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CE

# DABIGATRAN CONTROL PLASMA
# Ref 224701

Human plasmas at two levels of dabigatran for the quality control of dabigatran measurements with anti-IIa method

For in vitro diagnostic use only

**Not for Sale in the US**

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## ENGLISH

## INTENDED USE:
Dabigatran Control Plasma Kit is a set of control plasmas for the quality control of dabigatran measurements, using anti-IIa clotting assay. This kit is optimised for being used with the HEMOCLOT THROMBIN INHIBITORS assay (#CK002K/CK002L).

## CLINICAL INTEREST:
Dabigatran is the active moiety of the oral anticoagulant pro-drug, dabigatran etexilate (Pradaxa®). When required, dabigatran can be measured in plasma in case of suspicion of excess of anticoagulant activity.

## REAGENTS:
12 vials (6 sets of 2 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 a dabigatran concentration in the range 50 – 200 ng/mL. 6 vials of 1 mL

**C2:** ***Control 2:***
Human plasma, freeze-dried, with a dabigatran concentration in the range 200 – 400 ng/mL. 6 vials of 1 mL

The dabigatran concentrations and the acceptance ranges are indicated for each lot on the flyer provided within the kit.

**Note:**
- Control plasmas contain an antibiotic as preservative.
- Each donor unit used for the preparation of control plasmas is a human plasma, which 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.

## REAGENTS REQUIRED BUT NOT PROVIDED:
***Reagents*:**
Hemoclot Thrombin Inhibitor (ref. CK002K/CK002L) or equivalent
Dabigatran Plasma Calibrator (ref. 222801) or equivalent
Distilled water

***Materials:***
Spectrophotometer or automated analysers for clotting assays.
Calibrated pipettes.

## TRACEABILITY:
Dabigatran Controls 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 reagents, 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 (18-25°C) for 30 min, while shaking the vial from time to time.
- Homogenize the content before each use.

**Stability after reconstitution:**
- 7 days at 2-8°C.
- 48 hours at room temperature (18-25°C).
- Up to 6 month frozen at - 20°C or below.

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

## CAUTIONS:
- Vials are closed under vacuum. Remove carefully the stopper, in order to avoid any loss of powder when opening the vials.
- In order to ensure stability, reagents must be closed with their original screw cap following each use, or stored 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, e.g. by using chimneys, when available.
- The disposal of waste materials will be carried out according to current local regulations.

## PROCEDURE:
Refer to the packaging insert of the reagent used.

## QUALITY CONTROL:
If controls are out of the acceptance range, the test series must be invalidated, and the assay should be rerun. Check all the components of the test system, before repeating the assay.
If used with anti IIa assays from other manufacturers, measured values can vary according to the assay reactivity and its standardization: each laboratory must then determine and validate the acceptance ranges in its specific test conditions.

## PERFORMANCE:
The Dabigatran concentrations of controls may vary from lot to lot, but they are exactly indicated, for each lot, on the flyer provided.
The following Dabigatran concentrations are provided for information only:

| Dabigatran Control | Dabigatran (ng/ml) | Intra assay | | Inter assay | |
|---|---|---|---|---|---|
| | | N | SD | N | SD |
| **Level 1** | 120 | 20 | 3 | 11 | 7 |
| **Level 2** | 300 | 20 | 8 | 11 | 12 |

Dabigatran Control Plasma (lot 03001, obtained on KC10 and STAR):

## CARACTERISTICS:
Dabigatran Control Plasmas (level 1 and 2) are proposed for the quality control of calibration curves established for the measurements of dabigatran in plasma. They allow validating these calibration curves. They are especially useful for controlling the stability of the calibration curves, from run to run, when using a same lot of reagents.
The target values for controls have been made determined using the anti-II assays (Hemoclot Thrombin Inhibitor kit).

## LIMITATIONS:
- As all lyophilized plasmas, control plasmas are more or less cloudy after reconstitution. This is due essentially to 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.