2024 Participant Survey Report:
[2023 scheme year]

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1. Introduction

- The ERNDIM Participant Survey was sent to 822 contacts from 411 centres, on 8th January 2024. and was closed on 9th February 2024. We asked participants to answer questions relating to the 2023 EQA schemes

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 again highlighted areas where we need to improve, such as low sample volume for some schemes, and issues with the qualitative schemes' submission website.
- Some of the best scoring aspects for ERNDIM EQA scheme was for the 'Usefulness…' and 'Adequacy of the annual report'. We are pleased to hear that these reports are helpful, and we are working with the scientific advisors to publish these in a timely manner, and to increase the consistency of detail across different schemes and centres.
- We are pleased that 95.4% of respondents rated the quality of services provided by ERNDIM as 'excellent' or 'good'; with 96% of respondents having 'complete' or 'a lot' of confidence that ERNDIM can deliver the service required by participants. We will continue to make further improvements to our services as we work towards applying for accreditation.
- Based on comments and suggestions from previous participant surveys, we have launched a Lipids in Serum (LIS) pilot scheme. We anticipate this running as a pilot for 2 years before being considered as an official ERNDIM EQA Scheme. We are also investigating the feasibility of other suggested schemes such as lysosomal enzymes in dried blood spots. Future pilots for qualitative schemes are dependent on sample availability. Please contact ERNDIM for further information about donating samples.
- The worst scoring aspects were due to issues with sample volume, in particular with the Congenital Disorders of Glycosylation (CDG) scheme. 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. 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.
- 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 useful (see page 11) and we would welcome any other comments or suggestions for improvements.

3. Survey Responses

- 194 individuals from 411 centres in 35 countries responded to the survey. The response rate is significantly higher than for the 2022 scheme year survey, with the response rate by centre being 45.0% (compared to 30% in the 2022 scheme year 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 the Amino Acids Interpretation scheme; this is the first year it has been included in the survey (58.5% of 2023 scheme participants). The lowest response rate was for Neurotransmitters in CSF (35% of 2023 scheme participants).
- The response rate was the same or higher for all schemes compared to the 2022 scheme year survey, except for Neurotransmitters in CSF.

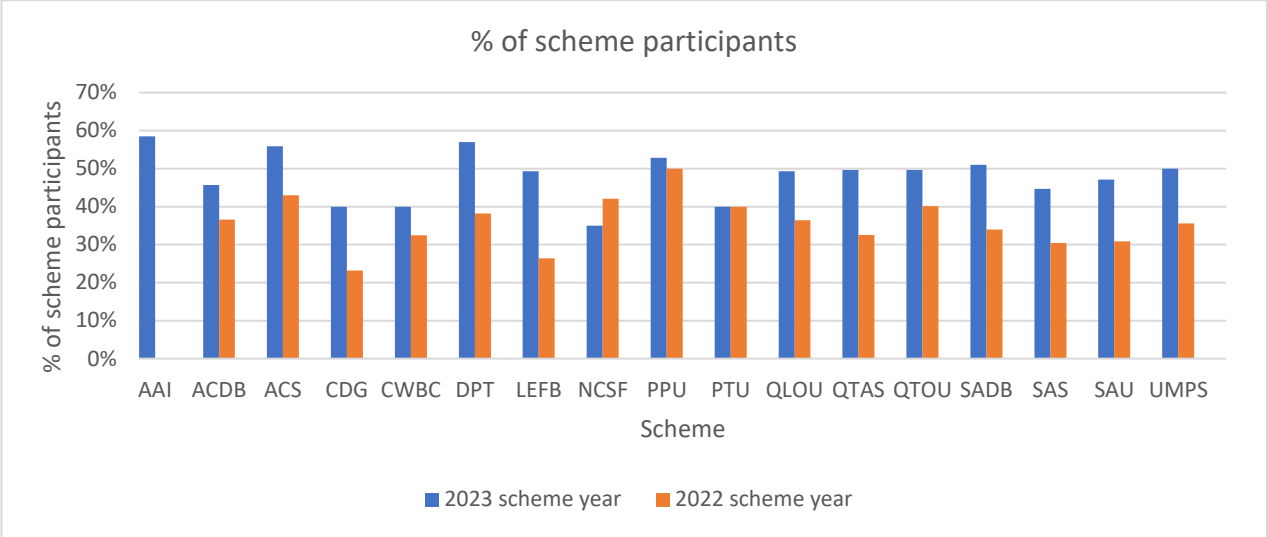


Figure 1. Survey responses per EQA scheme (Question 1) as a percentage of the EQA scheme participants

Key

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

- 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 2012 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 2022 scheme year.
- Twelve of the EQA schemes had the same score as last year, four schemes had a worse score than last year (CDG, LEFB, NCSF, UMPS) and no schemes had a better score.
- The average score for individual aspects remained unchanged when compared to the 2022 scheme year.
- The worst scoring aspects were ‘Sample volume’, ‘Website display’, ‘Value for money’ and ‘Billing arrangements’ which all had 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	**2023**	**2022**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2015**	**2014**	**2013**	**2012**
All schemes	**1.7**	**1.7**	**1.7**	**1.7**	**1.7**	**1.8**	**1.7**	**1.7**	**1.7**	**1.8**	**1.7**	**1.7**
AAI	1.7	-	-	-	-	-	-	-	-	-	-	-
ACDB	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.9	1.9	2.0	1.9
ACS	1.7	1.7	1.7	1.7	1.7	1.7	1.6	-	-	-	-	-
CDG	2.0	1.9	1.8	1.9	1.9	1.9	1.8	1.9	1.9	2.0	2.0	1.9
CWBC	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.6
DPT	1.7	1.7	1.6	1.6	1.7	1.8	1.6	1.7	1.7	1.7	1.7	1.7
LEFB	1.8	1.7	1.7	1.8	1.9	1.8	1.7	1.8	1.9	1.9	2.0	1.9
NCSF	1.8	1.7	1.6	1.9	1.8	1.8	1.9	1.7	-	-	-	-
PPU	1.7	1.7	1.7	1.6	1.7	1.7	1.7	1.7	1.8	1.8	1.7	1.7
PTU	1.7	1.7	1.6	1.6	1.5	1.8	1.9	-	-	-	-	-
QLOU	1.7	1.7	1.7	1.7	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7
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
QTOU	1.7	1.7	1.7	1.8	1.7	1.8	1.7	1.7	1.7	1.8	1.7	1.7
SADB	1.8	1.8	1.7	1.7	1.8	-	-	-	-	-	-	-
SAS	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	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
UMPS	1.8	1.7	1.6	1.7	1.7	1.8	1.7	1.8	1.7	1.8	1.8	1.8

- The 'Sample volume' score for CDG was again the worst score (2.8) in the survey and is the same as in 2023. The only other score above 2.0 in the survey was for 'Website Display' for CDG (2.1).
- The best scores of the whole survey (1.4) were for 'Adequacy of the Annual Report' for DPT and QLOU.

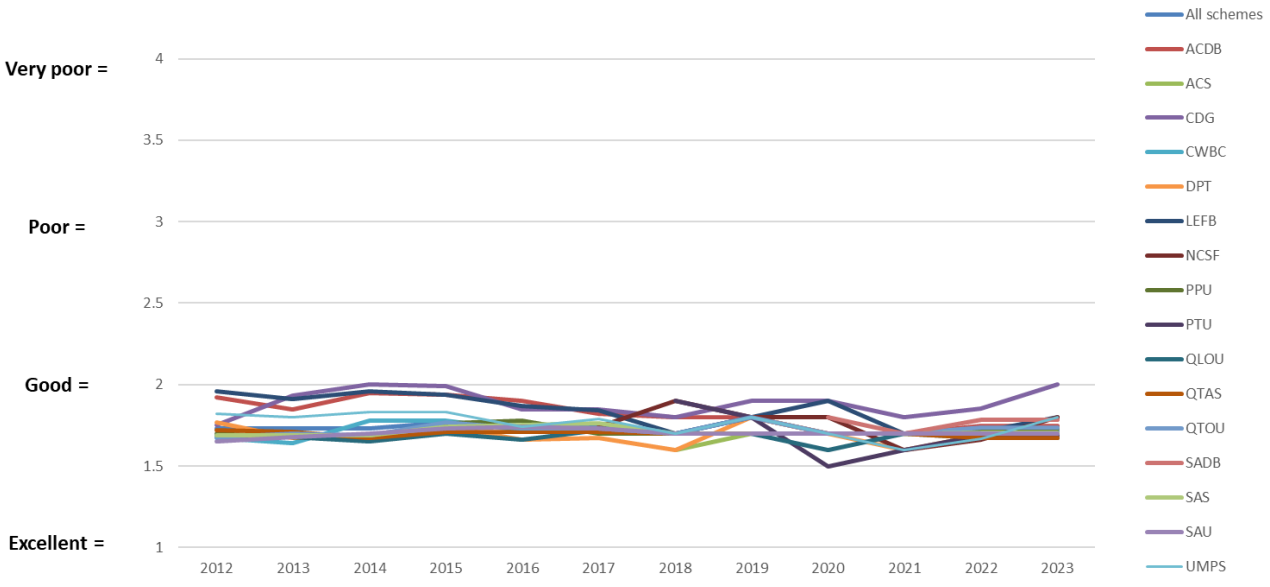


Figure 2. Average score per EQA scheme (Question 1) [See Figure 1 for key to scheme codes]

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

EQA Schemes	Frequency of samples	Sample volume	Appropriateness of analyte concentration	Website display	Adequacy of the report	Usefulness of the Annual Report	Value for money	Billing arrangements	Average per scheme	No. of responses (% of scheme participants)
AAI	1.7	-	-	1.9	1.6	1.6	1.8	1.7	1.7	82 (58.5%)
ACDB	1.7	1.8	-	1.9	1.6	1.6	1.7	1.7	1.7	66 (45.7%)
ACS	1.7	1.6	1.7	1.8	1.6	1.6	1.8	1.8	1.7	74 (55.9%)
CDG	1.6	2.8	-	2.1	1.8	1.8	1.9	1.9	2.0	25 (40.0%)
CWBC	1.6	1.9	1.5	1.6	1.7	1.5	1.8	1.8	1.7	19 (40.0%)
DPT	1.7	1.8	-	1.9	1.4	1.5	1.8	1.8	1.7	60 (57.0%)
LEFB	1.7	1.9	1.7	1.7	1.7	1.7	1.9	1.9	1.8	37 (49.3%)
NCSF	1.6	1.9	1.7	1.8	1.8	1.6	1.9	1.8	1.8	17 (35.0%)
PPU	1.6	1.6	1.7	1.8	1.6	1.7	1.8	1.8	1.7	31 (52.8%)
PTU	1.5	1.9	1.6	1.6	1.5	1.6	1.9	1.7	1.7	17 (40.0%)
QLOU	1.6	1.8	-	1.8	1.4	1.5	1.7	1.7	1.7	115 (49.3%)
QTAS	1.6	1.5	1.7	1.7	1.6	1.6	1.8	1.8	1.7	134 (49.6%)
QTOU	1.6	1.7	1.7	1.8	1.6	1.6	1.9	1.8	1.7	68 (49.6%)
SADB	1.6	1.8	1.6	1.8	1.8	1.7	1.9	1.8	1.8	56 (51.0%)
SAS	1.6	1.6	1.7	1.8	1.7	1.7	1.8	1.7	1.7	112 (44.7%)
SAU	1.6	1.6	1.7	1.7	1.6	1.7	1.8	1.8	1.7	94 (47.2%)
UMPS	1.6	1.9	-	2.0	1.7	1.7	1.9	1.8	1.8	47 (50.0%)
Average for all schemes	1.6	1.8	1.7	1.8	1.6	1.6	1.8	1.8	1.7	194 (45.0%)

3.2. Analytes in Quantitative & Hybrid Schemes (Q4 – Q.13)

- A total of 75 individuals (38.7% 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.

Q.3: Acylcarnitines – Serum

Suggested Analytes to be added (16 responses, 21.6% of ACS respondents)		**Suggested Analytes to be removed** 3 responses (4.1% of ACS respondents)	
Total suggested = 19		Total suggested = 2	
Analytes with >2 responses		**Analytes with >1 response**	
C6-DC	6	C3-DC	2
C18:1OH	5		
C10:1	3		
C14	3		
C14:2	3		

ERNDIM Response:

- There is a difficulty in the addition of these Acylcarnitines since there could be interference between these and the existing scheme analytes, unless chromatographic methods are used (which are used only by few

participants). That is why C14 was removed from the scheme previously, as there was interference between it and high concentrations of C14:1.

- C6-DC could be studied for possible addition, however, the quantification of C6-DC could be interfered by C8 non-derivatised and of C12-butylester, both already added.

Q.4: Lysosomal Enzymes – fibroblasts

Suggested Analytes to be added (10 responses, 27% of all LEFB respondents)		**Suggested Analytes to be removed** (7 responses, 18.9% of all LEFB respondents)	
Total suggested = 10		Total suggested = 5	
Analytes with >1 response		**Analytes with >1 response**	
arylsulfatase A	4	Lysosomal acid lipase	4
alfa iduronidase	3	Palmitoyl protein transferase	3
arylsulfatase B	2	Beta manosidase	2
hexosaminidases AB	2		

ERNDIM Response:

- Currently only 10 enzymes can be measured in each scheme round, so a selection must be made. There are a core set of 4 enzymes that are included every year, and 6 other enzymes are selected each year.

Q.5: Neurotransmitters – CSF

Suggested Analytes to be added (6 responses, 35.3% of NCSF respondents)		**Suggested Analytes to be removed**	
Total suggested = 8		Total suggested = 0	
Analytes with >1 response		**No Analytes suggested**	
Neopterin	4		
Biopterin	3		
MHPG	2		

ERNDIM Response:

- ERNDIM will send out a survey to assess the practicalities of adding pterins to NCSF samples.

Q.6: Purines & pyrimidines

Suggested Analytes to be added (5 responses, 16.1% of all PPU respondents)		**Suggested Analytes to be removed** (1 response, 3.2% of all PPU respondents)	
Total suggested = 16		Total suggested = 1	
Analytes with >1 response		**Analytes with 1 response**	
2,8-Dihydroxyadenine	3	Orotidine	1
SAICAR	2		

ERNDIM Response:

- No changes in 2025
- Instead of adding these analytes to the samples, there is a proposal to add two patient samples in 2025 samples: ADSL and APRT deficiency – this addresses SAICAr and 2,8-dihydroxyadenine.

Q.7: Pterins – Urine

Suggested Analytes to be added (2 responses, 11.8% of all PTU respondents)		**Suggested Analytes to be removed** (1 response, 5.9% of all PPU respondents)	
Total suggested = 4		Total suggested = 1	
All Analytes suggested		**Analytes with 1 response**	
Tetrahydrobiopterin (BH4)	1	Primapterin	1
Dihydrobiopterin (BH2)	1		
Dihydroneopterin (DHNTP)	1		
Sepiapterin	1		

ERNDIM Response:

- BH4, BH2, DHNTP are very unstable, are measured more for research purposes and by only a few laboratories, and they do not significantly help in the diagnosis of BH4 disorders.
- Sepiapterin is very unstable in solution.
- Primapterin is helpful in the diagnosis of a PCD deficiency, which can be symptomatic (developmental delay, hypotonia, maturity onset diabetes of the young).

Q.8: Quantitative amino acids

Suggested Analytes to be added (19 responses, 14.2% of all QTAS respondents)		**Suggested Analytes to be removed** (13 responses, 9.7% of all QTAS respondents)	
Total suggested = 13		Total suggested = 12	
Analytes with >1 response		**Analytes with >1 response**	
Homocitrulline	8	(pros)-methylhistidine	7
Homocystine	4	tele-methylhistidine	7
Phosphoylethanolamine	4	saccharopine	3
homocysteine	3	Arginino succinic acid	2
		Aspartyl glucosamine	2
		Pipecolic acid	2

Q.9: Quantitative organic acids

Suggested Analytes to be added (12 responses, 17.6% of all QTOU respondents)		**Suggested Analytes to be removed**	
Total suggested = 17		Total suggested = 0	
Analytes with >1 response		**No Analytes suggested**	
Malonic acid	3		
Orotic acid	3		
4-hydroxyphenyllactic acid	2		
Citric acid	2		
Propionylglycine	2		
Succinylacetone	2		

ERNDIM Response:

- Malonic acid will be added in 2025.
- Orotic acid is already included in the SAU scheme, it is not practical/cost effective to include it in both schemes.

Q.10: Special assays – Dried Blood Spots

Suggested Analytes to be added (14 responses, 25% of all SADB respondents)		**Suggested Analytes to be removed** (1 response, 1.8% of SADB respondents)	
Total suggested = 22		Total suggested = 2	
Analytes with >1 response		**Analytes with 1 response**	
methycitric acid	5	NTBC (nitisone)	1
ethylmalonic acid (EMA2)	2	C0 free carnitine	1
3-O-methyldopa (3OMD)	2		
2-OH Glutaric acid	2		

Q.11: Special assays – serum

Suggested Analytes to be added (19 responses, 17% of all SAS respondents)		**Suggested Analytes to be removed** (2 responses, 1.8% of all SAS respondents)	
Total suggested = 26		Total suggested = 2	
Analytes with >1 response		**Analytes with 1 response**	
Acetoacetate	5	Biotinidase	1
Lathosterol	2	C26:0 LPC	1
LysoSM509	2		
NTBC	2		

ERNDIM Response:

- Some of the suggested analytes may be added to the Lipids in Serum scheme that is currently in the pilot phase.
- In the past, there has been poor performance of Acetoacetate.
- Biotinidase is present in the sample matrix and cannot be removed.

Q.12: Special assays – urine

Suggested Analytes to be added (14 responses, 14.9% of all SAU respondents)		**Suggested Analytes to be removed** (1 response, 1.1% of all SAU respondents)	
Total suggested = 21		Total suggested = 5	
Analytes with >2 response		**Analytes with 1 response**	
Dermatan sulfate	3	Sulphocysteine	1
Heparan sulfate	3	Homocitrulline	1
phosphoethanolamine	2	Carnitine Free	1
		Mucopolysaccharides	1
		Guanidinoacetate	1

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.14)

- We received a total of 81 comments from 57 respondents that answered one or both questions asking for scheme related remarks or comments (Q.14), or overall suggestions for improvements (Q.25).
- We have selected a number of these comments to respond to in section 3.9.

3.4. Does your laboratory use any of the Internal Control Materials provided by MCA laboratories? (Q.15)

- 178/194 (91.7%) respondents answered this question

Response	Number of respondents
Yes	82 (46%)
No	75 (42.1%)
No, but we may use these in the future	21 (11.8%)

3.5. 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)

- 24/194 (12.4%) respondents answered this question. Analytes/scheme with >1 response are listed below:
  - Blood spot acylcarnitines (n=3)
  - Special assays in blood spots (n=6)
  - Special assays in Urine – addition of Homogentisic acid (n=3)
  - Lysosomal Enzymes in Fibroblasts (n=3)
  - Lysosphingolipids (n=4)

3.6. Potential sample exchange programmes (Q.17)

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.

There were 20 suggestions from this survey for sample exchange programmes, and these have been sent to the Scientific Advisory Board for discussion.

3.7. 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.

3.7.1. Is your laboratory currently providing an Untargeted Metabolomics test for diagnostic purposes? (Q.18)

- 166/194 (85.6%) respondents answered this question.

Response	Number of respondents
No, we do not have Untargeted Metabolomics in use or in development	141 (84.9%)
We are currently developing an Untargeted Metabolomics test for diagnostic use	13 (17.8%)
We have Untargeted Metabolomics available but for research use only	8 (4.8%)
Yes, we offer a diagnostic Untargeted Metabolomics test	4 (2.4%)

3.7.2. Would your laboratory be interested in participating in an Untargeted Metabolomics pilot scheme? (Q.19)

- 165/194 (85.1%) respondents answered this question.

Response	Number of respondents
No	86 (52.1%)
Not yet, perhaps in 5 or more years	18 (10.9%)
Not yet, perhaps in 2 or more years	41 (24.8%)
Yes	20 (12.1%)

3.7.3. If you are interested in participating in an Untargeted Metabolomics pilot scheme, what sample type would be of most interest to you? (Q.20)

- 56/194 (28.8%) respondents answered this question.

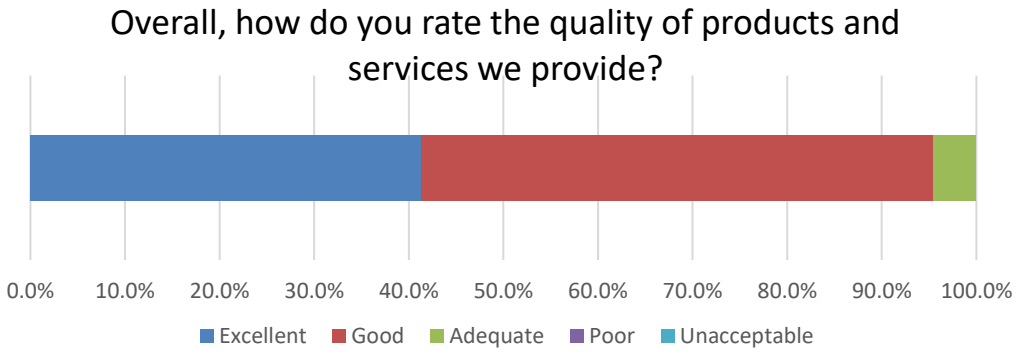
Response	Number of respondents
Urine	27 (48.2%)
Plasma	30 (54%)
Other (please specify)	7 (12.5%)
➢ DBS (n=5)	
➢ CSF (n=1)	
➢ Saliva (n=1)	

3.8. Comments on the overall performance of ERNDIM (Q.21 – 24)

- The aim of this section is to assess participants' perception of the overall performance of ERNDIM.
- In summary:
  - 95.4% of respondents rated the quality of services provided by ERNDIM as 'excellent' or 'good'; with 96% of respondents having 'complete' or 'a lot' of confidence that ERNDIM can deliver the service required by participants
  - 65.5% of respondents agreed that overall ERNDIM's performance is 'getting better' or 'getting much better'; with 98.2% of respondents stating that it was 'certain' or 'very likely' that they would use ERNDIM services in the future.

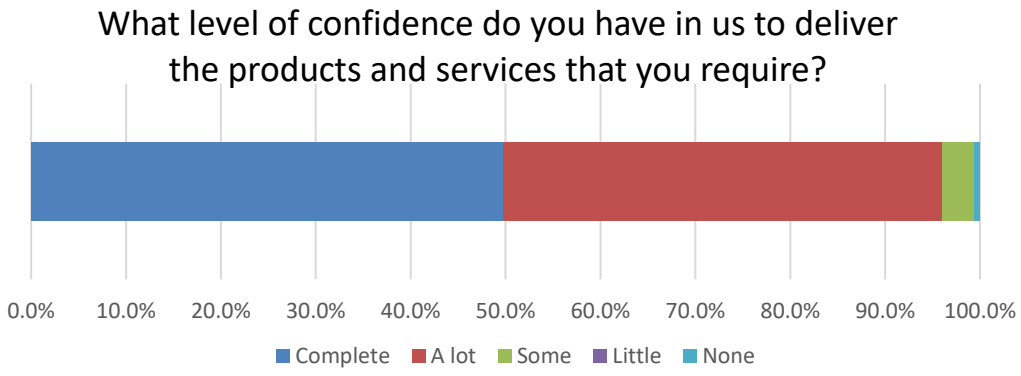
Q.21: Overall, how do you rate the quality of products and services we provide?

(177 responses, 91.2% of responders for this section)



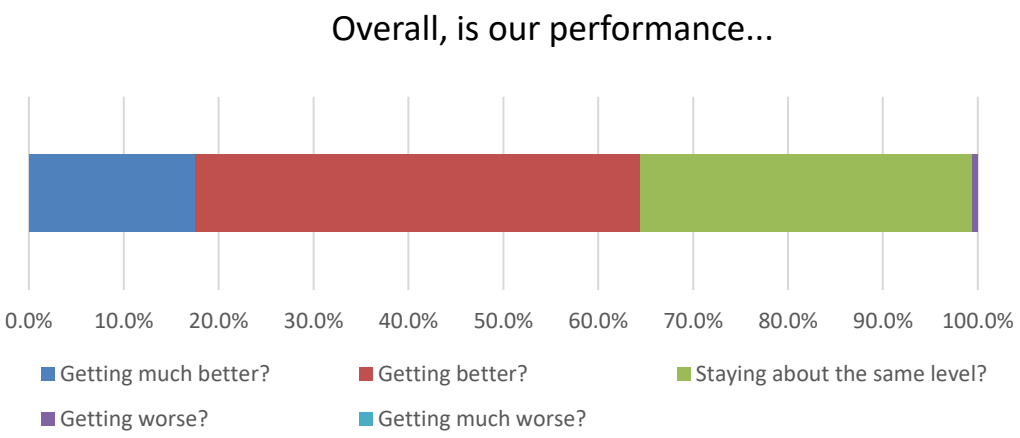
Q.22: What level of confidence do you have in us to deliver the products and services that you require?

(177 responses, 91.2% of responders for this section)



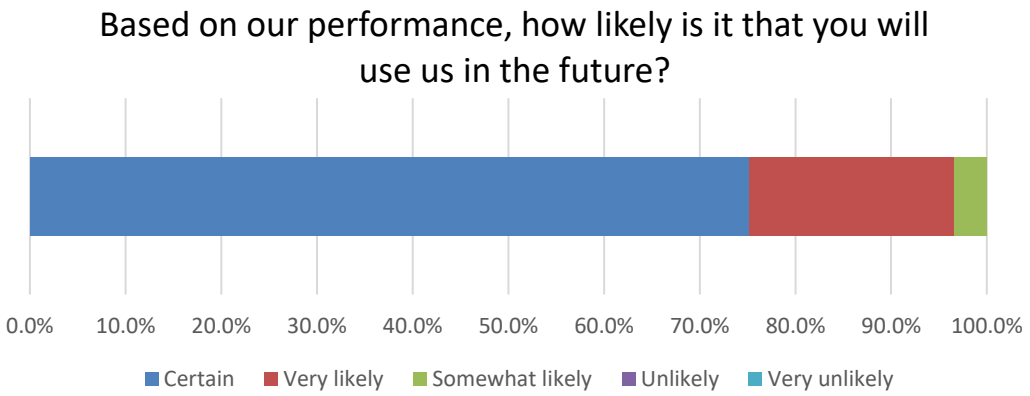
Q.23: Overall, is our performance…

(177 responses, 91.2% of responders for this section)



Q.24: Based on our performance, how likely is it that you will use us in the future?

(177 responses, 91.2% of responders for this section)



3.9. Summary of Remarks, comments or suggestions for improvements (Q.14 & Q.25)

- We received a total of 81 comments from 57 respondents that answered one or both questions asking for scheme related remarks or comments (Q.14), or overall suggestions for improvements (Q.25).
- We have selected a number of these comments to respond to below.

Participant Comment	ERNDIM Response
1. Administration	
• Please can ERNDIM become an ISO accredited EQA provider • ERNDIM HAS TO BECOME ACCREDITED	• We are working towards applying for accreditation but this is quite complex due to the variety of schemes that we offer and we appreciate your patience in this matter.
• Billing - The deadline is 1st April. Starting from December, we receive multiple requests/reminders to pay. However, our institution plans in advance to pay shortly before the deadline, but finds it irritating to receive monthly reminders well before that. • The frequency of the reminders for paying the invoice for the schemes is high. This is for our setting in our institute very inconvenient.	• For some participants who have experienced email receipt problems or have missed previous reminders these emails are very important. Although the payment deadline is in early April payment can be made earlier and once payment has been received no further payment reminders are sent.
• Invoice is sent out too early. Our hospital generally pays after delivery of a service.	• The invoices are sent out 3 months before the payment deadline as many institutions require this amount of time to process the payment.

Participant Comment	ERNDIM Response
• We are quite happy with the schemes. It would be nice to have the certificates a bit earlier. • We increasingly require quality certificates from our laboratory for external clinics. It would be great if there were proof of quality or confirmation that we participate in extern round robin tests. Thanks very much.	• Certificates of Participation for all eligible participants are published after the end of each scheme year. • The aim is for these to be published in by the end of March after the scheme year has ended. However, the 2022 and 2023 certificates were published later than this and we are working on improving this for next year.
• The participant survey is repetitive and some item may be filled as generic items (e.g. value for money, billing arrangement...)	• The annual participant survey has remained in the same format to easily compare and track responses over the years. However, we agree that some items such as billing do not need to be separated by scheme and the survey can be amended to reduce repetitiveness. We will look into this in advance of the next participant survey.
• We prefer digital meetings for the yearly workshops.	• In 2024 we have held several online technical and participant meetings, and these have been well received. We intend to keep some in-person events; however, we hope that there will be alternatives for participants who are unable to attend these.
2. EQA Schemes	
2.1. General	
• It would be useful to include some operations between January and March • The most important problem is not having samples for almost 5 months: from November to March	• For the quantitative schemes, the gap in EQA (November – March) relates to organisation issues which cannot be changed easily. • For the qualitative schemes, sample availability is the main reason for the gaps between the end one scheme year and the beginning of the next. • We have investigated options for extending the submission calendar but, due to operational issues this is not something that we can currently implement. However we will look at this again in the future.
• QTAS, QTOU, SAS, SAU and CWBC: 8 CQE samples a year to report is a lot and then we have nothing between November and March. One sample every 3 months is enough for most accreditation programs including ISO15189. Why don't we have only one result to report every 3 months (4 samples a year)? It would spread the work and be more regular. The labs who wants to perform more CQE analysis can do it by themselves (we do it between November and March). We have enough material for this	• The statistical design of the quantitative and hybrid schemes requires results to be submitted for at least 6 of the 8 samples in a scheme year
• It would be helpful to have documents for consent (for adults and children) and sample requirements on the website. Currently we have to contact the ERNDIM office, then the scheme organiser by which time the patient will have been treated, or discharged. It is not always possible to plan sample collection in advance.	• Further information regarding requirements for sample donation, including consent forms, are included on our website (https://www.erndim.org/eqa-schemes/sample-donations/). We ask that you still contact the ERDIM office, so that we can direct you to most appropriate scientific advisor.
• The system for reimbursement for submission of a sample is unclear. It would be easier to have the discount the year following sending in a sample. We have previously not received a discount when a sample has been used, and it is now difficult to keep track of this, particularly as we have submitted several samples.	• For some schemes we offer a 20% discount off the relevant scheme if a participating laboratory has donated a sample that was used as EQA material for the previous scheme year and we acknowledge the origin of donated samples in the relevant annual reports. As not all clinical samples are suitable for EQA, we only apply this discount if the sample was used. If you believe that a sample donation discount was mistakenly not added to your account, please contact admin@erndim.org

Participant Comment	ERNDIM Response
• Consider providing different costing for the quantitative amino acids in serum, that is, based on the number of amino acids per panel. Since the time we participated in ERNDIM, we are only participating in maximum of 27 amino acids. The rest, which is quite a number, we do not subscribe to. This would ease the burden of paying more for amino acids that we do not subscribe to.	• Quantitative EQA samples are manufactured in advance of registration, and we are therefore unable to manufacture individual samples for each participant. In addition, registration fees cover administrative costs of running the EQA scheme and are not based solely on the physical value of the EQA sample.
• Can we request the logistics company? I want to use the service of FedEx company because it delivers the sample direct to us.	• If you would like to specify a specific logistics company (DHL, FedEx, or TNT), please contact admin@erndim.org during registration.
• We would like to see more precise coding of the techniques and analysers. For example : immunoassay is not very discriminant. ELISA sandwich is more accurate, and ELISA sandwich with a COBAS e801 (ROCHE) would be perfect to compare with pairs. It's the same remark for LC MS MS methods : it would be interesting to compare with Water's users , like us.	• Overall performance is assessed against consensus values of all labs, and is independent of analysis method. Although labs may be interested in comparing their results against other labs with the same method, more precise coding of techniques may result in small sample groups and uninformative statistics. Therefore, we provide only limited statistics based on analysis method. However, we are currently in the process of reviewing the list of methods available on the results website, with the aim of harmonising these across the schemes, and will inform participants of any changes.
• It would be great if we could have the z-score according to the method	• See above. Currently z-scores are provided in the cycle review for a labs value compared to all other labs.
• For the qualitative programs - for patient anamnesis (medical history), include relevant treatment(s). We also would like to stress the opportunity to receive the anamnesis earlier for these programs to be able to reach a diagnosis before deadline.	• We will work with Scientific Advisors to standardise the level of detail in clinical information across schemes. • We release clinical information 3 weeks before the submission deadline to ensure analysis is conducted throughout the year. We ask that you analyse these samples in the way your laboratory would treat routinely tested patient samples. As we currently have very few late submissions requests, there are currently no plans to change this.
• The inclusion of informative mass spectra of specific new metabolites could be included in the reports. This information is not always provided.	• We are working to harmonise the level of detail in ERNDIM Annual Reports. We have internal guidelines for the generation of annual reports, and this suggestion can be included.
• Reports regarding qualitative schemes should be more detailed: explanation of pathologic profiles	• See above
2.2. Website reporting	
• The qualitative scheme website is complicated to navigate. • Qualitative UOA website is difficult to use (too much back and forth). Thanks! • the website remains slow despite the ongoing participants feedback about this issue. it would be great if ERNDIM could seriously consider improving the website.	• We are sorry participants are having problems with the results website for the qualitative schemes. We are continuing to work with the scheme organiser on improving this but if you have any specific suggestions for improvements please contact admin@erndim.org.
• a possibility to report concentrations below LLOQ, and take this point into account for statistical analysis, would be welcome • Special assay in urine - the website does not allow submission of results <LLOQ. We submit results below LLOQ in the text comment. However this then impacts our stats/reports as these results are not included etc. • Improve reporting capabilities for analytes that may be below the reportable range	• The instructions for the quantitative and hybrid schemes state that for values below a lab's LLOQ 'zero' should be entered. Please note if one or more result is entered that contains anything other than numbers or a decimal point, no results on the page will be saved by the website. However, for your own information, you can add a comment to the results submission page.

Participant Comment	ERNDIM Response
• Would it be possible to distinguish the figures of merit (recovery, accuracy, precision and linearity) based on two concentration levels/range, that is, low and high concentration range?"	• This was discussed at the 2023 Scientific Advisory Board meeting in Sitges, Spain. It was decided that this would not be informative for most labs, and there are currently no plans to implement this.
• It is unfortunate for the quantitative programs for AA, aCCA, SAS and SAU that errors such as entry in micromol/L instead of mmol/L can not be corrected. The result is that the next annual report is useless.	• We recommend that all participants review their results after submission and before the relevant cycle review has been published. If any mistakes are discovered you should contact admin@erndim.org as soon as possible. However, for the Quantitative and Hybrid schemes using the MCA results website, the 'cycle review' reports are published 2 weeks after the deadline, and it is not possible for any submitted results to be changed after these have been published.
2.3. Acylcarnitines in DBS	
• Qualitative BS acylcarnitine scheme - the interim reports take much too long to come back. • The DBS acylcarnitines qualitative scheme has not had a report for 2023 and we did not receive final versions of the 2022 report. • It would be helpful to have the reports of the schemes soon after the results have been submitted. The current situation with the DBS acylcarnitines is quite difficult.	• We apologise for the delay in these reports being published. The delays were due to software issues which we are working with the scheme organiser to resolve. • All reports for the 2022 and 2023 ACDB schemes should now have been published. However if you find you cannot access a scheme report please contact us at admin@erndim.org
2.4. Amino Acids Interpretation	
• Is it possible to add Interpretative aa to the web page?	• Unfortunately, this is not currently possible but we are investigating options for website submission for this scheme.
• We sincerely appreciate ERNDIM for offering the Amino Acid Interpretation. However, would it be possible to include the method parameters which were employed to obtain the amino acid results presented for interpretation? For instance, our lab is not measuring amino acids in urine but there was one case in which the amino acid concentrations provided were obtained from urine. We would also like to consider how the amino acid levels vary depending on the matrix.	• In 2024, the analysis method and the matrix are included in the case information.
2.5. 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.
2.6. Lysosomal Enzymes in fibroblasts scheme	
• Clearer reporting for lysosomal enzymes in fibroblasts scheme where enzymes not covered by the lab aren't included in the (negative) scoring as missed diagnosis if reported with a caveat of "not all LSDs excluded". • We cannot provide an accurate interpretation since we do not analyze all enzymes.	• If a participant does not find the diagnosis because it does not measure the enzyme involved, it will not be punished for that. Some participants did not fill in a diagnosis because they did not measure all 10 enzymes, which is incorrect: "No obvious enzyme deficiency" should be selected if a participant does not find an enzyme deficiency. In LEFB 2024 the instructions have been changed to "No obvious enzyme deficiency based on the enzymes measured". Moreover, it is even more emphasised that at least one option (diagnosis or no obvious..) must be chosen.
• Provide medical history to the samples in the lysosomal scheme	• Clinical symptoms, age and gender will be provided where possible, starting from LEFB 2024.
• Without arylsulfatase A, arylsulfatase B, hexosaminidase A, hexosaminidases AB, the Lysosomal Enzymes in Fibroblasts offers poor coverage for the range of enzymes our laboratory is in charge of.	• Currently only 10 enzymes can be measured in each scheme round, so a selection has to be made. There are a core set of 4 enzymes that are included every year, and 6 other enzymes are selected each year.

Participant Comment	ERNDIM Response
2.7. Qualitative Organic Acids	
• If you could revert to providing 3 cycles (3 samples x 3 cycle = 9 samples) for the Qualitative Organic Acids, our laboratory would highly appreciate it.	• The change from 9 samples to 6 samples was introduced due to difficulties in collecting sufficient samples of a large enough volume to deliver 9 samples from all 3 QLOU centres each year, and brings this scheme in line with the other qualitative schemes which all include 6 samples with 2 submission deadlines. • For information regarding sample donation please visit: https://www.erndim.org/eqa-schemes/sample-donations/
• Qualitative UOA sample volume does not allow full volume extraction, nor does it allow for repeat extraction when needed - sample is not treated like patient samples as a result	• Unfortunately, QLOU sample volume is limited by the availability of patient sample material. Additional sets of samples are available for purchase for the small number of participants requiring a larger volume for their method.
2.8. Special Assays in serum	
• NEFA: same concentration through the year is not optimal for quality control.	• NEFA is not added to the samples but is present in the serum matrix used to produce the samples. Due to demand from participants, NEFA values can be submitted to the results website to allow comparison between labs. As the concentration does not vary, it is not suitable for proficiency testing and therefore is not included on the certificates of performance or the annual reports.
• Phytanate concentration are never of a level seen in Refsum patient. It would be beneficial to assess/compare performance at a higher level.	• It is anticipated that VLCAs and phytanic/pristanic acids will be moved to the Lipids in Serum (LIS) scheme which is currently in pilot stage. This will be discussed with the scientific advisor of LIS.
• Add any of the PUFA to the SAS or the pilot Lipid Schemes (DHA, EPA, arachidonic...).	• This will be discussed with the scientific advisor of LIS (see above)
2.9. Special Assays in urine	
• Urine SAS could include a higher cystine concentration please	• We agree with this suggestion and are working to solve solubility problems for the 2025 scheme.
• Sulphocysteine highest conc in the last three years was around 35 umol/L. MoCo/SOD patients tend to be much higher than this, so a pair of samples at a higher concentration would be useful.	• For 2025, we will ask MCA Laboratories about the possibility of increasing the concentration to 100 umol/L in 2 pairs (dependant on costs).
• Can you elaborate why some organic acids are part of the special urine assay and not on the organic acids panel (eg. homogentistic acid)	• In the past, some labs had dedicated methods for a few organic acids (for example oxalate) and may not wish to take part in a full scheme of organic acids. In addition, some analytes are duplicated in both schemes. The scientific advisors of QTOU and SAU will discuss together any changes to their schemes.
3. Suggestions for future schemes	We do welcome suggestions for future schemes but unfortunately it is not possible to cater for every request.
• Lysosomal Enzymes in DBS	• This is something ERNDIM would like to be able to introduce. However, the ability to plan a future pilot scheme is dependent on sample availability. Please visit https://erndim.org/home/qascheme.asp for further information about donating samples.
• Lipids	• In 2024, ERNDIM is running a Lipids in Serum Pilot scheme. We anticipant this will be run as a pilot scheme for 2 years before being considered as an official ERNDIM EQA Scheme
• Untargeted Metabolomics	• This is something that ERNDIM is considering, see section 3.7 of the participant survey report.

END