BIOPHEN® DABIGATRAN CONTROL LOW
Ref 225001

CE

Human plasmas at two levels of Dabigatran for the quality control of Dabigatran measurements with anti-IIa methods

For in vitro diagnostic use only

Not for Sale in the US

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Last revision: 27/11/2014

ENGLISH

INTENDED USE:
BIOPHEN® DABIGATRAN Control Low Kit is a set of 2 levels control plasmas lyophilised and spiked with Dabigatran. They are titrated and optimised for anti-IIa clotting assays, such as HEMOCLOT Thrombin Inhibitors assay (low range protocol) (#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.
These control plasmas are then proposed for the quality control of Dabigatran measurements in plasma using anti-IIa clotting assays.

REAGENTS SUPPLIED:
The BIOPHEN® DABIGATRAN Control Low Kit contains 12 vials of 1 mL of human plasma supplemented at 2 different concentrations of Dabigatran (6 vials for each concentration).

C1: ***Control 1***
Human plasma, freeze-dried, with dabigatran concentration in the range 15-35 ng/mL. 6 vials of 1 mL

C2: ***Control 2:***
Human plasma, freeze-dried, with dabigatran concentration in the range 45-105 ng/mL. 6 vials of 1 mL

The concentrations of the controls may slightly vary from lot to lot. For the assay, refer to the concentration indicated on the flyer provided in the kit used.

Note:
- Control 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 Calibrator Low (ref. 222901) 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, controls 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 controls are out of the acceptance range, the test series can be invalid, and the assay should be rerun. Check all the components of the test system, before repeating the assay.
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 I precisely indicated, for each lot, on the flyer provided.
The following Dabigatran concentrations are provided for information only:

Dabigatran Control	Target Value of Dabigatran (ng/mL)	Acceptance Range (ng/mL)	Intra assay*		Inter assay**	
			N	SD (ng/mL)	N	SD (ng/mL)
Level 1	29.7	15 – 35	15	1.52	12	2.1
Level 2	81.2	45- 150	15	2.14	12	4.3

*: performed on Water bath using HEMOCLOT Thrombin Inhibitor (ref. CK002K/CK002L).
**: compilation of test performed on water bath, CS 5100 and STA-R, using HEMOCLOT Thrombin Inhibitor (ref. CK002K/CK002L).

CHARACTERISTICS:
BIOPHEN® DABIGATRAN Control Low (level 1 and 2) are proposed for the quality control of calibration curves established for the measurements of dabigatran in plasma, especially when used anti-IIa method. The results are guaranteed and optimised for being used with HEMOCLOT Thrombin Inhibitor (ref. CK002K/CK002L) assays.

LIMITATIONS:
- As all lyophilised plasmas, the control 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.
5. The pharmacokinetics, pharmacodynamics and tolerability of Dabigatran etexilate, a new oral direct thrombin inhibitor, in healthy male subjects, J Stangier et al, Br J Clin Pharmacol 2007, vol 63.
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