BIOPHEN® DABIGATRAN CALIBRATOR LOW
Ref 222901

CE

Set of human plasma assigned for Dabigatran intended to the calibration of the Dabigatran assays using anti-IIa method.

For in vitro diagnostic use only

Not for Sale in the US

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ENGLISH

INTENDED USE:
Dabigatran Plasma Calibrator is a set of calibration plasmas for Dabigatran measurements, titrated and optimised using the anti-IIa clotting assay **HEMOCLOT THROMBIN INHIBITORS (CK002K/CK002L).**

CLINICAL INTEREST:
Dabigatran (Pradaxa®) is an oral anticoagulant drug, used for curative or preventive indications although monitoring of this treatment is not necessary, when required, measuring the concentration in human plasma is helpful in some clinical case: in case of suspicion of excess of anticoagulant activity or emergency surgery.
BIOPHEN® DABIGATRAN Calibrator Low is proposed to establish the calibration curve for Dabigatran anti-IIa clotting assays.

REAGENTS:
The BIOPHEN® DABIGATRAN Calibrator Low contains 12 vials of 1 mL human plasma supplemented with different concentrations of Dabigatran (3 levels, 4 vials for each concentration).

CAL 1: ***Calibrator 1:***
Human plasma, freeze-dried, without Dabigatran concentration.
4 vials of 1 mL

CAL 2: ***Calibrator 2:***
Human plasma, freeze-dried, with Dabigatran concentration in the range 40-60 ng/mL. 4 vials of 1 mL

CAL 3: ***Calibrator 3:***
Human plasma, freeze-dried, with Dabigatran concentration in the range 80-120 ng/mL. 4 vials of 1 mL

The concentrations of the calibrators may slightly vary from lot to lot. For the assay, refer to the concentrations indicated on the flyer provided within the kit.

Note:
- Calibrator plasmas contain an antibiotic as preservative, and stabilizers.
- Each human plasma unit is from healthy donors. Each plasma has been tested with registered methods for the presence of Hepatitis B Surface Antigen, Hepatitis C Antibodies (HVC) and antibodies to HIV 1 and 2 and was found negative. However, no test can completely exclude the presence of infectious agents. Any product of human origin, and more especially plasma, must be considered as being potentially infectious and must be handled with all the required cautions for this kind of material.

REAGENT REQUIRED BUT NOT PROVIDED:
Reagents:
HEMOCLOT Thrombin Inhibitors (ref. CK002K/CK002L) or equivalent.
BIOPHEN® DABIGATRAN Control Low (ref. 225001) or equivalent.
Distilled water
Materials:
Spectrophotometer or automatic instrument for clotting assays.
Chronometer
Calibrated pipettes.

TRACEABILITY
These concentrations are accurately determined against an Internal Reference Standard, initially validated against fresh reference preparations of Dabigatran, spiked into a normal human citrated plasma pool, and confirmed with a physico-chemical method (HPLC).

STORAGE CONDITIONS:
Unopened vials, must be stored at 2–8 °C. Kept in their original packaging they are then stable until the expiration date printed on the label.

Note: The stability studies at 30°C show that the reagents can be shipped at room temperature without damage.

PREPARATION AND STABILITY OF REAGENTS:
Preparation:
- Reconstitute each vial with exactly **1 mL** of distilled water.
- Shake thoroughly until complete dissolution of the content (vortex).
- Incubate at room temperature, RT (18-25°C) for 30 min, while shaking the vial from time to time.
- Homogenise the content before each use.

Stability after reconstitution, in their original vial
- 7 days at 2-8°C.
- 48 hours at room temperature (18-25°C).
- 2 months at -20°C or below[7]

Cautions: freezing conditions and stability of the thawed product should be checked in the working conditions of the laboratory user.

CAUTIONS:
- Reagents vials are closed under vacuum. Remove carefully the stopper, in order to avoid any lost of powder when opening the vials.
- In order to ensure stability, reagents must be closed with their original screw cap following each use, or closed in the micro plastic containers in which the plasma could be aliquoted (depending on the protocol and the instrument used.
- Reagents must be handled with care, in order to avoid any contamination during use.
- It is recommended to homogenize each plasma before use, in order to have a good reproducibility (at all time).
- Incubating the reconstituted vials at RT allows stabilizing the reagents, and obtaining a homogeneous reactivity.
- Take care to limit as much as possible any evaporation of the reagents during use, eg. by using chimneys.
- The disposal of waste materials will be carried out according to current local regulations.

PROCEDURE:
Refer to the packaging insert of reagents used.

QUALITY CONTROL:
If used with other kits, measured values can vary according to the assay reactivity and its standardization: each laboratory must then determine and validate the suitability for use in its specific test conditions

PERFORMANCE:
The Dabigatran concentration of the control may vary from lot to lot, but it is precisely indicated, for each lot, on the flyer provided.
The following values, obtained for one lot of BIOPHEN® DABIGATRAN calibrator low are provided as an example only:

Callibrator	Target values of Dabigatran (ng/mL)*	Intra assay*		Inter assay**	
		N	SD (ng/mL)	N	SD (ng/mL)
CAL 1	0	15	1.31	11	0.69
CAL 2	57	15	1.80	11	2.99
CAL 3	107	15	2.92	11	5.95

*: performed on water bath using HEMOCLOT Thrombin Inhibitor
**: compilation of test performed on water bath, CS 5100 and STA-R, using HEMOCLOT Thrombin Inhibitor
The calibration curve covers the range from 0 to about 120 ng/mL.

CHARACTERISTICS:
BIOPHEN® DABIGATRAN Calibrator Low allows establishing the calibration curve for the measurement of Dabigatran in plasma, especially with anti-IIa methods: HEMOCLOT Thrombin Inhibitor (ref. CK002K/CK002L) kit.

LIMITATIONS:
- As all lyophilised plasmas, the calibration plasmas are more or less cloudy after reconstitution. This is due essentially to the lipids that, after lyophilisation, become less soluble and can form a small deposit.
- If necessary, let each vial 10 minutes at room temperature and shake gently before use in order to homogenise the content.
- Reagents must be handled with care, in order to avoid any contamination or activation during use. Any plasma containing a coagulum or contamination must be rejected.

REFERENCES:
1. Product Monograph Pradaxa® (Dabigatran etexilate) based on EU approval (Boehringer Ingelheim)
2. Oral Dabigatran etexilate vs subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the Re-MODEL randomized trial" Eriksson et al., J Thromb Haemost, 2007, 5:2178-85.
3. Dabigatran etexilate vs enoxaparin for the prevention of venous thromboembolism after total hip replacement: a randomised, double-blind, non inferiority trial" Eriksson et al., Lancet, 2007, 370:949-956.
4. Clinical Pharmacokinetics and Pharmacodynamics of the Oral Direct Thrombin Inhibitor Dabigatran Etexilate, J Stangier, Clin Pharmacokinet 2008; 47(5): 285-295.
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6. A new oral direct thrombin inhibitor, Dabigatran etexilate, compared with enoxaparin for prevention of thromboembolic events following total hip or knee replacement: the BISTRO II randomized trial; Eriksson et al, J Thromb Haemost 2005, 3: 103-111.
7. Stability of coagulation proteins in frozen plasma; Woodhams et al, Blood coagulation fibrinolysis 2001; 12(4):229-236