2023 Participant Survey Report:
[2022 scheme year]

ERNDIM Administration Office
c/o EMQN CIC Office, Unit 4, Enterprise House,
Manchester Science Park,
Pencroft Way, Manchester, M15 6SE,
United Kingdom
Tel: +44 161 757 4952
Fax: +44 161 850 1145
Email: admin@erndim.org
Web: www.erndim.org

1. Introduction

- Participants (826 contacts from 413 centres) were sent the link to the ERNDIM Participant Survey on the Survey Monkey website (www.surveymonkey.com) on 11th January 2023. We asked participants to answer questions relating to the 2022 EQA schemes. The closing date for the survey was 8th February 2023.

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.
- 30.0% of the laboratories that participated in the 2022 schemes responded to the survey, with the response rate for each of the schemes being between 26.4% - 50.0%.
- The survey has again highlighted areas where we need to improve, such as low sample volume for some schemes, value for money and billing arrangements.
- It is gratifying to see that 95% of respondents rate the quality of products and services we provide as 'excellent' or 'good' and that 68% of respondents believe that the quality of service we offer is getting better. We will continue to make further improvements to our services as we work towards applying for accreditation.
- The issue of sample volume is more difficult. The schemes that use real clinical samples as the EQA materials are dependent on the Scientific Advisors sourcing suitable clinical samples of sufficient volume either by direct contact with clinicians or via donations from participating laboratories. However, we are investigating alternative routes for sample donation. Information on the types of samples that would be useful to ERNDIM can be found on the website https://www.erndim.org under EQA schemes\sample donations. Discounts on scheme fees are also available for some schemes if a donated sample is used as an EQA material. If you would be interested in donating a sample, please contact admin@erndim.org for more information.
- For manufactured samples (Quantitative and Hybrid schemes) larger sample volumes are possible but this would incur additional costs and ERNDIM aims to provide sufficient sample volume for most participants while minimising costs. For most schemes, it is possible for participants requiring a larger sample volume to purchase additional sets of samples.
- 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 where we answer some of your comments (see page 11) and we would welcome any other comments or suggestions for improvements.

3. Survey Responses

- 127 individuals from 124 centres in 35 countries responded to the survey. The response rate by centre was 30.0% (compared to 32.9% in the last survey).

3.1. Please rate the following aspects for each of the ERNDIM quality assurance schemes that you subscribe to (Q.1 & 2)

- 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 Purines & Pyrimidines in urine (50.0% of 2022 scheme participants) and the lowest was for Lysosomal enzymes in fibroblasts (26.4% of 2022 scheme participants).
- The response rate was lower for 7 schemes compared to the 2021 scheme year survey; the biggest decrease was for the Congenital disorders of glycosylation scheme (30.0% for 2022 compared to 38.8% in 2021).

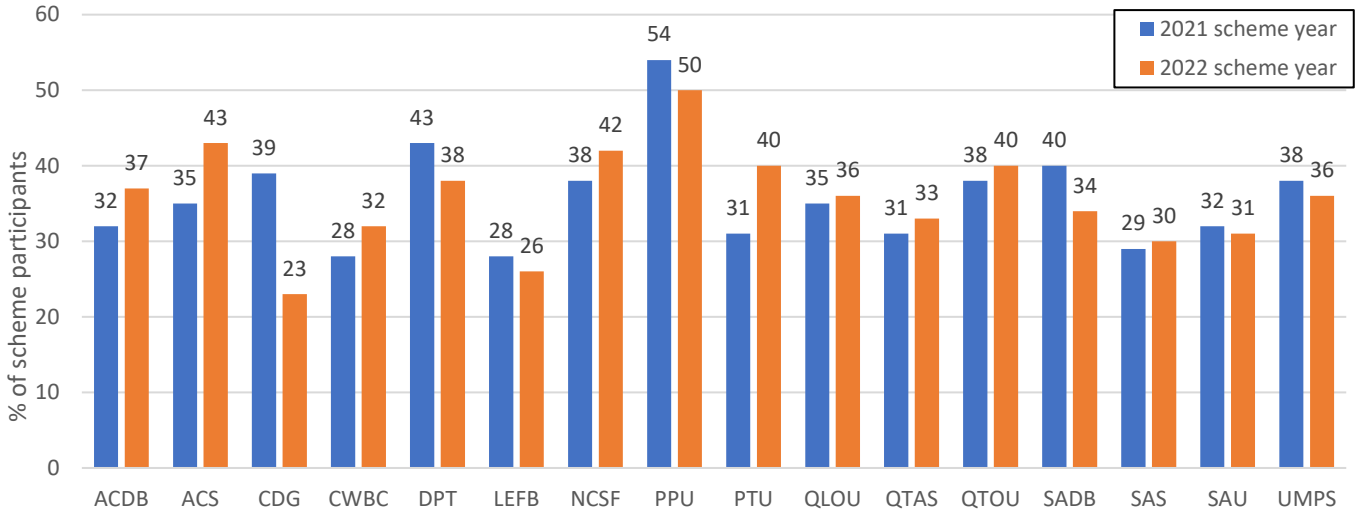


Figure 1. Survey responses per EQA scheme (Question 1) as a percentage of the EQA scheme participants

Key

EQA Scheme	Code	EQA Scheme	Code
Acylcarnitines in DBS	ACDB	Pterins in urine	PTU
Acylcarnitines in serum	ACS	Qualitative organic acids (urine)	QLOU
Congenital disorders of glycosylation	CDG	Quantitative amino acids (serum)	QTAS
Cystine in white blood cells	CWBC	Quantitative organic acids (urine)	QTOU
Diagnostic Proficiency Testing (urine)	DPT	Special assays - DBS	SADB
Lysosomal enzymes (fibroblasts)	LEFB	Special assays - serum	SAS
Neurotransmitters in CSF	NCSF	Special assays - urine	SAU
Purines & pyrimidines (urine)	PPU	Urine Mucopolysaccharides	UMPS

- Participants were asked to rate the following aspects of each scheme:
  - Frequency of samples
  - Appropriateness of analyte concentration
  - Website display
  - Value for money
  - Sample volume
  - Adequacy of the report
  - Usefulness of the annual report
  - 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
- The average scores per scheme since 2001 are shown in Table 1 and Figure 2 and scores ≤ 1.5 are highlighted in blue and scores ≥ 2.0 are highlighted in red.
- The overall score for all aspects of all schemes was 1.7, which is the same as for the 2021 scheme year.
- Ten of the EQA schemes had the same score as last year, six schemes had a worse score than last year (CDG, DPT, NCSF, PTU, SADB AND UMPS) and no schemes had a better score.
- The average score for individual aspects remained unchanged when compared to the 2021 scheme year with the exception of Billing arrangements, which was slightly worse (1.8) than for the 2021 scheme year (1.7).
- The worst scoring aspects were ‘Sample volume’, ‘Website display’, ‘Value for money’ and ‘Billing arrangements’ having an average score of 1.8. The best scoring aspects were ‘Frequency of samples’, ‘Adequacy of the report’ and ‘Usefulness of the annual report’ which all scored 1.6.

Table 1. Average scores per scheme (Question 1) *[See Figure 1 for key to scheme codes]*

	Average Scores												
EQA Scheme	**2022**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2015**	**2014**	**2013**	**2012**	**2011**	**2001**
All schemes	**1.7**	**1.7**	**1.7**	**1.7**	**1.8**	**1.7**	**1.7**	**1.7**	**1.8**	**1.7**	**1.7**	**1.7**	**1.7**
ACDB	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.9	1.9	2.0	1.9	1.9	2.0
ACS	1.7	1.7	1.7	1.7	1.7	1.6	-	-	-	-	-	-	-
CDG	1.9	1.8	1.9	1.9	1.9	1.8	1.9	1.9	2.0	2.0	1.9	1.8	-
CWBC	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.6	1.7	1.4
DPT	1.7	1.6	1.6	1.7	1.8	1.6	1.7	1.7	1.7	1.7	1.7	1.8	1.7
LEFB	1.7	1.7	1.8	1.9	1.8	1.7	1.8	1.9	1.9	2.0	1.9	2.0	-
NCSF	1.7	1.6	1.9	1.8	1.8	1.9	1.7	-	-	-	-	-	-
PPU	1.7	1.7	1.6	1.7	1.7	1.7	1.7	1.8	1.8	1.7	1.7	1.7	1.6
PTU	1.7	1.6	1.6	1.5	1.8	1.9	-	-	-	-	-	-	-
QLOU	1.7	1.7	1.7	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.6
QTAS	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
QTOU	1.7	1.7	1.8	1.7	1.8	1.7	1.7	1.7	1.8	1.7	1.7	1.7	1.7
SADB	1.8	1.7	1.7	1.8	-	-	-	-	-	-	-	-	-
SAS	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.7	1.7	1.7	1.7	1.7
SAU	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8
UMPS	1.7	1.6	1.7	1.7	1.8	1.7	1.8	1.7	1.8	1.8	1.8	1.8	-

- There was a total of 1 score above 2.0 in this survey: CDG ('Sample volume' = 2.8).
- The 'Sample volume' score for CDG was again the worst score in the survey (2.8), previous scores:2.5 for 2021, 2.6 for 2020, 2.4 for 2019, 2.4 for 2018.
- The best score of the whole survey (1.4) was for 'Usefulness of the Annual Report' for PPU.

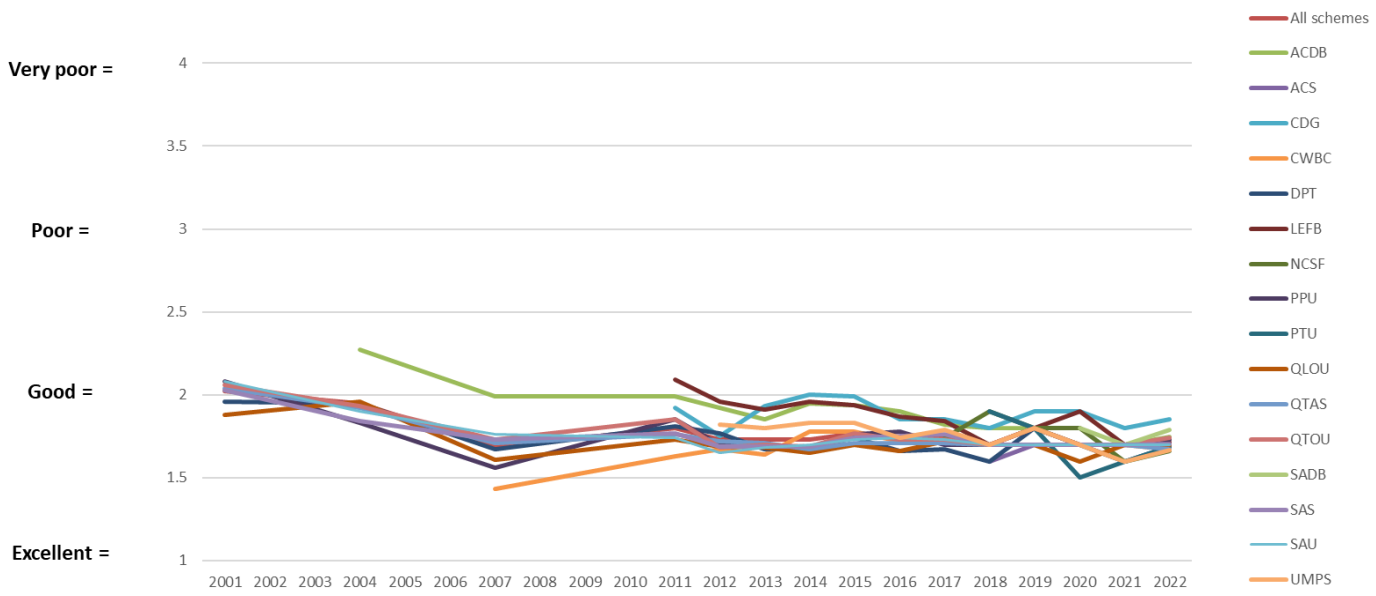


Figure 2. Average score per EQA scheme (Question 1) *[See Figure 1 for key to scheme codes]*

Table 2: Average scores per aspect of each scheme (Question 1) *[See Figure 1 for key to scheme codes]*

Scheme Aspects / EQA Schemes	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)
ACDB	1.6	1.8	-	1.6	1.9	1.6	1.8	1.8	1.7	49 (36.6%)
ACS	1.7	1.6	1.6	1.6	1.8	1.7	1.8	1.7	1.7	55 (43.0%)
CDG	1.5	2.8	-	1.5	2.0	1.7	1.7	1.8	1.9	24 (30.0%)
CWBC	1.7	1.8	1.6	1.6	1.7	1.6	1.7	1.7	1.7	12 (32.4%)
DPT	1.5	1.8	-	1.6	1.9	1.5	1.8	1.9	1.7	39 (38.2%)
LEFB	1.7	1.9	1.8	1.7	1.7	1.4	1.8	1.8	1.7	19 (26.4%)
NCSF	1.6	1.9	1.5	1.5	1.6	1.6	1.8	1.8	1.7	16 (42.1%)
PPU	1.6	1.5	1.8	1.7	1.9	1.6	1.9	1.9	1.7	25 (50.0%)
PTU	1.6	1.7	1.6	1.6	1.7	1.6	1.9	1.8	1.7	14 (40.0%)
QLOU	1.6	1.8	-	1.6	1.8	1.5	1.8	1.8	1.7	82 (36.4%)
QTAS	1.6	1.6	1.7	1.6	1.7	1.7	1.8	1.8	1.7	88 (32.6%)
QTOU	1.5	1.7	1.8	1.6	1.8	1.8	1.9	1.8	1.7	53 (40.2%)
SADB	1.6	1.9	1.7	1.7	1.9	1.7	1.9	1.9	1.8	34 (34.0%)
SAS	1.5	1.6	1.7	1.7	1.8	1.7	1.8	1.8	1.7	77 (30.4%)
SAU	1.5	1.8	1.7	1.6	1.7	1.6	1.8	1.8	1.7	62 (30.8%)
UMPS	1.5	1.9	-	1.5	1.8	1.5	1.7	1.8	1.7	32 (35.6%)
Average for all schemes	**1.6**	**1.8**	**1.7**	**1.6**	**1.8**	**1.6**	**1.8**	**1.7**	**1.7**	**124 (30.0%)**

3.2. Analytes in Quantitative & Hybrid Schemes (Q3 – Q.12)

- A total of 58 individuals (45.7% of respondents) made suggestions for analytes to be added to or removed from the Quantitative & hybrid schemes.
- Where possible we do try to incorporate suggestions for additional analytes 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 (pages 5 to 8).

Q.3: Acylcarnitines – Serum (7 responses, 5.5% of ACS participants)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 8		Total suggested = 1	
Analytes with >1 response		**All Analytes suggested**	
C14	2	C4-OH	1

ERNDIM Response:

- C14 was previously included but was removed in order to better quantify C14:1.
- C4-OH will not be removed at this time, one request is not sufficient for removal of an analyte.

Q.4: Lysosomal Enzymes (5 responses, 6.9% of LEFB participants)

Suggested Analytes to be added	Suggested Analytes to be removed
Total suggested = 6	Total suggested = 3
Analytes with >1 response	**Analytes with >1 response**

ERNDIM Response:

- No enzymes had more than 1 request for addition or removal, which is not sufficient for requests for changes to be implemented.

Q.5: Neurotransmitters – CSF (6 responses, 15.8% of all NCSF participants)

Suggested Analytes to be added		Suggested Analytes to be removed
Total suggested = 8		Total suggested = 0
Analytes with >1 response		**All Analytes suggested**
5 Methyltetrahydrofolate	3	
Biopterin	2	

ERNDIM Response:

- 5 Methyltetrahydrofolate will be included for the 2024 scheme.
- Biopterin inclusion may be complicated by differences in methods used by participants. Inclusion would require some further investigation.

Q.6: Purines & pyrimidines (7 responses, 14.0% of PPU participants)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 16		Total suggested = 3	
Analytes with >1 response		**All Analytes suggested**	
SAICAR	5	5-OH Methyluracil	1
2,8-dihydroxyadenine	3	Deoxy-insone	1
4 concentrations of Uric acid	2	Orotidine	1

ERNDIM Response:

- SAICAR will be re-evaluated to see if its inclusion might be possible.
- 2,8-dihydroxyadenine has been tested by the scheme organiser and Scientific Advisor but was chemically not possible.
- Uric acid is present at an inheritantly high concentration in the matrix, to include other concentrations would be difficult and costly.
- All suggestions for analyte removal had too few requests to be considered.

Q.7: Pterins – Urine (3 response, 8.6% of all PTU participants)

Suggested Analytes to be added		Suggested Analytes to be removed
Total suggested = 3		Total suggested = 0
All analytes suggested		**All Analytes suggested**
Sepiapterin	2	
Tetrahydrobiopterin	1	

ERNDIM Response:

- Sepiapterin may be useful as a qualitative parameter and will be considered, however this will require evaluation due to instability and is not likely to be possible for inclusion in the 2024 scheme.
- Tetrahydrobiopterin is also quite unstable and does not offer significant diagnostic purpose so will not be added at this time.

Q.8: Quantitative amino acids (8 responses, 3.0% of all QTAS participants)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 13		Total suggested = 20	
Analytes with >1 response		**Analytes with >3 response**	
Phosphoethanolamine	3	N(pros)-methylhistidine	5
		N(tele)-Methylhistidine	5
		Saccharopine	4

ERNDIM Response:

- Phosphoethanolamine is not stable enough to be included at this time.
- Pros and tele methyl histidine were included in the 2022 cycle reviews but not the Individual Lab Annual Reports as they demonstrated the difficulties in correctly identifying the 2 analytes. However they are not included in the 2023 scheme.
- Saccharopine will remain in the scheme at this time.

Q.9: Quantitative organic acids (18 responses, 13.6% of all QTOU participants)

Suggested Analytes to be added		Suggested Analytes to be removed
Total suggested = 72		Total suggested = 0
Analytes with >2 response		**All Analytes suggested**
2-methyl-3Ohbutyric acid	5	
Malonic acid	4	
Orotic acid	4	
Propionilglycine	4	
Succinic acid	4	

ERNDIM Response:

- Malonic acid and 2-methyl-3Ohbutyric acid will be considered for inclusion in the future.
- Orotic acid is already include in the SAU scheme, it is not practical/cost effective to include it in both schemes.
- 3-OH propionic acid and tiglyglycine are already included in the scheme so it is not considered worthwhile adding Propionylglycine at this time.
- Succinic acid does not offer enough benefit to be included compared to other analytes.

Q.10: Special assays – Dried Blood Spots (7 responses, 7.0% of all SADB participants)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 11		Total suggested = 1	
Analytes with >2 response		**All Analytes suggested**	
Methylmalonic acid	3	NTBC (nitisone)	1

ERNDIM Response:

- Methylmalonic acid is requested by too few participants to be considered for addition at this time.

Q.11: Special assays – serum (16 responses, 6.3% of all SAS participants)

Suggested Analytes to be added		Suggested Analytes to be removed	
Total suggested = 41		Total suggested = 2	
Analytes with >1 response		**All Analytes suggested**	
Sitosterol	4	Biotinidase	1
Desmosterol	3	Pipecolic acid	1

ERNDIM Response:

- Sitosterol and Desmosterol would be interesting analytes to include in the scheme, however currently the scheme has a large number of analytes and adding further analytes presents difficulties. This scheme will be reviewed and these analytes may potentially be added in the future as other changes are made.
- Biotinidase is present in the sample matrix and cannot be removed.

Q.12: Special assays – urine (17 responses, 8.5% of all SAU participants)

Suggested Analytes to be added		Suggested Analytes to be removed
Total suggested = 33		Total suggested = 2
Analytes with >1 response		**Analytes with >1 response**
Sulphatides	3	

ERNDIM Response:

- Sulphatides cannot be dissolved and therefore could not be included in this scheme, in a clinical scenario sulphatides are present within cells found in the urine.

3.3. Do you have any other remarks, comments or suggestions for any of the schemes you subscribed to? (Q.13)

- Number of individual responses = 31 (24.4% of all responses).
- These comments are summarised under 3.11 (page 11) with the comments made in response to Q.21 (see page 8).

3.4. Does your laboratory use any of the Internal Control Materials provided by MCA laboratories? (Q.14)

- 120/127 (94.5%) respondents answered this question

Response	Number of respondents
Yes	55 (45.8%)
No	48 (40.0%)
No, but we may use these in the future	17 (14.2%)

3.5. Would your laboratory purchase a control material for uracil and dihydrouracil in plasma/serum if this control material were to be produced in the future? (Q.15)

- 113/127 (89.0%) respondents answered this question.

Response	Number of respondents
Yes	22 (19.5%)
No	91 (80.5%)

3.6. Control materials are currently available to complement a number of ERNDIM schemes, would your laboratory like control materials to be produced to complement any other ERNDIM Quantitative or Hybrid schemes? (Q.16)

- 12/127 (9.4%) respondents answered this question, these responses are listed below:
  - Blood spot acylcarnitines
  - We would like to use neurotransmitters CSF kit
  - Amino acids kit, Organic acids kit, Pterins in urine kit
  - Pterins in urine and Neurotransmitters in CSF are of great interest
  - Yes. We are already using CAR1 and CAR2 control materials for plasma acylcarnitine analysis
  - Yes, lysosomal enzymes
  - Special assays in blood spots kit
  - Homocysteine Dried blood spot, Methylmalonic acid blood spot, Ethylmalonic acids
  - 5-MTHF in CSF, pterins in CSF
  - CDG – although I appreciate this would be close to impossible!
  - Oxalic and neopterin in plasma
  - Methylmalonic acid + methylcitric acid

3.7. Potential sample exchange programmes

Unfortunately, it's not possible for ERNDIM to provide EQA schemes for all analytes requested by participants. ERNDIM can however support laboratories looking to set up sample exchanges by helping identify other laboratories with the same needs.
Please note, the proposed sample exchanges listed below are not endorsed or validated by ERNDIM. ERNDIM is solely facilitating contact between laboratories and is not responsible for organising or supporting these sample exchanges in any other way.

3.7.1. Proposed exchange programme 1: (Q.17)

Bile Acids in plasma/urine

Organising laboratory& institution: Department of Clinical Chemistry, Sheffield Children's' Hospital

Analytes: Bile Acids/Salts

Matrix: Plasma and urine

Format: It is likely this would have a qualitative focus (i.e., what are the findings and what is the diagnostic significance if any) similar to the Qualitative Organic acids in urine EQA scheme. Although a quantitative element for the primary bile salts may perhaps be included if the participating labs desire it. Participating laboratories would be asked to take it in turns to send out samples to the other laboratories.

Geographical restrictions: limited to UK and EU labs only (due to sample transport), but would like to know if any labs outside this area are also interested in these analytes (with a view to proposing an ERNDIM pilot scheme if the sample exchange is successful).

Question: Are you interested in being contacted about this potential sample exchange?

- 108/127 (85.0%) respondents answered this question.

Response	Number of respondents
Yes	8 (7.4%)
No	97 (89.8%)
Other (please specify)	3 (2.8%)

Other:

- My lab outside UK or EU
- We already do a bile acids comparison with 2 other labs
- We don't have enough samples to share

3.7.2. Proposed exchange programme 2: (Q.18)

Palmitoyl phosphocholine serine (PPCS, formerly lysoSM-509)

Organising laboratory & institution: Willink Biochemical Genetics Laboratory, Manchester University Hospitals NHS Foundation Trust, UK

Analytes: PPCS (lyso-SM-509)

Matrix: Plasma

Format: Quantitative, single analyte in the first instance but there is undoubtedly potential value to the inclusion of other related analytes (e.g., lyso-sphingomyelin, glucosyl-sphingosine) with an interpretative element of the overall profile. However, this may give rise to additional shipping / stability considerations – to be decided depending on the level of interest.

Geographical restrictions: PPCS itself is proven stable in plasma at 25°C for at least 2 weeks but stability at elevated temperatures is unknown. Lyso-sphingomyelin and glucosyl-sphingosine may require special shipping conditions that could prove to be prohibitively expensive. For this reason, global sample distribution may not be possible but will be considered dependent on the level of interest received.

Question: Are you interested in being contacted about this potential sample exchange?

- 108/127 (85.0%) respondents answered this question.

Response	Number of respondents
Yes	11 (10.2%)
No	97 (89.8%)
Other (please specify)	0 (0.0%)

3.8. Metabolomics

ERNDIM has an interest in the introduction of Untargeted Metabolomics in a diagnostic setting. While there are currently no immediate plans for an ERNDIM Untargeted Metabolomics EQA pilot scheme we are periodically reviewing the level of interest expressed by our participants. We would therefore appreciate your response to the following questions.

3.8.1. Is your laboratory currently providing an Untargeted Metabolomics test for diagnostic purposes? (Q.22)

- 119/127 (93.7%) respondents answered this question.

Response	Number of respondents
No, we do not have Untargeted Metabolomics in use or in development	96 (80.7%)
We are currently developing an Untargeted Metabolomics test for diagnostic use	12 (10.1%)
We have Untargeted Metabolomics available but for research use only	5 (4.2%)
Yes, we offer a diagnostic Untargeted Metabolomics test	6 (5.0%)

3.8.2. Would your laboratory be interested in participating in an Untargeted Metabolomics pilot scheme? (Q.23)

- 117/127 (92.1%) respondents answered this question.

Response	Number of respondents
No	55 (47.0%)
Not yet, perhaps in 5 or more years	11 (9.4%)
Not yet, perhaps in 2 or more years	34 (29.1%)
Yes	17 (14.5%)

3.8.3. If you are interested in participating in an Untargeted Metabolomics pilot scheme, what sample type would be of most interest to you? (Q.24)

- 52/127 (40.9%) respondents answered this question.

Response	Number of respondents
Urine	22 (42.3%)
Plasma	20 (38.5%)
Other (please specify)	10 (19.2%)

Other:

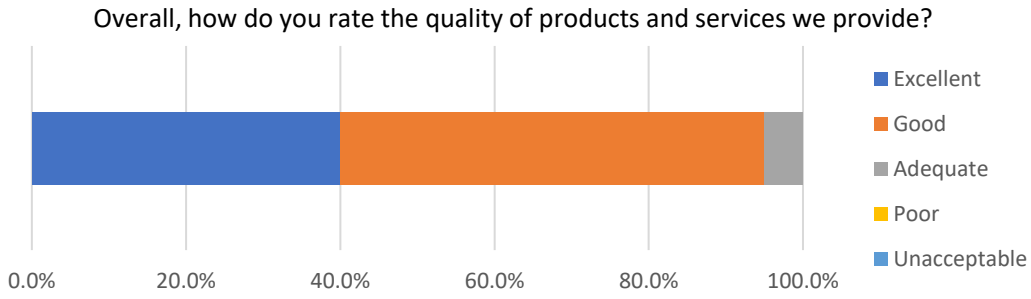
- Urine and plasma (n=5)
- Urine and DBS (n=1)
- Urine, plasma and DBS (n=1)
- Blood, plasma and cells (n=1)
- Cerebrospinal fluid (n=1)
- Not decided (n=1)

3.9. Comments on the overall performance of ERNDIM (Q.25 – 28)

- The aim of this section is to assess participants' perception of the overall performance of ERNDIM.
- In summary:
  - 95.0% of respondents rated the quality of services provided by ERNDIM as 'excellent' or 'good'; with 97.5% of respondents having 'complete' or 'a lot' of confidence that ERNDIM can deliver the service required by participants.
  - 67.5% of respondents agreed that overall ERNDIM's performance is 'getting better' or 'getting much better'; with 97.5% of respondents stating that it was 'certain' or 'very likely' that they would use ERNDIM services in the future.

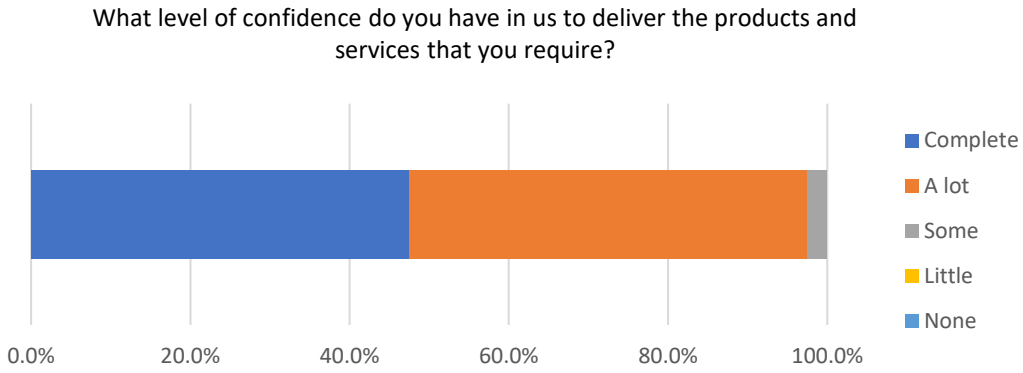
Q.25: Overall, how do you rate the quality of products and services we provide?

(120 individual responses, 94.5% of all responses for this section)



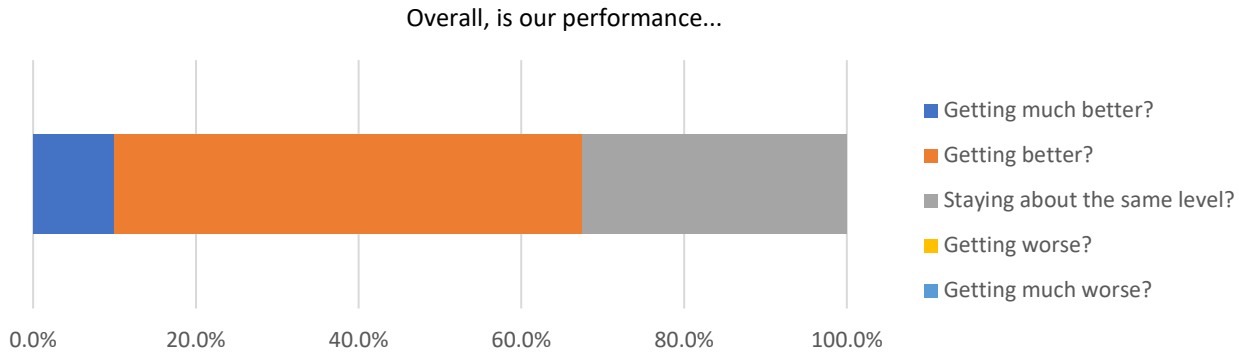
Q.26: What level of confidence do you have in us to deliver the products and services that you require?

(120 individual responses, 94.5% of all responses for this section)



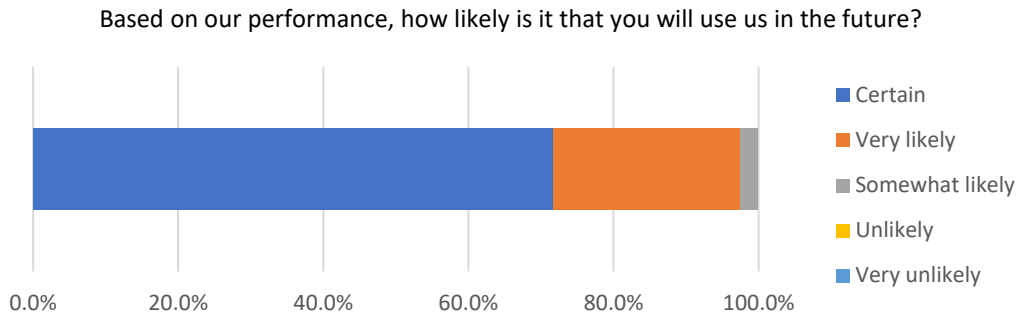
Q.27: Overall, is our performance…

(120 individual responses, 94.5% of all responses for this section)



Q.28: Based on our performance, how likely is it that you will use us in the future?

(120 individual responses, 94.5% of all responses)



3.10. Do you have any other remarks, comments or suggestions for how we could improve the services we provide? (Q.29)

- Number of individual responses = 21 (16.5% of all responses).
- These comments are summarised below with the comments made in response to Q13.

3.11. Summary of Remarks, comments or suggestions for improvements (Q.13 & Q.29)

- Total number of responses was 52 from 42 individuals (= 33.1% 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
2.1. General	
• Previous deadlines for submission of qualitative DPT and acylcarnitine schemes have been on the same date, which is a lot of work and can be challenging for labs with a small clinical team or when staff are on leave/off sick.	• While this may be challenging for some participants others prefer to have coinciding deadlines to reduce the number of submission dates throughout the year. All deadlines are available in advance to assist with planning around scheduled absences, however we understand that unplanned absences can still cause difficulties but should be minimal.

Participant Comment	ERNDIM Response
• Consideration should be give to late submissions, particularly for Qualitative Schemes. There is a need to differentiate between late submissions and no submissions. We participate in other EQA schemes that allow late submissions (prior to the day reports get released), however the submission is recorded as LATE. This differentiates labs that are able proficiently diagnose, but unable to meet deadlines. A lab that submits a late results does not mean they are unable to diagnose correctly. This information cannot be ascertained in the current format of the scheme, as after 1 late submission ALL late results are rejected. This is more important in the Qualitative schemes than the Quantitative schemes. Marks could be deducted for late submissions, instead of rejecting Qualitative results outright.	• There are currently a relatively low number of late submission requests each year, particularly with regards to the Qualitative schemes. Currently the Scientific Advisory Board is working towards a reduction in the number of late submissions rather than allowance for a greater number. It is useful of course to receive this feedback and it will be included as a point of discussion when the late submission policy is next reviewed.
2.2. Website reporting	
• To improve the site interface and accessibility. Make one site to all schemes (qualitative and quantitative).	• The functionality of the results submission websites for Qualitative and Quantitative/Hybrid schemes for scoring is quite distinct. At the time of creating these websites the most appropriate hosts were contracted to deliver these websites. There are no plans to merge these websites as this would require a large investment of resources. ERNDIM is currently prioritising improvement of schemes and progress towards accreditation, however, result submission website redevelopment may be considered in the future.
2.3. Acylcarnitines in serum	
• Low carnitine levels in "acyl carnitines in serum" are of importance (< 10 µmol/L)	• It is not possible to eliminate free carnitine form the sample matrix to produce such low levels in the samples.
2.4. CDG scheme	
• CDG scheme: The sample volume is too small.	• Additional sets of samples are available for purchase at a discounted rate for participants requiring a larger volume for their method. However the volume of sample is limited by the availability of patient sample material.
2.5. Cystine in white blood cells	
• How have the samples for the lkc-cystin scheme been prepared and the protein precipitated?	• Details can be found in the scheme annual report on the ERNDIM website www.erndim.org, further details can be requested by contacted admin@enridm.org if necessary.
2.6. Lysosomal Enzymes in fibroblasts scheme	
• How have the fibroblasts for the lysosomal scheme been cultivated and harvested?	• Preparation of material for this scheme is very labour intensive. Cell lines have to be retrieved from the cell bank and vast quantities grown up to provide sufficient to accommodate all participating laboratories. The process continues at MCA lab where all the cells are lyophilized and aliquoted into vials. All enzymes in all the samples then have to be assayed to validate the results. We understand there will be differences when measuring enzyme levels in cells from different labs and/or cells that have gone through the process of lyophilization. For this reason we now include a normal sample so labs can provide some comparison of values when they assay the other samples. The samples provided are always from patients with a clear enzyme deficiency, and so hopefully labs will be able to detect this in their system.
• As there is only one control sample, analysis of all the samples in the same series (and consequently only one submission deadline) should be more appropriate	• The enzyme assays in each lab should be optimized and therefore the difference between assay runs should be minimal. Providing more normal controls is not essential for the purpose of this scheme.

Participant Comment	ERNDIM Response
2.7. Qualitative Organic Acids	
• State that patients are under treatment if appropriate (Qualitative Organic acids, Proficiency QC programs).	• The Scientific Advisors try to avoid the inclusion of samples from patients undergoing treatment where possible, however sample availability at times prevents this. Where the information is provided by the donating centre this will be included in the sample clinical information.
2.8. Quantitative Amino acids in serum	
• Hydroxyproline, we would like to include concentrations >100 micro mol/L	• We will try to do this in the 2024 scheme.
• The inclusion of homocitrulline in the quant AA scheme means that as a Biochrom user we don't have any EQA for our methionine assay. If there was at least one sample with no homocitrulline that would be helpful, or remove homocitrulline altogether.	• Homocitrulline has not been included in the 2023 scheme.
• Why is the sarcosine range in the Amino Acids in Serum scheme so restricted?	• The concentrations set are intended to highlight interference from alanine on some MS methods.
2.9. Quantitative Organic acids in urine	
• Testing higher concentrations for some analytes (e.g. methylmalonic acid, 3-hydroxypropionic acid, glutaric acid...) could help.	• Very high concentrations may result in wider distribution of results and may also cause some extraction issues. However the inclusion of some higher concentrations will be consideredfor the 2024 scheme year.
2.10. Special Assays in DBS	
• In dried blood spots, we observed that all labs reported NTBC concentrations lower than the added amounts. If we remove our correction factors from the analysis, we get similar results as the other labs. It would be helpful to know, if we should include these factors in the future, as we would fail the NTBC scheme if we did so - although we in that case would get results that fit nicely to the added amounts.	• Participants should report EQA returns as they do patient samples.
2.11. Special Assays in serum	
• For the Special Assays in Serum program, is it possible to include the peer group of measurement system / analyser for comparing lactate, pyruvic acid and 3 OH Butyrate?	• This is a good idea, but interlab CV% is optimal for lactate (5%) and good for the others (around 11%).
2.12. Special Assays in urine	
• In 9 out of 20 metabolites, the CV% among laboratories showed a value >15% (being homogentisic, newly metabolite added in 2022 the highest = 54%.	• The Scientific Advisor will request an additional set of 2022 samples to review the stability of homogentisic acid, followed by 5-aminolevulinic and succinylacetone (35% and 27% respectively). A number of different technologies are employed for 5-aminolevulinic and succinylacetone determination, and this fact would explain this high variability.

3.12. Please complete your name and institute address details (Q.22-23)

- Number of individual responses = 80 (63.0% of all responses).