



ERNDiM

QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

DECEMBER 2019

Annual Report 2018

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EUROPEAN RESEARCH NETWORK FOR EVALUATION AND
IMPROVEMENT OF SCREENING, DIAGNOSIS AND
TREATMENT OF INHERITED DISORDERS OF
METABOLISM

Chair's Introduction

It is a pleasure to present to you the 2018 ERNDIM Annual Report, providing an overview of ERNDIM activities, overall features and results of EQA schemes as well as finance information.

ERNDIM is an international organisation aiming at consensus between European Biochemical Genetics Centres on reliable and standardised procedures for diagnosis, treatment and monitoring of inherited metabolic diseases. This is achieved through provision of quality control schemes operated according to accepted norms and on a global scale. We also provide education through meetings and provision of relevant documentation such as recommended operating procedures and annual reports of schemes on the internet. In

addition, we supply control and reference materials in conjunction with our partner organisation, MCA laboratory.

The ERNDIM Foundation was formally registered on September 5th 1994, at the Dutch Chamber of Commerce in Maastricht, and EQA schemes were operated for Quantitative Amino Acids, Organic Acids and Special Metabolite Assays, in addition to an interpretative scheme for Organic Acids.

Since these early years much progress has been made and ERNDIM has evolved into an organisation with professional governance and strong increases in the number of EQA schemes, and number of participating laboratories.



**Dr George Ruijter, Chair,
Executive Committee**

ERNDIM 2018

...an organisation with professional governance & strong increases in the number of EQA schemes, and number of participating laboratories...



2018 Activities

ERNDIM continues to grow and in 2018 we again saw an increase in the number of registered laboratories.

We maintain a strong European basis with 61% of participating laboratories in 2018 (Figure 1) being European, however a significant number of participating laboratories now also come from Asia, North America, Oceania, South America and Africa (Figures 1 & 2).

We provided two pilot schemes in 2018. These are fully funded by ERNDIM during the pilot phase, i.e. free to participants. Surveys have shown that there is sufficient interest worldwide to make the schemes viable. The 2018 pilots were: Cognitive Amino Acids and Special Assays in dried blood spots (DBS).

The results submission websites for the Qualitative Organic Acids and Acylcarnitines in DBS schemes were successfully launched in 2018.

The changes made to the EQA calendar in 2018 allowed the 2018 certificates to be published in April 2019. While this was slightly later than planned it was still earlier than for the 2017

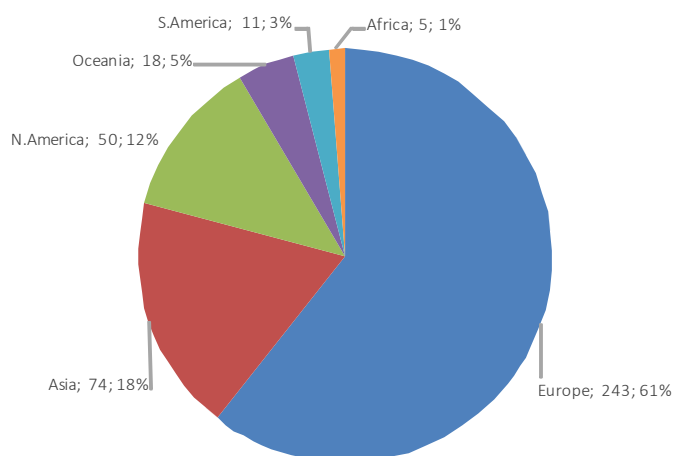


Figure 1: Number of registered laboratories in 2018, by continent

certificates which were published in May 2018.

The ERNDIM participant meeting was held in September 2018 in Athens, Greece and was well received and attended. The presentations from the 2018 ERNDIM Participant meeting can be found on www.erndim.org under 'Meetings'.

ERNDIM collaborated with the Education and Training Committee (ETAC) of SSIEM to provide the 2018 Academy training course which was held in

April in Slough, United Kingdom.

SSIEM continued to fund a full time Scientific Administrator post in the Administration Office ERNDIM is extremely grateful to SSIEM for this funding which is helping to speed up our slow, but steady, progress towards applying for accreditation.

2018 Activities *(continued)*

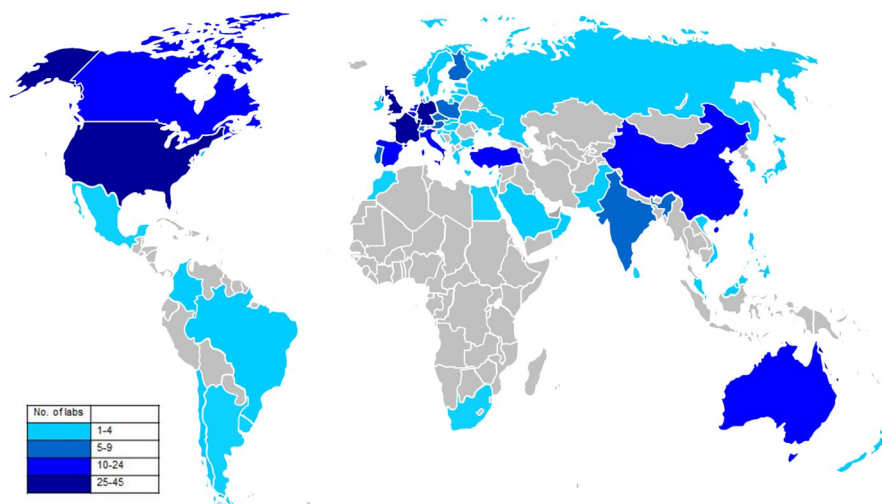


Figure 2: Number of participants per country



Finance Summary

Figures 3 and 4 are summaries of our 2018 income and expenditure. The main source of our income was the EQA scheme fees paid by participants however, we also receive significant support from SSIEM for staff costs (included under 'Admin' in Figure 3).

As would be expected our major expense is the provision of the EQA schemes, which in 2018 made up 69% of our expenditure; while Administration (staff costs, office consumables etc.) and Meetings, respectively, accounted for 23% and 5% of our expenditure.

ERNDIM 2018

...our major expense is the provision of the EQA schemes...

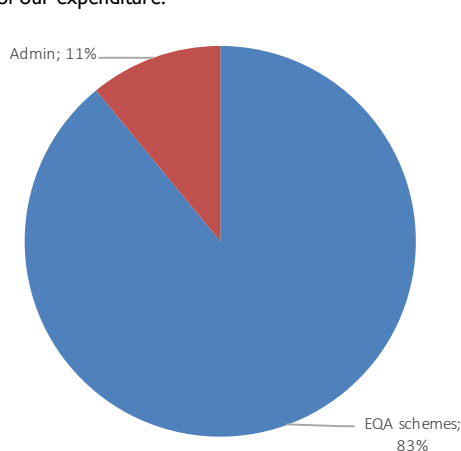


Figure 3: Summary of 2018 income

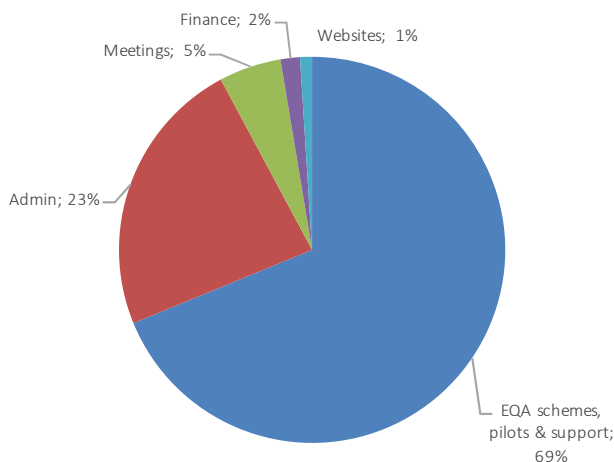


Figure 4: Summary of 2018 expenditure

2019-20 plans

EQA Calendar

We are continuing to make changes to the EQA scheme calendar to allow the scheme results to be finalised within the scheme year, with the aim of allowing certificates of participation to be published in the first quarter of the next year, which we know would be welcomed by many participants.

Sample Dispatch

The 2019 DPT,[†] QLOU[†] and ACDB[†]

samples were combined into one sample dispatch by CSCQ. This will improve service to participants by making it easier to track which samples have been received and reduce costs for ERNDIM.

Results websites

Online submission for the CDG[†] scheme launched for the first 2019 submission round.

Evaluation & Scoring

Scored interpretative elements for the CWBC[†], NCSF[†], PTU[†] and LEFB[†] schemes will be piloted.

Pilot schemes

The Cognitive Amino Acids pilot scheme has continued in 2019.



[†] = see Appendix (page 8) for full EQA scheme names

EQA Registrations



In 2018 401 laboratories, from 60 countries participated in the 15 EQA schemes that we offered, with 1788 individual scheme registrations.

ERNDIM received 627 registrations for qualitative schemes in 2018 (an increase of 6 [+1.0%] compared to 2017) and 1161 registrations for quantitative schemes (an increase of 30 [+2.7%] compared to 2017). Overall, registrations increased by 2.1% compared to 2017 (Figure 5) with twelve of the fifteen EQA schemes having an increase in registrations compared to 2017 (see Table 1).

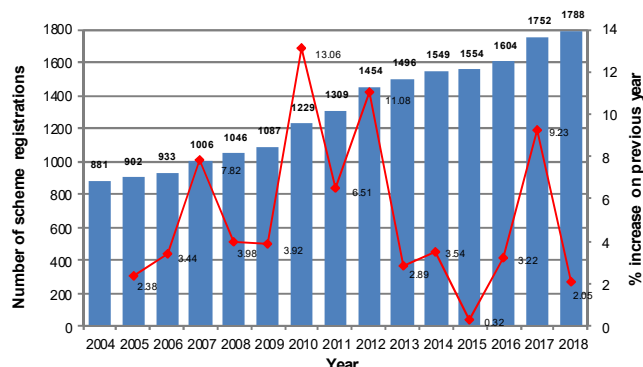


Figure 5: Total EQA scheme registrations by year (and % increase compared to previous year)

Table 1: 2018 Registrations per scheme

EQA Schemes [†]	No. of 2018 registrations	Difference to 2017	
		No.	%
ACDB	127	+4	+3.3%
ACS*	102	+14	+15.9%
CDG	68	+2	+3.3%
CWBC	37	0	0.0%
DPT	110	+1	+0.9%
LEFB	76	+1	+1.3%
NCSF	31	+2	+6.9%
PTU	33	+3	+10.0%
PPU	54	+3	+6.9%
QLOU	221	+1	+0.5
QTAS	268	+2	+0.8%
QTOU	127	+1	+0.8%
SAS	247	-2	-0.8%
SAU	186	+6	+3.3%
UMPS	101	-2	-1.9%
Total Registrations	1788	+36	+2.1%

[†] = see Appendix (page 8) for full EQA scheme names

Laboratories from 60 countries registered for the 2018 EQA schemes (Figure 6). For just under half these countries (29/60) only 1-2 laboratories were registered with ERNDIM (= 37 participants; 9.2%) While over 36% of participants (=146 participants) came from one of 4 countries (UK, France, USA and Germany).

Pilot Schemes

In 2018 there were 2 pilot schemes running: Cognitive Amino Acids (CAA, 53 participants from 8 countries) and Special Assays in DBS (SADB, 93 participants from 30 countries). For the CAA pilot all but one participant were European laboratories while for the SADB pilot 42.4% of participating laboratories were from outside of Europe.

ERNDIM 2018
15 EQA schemes
401 labs
60 countries
1788 registrations

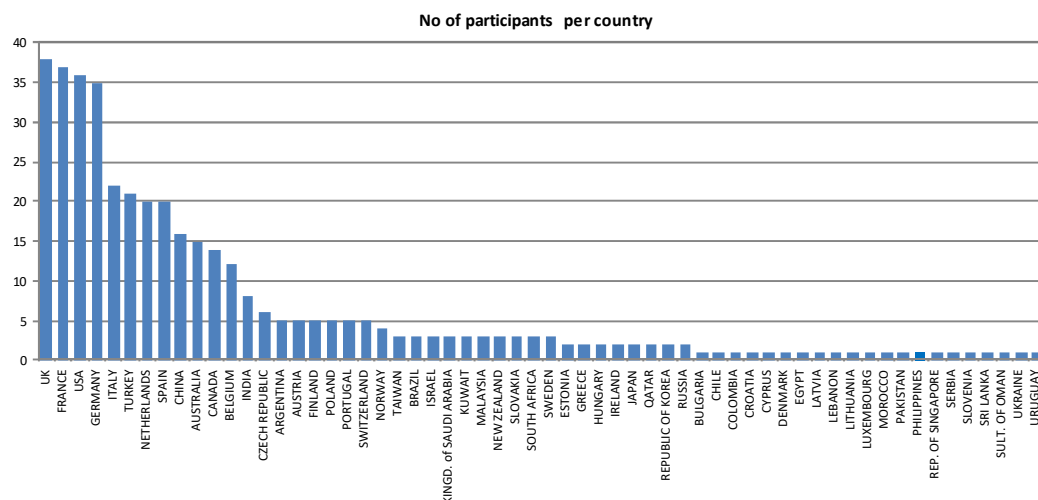


Figure 6: Number of participants per country

EQA Samples

Across all the 2018 EQA schemes we used 161 different EQA samples and 14,869 aliquots were prepared by the scheme organisers.

The main source of materials used for the 2018 EQA schemes were samples of patient urine collected by the Scientific Advisor/scheme organiser (57/161 samples).

A total of 13 samples used in the 2018 schemes were donated by participating laboratories (DPT[†] = 7, UMPS[†] = 4, QLOU[†] = 2, ACDB[†] = 1)

and a patient organisation (1 sample used in the DPT scheme).

We would like to thank all the individual laboratories that donated patient samples and also the Dutch Patient Association, VKS for their help.

Information on the types of donated samples that are useful to ERNDIM can be found on www.erndim.org under EQA schemes. Discounts on scheme fees are offered to participating labs that donate samples;

for more information contact admin@erndim.org.

If your laboratory has a sample you think might be useful to one of the ERNDIM EQA schemes please contact admin@erndim.org.

[†] = see Appendix (page 8) for full EQA scheme names

ERNDIM 2018

...161 different EQA samples and over 14,869 aliquots were prepared...

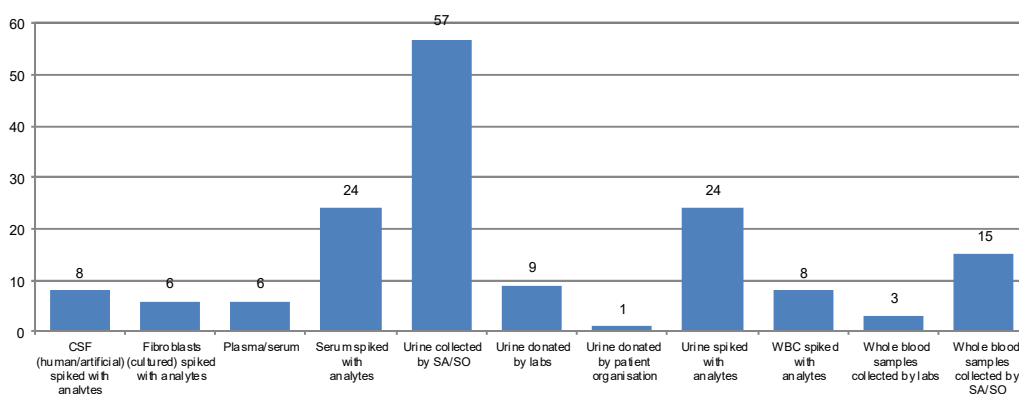


Figure 7: Materials used as EQA materials in 2018 schemes [SA = Scientific Advisor; SO = Scheme Organiser]

Extra sample requests

We received 87 requests for extra material for the 2018 schemes, from 62 laboratories (15.5% of all labs).

The main reasons for the requests were: the sample parcel not being received (21 requests; 5.2% of all labs); labs wishing to test/validate a new method* (21 requests; 5.2% of all labs); vials broken/leaked in transit (16 requests; 4.0% of all labs); labs requesting extra material to reanalyse (10 requests; 2.5% of all labs); and lab errors (8 requests; 2.0% of all labs) which together made up over 87% of all requests for extra material. [^{*} these requests are only fulfilled after the last submission deadline in the scheme year]

It should be noted that a almost a quarter of all requests were for samples to help with testing or validating a new method. Where this leads to a publication, labs should ask ERNDIM for consent (admin@erndim.org) for the use of the data from ERNDIM samples and ERNDIM should be acknowledged in the publication.

For the CDG and UMPS schemes, some laboratories require a larger sample volume due to their analysis method. For the CDG scheme, 22 labs (33% of scheme participants) requested extra sample volume due to their analysis method and were sent a total of 30 extra set of samples at a reduced fee. For the Urine MPS scheme 1 lab (1% of scheme participants) requested extra sample volume and was sent 1 extra set of samples at a reduced fee.

Table 2: Requests for extra 2018 EQA samples

EQA Schemes [†]	No. of extra materials requests	% of labs registered
ACDB	8	6.3%
ACS	5	4.9%
CDG	2	3.0%
CWBC	3	8.1%
DPT	1	0.9%
LEFB	4	5.5%
NSCF	5	16.1%
PTU	3	3.7%
PPU	2	9.4%
QLOU	4	1.8%
QTAS	11	4.2%
QTOU	7	5.6%
SAS	19	8.2%
SAU	9	5.1%
UMPS	4	4.0%
All requests	87	21.7%

[†] = see Appendix (page 8) for full EQA scheme names



Reporting Compliance Rates

Overall reporting compliance rates in 2018 were good, with 95% of results being submitted on time (Table 3), 1.1% of results were submitted after the submission deadlines (compared to 1.7% in 2017) & 4.0% of results were not submitted at all (compared to 4.4% in 2017).

The percentage of results submitted on time was 90% or above for all 2018 schemes, with 7 schemes have compliance rates above 95%. The lowest reporting compliance rates were for the LEFB[†] (90.0%) and ACDB[†] (90.7%).

Table 3: Reporting compliance rates for 2018 EQA schemes

EQA Schemes [†]	No of registered labs	% Results submitted on time	EQA Schemes [†]	No of registered labs	% Results submitted on time
ALL SCHEMES	401	94.8%	PTU	32	93.8%
ACDB	126	90.7%	PPU	54	95.8%
ACS	102	91.2%	QLOU	218	95.2%
CDG	67	92.8%	QTAS	264	94.6%
CWBC	37	98.6%	QTOU	126	94.1%
DPT	110	98.9%	SAS	233	95.9%
LEFB	73	90.0%	SAU	177	96.5%
NCSF	31	99.2%	UMPS	100	94.5%

[†] = see Appendix (page 8) for full EQA scheme names

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...95% of results were submitted on time...

Participations

Non- & Partial Submitters

330 labs (82.3%) participated in all their registered schemes, with an additional 56 labs (14.0%) participating in at least one scheme. 13 labs (3.2%) did not participate in any schemes (10 labs = 1-2 schemes; 1 lab = 3 schemes; 1 lab = 4 schemes; 1 lab = 5 schemes); while 2 labs were Educational Participants in all the schemes they registered for. All non- and partial submitters are sent a letter asking for the reason for the non-submission of results and offering advice and support if needed.

Educational Participants* (EP)

15 labs registered as EP. 11 labs were EPs in 1 scheme each and 4 labs were EPs in 2 schemes.

Any labs registered as an EP for only some of the analytes in a Quantitative scheme (= 0 labs for 2018) would not be included in Figure 8 as their performance would be assessed for the remaining analytes.

* = Labs can only apply for EP they are not offering a clinical service for the relevant analyte or test and acceptance is dependent on the approval of the appropriate Scientific Advisor,

Withdrawn labs

Five labs withdrew from one 2018 EQA scheme each (= 5 EQA registrations, 0.3% of all registrations): 1 lab was no longer offering a service, 3 labs had technical issues, and 1 lab withdrew from the UMPS[†] scheme and registered for the SAU[†] instead.

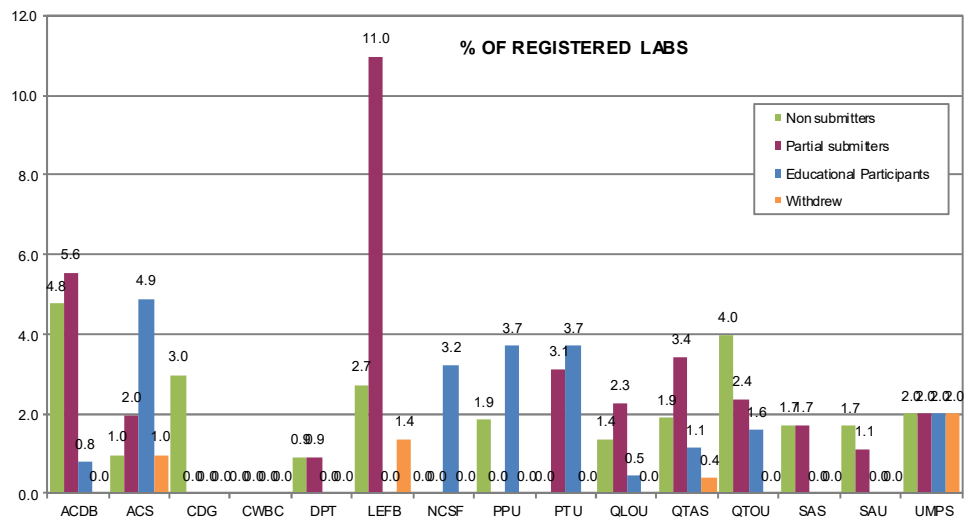


Figure 8: Non-submitters etc. per EQA scheme [† see Appendix (page 8) for full EQA scheme names and full scheme results]

Performance

Performances in all the ERNDIM EQA schemes are reviewed and agreed at meetings of the Scientific Advisory Board (SAB) which includes the Scientific Advisors for all the full EQA and pilot schemes.

The full results for all the EQA schemes are given in Table 5 (page 8) but a summary is given in Figure 9 below.

Poor Performance

Of the 386 labs that participated in one or more 2018 EQA schemes, 82 labs (21.2% of participating labs) were classed as a poor performer

for score and/or critical error in one or more of the EQA schemes they participated in.

Twenty-four critical errors were agreed by the SAB for the 2018 schemes, which resulted in 17 additional instances of poor performance (i.e. poor performance for critical error only, see Table 5, page 8). The details of the agreed critical errors can be found on www.erndim.org under 'Reports.'

Satisfactory Performance

78.8% of participating labs (= 304/386) obtained satisfactory

performance in all of the EQA schemes they participated in (compared to 82.9% in the 2017 schemes).

The level of satisfactory performance in the 2018 schemes ranged from 84.3% (PPU[†]) to 98.5% (CDG[†]) with the overall level of satisfactory performance for all schemes being 93.6% (see Table 5, page 8) compared to 95.3% in 2017.

ERNDIM 2018

...78.8% of participating labs obtained satisfactory performance in all of the EQA schemes they participated in...

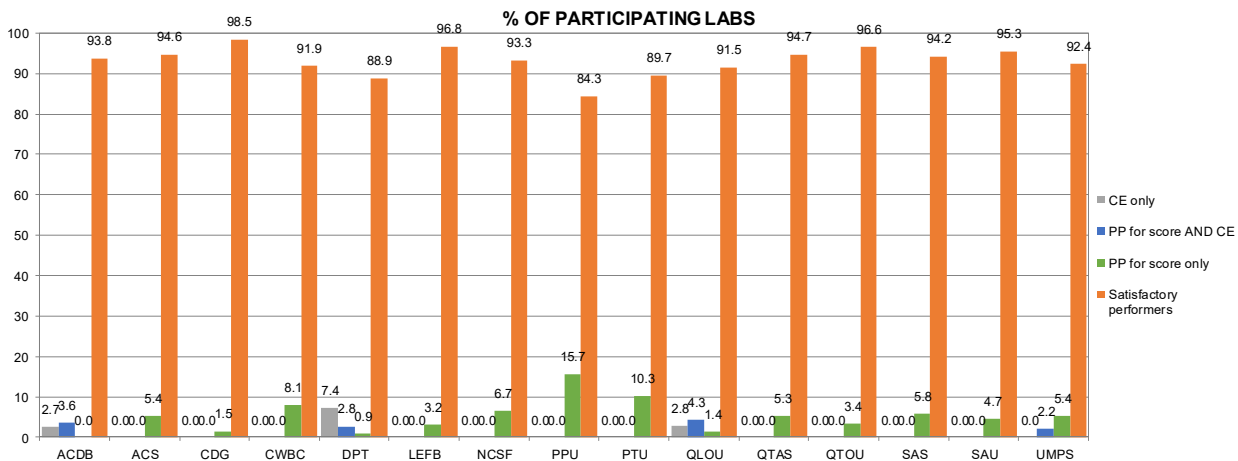


Figure 9: Performance per EQA scheme [see Appendix (page 8) for full EQA scheme names and full scheme results]

Persistent Poor Performance

Persistent Poor Performance (PPP) is defined as at least 2 years of poor performance in an EQA scheme within 3 participating years.

For 2016-2018, 25 labs had PPP (= 6.5% of participating labs) compared with 20 labs (5.2% of participating labs) for 2015-17.

Sixteen labs with PPP for 2016-2018

also had PPP for 2015-2017. Of these 16, 4 labs had poor performance in both 2016 & 2017 but were good performers in the 2018 schemes.

Two of the labs with PPP in 2016-2018 were PPP in more than one scheme (1 for 2 schemes & 1 for 3 schemes) and the remaining 23 labs only had PPP in one EQA scheme.

Appeals

We received 3 appeals against classification as a poor performer in the 2018 schemes, compared to 7 appeal for the 2017 schemes.

One 2018 appeal was upheld (CDG[†]) and the lab's performance was updated. The outcome of the successful appeal is included in the performance results in Figure 9 & Table 5 (page 8).

Global Poor Performance

Global Poor Performance (GPP) is poor performance in more than one EQA scheme in one year.

In 2018, nineteen labs had poor performance in more than one EQA scheme (= 4.9% of participating labs). This is higher than the rate of GPP in 2017 when 2.6% of participating labs had GPP (= 10/387).

Five of the labs with GPP in 2018 were poor performers in 2 separate EQA schemes, while the remaining 14 labs were poor performers in 3 separate schemes.

Four of the labs with GPP in 2018 also had GPP in 2017.

Change Requests

Requests for scores to be adjusted which would not result in a change to a lab's performance are classed as 'Change Requests'.

In 2018 one 'change request' related to the CDG[†] scheme was received, which was upheld.



Appendix

Table 4: Full EQA Schemes and scheme codes

Scheme Code	EQA Scheme Name
ACDB	Acylcarnitines in dried blood cells (DBS)
ACS	Acylcarnitines in serum
CDG	Congenital Disorders of Glycosylation (plasma/serum)
CWBC	Cystine in white blood cells (WBC)
DPT	Diagnostic Proficiency Testing (urine)
LEFB	Lysosomal Enzymes in fibroblasts
NSCF	Neurotransmitters in cerebrospinal fluid (CSF)
PPU	Purines & Pyrimidines (urine)
PTU	Pterins in urine
QLOU	Qualitative Organic Acids (urine)
QTAS	Quantitative Amino Acids (serum)
QTOU	Quantitative Organic Acids (urine)
SAS	Special Assays in serum
SAU	Special Assays in urine
UMPS	Urine Mucopolysaccharides

Table 5: Summary of all 2018 participations and performance results

EQA Scheme [†]	Registered labs	Non-submitters		Partial submitters		Withdrawn labs		Educational Participants		Participating labs		PP ¹ for score only		PP ¹ for score AND CE ²		PP ¹ for CE ² only		Satisfactory performers	
ACDB	126	6	4.8%	7	5.6%	0	0.0%	1	0.8%	112	88.9%	0	0.0%	4	3.6%	3	2.7%	105	93.8%
ACS	102	1	1.0%	2	2.0%	1	1.0%	5	4.9%	93	91.2%	5	5.4%	- ⁴	- ⁴	- ⁴	- ⁴	88	94.6%
CDG	67	2	3.0%	0	0.0%	0	0.0%	0	0.0%	65	97.0%	1	1.5%	0	0.0%	0	0.0%	64	98.5%
CWBC	37	0	0.0%	0	0.0%	0	0.0%	0	0.0%	37	100.0%	3	8.1%	- ⁴	- ⁴	- ⁴	- ⁴	34	91.9%
DPT	110	1	0.9%	1	0.9%	0	0.0%	- ³	- ³	108	98.2%	1	0.9%	3	2.8%	8	7.4%	96	88.9%
LEFB	73	2	2.7%	8	11.0%	1	1.4%	0	0.0%	62	84.9%	2	3.2%	- ⁴	- ⁴	- ⁴	- ⁴	60	96.8%
NSCF	31	0	0.0%	0	0.0%	0	0.0%	1	3.2%	30	96.8%	2	6.7%	- ⁴	- ⁴	- ⁴	- ⁴	28	93.3%
PPU	54	1	1.9%	0	0.0%	0	0.0%	2	3.7%	51	94.4%	8	15.7%	- ⁴	- ⁴	- ⁴	- ⁴	43	84.3%
PTU	31	0	0.0%	1	3.1%	0	0.0%	2	6.3%	29	90.6%	3	10.3%	- ⁴	- ⁴	- ⁴	- ⁴	26	89.7%
QLOU	220	3	1.4%	5	2.3%	0	0.0%	1	0.5%	211	95.9%	3	1.4%	9	4.3%	6	2.8%	193	91.5%
QTAS	264	5	1.9%	9	3.4%	1	0.4%	3	1.1%	246	93.2%	13	5.3%	- ⁴	- ⁴	- ⁴	- ⁴	233	94.7%
QTOU	126	5	4.0%	3	2.4%	0	0.0%	2	1.6%	116	92.1%	4	3.4%	- ⁴	- ⁴	- ⁴	- ⁴	112	96.6%
SAS	233	4	1.7%	4	1.7%	0	0.0%	0	0.0%	225	96.6%	13	5.8%	- ⁴	- ⁴	- ⁴	- ⁴	212	94.2%
SAU	177	3	1.7%	2	1.1%	0	0.0%	0	0.0%	172	97.2%	8	4.7%	- ⁴	- ⁴	- ⁴	- ⁴	164	95.3%
UMPS	100	2	2.0%	2	2.0%	2	2.0%	2	2.0%	92	92.0%	5	5.4%	2	2.2%	0	0.0%	85	92.4%
ALL SCHEMES	1752	35	2.0%	44	2.5%	5	0.3%	19	1.1%	1649	94.1%	71	4.3%	18	1.1%	17	1.0%	1543	93.6%

[†] = see Table 4 for full EQA scheme names; ¹ = Poor Performance; ² = Critical Error; ³ = Educational Participation does not apply to the DPT scheme;

⁴ = CE does not apply to these schemes



“Working towards a consensus between Biochemical Genetics Centres on reliable and standardised procedures for diagnosis, treatment and monitoring of inherited metabolic diseases”

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