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The Nordic Protein Project

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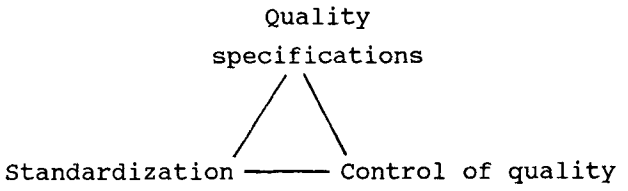
The Nordic Protein Project was decided by The Nordic Committee on Quality Control in 1986 and supported by NORDKEM from 1987. The project works in close co-operation with the Finnish non-profit company, Lab-quality and the Data Group in Uppsala. The activities are co-ordinated with the Finnish and the Danish Protein Groups and further with the Austrian Protein Group.

The project deals with the three main aspects of quality management:



QUALITY SPECIFICATIONS

The analytical quality specifications (analytical goals) develops from the goal that laboratories should be able to share common reference intervals for analytical components (here serum proteins) within regions where the populations are homogenous*. The statistical models are described in two articles assuming Gaussian (1) and log- Gaussian distributions (2). The preliminary goals are based on the Finnsh investigation (3) and on litterature, using the log-Gaussian model.

The analytical quality specifications are given as 'maximum allowable combined bias and imprecision', as percentage bias and CV % to be fullfilled for the concentration levels of both upper and lower reference limits.

For S-Haptoglobin, S-IgA and S-IgM the quality specifications are very wide, allowing a bias of + or -10% (when CV = 0 %) or CV ≈ 25% (when bias is 0%), whereas the specifications for S-Albumin are very restrictive with maximum allowable bias of ± 2% (CV = 0%) or CV = 4% (bias = 0%). For the remaining proteins (S-Transferrin, S-α1- Antitrypsin, S-Prealbumin, S-Orosomucoid, and S- IgG) allowable max bias from ± 3 to 5% (CV = 0%) or CV from 7 to 11% (bias = 0%).

STANDARDIZATION

For the standardization a common liquid frozen serum calibrator has been chosen. It is prepared as a serum pool from more than 1000 male blood-donors (all negative for hepatitis antigen and HIV-antibodies). The cryoprecipitates are removed from the frozen pool by centrifugation after thawing at 4°C and afterwards lipids are removed by ultracentrifugation. The calibrator is stored and mailed at -80°C (4).

The calibrator is clear, e.g. showed a preparation from 1981 an extinction (measured at 650 nm, undiluted, 10 mm cuvette) of 0.060 in 1981 and 0.079 in 1989.

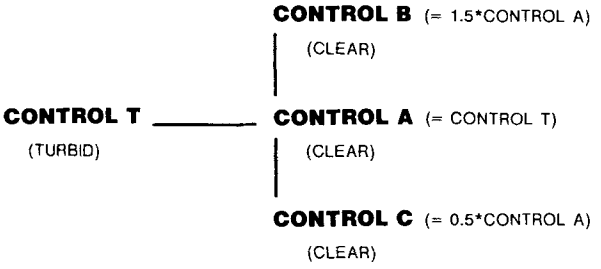
The proteins are genuine, i.e. behave like proteins in a fresh pool, e.g. they have identical electrophoretic mobility (also after eight years).

Further the production of the calibrator is reproducible and the proteins are stable. Since no other calibrator with long-term stable and genuine proteins is known, the combined reproducibility and stability is documentated indirectly by the low batch-to-batch variation, with CV below 2 % for batches from 1981, 1982 and 1984. Further 6 proteins show deviation of less than + or -2% from 1984 to 1987, whereas the acute phase reactants were lower in the 1987 præparation (3% for haptoglobin, 4% for α1-antitrypsin, and 5% for Orosomucoid). The first three pools were collected during winter and spring, the

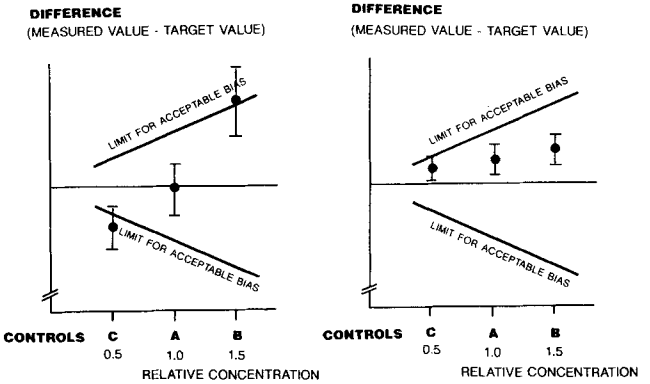
1987 preparation during late summer and autumn.

The concentration values are assigned from IFCC preparations of pure proteins and from the WHO reference preparation.

CONTROL OF QUALITY



The control samples are 4 serum pools with target values. Three controls are clear with different concentrations, to control standardization and linearity at three concentration levels. The fourth is turbid, to control how effective the different analytical principles (and equipments) are in giving a correct measurement for a turbid patient specimen (5).



The results are visualized by bias plots.

THE STEPS IN THE PROJECT

The procedure involves 3 steps:

A) The first assignment (January 1990) aims to registrate 'the state of art' (which we know is poor) and to evaluate performances in the 75 participating laboratories.

B) The second assignment (scheduled to May) includes for each laboratory

   a) Calibrator for daily use in two years

   b) The same controls as in A to be used

      I. in internal control of new calibration
      II. in control of the established quality
      III. repeated control (late 1990).

C) The co-ordinated projects on reference intervals in Denmark and Finland are planned to supply the laboratories with common reference intervals by May and September 1990, respectively. Depending on the results, specific reference intervals can be used in the two countries, or - hopefully - common reference intervals can be used in all the Nordic countries.

DISCUSSION

The aim of the project is to improve the quality of serum protein measurements in the Nordic countries to a specified level.

The quality is obtained by daily use of sommon calibrator of the highest quality and the quality is controlled by selected samples with target values, to control both the standardization and the interferenbce from turbid sera.

The quality specifications are based on the assumption of using common reference intervals - and these intervals are delivered by co-ordinated projects.

Other quality problems like measurements of M- components are not included in the project.

Other analytical quality specifications e.g. related to the use of serum proteins in defined clinical strategies, may be evaluated in co- operation with this 'umbrella project' on 'Medical need for quality specifications in laboratory medicine'.

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*The biological background for sharing reference intervals is investigated in two other projects in Finland and Denmark.

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