ERNDIM

QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

OCTOBER 2018

Annual Report 2017

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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 first ERNDIM Annual Report. This 2017 report provides an overview of ERNDIM activities 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.

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

2017 Activities

ERNDIM continues to grow and in 2017 we saw an increase in both the number of laboratories registering with us and the number of EQA schemes that we offer.

Although the Foundation maintains a strong European basis with 61% of participating laboratories in 2017 being European, a significant number of participating laboratories now also come from Asia, North America, Oceania, South America and Africa.

Two pilot schemes were implemented in 2017. 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 although these are for rare metabolites and the assays are often undertaken by only one laboratory in any country. The 2017 pilots were: Cognitive Amino Acids and Special Assays in DBS.

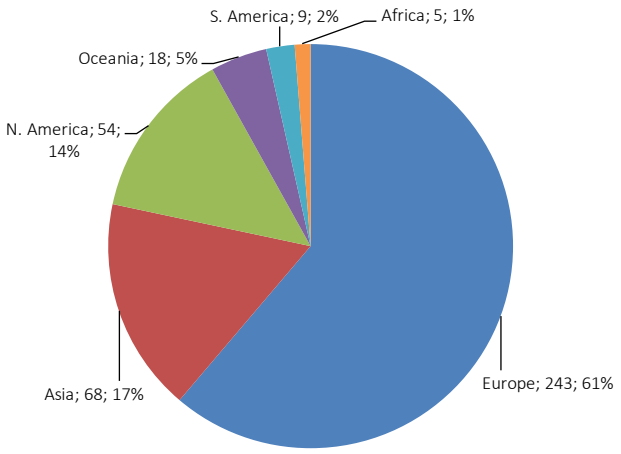

Figure 1: Number of registered laboratories in 2017, by continent

We held an extended ERNDIM Participant meeting in Manchester, United Kingdom, in November 2017. The meeting was well attended and received very positive feedback. ERNDIM was also represented at the ICIEM 2017 in Rio and the ICPLM 2017 in Durban. The presentations from the 2017 ERNDIM Participant meeting and the ERNDIM session at the ICIEM 2017 can be found on the ERNDIM website (www.erndim.org) under 'Meetings'.

ERNDIM collaborated with the Education and Training Committee (ETAC) of SSIEM to provide the 2017 Academy training course which was held in April in Lyon, France.

In August 2017, the

(Continued on page 3)

2017 Activities *(continued)*

(Continued from page 2)

Administration Office welcomed Jenny Barrett as the new Scientific Administrator in a post funded by SSIEM. The appointment of Jenny doubled the full time staff in the Administration Office! ERNDIM is extremely grateful to SSIEM for this funding which will help to speed up our slow, but steady, progress towards applying for accreditation.

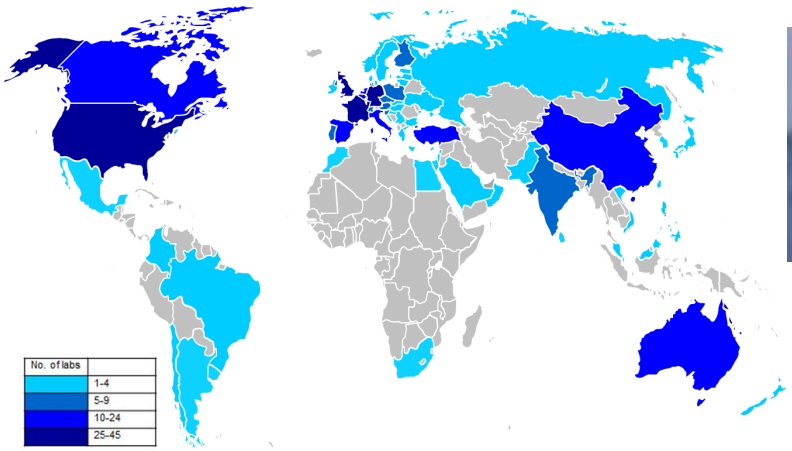

Figure 2: Number of participants per country

Finance Summary

Figures 3 and 4 are summaries of our 2017 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 in the 'Admin' in Figure 3) and website developments. The Meetings income was due to sponsorship and registration fees for the 2017 ERNDIM Participant Meeting which was held as a separate meeting in Europe due to ICIEM 2017 being held in Rio.

As would be expected our major expense is the provision of the EQA schemes, which in 2017 made up 62% of our expenditure; while Administration (staff costs, office consumables etc.) and Meetings, respectively, accounted for 23% and 12% of our expenditure.

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

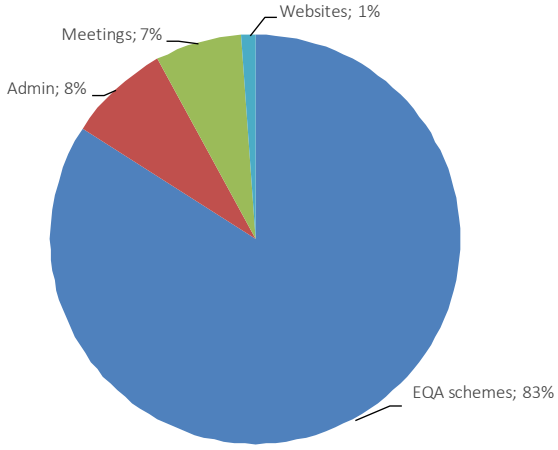

Figure 3: Summary of 2017 income

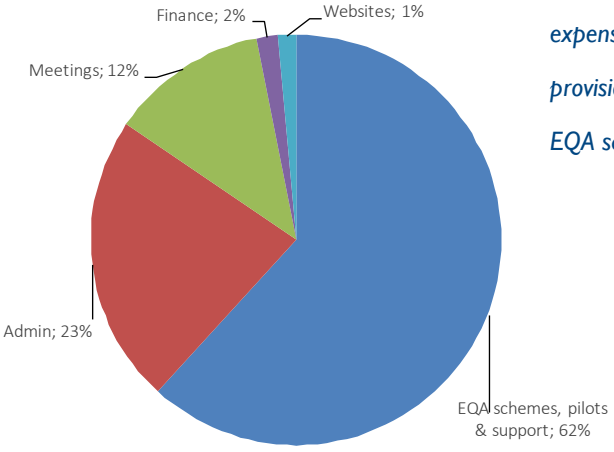

Figure 4: Summary of 2017 expenditure

2018-19 plans

EQA Calendar

Changes were made to the EQA scheme calendar to allow the scheme results to be finalised within the scheme year. The aim of this change is to allow the publication of the 2018 certificates of participation in the first quarter of the next year, which we know would be welcomed by many participants.

Sample Dispatch

The Acylcarnitines in DBS scheme moved to centralised dispatch by CSCQ in 2018.

In 2019 we are hoping to combine the dispatch of the DPT and Qualitative Organic Acids samples.

Results websites

Online submission for the Qualitative Organic Acids and Acylcarnitines in DBS schemes launched for the first 2018, submission rounds. The aim is to launch online submission for the CDG scheme later in 2018.

Pilot schemes

The Cognitive Amino Acids and Special Assays in DBS pilot schemes have both continued in 2018.

EQA Registrations

In 2017 397 laboratories, from 60 countries participated in the 15 EQA schemes that we offered, with 1752 individual scheme registrations.

ERNDIM received 621 registrations for qualitative schemes in 2017 and 1131 registrations for quantitative schemes. Overall, registrations were slightly increased compared to 2016 (Figure 5) with nine of the fifteen EQA schemes having an increase in registrations compared to 2016 (see Table 1). There were 2 new EQA schemes in 2017: the ACS† and PTU† schemes.

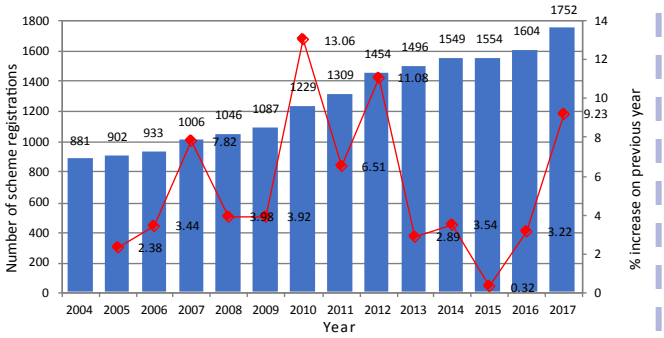

Figure 5: Total EQA scheme registrations by year (and % increase compared to previous year)

Table 1: 2017 Registrations per scheme

EQA Schemes†	No. of 2017 registrations	Difference to 2016	
		No.	%
ACDB	123	+2	+1.7%
ACS*	88	+88	-
CDG	66	+3	+4.8%
CWBC	37	-1	-2.6%
DPT	109	+1	+0.9%
LEFB	75	-3	-3.8%
NCSF	29	+3	+11.5%
PTU**	30	+30	-
PPU	51	0	0.0%
QLOU	220	+6	+2.8%
QTAS	266	0	0.0%
QTOU	126	+4	+3.3%
SAS	249	+7	+2.9%
SAU	180	+5	+2.9%
UMPS	103	+3	-3.0%
Total Registrations	**1752**	**+148**	**+9.2%**
(minus ACS & PTU)	*1634*	*+30*	*+1.9%*

Laboratories from 60 countries registered for the 2017 EQA schemes (Figure 6). For just over half these countries (31/60) only 1-2 laboratories were registered with ERNDIM. While over 38% of participants came from one of 4 countries (UK, France, USA and Germany).

Pilot Schemes

In 2017 there were 2 pilot schemes running: Cognitive Amino Acids (CAA, 32 participants from 5 countries) and Special Assays in DBS (SADB, 105 participants from 33 countries). For the CAA pilot all participants were European laboratories while for the SADB pilot 48.5% of participating laboratories were from outside of Europe.

† = see Appendix (page 8) for full EQA scheme names; * = 1st year as a full EQA scheme, (previously acyl-carnitines were part of the SAS scheme); ** = 1st year as a full EQA scheme, (ran as a pilot in 2014-2016, number of pilot registrations in 2016 was 27)

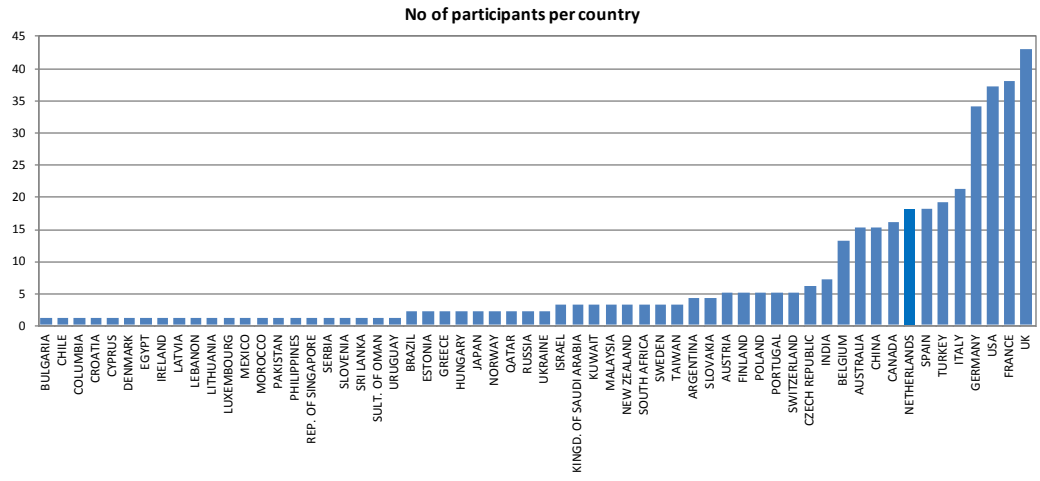

Figure 6: Number of participants per country

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15 EQA schemes

397 labs

60 countries

1752 registrations

EQA Samples

Across all the 2017 EQA schemes we used 152 different EQA samples and over 14,600 aliquots were prepared by the scheme organisers.

The main source of materials used for the 2017 EQA schemes were samples of patient urine collected by the Scientific Advisor/scheme organiser (42/152 samples).

A total of 16 samples used in the 2017 schemes were donated by participating laboratories (9 samples used in the DPT scheme and 3 samples used in the UMPS scheme) and a patient organisation (3 samples 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.

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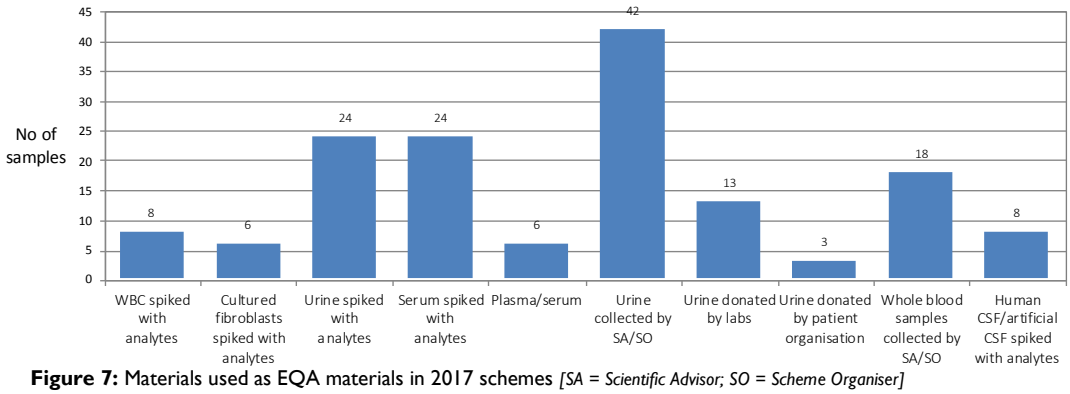

Figure 7: Materials used as EQA materials in 2017 schemes *[SA = Scientific Advisor; SO = Scheme Organiser]*

Extra sample requests

We received 72 requests for extra material for the 2017 schemes, from 54 laboratories (11.5% of all labs).

The main reasons for the requests were: the sample parcel not being received (24 requests; 6.0% of all labs); labs wishing to test/validate a new method (18 requests, 4.5% of all labs); vials broken/ leaked in transit (16 requests; 4.0% of all labs); and labs requesting extra material to reanalyse (11 requests; 2.8% of all labs), which together made up over 95% of all requests for extra material.

It should be noted that 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, 21 labs (32% of scheme participants) requested extra sample volume due to their analysis method and were sent a total of 26 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 2017 EQA samples

EQA Schemes†	No. of extra materials requests	% of labs registered
ACDB	9	7.3%
ACS	2	2.3%
CDG	0	0.0%
CWBC	8	21.1%
DPT	0	0%
LEFB	3	4.0%
NSCF	0	0.0%
PTU	2	3.9%
PPU	2	6.7%
QLOU	7	3.2%
QTAS	13	4.9%
QTOU	4	3.1%
SAS	10	4.0%
SAU	7	4.1%
UMPS	5	4.8%
All requests	**72**	18.1%

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

Reporting Compliance Rates

Overall reporting compliance rates in 2017 were good, with 94% of results being submitted on time (Table 3), 1.7% of results were submitted after the submission deadlines (compared to 1.2% in 2016) & 4.4% of results were not submitted at all (compared to 5.9% in 2016).

The percentage of results submitted on time was 90% or above for 13 schemes. The lowest reporting compliance rates were for the ACDB† (82.4%) and CDG† (84.6%) schemes, which were the only schemes in 2017 which did not have online submission available.

Table 3: Reporting compliance rates for 2017 EQA schemes

EQA Schemes†	No of registered labs	% Results submitted on time	EQA Schemes†	No of registered labs	% Results submitted on time
ALL SCHEMES	**397**	**94.0%**	PTU	30	90.0%
ACDB	122	82.4%	PPU	51	94.4%
ACS	88	92.0%	QLOU	218	95.9%
CDG	65	84.6%	QTAS	261	93.5%
CWBC	37	92.6%	QTOU	125	93.5%
DPT	109	99.1%	SAS	237	95.6%
LEFB	72	93.5%	SAU	172	97.5%
NCSF	29	91.8%	UMPS	102	96.6%

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

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...94% of results were submitted on time...

Participations

Non- & Partial Submitters:

320 labs (80.9%) participated in all the schemes they registered for, with an additional 67 labs (16.9%) labs participating in at least one scheme. While 9 labs (2.3%) did not participate in any schemes they registered for (7 labs = 1 schemes; 1 lab = 2 schemes; 1 lab = 3 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

10 labs registered as Educational Participants* (EP). 7 labs were EPs in 1 scheme each, 2 labs were EPs in 2 schemes and 1 lab was an EP in 3 schemes.

Labs that registered as an EP for only some of the analytes in a Quantitative scheme (= 4 labs) are not included in Figure 8 as their performance was assessed for the remaining analytes.

Withdrawn labs

Six labs withdrew from one or more 2017 EQA schemes (= 8 EQA registrations, 0.5% of all registrations): 3 labs were no longer offering a service, 1 lab had technical issues, and 2 labs did not receive their ACDB† samples parcels so were allowed to withdraw from the scheme.

* = Labs can only apply for Educational Participation 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,

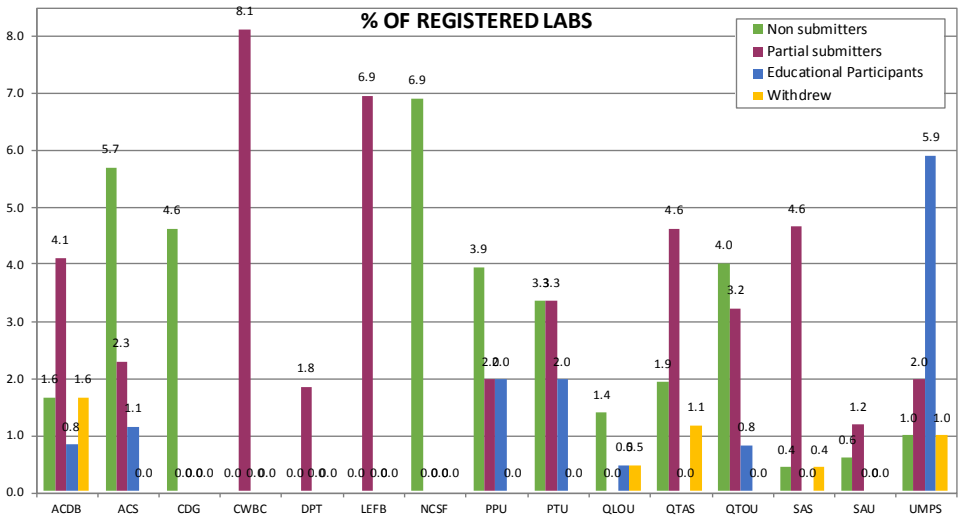

Figure 8: Non-submitters etc. per EQA scheme [† see Appendix (page 8) for full EQA scheme names and full scheme results]

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 387 labs that participated in one or more 2017 EQA schemes, 66 labs (17.1% 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.

Eight critical errors were agreed by the SAB for the 2017 schemes, which resulted in 9 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

82.9% of participating labs (= 321/387) obtained satisfactory performance in all of the EQA schemes they participated in (compared to 80.8% in the 2016 schemes).

The level of satisfactory performance in the 2017 schemes ranged from 85.7% (PTU†) to 98.5% (LEFB†) with the overall level of satisfactory performance for all schemes being 95.3% (see Table 5, page 8) compared to 93.9% in 2016.

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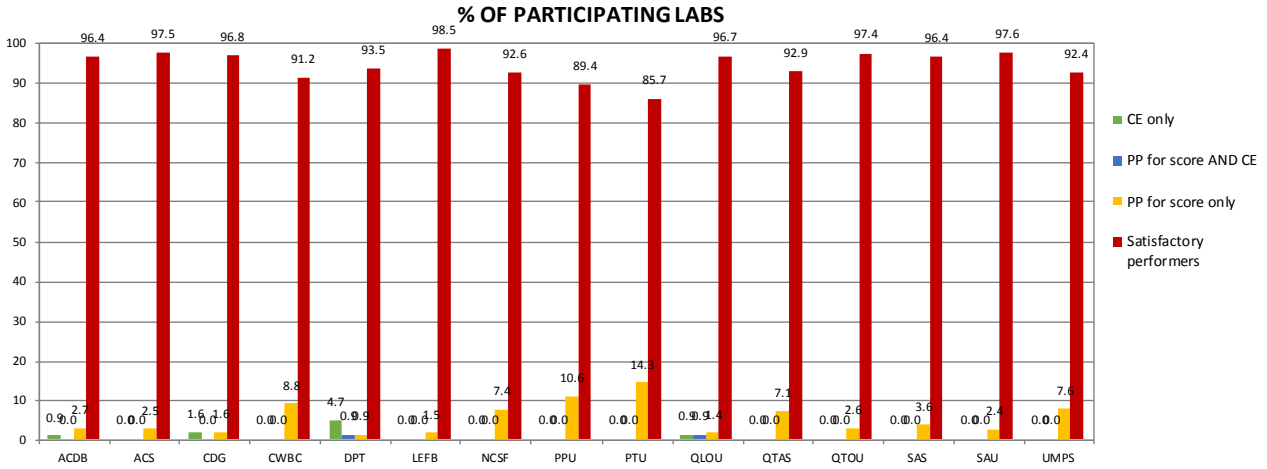

Figure 9: Performance per EQA scheme [† see Appendix (page 8) for full EQA scheme names and full scheme results]

Global Poor Performance

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

In 2017, ten labs had poor performance in more than one EQA scheme (= 2.6% of participating labs). This is lower than the rate of GPP in 2016 when 3.8% of participating labs had GPP (= 14/372).

The 10 labs with GPP in 2017 were all poor performers in 2 separate EQA schemes.

Persistent Poor Performance

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

For the period 2015-2017, 20 labs were classed as persistent poor performers (= 5.2% of participating labs) compared with 19 labs (5.1% of participating labs) for the period 2014-16.

Fifteen labs with PPP for 2015-2017 also had PPP for 2014-2016. Of these 15, 8 labs had poor performance in both 2015 & 2016 but were good performers in the 2017 schemes.

Two of the labs with PPP in 2015-2017 were PPP in 2 separate EQA schemes and the remaining 18 labs only had PPP in one EQA scheme.

Appeals

We received 7 appeals against classification as a poor performer in the 2017 schemes, compared to 1 appeal for the 2016. schemes.

Three 2017 appeals were upheld (LEFB† = 2; QTAS† = 1) and the labs' performances were updated. The outcomes of the successful appeals are included in the performance results in Figure 9 & Table 5 (page 8).

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 2017, 8 'change requests' were received. Seven of these were upheld, all of which related to the CDG† or ACDB† Annual reports.

Appendix

Table 4: Full EQA Schemes and scheme codes

Scheme Code	EQA Scheme Name
ACDB	Acylcarnitines in DBS
ACS	Acylcarnitines in serum
CDG	Congenital Disorders of Glycosylation (plasma/serum)
CWBC	Cystine in WBC
DPT	Diagnostic Proficiency Testing (urine)
LEFB	Lysosomal Enzymes in fibroblasts
NSCF	Neurotransmitters in 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 2017 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	**122**	2	*1.6%*	5	*4.1%*	2	*1.6%*	1	*0.8%*	**112**	*91.8%*	3	*2.7%*	0	*0.0%*	1	*0.9%*	108	*96.4%*
ACS	**88**	5	*5.7%*	2	*2.3%*	0	*0.0%*	1	*1.1%*	**80**	*90.9%*	2	*2.5%*	-[4]	-[4]	-[4]	-[4]	78	*97.5%*
CDG	**65**	3	*4.6%*	0	*0.0%*	0	*0.0%*	0	*0.0%*	**62**	*95.4%*	1	*1.6%*	0	*0.0%*	1	*1.6%*	60	*96.8%*
CWBC	**37**	0	*0.0%*	3	*8.1%*	0	*0.0%*	0	*0.0%*	**34**	*91.9%*	3	*8.8%*	0	*0.0%*	0	*0.0%*	31	*91.2%*
DPT	**109**	0	*0.0%*	2	*1.8%*	0	*0.0%*	-[3]	-[3]	**107**	*98.2%*	1	*0.9%*	1	*0.9%*	5	*4.7%*	100	*93.5%*
LEFB	**72**	0	*0.0%*	5	*6.9%*	0	*0.0%*	0	*0.0%*	**67**	*93.1%*	1	*1.5%*	-[4]	-[4]	-[4]	-[4]	66	*98.5%*
NSCF	**29**	2	*6.9%*	0	*0.0%*	0	*0.0%*	0	*0.0%*	**27**	*93.1%*	2	*7.4%*	-[4]	-[4]	-[4]	-[4]	25	*92.6%*
PPU	**51**	2	*3.9%*	1	*2.0%*	0	*0.0%*	1	*2.0%*	**47**	*92.2%*	5	*10.6%*	-[4]	-[4]	-[4]	-[4]	42	*89.4%*
PTU	**30**	1	*3.3%*	1	*3.3%*	0	*0.0%*	0	*0.0%*	**28**	*93.3%*	4	*14.3%*	0	*0.0%*	0	*0.0%*	24	*85.7%*
QLOU	**218**	3	*1.4%*	0	*0.0%*	1	*0.5%*	1	*0.5%*	**213**	*97.7%*	3	*1.4%*	2	*0.9%*	2	*0.9%*	206	*96.7%*
QTAS	**261**	5	*1.9%*	12	*4.6%*	3	*1.1%*	0	*0.0%*	**241**	*92.3%*	17	*7.1%*	-[4]	-[4]	-[4]	-[4]	224	*92.9%*
QTOU	**125**	5	*4.0%*	4	*3.2%*	0	*0.0%*	1	*0.8%*	**115**	*92.0%*	3	*2.6%*	-[4]	-[4]	-[4]	-[4]	112	*97.4%*
SAS	**237**	1	*0.4%*	11	*4.6%*	1	*0.4%*	0	*0.0%*	**224**	*94.5%*	8	*3.6%*	-[4]	-[4]	-[4]	-[4]	216	*96.4%*
SAU	**172**	1	*0.6%*	2	*1.2%*	0	*0.0%*	0	*0.0%*	**169**	*98.3%*	4	*2.4%*	-[4]	-[4]	-[4]	-[4]	165	*97.6%*
UMPS	**102**	1	*1.0%*	2	*2.0%*	1	*1.0%*	6	*5.9%*	**92**	*90.2%*	7	*7.6%*	0	*0.0%*	0	*0.0%*	85	*92.4%*
ALL SCHEMES	**1718**	**31**	***1.8%***	**50**	***2.9%***	**8**	***0.5%***	**11**	***0.6%***	**1618**	***94.2%***	**64**	***4.0%***	**3**	***0.2%***	**9**	***0.6%***	**1542**	***95.3%***

† = 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

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QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

"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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