

Annual Report ERNDIM-EQAS Purines/Pyrimidines 2002

1. Purpose

In 2002 the ERNDIM-EQAS pilot scheme for purines/pyrimidines has become an official regular scheme. 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

34 Laboratories subscribed and 29 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 85 - 89	Sample Pair 88 - 90	Sample Pair 87 - 91	Sample Pair 86 - 92
Uracil	U0750	391	235	78	0
5-OH methyluracil	H2627	91	55	18	0
Thymine	T0376	99	59	20	0
Guanine	G6779	93	55	19	0
Pseudo-Uridine	P1658	137	45	0	228
Uridine	U3750	53	17	0	88
Adenosine	A9251	62	20	0	102
Deoxy-adenosine	D7400	92	30	0	152
Orotidine	O9505	45	15	0	76
Hypoxanthine	H9377	48	0	240	144
Xanthine	X4002	58	0	289	173
Adenine	A8751	15	0	75	44
Thymidine	T9250	50	0	251	151
2,8-di-OH adenine	D7382	20	0	100	60
Orotic Acid	O2875	0	147	87	29
Inosine	I4125	0	102	61	20
Guanosine	G6752	0	80	48	16
Deoxy-inosine	D5287	0	151	91	31
Deoxy-guanosine	D7145	0	102	61	20

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 2002. 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 2002 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 2002). 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 2002). 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 2002

In this part the results as seen in the annual report 2002 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 2,8-di-OH adenine the mean of all labs is 45.5 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 78% for guanine to 113% for deoxy-guanosine. The overall recovery is 97%. 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 3.7% for creatinine to 31.7% for guanine. The overall intralab CV is 11.9%.

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 0.9528 for adenine to 0.9990 for uracil. The overall r is 0.9874.

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 uracil (29) whereas only 16 labs assayed 5-OH methyluracil. The Interlab CV ranges from 7.1% for creatinine to 421.9% for thymine. The mean Interlab CV for all analytes is 94.2%

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. Like in the pilot of 2001 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 2003*

The design of the scheme is the same as in 2002.

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)