ERNDIM - Quantitative Schemes
Special Assays in Serum

Dra. Begoña Merinero
Centro de Diagnóstico de
Enfermedades Moleculares
Facultad de Ciencias. Modulo 10
Universidad Autónoma de Madrid
28049 Madrid
Spain
e-mail: bmerinero@cbm.uam.es

Dr. C.W. Weykamp
Queen Beatrix Hospital
MCA Laboratory
P.O. Box 9005
NL – 7100 GG Winterswijk
The Netherlands
e-mail : c.w.weykamp@skbwinterswijk.nl

Annual Report ERNDIM-EQAS 2012

1. *Purpose*

The purpose of the ERNDIM External Quality Assurance Scheme for Special Assays in Serum is the monitoring of the analytical quality of the quantitative assay of a range of analytes in serum in laboratories involved in the diagnosis of patients with inherited metabolic disorders. For details see www.erndim.org / www.ERNDIMQA.nl

2. *Participants*

217 Datasets have been submitted by Laboratories from 36 countries. Of these, 8 labs did not submit any results and 5 labs submitted too few results to allow calculation of the annual report.

3. *Design*

The Scheme has been designed, planned and co-ordinated by the scientific advisor (Dra. Begoña Merinero) and Dr. Cas Weykamp as scheme organiser, both appointed by the ERNDIM Board. The design includes samples and reports which are connected to provide information with a balance between short-term and long-term reports and between detailed and aggregated information.

Samples

The scheme consisted of 8 lyophilized samples, all prepared from the same basic serum but with various amounts of added analytes. The samples were identical two by two: the pairs, analytes and their source as well as the added amounts are in the table below.

Analyte	Source:	Units	Added Amounts			
			Sample Pair 119-123	Sample Pair 121-125	Sample Pair 120-126	Sample Pair 122-124
3-OH-Butyric Acid	Aldrich 29,836-0	mmol/L	0	1,63	3,27	4,90
7-Dehydrocholesterol	Sigma D4429	µmol/L	0	65,3	130,7	196,0
C22:0	Aldrich 21,694-1	µmol/L	0	14,8	29,7	44,5
C24:0	Sigma L6641	µmol/L	0	22,4	44,9	67,3
C26:0	Sigma H0388	µmol/L	0	3,3	6,5	9,8
Carnitine Free	Sigma C0283	µmol/L	0	32,6	65,2	97,9

Cholestanol	Sigma D6128	µmol/L	0	33,0	66,0	98,9
Creatine	Sigma C3630	µmol/L	0	19,6	39,3	58,9
Galactose	Sigma G0750	µmol/L	0	646,8	1293,6	1940,4
Guanidine acetate	Sigma G6002	µmol/L	0	5,9	11,9	17,8
Homocysteine	Sigma H6010	µmol/L	0	32,7	65,5	98,2
Lactic Acid	Sigma L7022	mmol/L	0	2,18	4,36	6,53
Methylmalonic acid	Aldrich M5,405-8	µmol/L	0	323,4	646,8	970,2
Phytanic acid	Sigma P4060	µmol/L	0	7,1	14,2	21,3
Pipecolic Acid	Aldrich P4,585-0	µmol/L	0	13,0	26,1	39,1
Pristanic acid	Sigma P6617	µmol/L	0	2,8	5,6	8,4
Pyruvic Acid	Sigma B8574	mmol/L	0	0,098	0,196	0,294

Reports

All data-transfer, the submission of data as well as request and viewing of reports proceeded via the interactive website www.erndimqa.nl which can also be reached through the ERNDIM website (www.erndim.org).

An important characteristic of the website is that it supplies short-term and long-term reports. Short-term reports are associated with the four individual specimens, for each of which there has been a specific deadline in the year 2012. Two weeks after the respective deadlines participants could request their reports and as such had four times up-to-date information on their analytical performance. Although technically not required (the website can work with a delay time zero) a delay time of 14 days has been chosen to enable the scientific advisor to inspect the results and add his comment to the report. Contrary to the fast short-term report is the annual long-term report. The annual report is based on the design-anchored connection between samples which enables to report a range of analytical parameters (accuracy, precision, linearity, recovery and interlab dispersion) once an annual cycle has been completed. The annual report is discussed below.

A second important characteristic of the website is the wide range in aggregation of results which permits labs to make an individual choice for detailed and/or aggregated reports. The most detailed report which can be requested from the website is the "Analyte in Detail" which shows results of a specific analyte in a specific sample (144 such Analyte-in-Detail-reports can be requested in the 2012 cycle). A more condensed report is the "Cycle Review" which summarizes the performance of all analytes in a specific sample (8 such Cycle-Review-Reports can be requested in 2012). The highest degree of aggregation has the Annual Report which summarizes the performance of all analytes of all 8 samples (1 such Annual-Report can be requested in 2012).

4. Discussion of Results in the Annual Report 2012

In this part the results as seen in the annual report 2012 will be discussed. Subsequently we will regard accuracy, recovery, precision, linearity, interlab CV and crosssectional relations. Please print your annual report from the Interactive Website when you read the "guided tour" below and keep in mind that we only discuss the results of "all labs": it is up to you to inspect and interpret the specific results of your laboratory.

4.1 Accuracy

A first approach to describe the accuracy is to compare mean outcome in your lab of the eight samples with the mean outcome of all labs. This is done in the first columns

of the annual report. It can be seen that the mean outcome for all labs for free Carnitine free is 89.2 micromol/L.

4.2 Recovery

A second approach to describe accuracy is the percentage recovery of added analyte. In this approach it is assumed that the recovery of the weighed quantities is the target value. The correlation between weighed quantities as added to the samples (on the x-axis) and your measured quantities (on the y-axis) has been calculated. The slope of the correlation multiplied with 100% is your recovery of the added amounts. Outcome for your lab in comparison to median outcome of all labs is shown in the column “Recovery” in the Annual Report. For all labs the recovery ranges from 73% for C24:0 Lignoceric acid to 135% for 7-Dehydrocholesterol. The overall recovery is 102%. All recoveries are not too far away from 100% which is quite satisfying.

4.3 Precision

Reproducibility is an important parameter for quality in the laboratory and is encountered in the schemes’ design. Samples come in pairs which can be regarded as duplicates from which CV’s can be calculated (Intra laboratory CV as indicator for reproducibility). Outcome for your lab in comparison to the median of all labs is shown in column “Precision”of the Annual Report. Precision ranges from 3.2% for lactic acid to 11.8% for 7-Dehydrocholesterol. The overall precision of 7.1% is quite satisfying.

4.4 Linearity

Linearity over the whole relevant analytical range is another important parameter for analytical quality. Again this is encountered in the Schemes’ design. With weighed quantities on the x-axis and your measured quantities on the y-axis the coefficient of regression (r) has been calculated. Outcome for your lab in comparison to the median of all labs is in the column “Linearity” of the annual report. It can be seen that the coefficient of regression is best for NEFA (0.999). For none of the analytes we observe an r below 0.95.

4.5 Interlab CV

For comparison of outcome for one patient in different hospitals and for use of shared reference values it is relevant to have a high degree of harmonization between results of various 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. It can be seen that most laboratories submitted results for 3-OH Butyric acid (111 labs) whereas only 11 labs submitted results for Galactose. The Interlab CV ranges from 6.03% for Lactic Acid to 21.7% for 7-Dehydrocholesterol.

4.6 Cross Sectional Relations

The various parameters as described above often have an interrelation: more than one parameter directs towards good or bad analytical control.
A typical example of good analytical control is lactic acid: many (104) laboratories submitted results, the reproducibility within the labs is good (precision of 3.2%), the interlab CV is good (6.03%), linearity is good (0.998) as is the recovery (112%).

4.7 Your performance: red and green flags

After some years of discussion and planning a system to judge performance of individual laboratories is implemented starting from January 2009. In the annual report of an individual laboratory red flags indicate poor performance for accuracy, precision, linearity and recovery. Special assays with satisfactory performance for at least three of the four parameters (thus no or only one red flag or no result) receive a

green flag. Thus a green flag indicates satisfactory performance for analysis of that particular analyte while a red flag indicates that your laboratory has failed to attain satisfactory performance. Criteria for red flags can be found in the general information on the website (general information; interactive website, explanation annual report).

4.8 Poor Performance Policy

A wide dispersion in the overall performance of individual laboratories is evident. Table 2 shows the percentage of red flags observed. 53% of the laboratories have no red flag at all and thus have attained excellent overall performance. In contrast, at the other extreme there are also 3% of laboratories with more than 25% red flags. Following intensive discussion within the ERNDIM board and Scientific Advisory Board (SAB) and taking into account feedback from participants we have been able to agree on a harmonised scoring system for the various branches of the Diagnostic Proficiency schemes and qualitative schemes. We have also tested a scoring system for the quantitative schemes as described in our Newsletter of Spring 2009. In parallel to this the SAB has agreed levels of adequate performance for all the schemes and these will be re-evaluated annually. The scoring systems have been carefully evaluated by members of the SAB and have been applied to assess performance in our schemes from 2007 onwards. The ERNDIM Board has decided that the Scientific Advisor will judge the performance of the individual laboratories based on these levels of satisfactory performance and issue a letter of advice of failure to achieve satisfactory performance to those laboratories which do not achieve satisfactory performance. The letter is intended to instigate dialogue between the EQA scheme organiser and the participating laboratory in order to solve any particular analytical problems in order to improve quality of performance of labs in the pursuit of our overall aim to improve quality of diagnostic services in this field.

Table 2. Percentage Red Flags

% Red Flags seen in Annual Report	Percentage Labs In this Category	Cumulative Percentage Of Labs
>25%	3%	3%
20 – 25%	3%	6%
15 – 20%	6%	12%
10 – 15%	8%	20%
5 – 10%	18%	38%
0 – 5%	9%	47%
0%	53%	100%

4.9 Certificates

As for other schemes the performance as it is indicated by the red/green flags in the individual laboratories annual report is summarised in the new style of annual participation certificate. The certificate lists the total number of special assays in the scheme, the number for which results have been submitted and the number for which satisfactory performance has been achieved. It is important to bear in mind that the certificate has to be backed up by the individual annual report in the case of internal or external auditing.

5. Summary

The Annual Report, dealing with analytical performance in terms of accuracy, precision, linearity, recovery and interlab CV, shows a performance with similarities to previous years. For some analytes the performance is good, for others there is still something to do to achieve sufficient intra- and interlaboratory quality. In comparison to the previous scheme improvement is seen for all analytical parameter

6. Preview Scheme 2013

There are no major changes in 2013.

7. Questions, Comments and Suggestions

If you have any questions, comments or suggestions please address to the scientific advisor of the scheme Dra. Begoña Merinero (bmerinero@cbm.uam.es) and/or to the scheme organiser Dr. Cas Weykamp (c.w.weykamp@skbwinterswijk.nl)