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Package insert, version 02, deks@deks.dk

INR Calibrator High
(INR Calibrator High)

Produktkode 3252 DK

LOT **22-06** **2030** IVD CE

Assigned Value

P-Coagulation, tissue factor-induced; rel.time (actual/norm; INR[1]; IRP 67/40)	**3.57 INR**	U=0.084 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

Upon receipt it is checked that the calibrators are frozen.
Are the calibrators *not* frozen, the validity can be reduced, or the calibrators 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 samples 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 samples 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 drawn from patients during stabile anti-coagulation treatment.
Whole blood collected from these patients are diluted with natrium citrate 0.109 M 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 and stored at -80 °C.

Shelf-life

The calibrator is at -80 °C valid until the end of year 2030 and at –20 °C it is valid for 2 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 the manufacturer's procedure. The equipment must be maintained regularly and adequately suited for the examination of P-Coagulation, tissue factor-induced; rel.time (actual/norm; INR; IRP 67/40).
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 show a need.

Handling and Use

1. The calibrator is thawed at a water bath or a heating block 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 180° 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: *Beregning af ISI og MNPT (normalkoagulationstid)*:
   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. [1].

Value Assignment and Traceability

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) [2-3].
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 determination of P-Coagulation, tissue factor-induced; rel.time (actual/norm; INR; IRP 67/40) was performed by 3 expert laboratories: Zealand University Hospital, Roskilde; Southwest Jutland Hospital, Esbjerg and Linköping University Hospital.
The expanded uncertainty, U, that indicates the 95%-confidence interval of the value (3,57 INR), is determined to 0,084 INR with the coverage factor k=2,0.
The calibrator, the 4th 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 verify that the national level is not changed over time.

[2] 3-point calibration follows the WHO recommendations [4] for the use of plasma pools and ensures a calibration of the assay over a wide range
[3] The spreadsheet performs an orthogonal regression as described by van den Besselaar, AMHP [1].

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 INR.

Orders and Shipment of the Calibrator

INR Calibrator High is found in packages of 2 vials or in a tripple pack with med *INR Calibrator Therapeutic* and *Coagulation Calibrator Normal* (product code 3457 DK) 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 ☎ +45 3863 4400 or ☜ deks@deks.dk.
The materials are shipped as dry-ice shipment.

Literature references

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

[2] The National Institute for Biological Standards and Control (NIBSC), WHO 5th International Standard 2016. Thromboplastin, Human, Recombinant, Plain. NIBSC Code: rTF/16. Instructions for use (Version 2.0) 1-3. 2021-02-03.

[3] The National Institute for Biological Standards and Control (NIBSC), WHO 5th International Standard 2016. Thromboplastin, Rabbit, Plain. Code: RBT/16. Instructions for use (Version 4.0). 1-3. 2021-02-03.

[4] WHO, WHO Expert Committee Biological Standardization, Guidelines for thromboplastins and plasma used to control oral anticoagulant therapy with vitamin K antagonists. 271-303. 2013. Genova. WHO Technical Report Series no. 979

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Revision history

Version	Year-month	
01	2022-06	Package insert created
02	2023-06	