2025 Participant Survey Report:
[2024 scheme year]

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1. Introduction

- The ERNDIM Participant Survey was sent to 822 contacts from 413 centres, on 3rd February 2025, and was closed on 3rd March 2025. We asked participants to answer questions relating to the 2024 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.
- One of the best scoring aspects for ERNDIM EQA scheme was for the 'Usefulness 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 98.6% of respondents rated the quality of services provided by ERNDIM as 'excellent' or 'good'; with 95.8% 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.
- 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 basis of 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.
- The Lipids in Serum (LIS) pilot scheme has now been running for two years, and discussions are underway to consider establishing it as an official ERNDIM EQA scheme. We are also investigating the feasibility of other suggested schemes such as lysosomal enzymes in dried blood spots and amino acids in dried urine samples. Future pilots for qualitative schemes are dependent on sample availability. Please contact ERNDIM for further information about donating 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 useful (see page 13) and we would welcome any other comments or suggestions for improvements.

3. Survey Responses

- 153 individuals from 143 centres in 44 countries responded to the survey. The response rate is lower than in the 2023 scheme year survey. The response rate by centre was 35.0% (compared to 45% in the 2023 scheme year survey).

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

- The response rate was lower for all but two schemes than for the 2023 scheme year survey. The biggest decrease was for AAI (41% for 2024 compared to 58.5% for the 2023 scheme year). 2024 is the second year that AAI has been a full scheme.
- The response rate was higher for CDG than in the 2023 scheme year survey (45% for 2024 compared to 40% for 2023). For NCSF, the response rate was marginally improved (37% for 2024 compared to 35% in 2023).

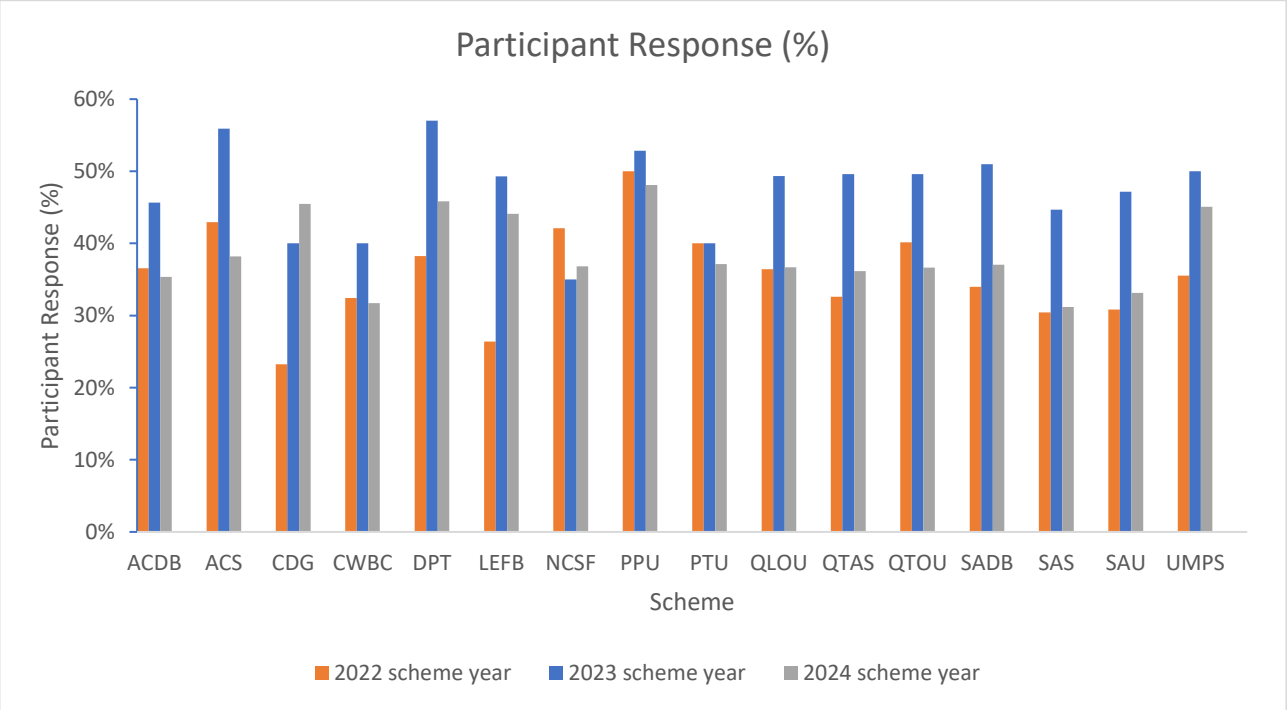


Figure 1. Survey responses per EQA scheme (Question 1) as a percentage of the EQA scheme participants

Key

EQA Scheme	Code	EQA Scheme	Code
Amino Acids Interpretation	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
- 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 1.6, which is an improvement from the 2023 scheme year (1.7).
- Two EQA schemes had the same score as last year (ACS, LEFB), 14 schemes had a better score than last year (ACDB, CDG, CWBC, DPT, NCSF, PPU, PTU, QLOU, QTAS, QTOU, SADB, SAS, SAU, & UMPS) and no schemes had worse scores. 2024 is the second year that AAI has been a full scheme and had an average score of 1.6. All schemes scored ≤ 1.8.
- The CDG and LEFB schemes had the lowest score (1.8). However, for CDG, this was an improvement from 2023 (2). There was no change in score for LEFB from 2023.
- The average score for individual aspects marginally improved when compared to the 2023 scheme year (1.7 in 2023 to 1.6 in 2024).
- The worst scoring aspects were 'Value for Money' with an average score of 1.8, and 'Sample Volume', 'Website Display', and 'Appropriateness of Analyte Concentration' with an average score of 1.6. The best scoring aspects were 'Frequency of Samples', 'Adequacy of the Report' and 'Usefulness of the Annual Report' which all scored 1.5.

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

	Average Scores												
EQA Scheme	**2024**	**2023**	**2022**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2015**	**2014**	**2013**	**2012**
All schemes	**1.6**	**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	1.6	1.7	-	-	-	-	-	-	-	-	-	-	-
ACDB	1.6	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	1.7	1.6	-	-	-	-	-
CDG	1.8	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	1.6	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	1.5	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	1.8	1.7	1.7	1.8	1.9	1.8	1.7	1.8	1.9	1.9	2.0	1.9
NCSF	1.6	1.8	1.7	1.6	1.9	1.8	1.8	1.9	1.7	-	-	-	-
PPU	1.5	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	1.6	1.7	1.7	1.6	1.6	1.5	1.8	1.9	-	-	-	-	-
QLOU	1.6	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	1.6	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	1.6	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	1.6	1.8	1.8	1.7	1.7	1.8	-	-	-	-	-	-	-
SAS	1.6	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	1.6	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	1.6	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 in the survey, with a score of 2.5, marginally improved from 2023 (2.8). No other aspects of any scheme scored above 2.0 in the survey.
- The best scoring aspects in the survey was for ‘Sample Volume’ for PPU (1.3).

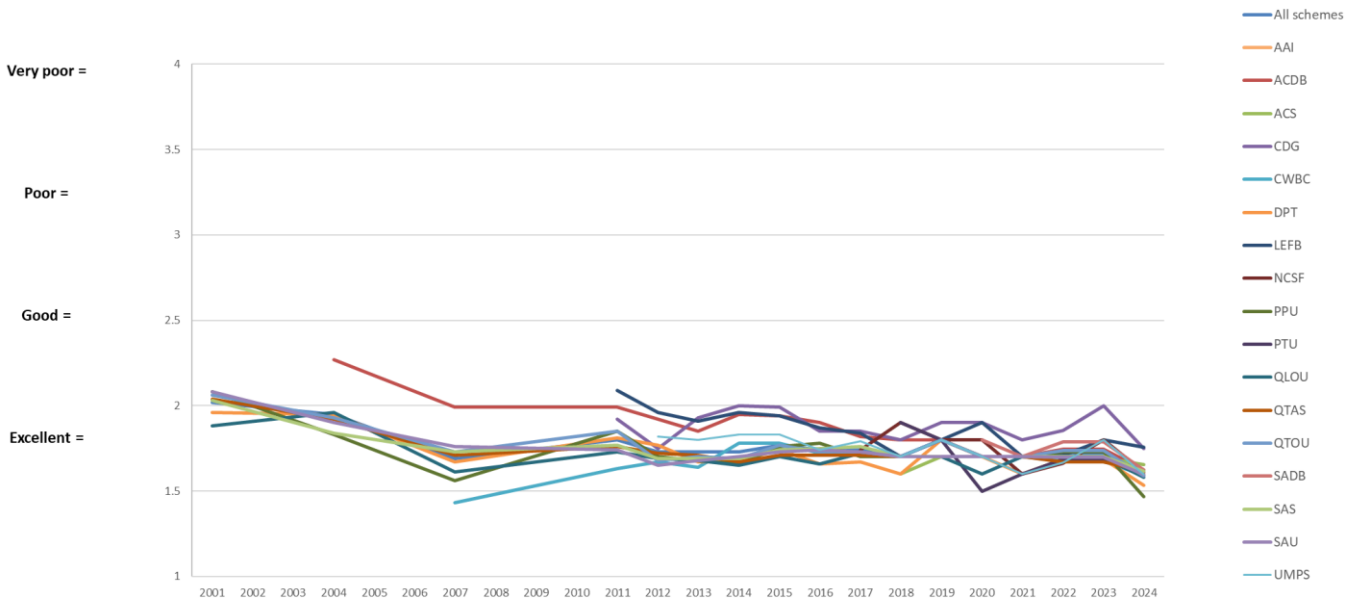


Figure 2. Average score per EQA scheme (Question 1) [See Figure 1 for key to scheme codes]

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	Average per scheme	No. of responses (% of scheme participants)
AAI	1.6	-	-	1.8	1.6	1.5	1.7	1.6	58 (41%)
ACDB	1.6	1.8	-	1.7	1.4	1.4	1.8	1.6	47 (35%)
ACS	1.6	1.6	1.7	1.7	1.7	1.6	1.7	1.7	48 (38%)
CDG	1.4	2.5	-	1.7	1.6	1.4	1.8	1.8	26 (45%)
CWBC	1.5	1.7	1.5	1.6	1.6	1.6	1.7	1.6	13 (32%)
DPT	1.4	1.6	-	1.8	1.4	1.4	1.6	1.5	45 (46%)
LEFB	1.6	1.9	1.8	1.7	1.7	1.7	1.9	1.8	34 (44%)
NCSF	1.5	1.9	1.6	1.6	1.5	1.5	1.7	1.6	14 (37%)
PPU	1.4	1.3	1.6	1.4	1.4	1.5	1.6	1.5	25 (48%)
PTU	1.5	1.8	1.8	1.4	1.5	1.4	1.9	1.6	13 (37%)
QLOU	1.5	1.8	-	1.7	1.4	1.4	1.7	1.6	86 (37%)
QTAS	1.5	1.5	1.7	1.6	1.6	1.6	1.8	1.6	96 (36%)
QTOU	1.5	1.5	1.6	1.6	1.6	1.6	1.7	1.6	49 (37%)
SADB	1.6	1.7	1.6	1.6	1.6	1.6	1.8	1.6	40 (37%)
SAS	1.5	1.6	1.6	1.6	1.6	1.7	1.7	1.6	79 (31%)
SAU	1.4	1.6	1.6	1.6	1.5	1.6	1.8	1.6	65 (33%)
UMPS	1.4	1.8	-	1.7	1.5	1.4	1.8	1.6	41 (45%)
Average for all schemes	1.5	1.7	1.6	1.6	1.5	1.6	1.7	1.5	143 (35%)

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

- A total of 58 individuals (37.9% 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.

4.1. Acylcarnitines – Serum (ACS)

Suggested Analytes to be added (8 responses, 17% of ACS respondents)		**Suggested Analytes to be removed** 1 response (2% of ACS respondents)	
Total suggested = 10		Total suggested = 3	
Analytes with >1 responses		**Analytes with ≥ 1 response**	
C14	2	Tripeptidyl peptidase I	1
C18:2OH	2	Arylsulfatase B	1
		β mannosidase	1

ERNDIM Response:

- No changes are planned for the 2026 scheme year.
- There is the potential for interference between C14 and the existing scheme analytes which is why C14 was removed from the scheme previously.
- C18:2OH could be included in the future, provided C18:1-OH is not introduced. This precaution is necessary as the majority of participants employ FIA methods and C18:2OH concentrations could interfere with C18:1-OH in FIA.

4.2. Lysosomal Enzymes (LEFB)

Suggested Analytes to be added (11 responses, 32% of all LEFB respondents)		**Suggested Analytes to be removed** (6 responses, 18% of all LEFB respondents)	
Total suggested = 10		Total suggested = 5	
Analytes with >1 response		**Analytes with >1 response**	
β-Hexosaminidase (A+B)	5	Acetyl-CoA-glucosamine acetyltransferase,	3
Sphingomyelinase	3	β mannosidase	2
β-Hexosaminidase A	3		
N-acetylglucosamine-6-sulfatase	2		
β-Glucuronidase	2		
β-galactocerebrosidase (Krabbe)	2		
α-fucosidase	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.

4.3. Neurotransmitters – CSF (NCSF)

Suggested Analytes to be added (1 response, 7% of NCSF respondents)		**Suggested Analytes to be removed**	
Total suggested = 8		Total suggested = 0	
Analytes with >1 response		**No Analytes suggested**	
Pyridoxal-Phosphate	1		

ERNDIM Response:

- No changes planned.
- Pyridoxal phosphate will not be added at this time as there are potential problems with stability on freeze-thawing in artificial CSF.

4.4. Purines & Pyrimidines – Urine (PPU)

Suggested Analytes to be added (3 responses, 12% of all PPU respondents)		**Suggested Analytes to be removed**	
Total suggested = 16		Total suggested = 1	
Analytes with >1 response		**Analytes with 1 response**	
2,8-Dihydroxyadenine	2		
SAICAR	1		
Orotidine	1		

ERNDIM Response:

- While we planned to include orotidine in the 2025 scheme samples, unforeseen issues led to its removal from assessment. We are optimistic that orotidine will be present in the 2026 samples.
- The inclusion of 2,8-Dihydroxyadenine is chemically not possible and the inclusion of SAICAR is not economically viable for participants or ERNDIM.
- We would like to distribute APRT and ADSL clinical samples in a future PPU scheme, however, we require donations of untreated APRT and ADSL urine samples. If you are able to donate, please contact the ERNDIM office at admin@erndim.org.

4.5. Pterins – Urine (PTU)

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 = 0		Total suggested = 1	
No Analytes suggested		**No Analytes Suggested**	

ERNDIM Response:

- There are currently no changes planned for 2026.

4.6. Quantitative Amino Acids (QTAS)

Suggested Analytes to be added (13 responses, 14% of all QTAS respondents)		**Suggested Analytes to be removed** (8 responses, 8% of all QTAS respondents)	
Total suggested = 22		Total suggested = 7	
Analytes with >1 response		**Analytes with >1 response**	
Homocystine	7	Sulfocysteine	4
phosphoethanolamine	4	Argininosuccinic acid	2
Homocitruline	3	SARCOSINE	2

ERNDIM Response:

- There are currently no changes planned for 2026.
- Homocysteine was requested by 7 participants, however, it lacks the stability to be included.

4.7. Quantitative Organic Acids (QTOU)

Suggested Analytes to be added (6 responses, 12% of all QTOU respondents)		**Suggested Analytes to be removed** (2 responses, 4% of all QTOU respondents)	
Total suggested = 8		Total suggested = 3	
Analytes with >1 response		**Analytes with ≥ 1 response**	
methylsuccinic acid	2	malic acid	1
succinic acid	2	Malonic acid	1
propionylglycine	2	2-hydroxyglutaric acid	1
orotic acid	2		

ERNDIM Response:

- The removal of Malonic acid was requested; however, it was only recently added following a request from a previous survey.
- Orotic acid is already included in the SAU scheme, it is not practical/cost effective to include it in both schemes.
- No relevant proposition for adding or removing compounds.

4.8. Special Assays – Dried Blood Spots (SADB)

Suggested Analytes to be added (9 responses, 23% of all SADB respondents)		**Suggested Analytes to be removed**	
Total suggested = 22		Total suggested = 0	
Analytes with >1 response		**No Analytes Suggested**	
methylcitric acid	4		
methylmalonic acid	4		

ERNDIM Response:

- SADB contains many unrelated analytes which are analysed using several different assays. This makes assessing the scheme results and writing the annual report difficult. Therefore, there are no proposed changes to the analyte list for the 2026 scheme year.

4.9. Special Assays – Serum (SAS)

Suggested Analytes to be added (15 responses, 19% of all SAS respondents)		**Suggested Analytes to be removed** (1 response, 1% of all SAS respondents)	
Total suggested = 25		Total suggested = 1	
Analytes with >1 response		**Analytes with 1 response**	
C24-LPC	2	L-Pipecolic acid	1
more Carnitines	2		
desmosterol	2		
lathosterol	2		

ERNDIM Response:

- Lipids are currently available in the Lipids in Serum (LIS) pilot scheme and discussions are underway to establish LIS as a full ERNDIM scheme. As the SAS scheme currently includes a large number of analytes, lipids will not be added.
- We do not anticipate adding more carnitines as there is already an acylcarnitine in serum scheme where these can be tested.

4.10. Special Assays – Urine (SAU)

Suggested Analytes to be added (11 responses, 17% of all SAU respondents)		**Suggested Analytes to be removed** (2 response, 3% of all SAU respondents)	
Total suggested = 18		Total suggested = 2	
Analytes with >1 response		**Analytes with 1 response**	
Phosphoethanolamine	2	homogentisic	1
		Orotic acid	1

ERNDIM Response:

- We are exploring adding Phosphoethanolamine, but due to the large number of analytes included in the SAU scheme, it may not be possible to include more analytes at this time due to solubility and possible interactions of analytes.

5. Special Questions

5.1. Does your laboratory use any of the Internal Control Materials provided by MCA laboratories?

- 141/153 (92.2%) respondents answered this question.

Response	Number of respondents
Yes	68 (48%)
No	55 (39%)
No, but we may use these in the future	15 (13%)

5.2. 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?

- 26/153 (17%) respondents answered this question, several of these responses are included below:
  - Biotinidase (n=1)
  - Homocystein (n=2)
  - Methylmalonic acid DBS controls (n=2)
  - Calibrators for lyso-GB1 and lyso-GB3 (n=1)
  - Glycine in CSF (n=1)
  - Methylcitric acid in DBS (n=1)
  - Neurotransmitters in CSF (n=1)
  - Special assays in serum kit (n=1)
  - IQCS for mucopolysaccharides - chondroitin, heparan and dermatan sulfates (n=1)
  - Urine cystine, ornithine, arginine and lysine (n=1)

5.3. Does your laboratory use any of the organic acid standards provided by AUMC in Amsterdam? If yes, please specify since which year. *Only QTOU participants answered this question*.

- 47/48 (98%) respondents answered this question.

Response	Number of respondents
Yes	12 (25.5%)
No	35 (74.5%)

- 2025 (n=1), 2023 (n=1), 2022 (n=1), 2020 (n=1), 2018 (n=2), 2017 (n=1), 2016 (n=1), 2015 (n=2).

5.4. Does your institute currently perform dried urine amino acid analysis? If yes (please specify the method your laboratory uses for this analysis).

- 126/153 (82.4%) respondents answered this question.

Response	Number of respondents
Yes	6 (4.8%)
No	103 (81.8%)
No, but we may in the future	14 (11.1%)

- Methods of analysis: Tandem mass spectrometry coupled to UPLC (n=1), MS/MS (n=1), Waters AccQ.Tag with UPLC-UV (n=1).

5.5. Would you be interested in an EQA scheme that analyses amino acids in dried urine samples?

- 119/153 (77.8%) respondents answered this question.

Response	Number of respondents
Yes	27 (22.7%)
No	92 (77.3%)

5.6. Would your laboratory be interested in adding NTBC for monitoring patients with Tyrosinemia type I to the Special Assays in Serum scheme?

- 83/153 (54.2%) respondents answered this question.

Response	Number of respondents
Yes	11 (13.2%)
No	33 (39.8%)
N/A	39 (47%)

5.7. Would your laboratory be interested in adding Cysteamine for monitoring patients with Cystinosis to the Special Assays in Serum scheme?

- 78/153 (51%) respondents answered this question.

Response	Number of respondents
Yes	4 (5.1%)
No	30 (38.5%)
N/A	44 (56.4%)

5.8. 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.

There were 13 suggestions from this survey for sample exchange programmes, and these have been sent to the Scientific Advisory Board for discussion.

5.9. 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.

5.9.1. Is your laboratory currently providing an Untargeted Metabolomics test for diagnostic purposes?

- 137/153 (89.5%) respondents answered this question.

Response	Number of respondents
No, we do not have Untargeted Metabolomics in use or in development	119 (86.9%)
We are currently developing an Untargeted Metabolomics test for diagnostic use	10 (7.3%)
We have Untargeted Metabolomics available but for research use only	8 (5.8%)
Yes, we offer a diagnostic Untargeted Metabolomics test	0 (0%)

5.9.2. Would your laboratory be interested in participating in an Untargeted Metabolomics pilot scheme?

- 135/153 (88.2%) respondents answered this question.

Response	Number of respondents
No	70 (51.9%)
Not yet, perhaps in 5 or more years	20 (14.8%)
Not yet, perhaps in 2 or more years	33 (24.4%)
Yes	12 (8.9%)

5.9.3. If you are interested in participating in an Untargeted Metabolomics pilot scheme, what sample type would be of most interest to you?

- 45/153 (29.4%) respondents answered this question.

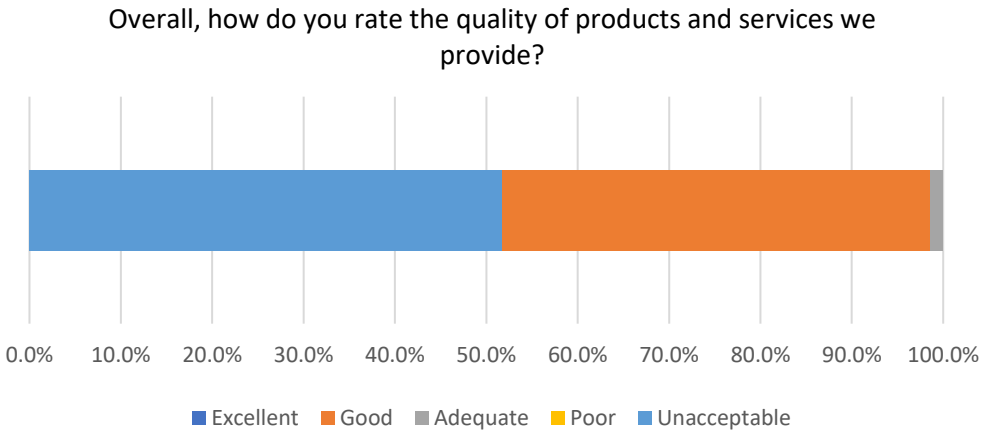
Response	Number of respondents
Urine	16 (11.9%)
DBS	2 (1.5%)
DBS and Serum/Plasma	1 (0.7%)
Urine and Plasma	1 (0.7%)
Plasma	25 (18.5%)

6. Comments on the overall performance of ERNDIM

- The aim of this section is to assess participants' perception of the overall performance of ERNDIM.
- In summary:
  - 98.6% of respondents rated the quality of services provided by ERNDIM as 'excellent' or 'good'; with 95.8% of respondents having 'complete' or 'a lot' of confidence that ERNDIM can deliver the service required by participants.
  - 71.7% of respondents agreed that overall ERNDIM's performance is 'getting better' or 'getting much better'; with 98.6% of respondents stating that it was 'certain' or 'very likely' that they would use ERNDIM services in the future.

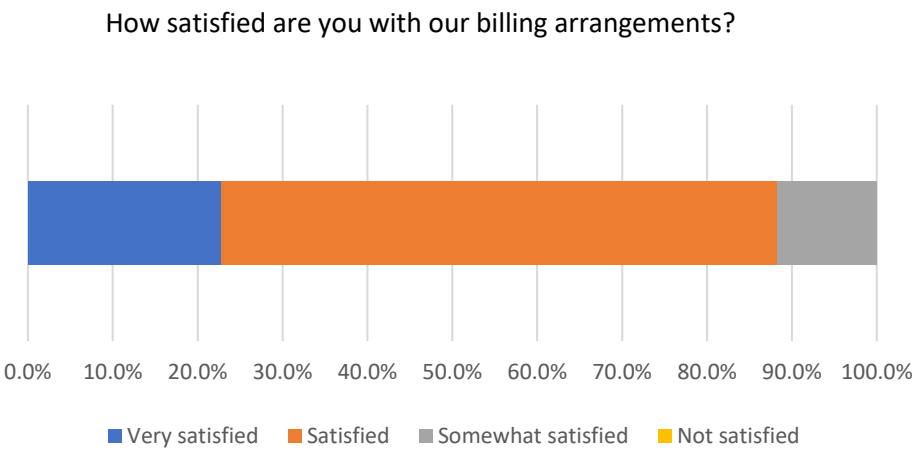
6.1. Overall, how do you rate the quality of products and services we provide?

(145 responses, 95% of responders for this section)



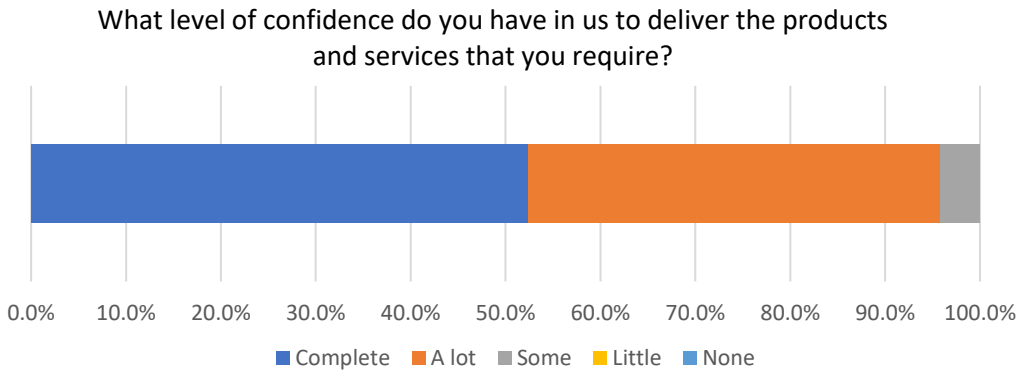
6.2. How satisfied are you with our billing arrangements?

(145 responses, 95% of responders for this section).



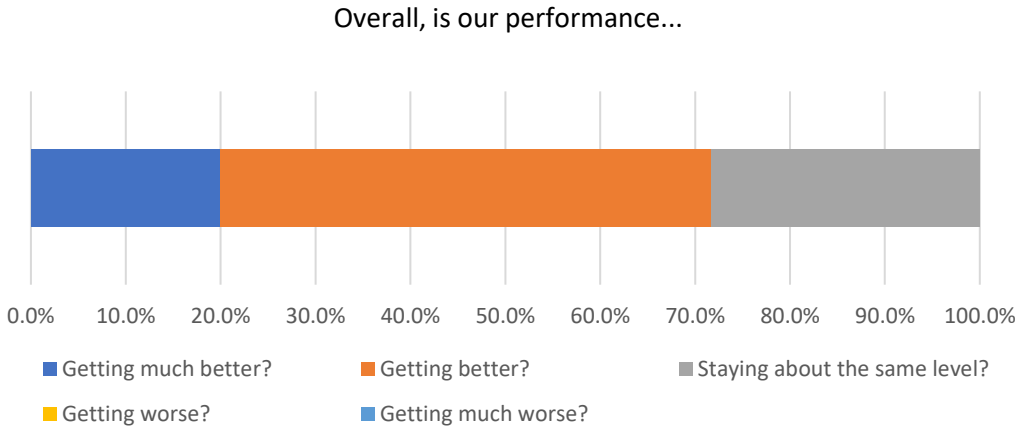
6.3. What level of confidence do you have in us to deliver the products and services that you require?

(145 responses, 95% of responders for this section)



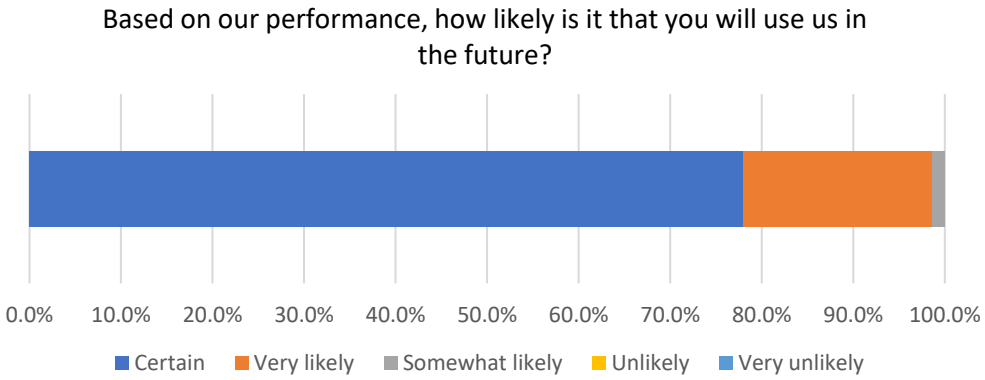
6.4. Overall, is our performance…

(145 responses, 95% of responders for this section)



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

(145 responses, 95% of responders for this section)



7. Summary of Remarks, comments or suggestions for improvements.

- We received a total of 59 comments from 38 respondents that answered one or both questions asking for scheme related remarks or comments, or overall suggestions for improvements.
- We have selected a number of these comments to respond to below.

Participant Comment	ERNDIM Response
Administration	
• If possible, please continue with the conduct of the ERNDIM Online Participants' workshop. This is for other participants who may not be able to attend SSIEM where the in person ERNDIM participant's workshop is usually held.	• While we understand that an online workshop format offers advantages in terms of accessibility and convenience for a broad range of participants, we also recognise the unique benefits of in-person events such as in-depth discussions and collaborations which is why our 2025 Workshop will be held in person. • However, our intention is to maintain a balance and we will continue to host online events such as the two technical meetings in 2025. We also aim to explore and direct participants to external travel bursaries and grants where applicable.
• Your service is great, thanks a lot for that. However, I would suggest trying to reduce the number of emails sent and try to send shorter concise text.	• We aim to minimise the number of emails and only send scheme-specific messages to relevant participants. However, we acknowledge that those registered for multiple schemes may receive a larger number of communications. We will work on making our messages more concise for clarity.
• To countries outside EU the delivery of EQA and QC materials should be more efficient to prevent materials exposed to high temperature also make sure that the courier delivers the materials in time keeping samples at the recommended temperatures.	• Unfortunately, once the courier has the package, delivery timing is outside our direct control and can be impacted by destination country customs, which can cause delays. However, EQA and QC materials have been either heat treated, or lyophilised, and have been extensively tested by the Scientific Advisor to ensure the metabolic profiles are preserved during transit. In all samples, the typical metabolic profiles are preserved. However, if you believe your samples may have been compromised by extreme temperatures, please contact admin@erndim.org and we can arrange a repeat sample dispatch.
• ISO17043 accreditation.	• We are working towards applying for accreditation, but this is quite complex due to the variety of schemes that we offer. We appreciate your patience on this matter.
• There could be more participants, if the cost of schemes were reduced or if a buy one get one free scheme is started.	• As a not-for-profit foundation, we aim to provide value for money through minimal administration costs while delivering high quality EQA schemes. While wider participation is a goal this would not lead to a reduction in costs. However, we do offer Laboratory Support Grants for institutions with financial constraints and a 20% discount for labs donating samples. Further information on donating samples can be found on our website https://www.erndim.org/eqa-schemes/sample-donations/.
• We have a new person in the hospital's quality area, so he asks us for training in the interpretation of the results obtained in the schemes registered with you; is it possible to get support on this issue from you? To whom should I escalate the request?	• Assessment frameworks are available on the ERNDIM participant website (https://eqa.erndim.org/information/view/14). • Please also see the relevant scheme annual reports available on our website (https://www.erndim.org/meetings-reports-cat/eqa-scheme-annual-reports/). • For further assistance, please contact the administration office, or the scientific advisor of the scheme.

Participant Comment	ERNDIM Response
EQA Schemes	
General Quantitative Scheme Comments	
• Quantitative assays are very intense and can be reduced. • Ideally, amino acids should be every month. At present, the scheme only offers an 8 months' supply. • My main comment concerns the distribution of EQA operations over the year. In fact, the number of operations over the year is correct, but there are no operations between November and March, which is unsatisfactory (5 months of the year with no external quality assessment).	• Decreasing the number of submissions per year for the Quantitative schemes would mean very long periods without EQA coverage which would not be acceptable. • For the quantitative schemes, the gap in EQA (November – March) relates to operational requirements which cannot be changed easily. • 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.
• We suggest to improve method field description and add specific fields in website for quantitative schemes for: 1) which specific internal standard is used for stable isotope dilution LC-MS/MS or GC-MS 2) and/or specify the use of an external calibration curve moreover as regards results data 3) add a field in the results visualization of "Analyte in detail" with the amount added to the sample	• We agree that it may be interesting to obtain such information from participants, although this information is not necessary for the evaluation of our schemes • The wide variety of different analysis methods that participants might require could make all that information unmanageable, and/or the statistics uninformative. We occasionally circulate surveys asking specific scheme related questions which allows for more careful, curated data collection.
• We would be interested in knowing which instruments/methods the other participants are using. This is often provided as information in other programmes.	• For quantitative schemes, methods used by other participants can be viewed on the MCA results website under the 'Analyte in Detail' report, however specific information regarding instruments used is not collected. • For qualitative schemes, method data is collected during result submission but is not routinely included in annual reports. We aim for consistency across reports and will explore whether this information can be included more broadly.
• Please include units of measurement for analytes on the report cycle review. This would be particularly useful for schemes with a range of unrelated analytes e.g. SAS. It would be interesting to read more detailed discussions about the varying analytical performance for different analytes in a scheme, for example the amino acids scheme has some analytes where all labs produce the expected results with very little variation, whereas other amino acids show wide variation in performance. Why is this? Are there recommendations for improvement in performance? It would be useful to have a mechanism for recording long-term assay performance. Currently we add all our results to a spreadsheet so we can compare results year-on-year, but would it be possible for ERDIM to provide this for laboratories to review their own long-term results?	• Thank you for your suggestion to add the units of measurement for analytes on the report cycle review. We will work with the website developers to see if it is feasible to implement this. • For further discussion of the analytical performance for different analytes in a scheme, please see the scheme annual reports. Please note that some schemes contain a large number of analytes, and it is not practical to comment on all analytes in a scheme. • If you would like specific advice on how to improve performance, please contact the scientific advisor of the scheme. • We welcome your thoughts on how to improve the reporting of results. Please contact admin@erndim.org with your suggestions.
• Reporting: inclusion of SD improves interpretation of the z-score. Please provide systematic explanation of all indicators on every report.	• The standard deviation is reported on the 'Analyte in detail' page on the MCA result website. If you would like to suggest additional indicators to be included on each report, please contact admin@erndim.org. The explanation of reports can be found on the MCA results website under 'General Information' → 'Use Website'.

Participant Comment	ERNDIM Response
• The internet page www.erndimqa.nl is a bit slow.	• We are sorry participants are having problems with the results website for the quantitative 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.
General Qualitative Scheme Comments	
• In the reports we receive for qualitative organic acids, MPS and lysosomal enzymes, we sometimes disagree with the score received, so we would like to know how these requests are managed and have a clear explanation of them.	• If you wish to query a score, please contact admin@erndim.org and we will refer it to the Scientific Advisor where appropriate. Please note that interim scores in qualitative schemes are provisional and may be reviewed by the Scientific Advisory Board at year-end. • Further details regarding the scoring policy and appeals are available on the ERNDIM participant website (https://eqa.erndim.org/information/view/14). Further information can also be found in the annual reports.
• The SOPs for different assays may be provided e.g. SOP for urine qualitative organic acid profile.	• For technical advice, please contact the Scientific Advisor of the scheme. • Please see diagnostic method overviews on our website https://www.erndim.org/resources/ • We highly recommend the following textbook: 'Laboratory Guide to the Methods in Biochemical Genetics' by N Blau and F Vaz.
• For some operations (e.g. AA interpretation and Qualitative organic acid), the proposed cases are not always relevant in the sense that the techniques are not the most suitable for making the diagnosis. For example, detecting an aminoacidopathy using organic acid chromatography may be obvious in some cases, but in others the cases presented are a bit "far-fetched". You should sometimes consider simpler cases, closer to what is observed in everyday life (rather than these "exotic" cases). This applies in particular to the AA interpretation scheme.	• We understand that there are mix of participants who will appreciate a range from 'normal' healthy profiles to more frequent disease profiles and rarer cases. Every condition included in a scheme is expected to be able to be detectable by all participants and we are not trying to trick any labs. The cases in AAI are based on real world patients. We are trying to cover a range of disorders and will consider any responses to poor performance letters based on the experience of the laboratory. • On occasion we do recognise that a sample may be more challenging than initially expected, in these circumstances the Scientific Advisory Board will discuss whether it is appropriate to include this sample in the scoring. Under these circumstances a sample may be classified as an "educational sample" and excluded from scoring to ensure participants are not disadvantaged.
• Better repartition over the year: instead of stopping 4 consecutive months during winter, it may be better to stop 2 months in summer (July and August) and 2 months in winter (December and January). • Interpretative assays are very educational, and we are happy to perform more intense (eg 3-4 times a year).	• For the qualitative schemes, limited sample availability is the main reason for the gaps between the end of one scheme year and the beginning of the next. We have investigated options for extending the submission calendar but, due to operational constraints this is not something that we can currently implement. However, we will look at this again in the future.
• The CSCQ website continues to be a pain. Very clunky and I curse at it regularly. Would love to see that changed but understand that it's not that simple.	• 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

Acylcarnitines in Serum	
• Concentration range for quantitative acylcarnitine in serum is quite high; might consider decreasing the concentration range of the acylcarnitine to within the normal reference ranges (regardless of the country of origin/population).	• The concentration range covers normal and pathological values. In some ACS samples, most of the values on the calibration curve approach normality, thus ensuring better measurement. However, in other cases, it is also important to maintain accuracy at high values, for when the patient is under follow-up and usually presents values above the reference values, such as C3 in propionic or methylmalonic acidemias.
CDG scheme	
• No penalties for CDG-patients with normal profiles.	• The cases in the CDG scheme aim to cover a range of disorders and it is expected that every condition we send out will be picked up by all labs. 'Penalties' or 'Critical Errors' are assigned to interpretations that would be unacceptable to the majority of labs and would have a serious adverse effect on patient management. Further details regarding the scoring policy and appeals are available on the ERNDIM participant website (https://eqa.erndim.org/information/view/14). Additional information can also be found in the annual reports.
• CDG syndromes: we have switched our method to capillary electrophoresis and minimal sample volume is 150µL, so we can no longer participate in CDG scheme because of insufficient volume. • I rated volume of CDG poor for 1 set of samples. We need 3 sets of samples. the organizer is, however, helpful in providing multiple sets so excellent scheme.	• 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. If sample volume issues related to your method persist, please contact admin@erndim.org for further advice from the Scientific Advisor for the CDG scheme. • Thank you for the positive feedback. We're pleased that you find the ability to purchase extra sample sets for a reduced fee useful.
• Results submissions to the website for CDG are very laborious. Possibly, I'm missing something but currently having to complete several fields separately is time-consuming and possibly prone to errors.	• We are sorry you're having difficulties with the CDG results website. 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
Cystine in White Blood Cells Scheme (CWBC)	
• As noted in previous years, it would be of great value to provide the "Cystine white blood cells" scheme with blood and not protein and Cystine apart, as we know the extraction method have great impact on the results.	• Due to the number of participants, sample size required, and distribution of samples, it is not possible for real blood samples to be used for this scheme.
Diagnostic Proficiency Testing Scheme (DPT)	
• On the DPT scheme it needs to be made clearer that putting results into the comments section means they are not included in the scoring.	• Results that are included in the 'Comments' section of the CSCQ results website are not included in the evaluation programme for scoring. This is stated in the scheme instructions and in the annual reports.
Lysosomal Enzymes in fibroblasts scheme	
• It would be better if there is an option to switch for another lysosomal enzyme when we are not able to test a particular enzyme that is included in the scheme.	• All enzymes included in the scheme are assayed and validated in the samples prior to distribution. Participants can therefore not switch enzymes to test for, as they have not been validated in all cell lines. • Laboratories can participate in as many of the ten enzymes offered in the scheme. Participants do not receive a lower score when they do not measure an enzyme that is deficient in a sample.

Qualitative Organic Acids (QLOU)	
• If a particular laboratory is not able to pick up some specific metabolites, that lab won't be able to make the particular diagnosis. In that case, please share your SOPs for that test so that it helps to improve the lab's ability to make that particular diagnosis in future.	• For technical advice, please contact the scientific advisor of the scheme. • Additionally, we highly recommend the following textbook: 'Laboratory Guide to the Methods in Biochemical Genetics' by N Blau.
• Regarding the sample volume for urine organic acid analysis, please consider increasing the volume of the urine samples. Some of the samples especially those with low creatinine levels, are not enough for replicate analysis.	• Unfortunately, QLOU sample volume is limited by the availability of patient sample material. We always send 2ml to all participants. Additional sets of samples are available for purchase for the small number of participants requiring a larger volume for their method. • For information regarding sample donation please visit: https://www.erndim.org/eqa-schemes/sample-donations/
Quantitative amino acids in Serum (QTAS)	
• We would love to see the results from the Amino Acids Serum data broken down not only by class of analytical method but further to the level of the individual manufacturer. We could then use the data from the sub-set linked to Biochrom instruments for our Post-Market Surveillance Report. We use the PMSR as a part of the evidence to support compliance with IVD regulations. I do appreciate this might put at risk the anonymity of some users where the number using certain manufacturers could be very small or even unique.	• Information on the instruments used by participants is not routinely collected. We agree that it may be interesting although this information is not necessary for the evaluation of the schemes. We occasionally circulate surveys asking specific scheme related questions which allows for more careful, curated data collection.
• Level of allo-isoleucine was somewhat too low for detection. Might consider checking on the general method's detection limit or limit of quantitation.	• A variety of concentrations are included and may vary between scheme years. The levels are selected by the Scientific Advisor for the scheme based on levels they expect to be of clinical interest or realistic to a clinical scenario. In some instances, levels may be restricted by the solubility of the analyte or it's interaction with other analytes in the scheme. For example, Allo-isoleucine spiked concentrations have ranged from 0 to 195 umol/L. If you have a result which is below your limit of detection this should be entered as 0 (zero). Further information can be found in the scheme instructions here: https://eqa.erndim.org/information/view/10.
• For the quantitative amino acids program, samples that are spiked with several analytes in high concentrations, can cause ion suppression for our method	• This is a valid point and a known a limitation of the scheme. The samples are non-physiological as they are designed to cover measuring ranges for multiple analytes.
Special Assays in Dried Blood Spots (SADB)	
• My suggestion is to add an extra spot to DBS filter cards. Our lab also uses Erndim samples to validate standards and controls. It would be helpful to have extra sample for that purpose and/or for troubleshooting observed biases on results.	• The provision of additional DBS as part of the EQA schemes would increase costs for all participants. However, if you require additional DBS, these can be purchased during the registration period. • If you require extra samples for repeat testing to troubleshoot poor performance during the scheme year, please contact admin@erndim.org. • Alternatively, archived scheme samples are sold the following year through our partners at MCA Laboratories (https://www.erndimqa.nl/Information.aspx?I=1069).

• SADB: lots of potential, still to be expanded (acylcarnitines, enzymatic activities)	• There is a separate Acylcarnitines in DBS scheme. • SADB contains analytes that do not neatly fit into the current dedicated DBS schemes that we offer. There are currently no plans to expand the range of analytes in SADB.
Special Assays in Serum (SAS) / Urine (SAU)	
• SAS: a lot of analytes for limited sample volume with limited stability	• We are aware the SAS scheme includes a large number of analytes, making it difficult to add new analytes of interest due to issues surrounding solubility and analyte interactions. We have identified lipids as a convenient group of analytes to move from SAS to a new EQA scheme. If the Lipids in Serum (LIS) pilot scheme is successful, this will enable us to remove a number of analytes from SAS.
• I rated special assays urine website good as the fact that creatinine has to be reported in mmol/L and the rest in micromol/L introduces a risk of errors. Obvious errors are not corrected by the organizer.	• It is the responsibility of participants to check all submitted results have been entered correctly before the relevant submission deadline. • However, it is sometimes possible to correct an error in results entry after the deadline if you contact us (admin@erndim.org) before the cycle review has been published. • Once reports are published, results cannot be changed.
Suggestions for future schemes	
• What about a bile acids scheme? Or a complete fatty acid profile (not just the 5 analytes offered in SA serum)	• We are aware of other participants wishing to organise a bile acids sample exchange. Please contact admin@erndim.org so we can put you in touch the organiser.
• It would be good to see CSF and Urine quantitative amino acid scheme	• These are not being investigated at this time.
• Lysosomal Enzymes in Dried Blood Spots.	• There has been a short Lysosomal Enzymes in DBS pilot scheme in the past, but it was not possible to continue it due to limited sample availability at that time. However, discussions on whether this could be reintroduced are in progress.

7.1. Positive Feedback

- Thank you!
- Many thanks. We understand that it is very time consuming providing the annual reports so we are grateful when they come through.
- We appreciate your decision to dispatch the samples of Qualitative Organic Acids (urine) by MCA Laboratories in the Netherlands to prevent the delivery issues experienced Italian labs in 2023 and 2024.
- We had a problem with two laboratories which we are cooperate LC-MS/MS tests for QTAS 2024 sample number of 6. We wrote to ERNDIM by email and explained our problem. After some investigations we received an apology email and a report for explanation of the double pipetting mistake. We are grateful for ERNDIM professional attitude. It is very important case for us for the trustability.
- Your service is great, thanks a lot for that.
- Thank you for the excellent service!
- Thank you for your continued efforts to maintain and improve this proficiency program!

END