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Acylcarnitines in Dried Blood Spots

Centre: London - United Kingdom

Final Report 2022

prepared by
Mr Charles Turner

Note: This annual report is intended for participants of the ERNDIM ACDB scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

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1. Introduction

The ERNDIM Acylcarnitine in dried blood spots scheme offers dried blood spots obtained from confirmed patients with confirmed diagnoses to enable laboratories to gain or maintain experience to identify organoacidopathies and fatty acid β-oxidation defects. The scheme is organised by Mr Charles Turner (Evelina London Children's Hospital) in conjunction with CSCQ, the Swiss organisation for quality assurance in medical laboratories.

As in previous years, samples were sent out to cover the spectrum of what is typically observed in the metabolic laboratory. A mix of clearly diagnostic profiles and some more challenging profiles were provided. As in previous years normal profiles were also sent out. The requirement to interpret a normal profile, as such, is as important as correctly identifying abnormal profiles. Correctly identifying a profile as normal can avoid unnecessary further investigation and distress to the patient and family.

2. Geographical distribution of participants

In 2022 43 laboratories from many different countries participated in the ACDB London scheme.
There was no educational participant in 2022 (one in 2021). Educational participants take part in all aspects of the scheme and receive interim reports with scores, but performance is not indicated on the ERNDIM certificate of performance.

[1] If this report is not Version 1 for this scheme year, go to APPENDIX 1 for details of the changes made since the last version of this document.

Participants and new applicants are distributed between the Heidelberg, London and Rome acylcarnitine in dried blood spots schemes which are run separately. The three organising laboratories each participate in the other's scheme by rotation.

Country	Number of participants
Australia	4
Brazil	1
Canada	3
Chile	1
Ireland	1
Italia	13
New Zealand	1
Oman	1
Qatar	1
Taiwan	1
Turkey	2
United Kingdom	13
Russia	1

3. Design and logistics of the scheme including sample information

As usual, the samples used in 2022 were authentic human blood spot samples, 5 from affected patients and one showing a normal profile.

The scheme has been designed and planned by Charles Turner as Scientific Advisor and coordinated by CSCQ, the Swiss organisation for quality assurance in medical laboratories, both appointed by and according to procedures laid down by the ERNDIM Board

All samples selected by the Scientific Advisor are prepared from 30-50µl of lithium heparin anticoagulated whole blood on Whatman (Schleicher & Schuell) 903™ paper. All samples are obtained following local ethical and consent guidelines.

In 2022 CSCQ dispatched the ACDB EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports. Existing QLOU, ACDB, DPT and Urine MPS scheme participants can log on to the CSCQ results submission website at:

https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php

Labelled copies of scan/chromatograms can be uploaded on the CSCQ website.

4. Schedule of the scheme

Time schedule in the 2022 ERNDIM ACDB London scheme.

	1st Submission Round	2nd Submission Round
Sample ID's:	ACDB-UL-2022-A ACDB-UL-2022-B ACDB-UL-2022-C	ACDB-UL-2022-D ACDB-UL-2022-E ACDB-UL-2022-F
4.1. Shipment of samples	February 12th, 2022	
4.2. **Start of analysis (clinical data available)**	March 9th, 2022	June 8th, 2022
Reminder for result submission	March 23th, 2022	July 15th, 2022
Results submission deadline:	March 30th, 2022	July 22nd, 2022
Interim reports available on CSCQ website	September 1st, 2022	September 17th, 2022

To be able to continue this scheme we need a steady supply of new patient samples. Several laboratories have donated samples to the ACDB scheme in the past, for which they are gratefully acknowledged. If you have one or more samples available and are willing to donate these to the scheme, please contact us at admin@erndim.org.
Laboratories which donate samples that are used in the scheme are eligible for a 20% discount on their participation in the ACDB scheme in the following year.

Samples included in the 2022 ERNDIM ACDB London scheme.

Survey	Sample no.	Diagnosis
22-03-ACL	ACDB-UL-2022-A	3-Hydroxy-3-methy-glutaryl-CoA lyase deficiency (HMG)
	ACDB-UL-2022-B	Mild Multiple AcylCoA dehydrogenase deficiency (MADD, OMIM 231680).
	ACDB-UL-2022-C	Propionyl CoA carboxylase deficiency (OMIM 606054)
22-06-ACL	ACDB-UL-2022-D	Long chain hydroxyacylCoA dehydrogenase deficiency (OMIM 609016)
	ACDB-UL-2022-E	Methylmalonyl CoA mutase deficiency (OMIM 609058)
	ACDB-UL-2022-F	Cobalamin C deficiency (OMIM 277400)

The scheme format was kept identical to those of previous years. Samples were shipped by regular mail. Details regarding stability of samples are provided in the sample package.
Interim reports were generated by the evaluation program developed by CSCQ.
Origin of patients: all urine samples have been provided by the scheme organizers or specified participants.

Patient A: 3-Hydroxy-3-methy-glutaryl-CoA lyase deficiency (HMG)
Patient C: Propionyl CoA carboxylase deficiency (OMIM 606054)
Patient D: Long chain hydroxyacyl CoA dehydrogenase deficiency (OMIM 609016)
Patient E: Methylmalonyl CoA mutase deficiency (OMIM 609058)
Patient F: Cobalamin C deficiency (OMIM 277400)

5. Results

Returned results in the 2022 ERNDIM ACDB London scheme.

	Survey 1	**Survey 2**
Receipt of results	43	42
No answer	0	1

6. Web site reporting

The website reporting system is compulsory for all centers. Please read carefully the following advice:

- Results
  - Give quantitative data as much as possible.
  - Enter the key metabolites with the evaluation **in the tables** even if you don't give quantitative data.
  - If the profile is normal: enter "Normal profile" in "Key metabolites".
  - **Don't enter results in the "comments" window**, **otherwise your results will not be included in the evaluation program.**
- ***Diagnosis***
  - **Don't enter the diagnosis in the "comments" window**, **otherwise your results will not be included in the evaluation program.**
- Recommendations = **advice for further investigation**.
  - Scored together with the interpretative score.
  - Advice for treatment are not scored.
  - **Don't give advice for further investigation in "Comments on diagnosis"**: it will not be included in the evaluation program.

7. Scoring and evaluation of results

A scoring system was developed in 2012 and approved by the ERNDIM Scientific Advisory Board. Similar to other qualitative (proficiency testing) ERNDIM schemes, the maximum score for a sample is 4 points.
Qualitative results and diagnostic proficiency of the 2022 samples were scored using the criteria given below. These criteria have been set by the Scientific Advisor, approved by the Scientific Advisory Board. The final decision about scoring of the scheme is made in the Scientific Advisory Board (SAB) during the Autumn meeting (November 19th, 2022).
General criteria used to score results

Item	Description of scoring criteria	Score
Quantitative results	Correct classification of quantitative results (i.e. normal or increased) according to reference values	1
	Incorrect classification of quantitative results	0
Qualitative results	Correct results according to criteria set for the sample	1
	Incorrect: minimally required results not reported	0
Diagnostic proficiency	Correct according to criteria set for the sample	2
	Partially correct	1
	Unsatisfactory or misleading	0
	Maximum total score	**4**

Starting with the 2014 schemes the concept of 'critical error' is introduced to the assessment of the qualitative schemes. Labs failing to make a correct diagnosis of a sample considered eligible for this category will be deemed not to have reached a satisfactory performance even if their total points for the year is sufficient according to the requirement set by the SAB. The classification of samples to be judged for critical error was undertaken at the SAB meeting held on November 19th, 2022.

7.1. Score for satisfactory performance

At least 17 points from the maximum of 24 (70%). We are required to define "Participation" for the purpose of the ERNDIM Annual Certificate which covers all ERNDIM schemes. For this acylcarnitine in dried blood spots scheme we have defined "Participation" as requiring two returns during the year. Failure to meet this requirement will result in the certificate of participation showing 'non-submitter' rather than 'satisfactory' or 'unsatisfactory'.

8. Results of samples and evaluation of reporting

8.1. Patient A

3-Hydroxy-3-methy-glutaryl-CoA lyase deficiency (HMG) on treatment with carnitine

Patient details provided to participants

Patient admitted for vomiting, diarrhea, hypoglycemia and metabolic acidosis. In treatment with carnitine

Patient details

This acylcarnitine (AC) profile is typical of 3-HMG-CoA lyase deficiency. The sample was distributed by the ACDB centre Rome as a common sample for all three centres.

Analytical performance

Diagnostic markers for HMG CoA Lyase deficiency are C6-DC and C5-OH carnitines. Depending on the method applied for detection of ACs, one or both markers can have isobaric interfering analytes. For this sample, 43 out of 43 participants reported results. C5OH and C6DC carnitine concentrations were both reported as elevated or even grossly elevated by 93% of these labs (40/43), 2/43 did not comment on the elevation of C6DC and only 1 did not comment on either. Other frequently reported ACs were C0 (n=26, 19 normal and 7 elevated), and C3 (n=6, 5 normal and 1 elevated).
The results from other centres suggested that C6DC/methylglutarylcarnitine is not included in the scope of AC analyses in some laboratories, and it was not commented upon by 2/43 laboratories in the London scheme. In the case of HMG CLD it is a helpful marker for a targeted diagnosis. Following agreement with the scientific advisors of all three centres for ERNDIM ACDB schemes, we gave 2 points for analysis to all laboratories reporting elevations in either C5OH or C6DC but would encourage participants to expand their methods to include C6DC if missing, and will consider this when evaluating future HMG CLD samples accordingly

Diagnosis / Interpretative proficiency

3-HMG-CoA lyase deficiency was given as primary diagnosis by 39 participants. Two participants suggested 3-methylcrotonyl CoA carboxylase deficiency, one isovaleric acidaemia and one described the profile as normal. One of those suggesting 3MCC deficiency as most likely had 3-HMG CoA synthase deficiency as their alternative diagnosis.

Recommendations

40/43 participants would follow up the patient with analysis of urinary organic acids to clarify the diagnosis, with 32 of these suggesting mutation analysis targeting the HMG CoA lyase gene for confirmation. 12 would repeat the acylcarnitine analysis on plasma. 3 mentioned that enzyme assay in leucocytes or fibroblasts could be useful, particularly if a mutation of unknown significance was found. 3 suggested assay of plasma biotinidase activity and one holocarboxylase synthase activity as part of the follow-up of a raised C5OH carnitine.

Scoring

Reporting of C5-OH gave 2 points for analytical performance. For interpretive proficiency, two points were awarded for either reporting HMG CLD as primary or secondary diagnosis – in the latter case, a method suitable to find the correct diagnosis must have been given in the recommendations.

Overall impression

Overall proficiency on this sample was excellent: 98% for analytical, 93% for interpretation giving 95% overall.

8.2. Patient B

Mild Multiple AcylCoA dehydrogenase deficiency (MADD,OMIM 231680). The patient was well at a routine clinic visit.

Patient details provided to participants
Hypoglycaemia in infancy, currently well

Patient details
Mild Multiple Acyl CoA dehydrogenase deficiency (MADD,OMIM 231680)

Analytical performance
All 43 respondents noted elevated octanoyl (C8) and decanoyl (C10) carnitine, and 40 an elevated hexanoyl (C6) carnitine. 15 also mentioned an elevated C12 carnitine. 9 commented on the normal C8/C10 ratio.

Diagnosis / Interpretative proficiency
24 participants suggested MADD (GA2) as their most likely diagnosis whilst 19 considered MCADD most probable. 36 (84%) included MADD in their differential diagnosis. Of those who did not consider MADD, 5 would exclude MCADD before considering an alternative and 2 included VLCADD as a possibility on the basis of a slightly increased C14:1 carnitine.

Recommendations
36 participants suggested urinary organic acid analysis and 18 plasma acylcarnitine analysis as suitable follow-up tests to clarify the diagnosis. 40 would use genotyping to confirm a diagnosis concentrating on the ACADM, ETFA, ETFB & ETFDH genes as appropriate, either guided by urine organic acids or as the first follow-up test. 7 suggested enzyme activity measurements in leucocytes or fibroblasts. 7 of those suggesting MADD suggested a trial of riboflavin therapy.

Scoring
2 points for analysis were given for raised C8 and C10. 2 points for interpretation were given for MADD as primary diagnosis or if given as alternative diagnosis including a recommendation suitable to find the correct diagnosis.

Overall impression
The overall analytical proficiency was 100%, interpretation 90% giving an overall proficiency of 95%. The majority of participants included MADD in their differential diagnosis and suggested appropriate follow-up tests to allow a conclusion to be made.

8.3. Patient C

The sample was from a patient at presentation with propionyl CoA carboxylase deficiency (OMIM 606054).

Patient details provided to participants

Hyperammonaemia

Patient details

The sample was from a patient shortly after being admitted to Intensive care with hyperammonaemia. Carnitine had been given. The final diagnosis, genetically confirmed, was propionyl CoA carboxylase deficiency (OMIM 606054)

Analytical performance

Analytical performance was excellent, all participants (43/43) detected the high C3 (propionyl) carnitine in this sample.

Diagnosis / Interpretative proficiency

All participants included propionic acidaemia (propionyl CoA carboxylase deficiency) in their differential diagnosis. Most suggested PA as the most likely diagnosis (41/43), with 1 making methylmalonic acidaemia more likely and 1 suggesting biotinidase deficiency. Both of these included propionic acidaemia as a possible diagnosis and both suggested appropriate follow-up tests to confirm the diagnosis.

Recommendations

40/43 participants suggested appropriate tests to differentiate between causes of a raised C3 carnitine and/or confirm the diagnosis. All 40 suggested urinary organic analysis, 13 plasma total homocysteine, and 10 plasma methylmalonic acid, largely to distinguish between PA and MMA and further guide investigation. Definitive diagnosis by genotyping of the PCCA and PCCB genes was suggested by 28.

Scoring

Two points for analysis were awarded when reporting C3 as elevated or grossly elevated. To achieve 2 points for interpretation PA had to be reported either as the primary diagnosis or as an alternative diagnosis. In the latter case, a method suitable for finding the correct diagnosis must also have been recommended.

Overall impression

Proficiency on this sample was excellent. Analytical proficiency was 100%, Interpretive proficiency 97%, overall 100%.

8.4. Patient D

The sample was from a patient with long chain hydroxyacyl CoA dehydrogenase deficiency (OMIM 609016), on admission to hospital, before specific treatment was started

Patient details provided to participants

Hypoglycaemia, hypotonia

Patient details

The sample was from a patient with Long chain 3-hydroxyacyl CoA dehydrogenase deficiency (LCHADD, OMIM 609016) shortly after clinical presentation with hypoglycaemia and hypotonia.

Analytical performance

Analytical performance was uniformly excellent. All respondents who reported results noted increased long-chain 3-hydroxyacyl carnitines: 42/42 C16OH, 40/42 C18:1OH, 34/42 C18OH and 24/42 C16:1OH. 31/42 commented on the elevated tetradecenoyl carnitine (C14:1. 33/42 noted the low free carnitine. 3 commented on elevated C5DC (glutaryl carnitine) but one of these made the point that C5DC and C10-OH carnitines are isobaric when butylated. Overall the analytical proficiency was 100%.

Diagnosis / Interpretative proficiency

40/42 respondents included LCHADD/TFP deficiency as the most likely diagnosis. One suggested MADD because of an elevated C5DC (glutaryl) carnitine but included LCHADD/TFP in their differential diagnosis and suggested confirmatory tests to clarify. One respondent only suggested VLCADD on the basis of the elevated C14:1 carnitine. Overall interpretive proficiency was 98%

Recommendations

29/42 participants would confirm the biochemical findings with urinary organic acid analysis and 19/42 with plasma acylcarnitine profiling. Most made the point that LCHADD and TFP deficiency cannot be distinguished by metabolite profiling and 40/42 suggested genotyping of the HADHA and HADHB genes for definitive diagnosis. 17/42 also included enzyme assay in cultured fibroblasts as an alternative method.

Scoring

2 points for analysis were given for reporting one or more elevated long chain hydroxyacyl carnitines. 2 points for interpretation were awarded for reporting LCHADD as primary or secondary diagnosis – in the latter case, a method suitable to find the correct diagnosis must have been given in the recommendations.

Overall impression

Overall performance for this sample was excellent with an overall proficiency of 99%

8.5. Patient E

The sample was from a patient with methylmalonyl CoA mutase deficiency (OMIM 609058), with a degree of chronic kidney disease on treatment with carnitine.

Patient details provided to participants

Acidosis in infancy, currently well, on carnitine

Patient details

The sample was from a patient with Methylmalonyl CoA mutase deficiency and reduced renal function on carnitine supplementation. At the time of sampling the patient was well at a clinic visit for assessment of renal function.

Analytical performance

Analytical performance was excellent (100%). All participants who returned results (42/42) detected the massively raised propionyl carnitine with 22 also commenting on the raised C3/C2 or C3/C16 ratios. 11 commented on an elevated(2) or grossly elevated (9) C4DC (methylmalonyl carnitine). 34 respondents noted the high free carnitine.

Diagnosis / Interpretative proficiency

One respondent did not return a suggested diagnosis, and one did not include methylmalonyl CoA mutase deficiency in their differential diagnosis. 34/41 made methylmalonic aciduria their most likely diagnosis, and 6/7 of the remainder included MMA in the differential. Overall interpretative proficiency was 96%.

Recommendations

Two respondents did not make any recommendations for followup tests to confirm the diagnosis. 38/39 would perform urine organic acid analysis to clarify the diagnosis, 22 plasma total homocysteine, 19 plasma amino acids and 14 plasma methylmalonic acid. 5 respondents suggested followup tests on the dried blood spot (MMA, methylcitrate, 3hydroxypropionate and propionylglycine. For definitive diagnosis 33 suggested genotyping and 3 enzyme assay. One respondent had already performed methylmalonic acid measurement on the dried blood spot and would proceed directly to genotyping without urinary organic acid analysis.

Scoring

Analytical: 2 points for C3 as elevated or grossly elevated. Interpretive: MMA had to be reported either as the primary diagnosis or as an alternative diagnosis to achieve two points. In the latter case, a method suitable for finding the correct diagnosis must also have been recommended.

Overall impression

Performance was excellent: 98%

8.6. Patient F

Mild Cobalamin C deficiency (OMIM 277400) on treatment with hydroxocobalamin and low dose carnitine

Patient details provided to participants

Developmental delay, raised homocysteine, on treatment

Patient details

The sample was from a patient with a relatively mild Cobalamin C deficiency OMIM 277400 on treatment with hydroxocobalamin and low dose carnitine, at a routine follow up clinic visit.

Analytical performance

The acylcarnitine profile from this patient was essentially normal, as described by all participants. One participant commented on an abnormal (C16 + C18:1)/C2 ratio. Analytical proficiency was 98%

Diagnosis / Interpretative proficiency

The acylcarnitine profile was uninformative/normal. Interpretation as normal was appropriate. Most participants indicated that further investigation of hyperhomocystinaemia was indicated. 23/42 specifically suggested that cobalamin disorders where methylmalonic acidaemia is expected could be the cause, and made the point that effective treatment may result in complete normalisation of the acylcarnitine profile while hyperhomocystinaemia persists. Interpretive proficiency was 74%

Recommendations

Most respondents suggested further tests to enable a cause for the described hyperhomocystinaemia: most commonly urinary organic acid analysis (26/42), plasma amino acid analysis (21/42), plasma methylmalonic acid (16/42) and genotyping (14/42). 17/42 would confirm the raised homocysteine by plasma total homocysteine measurement, 6 had already done so by analysis of total homocysteine on the supplied blood spot (all 6 found it raised). 5 respondents measured methylmalonic acid on the dried blood spot, 3 finding it elevated and 2 within their reference ranges

Scoring

The sample was designated as “Educational” following discussion at the ERNDIM SAB meeting in November 2022 and removed from the scoring for the year.
Had it been included, 2 points for analysis would have been given for a “normal acylcarnitine profile” and 2 points for interpretation if the profile was referred to as normal. Points would not have been deducted if reasonable recommendations for investigations to elucidate the cause of hyperhomocystinaemia were made.

Overall impression

This was a normal acylcarnitine profile from a patient with a disorder which untreated would be expected to lead to elevated propionyl and methylmalonyl carnitine. Overall participants avoided over-interpreting any minor acylcarnitine variations and made appropriate suggestions for further non-acylcarnitine tests to achieve a final diagnosis. Overall proficiency was 86%.

9. Scores of participants

All data transfer, the submission of data as well as the request and viewing of reports proceed via the ACDB-CSCQ results website. The results of your laboratory are confidential and only accessible to you (with your username and password). The anonymous scores of all laboratories are accessible to all participants and only in your version is your laboratory highlighted in the leftmost column.

If your laboratory is assigned poor performance and you wish to appeal against this classification please email the ERNDIM Administration Office (admin@erndim.org), with full details of the reason for your appeal, within one month receiving your Performance Support Letter. Details of how to appeal poor performance are included in the Performance Support Letter sent to poor performing laboratories.

Detailed scores – Round 1

	Patient A			Patient B			Patient C		
Lab No	**3-HMG-CoA lyase deficiency, OMIM 246450**			**Multiple Acyl CoA dehydrogenase deficiency (MADD, OMIM 231680)**			**Propionyl CoA carboxylase deficiency (OMIM 606054)**		
	A	**I**	**Total**	**A**	**I**	**Total**	**A**	**I**	**Total**
1	2	2	4	2	2	4	2	2	4
2	2	2	4	2	2	4	2	2	4
3	2	2	4	2	2	4	2	2	4
4	2	2	4	2	2	4	2	2	4
5	2	2	4	2	2	4	2	2	4
6	2	2	4	2	2	4	2	2	4
7	2	2	4	2	2	4	2	2	4
8	2	2	4	2	2	4	2	2	4
9	2	2	4	2	2	4	2	2	4
10	2	2	4	2	2	4	2	2	4
11	2	1	3	2	2	4	2	2	4
12	2	2	4	2	2	4	2	2	4
13	2	2	4	2	1	3	2	2	4
14	2	2	4	2	2	4	2	2	4
15	2	2	4	2	2	4	2	2	4
16	2	2	4	2	2	4	2	2	4
17	2	2	4	2	2	4	2	2	4
18	2	2	4	2	2	4	2	2	4
19	2	2	4	2	2	4	2	2	4
20	2	2	4	2	2	4	2	2	4
21	2	2	4	2	2	4	2	2	4
22	2	2	4	2	1	3	2	2	4
23	2	2	4	2	1	3	2	2	4
24	2	2	4	2	2	4	2	2	4
25	2	2	4	2	2	4	2	2	4
26	2	2	4	2	2	4	2	2	4
27	2	2	4	2	2	4	2	2	4
28	2	2	4	2	1	3	2	2	4

29	2	2	4	2	2	4	2	2	4
30	2	2	4	2	2	4	2	2	4
31	2	2	4	2	1	3	2	2	4
32	2	2	4	2	2	4	2	2	4
33	2	2	4	2	2	4	2	2	4
34	2	2	4	2	2	4	2	2	4
35	2	2	4	2	2	4	2	2	4
36	2	2	4	2	1	3	2	2	4
37	2	2	4	2	1	3	2	2	4
38	2	2	4	2	2	4	2	2	4
39	2	2	4	2	2	4	2	2	4
40	0	0	0	2	2	4	2	2	4
41	1	1	2	2	1	3	2	2	4
42	2	0	2	2	1	3	2	2	4
43	2	2	4	2	2	4	2	2	4

Detailed scores – Round 2

	Patient D			Patient E			Patient F		
Lab No	Long chain hydroxyacyl CoA dehydrogenase deficiency LCHADD (OMIM 609016)			Methylmalonyl CoA mutase deficiency (OMIM 609058)			Mild Cobalamin C deficiency OMIM 277400 Educational Sample		
	A	I	Total	A	I	Total	A	I	Total
1	2	2	4	2	2	4	–	–	–
2	2	2	4	2	2	4	–	–	–
3	2	2	4	2	2	4	–	–	–
4	2	2	4	2	2	4	–	–	–
5	2	2	4	2	2	4	–	–	–
6			0			0	–	–	–
7	2	2	4	2	2	4	–	–	–
8	2	2	4	2	2	4	–	–	–
9	2	2	4	2	2	4	–	–	–
10	2	2	4	2	2	4	–	–	–
11	2	2	4	2	2	4	–	–	–
12	2	2	4	2	2	4	–	–	–
13	2	2	4	2	2	4	–	–	–
14	2	2	4	2	2	4	–	–	–
15	2	2	4	2	2	4	–	–	–
16	2	2	4	2	2	4	–	–	–
17	2	2	4	2	2	4	–	–	–
18	2	2	4	2	2	4	–	–	–
19	2	2	4	2	2	4	–	–	–
20	2	2	4	2	2	4	–	–	–
21	2	2	4	2	2	4	–	–	–
22	2	2	4	2	2	4	–	–	–
23	2	2	4	2	2	4	–	–	–
24	2	2	4	2	2	4	–	–	–
25	2	2	4	2	2	4	–	–	–
26	2	2	4	2	2	4	–	–	–
27	2	2	4	2	2	4	–	–	–
28	2	2	4	2	2	4	–	–	–
29	2	2	4	2	2	4	–	–	–
30	2	2	4	2	2	4	–	–	–
31	2	2	4	2	2	4	–	–	–
32	2	2	4	2	2	4	–	–	–
33	2	2	4	2	2	4	–	–	–
34	2	2	4	2	2	4	–	–	–
35	2	2	4	2	2	4	–	–	–

36	2	2	4	2	2	4	–	–	–
37	2	2	4	2	2	4	–	–	–
38	2	2	4	2	2	4	–	–	–
39	2	2	4	2	2	4	–	–	–
40	2	2	4	2	1	3	–	–	–
41	2	2	4	2	2	4	–	–	–
42	2	0	2	2	2	4	–	–	–
43	2	2	4	2	2	4	–	–	–

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	4	4	4	4	–	20	100	
2	4	4	4	4	4	–	20	100	
3	4	4	4	4	4	–	20	100	
4	4	4	4	4	4	–	20	100	
5	4	4	4	4	4	–	20	100	
6	4	4	4	0	0	–	12	60	
7	4	4	4	4	4	–	20	100	
8	4	4	4	4	4	–	20	100	
9	4	4	4	4	4	–	20	100	
10	4	4	4	4	4	–	20	100	
11	3	4	4	4	4	–	19	95	
12	4	4	4	4	4	–	20	100	
13	4	3	4	4	4	–	19	95	
14	4	4	4	4	4	–	20	100	
15	4	4	4	4	4	–	20	100	
16	4	4	4	4	4	–	20	100	
17	4	4	4	4	4	–	20	100	
18	4	4	4	4	4	–	20	100	
19	4	4	4	4	4	–	20	100	
20	4	4	4	4	4	–	20	100	
21	4	4	4	4	4	–	20	100	
22	4	3	4	4	4	–	19	95	
23	4	3	4	4	4	–	19	95	
24	4	4	4	4	4	–	20	100	
25	4	4	4	4	4	–	20	100	
26	4	4	4	4	4	–	20	100	
27	4	4	4	4	4	–	20	100	
28	4	3	4	4	4	–	19	95	
29	4	4	4	4	4	–	20	100	
30	4	4	4	4	4	–	20	100	
31	4	3	4	4	4	–	19	95	
32	4	4	4	4	4	–	20	100	
33	4	4	4	4	4	–	20	100	
34	4	4	4	4	4	–	20	100	
35	4	4	4	4	4	–	20	100	
36	4	3	4	4	4	–	19	95	
37	4	3	4	4	4	–	19	95	
38	4	4	4	4	4	–	20	100	
39	4	4	4	4	4	–	20	100	
40	0	4	4	4	3	–	15	75	

41	2	3	4	4	4	–	17	85	
42	2	3	4	2	4	–	15	75	
43	4	4	4	4	4	–	20	100	

Performance

	Number of labs	% total labs
Satisfactory performers **(≥ 70 % of adequate responses)**	41	95.4
Unsatisfactory performers **(< 70 % adequate responses and/or critical error)**	1	2.3
Partial and non-submitters	1	2.3

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
ACDB-UL-2022-A	3-HMG-CoA lyase deficiency, OMIM 246450	97	93	95
ACDB-UL-2022-B	Multiple Acyl CoA dehydrogenase deficiency (MADD, OMIM 231680)	100	90	95
ACDB-UL-2022-C	Propionyl CoA carboxylase deficiency (OMIM 606054)	100	100	100
ACDB-UL-2022-D	Long chain hydroxyacyl CoA dehydrogenase deficiency LCHADD (OMIM 609016)	100	98	99
ACDB-UL-2022-E	Methylmalonyl CoA mutase deficiency (MMA) OMIM 251000	100	98	99
ACDB-UL-2022-F	Cobalamin C deficiency (OMIM 277400)	-	-	-

10. Preview of the scheme in 2023

The timetable for samples in 2023:

	1st Submission Round	2nd Submission Round
Sample ID's:	ACDB-UL-2023-A ACDB-UL-2023-B ACDB-UL-2023-C	ACDB-UL-2023-D ACDB-UL-2023-E ACDB-UL-2023-F
Shipment of samples	February 8th 2023	
Start of analysis (clinical data available)	March 13th 2023	June 5th 2023
Reminder for result submission	March 27th 2023	June 19th 2023
Results submission deadline:	April 3rd 2023	June 26th 2023

11. ERNDIM certificate of participation

A combined certificate of participation covering all EQA schemes will be provided to all participants who take part in any ERNDIM scheme. For the ACDB scheme this certificate will indicate if results were submitted and whether satisfactory performance was achieved in the scheme.

12. Questions, Comments and Suggestions

If you have any questions, comments or suggestions please address to the Scientific Advisor of the scheme, Mr. Charles Turner (chas.turner@kcl.ac.uk) and/or to the ERNDIM Administration Office (admin@erndim.org)

Date of report, 2024-03-18
Name and signature of Scientific Advisor

Mr Charles Turner
Scientific Advisor

APPENDIX 1. Change log (changes since the last version)

Version Number	Published	Amendments
1	19 March 2024	2022 annual report published

END