ERNDIM - Quantitative Schemes
Special Assays in Urine

Dr. A. Burlina
University Hospital
Department of Pediatrics
Division of Metabolic Disorders
Via Giustiniani 3
IT – 35128 Padova
e-mail : burlina@pediatria.unipd.it

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

Annual Report ERNDIM-EQAS 2007

1. *Purpose*

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

2. *Participants*

148 Laboratories from 25 countries participated in the Scheme

3. *Design*

The Scheme has been designed , planned and coordinated 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 lyophilised samples, all prepared from the same basic urine but with various amounts of added analyte. 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 79-83	Sample Pair 82-86	Sample Pair 81-84	Sample Pair 80-85
5-OH indolacetic acid	H8876	µmol/L	0	32.4	65.8	98.2
Carnitine free	C0283	µmol/L	0	146.3	297.1	443.4
Creatinine	C6257	mmol/L	0	3.2	6.6	9.8
Creatine	C3630	µmol/L	0	147.1	298.6	445.6
Guanidinoacetate	G6002	µmol/L	0	32.3	65.5	97.8
Homovanillic acid	H1252	µmol/L	0	32.3	65.6	98.0
Hydroxyproline	56250 (Fluka)	µmol/L	0	323.3	656.4	979.8
Lactic acid	L7022	mmol/L	0	3.2	6.6	9.8

MPS	C6737	mg/L	0	23.1	46.9	70.0
Orotic acid	O3000	µmol/L	0	29.6	60.1	89.7
Pipecolic acid	P4585-0	µmol/L	0	16.1	32.8	48.9
Sialic acid	A2388	µmol/L	0	97.1	197.2	294.3
Succinylacetone	D1415	µmol/L	0	13.2	26.8	40.0

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 2007. 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 2007 cycle). A more condensed report in the "Cycle Review" which summarizes the performance of all analytes in a specific sample (8 such Cycle-Review-Reports can be requested in 2007). 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 2007).

4. *Discussion of Results in the Annual Report 2007*

In this part the results as seen in the annual report 2007 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 accuracy is to compare the mean outcome of the eight samples in your lab with the mean of all labs. This is done in the first columns of the annual report. It can be seen that for 5-OH-Indolacetic acid the mean outcome of all labs is 53.7 micromol/liter

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 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 Succinyl acetone to 146% for Mucopolysaccharides. The overall recovery is 104%.

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 3.4% for Creatinine to 36.3% for Succinylacetone.

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 ranges from 0.8865 for Succinylacetone to 0.9981 for Lactic acid.

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 Creatinine (100) whereas only 21 submitted results for Sialic acid. The Interlab CV ranges from 5.7% for Creatinine to 142.1% for Hydroxyproline. The majority of the interlab CV's are worrying because these values reflect the wide dispersion of data.

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 Creatinine: many (100) laboratories submitted results, the reproducibility within the labs is good (precision of 3.4%), the Interlab CV is good with 5.7%, linearity is excellent (0.9977) and recovery is 104%. Creatinine will be measured in many institutes by the general clinical chemistry lab using commercial analyzers. It is, therefore, not logical to compare it's results with those of chromatographic analyzers.

5. Summary

The Annual Report, dealing with analytical performance in terms of accuracy, precision, linearity, recovery and interlab CV, shows a pattern similar to previous years. For some analytes the overall performance is good, for others results are less satisfying, especially the interlaboratory dispersion. The heterogeneity of the analytes makes it difficult to give a general advise.

6. Preview Scheme 2008

The design of the scheme in 2008 is the same as in 2007.

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)