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Acylcarnitines in dried blood spots

Centre: London United Kingdom

Final Report 2025

prepared by
Mrs Erin Emmett

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 Mrs Erin Emmett (Great Ormond Street Hospital for Children, London UK) 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. No normal profiles were sent out this year, however 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

Participants and new applicants were 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.

[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.

In 2025, 47 laboratories from many different countries participated in the ACDB London scheme. There were no educational participants in 2025. 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.

Country	Number of Participants	Country	Number of Participants
Australia	4	New Zealand	1
Brazil	2	Oman	1
Canada	4	Poland	2
Chile	1	Taiwan	1
Finland	1	Turkey	2
Germany	1	United Kingdom	14
Ireland	1	United States	1
Italy	11		

3. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Mrs Erin Emmett 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. As usual, the samples used in 2025 were authentic human blood spot samples, all six from affected patients.

All samples selected by the Scientific Advisor are prepared from 25-50 µL of lithium heparin anticoagulated whole blood on Whatman (Schleicher & Schuell) 903™ paper. All samples are obtained following local ethical and consent guidelines.

In 2025 CSCQ dispatched the ACDB EQA samples to the scheme participants and provides a website for online 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.

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 2025 ERNDIM ACDB London scheme:

Survey	Sample no.	Diagnosis
25-03-ACL	ACDB-UL-2025-A	Very long chain acyl-CoA dehydrogenase (VLCAD) deficiency (common sample)
	ACDB-UL-2025-B	3-hydroxyisobutyryl-CoA hydrolase (HIBCH) deficiency
	ACDB-UL-2025-C	Isovaleryl-CoA dehydrogenase deficiency (Isovaleric acidaemia; IVA)
25-06-ACL	ACDB-UL-2025-D	Medium chain acyl-CoA dehydrogenase (MCAD) deficiency
	ACDB-UL-2025-E	Cobalamin C (Cbl C) deficiency
	ACDB-UL-2025-F	Malonyl-CoA decarboxylase deficiency (malonic aciduria)

The scheme format was kept identical to those of previous years. All samples selected by the Scientific Advisor have been tested for suitability in the Scientific Advisor's laboratory before and after shipping process. Samples were sent by DHL; FedEx or the Swiss Post at room temperature. The

samples are stable for the duration of the scheme's submission calendar when stored under defined conditions. Interim reports were generated by the evaluation program developed by CSCQ.

Origin of patients: Five clinical samples were provided by the scheme organiser, and one clinical sample was donated by a participant laboratory.

4. Schedule of the scheme

Time schedule in the 2025 ERNDIM ACDB London scheme:

	1st Submission Round	2nd Submission Round
Sample ID's	ACDB-UL-2025-A ACDB-UL-2025-B ACDB-UL-2025-C	ACDB-UL-2025-D ACDB-UL-2025-E ACDB-UL-2025-F
Shipment of samples	05 Feb 2025	
Start of analysis (clinical data available)	17 Mar 2025	02 Jun 2025
Reminder for result submission	31 Mar 2025	16 Jun 2025
Results submission deadline	07 Apr 2025	23 Jun 2025
Interim reports available on CSCQ website	May 2025	Aug 2025

5. Results

Returned results in the 2025 ERNDIM ACDB London scheme.

	Survey 1	Survey 2
Receipt of results	46	46
No results submitted	1	1

6. Website 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. For further information, please refer to the Framework for Assessment and Education for Qualitative Schemes on our website (https://eqa.erndim.org/information/view/14)

Qualitative results and diagnostic proficiency of the 2025 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 27th, 2025).

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**

ERNDIM applies the concept of 'critical error' in the scoring of results. In principle this is a category of error that would be unacceptable to the majority of labs and would have a serious adverse effect on patient management. 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 are 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 27th November 2025

7.1. Score for satisfactory performance

At least 17 points from the maximum of 24 (70%). In instances where the SAB agrees that a sample will be classed as an Educational Sample, the scores associated with the sample will be not included in the performance evaluation of the participating laboratories' overall scheme.
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

Very long chain acyl-CoA dehydrogenase (VLCAD) deficiency due to mutation in the *ACADVL* gene, OMIM 201475.

Patient details provided to participants
Occasional cramps and dark urine as child. Episodes of rhabdomyolysis as young adult, two episodes requiring dialysis.

Patient details
This sample was the common sample for 2025 and was collected from a 57 year old male with history of episodes of rhabdomyolysis associated with intense exercise. He received genetic confirmation of VLCAD deficiency at the age of 55 following another episode of rhabdomyolysis requiring admission to A&E with a CK of >10,000 IU/L. Patient now well controlled on a lower fat diet with avoidance of large intakes of alcohol, and use of SOS carbohydrate supplement prior to increased exercise. At the time of sample collection, the patient was not formally using MCT supplementation.

Analytical performance
Results were returned by 98% of participating laboratories (46/47).
This was a highly scoring sample with all participants who returned a result scoring two analytical marks. All participants identified the elevated or grossly elevated C14:1, C14, C14:2 and/or relevant ratios, including C14:1/C12:1, C14:/C2, C14:1/C16.

Diagnosis / Interpretative proficiency
All participants who returned a result identified very long chain acyl-CoA dehydrogenase (VLCAD) deficiency as the likely diagnosis.
Other possible diagnoses provided included MADD, CPT2, CACT deficiency and TANGO2, however the majority of participants who suggested these identified that VLCADD was the most likely diagnosis in light of the clinical details provided.

Recommendations
100% of participating laboratories recommended genetic analysis for confirmation of the suspected diagnosis, with the majority specifying analysis of the *ACADVL* gene. Other commonly suggested recommendations included urine organic acid analysis (25/46), plasma or repeat bloodspot acylcarnitines (21), enzyme studies (either VLCAD specifically or FAOD flux studies) (20), and a number of routine Chemistry tests including CK.
24/46 participants provided recommendations on patient management, including referral to a specialist metabolic team and family testing.

Scoring
The scoring criteria were –
Analytical: 2 points for increased C14:1, or other long chain acylcarnitines such as C14, C14:2, C16:1 etc, and/or appropriate ratios including C14:1/C12:1 and C14:1/C2.
Interpretative: 1 point for VLCADD as the primary or secondary likely diagnosis and 1 point for appropriate recommendations (plasma acylcarnitines, genetics, enzyme analysis).

Overall impression
This was a sample with clear acylcarnitine abnormalities, and as such all participants who returned results scored full marks for analysis and interpretation.

8.2. Patient B

3-hydroxyisobutyryl-CoA hydrolase (HIBCH) deficiency due to mutation in the *HIBCH* gene, OMIM 250620.

Patient details provided to participants
Viral illness age 3 triggering metabolic decompensation and encephalopathy. Seizures, abnormal brain MRI. Now on carnitine.

Patient details
This sample was collected from a 4 year old patient with 3-hydroxyisobutyryl-CoA hydrolase (HIBCH) deficiency. The patient was diagnosed at the age of 3 years during an episode of acute metabolic decompensation following a febrile illness and subsequent period of fasting. His presenting features at the time included seizures, ketotic hypoglycaemia, encephalopathy and significant basal ganglia injury with brainstem involvement. A bloodspot sample at this time showed a significantly increased bloodspot C4OH-carnitine and the diagnosis of HIBCH deficiency was confirmed with genetics. Prior to this event, there was minimal history of note aside from a mild isolated speech delay, which may have been due to a second separate gene mutation associated with neurodevelopmental delay identified in this patient.
At the time of sample collection, this patient was on carnitine and a low-protein diet supplemented with controlled branched chain amino acid intake.

HIBCH is an enzyme involved in valine metabolism located in the mitochondria; deficiency results in Leigh-like disease and hypotonia. The first patient with metabolic and clinical abnormalities associated with deficiency of this enzyme was described in the literature in 1982 (1), with the molecular basis of the deficiency described in a second patient in 2007 (2).
Increased C4OH acylcarnitine is often observed in HIBCH deficiency, but not in another related disorder of valine metabolism, ECHS1 deficiency. Compounds increased in both HIBCH and ECHS1 deficiencies can be seen on urine organic acid analysis (2-methyl-2,3-dihydroxybutyrate) and urine amino acid analysis (cysteine and cysteamine metabolites of methacrylyl-CoA and acryloyl-CoA) (3).
(1) G K Brown et al, 1982. Pediatrics, 70(4):532-8
(2) F J Loupatty et al, 2007. AJHG, 80:195-9
(3) H Peters et al, 2015. Mol Genet Metab, 115(4):168-73

Analytical performance
Results were returned by 98% of participating laboratories (46/47).
The acylcarnitine pattern in this sample was dominated by the gross increase in free carnitine, observed by 45/46 participants. The diagnostic abnormality, increased C4OH, was very subtle and only noted to be elevated by 24% of participants (11/46). A wide range of other acylcarnitines were mentioned by participants, including most commonly C2, but also mild elevations in C3, C5DC, C6, C8, C10 and C16- and C18-derived long chain acylcarnitines.
Full marks were awarded for labs that identified elevated free carnitine and C4OH. One mark was given for only identifying the increased free carnitine (plus other acylcarnitine abnormalities).
Excluding one non-submitter, overall analytical proficiency for this sample was 60.9%.

Diagnosis / Interpretative proficiency
Two points were awarded to two participants who included HIBCH deficiency in their differential diagnosis. All participants who scored one mark suggested a wide range of possible diagnoses, including CPT2 deficiency (13), carnitine-acylcarnitine translocase (CACT) deficiency (9), carnitine supplementation with no specified reason (10), primary carnitine deficiency (7), MCADD (6), MADD (7), GA1 (7), and other metabolic disorders (17), including other fatty acid oxidation defects, ketogenesis defects, CoPAN, propionic and methylmalonic acidaemias. Participants who only suggested CPT1 deficiency without reference to appropriate recommendations that could have led to identification of HIBCH as the diagnosis (including urine organic acid analysis and referral to a clinical team) scored zero marks, as it was stated in the clinical information provided that the patient was on carnitine.
Excluding one non-submitter, overall interpretative proficiency for this sample was 48.9%.

Recommendations
A wide range of recommendations were provided, reflecting whichever diagnosis (or diagnoses) the participant included in their response, but largely included urine organic acid analysis, plasma and/or repeat bloodspot acylcarnitines and a variety of genetic investigations.

Scoring
The scoring criteria were –
Analytical: 2 points for increased C0 and C4OH. 1 point for increased C0 and/or any other abnormalities identified.
Interpretative: 2 points for HIBCH deficiency with appropriate recommendations. 1 point if organic acids or clinical referral suggested regardless of diagnosis. Zero points if CPT1 was suggested (as clinical details clearly state ‘now on carnitine’) with no recommendations provided.

However, at the Scientific Advisory Board meeting it was agreed that due to the subtle nature of the abnormalities in this patient sample and the low overall proficiency of this sample of 54.9%, this sample is designated educational and therefore no critical errors are awarded and this sample is excluded from the overall scoring.

Overall impression
This sample highlights the difficulty in obtaining samples from real patients that reflects the reality of what participants may encounter in their laboratories when analysing ‘real-time’ samples from acutely unwell patients. Due to the logistical and sometimes ethical barriers preventing samples being obtained from patients during acute presentation, many samples collected and distributed are from treated, well patients. In this case, the large amount of free carnitine in the patient sample prevented the diagnostic abnormality, which was subtle, from being elucidated by the majority of participants.

8.3. Patient C

Isovaleric acidaemia (IVA) ; Isovaleryl-CoA dehydrogenase deficiency due to mutation in the *IVD* gene, OMIM 243500.

Patient details provided to participants
Pale and sleepy with poor weight gain at 3 weeks. Presented with acute D&V, high ammonia. Currently well.

Patient details
This sample was kindly donated by a participant lab and was obtained from a 16 year old patient with isovaleric acidaemia (isovaleryl-CoA dehydrogenase deficiency), currently treated and well managed,

including with carnitine supplementation. Initial concern for this patient was at 3 weeks old with poor weight gain. However it was not until an acute presentation with D&V and hyperammonaemia at 11 months old that further investigations were performed and the diagnosis of IVA made.

Analytical performance
Results were returned by 98% of participating laboratories (46/47).
This was a highly scoring sample with all participants who returned a result scoring two analytical marks. All participants identified the elevated or grossly elevated C5 and/or relevant ratios, including C5/C2 and C5/C3.

Diagnosis / Interpretative proficiency
All participants who returned a result identified isovaleric acidaemia (IVA) as the likely diagnosis.
Other possible causes provided to explain this acylcarnitine pattern included 2-methylbutyryl-CoA dehydrogenase deficiency (SBCAD deficiency) (28/46) and pivaloyl-containing antibiotics (16).

Recommendations
100% of participating laboratories recommended urine organic acid analysis to confirm the diagnosis. 44/46 suggested genetic diagnosis, with the majority specifying analysis of the *IVD* gene.
Other commonly suggested recommendations included plasma or repeat bloodspot acylcarnitines (21), ammonia (10) and C5 isobars (8) to exclude pivaloyl-CoA as a cause of the increased C5-carnitine.
24/46 participants provided recommendations on patient management, including referral to a specialist metabolic team and family testing.

Scoring
The scoring criteria were –
Analytical: 2 points for increased C5 and/or appropriate ratios including C5/C2 and C5/C3.
Interpretative: 2 points for IVA as the primary or secondary likely diagnosis with appropriate recommendations (urine organic acids, genetics, enzyme analysis), or 1 point for IVA without recommendations.

Overall impression
This was a sample with clear acylcarnitine abnormalities, and as such all participants who returned results scored full marks for analysis and interpretation.

8.4. Patient D

Medium chain acyl-CoA dehydrogenase (MCAD) deficiency due to mutation in the *ACADM* gene, OMIM 201450.

Patient details provided to participants
Presented with encephalopathy and respiratory distress at 4 days old. Metabolic acidosis, hypoglycaemia, high ketones.

Patient details
This sample is from a currently treated and well patient with a confirmed genetic diagnosis of medium chain acyl-CoA dehydrogenase deficiency (MCADD). An acute sample from the same patient at the time of the above symptoms was distributed in 2024 (sample ACDB-L-2024-F).
The patient presented in a state of acute metabolic decompensation at the age of 4 days old (prior to the newborn screening sample being taken) with significant ketotic hypoglycaemia and mild hyperammonaemia.
The initial metabolic investigations at that time included acylcarnitine and urine organic acid analysis, which were both consistent with a diagnosis of MCADD and showed evidence of ketosis/ketonuria. A referral for MCADD was made by Newborn Screening a few days later.
The patient was 10 months old at the time of this sample. He is developmentally well, has not had any decompensations since initial presentation, has not required emergency regimen and is able to go without feed overnight.

Analytical performance
Results were returned by 98% of participating laboratories (46/47).

This was a highly scoring sample with all participants who returned a result scoring two analytical marks. All participants identified the elevated or grossly elevated C6, C8, C10:1 and/or C8/C10 ratio.

Diagnosis / Interpretative proficiency
44/46 participants who returned a result identified MCADD as the likely diagnosis and scored 2 marks. Despite identifying the abnormal acylcarnitines, it is unclear why the remaining two labs did not suggest MCADD.
The major other possible diagnosis suggested was multiple acyl-CoA dehydrogenase deficiency (11/46).
Excluding one non-submitter, overall interpretative proficiency for this sample was 95.7%.

Recommendations
The majority of participating laboratories (42/46) recommended genetic analysis for confirmation of the suspected diagnosis of MCADD, with most specifying analysis of the *ACADM* gene. Other commonly suggested recommendations included urine organic acid analysis (41/46), plasma or repeat bloodspot acylcarnitines (23), enzyme studies (specifically MCAD) (11), and a number of routine Chemistry tests including ammonia, glucose, CK, LFTs, lactate, ketones and blood gas analysis.
27/46 participants provided recommendations on patient management, including referral to a specialist metabolic team and family testing.

Scoring
The scoring criteria were –
Analytical: 2 points for increased C8, C6, C10:1 etc and/or appropriate ratio such as C8/C10.
Interpretative: 2 points for MCADD as the primary or secondary likely diagnosis with appropriate recommendations or 1 point for an alternative diagnosis with recommendations that would identify MCADD as the diagnosis (such as urine organic acid analysis or FAOD gene panel).

Overall impression
This was a sample with clear acylcarnitine abnormalities. Overall proficiency for this sample was 97.8% (excluding one non-submitter).

8.5. Patient E

Cobalamin C deficiency due to mutation in the *MMACHC* gene, OMIM 277400.

Patient details provided to participants
Mild dev delay, diagnosed after younger sister investigated for seizures.

Patient details
This sample was collected from an 11 year female who has some mild developmental delay but is otherwise well. Following investigation of her sister for seizures, a genetic diagnosis of cobalamin C deficiency was made in both siblings.
At the time of sample collection, this patient was receiving betaine, vitamin B12, calcium folinate and carnitine.

Analytical performance
Results were returned by 98% of participating laboratories (46/47).
The acylcarnitine pattern in this sample was subtle. Propionylcarnitine is either only mildly increased or identified as increased via use of a ratio, such as C3/C2 or C3/C16.
These abnormalities were identified by 26/46 participants (56.5%) who all scored 2 marks. 19 laboratories reported a normal profile (41.3%). One participant identified findings associated with glutaric aciduria type 1.
Excluding one non-submitter, overall analytical proficiency for this sample was 54.3%.

Diagnosis / Interpretative proficiency
A diagnosis of cobalamin C deficiency was made by 13/46 participants. Other suggested diagnoses included an unspecified cobalamin defect (13), a specific cobalamin defect (D, F, J, E), vitamin B12 deficiency (14), other disorder of methylmalonate metabolism (including mutase and epimerase defects)

(10), propionic acidaemia (8), remethylation defects (3), multiple carboxylase / biotinidase deficiency (3), SUCLA2 deficiency (2) and other unrelated IMD (7).
25/46 participants scored either 3 or 4 total points. Eight participants scored 0 marks but no critical errors have been made due to the subtlety of the abnormal findings.
It should be noted that additional second-line analyses, including in this sample total homocysteine, should not contribute to the interpretation and suggestions submitted. Following a discussion of this matter at the Scientific Advisory Board meeting, the reduced points awarded for these participants reflects this. This is not a diagnostic proficiency scheme, but a scheme for acylcarnitine analysis and interpretation.
Excluding one non-submitter, overall interpretative proficiency for this sample was 67.4%.

Recommendations
A wide range of recommendations were provided, but commonly included urine organic acid analysis (33/46), plasma total homocysteine (21), amino acids (mainly in plasma but urine and CSF also suggested) (21), plasma or repeat dried bloodspot acylcarnitines (16), vitamin B12 (15), plasma MMA (12), plasma folate (5) and various other routine laboratory tests.
22/46 participants suggested genetic analysis, with the genes specified varying depending on the diagnoses suggested by each lab.

Scoring
The scoring criteria were –
Analytical: 2 points for increased C3 and/or appropriate ratio including C3/C2 and C3/C16.
Interpretative: 2 points if a cobalamin defect, MMA, PA or other related IMD included in the primary or secondary likely diagnosis with appropriate recommendations (urine organic acids, plasma MMA, total homocysteine, vitamin B12, genetics, enzyme analysis). 1 point if further investigations provided that would identify abnormalities in MMA metabolism.

Overall impression
This sample was obtained from an otherwise well patient with a mild deficiency of cobalamin C and only subtle abnormalities in the acylcarnitine profile. This was reflected in the relatively low overall proficiency for this sample of 60.9%. It was agreed at the Scientific Advisory Board meeting that no critical errors would be made for this sample.

8.6. Patient F

Malonic aciduria; Malonyl-CoA carboxylase deficiency due to a mutation in the *MLYCD* gene, OMIM 248360.

Patient details provided to participants
Mild motor and speech delay and mild left ventricular hypertrophy aged 3.

Patient details
This sample was obtained from a 14 year old treated and well patient with a genetic diagnosis of malonyl-CoA decarboxylase deficiency (malonic aciduria). The patient was diagnosed at the age of three after investigation for mild motor and speech delay and mild left ventricular hypertrophy. The patient no longer has any cardiac issues, is receiving carnitine, and has an emergency regimen but rarely requires it. She attends a mainstream school although some speech and language support continues to be required.

Analytical performance
Results were returned by 98% of participating laboratories (46/47).
There was a divide in analytical proficiency with 39/46 participants identifying the increased malonylcarnitine (C3DC) and scoring 2 marks. The remaining seven participants did not identify any abnormality; it is not clear whether this is because these participants do not identify and/or quantitate C3DC in their methods.
Analytical methods that do not employ derivatisation are not able to distinguish between isobaric C3DC and C4OH acylcarnitines. Nine of the participants who identified the diagnostic abnormality reported increased C3DC+C4OH and went on to correctly suggest malonic aciduria as the diagnosis.
Excluding one non-submitter, overall analytical proficiency for this sample was 82.6%.

Diagnosis / Interpretative proficiency

All participants who identified increased C3DC (or C3DC+C4OH) identified malonic aciduria as the likely diagnosis and therefore scored the full 4 marks.
The seven participants who did not identify the diagnostic abnormality scored overall 0 or 1 marks depending on any recommendations provided. Four participants scored zero points and critical errors were confirmed by the Scientific Advisory Board. The other three participants, who scored one point, were saved from a critical error by recommending urine organic acid analysis.
The main other possible diagnosis suggested was combined malonic and methylmalonic aciduria (CMAMMA) (12/46).
Excluding one non-submitter, overall interpretative proficiency for this sample was 88.0%.

Recommendations
All participants who identified the correct diagnosis suggested confirmation by genetic analysis of the *MLYCD* gene, and three labs additionally suggested analysis of the *ACSF3* gene (for CMAMMA). The most commonly suggested biochemical investigation was urine organic acids (39/46), then plasma or repeat acylcarnitines (17), with some participants recommending to ensure derivatised analysis for accurate identification of C3DC and C4OH. In view of the cardiac clinical presentation, 11 participants suggested acid alpha-glucosidase enzyme analysis to exclude Pompe disease. A wide range of routine Chemistry tests were suggested.
22/46 participants provided recommendations on patient management, including referral to a specialist metabolic team and family testing.

Scoring
The scoring criteria were –
Analytical: 2 points for increased C3DC (or C3DC+C4OH).
Interpretative: 2 points for malonic aciduria as the primary or secondary likely diagnosis with appropriate recommendations. 1 point for an alternative diagnosis with recommendations that would identify malonic aciduria (i.e. urine organic acids).
Critical error if the diagnostic metabolite was not identified and no recommendations provided.

Overall impression
This was a sample with a clear acylcarnitine abnormality, and as such all participants who identify C3DC in their acylcarnitine repertoire scored full marks for analysis and interpretation. Overall proficiency for this sample was 85.3% (excluding one non-submitter).

9. Scores of participants

All data transfer, the submission of data as well as the request and viewing of reports proceed via the 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.	VLCADD (common sample)			HIBCH (educational sample)			IVA			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	1	1	2	2	2	4	10
2	2	2	4	1	1	2	2	2	4	10
3	2	2	4	2	1	3	2	2	4	11
4	2	2	4	2	1	3	2	2	4	11
5	2	2	4	1	1	2	2	2	4	10
6	2	2	4	1	1	2	2	2	4	10
7	2	2	4	1	1	2	2	2	4	10
8	2	2	4	1	1	2	2	2	4	10
9	2	2	4	1	1	2	2	2	4	10
10	2	2	4	1	1	2	2	2	4	10
11	2	2	4	2	2	4	2	2	4	12
12	2	2	4	1	1	2	2	2	4	10
13	2	2	4	2	0	2	2	2	4	10
14	2	2	4	2	1	3	2	2	4	11
15	2	2	4	1	1	2	2	2	4	10
16	2	2	4	2	1	3	2	2	4	11
17	2	2	4	1	1	2	2	2	4	10
18	2	2	4	2	1	3	2	2	4	11
19	2	2	4	1	1	2	2	2	4	10
20	2	2	4	2	1	3	2	2	4	11
21	2	2	4	1	1	2	2	2	4	10
22	2	2	4	1	1	2	2	2	4	10
23	2	2	4	2	1	3	2	2	4	11
24	2	2	4	1	1	2	2	2	4	10
25	2	2	4	1	1	2	2	2	4	10
26	2	2	4	1	1	2	2	2	4	10
27	2	2	4	1	1	2	2	2	4	10
28	2	2	4	1	1	2	2	2	4	10
29	2	2	4	1	1	2	2	2	4	10

	Patient A			Patient B			Patient C			
Lab no.	VLCADD (common sample)			HIBCH (educational sample)			IVA			
	A	I	Total	A	I	Total	A	I	Total	Total
30	2	2	4	1	1	2	2	2	4	10
31	2	2	4	1	1	2	2	2	4	10
32	2	2	4	1	1	2	2	2	4	10
33	2	2	4	1	0	1	2	2	4	9
34	2	2	4	1	1	2	2	2	4	10
35	2	2	4	1	1	2	2	2	4	10
36	2	2	4	1	1	2	2	2	4	10
37	2	2	4	1	1	2	2	2	4	10
38	2	2	4	2	1	3	2	2	4	11
39	2	2	4	1	1	2	2	2	4	10
40	2	2	4	2	2	4	2	2	4	12
41	2	2	4	1	1	2	2	2	4	10
42	2	2	4	0	1	1	2	2	4	9
43	2	2	4	1	1	2	2	2	4	10
44	2	2	4	1	0	1	2	2	4	9
45	2	2	4	1	1	2	2	2	4	10
46	2	2	4	1	1	2	2	2	4	10
47										Non-Submitter

Detailed scores – Round 2

	Patient D			Patient E			Patient F			
Lab no.	MCADD			Cobalamin C			Malonic aciduria			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	0	0	0	8
2	2	2	4	2	2	4	0	0	0	8
3	2	2	4	0	0	0	2	2	4	8
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	0	1	1	2	2	4	9
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	2	2	4	2	2	4	12
8	2	2	4	2	2	4	2	2	4	12
9	2	2	4	2	2	4	2	2	4	12
10	2	2	4	0	1	1	2	2	4	9
11	2	2	4	2	2	4	2	2	4	12
12	2	2	4	2	2	4	2	2	4	12
13	2	2	4	2	1	3	2	2	4	11
14	2	2	4	0	1	1	2	2	4	9

	Patient D			Patient E			Patient F			
Lab no.	MCADD			Cobalamin C			Malonic aciduria			
	A	I	Total	A	I	Total	A	I	Total	Total
15	2	2	4	2	1	3	0	0	0	7
16	2	2	4	2	2	4	2	2	4	12
17	2	2	4	2	2	4	2	2	4	12
18	2	2	4	0	0	0	2	2	4	8
19	2	0	2	2	2	4	2	2	4	10
20	2	2	4	2	1	3	2	2	4	11
21	2	2	4	0	1	1	0	1	1	6
22	2	2	4	0	0	0	2	2	4	8
23	2	2	4	0	0	0	2	2	4	8
24	2	2	4	0	2	2	2	2	4	10
25	2	2	4	0	1	1	2	2	4	9
26	2	2	4	2	2	4	2	2	4	12
27	2	1	3	0	0	0	0	1	1	4
28	2	2	4	2	2	4	2	2	4	12
29	2	2	4	0	0	0	2	2	4	8
30	2	2	4	2	2	4	0	1	1	9
31	2	2	4	2	2	4	2	2	4	12
32	2	2	4	2	2	4	2	2	4	12
33	2	2	4	2	2	4	2	2	4	12
34	2	2	4	0	2	2	0	2	2	8
35	2	2	4	0	1	1	2	2	4	9
36	2	2	4	2	2	4	2	2	4	12
37	2	1	3	0	1	1	2	2	4	8
38	2	2	4	2	2	4	2	2	4	12
39	2	2	4	0	1	1	2	2	4	9
40	2	2	4	0	2	2	2	2	4	10
41	2	2	4	0	0	0	2	2	4	8
42	2	2	4	0	0	0	2	2	4	8
43	2	2	4	0	1	1	2	2	4	9
44	2	2	4	2	1	3	2	2	4	11
45	2	2	4	2	2	4	2	2	4	12
46	2	2	4	0	1	1	0	0	0	5
47										Non-Submitter

Total scores

Excluding scores for sample B which is designated an educational sample

Lab no.	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	-	4	4	4	0	16	80	Sample F
2	4	-	4	4	4	0	16	80	Sample F
3	4	-	4	4	0	4	16	80	
4	4	-	4	4	4	4	20	100	
5	4	-	4	4	1	4	17	85	
6	4	-	4	4	4	4	20	100	
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	1	4	17	85	
11	4	-	4	4	4	4	20	100	
12	4	-	4	4	4	4	20	100	
13	4	-	4	4	3	4	19	95	
14	4	-	4	4	1	4	17	85	
15	4	-	4	4	3	0	15	75	Sample F
16	4	-	4	4	4	4	20	100	
17	4	-	4	4	4	4	20	100	
18	4	-	4	4	0	4	16	80	
19	4	-	4	2	4	4	18	90	
20	4	-	4	4	3	4	19	95	
21	4	-	4	4	1	1	14	70	
22	4	-	4	4	0	4	16	80	
23	4	-	4	4	0	4	16	80	
24	4	-	4	4	2	4	18	90	
25	4	-	4	4	1	4	17	85	
26	4	-	4	4	4	4	20	100	
27	4	-	4	3	0	1	12	60	
28	4	-	4	4	4	4	20	100	
29	4	-	4	4	0	4	16	80	
30	4	-	4	4	4	1	17	85	
31	4	-	4	4	4	4	20	100	
32	4	-	4	4	4	4	20	100	
33	4	-	4	4	4	4	20	100	
34	4	-	4	4	2	2	16	80	
35	4	-	4	4	1	4	17	85	
36	4	-	4	4	4	4	20	100	
37	4	-	4	3	1	4	16	80	
38	4	-	4	4	4	4	20	100	
39	4	-	4	4	1	4	17	85	

Lab no.	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
40	4	-	4	4	2	4	18	90	
41	4	-	4	4	0	4	16	80	
42	4	-	4	4	0	4	16	80	
43	4	-	4	4	1	4	17	85	
44	4	-	4	4	3	4	19	95	
45	4	-	4	4	4	4	20	100	
46	4	-	4	4	1	0	13	65	Sample F
47		-					Non-Submitter		

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 70 % of adequate responses)	41	87
Unsatisfactory performers (< 70 % adequate responses and/or critical error)	5	11
Partial and non-submitters	1	2

Overall Proficiency

(excluding non-submitters)

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
ACDB-UL-2025-A	VLCADD (common sample)	**100**	**100**	**100**
ACDB-UL-2025-B	HIBCH (educational sample)	**61**	**49**	**55**
ACDB-UL-2025-C	IVA	**100**	**100**	**100**
ACDB-UL-2025-D	MCADD	**100**	**96**	**98**
ACDB-UL-2025-E	Cobalamin C	**54**	**67**	**61**
ACDB-UL-2025-F	Malonic aciduria	**83**	**88**	**85**

10. Preview of the scheme in 2026

Sample distribution	4th February 2026
Start of analysis of Survey 2026/1 - Website open	17th March 2026
Survey 2026/1 - Results submission	7th April 2026
Survey 2026/1 - Reports	2nd June 2026
Start of analysis of Survey 2026/2 - Website open	1st June 2026
Survey 2026/2 – Results submission	22nd June 2026
Survey 2026/2 - Reports	17th August 2026
Annual Report 2026	Jan-Mar 2027

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, Suggestions and Complaints

If you have any questions, comments or suggestions please address to the Scientific Advisor of the scheme, Mrs Erin Emmett and/or to the ERNDIM Administration Office (admin@erndim.org).

Most complaints received by ERNDIM consist of minor misunderstandings or problems with samples, which can usually be resolved via direct contact with the ERNDIM administrative staff. If you wish to file a formal complaint, please email your complaint with details of your issue to admin@erndim.org or contact us through our website at https://www.erndim.org/contact-us/

Date of report, 2026-03-05
Name and signature of Scientific Advisor

Mrs Erin Emmett
Scientific Advisor

Please 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 scheme advisor.

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

Version Number	Published	Amendments
1	5th March 2026	2025 annual report published

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