ERNDIM - Quantitative Schemes
Cystine in White Blood Cells

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Annual Report ERNDIM-EQAS 2006

1. Purpose

The purpose of the ERNDIM External Quality Assurance Scheme for Cystine in White Blood Cells is the monitoring of the analytical quality of the quantitative assay of cystine in white blood cells in the management and diagnosis of patients with cystinosis. For details see www.erndimqa.nl

2. Participants

27 Laboratories from 13 countries participate in the scheme.

3. Design

The Scheme has been designed, planned and co-ordinated by Dr. Mick Henderson as scientific advisor and Dr. Cas Weykamp as scheme organiser, both appointed by the ERNDIM Board. The design includes special attention to sample composition and to the layout of the reports.

Samples

The scheme consisted of 2 series of lyophilised samples: one series containing protein pellets and the other supernatants of lysed white blood cells spiked with cystine. As can be seen from table 1 the weighed amounts of protein and cystine were identical in pairs of samples. The nature, source and added amounts of the analytes are summarised in table 1.

Table 1. Pair identification, source and amount of added analytes.

Analyte	Source	Added Quantities Protein (mg/vial)+Cystine (nmol/vial)			
		Sample Pair 29-35	Sample Pair 30-33	Sample Pair 32-36	Sample Pair 31-34
Protein	Serva 11930	0.45	1.00	1.25	1.50
Cystine	Sigma C8755	1.25	3.50	0.70	0

Reports

All data-transfer, the submission of data as well as request and viewing of reports proceeded via the interactive website www.erndimqa.nl

An important characteristic of the website is that it supplies short-term and long-term reports.

Short-term reports on the eight individual specimens are available two weeks after the submission deadline and provide up-to-date information on analytical performance. Although technically reports could be immediately available a delay time of 14 days has been introduced to enable the scientific advisor to inspect the results and add his comment to the report.

The **annual long-term report** summarises the results of the whole year.

A second important characteristic of the ERNDIM website is the different levels of detail of results which allows individual laboratories the choice of fully detailed and/or summarised reports.

The "Analyte in Detail" is the most detailed report and shows results of a specific analyte in a specific sample.

A more condensed report is the "Current Report" which summarises the performance of all analytes in a specific sample.

The Annual Report summarizes all results giving an indication of overall performance for all analytes in all 8 samples.

Depending on the responsibilities within the laboratory participants can choose to inspect the annual report (QC managers) or all (or part of) detailed reports (scientific staff).

4. Discussion of Results in the Annual Report 2006

In this part the results as seen in the annual report 2006 will be discussed. Please print out your annual report from the website when you follow the various aspects below and keep in mind that we only discuss the results of "all labs". It is up to you to inspect and interpret the results of your own laboratory.

4.1 Accuracy

A first approach to evaluating your performance in terms of accuracy is comparison of your mean values in the eight samples with those of all labs. This is shown in the columns "your lab" and "all labs" under the heading "Accuracy". For example for protein the mean of all labs is 1.07 mg/vial. with which you can compare the mean of your lab.

4.2 Recovery

A second approach to describe accuracy is the percentage recovery of added analyte. In this approach the amounts of weighed quantities added to the samples are the assumed target values after adjustment for blank values. The correlation between weighed amounts (on the x-axis) and your measured quantities (on the y-axis) has been calculated. The slope of the resulting relationship (a in $y = ax + b$) in this formula multiplied by 100% is your recovery of the added amounts. The outcome for your lab in comparison to the median outcome of all labs is shown in the column "Recovery".

It can be seen that the mean recovery of cystine is 97% and of protein 100% which is excellent and very reassuring. We are all measuring the same thing.

4.3 Precision

Reproducibility is an important parameter for the analytical performance of a laboratory and is addressed in the schemes' design. Samples provided in pairs can be regarded as duplicates from which CV's can be calculated. The column "Precision" in the annual report shows your CV's in comparison to median values for all labs. The best median CV is observed for cystine (10.1%). 11.0% and 23.4% are seen for protein and cystine (nmol ½ cys/mg protein), respectively.

4.4 Linearity

Linearity over the whole relevant analytical range is another important parameter for analytical quality and is also examined within the schemes. A comparison of the weighed quantities on the x-axis and your measured quantities on the y-axis allows calculation of the coefficient of regression (**r**). The column "Linearity" in the annual report shows your **r** values in comparison to the median **r** values for all labs. Ideally the **r** value is close to 1.000 and this is indeed observed with values of 0.9686 for protein and 0.9960 for cystine.

4.5 Interlab CV

For comparison for diagnosis and monitoring of treatment for one patient in different hospitals and for use of shared reference values it is essential to have a high degree of harmonization between results of laboratories. Part of the schemes' design is to monitor this by calculating the Interlaboratory CV. This, along with the number of laboratories who submitted results is shown in the column "Data all labs" in the annual report. We see an interlab CV of 17.0% for protein and of 90.9% for cystine (nmol ½ cys/mg protein). The interlab CV for cystine is disappointing and is caused by some labs with extreme results.

4.6 Number of participating labs and submitting results

In total 27 labs received samples and 27 submitted results.

4.7 Interrelationships between results

Cystine (nmol ½ cys/mg protein) is a ratio of the assays of cystine (nmol/aliquot) and protein. The precision will be the cumulated precision of both assays.

4.8 Report in correct numbers

As we have indicated in previous reports it is important to report in the correct units. Although we feel that nearly all labs do that now, some strange results of individual labs might be traced back to "clerical errors". So if you have a deviating result, please check if you reported your result in the correct units.

5. *Summary*

We feel that, after some pilots, the scheme is well-established now. The mean performance of the labs, especially the recovery of added cystine and protein, is fine. Of course the performance of some individual labs require improvement. The Interlab CV demonstrates lack of standardisation which requires improvement. We would like to emphasise the need for all laboratories to use internal quality control. At its simplest

this can be made from pooling surplus supernatants from assayed samples. We think that some of the aberrant results are still caused by simple calculating errors.

6. *Preview of the Scheme in 2007*

The design of the 2007-scheme is the same as in 2006.

7. Questions, Comments and Suggestions

If you have any questions, comments or suggestions please address to the scientific advisor of the Scheme, Dr. Mick Henderson (mick.henderson@leedsth.nhs.uk) and/or the scheme organiser Dr. Cas Weykamp (c.w.weykamp@skbwinterswijk.nl).