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Package insert, version 6, deks@deks.dk

INR Kalibrator Høj

Product code 3252 DK LOT **14-08** **2022-08** IVD CE

Assigned Values

P-Coagulation, tissue factor-induced; rel.time (actual/norm; INR[1]; IRP 67/40)	**3,50 INR**	U=0,10 INR (k=2)

Expected Use

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

Receipt

Receiving the samples, it is checked that the samples are frozen.
Are the samples *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 and C plus HIV. The samples may only be handled by educated persons qualified to perform calibration.
The samples may not be used for calibration if they were thawed at receipt, have exceeded the shelf-life or maximum in-use stability after thawing or if they have been thawed-frozen-and-thawed again, as the assigned values may be altered.

Material

The calibrator is produced from plasma from patients in stabile anti-coagulation treatment.
Full blood from these patients are when collected diluted with 3,2 % natrium citrate in the proportion 9-part blood and 1-part citrate. Subsequently, the plasma is separated and frozen at -80°C. The separate portions are thawed and mixed in a pool, which is then aliquoted into vials of 0,5 mL (filling volume). The material is frozen and kept at -80°C.

Shelf-life

The calibrator is at -80 °C valid until August 2022 and at –20°C it is valid for two weeks.

In-use Stability

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

[1] INR is short for International Normalized Ratio.

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Calibration of Analytical Equipment

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 performed when the internal controls show a need.
Calibration must be performed with equipment and with a reagent intended for the relevant tests and in correspondence with the manufacturer of the equipment's procedure. The equipment must be maintained and adequately suited for the examination of the chosen components.

Handling and Use

Defrosting 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 2.
   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*. [5].

Value Assignment and Traceability

The determination of P-Coagulation, tissue factor-induced; rel.time is performed by 3 expert laboratories: Linköping University Hospital, Aalborg University Hospital, Region Northern Jutland and Roskilde Hospital, Region Zealand.
The material is determined in relation to the three international reference preparations of thromboplastins: WHO 4th IRP, Human Recombinant Plain (rTF/09), WHO IRP, Rabbit Plain (RBT/05), and WHO 2nd IRP, Bovine Combined (OBT/79) [1-3]. The measurements are performed by each expert laboratory by the manual reference method, in relation to a protocol, that complies with the WHO guidelines [4].
The expanded uncertainty, U, that indicates the 95%-confidence interval of the value (3,50 INR), is determined to 0,10 INR with the expansion factor k=2, which corresponds to a standard deviation of the mean (SEM) of 0,0486 INR.
The calibrator, the 3rd national INR Calibrator High, is just as with previous changes of batches tested in relation to previous Danish INR-Calibrators with the use of routine thromboplastin-reagents to control 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 High' DEKS also offers 'Coagulation Calibrator Normal' (product code 2004 DK) and 'INR Calibrator Therapeutic' (product code 3346 DK) for calibrating the quantity P-Coagulation, tissue factor-induced; rel.time (actual/norm; INR; IRP 67/40).

Orders and Shipment of the Calibrator

INR Calibrator *High* is found in packages of 2 vials or in a twin pack with med INR Calibrator *Therapeutic* and Coagulation calibrator *Normal* and is ordered via DEKS. The order is placed via the on-line ordering system at www.deks.dk.
DEKS can be reached at tel. +45 3863 4400 or e-mail: deks@deks.dk.
The materials are shipped as dry-ice shipment.

Expert

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Literature references

[1] Institute for Reference Materials and Measurements (IRMM). Certificate of Analysis, ERM-AD148 Thromboplastin bovine (OBT/79). 1-10. 2004-5-1.

[2] The National Institute for Biological Standards and Control (NIBSC), WHO 4th International Standard Thromboplastin, Human, Recombinant, Plain, NIBSC code: rTF/09, Instructions for use (Version 2.0). 1-3. 2012-11-30.

[3] The National Institute for Biological Standards and Control (NIBSC), WHO International Standard Thromboplastin, Rabbit, Plain, NIBSC code: RBT/05, Instructions for use (Version 3.0). 1-3. 2012-12-13.

[4] 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.

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

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Revision history

2015-10: Version 1
2017-02: Version 2. New DEKS logo
2017-11: Version 3. New document template
2019-01: Version 4. A few linguistic corrections
2019-08: Version 5. A few misspellings have been changed
2020-01: Version 6. A new link www.deks.dk/laboratorier/pakningsvedlaeg and linguistic corrections