Annual Report ERNDIM-EQAS Purines/Pyrimidines 2003

1. Purpose

The purpose of the ERNDIM External Quality Assurance Scheme for Quantitative Purines and Pyrimidines in Urine is the monitoring of the analytical quality of the quantitative assay of purines and pyrimidines in urine in laboratories involved in the screening and diagnosis of patients with inherited metabolic disorders. For details see www.erndimqa.nl

2. Participants

40 Laboratories subscribed and 33 laboratories from 12 countries submitted results.

3. Design

The Scheme has been designed, planned and co-ordinated by Dr. Albert van Gennip as scientific advisor 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 pilot 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 (all Sigma)	Added Quantities in micromol/liter			
		Sample Pair 96-100	Sample Pair 93-99	Sample Pair 95-97	Sample Pair 94-98
Uracil	U0750	361	218	73	0
5-OH methyluracil	H2627	85	51	17	0
Thymine	T0376	82	49	16	0
Guanine	G6779	85	51	17	0
Pseudo-Uridine	P1658	125	42	0	209
Uridine	U3750	49	16	0	81
Adenosine	A9251	56	18	0	91
Deoxy-adenosine	D7400	85	28	0	139
Orotidine	O9505	34	12	0	59
Hypoxanthine	H9377	34	0	170	102
Xanthine	X4002	53	0	266	160
Adenine	A8751	14	0	69	41
Thymidine	T9250	46	0	232	139
Uric Acid	U2875	0	180	360	540
Orotic Acid	O2875	0	138	83	28
Inosine	I4125	0	95	57	19
Guanosine	G6752	0	72	43	14
Deoxy-inosine	D5287	0	140	84	28
Deoxy-guanosine	D7145	0	90	54	18
Creatinine	-	0	0	0	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 eight individual specimens, for each of which there has been a specific deadline in the year 2003. Two weeks after the respective deadlines participants could request their reports and as such had eight 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 (168 such Analyte-in-Detail-reports can be requested in the year 2003 cycle). A more condensed report is the "Current Report" which summarizes the performance of all analytes in a specific sample (8 such Current Reports can be requested in 2003). 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 2003). Depending on their position in the laboratory one can choose to have a glance at only the annual report (managers) or at all 168 detailed reports (technicians).

4. *Discussion of Results in the Annual Report 2003*

In this part the results as seen in the annual report 2003 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 comparison of your mean outcome in the eight samples with the mean of all labs. This is shown in the columns "your lab" and "all labs" under the heading "Accuracy", respectively. For Adenine the mean of all labs is 27.0 micromol/Liter 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 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 81% for xanthine to 134% for hypoxanthine. The overall recovery is 98%. None of the analytes shows an extremely low or high recovery.

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 the column "Precision" of the Annual Report. Precision ranges from 3.6% for creatinine to 27.8% for adenine. The overall intralab CV is 8.9%.

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 0.9793 for adenine to 0.9991 for uracil. The overall r is 0.9934.

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 orotic acid (32) whereas only 18 labs assayed 5-OH methyluracil. The Interlab CV ranges from 5.3% for creatinine to 297.9% for thymine. The mean Interlab CV for all analytes is 72.9%

4.6 Cross Sectional Relations

The various parameters as described above often have an interrelation: often more than one parameter directs towards good or bad analytical control.
This pattern, clearly seen in the other ERNDIM schemes is less prominent in the Purines and Pyrimidines.

5. Summary

The purpose of the ERNDIM scheme for Purines and Pyrimidines was the monitoring of the analytical quality of the quantitative assay of these compounds in urine. The most dominating in the outcome is the huge Interlab Variation for all analytes except creatinine whereas precision, linearity and mean recovery are quite acceptable. This seems to confirm the relevance of the scheme and an indication that improvement of standardization to achieve harmonisation between laboratories seems a major task associated with the organisation of this scheme.

6. *Preview Scheme 2004*

The design of the scheme is the same as in 2003.

7. *Questions, Remarks, Suggestions*

If you have any questions, remarks or suggestions please address to the scientific advisor Dr. Albert van Gennip (Albert.vanGennip@gen.unimaas.nl) or the scheme organiser Dr. Cas Weykamp (c.w.weykamp@skbwinterswijk.nl)