ERNDIM

QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

2014 Participant Survey Report:

[2013 scheme year]

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European Research Network for evaluation and improvement of screening, Diagnosis and treatment of Inherited disorders of Metabolism

1. Introduction

- Participants (565 contacts from 362 centres) were sent the link to the ERNDIM Participant Survey on the Survey Monkey website (www.surveymonkey.com) on 9th May 2014. We asked participants to answer questions relating to the 2013 EQA schemes. The closing date for the survey was 30th June 2014.

2. Summary

- Thank you to everyone who took the time to complete this survey. This report is a summary of all the responses we received. The results from the survey will help us to continue to improve the quality and efficiency of the ERNDIM EQA schemes.
- The survey has highlighted areas where we need to improve such as the lack of website reporting for all of the qualitative schemes and low sample volume for some of the qualitative schemes. However it is also gratifying to see that the majority of respondents believe that the quality of service we offer is getting better and we will continue to make further improvements to the service that we offer in the future.
- We are especially pleased that so many of you took the time to complete the survey and to send comments on the schemes. We hope you find the summary on pages 8 - 10, where we answer some of your comments, interesting and we would welcome any other comments or suggestions for improvements.

3. Survey Responses

- 201/565 contacts from 188/362 centres in 49 countries responded to the survey. The response rate by centre was 51.9% (compared to 43.9% in the last survey) and the individual response rate was 35.6% (compared to 34.8% in the last survey).

Question 1: Please rate the following aspects for each of the ERNDIM quality assurance schemes that you subscribe to

- Number of centre responses = 188 centres (= 100% of all responses).
- The response rate for each EQA scheme is shown in Figure 1 and Table 2. For the individual schemes the highest response rate was for Diagnostic Proficiency Schemes (64% of scheme participants) and the lowest was for Acyl carnitines (45% of scheme participants). The response rate for all the schemes is higher than in 2013 (Figure 1).

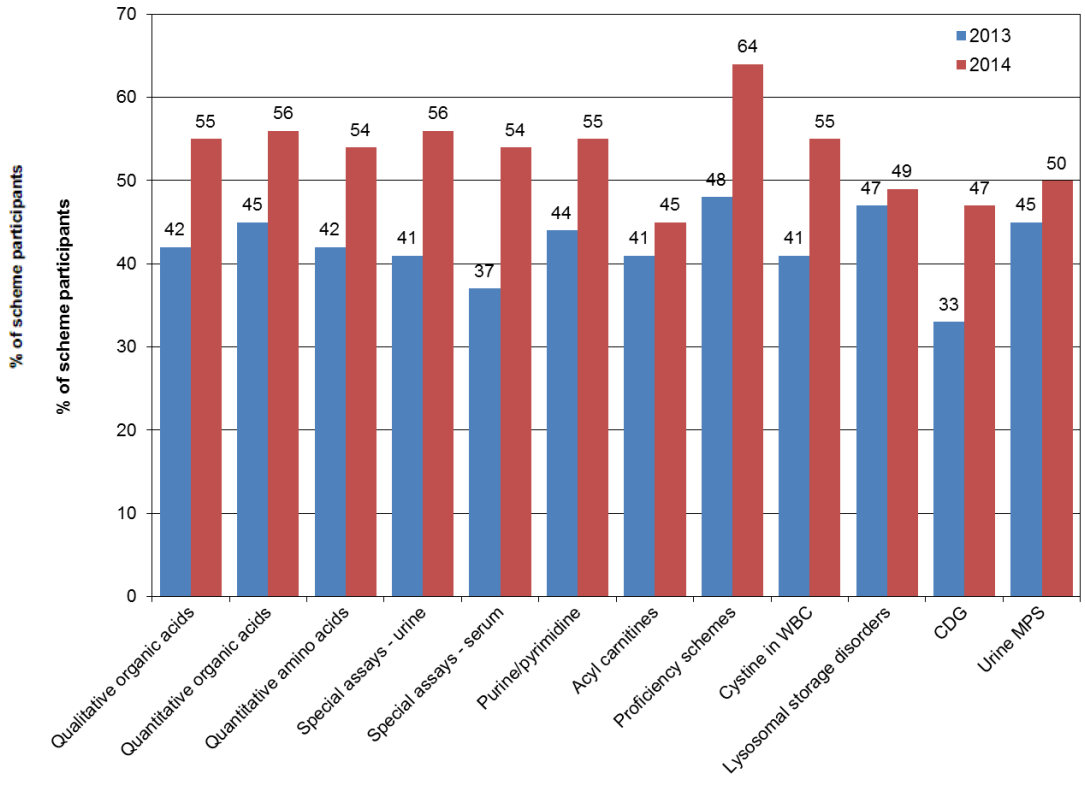


Figure 1. Survey responses per EQA scheme (Question 1) as a percentage of the EQA scheme participants

- Participants were asked to rate the following aspects of each scheme:
  1. Frequency of samples
  2. Sample volume
  3. Appropriateness of analyte concentration
  4. Adequacy of the report
  5. Website display
  6. Usefulness of the annual report
  7. Value for money
  8. Billing arrangements
- Each of the aspects of individual EQA schemes was rated according to the following scoring system:
  1 = Excellent 2 = Good 3 = Poor 4 = Very poor
- Scores ≤ 1.5 are highlighted in blue and scores ≥ 2.0 are highlighted in red.

Table 1. Average scores per scheme (Question 1)

	Average Scores						
EQA Scheme	**2014**	**2013**	**2012**	**2011**	**2007**	**2004**	**2001**
All schemes	**1.7**	**1.7**	**1.7**	**1.8**	**1.7**	**2.0**	**2.0**
Qualitative organic acids	1.7	1.7	1.7	1.7	1.6	2.0	1.9
Quantitative organic acids	1.7	1.7	1.7	1.9	1.7	1.9	2.1
Quantitative amino acids	1.7	1.7	1.7	1.8	1.7	1.9	2.0
Special assays - urine	1.7	1.7	1.7	1.7	1.8	1.9	2.1
Special assays - serum	1.7	1.7	1.7	1.8	1.7	1.8	2.0
Purine/pyrimidine	1.7	1.7	1.7	1.9	1.6	1.8	2.1
Acyl carnitines	2.0	1.9	1.9	2.0	2.0	2.3	-
Proficiency schemes	1.7	1.7	1.8	1.8	1.7	2.0	2.0
Cystine in white blood cells	1.8	1.6	1.7	1.6	1.4	-	-
Lysosomal storage disorders	2.0	1.9	2.0	2.1	-	-	-
Congenital disorders of glycosylation	2.0	1.9	1.8	1.9	-	-	-
Urine Mucopolysaccharides	1.8	1.8	1.8	-	-	-	-

- The overall score for all aspects of all schemes was 1.7, the same as in 2013 and 2012. Eight of the EQA schemes had the same score as last year while the remaining four schemes had worse scores than last year.
- The best scoring schemes were Qualitative Organic Acids, Quantitative Organic Acids, Quantitative Amino Acids, Special Assays in serum and urine, Purines and Pyrimidines and the DPT scheme which all scored 1.7. The worst scoring schemes were CDG, LSDs and Acylcarnitines which all scored 2.0.
- The average scores per scheme since 2001 are shown in Table 1 and Figure 2, and show a general trend of improvement.
- The score for 7 out of the 8 of the individual aspects have improved or stayed the same since 2013, with only 'Usefulness of the annual report' having a worse score in 2014 than in 2013 (1.7 in 2014 compared to 1.6 in 2013).
- The worst scoring aspects were 'Sample volume', 'Appropriateness of analyte concentration', 'Website display', 'Value for money' and 'Billing arrangements' which all scored 1.8; with the best scoring aspect being 'Frequency of samples' (1.6).
- The score for 'Sample volume' has remained the same as in 2013 (1.8) however four schemes still scored 2.0 or more (DPT = 2.0, CDG = 2.6; Urine MPS = 2.1; LSDs = 2.3) for this aspect. The 'Sample volume' score for CDG was the worst score in the survey.
- The best scores of the whole survey (all 1.5) were for 'Frequency of samples' (Qual Organic Acids, Specials Assays in urine & Purines and pyrimidines), 'Sample volume' (Quant Organic Acids and Purines and pyrimidines), 'Adequacy of the report (Qual Organic Acids & DPT) and 'Usefulness of the Annual Report' (DPT).
- The most improved scores of the whole survey were for Lysosomal Enzymes (value for money, 1.9 compared to 2.1 in 2013), Qualitative Organic Acids (website display, 1.9 compared to 2.1 in 2013) and Urine MPS (sample volume, 2.1 compared to 2.3).

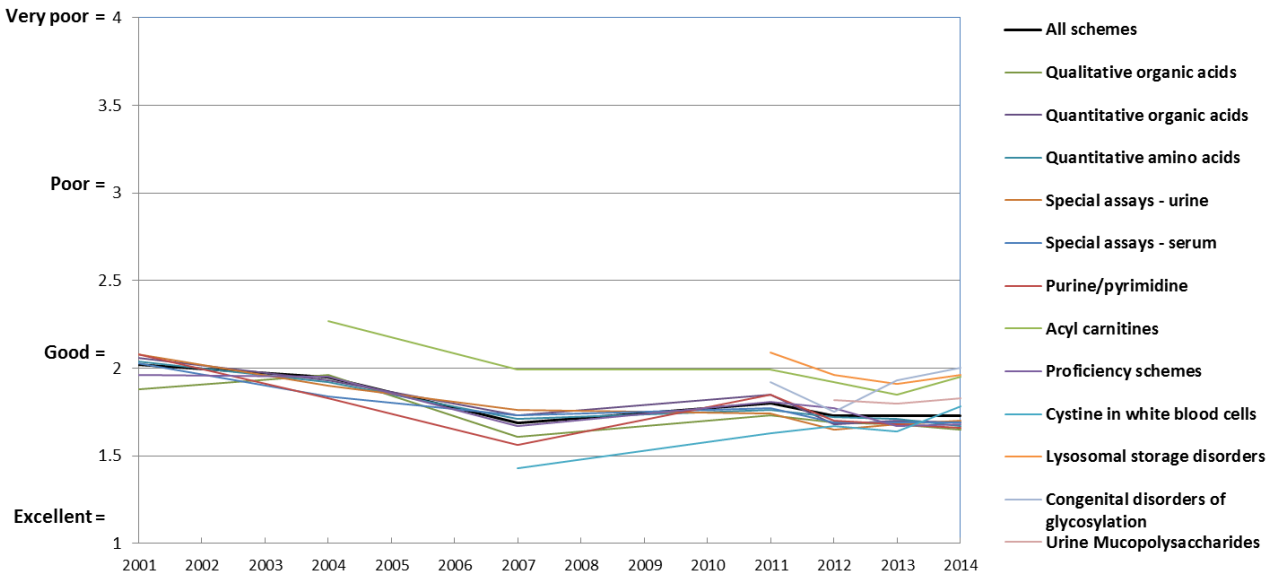


Figure 2. Average score per EQA scheme (Question 1)

Table 2: Average scores per aspect of each scheme (Question 1)

Scheme Aspects	Frequency of samples	Sample volume	Appropriateness of analyte concentration	Adequacy of the report	Website display	Usefulness of the annual report	Value for money	Billing arrangements	Average per scheme	No. of responses (% of scheme participants)
Qual. organic acids	1.5	1.7	1.6	1.5	1.9	1.6	1.7	1.8	**1.7**	104 (55.0%)
Quant. organic acids	1.6	1.5	1.8	1.7	1.7	1.8	1.8	1.7	**1.7**	62 (55.9%)
Quant. amino acids	1.6	1.6	1.7	1.7	1.7	1.7	1.8	1.7	**1.7**	136 (53.8%)
Special assays - urine	1.5	1.8	1.8	1.6	1.7	1.7	1.8	1.7	**1.7**	93 (56.0%)
Special assays - serum	1.6	1.6	1.8	1.6	1.7	1.7	1.8	1.7	**1.7**	114 (54.3%)
Purines/pyrimidines	1.5	1.5	1.9	1.6	1.7	1.7	1.8	1.7	**1.7**	31 (55.4%)
Acyl carnitines	2.2	1.8	1.8	2.0	2.2	1.9	2.0	1.8	**2.0**	55 (45.1%)
Proficiency schemes	1.6	2.0	1.7	1.5	1.8	1.5	1.7	1.7	**1.7**	66 (63.5%)
Cystine in WBC	1.7	1.9	1.9	1.7	1.8	1.6	1.7	1.9	**1.8**	18 (54.5%)
LSD	1.7	2.3	2.0	2.0	1.9	2.1	1.9	1.9	**2.0**	35 (48.6%)
CDG	1.8	2.6	1.9	1.9	2.1	1.9	2.0	1.9	**2.0**	28 (46.7%)
Urine MPS	1.7	2.1	1.8	1.8	1.9	1.8	1.8	1.8	**1.8**	52 (50.0%)
Average for all schemes	**1.6**	**1.8**	**1.8**	**1.7**	**1.8**	**1.7**	**1.8**	**1.8**		

Question 2: Do you have any other remarks, comments or suggestions for improvements in Quantitative Schemes?

- Number of individual responses = 69 (= 34% of all responses)
- These comments are summarised with the comments made in response to Q13 on pages 8 - 10.

Questions 3 to 8: Analytes in Quantitative Schemes

- A total of 77/201 individuals (38%) made suggestions for analytes to be added to or removed from the Quantitative schemes.
- Where possible we do try to incorporate suggestions for additional analytes and but unfortunately this is not always possible. A summary of the suggestions for analytes to added or removed, with some responses from ERNDIM, is below.

Q.3: Quantitative amino acids (38 responses, 19% of all respondents)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 20		Total suggested = 9	
Analytes with >1 response		**Analytes with >1 response**	
arginosuccinic acid (ASA)	n = 10	sarcosine	n = 8
sulfocysteine	n = 5	3-methylhistidine	n = 4
tryptophan	n = 5	saccharopine	n = 4
alloisoleucine	n = 3	1-methylhistidine,	n = 3
Beta- alanine	n = 2	pipecolic acid	n = 3
cystathionine	n = 2	Tryptophan (TRP)	n = 2
Gamma-Amino Butyric Acid (GABA)	n = 2		
homocystine	n = 2		
Phenylethylamine (PEA)	n = 2		
phosphoetanolamine	n = 2		

Q.4: Quantitative organic acids (21 responses, 10% of all respondents)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 66*		Total suggested = 1	
Analytes with >1 response		**All Analytes suggested**	
3-methylglutaconic acid	n = 5	3-hydroxyisobutyric acid	n = 1
3-OH-glutaric acid	n = 4		
3-hydroxybutyric acid	n = 3		
3-methylglutaconic	n = 3		
isovalerylglycine	n = 3		
Suberylglycine	n = 3		
3-methylcrotonylglycine	n = 2		
butyrylglycine	n = 2		
glutaconic acid	n = 2		
lactic acid	n = 2		
malonic	n = 2		
methylsuccinic acid	n = 2		
oxalic acid	n = 2		

***** = one respondent suggested 39 different analytes to be added

Q.5: Purines & pyrimidines (6 responses, 3% of all respondents)

Suggested Analytes to be added		Suggested Analytes to be removed
Total suggested = 4		Total suggested = 0
Analytes with >1 response		**All Analytes suggested**
SAICAR	n = 5	NONE
Succinyladenosine (SAdo)	n = 4	
2,8-dihydroxyadenine;	n = 2	

ERNDIM Response:

- The addition of 2,8-dihydroxyadenine was attempted a few years ago, but proved to be impossible due to its insolubility. The availability of both succinyladenosine (SAdo) and SAICAriboside (SAICAR) is very limited and unfortunately the addition of these compounds is financially not feasible.

Q.6: Lysosomal Enzymes (12 responses, 6% of all respondents)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 13		Total suggested = 6	
Analytes with >1 response		**All Analytes suggested**	
Acid esterase (Wolman disease)	n = 3	Heparan sulphamidase	n = 2
arylsulfatase B**	n = 3	arylsuphatase 37ºC	n = 1
MPS Type IV	n = 2	Beta hex A	n = 1
MPS VI	n = 2	galactocerebrosidase	n = 1
N-acetylgalactosamine-6-sulfatase	n = 2	MPS IIIA	n = 1
		MPS IVA	n = 1

** = one respondent suggested arylsulfatase 0 ºC

Q.7: Special assays – serum (30 responses, 14% of all respondents)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 27		Total suggested = 1	
Analytes with >1 response		**All Analytes suggested**	
Non-esterified fatty acids (NEFA)	n = 5	Free fatty acids	n = 1
Biotinidase	n = 4		
Free Fatty Acids (FFA)	n = 4		
more acylcarnitines - C3, C5, C14:1	n = 2		
total carnitine	n = 2		

ERNDIM Response:

- The addition C14:1 carnitine has already been studied but the analyte is not yet commercially available.
- The feasibility of adding C3 and C5 carnitines will be studied by the next SAB meeting.
- Biotinidase and Total carnitine are not commercial available. However an EQA scheme for Biotinidase in dried blood spots is available from the Newborn Screening Quality Assurance Program, Atlanta (www.cdc.gov/nsqap).

Q.8: Special assays – urine (14 responses, 7% of all respondents)

Suggested Analytes to be added		Suggested Analytes to be removed
Total suggested = 27		Total suggested = 0
Analytes with >1 response		**All Analytes suggested**
arabitol	n = 2	NONE
Delta 4 aminolevulinic acid	n = 2	
fructose	n = 2	
sorbitol	n = 2	
Vanillylmandelic acid (VMA)	n = 2	

ERNDIM Response:

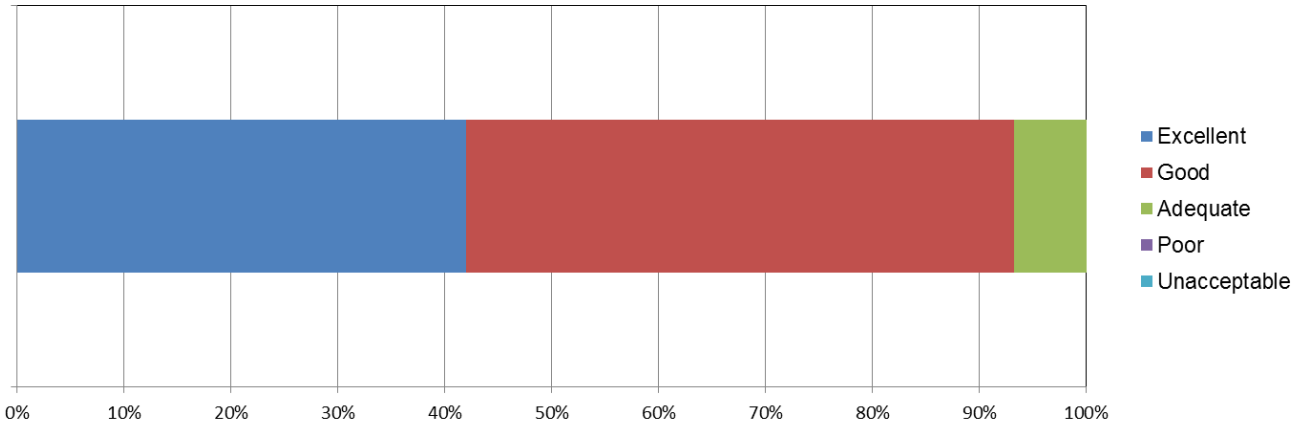
- The feasibility of the addition of delta-aminolevulinic acid, vanillylmandelic acid (VMA), arabitol and carbohydrates (fructose, sorbitol) will be discussed by the next SAB meeting

Questions 9 to 12: Comments on the overall performance of ERNDIM

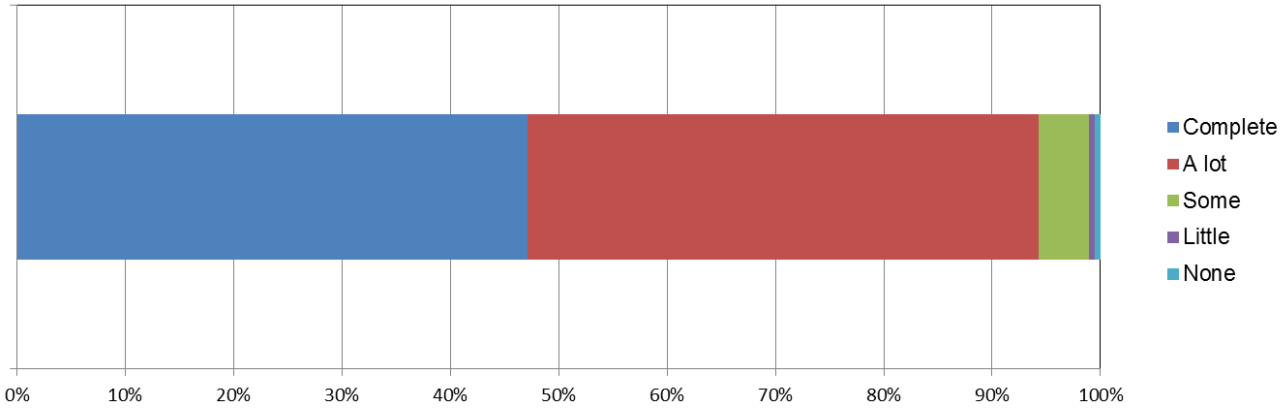
- This aim of this section is to assess participants' perception of the overall performance of ERNDIM.
- In summary, 93% of respondents rated the quality of services provided by ERNDIM as 'excellent' or 'good'; with 94% of respondents having 'complete' or 'a lot' of confidence that ERNDIM can deliver the service required by participants.
- 72% of respondents agreed that overall ERNDIM's performance is 'getting better' or 'getting much better'; with 96% of respondents stating that it was 'certain' or 'very likely' that they would use ERNDIM services in the future.

Q.9: Overall, how do you rate the quality of products and services we provide?

(193 individual responses, 96% of all responses)

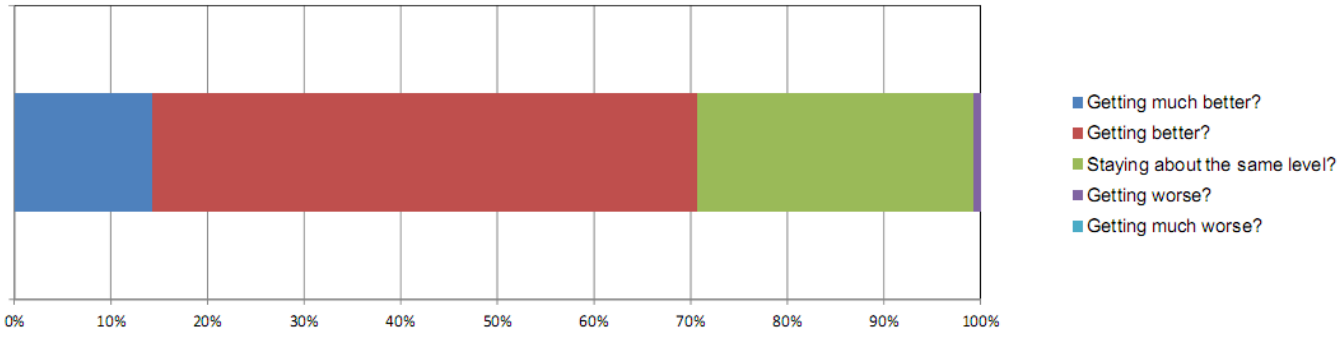


Q.10: What level of confidence do you have in us to deliver the products and services that you require? (193 individual responses, 96% of all responses)

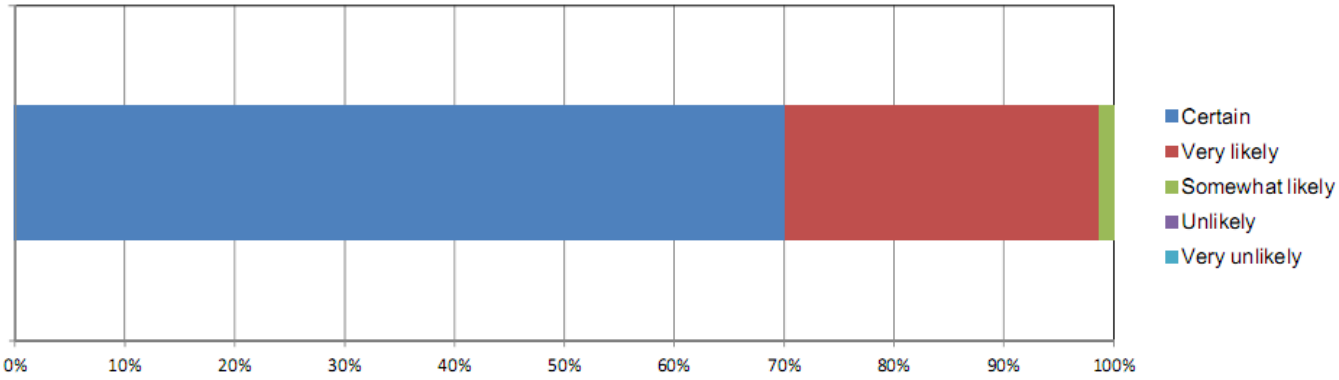


Q.11: Overall, is our performance...

(189 individual responses, 94% of all responses)



Q.12: Based on our performance, how likely is it that you will use us in the future?
(194 individual responses, 97% of all responses)



Question 13: Do you have any other remarks, comments or suggestions for how we could improve the services we provide?

- Number of individual responses = 37 (= 18% of all responses)
- These comments are summarised below with the comments made in response to Q2.

Questions 2 & 13: Remarks, comments or suggestions for improvements

- Total number of responses was 106 from 82 individuals (= 41% of all responses)
- There were a large number of comments and suggestions for improvement. Below is a summary of some of the most frequent comments with responses from ERNDIM.

Participant Comment	ERNDIM Response
1. General Comments	
1.1. There were a number of comments on the frequency of submission deadlines – some wanting more frequent (up to 12 or 24 per year) and some wanting less frequent deadlines (4 per year).	• There are no plans at the moment to alter the number or frequency of submission deadlines for the EQA schemes.
1.2. Increased number of sample distributions for some of the qualitative schemes.	• For the qualitative schemes there are often problems sourcing suitable clinical material of a sufficient volume to use as the EQA materials. For most of these schemes the Scientific Advisor sources all the EQA materials themselves and we would welcome offers to donate suitable samples from participating centres. Please contact the Administration office if you would be interested in donating a sample.
1.3. Lack of website reporting for all the qualitative schemes.	• ERNDIM's long term aim is to move all of the qualitative schemes to the CSCQ Results website. The Urine MPS scheme moved to website reporting in 2014 and it planned that the CDG scheme will move to website reporting in 2015 with the other qualitative schemes moving over gradually in the next few years.
1.4. Faster access to the annual reports.	• The final results for each scheme are ratified by the Scientific Advisory Board at its Spring meeting so all annual reports are published as soon as possible after that meeting.
1.5. Certificates of Participation to be sent earlier.	• In the past the Certificates have sometimes been published in August which, we agree, is too late. In 2013 and 2014 the certificates were published in July. This year we're hoping to publish them in June and we're working towards publishing them earlier next year.
2. EQA Schemes	
2.1. Acylcarnitines in DBS	
• Delivery of samples is delayed	• The EQA materials for the scheme are real clinical samples and delays in sample dispatch are due to difficulties obtaining suitable samples.

• Results for the first round should be available before the submission deadline for the second round is due.	• We are working towards online submission of results for this scheme which will make it easier for the Scientific Advisor to evaluate the results and send out reports earlier.

2.2. DPT scheme

• Comments from some participants that the DPT results website is not sufficiently user-friendly.	• The manuals for website reporting will be sent to participants again in 2015.
• DPT samples have poor clinical information.	• As the DPT samples are real clinical samples the clinical information provided with them reflects the real life situation.

2.2. CDG scheme

• The reports should be available sooner or if that is not possible, at least the 'answers' should be sent out in a timely fashion.	• For the 2014 scheme the Scientific Advisor sent the diagnoses for the EQA materials to participants in November instead of waiting until the Annual Report has been approved by the SAB this Spring. The planned on-line submission of results will make it easier for the Scientific Advisor to evaluate the results and send out reports earlier.

2.3. Lysosomal Enzymes

• Improve the annual report.	• The Scientific Advisor and the Scheme Organiser are looking at ways to improve the annual report.

2.4. Qualitative Organic Acids

• Analyte concentrations in the samples are too low for diagnosis. The real patient samples are generally different then these samples.	• All samples are from real patients - some are taken outside of crisis but the scheme organisers feel it is important for participants not to miss the subtle/mild phenotypes.
• The inclusion of some complicated samples would promote learning and would be more realistic (e.g. concurrent ketosis, patient under treatment etc). These could be included as "educational" samples with similar report commitments as "ordinary" samples but without the inclusion of their score in the overall result.	• Some complicated samples were included in the 2014 scheme.
• The EQA samples included are very often 'classic' cases with extreme elevations, which pose little challenge to identify. Inclusion of more subtle variant cases would be valuable educationally.	• We attempt to distribute both complex and classical samples to meet the requirements of all participants.
• Online submission of results.	• We are working on website submission of results and hope to implement this in 2016/17.

2.5. Quantitative Amino Acids

• A report that can be down loaded with one keystroke from the results website	• This has been implemented for all the quantitative schemes

2.6. Special Assays in Serum

• Some participants complained that NEFA had been removed from the scheme.	• Although NEFA was in the list of analytes in SAS from 2010 to 2013, it was not an added analyte and was not scored during that period so did not appear in the Annual Reports. We will discuss in the next SAB meeting whether to include NEFA again in the 2015 program and will try to change the software so that it will be scored in the annual report.
• Lower concentration of some analytes (e.g. carnitine, homocysteine) would be much more interesting and helpful.	• Concentrations of these analytes in the low-normal range are not technically possible since the matrix is pooled human serum, where concentrations are already within the control range.
• The concentrations of methylmalonic acid are geared too much towards the high end	• The concentration of MMA has already been decreased in the 2014 scheme.

2.7. Special Assays in Urine

• Please standardise the units for creatinine as it is used in many of the schemes.	• This has been done.

• The concentrations of succinylacetone are geared too much towards the high end	• The concentration of succinylacetone has already been decreased in the 2014 scheme.
2.8. Urine MPS	
• Some participants commented that the MPS results website is not sufficiently user-friendly.	• The manuals for website reporting will be sent to participants again in 2015.
• Sample volume is inadequate.	• The reason for sending 5 ml samples is the limited sample availability (size and number). Hence, sample volumes can't be larger than 5 ml. We prepare 120 aliquots of 5 ml, which requires 600 ml of urine. Larger aliquots would require proportionally larger stock samples. Since the Urine MPS scheme uses authentic human urine samples, we depend on participants to donate these but only a very small number of participants do send samples. A possible option could be to send 2 vials per sample upon request however this would be possible only for 5 - 10 participants. We urge participants to donate samples and we would welcome offers to donate suitable samples. Please contact the Administration office if you would be interested in donating a sample.
• It would be better if the results and reports from urine mucopolysaccharides were at the same website.	• The Scientific Advisor will discuss with the scheme organiser whether it would be possible to put the interim and annual reports on the CSCQ website.
• Concern over the requirement to be specific in the diagnosis of MPS subtype for urine mucopolysaccharides scheme when dermatan sulphate is present when this could indicate MPS I, II, VI or VII. Participants are marked as partially correct if exact subtype is not reported. This is not best practice in reality as the subtype can only be confirmed by enzyme analysis and not on urine analysis alone.	• The scoring is context-dependent. If for example in case of an MPS VI sample the majority of the participants does report absence of HS and concludes MPS VI, then it is apparently feasible to make such a specific diagnosis. The Scientific Advisor feels this majority should be rewarded by scoring less specific diagnoses as partially correct (i.e. 1 point instead of 2). However this issue will be discussed at the next SAB meeting.
• A short clinical description would be very informative and helpful.	• The Urine MPS scheme is developed to test analytical performance plus interpretation of results for MPS testing only. It is method-oriented and not to test knowledge on phenotypes, which is a feature in DPT schemes. MPS phenotypes are very typical and we have decided not to provide clinical info, since this would make it rather easy to establish diagnosis. In other qualitative schemes such as organic acids and CDG clinical phenotypes are much less helpful/suggestive compared to MPS.
3. Suggestions for future schemes	We do welcome suggestions for future schemes but unfortunately it is not possible to cater for every request.
• Plasma acyl carnitines	• A very small pilot study is currently running for plasma Acyl carnitines and the feasibility of extending this will be looked at.
• Cognitive scheme for amino acids	• Plans are being developed for a pilot cognitive scheme for amino acids

Question 14 Please complete your name and institute address details.

- Number of individual responses = 182 (= 91% of all responses).