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Published: 26 April 2022[1]

Acylcarnitines in dried blood spots Rome: Italy

Final Report 2021

prepared by
Dr. Cristiano Rizzo

Note: This annual report is intended for participants of the ERNDIM Acylcarnitines in dried blood spots (ACDB) Rome scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

The fact that your laboratory participates in ERNDIM schemes is not confidential. However, the raw data and performance scores are confidential and will only be shared within ERNDIM for the purpose of evaluating performance of your laboratory, unless ERNDIM is required to disclose performance data by a relevant government agency. For details, please see the terms and conditions in the EQA Schemes Catalogue and Participant Guide and the ERNDIM Privacy Policy on www.erndim.org.

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 Dr Cristiano Rizzo (Laboratory of metabolic disease Bambino Gesù 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 2021 47 laboratories from many different countries participated in the ACDB Rome scheme.
There was one educational participant 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.
Participants and new applicants will 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.

Country	*Number of participants*		*Country*	*Number of participants*
BELGIUM	6		MOROCCO	1
BULGARIA	1		PORTUGAL	3
CROATIA	1		REPUBLIC OF SINGAPORE	1
CZECH REPUBLIC	2		SLOVAKIA	2
GREECE	1		SLOVENIA	1
ISRAEL	2		UK	2
KINGDOM of SAUDI ARABIA	1		SPAIN	8
LEBANON	1		SWITZERLAND	2
LITHUANIA	1		TAIWAN	1
MALAYSIA	3		USA	6

3. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Cristiano RIzzo as Scientific Advisor and coordinated by CSCQ as scheme organiser (sub-contractor on behalf of ERNDIM), both appointed by and according to procedures laid down the ERNDIM Board.
As usual, the samples used in 2021 were authentic human blood spot samples, 5 from affected patients and one from a healthy individual.
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 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 Rome scheme.

	1st Submission Round	**2nd Submission Round**
Sample ID's:	ACDB-IR-2021-A ACDB-IR-2021-B ACDB-IR-2021-C	ACDB-IR-2021-D ACDB-IR-2021-E ACDB-IR-2021-F
4.2. Shipment of samples	February 10th, 2021	
4.3. **Start of analysis (clinical data available)**	March 8, 2021	June 7, 2021
Reminder for result submission	March 22, 2021	June 21, 2021
Results submission deadline:	March 29, 2021	June 28, 2021
Interim reports available on CSCQ website	April 12, 2021	July 12, 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 Rome scheme.

Survey	Sample no.	Diagnosis
1	ACDB-IR-2021-A	Propionyl-CoA carboxylase deficency
	ACDB-IR--2021-B	Normal acylcarnitines profile
	ACDB-IR-2021-C	Very long Chain Acyl-CoA dehydrogenase deficency (VLCAD)
2	ACDB-IR-2021-D	HMG
	ACDB-IR-2021-E	cblC
	ACDB-IR-2021-F	CPT1

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 DBS samples have been provided by the scheme organizer

Patient A: Propionyl-CoA carboxylase deficency
Patient B: Normal acylcarnitines profile
Patient C: Very long Chain Acyl-CoA dehydrogenase deficency (VLCAD)
Patient D: HMG
Patient E: cblC
Patient F: CPT1

5. Results

Returned results in the 2021 ERNDIM ACDB Rome scheme.

	Survey 1	**Survey 2**
Receipt of results	43	43
No answer	4	4

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.

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.

7.2. Score for satisfactory performance

At least 17 points from the maximum of 24 (70%). **Satisfactory performance** is defined as **70% of maximum score** i.e. **14/20** points considering **sample ACDB-IR D as educational sample.**

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

Propionyl-CoA Carboxylase deficency

Patient details provided to participants

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

Patient details

Analytical performance

43/43 (100%) respondents reported a significant increase of C3 (propionylcarnitine) levels, 21 noted a significant elevated C3/C2 ratio, 13 noted a significant elevated C3/C16 ratio, 21 respondents comment that the concentration of C4DC (methylmalonilcarnitine+succinylcarnitine) was normal.
36 respondents considered C0 concentration as elevated.
5 respondents performed a II tier test which provided measurement of 3-hydroxy-propionate, methylmalonate, methylcitrate and homocysteine on the blood spot. MMA was found to be normal

Diagnosis / Interpretative proficiency All 43/43 (100%) respondents considered a disorder of the propionate pathway as the most likely diagnosis, 11 of these specified just a propionic acidemia, 31/44 included propionic and methylmalonic acidemias and 8 of them included defects in B12 synthesis and transport, as part of their differential diagnosis.
2/44 respondents considered the alteration due to maternal B12 deficiency

Recommendations
43 respondents suggested test to distinguish those disorders, 43 would have initially performed an organic acids analysis, 19 plasma aminoacids, 15 plasma acylcarnitines, 15 plasma homocysteine, 13 plasma methylcitrate and methylmalonic acids, 10 ammonia, 12 serum vitamin B12, to formulate a definitive diagnosis.
35 respondents suggested confirming the diagnosis by genetic genotyping and 18 mentioned enzyme activity in fibroblast in conjunction with genotyping.
The need for a low protein intake together with carnitine supplementation was mentioned by 19 respondents. Metronidazole therapy was mentioned by 6 respondents.
Referral to a metabolic physician was mentioned by 12 respondents

8.2. Patient B

Normal acylcarnitines profile

Patient details provided to participants
Patient admitted for asthenia and psychomotor retardation

Diagnosis / Interpretative proficiency
41/44 (93%) respondents reported a normal acylcarnitines profile. One respondent considered glutaryl-CoA dehydrogenase deficency and an another respondent considered Very long Chain Acyl-CoA dehydrogenase deficiency as the most likely diagnosis

Recommendations

1. Repeat Acylcarnitines profile in plasma to avoid missing CPT2 deficiency (CPT II can be missed on dried blood spot) (n=4);
2. Measure Free and total carnitine in plasma (n=4)
3. CPK in serum (n=4)
4. organic acids analysis (n=11),
5. liver enzymes (n=4),
6. blood gases (n=2)
7. blood glucose (n=3)
8. lactic acid and pyruvate (n=4)
9. ammonia (n=4)
10. cortisol (n=3)
11. amino acids (n=9)
12. purine and pyrimidine (n=3)
13. oligosaccharides (n=2)
14. creatine (n=1)
15. Consider mitochondrial disorders (n=2)
16. Consider lysosomal disorders (n=2)
17. Transferrin isoform analysis (1)
18. Redox state (n=1)
19. Full clinical evaluation genetic & neurologic) etc. (n=6)
20. No special recommendations (n=5)

8.3. Patient C

Very Long Chain Acyl-CoA Dehydrogenase Deficency (VLCADD)

Patient details provided to participants
Patient admitted for vomit, hypoglycemia, acidosis and hypertrophic cardiomyopathy. In treatment with vitamins, DHA and MCT

Diagnosis / Interpretative proficiency
43/43 (100%) respondents considered Very Long Chain Acyl-CoA Dehydrogenase deficiency (VLCADD) as the most likely diagnosis, 4 respondents considered as an alternative diagnosis CPT2 deficiency 3 respondents considered Carnitine Acylcarnitine Translocase deficiency (CACT) and 1 responders Multiple Acyl-CoA Dehydrogenase deficiency (MADD).

8.4. Patient D

3-Hydroxt-3-methyl-glutaryl-CoA lyase deficency

Patient details provided to participants

Patient admitted for vomit, dehydration and acidosis. In treatment with carnitine

Analytical performance

This is a very complex acylcarnitine profile. The sample was taken during an acute crisis of hypoglycemia and acidosis. The patient was supplemented with carnitine therefore, the interpretation of this sample is extremely difficult

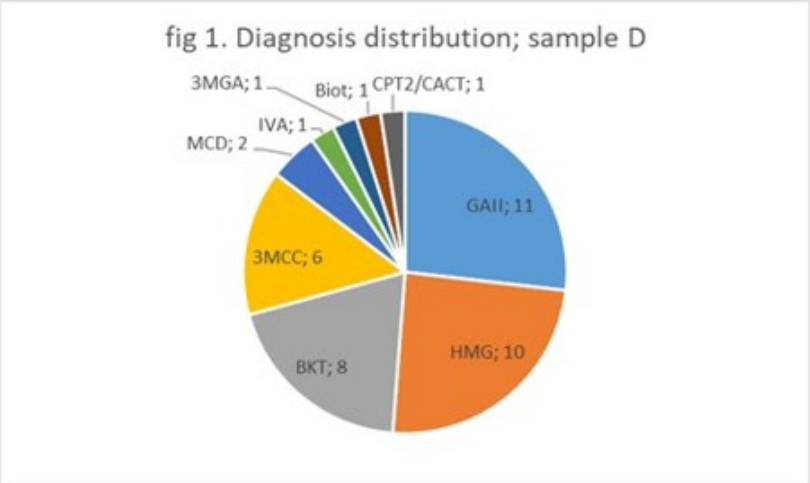
In this dried blood spot sample, the concentrations of almost all acylcarnitine species (C0 to C18) were elevated. In particular, free carnitine (C0) and C5-OH acylcarnitine were markedly elevated and several other carnitine species were mildly elevated.

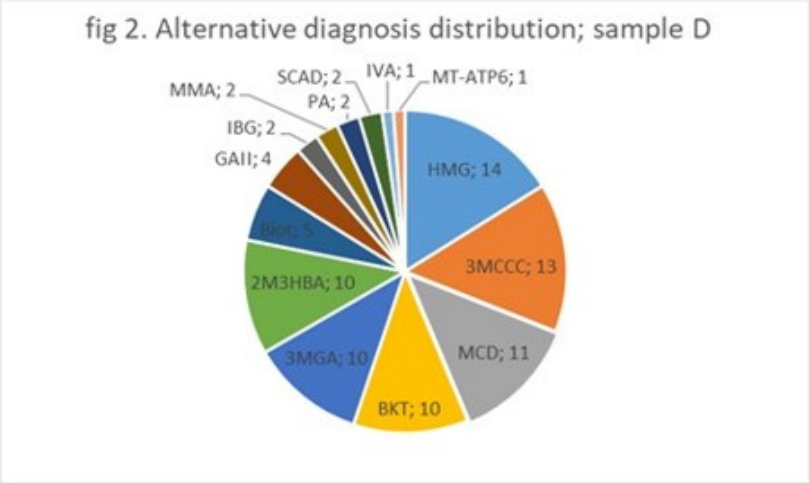
Diagnosis / Interpretative proficiency

The differential diagnosis of elevated C5-OH includes 3-methylcrotonyl-CoA carboxylase deficiency (3-MCC deficiency), 3-hydroxy 3-methylglutaryl-CoA lyase deficiency (HMG), beta-ketothiolase deficiency, 2-methyl 3-hydroxy butyryl-CoA dehydrogenase deficiency, 3-methylglutaconic aciduria type I-IV, biotinidase deficiency and holocarboxylase deficiency.

Furthermore, the profile could be suspected for multiple dehydrogenase deficency (MADD) due to the many altered acylcarnitines in the sample.

Figure 1 & 2 show the suggested diagnosis and alternative diagnosis distribution





Recommendations
42 respondents suggested these follow up test to confirm the diagnosis.
42 respondents suggested the mutation analysis guided by the results of the urinary organic acids analysis (11 labs specified ETFA, ETFB , ETFDH genes; 6 labs specified ACAT1 gene; 5 labs specified HMGCS2 gene, 3 labs specified MCCC1 and MCCC2 genes, 1 lab specified SLC25A20 gene; 1 lab specified CPT2 gene; 1 lab specified riboflavin transport genes; 1 lab specified IVD gene; 3 lab specified BTD gene; 1 lab specified AUH gene; 1 lab specified CLPB gene; 1 lab specified DNAJC19 1 lab specified HLCS gene, 1 lab specified HSD17B10 gene, 1 lab specified OPA3 gene, 1 lab specified SERAC1 gene, 1 lab specified TAE gene)
8 respondents suggested enzyme assay in cultured fibroblasts, 17 respondents suggested plasma carnitine/acylcanitines analysis, 7 respondents suggested plasma aminoacids analysis, 8 respondents suggested biotinidase assay,3 respondent suggested ammonia, glucose and methionine assay
The implementation of appropriate dietary management (2 labs suggested biotine supplementation, 5 labs suggested carnitine supplementation) was mentioned by 7 respondents.

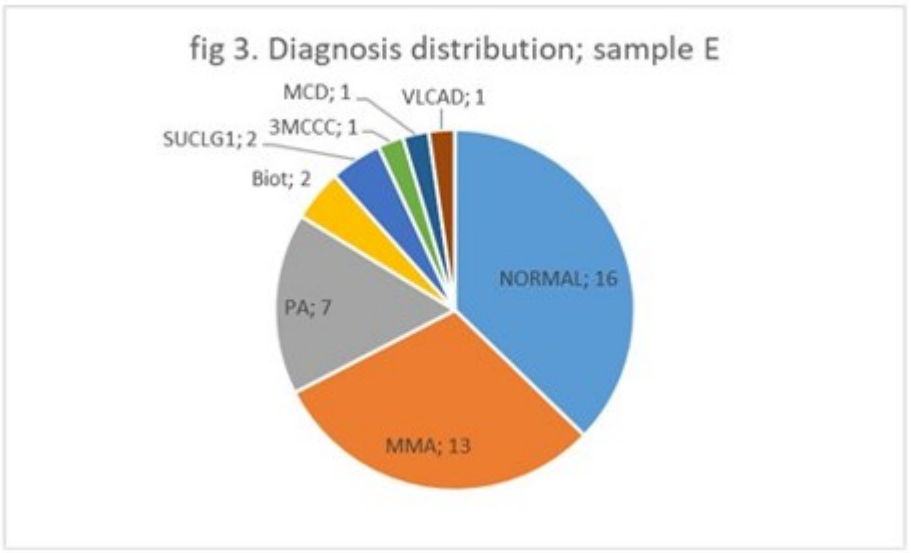
8.5. Patient E

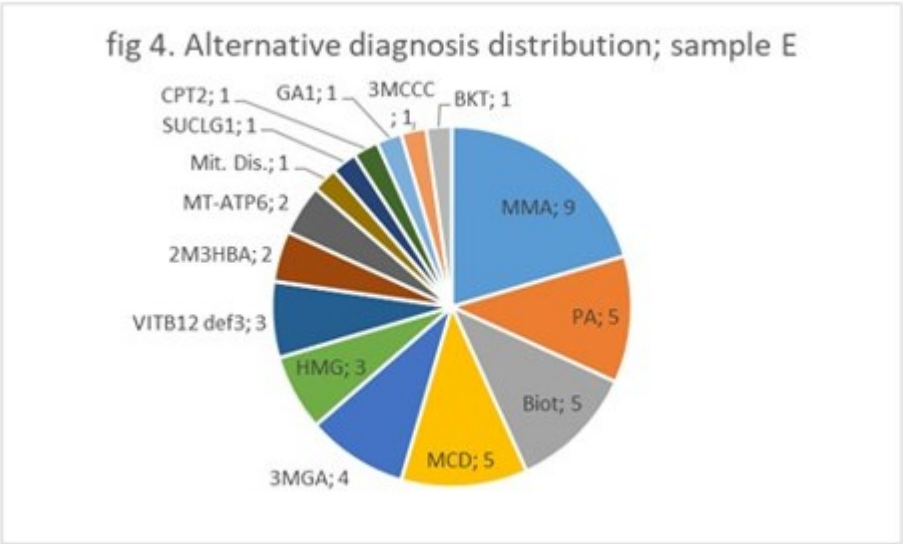
Methylmalonic aciduria and homocystinuria, cblC type

Patient details provided to participants
Patient admitted for severe intellectual disability and epileptic encephalopathy. In treatment.

Analytical performance and Diagnosis / Interpretative proficiency

The patient was supplemented with carnitine therefore the interpretation of this sample could be difficult
Figures 3 and 4 show the suggested diagnoses.
16 laboratories reported "normal sample" as the main diagnosis. Interestingly, 7 of the 16 laboratories that defined the diagnosis as "normal sample" had reported elevated C3 values (3.4; 4.0; 5.0; 3.99; 4.0, 4.2; 4.19)





Recommendations
42 respondents suggested test to distinguish those disorders, 34 would have initially performed an organic acids analysis, 7 plasma aminoacids, 9 plasma acylcarnitines, 13 plasma homocysteine, 8 plasma methylmalonic acids, 9 ammonia, 5 serum vitamin B12, 4 folate, to formulate a definitive diagnosis. 19 respondents suggested confirming the diagnosis by genetic genotyping and 4 mentioned enzyme activity in fibroblast in conjunction with genotyping.
The need for a low protein intake together with carnitine supplementation was mentioned by 7 respondents

8.6. Patient F

Carnitine Palmitoyl Transferase I Deficiency

Patient details provided to participants
Patient admitted at the age of 2 months with hypoglycemic coma. He currently has a slight delay in speech. In treatment.

Diagnosis / Interpretative proficiency
41/43 (95%) respondents reported a Carnitine Palmitoyl Transferase I Deficency
One respondent considered Very long Chain Acyl-CoA dehydrogenase deficiency an another respondent considered normal acylcarnitines profile as the most likely diagnosis.

Recommendations
41 respondents suggested these follow up test to confirm the diagnosis:41 respondents suggested the CPT1A mutation analysis, 13 respondents suggested enzyme assay in cultured fibroblasts, 19 respondents suggested plasma carnitine/acylcanitines analysis, 4 respondents suggested urinary carnitine analysis, 7 respondent suggested organic acid analysis, 3 respondents suggested ketones analysis, 3 respondent suggested ammonia, liver enzymes and CPK assay
The implementation of appropriate dietary management to avoiding fasting (carbohydrate rich diet, low fat diet supplement with MCT and essential fatty acids) was mentioned by 9 respondents.

9. Scores of participants

All data transfer, the submission of data as well as the request and viewing of reports proceed via the QLOU-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.

Detailed scores – Round 1

Lab n°	Patient A Propionyl-CoA carboxylase deficiency			Patient B Normal acylcarnitines profile			Patient C Very long Chain Acyl-CoA dehydrogenase deficiency (VLCAD)			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	2	2	4	2	2	4	2	2	4	12
3	2	2	4	2	2	4	2	2	4	12
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	2	2	4	2	2	4	12
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	0	0	0	0	0	0	0	0	0	0
10	2	2	4	2	2	4	2	2	4	12
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	2	4	2	2	4	12
14	2	2	4	2	2	4	2	2	4	12
15	2	2	4	2	2	4	2	2	4	12
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	2	2	4	2	2	4	12
19	2	2	4	2	2	4	2	2	4	12
20	2	2	4	2	2	4	2	2	4	12
21	0	0	0	0	0	0	0	0	0	0
22	2	2	4	2	2	4	2	2	4	12
23	2	2	4	2	2	4	2	2	4	12
24	2	2	4	2	2	4	2	2	4	12
25	2	2	4	2	2	4	2	2	4	12
26	2	2	4	2	2	4	2	2	4	12

Lab n°	Patient A Propionyl-CoA carboxylase deficiency			Patient B Normal acylcarnitines profile			Patient C Very long Chain Acyl-CoA dehydrogenase deficiency (VLCAD)			
	A	I	Total	A	I	Total	A	I	Total	Total
27	2	2	4	0	0	0	2	2	4	8
28	2	2	4	2	2	4	2	2	4	12
29	2	2	4	2	2	4	2	2	4	12
30	2	2	4	2	2	4	2	2	4	12
31	2	2	4	0	0	0	2	2	4	8
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	2	2	4	2	2	4	12
35	2	2	4	2	2	4	2	2	4	12
36	2	2	4	2	2	4	2	2	4	12
37	2	2	4	2	2	4	2	2	4	12
38	2	2	4	2	2	4	2	2	4	12
39	2	2	4	2	2	4	2	2	4	12
40	2	2	4	2	2	4	2	2	4	12
41	2	2	4	2	2	4	2	2	4	12
42	2	2	4	2	2	4	2	2	4	12
43	2	2	4	2	2	4	2	2	4	12
44	2	2	4	2	2	4	2	2	4	12
45	0	0	0	0	0	0	0	0	0	0
46	2	2	4	2	2	4	2	2	4	12
47	0	0	0	0	0	0	0	0	0	0

Detailed scores – Round 2

Lab n°	Patient D HMG			Patient E cblC			Patient F CPT1			
	A	I	Total	A	I	Total	A	I	Total	Total
1	--	--	--	2	2	4	2	2	4	8
2	--	--	--	2	2	4	2	2	4	8
3	--	--	--	2	0	2	2	2	4	6
4	--	--	--	2	1	3	2	2	4	7
5	--	--	--	0	0	0	2	2	4	4
6	--	--	--	2	2	4	2	2	4	8
7	--	--	--	0	0	0	2	2	4	4
8	--	--	--	2	2	4	2	2	4	8
9	--	--	--	0	0	0	0	0	0	0
10	--	--	--	2	2	4	2	2	4	8
11	--	--	--	2	2	4	2	2	4	8
12	--	--	--	2	2	4	2	2	4	8
13	--	--	--	0	0	0	2	2	4	4
14	--	--	--	2	2	4	2	2	4	8
15	--	--	--	0	0	0	0	0	0	0
16	--	--	--	1	2	3	2	2	4	7
17	--	--	--	2	2	4	2	2	3	8
18	--	--	--	2	2	4	2	2	4	8
19	--	--	--	2	0	2	2	2	4	6
20	--	--	--	2	0	2	2	2	4	6
21	--	--	--	2	2	4	2	2	4	8
22	--	--	--	2	2	4	2	2	4	8
23	--	--	--	2	2	4	2	2	4	8
24	--	--	--	1	1	2	2	2	4	6
25	--	--	--	2	2	4	2	2	4	8
26	--	--	--	2	1	3	2	2	4	7
27	--	--	--	0	0	0	2	2	4	4
28	--	--	--	1	2	3	2	2	4	7
29	--	--	--	0	0	0	2	2	4	4
30	--	--	--	2	2	4	0	0	0	4

Lab n°	Patient D HMG			Patient E cblC			Patient F CPT1			
	A	I	Total	A	I	Total	A	I	Total	Total
31	--	--	--	1	2	3	2	2	4	7
32	--	--	--	2	2	4	2	2	4	8
33	--	--	--	0	0	0	2	2	4	4
34	--	--	--	2	2	4	2	2	4	8
35	--	--	--	1	1	2	2	2	4	6
36	--	--	--	1	0	1	2	2	4	5
37	--	--	--	2	2	4	2	2	4	8
38	--	--	--	2	1	3	2	2	4	7
39	--	--	--	0	0	0	2	2	4	4
40	--	--	--	1	1	2	2	2	4	6
41	--	--	--	2	2	4	2	2	4	8
42	--	--	--	2	2	4	2	2	4	8
43	--	--	--	1	2	3	2	2	4	7
44	--	--	--	0	0	0	2	0	2	2
45	--	--	--	0	0	0	0	0	0	0
46	--	--	--	2	2	4	2	2	4	8
47	--	--	--	0	0	0	0	0	0	0

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error/partial submitter/ non submitter
1	4	4	4	--	4	4	20	100	
2	4	4	4	--	4	4	20	100	
3	4	4	4	--	2	4	18	90	
4	4	4	4	--	3	4	19	95	
5	4	4	4	--	0	4	16	80	
6	4	4	4	--	4	4	20	100	
7	4	4	4	--	0	4	16	80	
8	4	4	4	--	4	4	20	100	
9	0	0	0	--	0	0	0	0	NS
10	4	4	4	--	4	4	20	100	
11	4	4	4	--	4	4	20	100	
12	4	4	3	--	4	4	19	95	
13	4	4	4	--	0	4	16	80	
14	4	4	4	--	4	4	20	100	
15	4	4	4	--	0	0	12	60	PS
16	4	4	4	--	3	4	19	95	
17	4	4	4	--	4	3	19	95	
18	4	4	4	--	4	4	20	100	
19	4	4	4	--	2	4	18	90	
20	4	4	4	--	2	4	18	90	
21	0	0	0	--	4	4	8	40	PS
22	4	4	4	--	4	4	20	100	
23	4	4	4	--	4	4	20	100	
24	4	4	4	--	2	4	18	90	
25	4	4	4	--	4	4	20	100	
26	4	4	4	--	3	4	19	95	
27	4	0	4	--	0	4	12	60	
28	4	4	4	--	3	4	19	95	
29	4	4	4	--	0	4	16	80	
30	4	4	4	--	4	0	16	80	CE

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error/partial submitter/ non submitter
31	4	0	4	--	3	4	15	75	
32	4	4	4	--	4	4	20	100	
33	4	4	4	--	0	4	16	80	
34	4	4	4	--	4	4	20	100	
35	4	4	4	--	2	4	18	90	
36	4	4	4	--	1	4	17	85	
37	4	4	4	--	4	4	20	100	
38	4	4	4	--	3	4	19	95	
39	4	4	4	--	0	4	16	80	
40	4	4	4	--	2	4	18	90	
41	4	4	4	--	4	4	20	100	
42	4	4	4	--	4	4	20	100	
43	4	4	4	--	3	4	19	95	
44	4	4	4	--	0	2	14	70	
45	0	0	0		0	0	0	0	NS
46	4	4	4	--	4	4	20	100	
47	0	0	0		0	0	0	0	NS

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 70 % of adequate responses)	40	85
Unsatisfactory performers (< 70 % adequate responses and/or critical error)	2	4
Partial and non-submitters	5	10

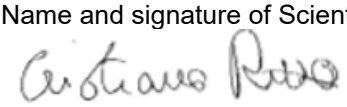
Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
ACDB-IR-2021-A	Propionyl-CoA carboxylase deficiency	100	100	100
ACDB-IR-2021-B	Normal acylcarnitines profile	95.3	95.3	95.3
ACDB-IR-2021-C	Very long Chain Acyl-CoA dehydrogenase deficiency (VLCAD)	100	100	100
ACDB-IR-2021-D	HMG	--	--	--
ACDB-IR-2021-E	cblC	72.1	65.1	68.6
ACDB-IR-2021-F	CPT1	97.7	95.3	96.5

10. 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 QLOU scheme this certificate will indicate if results were submitted and whether satisfactory performance was achieved in the scheme.

Date of report, 2021-12-13
Name and signature of Scientific Advisor



Dr. Cristiano Rizzo
Scientific Advisor

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

Version Number	Published	Amendments
1	26 April 2022	2021 annual report published

END