ERNDIM

QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

JUNE 2020

Annual Report 2019

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

Chair's Introduction

Dr George Ruijter, Chair, Executive Committee

It is a pleasure to present to you the 2019 ERNDIM Annual Report, providing an overview of ERNDIM activities, overall features and results of EQA schemes as well as finance information. This annual report was prepared by the ERNDIM office led by Dr Sara Gardner.

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 relevant documentation such as recommended operating procedures and annual reports of schemes on our website. 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.

ERNDIM 2019

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

2019 Activities

ERNDIM continues to grow and in 2019 we again saw an increase in the number of registered laboratories.

We maintain a strong European basis with 59% of participating laboratories in 2019 (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 introduced a new EQA scheme in 2019, the Special Assays in DBS scheme which previously ran as a pilot in 2017 and 2018.

We provided one pilot scheme in 2019: Cognitive Amino Acids. These schemes 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.

For the first time in 2019 the samples for the ACDB† DPT† and QLOU† schemes were sent in one combined sample dispatch by our sub-contractor, CSCQ, rather than in separate parcels as in previous years.

The results submission website for the CDG† scheme was successfully launched in 2019.

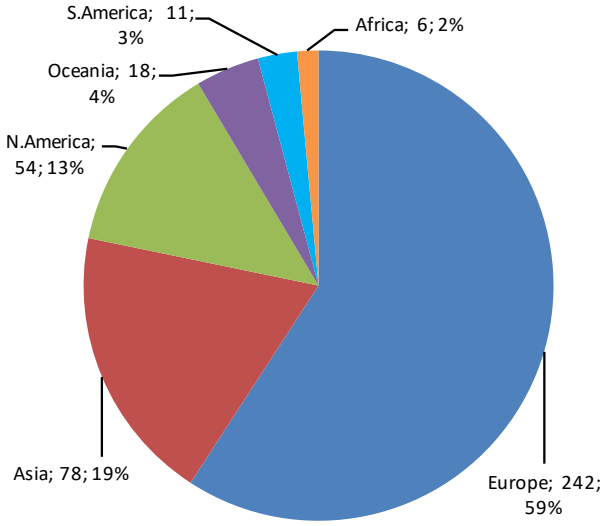

Figure 1: Number of registered laboratories in 2019, by continent

The scoring of interpretative elements for the NCSF†, PTU† and LEFB† schemes were piloted.

Unfortunately, due to difficulties caused by the Covid-19 pandemic the final evaluation of some schemes was delayed and the 2019 Certificates of Participation were not published until June 2020.

The ERNDIM participant meeting was held in September 2019 in Rotterdam, Netherlands and was well received and attended. The presentations from the 2019 ERNDIM Participant meeting can be found on www.erndim.org under 'Meetings'.

ERNDIM continued to collaborate with the Education and Training Committee (ETAC) of SSIEM to provide the 2019 Academy training course which was held in April in Winterthur, Switzerland.

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.

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

2019 Activities *(continued)*

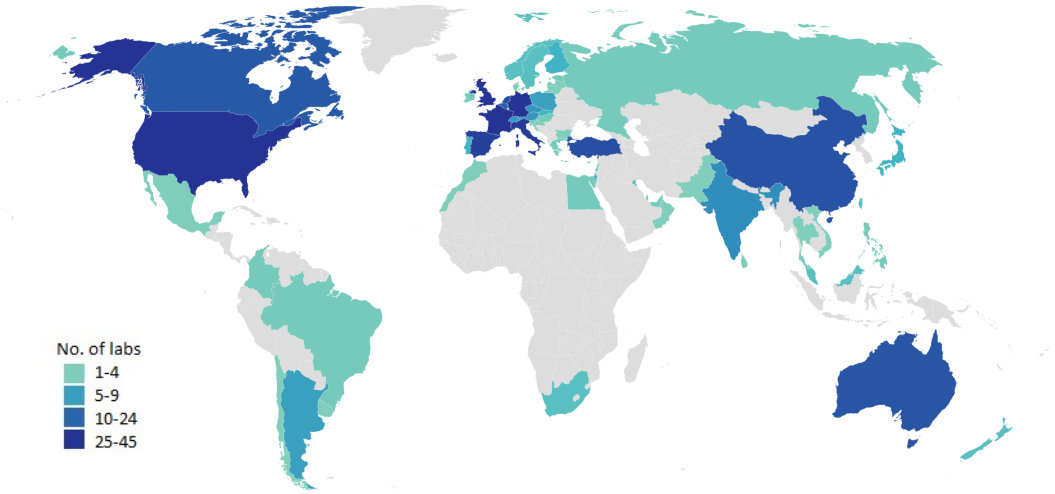

Figure 2: Number of participants per country

Finance Summary

Figures 3 and 4 are summaries of our 2019 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 2019 made up 65% of our expenditure; while Administration (staff costs, office consumables etc.) and Meetings, respectively, accounted for 28% and 5% of our expenditure.

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

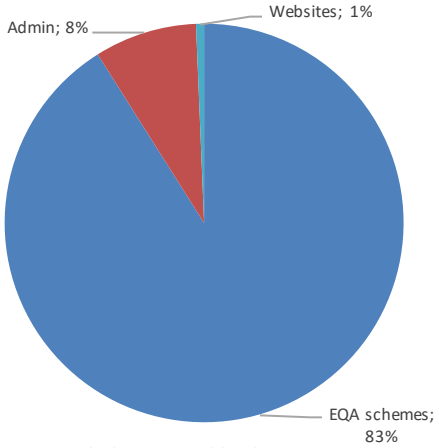

Figure 3: Summary of 2019 income

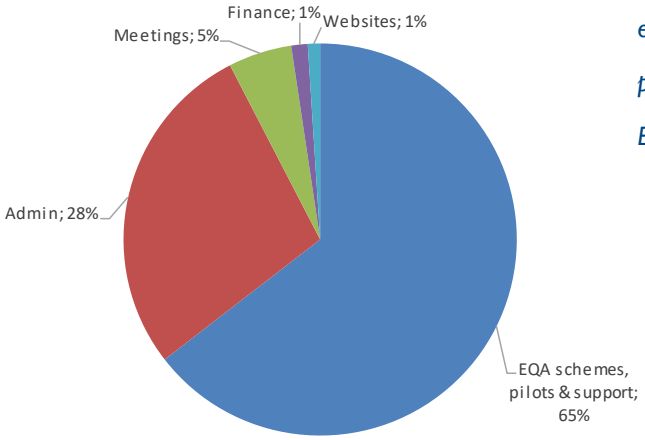

Figure 4: Summary of 2019 expenditure

2020-21 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.

Evaluation & Scoring

After successful pilots in 2019, scored interpretations for the NCSF†, and LEFB† schemes will be part of the performance evaluation for these schemes in 2020. While pilots for scored interpretative elements will continue in 2020 for the PTU† scheme and start for the CWBC† scheme.

EQA scheme format

After a review it has been agreed to reduce the number of samples in the QLOU† scheme from 9 to 6 per scheme year, from 2021 onwards. This change will make it easier for the Scientific Advisors to source a sufficient number of clinical samples to be used as the EQA materials, and will bring this scheme inline with the other qualitative schemes which all include 6 samples per scheme year.

Pilot schemes

The Cognitive Amino Acids pilot scheme will continue in 2020.

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

EQA Registrations

In 2019, 409 laboratories, from 63 countries participated in the 16 EQA schemes that we offered, with 1924 individual scheme registrations.

ERNDIM received 630 registrations for qualitative schemes in 2019 (an increase of 3 [+0.5%] compared to 2018) and 1294 registrations for quantitative schemes (an increase of 161 [+11.5%] compared to 2018) . However, this large increase was mainly due to the introduction of a new full quantitative EQA scheme (the SADB† scheme). If the registrations for this scheme are taken out of the 2019 quantitative registrations then there was a 3.9% increase compared to 2018. .

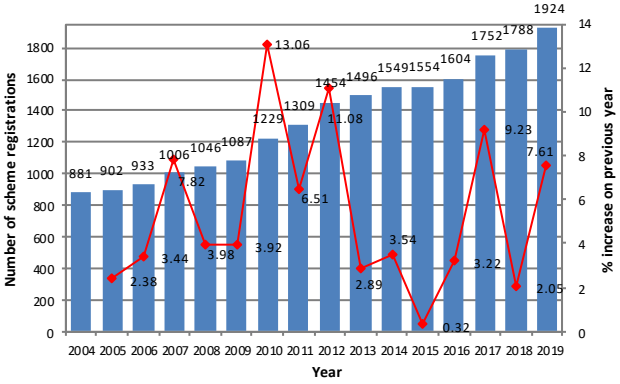

Figure 5: Total EQA scheme registrations by year (and % increase compared to previous year)

Table 1: 2019 Registrations per scheme

EQA Schemes†	No. of 2019 registrations	Difference to 2018	
		No.	%
ACDB	136	+9	+7.1%
ACS	123	+21	+20.6%
CDG	69	+1	+1.5%
CWBC	36	-1	-2.7%
DPT	108	-2	-1.2%
LEFB	77	+1	+1.3%
NCSF	34	+3	+9.8%
PTU	35	+2	+6.1%
PPU	56	+2	+3.7%
QLOU	220	-1	-0.5%
QTAS	276	+8	+3.0%
QTOU	129	+2	+1.6%
SADB*	88	n/a	n/a
SAS	251	+4	+1.6%
SAU	189	-3	-1.6%
UMPS	97	-4	-4.0%
Total Registrations	**1924**	**+48**	**+7.6%**

Overall, registrations increased by 7.6% compared to 2018 (Figure 5) with ten of the sixteen EQA schemes having an increase in registrations compared to 2018 (see Table 1).

Laboratories from 63 countries registered for the 2019 EQA schemes (Figure 6). For just over half these countries (32/63) only 1-2 laboratories were registered with ERNDIM (= 44 participants; 10.8%) While just over 36% of participants (=148 participants) came from one of 4 countries (UK, France, USA and Germany).

Pilot Schemes

In 2019 there was 1 pilot scheme running, the Cognitive Amino Acids scheme which had 45 participants from 9 countries. All but 3 of these participants were European laboratories.

† = see Appendix (page 8) for full EQA scheme names;
* = 1st year as a full EQA scheme, (ran as a pilot in 2017-2018, number of pilot registrations in 2018 was 93)

ERNDIM 2019

16 EQA schemes

409 labs

63 countries

1924 registrations

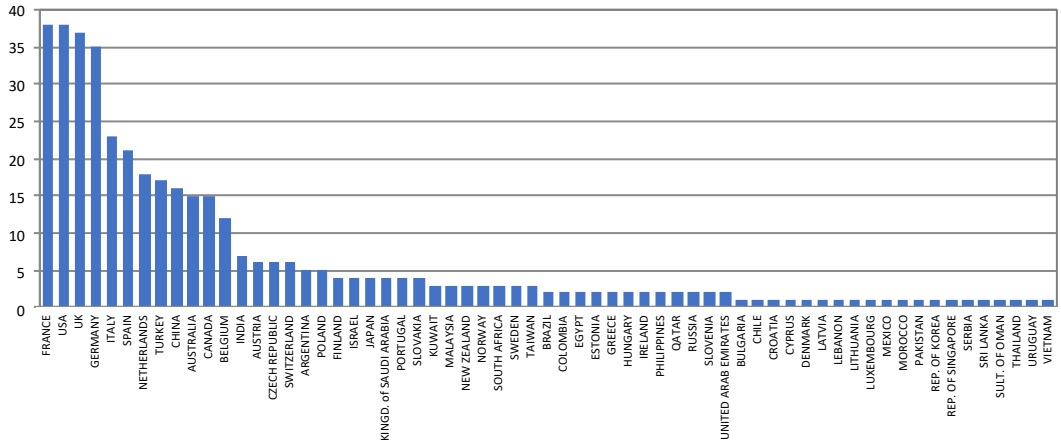

Figure 6: Number of participants per country

EQA Samples

Across all the 2019 EQA schemes we used 171 different EQA samples and 16,624 aliquots were prepared by the scheme organisers.

The main source of materials used for the 2019 EQA schemes were samples of patient urine collected by the Scientific Advisor/scheme organiser (47/171 samples).

A total of 14 samples used in the 2019 schemes were donated by participating laboratories (DPT† = 7, UMPS† = 2, QLOU† = 3, ACDB† = 2).

We would like to thank all the individual laboratories that donated patient samples without which it would be extremely difficult for us to runs the qualitative EQA schemes.

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

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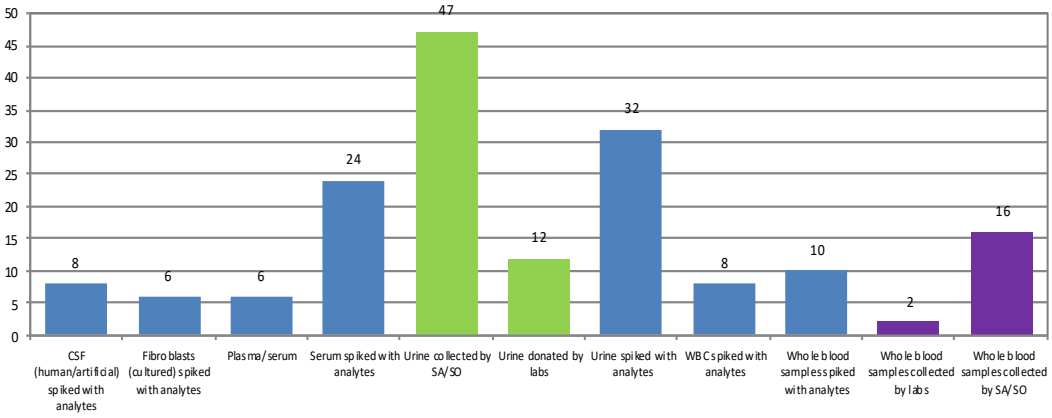

Figure 7: Materials used as EQA materials in 2019 schemes *[SA = Scientific Advisor; SO = Scheme Organiser]*

Extra sample requests

We received 104 requests for extra material for the 2019 schemes, from 66 laboratories (16.1% of all labs).

The main reasons for the requests were: the sample parcel not being received (29 requests; 7.1% of all labs); labs requesting extra material to reanalyse (19 requests; 4.6% of all labs); labs wishing to test/validate a new method* (16 requests, 3.9% of all labs); vials broken/ leaked in transit (13 requests; 3.2% of all labs); and lab errors (12 requests; 2.9% of all labs) which together made up over 85% 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 13/104 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, 24 labs (36% 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 2019 EQA samples

EQA Schemes†	No. of extra materials requests	% of labs registered
ACDB	3	2.2%
ACS	4	3.3%
CDG	3	4.5%
CWBC	12	33.3%
DPT	2	1.9%
LEFB	2	2.7%
NSCF	2	5.9%
PTU	3	8.8%
PPU	4	7.1%
QLOU	8	3.7%
QTAS	13	4.8%
QTOU	10	7.8%
SADB	4	4.7%
SAS	17	7.1%
SAU	11	6.2%
UMPS	6	6.3%
All requests	**104**	25.4%

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

Reporting Compliance Rates

Overall reporting compliance rates in 2019 were good, with 95% of results being submitted on time (Table 3), 0.6% of results were submitted after the submission deadlines (compared to 1.1% in 2018) & 4.4% of results were not submitted at all (compared to 4.0% in 2018).

The percentage of results submitted on time was 90% or above for 14/16 2019 schemes, with 8 schemes have compliance rates above 95% The lowest reporting compliance rates were for the PTU† (85.3%) and SADB† (89.0%) schemes.

Table 3: Reporting compliance rates for 2019 EQA schemes

EQA Schemes†	No of registered labs	% Results submitted on time	EQA Schemes†	No of registered labs	% Results submitted on time
ALL SCHEMES	**409**	**95.0%**	PPU	56	91.3%
ACDB	134	91.6%	QLOU	219	95.6%
ACS	122	90.2%	QTAS	269	93.9%
CDG	67	90.5%	QTOU	128	99.7%
CWBC	36	95.1%	SADB	86	89.0%
DPT	108	98.8%	SAS	236	99.0%
LEFB	73	98.4%	SAU	177	97.2%
NCSF	34	96.0%	UMPS	96	93.2%
PTU	34	85.3%			

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

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

Participations

Non- & Partial Submitters

318 labs (77.8%) participated in all their registered schemes, with an additional 68 labs (16.6%) participating in at least one scheme. 20 labs (4.9%) did not participate in any schemes (17 labs = 1-2 schemes; 2 labs = 3 schemes; 1 lab = 4 schemes). 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: 12 labs were EPs in 1 scheme each, 1 lab was an EP in 2 schemes; 1 lab was an EP in 3 schemes; and 1 lab was an EP in 6 schemes.

Any labs registered as an EP for only some of the analytes in a Quantitative scheme (= 1 lab for 2019) would not be included in Figure 8 as their performance would be assessed for the remaining analytes.

* = Labs can only apply for EP if 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

Seven labs withdrew from one to two 2019 EQA scheme each (= 9 EQA registrations, 0.5% of all registrations): 3 labs were no longer offering a service, 2 labs had technical issues, 1 lab ordered a scheme by mistake and 1 lab did not give a reason.

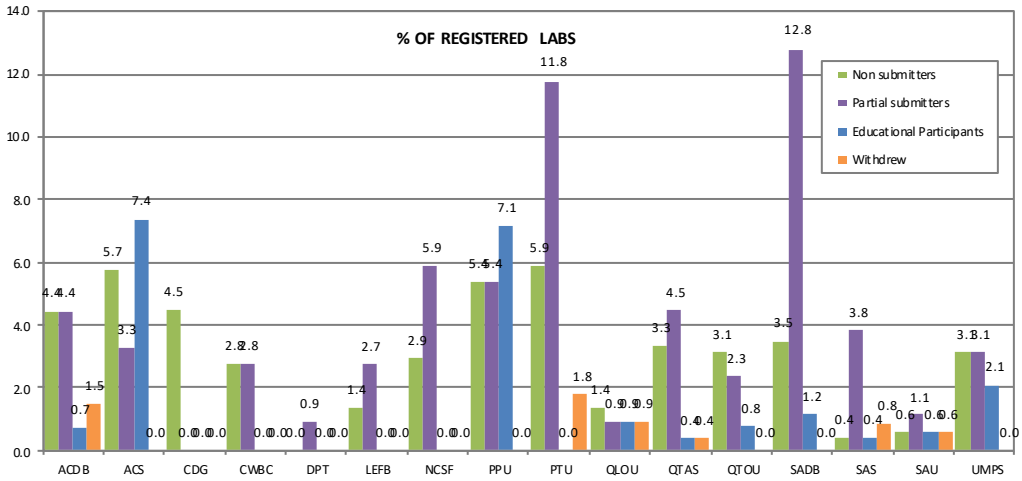

Figure 8: Non-submitters etc. per EQA scheme [† see Appendix (page 8) for full EQA scheme names and full scheme results]

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 2019 EQA schemes, 84 labs (21.8% 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.

Twelve critical errors were agreed by the SAB for the 2019 schemes, which resulted in 21 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

78.2% of participating labs (= 302/386) obtained satisfactory performance in all of the EQA schemes they participated in (compared to 78.8% in the 2018 schemes).

The level of satisfactory performance in the 2019 schemes ranged from 88.2% (CWBC†) to 96.9% (CDG†) with the overall level of satisfactory performance for all schemes being 93.6% (see Table 5, page 8) which is the same as for the 2018 schemes.

ERNDIM 2019

...78.2% of participating labs obtained satisfactory performance in all of the EQA schemes they participated in...

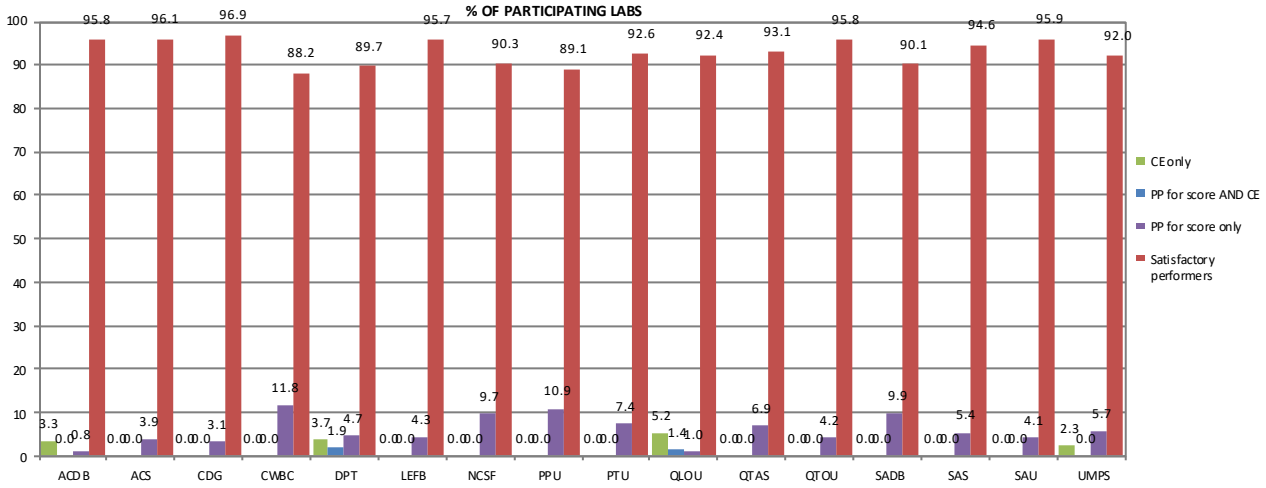

Figure 9: Performance per EQA scheme [† see Appendix (page 8) for full EQA scheme names and full scheme results]

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 2017-2019, 29 labs had PPP (= 7.5% of participating labs) compared with 25 labs (6.5% of participating labs) for 2016-18.

Nine labs with PPP for 2017-2019 also had PPP for 2016-2018. Of these 9, 6 labs had PPP in 2016-18 and 2017-19 for the same &/or additional schemes.

Two of the labs with PPP in 2017-2019 were PPP in more than one scheme (one for 2 schemes & one for 3 schemes) and the remaining 27 labs only had PPP in one EQA scheme.

Appeals

We received 2 appeals against classification as a poor performer in the 2019 schemes (one for the ACDB† scheme and one for the QLOU† scheme), compared to 3 appeals for the 2018 schemes. Both 2019 appeals were rejected.

Global Poor Performance

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

In 2019, sixteen labs had poor performance in more than one EQA scheme (= 4.1% of participating labs). This is lower than the rate of GPP in 2018 when 4.9% of participating labs had GPP (= 19/386).

Eleven of the labs with GPP in 2019 were poor performers in 2 separate EQA schemes, while the remaining 5 labs were poor performers in 3 schemes (n = 2), 4 schemes (n = 3) or 6 schemes (n = 1).

Three of the labs with GPP in 2019 (= 0.8% of participating labs) also had GPP in 2018.

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 2019 eight 'change requests' were received and 7 of these were upheld (LEFB† = 5, DPT† = 1, QLOU† = 1).

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

Appendix

Table 4: Full EQA Schemes and scheme codes

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

Table 5: Summary of all 2019 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	**135**	6	4.4%	6	4.4%	2	1.5%	1	0.7%	120	88.9%	1	0.8%	0	0.0%	4	3.3%	115	95.8%
ACS	**122**	7	5.7%	4	3.3%	0	0.0%	9	7.4%	102	83.6%	4	3.9%	-[4]	-[4]	-[4]	-[4]	98	96.1%
CDG	**67**	3	4.5%	0	0.0%	0	0.0%	0	0.0%	64	95.5%	2	3.1%	0	0.0%	0	0.0%	62	96.9%
CWBC	**36**	1	2.8%	1	2.8%	0	0.0%	0	0.0%	34	94.4%	4	11.8%	-[4]	-[4]	-[4]	-[4]	30	88.2%
DPT	**108**	0	0.0%	1	0.9%	0	0.0%	-[3]	-[3]	107	99.1%	5	4.7%	2	1.9%	4	3.7%	96	89.7%
LEFB	**73**	1	1.4%	2	2.7%	0	0.0%	0	0.0%	70	95.9%	3	4.3%	-[4]	-[4]	-[4]	-[4]	67	95.7%
NSCF	**34**	1	2.9%	2	5.9%	0	0.0%	0	0.0%	31	91.2%	3	9.7%	-[4]	-[4]	-[4]	-[4]	28	90.3%
PPU	**56**	3	5.4%	3	5.4%	0	0.0%	4	7.1%	46	82.1%	5	10.9%	-[4]	-[4]	-[4]	-[4]	41	89.1%
PTU	**34**	2	5.9%	4	11.8%	1	1.8%	0	0.0%	27	79.4%	2	7.4%	-[4]	-[4]	-[4]	-[4]	25	92.6%
QLOU	**219**	3	1.4%	2	0.9%	2	0.9%	2	0.9%	210	95.9%	2	1.0%	3	1.4%	11	5.2%	194	92.4%
QTAS	**269**	9	3.3%	12	4.5%	1	0.4%	1	0.4%	246	91.4%	17	6.9%	-[4]	-[4]	-[4]	-[4]	229	93.1%
QTOU	**128**	4	3.1%	3	2.3%	0	0.0%	1	0.8%	120	93.8%	5	4.2%	-[4]	-[4]	-[4]	-[4]	115	95.8%
SADB	**86**	3	3.5%	11	12.8%	0	0.0%	1	1.2%	71	82.6%	7	9.9%	-[4]	-[4]	-[4]	-[4]	64	90.1%
SAS	**236**	1	0.4%	9	3.8%	2	0.8%	1	0.4%	223	94.5%	12	5.4%	-[4]	-[4]	-[4]	-[4]	211	94.6%
SAU	**177**	1	0.6%	2	1.1%	1	0.6%	1	0.6%	172	97.2%	7	4.1%	-[4]	-[4]	-[4]	-[4]	165	95.9%
UMPS	**96**	3	3.1%	3	3.1%	0	0.0%	2	2.1%	88	91.7%	5	5.7%	0	0.0%	2	2.3%	81	92.0%
ALL SCHEMES	**1876**	**48**	**2.6%**	**65**	**3.5%**	**9**	**0.5%**	**23**	**1.2%**	**1731**	**92.3%**	**84**	**4.9%**	**5**	**0.3%**	**21**	**1.2%**	**1621**	**93.6%**

† = see Table 4 for full EQA scheme names; * = Percentages in these columns are a proportion of the number of participating labs rather than the number of registered labs;
[1] = Poor Performance; [2] = Critical Error; [3] = Educational Participation does not apply to the DPT scheme; [4] = CE does not apply to these schemes

ERNDIM

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"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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