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Certificate of analysis NFKK Reference Serum X: a reprint

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This is a reprint of the first official version of the certificate of analysis for NFKK Reference Serum X. It should be noted that the content of the certificate might be subject to changes in the future and one always must use a valid certificate. The official version of the certificate at all times is available at the homepage of the Nordic Reference Interval Project, NORIP at www.furst.no/norip. Further information is also available in articles elsewhere in this issue and at the NORIP homepage.

POSSIBLE USE OF X: PRACTICAL IMPLEMENTATION OF NORIP REFERENCE INTERVALS

X could be used to verify the measurement equipment before implementation of the reference intervals obtained in The Nordic Reference Interval Project. The verification could be evaluated using an Excel spreadsheet [1]. The principle [2] in the spreadsheet is a suggestion agreed on by EQAnord, the liaison organization for the Nordic EQA organizers.

The Scandinavian Society of Clinical Chemistry (NFKK) and EQAnord previously decided on a common strategy: a coordinated implementation of the reference intervals, where information of the benefits was central. In Norway, the information has resulted in smooth implementation of the new reference intervals for enzymes and a marked decrease in deviation of measurement results.

REFERENCES

1 Rustad P. Evaluation of method bias using NFKK Reference Serum X. http://www.furst.no/norip/X/x_spreadsheet.xls. 27-12-0003.
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CERTIFICATE OF ANALYSIS

NFKK Reference Serum X

Components in Human Serum, Lot Number: NFKK2002a

Description of the material

The NFKK Reference Serum X is an unmodified fresh frozen human serum.[1] It is intended for use in evaluation and verification of the trueness of measurement procedures in laboratory medicine for the components listed in Table 1. One unit consists of 5 mL serum in a polypropylene vial with a Teflon-coated stopper.

Source of the material

The serum was collected from Danish blood donors by Hjørring County Hospital, Denmark.

Preparation of the material

After collection in blood bags without anti-coagulant, the serum was pooled and frozen. Later the pool was sterile-filtered and distributed into vials by Statens Serum Institut, Denmark [1].

Date of expiry

The values and uncertainties specified in this certificate are valid from 2003-11-21 until 2004-11-21 provided the handling, storage and use of the material are in accordance with the below instructions. The material is regularly monitored and the purchasers will be notified of any significant changes resulting in recertification or withdrawal of the material during the period of validity.

WARNINGS

THE NFKK REFERENCE SERUM X IS INTENDED FOR *IN-VITRO* USE ONLY. The material is of human origin. HANDLE THE MATERIAL AS A BIOHAZARDOUS MATERIAL CAPABLE OF TRANSMITTING INFECTIOUS DISEASES. Each donor unit of serum or plasma used in the preparation of this material have been tested and are found to be non-reactive for HBsAg, HCV and HIV-1 antibodies. However, no test procedure can offer complete assurance that hepatitis B virus, hepatitis C virus, HIV or other infectious agents are absent from this material. Therefore this material based on human blood should be handled as a POTENTIALLY INFECTIOUS HUMAN SERUM, according to the laboratory's procedure(s) and good laboratory practices.

Intended use

The material is intended for evaluation and verification of trueness of measurement procedures, usually involving *in-vitro* diagnostic (IVD) medical devices. If the user of the IVD product obtains a measurement result that does not agree with the values specified in this certificate (taking into account the respective uncertainties), further investigations may be necessary. The user should first investigate if the disagreement originates from within the laboratory, e.g. due to sample handling, calibration, maintenance and/or reagents. If the error is not found in the laboratory, contact the manufacturer. It is also recommended to contact other users of the same measuring system. The results may be used to document a complaint intended for the manufacturer of the IVD, taking into account the quality specifications that are stated by the manufacturer.

[1] The term 'fresh frozen' refers to a material that does not undergo further processing or modifications other than pooling, and for which the time in thawed state is kept at a minimum.

Storage and stability

Store the material only at < – 70 °C and do not expose it to sunlight or ultraviolet radiation, otherwise the concentrations of the components may be affected.

Instructions for use

1. Remove the material from the freezer and place the vial on absorbing material in darkness at room temperature for two hours
2. After thawing, gently mix the serum for 10 minutes, e.g. by placing it in a slow turning mixer
3. Analyse within two hours.

Property values

Certified (Table 1) and indicative (Table 2) property values relate to the total amount-of-substance concentration, mass concentration or catalytic activity concentration of the components in the material. The indicative values are for information only.

Certified Values

Table 1: Certified values and their expanded uncertainties.

Component	Unit	Certified value	Expanded uncertainty $U=2\cdot u_c$
Albumin	g/L	41,5	2,7
Calcium (Ca)	mmol/L	2,325	0,008
Cholesterol	mmol/L	5,220	0,023
Creatininium	µmol/L	73,90	0,60
Iron (Fe)	µmol/L	20,00	0,56
gamma-Glutamyltransferase (GGT)	U/L	35,42	0,95
Glucose	mmol/L	4,405	0,034
Potassium (K)	mmol/L	3,732	0,022
Magnesium (Mg)	mmol/L	0,810 0	0,006 5
Sodium (Na)	mmol/L	140,65	0,75
Thyroxine (T4)	nmol/L	99,4	3,1
Triglyceride	mmol/L	1,287	0,038
Carbamide (Urea)	mmol/L	4,910	0,026
Urate (Uric acid)	µmol/L	309,9	5,8

Measurement techniques used for the certification

In the Nordic Trueness Project 2002, 136 laboratories from five countries performed replicate analyses on IMEP-17 Material 1 and/or Reference Serum CAL and NFKK Reference Serum X for up to 5 days [2]. All laboratories used routine measurement procedures. Afterwards the transferrals of values from the IMEP-17 Material 1 or the Reference Serum CAL to the NFKK Reference Serum X were done [2]. Reference serum CAL is the calibrator used in the Nordic Reference Interval Project (NORIP) [3]. IMEP-17 Material 1 is used in the Nordic Trueness Project. All materials are manufactured similar to NFKK Reference Serum X.

Indicative values

Table 2: Indicative values for components in NFKK Reference Serum X, obtained in the NORIP project.

Component	Unit	Indicative value* and (standard deviation of mean of laboratory mean)# traceable	
		to consensus mean value in NORIP [Enzymes: IFCC 37 °C]	via CAL to certified reference value by DGKC 1997
Alkaline phosphatase (ALP)	U/L	72,5 (0,7)	-
Alanine transaminase (ALT)	U/L	-	24,2 (0,2)
Amylase	U/L	60,7 (1,4)	-
Aspartate transaminase (AST)	U/L	25,5 (0,2)	-
Bilirubin	µmol/L	-	8,97 (0,04)
Creatine kinase (CK)	U/L	-	133,3 (0,4)
HDL-cholesterol§	mmol/L	1,387 (0,003)	-
Lactate dehydrogenase (LD)	U/L	147,8 (3,1)	-
Pancreatic amylase	U/L	28,6 (0,4)	-
Phosphate§	mmol/L	-	1,043 (0,002)
Protein (total protein)§	g/L	-	68,7 (0,11)
Transferrin	g/L	2,709 (0,025)	-

* For values in the first column, the value is the mean of laboratory means. For values in the second column, the indicative value is the mean of factors M(X)/M(CAL) multiplied with certified reference value for CAL, where M(X) and M(CAL) is laboratory mean of X and CAL respectively.
# No expanded uncertainties can be provided for these components, however the obtained standard deviation of mean of laboratory means (SDM), from approximately 102 laboratories using routine measurement systems can be used to judge upon the reliability of the value (first column) and the reliability of the value relative to CAL (second column). For the enzymes a lower number of laboratories were involved (ALT: 86, Amylase: 24, AST: 79, CK: 81, Pancreatic amylase: 21, ALP: 23, LD: 3). For values in the second column the SDM is without the main source of uncertainty from the target value of CAL.
§ In the Nordic Trueness Project 2002, these components were re-assigned with transferred values via CAL. No significant difference between the two sets of values was observed ($p<0,05$).

Traceability

The certified values are traceable to SI or to an international measurement standard (GGT) via the IMEP-17 Material 1 and Material CAL through reference measurement procedures and international certified reference materials [4-5]. The indicative values are obtained in the frame of NORIP, as either the arithmetic mean of all participants' mean measurement values or traceable to the certified value from DGKC 1997 [2] via the arithmetic mean of all participants mean values transferred via CAL. For enzymes the values are obtained using IFCC 37 °C compatible routine measuring systems [3].

Homogeneity

Note, that because the values are averages of observations done on many vials, no separate contribution from the between-vial variation is included in the uncertainty statement. Statistical analysis has concluded that the vial-to-vial variation including sample treatment will be of very little practical importance to the routine laboratories [2].

Commutability

No specific commutability study was performed for this material. However, the entire production process has been outlined to ensure commutability provided the instructions given here are adhered to.

Further information

Information concerning homogeneity, calculations of the transferred values and uncertainties, the ongoing monitoring of the material are available in [2].

Legal Notice

It is a prerequisite that the necessary precautions are taken, by the user, for storage, handling and use especially in regard to safety. The material(s) must be treated as a patient sample that is POTENTIALLY INFECTIUS AND CAPABLE OF TRANSMITTING INFECTIUS DISEASE. This precaution also applies to materials screened and found non-reactive for HIV, HBsAG and HCV antibodies. However no known test procedure can offer complete assurance that HIV, hepatitis B virus, hepatitis C virus, or other infectious agents are absent from the material(s). NFKK, DEKS, NOBIDA and the suppliers do not take responsibility for infections with HIV, hepatitis B virus or hepatitis C virus. Neither shall they be liable for any particular, indirect, incidental and consequential damage caused by delays and erroneous transportation, storage, handling and use.

Analysts, investigators and participating laboratories

- M. Blom and I. Nørgaard, Hjørring County hospital, Denmark collected serum from Danish blood donors and performed the viral screening.
- L. Blou, Statens Serum Institut, Denmark performed the filtration and distribution into the vials.
- Many Nordic laboratories who most kindly assisted with their careful measurements of the reference materials.
- The Nordic Reference Interval Group (P. Felding, L. Franzson, K. Hellsing, P. Simonsson, V. Kairisto, P.H. Pedersen and P. Rustad) performed the protocol for the measurement procedures at the Nordic laboratories.
- G. Nordin and U. Örnemark, EQUALIS, Sweden, collected and compiled the data.
- G.M. Henriksen, A. Marker and J. Hervel, DEKS, planned and performed the initial homogeneity study.
- P. Rustad, Fürst Medisinsk Laboratorium, Norway, performed the data treatment and transferral of values and uncertainties. He also evaluated the homogeneity.
- M.M. Pedersen, DEKS, Denmark performed the protocol for the long-term and accelerated stability studies and monitors the outcome.
- A. Uldall, DEKS coordinated and monitored the overall work leading to the establishment and issuance of this certificate.

Supplier of the serum

Information about suppliers can be obtained from DEKS, 52M1, Herlev University Hospital, DK-2730 Herlev, Denmark, Phone: +45 4488 3266, Fax: +45 4453 5369 e-mail: deks@deks.dk.

Certifying officers

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Revision history

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