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Package insert, version 06 deks@deks.dk

INR Kalibrator Terapeutisk
(INR Calibrator Therapeutic)

Product code 3346 DK

LOT 04-18 2027-04 IVD CE

Assigned Value

P-Coagulation, tissue factor-induced; rel.time (actual/norm; INR; IRP 67/40) **2,35 INR** U=0,05 INR (k=2)

Expected Use

The calibrator is used for calibration of INR[1]-analysis P-Coagulation, tissue factor-induced; rel.time (actual/norm; INR; IRP 67/40) (INR), together with *Coagulation Calibrator Normal* and *INR Calibrator High.* This is done with the determination of the International Sensitivity Index (ISI) and the normal coagulation time (MNPT) for each laboratory's testing system (procedure, reagent and instrument).

Receipt

Upon receipt it is checked that the calibrators are frozen.
Are the calibrators *not* frozen, the validity can be reduced, or the samples can be totally useless – please contact DEKS.

Safety

The material must be handled with the same precautions as patient samples.
The used donor plasma has individually tested negative for hepatitis B, hepatitis C and HIV.
The calibrator and waste products should be handled as potentially infectious patient specimens according to the laboratory's internal instructions and good laboratory practice.

The calibrators may only be handled by educated persons qualified to perform calibration.

The calibrators may not be used for calibration:

- if they were thawed at receipt
- if they have exceeded the shelf-life
- if they have exceeded the maximum in-use stability after thawing
- if they have been thawed-frozen-and-thawed again

as the assigned values may be altered.

Material

The calibrator is produced from plasma taken from patients during stabile anti-coagulation treatment.
Whole blood collected from these patients are diluted with 3,2 % natrium citrate at a ratio of 9-part whole blood and 1-part citrate. Subsequently, the plasma is separated and frozen at -80°C. The separate portions are thawed and pooled before it is aliquoted into vials of 0,5 mL (filling volume) and frozen at -80°C.

Shelf-life

The calibrator is at -80 °C valid until the end of April 2027 and at –20°C it is valid for two weeks.

[1] INR is short for International Normalized Ratio.

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In-use Stability

After thawing the calibrator can be used for a maximum of 4 hours.

Calibration of Analytical Equipment

Calibration must be performed with equipment and with a reagent intended for the relevant tests and according to manufacturer's procedure. The equipment must be maintained regularly and adequately suited for the examination of the chosen components.
The analytical equipment should as minimum be calibrated following the change of reagent batch, following equipment adjustments or when service has been made on the equipment.
Calibration must always be carried out when the internal controls do not meet acceptance criteria.
It is recommended that the calibration of the quantity of INR is performed as a three-point calibration[2] where calibrators are used with levels corresponding to normal, therapeutic, and high INR-level.

Handling and Use

Thawing and preparation of the calibrator

1. The calibrator is thawed at a water bath at 37 °C in exactly 5 minutes, mixed in a turning device at ambient temperature for 5-10 minutes.
   Mixing without a turning device is possible by holding the calibrator between thumb and index finger and tilting it carefully 180º approx. 20 times.
   The calibrator must have room temperature before use.

2. Coagulation times for *INR Calibrator Therapeutic*, *Coagulation calibrator Normal* and *INR Calibrator High* is decided with the laboratory's routine method.
   At least five measurements are made on each set of material. Mean values of the results are calculated.
   If one result deviates more than 5% from the mean value, the result should be omitted.

3. Find the spreadsheet: www.deks.dk/laboratorier/pakningsvedlaeg
   and fill in the measurement results[3].
   USE ONLY THE LATEST VERSION OF THE SPREADSHEET AND CHECK THAT THE VALUES ARE CONSISTENT WITH THE USED LOT OF CALIBRATORS.
   The spreadsheet calculates 'Mean Normal Prothrombin Time' (MNPT) and 'International Sensitivity Index' (ISI) and follows the principle from van den Besselaar, et al. [4].

Value Assignment and Traceability

The determination of P-Coagulation, tissue factor-induced; rel.time (actual/norm; INR; IRP 67/40) was performed by 3 expert laboratories: Linköping University Hospital, Aalborg University Hospital, Region Northern Jutland and Hospital of South West Jutland, Region Southern Denmark.
The material is determined in relation to the two international reference preparations of thromboplastins: WHO 5th IRP, Human Recombinant Plain (rTF/16) and WHO 5th IRP, Rabbit Plain (RBT/16) [1-2]. The measurements are performed by each expert laboratory by the manual reference method, in correspondence to a protocol, that complies with WHO guidelines [3].
The expanded uncertainty, U, that indicates the 95%-confidence interval of the value (2,35 INR), is assigned to 0,05 INR with the coverage factor k=2, which corresponds to a standard deviation of the mean (SEM) of 0,025 INR.
The calibrator, the 7th national INR Calibrator Therapeutic, is just as with previous changes of batches examined in relation to previous Danish INR-Calibrators with the use of routine thromboplastin-reagents to verify that the national level is not changed over time.

[2] 3 point calibrating complies with WHO's recommendations [4] for the use of plasma pools and ensures a calibration of the test over a wide area.
[3] The spreadsheet performs a orthogonal regression as described by van den Besselaar, AMHP [5].

Reference

In addition to *INR Calibrator Therapeutic* DEKS also offers *Coagulation Calibrator Normal* (product code 2004 DK) and *INR Calibrator High* (product code 3252 DK) for calibrating the INR.

Orders and Shipment of the Calibrator

INR Calibrator Therapeutic is found in packages of 2 vials or in a twin pack with med INR Calibrator *High* and Coagulation Calibrator *Normal* and is ordered via DEKS. The order is placed via the online ordering system at www.deksonline.dk (login required).
DEKS can be reached at tel. +45 3863 4400 or e-mail: deks@deks.dk.
Please stated Purchase Order number
The materials are shipped as dry-ice shipment.

Literature references

[1] The National Institute for Biological Standards and Control (NIBSC), WHO 5th International Standard Thromboplastin, Human, Recombinant, Plain, NIBSC code: rTF/16, Instructions for use (Version 1.0). 1-3. 2016-10-24.

[2] The National Institute for Biological Standards and Control (NIBSC), WHO 5th International Standard Thromboplastin, Rabbit, Plain, NIBSC code: RBT/16, Instructions for use (Version 3.0). 1-3. 2016-10-24.

[3] WHO, WHO Expert Committee Biological Standardization Guidelines for Thromboplastines and Plasma Used to Control Oral Anticoagulant Therapy. 64-93. 1999. Genova. WHO Technical Report Series no. 889.

[4] van den Besselaar, AMHP. *et al*. Journal of Thrombosis and Haemostasis. 1946-1953, 2, 2004.

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Revision history

2018-12: Version 01: Prepared

2019-08: Version 02: A few misspellings have been changed.

2020-01: Version 03: A new link www.deks.dk/laboratorier/pakningsvedlaeg and linguistic corrections

2021-03: Version 04: New name in heading

2022-04: Version 05: Linguistic changes. *Expert information* removed

2023-03: Version 06: Shelf-life listed incorrectly in the former versions