Annual Report ERNDIM-EQAS Special Assays in Serum 2005

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.erndimqa.nl

2. Participants

149 Laboratories from 25 countries participated in the Scheme

3. Design

The Scheme has been designed, planned and co-ordinated by the scientific advisor (Dr. Alberto Burlina) 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: Sigma	Units	Added Amounts			
			Sample Pair 64-69	Sample Pair 66-70	Sample Pair 65-67	Sample Pair 63-68
Lactic Acid	L7022	-mmol/L	0	2.2	4.4	6.5
3-OH Butyric Acid	B29,836-0	-mmol/L	0	1.3	2.6	3.9
Phytanic Acid	P4060	-µmol/L	0	9.3	18.5	27.8
C22:0	B7644	-µmol/L	0	15	30	45
C24:0	L6641	-µmol/L	0	22	45	68
C26:0	H0388	-µmol/L	0	3.3	6.7	10.0
Carnitine Free	C7518	-µmol/L	0	33	66	98
Creatine	C3630	-µmol/L	0	20	39	59
Guanidine Acetic Acid	G6002	-µmol/L	0	6.2	12.4	18.6
Homocysteine	H6010	-µmol/L	0	32.9	65.9	98.8
Phenylalanine	P8324	-µmol/L	0	229	457	686
Uric Acid	U2875	-µmol/L	0	133	267	400
7-Dehydrocholesterol	D4429	-µmol/L	0	65	131	196
Cis-4 Deconic Acid	Brunet	-µmol/L	0	31	63	94
Pipecolic Acid	P4,585-0	-µmol/L	0	13	26	39
Pyruvic Acid	B8574	-mmol/L	0	0.16	0.33	0.49

Reports

All data-transfer, the submission of data as well as the request 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 are associated with the four individual specimens, for each of which there has been a specific deadline in the year 2005. 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 (120 such Analyte-in-Detail-reports can be requested in the 2005 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 2005). 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 2005).

4. *Discussion of Results in the Annual Report 2005*

In this part the results as seen in the annual report 2005 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 is 90.0 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 40% for Cis-4-decanoic acid to 127% for 7Dehydrocholesterol. The overall recovery is 99%. Quite

an unsatisfying recovery (40%)is seen for cis-4-decenoic acid. All other recoveries are not too far away from 100%.

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 1.9% for Uric Acid to 18.0% forcis-4-decanoic acid. The overall precision of 8.8% 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 uric acid (0,9982). For none of the analytes we observe an r below 0.9.

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 lactic acid (103 labs) whereas only 12 labs submitted results for cis-4-decenoic acid. The Interlab CV ranges from 3.5% for Uric Acid to 189.7% for cis-4-decanoic acid. It can be deduced that those assays which are probably being performed most frequently (homocysteine, phenylalanine) have the lowest interlab CV.

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 homocysteine: many (102) laboratories submitted results, the reproducibility within the labs is good (precision of 5.2%), the interlab CV is good (11.1%), linearity is good (0.9944) as is the recovery (103%).
On the opposite side is cis-4-decanoic acid: only 12 laboratories submitted results, the reproducibility is rather poor with 18.0%, the inter lab CV is wide with 189.7%, and the recovery (40%) is poor.

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 2006

There are no major changes 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. Alberto Burlina (burlina@pediatria.unipd.it) and/or to the scheme organiser Dr. Cas Weykamp (c.w.weykamp@skbwinterswijk.nl)