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|  | ERNDIM - Quantitative Schemes Special Assays in Urine | |
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Annual Report ERNDIM-EQAS 2006

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*

149 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 71-75 | Sample Pair 74-78 | Sample Pair 73-76 | Sample Pair 72-77 |
| Lactic Acid | L7022 | mmol/L | 0 | 3.3 | 6.6 | 9.8 |
| Creatine | C3630 | µmol/L | 0 | 149 | 297 | 445 |
| Carnitine Free | C0283 | µmol/L | 0 | 148 | 295 | 443 |
| Creatinine | C6257 | mmol/L | 0 | 3.3 | 6.6 | 9.8 |
| Guanidino Acetate | G6002 | µmol/L | 0 | 33 | 66 | 97 |
| Hydroxyproline | 56250 (Fluka) | µmol/L | 0 | 327 | 654 | 981 |

| | | | | | | |
|------------------------|---------|--------|---|------|------|------|
| Uric Acid | U2875 | µmol/L | 0 | 0.20 | 0.40 | 0.60 |
| Orotic Acid | O3000 | µmol/L | 0 | 30 | 59 | 90 |
| Sialic Acid | A2388 | µmol/L | 0 | 98 | 197 | 294 |
| MPS | C6737 | mg/L | 0 | 33 | 66 | 99 |
| Succinylacetone | D1415 | µmol/L | 0 | 13 | 27 | 40 |
| Homovanillic Acid | H1252 | µmol/L | 0 | 33 | 67 | 98 |
| 5-OH Indol acetic Acid | H8876 | µmol/L | 0 | 32.6 | 65.3 | 98.0 |
| Pipecolic Acid | P4585-0 | µmol/L | 0 | 17 | 32 | 49 |
| Thiosulfate | S7026 | µmol/L | 0 | 20 | 39 | 59 |

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 2006. 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 2006 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 2006). 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 2006).

4. *Discussion of Results in the Annual Report 2006*

In this part the results as seen in the annual report 2006 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 55.2 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 75% for Sodium Thiosulfate to 115% for Sialic Acid. The overall recovery is 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 3.5% for Creatinine to 59.8% 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 0.9026 for Succinylacetone to 0.9979 for Creatinine.

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 (97) whereas only 6 submitted results for Thiosulfate. The Interlab CV ranges from 6.1% for Creatinine to 156.4% for pipecolic acid. 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 (97) laboratories submitted results, the reproducibility within the labs is good (precision of 3.5%), the

Interlab CV is good with 6.1%, linearity is excellent (0.9979) and recovery is 105%. Creatinine will be measured in many institutes by the general clinical chemistry lab using commercial analyzers. It is, therefore, not logical to compare its results with those of chromatographic analyzers.

On the opposite side is Sodium Thiosulfate with only 6 participating labs, a recovery of 75%, a linearity of 0.9235, an Intralab CV of 28.1% and an Interlab CV of 99.9%.

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 2007*

The design of the scheme in 2007 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. Alberto Burlina (burlina@pediatria.unipd.it) and/or to the scheme organiser Dr. Cas Weykamp (c.w.veykamp@skbwinterswijk.nl)