

<p>Scientific Advisor Camilla Scott Sharon Colyer Department of Clinical Chemistry Sheffield Childrens NHS Foundation Trust Western Bank Sheffield South Yorkshire England S10 2TH</p>	<p>Website for reporting results</p> <p>Dr. Xavier Albe CSCQ Swiss Center for Quality Control 2 chemin du Petit-Bel-Air CH-1225 Chêne-Bourg Switzerland e-mail : Xavier.Albe@hcuge.ch</p>	<p>Administration office:</p> <p>ERNDIM Admsintration Office Manchester Centre for Genomic Medicine 6th Floor, St Mary's Hospital, Oxford Road, Manchester M13 9WL, United Kingdom. e-mail: admin@erndim.org</p>
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22nd January 2019

30 July 2019*

1. Introduction

The ERNDIM Qualitative Organic Acids in urine scheme offers urine samples obtained from confirmed patients with confirmed diagnoses to enable laboratories to gain or maintain experience to identify organic acid disorders. The scheme is organised by *Camilla Scott and Sharon Colyer at Sheffield Children's Hospital NHS foundation Trust* in conjunction with CSCQ, the Swiss organisation for quality assurance in medical laboratories.

As in previous years, samples were sent out to cover the spectrum of what is typically observed in the metabolic laboratory. A mix of clearly diagnostic profiles and some more challenging profiles were provided. As in previous years normal profiles were also sent out. The requirement to interpret a normal profile, as such, is as important as correctly identifying abnormal profiles. Correctly identifying a profile as normal can avoid unnecessary further investigation and distress to the patient and family.

2. Participants

In 2018 73 laboratories from many different countries participated in the QLOU Sheffield scheme.

The numbers of participants continues to increase and as a result a third organising centre, Barcelona, was added to the QLOU scheme for 2018 and participants were split between the three organising centres. New applicants will distributed between the Barcelona, Sheffield and Heidelberg qualitative urinary organic acid schemes which are run separately. The three organising laboratories each participate in the other's scheme by rotation.

3. Design of the scheme and logistics

As usual, the samples used in 2018 were authentic human urine samples, 7 from affected patients and 2 from a healthy individual. Samples were selected by the Scientific Advisor and tested for suitability in the Scientific Advisor's laboratory. In 2018 CSCQ dispatched the QLOU EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports. Existing QLOU, ACDB, DPT and Urine MPS scheme participants can log on to the CSCQ results submission website at: <https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php>

To be able to continue this scheme we need a steady supply of new patient samples. Several laboratories have donated samples to the qualitative urine organic acid scheme in the past, for which they are gratefully acknowledged. If you have one or more samples available and are willing to donate these to the scheme, please contact us at admin@erndim.org. Laboratories which donate samples that are used in the scheme are eligible for a 20% discount on their participation in the QLOU scheme in the following year.

Version Number (& Date)	Amendments
1 version 2 (30 th July 2019)	<ul style="list-style-type: none"> Page 2: Addition of reference to donated sample used in the 2018 scheme.

Table 1. Samples included in the 2018 ERNDIM QLOU Sheffield scheme. One sample used in the 2018 was donated by University Hospital Wales, Cardiff.

Survey, reporting deadline	Sample no.	Sample type
2018A, 1 st June 2018	QLOU-US-2018-A	Alkaptonuria
2018B, 1 st June 2018	QLOU-US-2018-B	Glutaric Aciduria Type 1
2018C, 1 st June 2018	QLOU-US-2018-C	Normal
2018D, 27 th July 2018	QLOU-US-2018-D	Methylmalonic Aciduria
2018E, 27 th July 2018	QLOU-US-2018-E	3-Methylglutaconic Aciduria (NOS)
2018F, 27 th July 2018	QLOU-US-2018-F	3-Methylglutaconic Aciduria (NOS)
2018G, 28 th September 2018	QLOU-US-2018-G	Propionic Acidaemia
2018H, 28 th September 2018	QLOU-US-2018-H	Normal
2018I, 28 th September 2018	QLOU-US-2018-I	Ethylene glycol poisoning

The scheme format was kept identical to those of previous years. Samples were shipped by regular mail in *March 2018* along with other ERNDIM samples. Details regarding stability of (reconstituted) samples are provided in the sample package.

Participants submitted results to the CSCQ website <https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php>. The due dates for submitting results in 2018 were *1st June, 27th July and 28th September 2018*. The website includes a section to specify methods.

In 2018 a total of 72/73 reports were received for survey 1 (samples 2018 A to C), 71/73 reports for survey 2 (samples 2018 D to F) and 71/73 reports for survey 3 (samples 2018 G to I). 69 labs submitted results for all three surveys and 3 of the participants submitted two of the three reports. 1 laboratory submitted only one full survey.

Evaluation of results was performed using a combination of both Microsoft access and excel databases with the submitted results extracted from the database by the website manager.

4. Scoring of results

A scoring system was developed in 2012 and approved by the ERNDIM Scientific Advisory Board. Similar to other qualitative (proficiency testing) ERNDIM schemes, the maximum score for a sample is 4 points. Scores are allocated to different elements of the results reported (Table 3). Qualitative results and diagnostic proficiency of the 2018 samples were scored using the criteria given in Table 4 and 5. These criteria have been set by the Scientific Advisor, approved by the Scientific Advisory Board. The final decision about scoring of the scheme is made in the Scientific Advisory Board (SAB) during the Autumn meeting (November 30th, 2018 for the 2018 scheme).

A note on scoring of diagnostic proficiency and the use of check boxes and the comment box:

To indicate the most likely diagnosis check boxes must be used to facilitate evaluation of results. The use of the 'comments' box in the website form is recommended to explain your interpretation of results. Comments will be taken into account to score interpretation.

Table 2. General criteria used to score results

Satisfactory	4	Helpful but incomplete	3
Not helpful	2	Slightly misleading	1
Misleading	0		

Starting with the 2014 schemes the concept of 'critical error' is introduced to the assessment of the qualitative schemes. Labs failing to make a correct diagnosis of a sample considered eligible for this category will be deemed not to have reached a satisfactory performance even if their total points for the year is sufficient according to the requirement set by the SAB. The classification of samples to be judged for critical error was undertaken at the SAB meeting held on November 30th, 2018. Samples **QLOU-US-2018-B (GA-1), QLOU-US-2018-D (MMA), QLOU-US-2018-E & F (3-methyl glutaconic aciduria), QLOU-US-2018-G (PA)**, were eligible for critical error. Five laboratories were awarded critical error in 2018. Details are given under item 7 'Results of individual samples and evaluation of reporting'.

We are required to define "Participation" for the purpose of the ERNDIM Annual Certificate which covers all ERNDIM schemes. For this urinary organic acid scheme we have defined "Participation" as requiring at least two full returns during the year. Failure to meet this requirement will result in the certificate of participation showing 'non-submitter' rather than 'satisfactory' or 'unsatisfactory'.

In 2018 the satisfactory performance score has changed from 61% to **70%** which equates to **25/36** for 3 returns and **17/24** for two returns.

5. Communication of results

Interim reports with diagnoses, summaries of the results submitted and interim scores were made available 27/07 (survey 2018-1), 19/09 (survey 2018-2) and 07/12 (survey 2018-3).

ERNDIM provides a single certificate for all its schemes with details of participation and performance.

Five Performance Support letters will be sent for the 2018 surveys. *Two* of these *five* participants have also received a performance support letter in 2016 or 2017. Unsatisfactory performance (either due to overall score or due to critical error) within an EQA scheme for at least 2 out of 3 years that the participant has subscribed for will result in a notification letter of unsatisfactory performance to the quality manager or head of department.

6. Proficiency of the 2018 surveys

In 2018, 69 participants submitted 3 reports, 3 participants submitted 2 reports. 1 laboratory submitted one full report. From the 73 ordinary (non-educational) participants 68 (93%) achieved satisfactory performance (score ≥ 25 no critical error). Five participants did not accomplish satisfactory performance. Four of these were for critical error alone. Overall proficiencies of each sample are depicted in Table 6.

Table 6. Overall proficiencies of the 2018 surveys.

Sample ID	Sample type	Proficiency (%)
QLOU-US.2018.A	Alkaptonuria	100
QLOU-US.2018.B	Glutaric Aciduria Type 1	96
QLOU-US.2018.C	Normal	100
QLOU-US.2018.D	Methylmalonic Aciduria	92
QLOU-US.2018.E	3-Methylglutaconic aciduria (NOS)	94
QLOU-US.2018.F	3-Methylglutaconic aciduria (NOS)	94
QLOU-US.2018.G	Propionic Acidaemia	97
QLOU-US.2018.H	Normal	99
QLOU-US.2018.I	Ethylene glycol poisoning	94

7. Results of individual samples and evaluation of reporting

The samples sent out in 2018 achieved good proficiency across the board. It is reassuring to see the majority of laboratories were successful in identifying the key metabolites and advising on the correct diagnosis in the majority of cases. The methylmalonic aciduria sample 2018/D had the lowest proficiency and this was mainly due to the failure to identify the methylmalonic peak by some participants. Interestingly most participants were able to identify the methylcitrate and 3-hydroxypropionate peaks in this profile. The ethylene glycol sample (oxalate and glycolate peaks) (2018/I) and the 3-methylglutaconic aciduria (2018/D and E) were also missed by some participants. These samples have proved challenging in previous distributions and the proficiency was greatly improved in 2018 compared to previous distributions.

8. Preview of the scheme in 2019

The format of the QLOU 2019 scheme will be similar to that of previous years.

2018 was the first year for electronic reporting via the CSCQ website. We will continue to evaluate results via the website for 2019.

Scientific Advisors name



Camilla Scott
Scientific Advisor

Sharon Coyler
Deputy Scientific Advisor

Please note:

This annual report is intended for participants of the ERNDIM QLOU scheme. The contents should not be used for any publication without permission of the scheme advisor