrate.
The yellow colour emitted is in direct relationship with the residual factor Xa activity. There is an inverse relationship between the concentration of DiXaI in the tested sample and the colour development.



PERFORMANCE CHARACTERISTICS

The assay is calibrated and optimised for Rivaroxaban.
The curves are constructed in function of the Rivaroxaban concentration expressed in µg/ml.

The dynamic range is from 0 to about 0.5 µg/ml for Rivaroxaban in plasma, which covers the recommended plasma levels widely. If a higher working range is required, the standard assay dilution can be adjusted accordingly.

The assay is designed for minimizing the interference of plasma factors. The assay is totally insensitive to the presence of heparin-like indirect anti-FXa activities such as UFH, LMWH, Fondaparinux and Sodium Danaparoid at usual therapeutic doses

Automated Methods

This method is easy to adapt on automated systems. Validated applications are available for the most common coagulation analysers.

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