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# Acylcarnitines in dried blood spots

# Centre: United Kingdom

# Final Report 2021

prepared by
Mr Charles Turner

**Note**: This annual report is intended for participants of the ERNDIM Acylcarnitines in dried blood spots (ACDB) London 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 Charles Turner (Evelina London Children's Hospital) in conjunction with CSCQ (sub-contractor on behalf of ERNDIM), both appointed by and according to procedures laid down the ERNDIM Board. CSCQ dispatches the EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports.

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. This year no normal profiles were sent out. 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

In 2021 44 laboratories from many different countries participated in the ACDB London scheme.

[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.

There was 1 educational participant in 2021 (none in 2020). 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.

Participants and new applicants will be 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 | Country | Number of Participants |
|---|---|---|---|
| UK | 13 | Germany | 1 |
| Italy | 11 | Ireland | 1 |
| Canada | 5 | New Zealand | 1 |
| Australia | 4 | Oman | 1 |
| Turkey | 2 | Qatar | 1 |
| Brazil | 1 | Russian Federation | 1 |
| Chile | 1 | Taiwan | 1 |

## 3. Design and logistics of the scheme including sample information

As usual, the samples used in 2021 were authentic human blood spot samples, all 6 from affected patients.

All samples selected by the Scientific Advisor are prepared from 30-50µl of lithium heparin anticoagulated whole blood on Whatman (Schleicher & Schuell) 903™ /Perkin Elmer Ahlstrom 226 paper. All samples are obtained following local ethical and consent guidelines.

In 2021 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 2021 ERNDIM ACDB London scheme.

| | 1st Submission Round | 2nd Submission Round |
|---|---|---|
| **Sample ID's:** | ACDB-UL-2021-A<br>ACDB-UL-2021-B<br>ACDB-UL-2021-C | ACDB-UL-2021-D<br>ACDB-UL-2021-E<br>ACDB-UL-2021-F |
| **Shipment of samples** | February 12th, 2021 | |
| **Start of analysis (clinical data available)** | March 9th, 2021 | June 8th, 2021 |
| **Reminder for result submission** | March 23rd, 2021 | July 15th, 2021 |
| **Results submission deadline:** | March 30th, 2021 | July 22nd, 2021 |
| **Interim reports available on CSCQ website** | September 1st, 2021 | September 17th, 2021 |

***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 2021 ERNDIM ACDB London scheme.

| Survey | Sample no. | Diagnosis |
|---|---|---|
| 20-05-OUH | ACDB-UL-2021-A | Propionyl CoA carboxylase deficiency: OMIM 606054 |
| | ACDB-UL-2021-B | Propionyl CoA carboxylase deficiency: OMIM 606054 |
| | ACDB-UL-2021-C | LCHADD, OMIM 609016 |

| Survey | Sample no. | Diagnosis |
|---|---|---|
| 20-07-OUH | ACDB-UL-2021-D | The sample was from a patient presenting with infantile carnitine palmitoyl transferase deficiency. |
| | ACDB-UL-2021-E | Methylmalonyl CoA mutase deficiency, OMIM 251000. |
| | ACDB-UL-2021-F | Holocarboxylase synthetase deficiency, OMIM 253270 |

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 Dried blood spot samples have been provided by the scheme.

## 5. Results

Returned results in the 2021 ERNDIM ACDB London scheme.

| | Survey 1 | Survey 2 |
|---|---|---|
| Receipt of results | 41 | 42 |
| No answer | 3 | 2 |

## 6. Web site reporting

The website reporting system is compulsory for all centres. 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 2021 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, 2021).

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, 2021.

## 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'.

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.

# 8. Results of samples and evaluation of reporting

## 8.1. Patient A

The sample was from a patient with propionyl CoA carboxylase deficiency (OMIM 606054), on treatment with carnitine. This sample was supplied by the Rome centre of the ERNDIM dried blood spot acylcarnitine scheme and was the "common sample" distributed to all participants in all three centres.

### Patient details provided to participants

Patient admitted for vomit, asthenia, cardiac insufficiency, and acidosis. In treatment with carnitine

### Patient details

The sample was from a patient with propionyl CoA carboxylase deficiency (OMIM 606054), on treatment with carnitine. This sample was supplied by the Rome centre of the ERNDIM dried blood spot acylcarnitine scheme and was the "common sample" distributed to all participants in all three centres.

### Analytical performance

All the participants who reported results (41/41) commented on the elevated propionyl(C3) carnitine (40/41) or associated ratios as well as the elevated free (C0) carnitine 41/41. The most commonly reported ratios were C3/C2 (21 participants), C3/C0 (9 participants) and C3/C16 (8 participants. Methylmalonyl carnitine was reported by 14 laboratories, with 12 of these finding it within their reference ranges, 1 low, and 1 finding it elevated.

### Diagnosis / Interpretative proficiency

All participants included propionyl CoA carboxylase deficiency in their differential diagnosis for this patient.

### Recommendations

All laboratories included urinary organic acid analysis as a first line follow-up test to confirm their findings and to exclude one of the methylmalonic acidaemias from the diagnosis. Most would then go on to genotyping to confirm the diagnosis. Several laboratories measured or suggested measuring confirmatory metabolites on the original blood spot: these included methylcitric acid, propionic acid, 3-hydroxypropionic acid, propionyl glycine, methylmalonic acid and total homocysteine.

### Scoring

All laboratories who returned results obtained a maximum score (41/41) 100% proficiency

**Overall impression**

All respondents correctly reported significantly raised propionyl (C3) carnitine in this sample, and all of them suggested appropriate tests to clarify and confirm the location of the deficiency in the propionate pathway.

## 8.2. Patient B

The sample was from a patient with propionyl CoA carboxylase deficiency (OMIM 606054) on treatment with carnitine.

**Patient details provided to participants**

Hyperammonaemia in infancy, currently well

**Patient details**

The sample was from a patient with propionyl CoA carboxylase deficiency (OMIM 606054) on treatment with carnitine

**Analytical performance**

All but one of the participants who reported results (41/41) commented on the elevated propionyl(C3)carnitine. Many also mentioned elevated ratios indicating a raised propionyl carnitine, most commonly C3/C2 (21 participants), C3/C0 (9 participants) and C3/C16 (8 participants. Methylmalonyl carnitine was reported by 11 laboratories, with 8 of these finding it within their reference ranges and 3 finding it elevated. All participants who reported free carnitine levels found it to be within their reference ranges.

**Diagnosis / Interpretative proficiency**

40 of the 41 participants who found a raised C3 included propionyl CoA carboxylase deficiency in their differential diagnosis for this patient. The remaining laboratory only suggested one of the methylmalonic acidaemias but included urinary organic acids as a first line follow-up test which would have clarified their interpretation.

**Recommendations**

All laboratories included urinary organic acid analysis as a first line follow-up test to confirm their findings and to exclude one of the methylmalonic acidaemias from the diagnosis. Most would then go on to genotyping to confirm the diagnosis. Several laboratories measured or suggested measuring confirmatory metabolites on the original blood spot: these included methylcitric acid, propionic acid, 3-hydroxypropionic acid, propionyl glycine, methylmalonic acid and total homocysteine.

**Scoring**

Overall diagnostic proficiency for this sample was 99.4%

**Overall impression**

Most respondents correctly reported significantly raised propionyl (C3) carnitine in this sample, and all of these suggested appropriate tests to clarify and confirm the location of the deficiency in the propionate pathway.

## 8.3. Patient C

The sample was from a patient with long chain hydroxyacyl CoA dehydrogenase deficiency (LCHADD, OMIM 609016)

**Patient details provided to participants**

Muscle pain, mild cardiac arrhythmia

**Patient details**

Patient with long chain hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency (OMIM 609016)

**Analytical performance**

41 laboratories reported results for this sample. 39 reported at least one elevated long chain hydroxy acylcarnitine species (38/39 C18:1OH, 37/39 C18OH, 37/39 C16OH). 1 respondent reported the profile as normal and one noted the low acetyl (C2) carnitine but did not comment on the long chain hydroxyacyl carnitines.

**Diagnosis / Interpretative proficiency**

38/41 respondents suggested long chain hydroxyacyl CoA dehydrogenase deficiency (LCHADD) either due to mutations in the HADHA gene, or trifunctional protein (MTP) deficiency due to mutations in HADHB, as the most likely diagnosis on the basis of the high long chain hydroxy acylcarnitine species. One respondent suggested carnitine palmitoyl transferase type 2 (CPT2) deficiency on the basis of the low C2 and consequently raised (C16+C18:1)/C2 ratio, despite detecting elevations in long chain hydroxyacyl carnitines. The other two respondents suggested investigations for lysosomal storage disorders on the basis of the clinical description and no diagnostic acylcarnitine abnormalities.

**Recommendations**

38 of the 39 respondents who detected elevations of long chain hydroxyacyl carnitine species suggested tests to confirm the diagnosis and distinguish between long chain hydroxyacyl CoA dehydrogenase deficiency and trifunctional protein deficiency. A number indicated that plasma acylcarnitine analysis might be appropriate to confirm the dried blood spot findings. Most suggested genotyping of the HADHA and HADHB genes, with several also advocating fat oxidation studies in cultured fibroblasts either as a first confirmation or as a second line test if a mutation of uncertain significance was found.

The laboratory who suggested CPT2 despite detecting elevations in long chain hydroxyacyl carnitines suggested genotyping of the CPT gene as their only follow-up test.

**Scoring**

Diagnostic proficiency was 93.9%

**Overall impression**

The overwhelming majority (39/41) respondents detected the elevated long chain hydroxyacyl carnitines in this sample and suggested appropriate tests to clarify and confirm the diagnosis, including distinguishing between LCHADD and MTP deficiency. It was agreed at the November Scientific Advisory Board meeting that failure to detect the elevated long chain hydroxyacyl carnitines in this sample would constitute a “Critical Error”.

## 8.4. Patient D

Carnitine palmitoyl transferase deficiency OMIM 600649

**Patient details provided to participants**

Hypoglycaemia, cardiomyopathy

**Patient details**

The sample was from a patient presenting acutely in the neonatal period with carnitine palmitoyl transferase 2 (CPT2) deficiency (OMIM 600649).

**Analytical performance**

Most participants reported the marked elevation of long chain acylcarnitine species in particular C16 (palmitoyl carnitine) and (C16+C18:1)/C2 ratio. One laboratory reported a raised C3 and C5OH carnitine in this sample

**Diagnosis / Interpretative proficiency**

The majority of participants 31/41 included CPT2/CACT in their differential diagnosis, and suggested appropriate further tests to elucidate the precise defect. The most common alternative diagnosis considered was multiple acylCoA dehydrogenase deficiency (MADD), all 10 who did not suggest CPT2/CACT included MADD as a likely diagnosis.

**Recommendations**

Those participants who included CACT/CPT2 in their differential diagnosis suggested appropriate tests to clarify the diagnosis. The most common tests suggested were plasma acylcarnitine analysis (19/31), urinary organic acid analysis (23/31), genotyping directed towards the CPT2 gene and the SLC25A20 (CACT) genes to differentiate between these diagnoses (27/31). 4 respondents also suggested fatty acid oxidation studies in fibroblasts.

**Scoring**

Proficiency was 83.3%

**Overall impression**

It was surprising that so many participants did not recognise the disproportionate elevation of long chain acylcarnitines as indicating a possible CPT2/CACT deficiency, and considered MADD as a more likely diagnosis

## 8.5. Patient E

The sample was from a patient with methylmalonyl CoA mutase deficiency, OMIM 251000.

**Patient details provided to participants**

Acidosis, renal dysfunction

**Patient details**

The sample was from a patient with methylmalonyl CoA mutase deficiency (OMIM 251000), on carnitine supplementation, at a routine clinic visit for assessment of renal function. The patient has a low glomerular filtration rate: a common secondary complication of methylmalonic acidaemia.

**Analytical performance**

All but one participant who returned results reported the grossly elevated propionyl (C3) carnitine and/or ratios indicating elevated C3 (most commonly C3/C2 and C3/C16). A number of participants commented that the elevations of some unrelated acylcarnitine species e.g. C5:1 carnitine could have been due to the renal insufficiency of this patient.

**Diagnosis / Interpretative proficiency**

The majority of participants included methylmalonic acidaemia (MMA) within their differential diagnosis, and all suggested further tests which would have clarified the diagnosis. Four laboratories did not explicitly mention MMA, all of these considered that the raised C5OH carnitine together with the raised C3 indicated a biotin related multiple carboxylase deficiency (biotinidase or holocarboxylase synthetase deficiency).

**Recommendations**

39/41 would have followed up with urinary organic acid analysis (uOA), to differentiate between MMA and propionic acidaemia (PA), or guide further investigation or genotyping. The 2 laboratories who would not have performed uOA both named MMA as the most likely or only probable diagnosis and suggested mutation analysis of the genes in the propionate pathway as their only confirmatory test. 7 laboratories measured methylmalonic acid on the dbs sample and found it raised. Other tests suggested to clarify the diagnosis included total plasma homocysteine (21/41), plasma methylmalonic acid (14/41), plasma amino acids 13/41 and vitamin B12 assay (13/41). 4 suggested biotinidase activity measurement. 25 respondents suggested mutation analysis to provide a definitive diagnosis whilst 5 suggested enzyme assay in fibroblasts.

**Scoring**

Proficiency was 94.6%

**Overall impression**

The majority of respondents identified the abnormal C3 acylcarnitine species in this sample and most included MMA as a likely diagnosis. The majority suggested appropriate follow-up tests which would

have led to a correct diagnosis. Failure to recognise the grossly elevated C3 carnitine would constitute a "Critical Error"

## 8.6. Patient F

Biotin responsive multiple carboxylase deficiency, holocarboxylase synthetase deficiency, OMIM 253270

**Patient details provided to participants**

Seizures in infancy, currently well

**Patient details**

The sample was from a patient with biotin responsive multiple carboxylase deficiency, holocarboxylase synthetase deficiency, OMIM 253270, on treatment with biotin, at a routine clinic visit to check biotin dosage.

**Analytical performance**

The most common abnormality noted was a raised 3-hydroxyisovaleryl (C5OH) carnitine (32 respondents).

**Diagnosis / Interpretative proficiency**

The majority of respondents included abnormalities in biotin related pathways in their differential diagnosis (31 participants). The most common alternative explanation for the raised C5OH carnitine was 3-methylcrotonyl CoA carboxylase (3MCC) deficiency.

**Recommendations**

Most respondents suggested urinary organic acid analysis to clarify the diagnosis, and many also would have measured biotinidase activity and holocarboxylase synthetase activity. Definitive diagnoses would have been provided either by enzyme assay or genotyping directed by the biochemical analyses.

**Scoring**

Proficiency 70.8%

**Overall impression**

The sample was not easy to interpret since the patient was already on biotin supplementation and the acylcarnitine abnormalities were mild. This led to some suggesting that the sample was essentially normal.

## 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.

### 9.1. Detailed scores – Round 1

| Lab n° | Patient A | | | Patient B | | | Patient C | | |
|---|---|---|---|---|---|---|---|---|---|
| | Propionyl CoA carboxylase deficiency: OMIM 606054 | | | Propionyl CoA carboxylase deficiency: OMIM 606054 | | | Long chain hydroxyacyl CoA dehydrogenase deficiency: OMIM 609016 | | |
| | 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 | 0 | 0 | 0 |
| **9** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **10** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 0 | 0 |
| **11** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **12** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **13** | 2 | 2 | 4 | 2 | 2 | 4 | 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** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **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 | 2 | 4 | 2 | 0 | 2 |
| **23** | 2 | 2 | 4 | 2 | 2 | 4 | 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** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **28** | 2 | 2 | 4 | 2 | 2 | 4 | 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 | 2 | 4 | 2 | 2 | 4 |
| **32** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **33** | 2 | 2 | 4 | 2 | 1 | 3 | 2 | 2 | 4 |
| **34** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |

| Lab n° | Patient A | | | Patient B | | | Patient C | | |
|---|---|---|---|---|---|---|---|---|---|
| | Propionyl CoA carboxylase deficiency: OMIM 606054 | | | Propionyl CoA carboxylase deficiency: OMIM 606054 | | | Long chain hydroxyacyl CoA dehydrogenase deficiency: OMIM 609016 | | |
| | A | I | Total | A | I | Total | A | I | Total |
| **35** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **36** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **37** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **38** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **39** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **40** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **41** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **42** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **43** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **44** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

## 9.2. Detailed scores – Round 2

| Lab n° | Patient D | | | Patient E | | | Patient F | | |
|---|---|---|---|---|---|---|---|---|---|
| | Carnitine palmitoyl transferase deficiency OMIM 600649 | | | Methylmalonyl CoA mutase deficiency, OMIM 251000 | | | Holocarboxylase synthetase deficiency, OMIM 253270 | | |
| | A | I | Total | A | I | Total | A | I | Total |
| **1** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 0 | 2 |
| **2** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **3** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **4** | 2 | 0 | 2 | 2 | 2 | 4 | 2 | 2 | 4 |
| **5** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **6** | 2 | 0 | 2 | 2 | 1 | 3 | 2 | 2 | 4 |
| **7** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 1 | 3 |
| **8** | 2 | 0 | 2 | 2 | 2 | 4 | 0 | 0 | 0 |
| **9** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 0 | 0 |
| **10** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 0 | 0 |
| **11** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **12** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **13** | 2 | 0 | 2 | 2 | 2 | 4 | 2 | 1 | 3 |
| **14** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **15** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 1 | 1 |
| **16** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **17** | 1 | 0 | 1 | 2 | 1 | 3 | 2 | 2 | 4 |
| **18** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 0 | 0 |
| **19** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **20** | 2 | 2 | 4 | 2 | 1 | 3 | 2 | 1 | 3 |
| **21** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **22** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **23** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 1 | 3 |
| **24** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| Lab n° | Patient D | | | Patient E | | | Patient F | | |
|---|---|---|---|---|---|---|---|---|---|
| | Carnitine palmitoyl transferase deficiency OMIM 600649 | | | Methylmalonyl CoA mutase deficiency, OMIM 251000 | | | Holocarboxylase synthetase deficiency, OMIM 253270 | | |
| | A | I | Total | A | I | Total | A | I | Total |
| **25** | 2 | 0 | 2 | 2 | 2 | 4 | 2 | 2 | 4 |
| **26** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **27** | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| **28** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **29** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **30** | 2 | 0 | 2 | 2 | 2 | 4 | 2 | 2 | 4 |
| **31** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **32** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **33** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **34** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **35** | 2 | 2 | 2 | 2 | 2 | 4 | 2 | 2 | 4 |
| **36** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 0 | 0 |
| **37** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 |
| **38** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 0 | 0 |
| **39** | 2 | 0 | 2 | 2 | 2 | 4 | 2 | 0 | 2 |
| **40** | 2 | 0 | 2 | 2 | 1 | 3 | 2 | 1 | 3 |
| **41** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 0 | 0 |
| **42** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 1 | 3 |
| **43** | 2 | 0 | 2 | 2 | 2 | 4 | 2 | 2 | 4 |
| **44** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

## 9.3. Total scores

| Lab n° | A | B | C | D | E | F | Cumulative score | Cumulative score (%) | Critical error (CE) / Non-Submitter (NS) / Partial Submitter (PS) |
|---|---|---|---|---|---|---|---|---|---|
| **1** | 4 | 4 | 4 | 4 | 4 | 2 | 22 | 92 | |
| **2** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **3** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **4** | 4 | 4 | 4 | 2 | 4 | 4 | 22 | 92 | |
| **5** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **6** | 4 | 4 | 4 | 2 | 3 | 4 | 21 | 88 | |
| **7** | 4 | 4 | 4 | 4 | 4 | 3 | 23 | 96 | |
| **8** | 4 | 4 | 0 | 2 | 4 | 0 | 14 | 58 | CE |
| **9** | 4 | 4 | 4 | 4 | 4 | 0 | 20 | 83 | |
| **10** | 4 | 4 | 0 | 4 | 4 | 0 | 16 | 67 | CE |
| **11** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **12** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **13** | 4 | 4 | 4 | 2 | 4 | 3 | 21 | 88 | |
| **14** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **15** | 4 | 4 | 4 | 4 | 4 | 1 | 21 | 88 | |
| **16** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |

| Lab n° | A | B | C | D | E | F | Cumulative score | Cumulative score (%) | Critical error (CE) / Non-Submitter (NS) / Partial Submitter (PS) |
|---|---|---|---|---|---|---|---|---|---|
| **17** | 0 | 0 | 0 | 1 | 3 | 4 | 8 | 33 | PS |
| **18** | 4 | 4 | 4 | 4 | 4 | 0 | 20 | 83 | |
| **19** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **20** | 4 | 4 | 4 | 4 | 3 | 3 | 22 | 92 | |
| **21** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **22** | 4 | 4 | 2 | 4 | 4 | 4 | 22 | 92 | |
| **23** | 4 | 4 | 4 | 4 | 4 | 3 | 23 | 96 | |
| **24** | 4 | 4 | 4 | 0 | 0 | 0 | 12 | 50 | CE |
| **25** | 4 | 4 | 4 | 2 | 4 | 4 | 22 | 92 | |
| **26** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **27** | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 4 | PS |
| **28** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **29** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **30** | 4 | 4 | 4 | 2 | 4 | 4 | 22 | 92 | |
| **31** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **32** | 4 | 4 | 4 | 0 | 0 | 0 | 12 | 50 | PS |
| **33** | 4 | 3 | 4 | 4 | 4 | 4 | 23 | 96 | |
| **34** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **35** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **36** | 4 | 4 | 4 | 4 | 4 | 0 | 20 | 83 | |
| **37** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **38** | 4 | 4 | 4 | 4 | 4 | 0 | 20 | 83 | |
| **39** | 4 | 4 | 4 | 2 | 4 | 2 | 20 | 83 | |
| **40** | 4 | 4 | 4 | 2 | 3 | 3 | 20 | 83 | |
| **41** | 4 | 4 | 4 | 4 | 4 | 0 | 20 | 83 | |
| **42** | 4 | 4 | 4 | 4 | 4 | 3 | 23 | 96 | |
| **43** | 4 | 4 | 4 | 2 | 4 | 4 | 22 | 92 | |
| **44** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | NS |

## 9.4. Performance

| | Number of labs | % total labs |
|---|---|---|
| **Satisfactory performers (≥ 70 % of adequate responses)** | 37 | 84 |
| **Unsatisfactory performers (< 70 % adequate responses and/or critical error)** | 3 | 7 |
| **Partial and non-submitters** | 4 | 9 |

## 9.5. Overall Proficiency

| Sample | Diagnosis | Analytical (%) | Interpretation (%) | Total (%) |
|---|---|---|---|---|
| ACDB-UL-2021-A | Propionyl CoA carboxylase deficiency: OMIM 606054 | 100.0% | 100.0% | 100.0% |
| ACDB-UL-2021-B | Propionyl CoA carboxylase deficiency: OMIM 606054 | 100.0% | 98.8% | 99.4% |
| ACDB-UL-2021-C | Long chain hydroxyacyl CoA dehydrogenase deficiency: OMIM 609016 | 95.1% | 92.7% | 93.9% |
| ACDB-UL-2021-D | Carnitine palmitoyl transferase deficiency OMIM 600649 | 95.2% | 71.4% | 83.3% |
| ACDB-UL-2021-E | Methylmalonyl CoA mutase deficiency, OMIM 251000 | 95.2% | 90.5% | 92.9% |
| ACDB-UL-2021-F | Holocarboxylase synthetase deficiency, OMIM 253270 | 76.2% | 65.5% | 70.8% |

## 10. Preview of the scheme in 2022

There will be no changes in the structure and design of the ACDB scheme in 2022.

## 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.

Date of original report, 2022-05-30

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 | 30 May 2022 | 2021 annual report published |
| 2 | 03 November 2022 | Page 7: item 8.4 - Diagnostic proficiency for sample D updated inline with changes to item 9.2<br>Page 11: item 9.2, Lab 35 - score for interpretation for sample D corrected<br>Page 12: item 9.3, Lab 35 – scores updated in line with changes to item 9.2<br>Page 13 : item 9.5 – Proficiency for sample D updated in line with changes to item 9.2 |
| | | |

**END**