ERNDIM Administration Office
c/o EMQN CIC, Unit 4, Enterprise House
Manchester Science Park, Pencroft Way
Manchester M15 6SE, United Kingdom
Email: admin@erndim.org

Scientific Coordination
Dr Joachim Janda
Metabolic Center Heidelberg
Im NeuenheimerFeld 669
69120 Heidelberg
Germany
e-mail:Joachim.Janda@med.uni-heidelberg.de

Scheme Organisation
CSCQ (Quality Control Centre, Switzerland)
1)Alessandro Salemma 2)Nicola Braik
2 chemin du Petit-Bel-Air
1225 Chêne-Bourg
Switzerland,
Tel: +41 22 305 52 36
Email: 1)alessandro.salemma@hcuge.ch
2)nicola.braik@hcuge.ch

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Acylcarnitines in dried blood spots

Centre: Germany

Final Report 2022

prepared by
Dr Joachim Janda

Note: This annual report is intended for participants of the ERNDIM Acylcarnitines in DBS 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 (AC) 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 Joachim Janda (metabolic centre Heidelberg) in conjunction with CSCQ, the Swiss organisation for quality assurance in medical laboratories, a subcontractor of ERNDIM.

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

2. Geographical distribution of participants

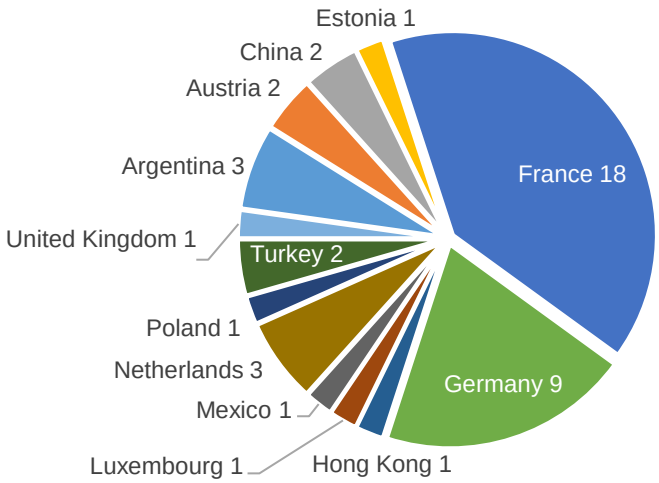
In 2022, 45 laboratories from many different countries participated in the ACDB Heidelberg scheme. As in the year before, there was no educational participants in 2022. Educational participants take part in all aspects of the scheme and receive interim reports with scores, but performance is not indicated 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.

[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
Argentina	3
Austria	2
China	2
Estonia	1
France	18
Germany	9
Hong Kong	1

Country	Number of participants
Luxembourg	1
Mexico	1
Netherlands	3
Poland	1
Turkey	2
United Kingdom	1

Geographical distribution and numbers of participants



3. Design and logistics of the scheme including sample information

As in earlier ACDB schemes, the samples used in 2022 were authentic human blood spot samples, five from affected patients and one from a healthy individual.
All samples selected by the Scientific Advisor are typically prepared from 30-50 µL of lithium heparin anticoagulated whole blood on Whatman (Schleicher & Schuell) 903™ paper. All samples are obtained following local ethical and consent guidelines.
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

Participants are also encouraged to make use of the option to upload labelled copies of scans and/or chromatograms on the CSCQ website together with their analytical and interpretative results.

4. Schedule of the scheme

Time schedule in the 2022 ERNDIM ACDB Heidelberg scheme.

	1st Submission Round	2nd Submission Round
Sample IDs	ACDB-DH-2022-A ACDB-DH-2022-B ACDB-DH-2022-C	ACDB-DH-2022-D ACDB-DH-2022-E ACDB-DH-2022-F
Shipment of samples	February 2, 2022	
Start of analysis (clinical data available)	March 14, 2022	June 6, 2022
Reminder for result submission	March 28, 2022	June 21, 2022
Results submission deadline	April 4, 2022	June 28, 2022
Interim reports available on CSCQ website	June 24, 2022	September 12, 2022

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

Samples included in the 2022 ERNDIM ACDB Heidelberg scheme.

Survey	Sample no.	Diagnosis
22-03-ACH	ACDB-DH-2022-A	Hydroxymethylglutaric aciduria (HMG CLD)
	ACDB-DH-2022-B	Glutaric acidemia type 1 (GA-I)
	ACDB-DH-2022-C	Methylmalonic aciduria, mut(0) type
22-06-ACH	ACDB-DH-2022-D	Hydroxymethylglutaric aciduria (HMG CLD)
	ACDB-DH-2022-E	Propionic acidemia (PA)
	ACDB-DH-2022-F	Normal profile

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 blood samples have been provided by the scheme organizer or participants as specified below.

Patient A:	Hydroxymethylglutaric aciduria (HMG CLD)	Common sample for the ACDB schemes provided by the ACDB centre in Rome
Patient B:	Glutaric acidemia type 1 (GA-I)	
Patient C:	Methylmalonic aciduria, mut(0) type	
Patient D:	Hydroxymethylglutaric aciduria (HMG CLD)	Kindly provided by the Department of Paediatrics and Inherited Metabolic Disorders of the General University Hospital Prague.
Patient E:	Propionic acidemia (PA)	
Patient F:	Normal profile	

Prior to the distribution of the first round, a validation set of samples was returned from the CSCQ to the organising laboratory and re-analysed.

5. Results

Returned results in the 2022 ERNDIM ACDB Heidelberg scheme.

	Survey 1	Survey 2
Receipt of results	41	36
No answer	4	9

6. Web site reporting

The website reporting system is compulsory for all centres. The participants are reminded to carefully read and consider the following advice:

- **Results**
  - Give quantitative data as much as possible.
  - Enter the key metabolites with the evaluation **in the tables** even if you do not give quantitative data.
  - If the profile is normal: enter “Normal profile” in “Key metabolites”.
  - **Do not enter results in the “comments” field**, **otherwise your results will not be included in the evaluation program.**
- **Diagnosis**
  - **Do not 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 on treatment will not be scored.
  - **Do not give recommendations in “Comments on diagnosis” field**: 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 (SAB). Similar to other qualitative (proficiency testing) ERNDIM schemes, the maximum score for a sample is 4 points.
Qualitative results and diagnostic proficiency of the 2022 samples were scored using the criteria given below. These criteria have been set by the Scientific Advisor and approved by the SAB of ERNDIM. The final decision on scoring of the scheme has been made by the SAB during its autumn meeting (November 25, 2022).

General criteria used to score results

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

Starting with the 2014 schemes, the concept of ‘critical error’ has been 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 14, 2022.

Score for satisfactory performance
A minimum of 17 points out of a maximum of 24 (71%) is necessary for a satisfactory performance.

The ERNDIM Annual Certificate covers all ERNDIM schemes in which a laboratory has participated during the scheme year. For the ‘acylcarnitine in dried blood spots’ scheme, “participation” is defined as requiring two returns during the year. Failure to meet this requirement will result in the certificate of participation showing ‘non-submitter’ rather than ‘satisfactory’ or ‘unsatisfactory’.

8. Results of samples and evaluation of reporting

8.1. Patient A

3-Hydroxy-3-methy-glutaryl-CoA lyase deficiency (HMG CLD)

This AC profile represents a 3-HMG-CoA lyase deficiency sample. The sample has been distributed by the ACDB centre Rome as a common sample for all three organising centres.

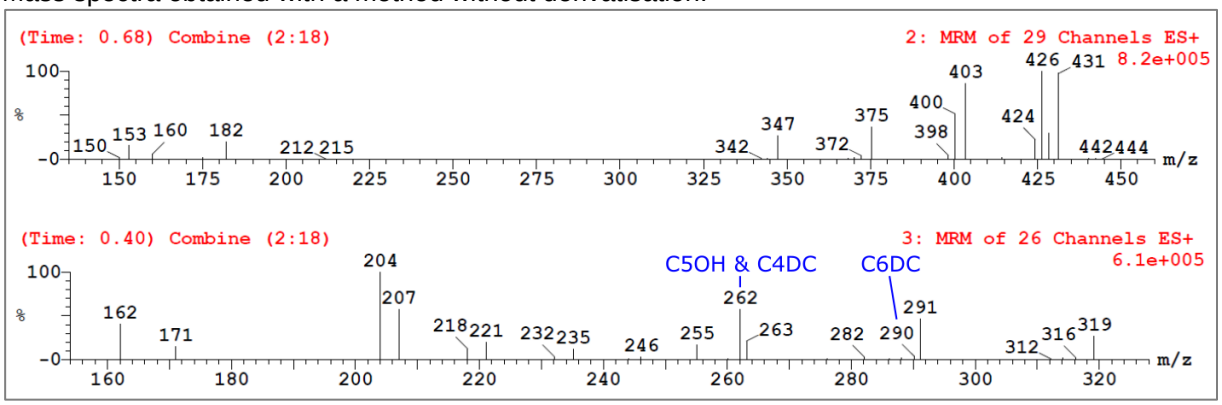
Clinical description provided to participants

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

Analytical performance

Diagnostic markers for HMG CLD are the C6-DC and C5-OH carnitines. Depending on the method applied for detection of ACs, one or both markers can have isobaric analytes. MS spectra obtained with a kit based on non-derivatised analysis are shown below.

Mass spectra obtained with a method without derivatisation.



For this sample, 41 out of 45 participants reported results. C5OH and C6DC carnitine concentrations were reported as elevated or even grossly elevated by 98% and 61% of these labs, respectively. Other frequently reported ACs were C0 (n=27, 22 normal and five elevated), C5:1 (n=9, seven normal and two elevated) and C3 (n=8, seven normal and one elevated).
The results show that C6DC/methylglutarylcarnitine is not in the scope of AC analyses in some laboratories, but in the case of HMG CLD it is a helpful marker for a targeted diagnosis.

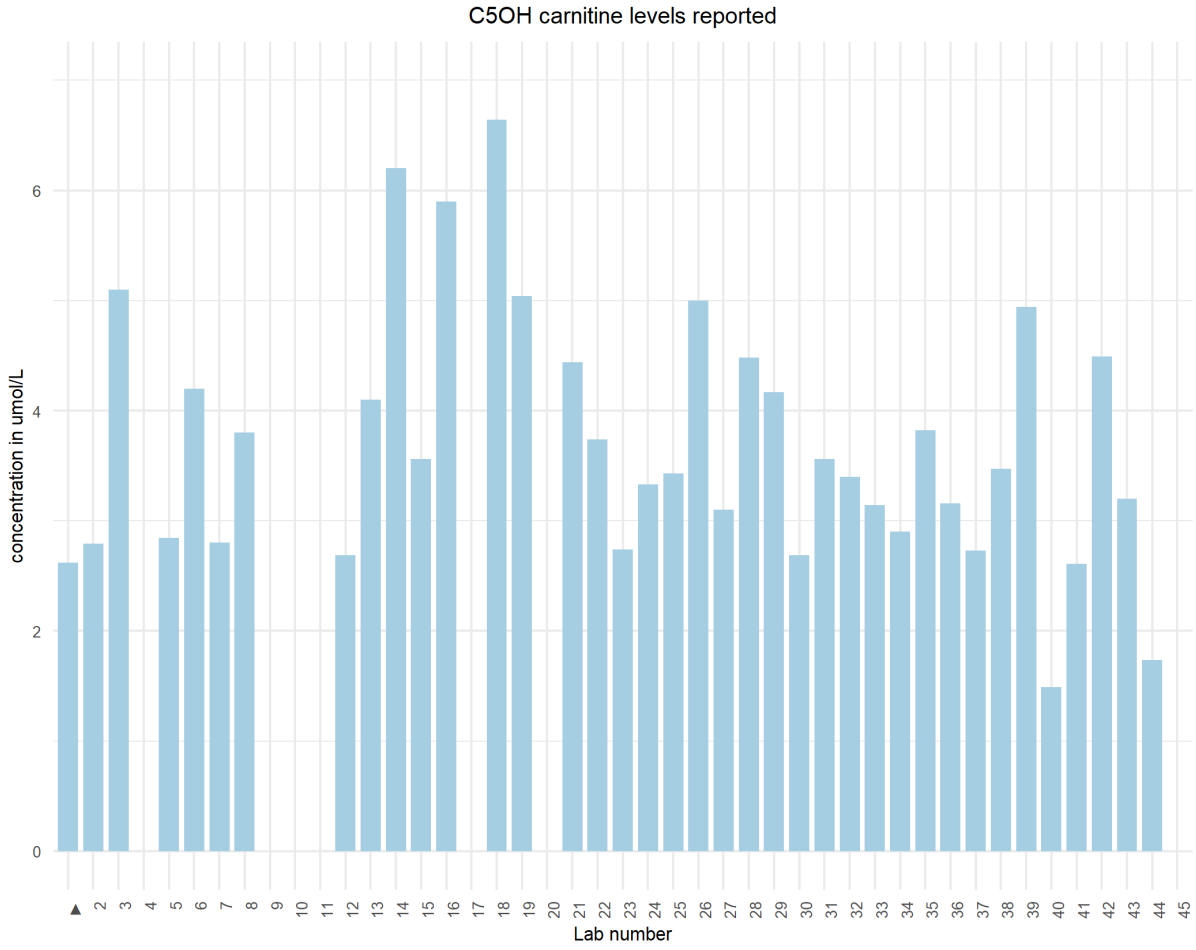
Following agreement with the scientific advisors of all three centres for ERNDIM ACDB schemes, we encourage participants to expand their methods to include C6DC/methylglutarylcarnitine and will consider this when evaluating future HMG CLD samples accordingly.

Diagnosis / Interpretative proficiency

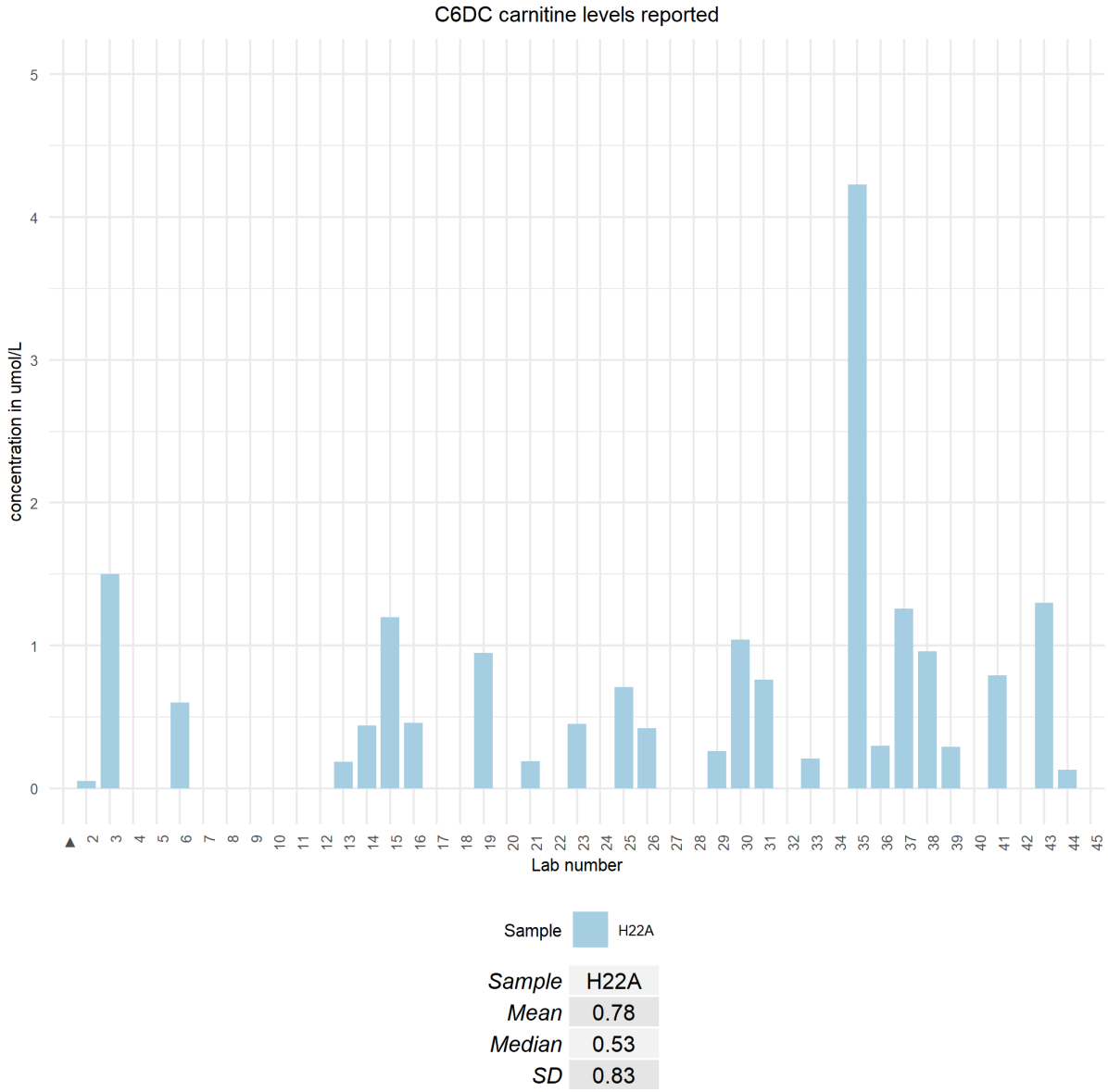
3-HMG-CoA lyase deficiency was given as primary diagnosis by 29 participants and as an alternative by nine participants. Other metabolic disorders reported as primary diagnosis were 3-methylcrotonyl-CoA carboxylase deficiency (n=7), 3-methylglutaconic aciduria type I (n=1), beta-ketothiolase deficiency (n=1), 2-methyl 3-hydroxy butyryl-CoA dehydrogenase deficiency (n=1) and glutaric aciduria (n=1).
Alternative diagnoses other than HMG CLD reported by the participants included 3-methylcrotonyl-CoA carboxylase deficiency (n=21), multiple carboxylase deficiency (n=11), 3-methylglutaconic aciduria type I (n=10), biotinidase deficiency (n=10), beta-ketothiolase deficiency (n=8), 2-methyl 3-hydroxy butyryl-CoA dehydrogenase deficiency (n=8), and glutaric aciduria (n=1).

Recommendations

In the recommendations for further investigation, the participants focused on confirmation and/or differentiation. Methods recommended were organic acids in urine (n=38), molecular genetic analyses (n=30), measurement of enzymatic activity (n=10), ACs in plasma (n=5), amino acids in plasma (n=2), or repetition of ACs in blood spots (n=2).
In addition, 11 participants gave recommendations on therapeutic measures.



Sample	H22A
Mean	3.49
Median	3.37
SD	1.22



Sample	H22A
Mean	0.78
Median	0.53
SD	0.83

Scoring

Two points were awarded if C5OH carnitine was reported at least as elevated. However, it may again be mentioned that in future HMG CLD samples reporting of methylglutaryl carnitine (C6DC) will also be required to achieve full analytical score.

For interpretation, two points were awarded for either reporting HMG CLD as primary or secondary diagnosis – in the latter case, a method suitable to find the correct diagnosis must be given in the recommendations.

One lab detected C5DC and C18:1 carnitines as elevated and interpreted its results as indicative for glutaric aciduria type 1. This was classified as a critical error by the SAB.

Overall impression

The participants performed excellent achieving analytical and interpretational proficiencies of 98% and 95%, respectively.

8.2. Patient B

Glutaryl-CoA dehydrogenase deficiency (glutaric aciduria type 1)

Patient details provided to participants

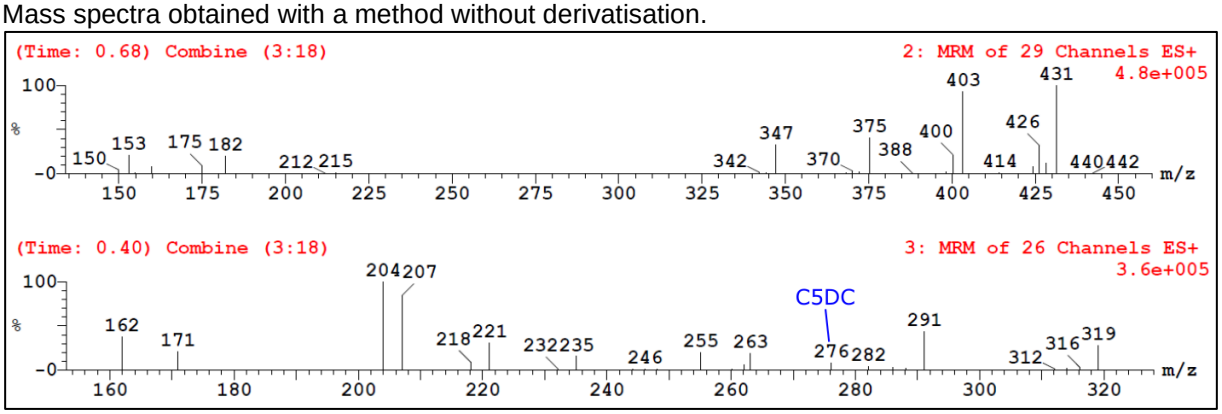
8-month-old boy referred with a history of fever and dystonia

The sample was from a patient with glutaric aciduria type 1.

Analytical performance

The AC profile contains an elevated signal for glutarylcarnitine (C5DC, marked in the MS spectrum below). Several diagnostic ratios, which can be used to substantiate the analytical result, such as C5DC/C8, C5DC/C16, or C5DC/C0, are also elevated.

Mass spectra obtained with a method without derivatisation.



Results were reported by 40 participants of 45 and most of them reported elevated or grossly elevated C5DC carnitine (95%). One lab categorised the C5DC concentration as normal. Free carnitine was reported to be normal (n=16) or low (n=4). Other ACs were less frequently reported, such as C2 (normal: n=2, low: n=2), C3 (normal: n=3, low: n=1), C4 (normal: n=2), C5 (normal: n=2), C6 (normal: n=3), C8 (normal: n=3), C10 (normal: n=2) or C16 (normal: n=1, low: n=3). Some laboratories reported diagnostic ratios indicative of GA 1, including C5DC/C16 (grossly elevated: n=8, elevated: n=5), C5DC/C8 (grossly elevated: n=7, elevated: n=5), C5DC/(C3DC & C4OH) (grossly elevated: n=4, elevated: n=1) and C5DC/C0 (grossly elevated: n=2, elevated: n=2). The ratios C14:1/C12:1 and C14:1/C16 were reported as elevated by one lab each.

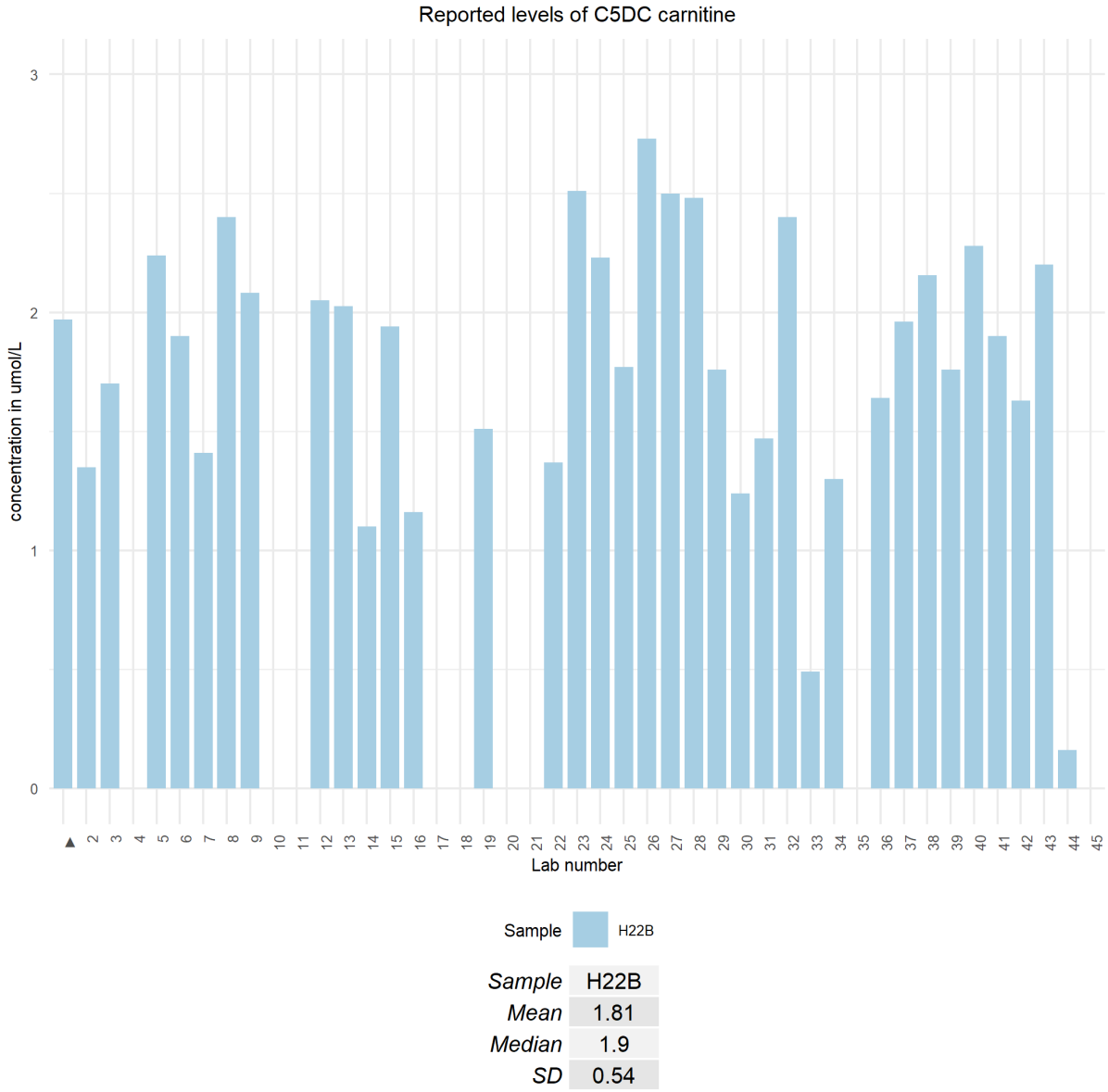
Diagnosis / Interpretative proficiency

Thirty-nine participants (97.5%) decided on glutaric aciduria type 1 as their main diagnosis. One lab did not report C5DC but found elevated C14:1-based ratios and opted for VLCAD instead – this was classified as critical error by the SAB.

Alternative diagnoses reported were glutaric acidaemia type 2 (n=6), glutaric aciduria type 3 (n=1), severe renal insufficiency (n=2), Reye syndrome (n=1), encephalitis (n=1), mitochondrial disorders (n=1) and VLCAD (n=1).

Recommendations

The participants were mostly certain of their diagnosis and recommended determination of urinary organic acids (95%), in some cases stating expected metabolites, such as glutaric and 3-OH-glutaric acid. Additional confirmatory methods recommended were molecular genetic testing (85%), measurement of enzymatic activity (52.2%), ACs in plasma (12.5%) and amino acids in plasma (7.5%). Twenty-one participants (37.5%) also recommended therapeutic measures.



Sample	H22B
Mean	1.81
Median	1.9
SD	0.54

Scoring

Analytical performance: Elevated or grossly elevated C5DC carnitine = 2 Points

Interpretational proficiency: 2 Points for GA 1 as primary diagnosis or if given as alternative diagnosis including a recommendation suitable to find the correct diagnosis.

Overall impression

The handling of this sample was straightforward for most labs and resulted in excellent proficiency, both analytical (97.5%) and interpretative (98.2%).

8.3. Patient C

Methylmalonic aciduria due to methylmalonyl-CoA mutase deficiency

Patient details provided to participants

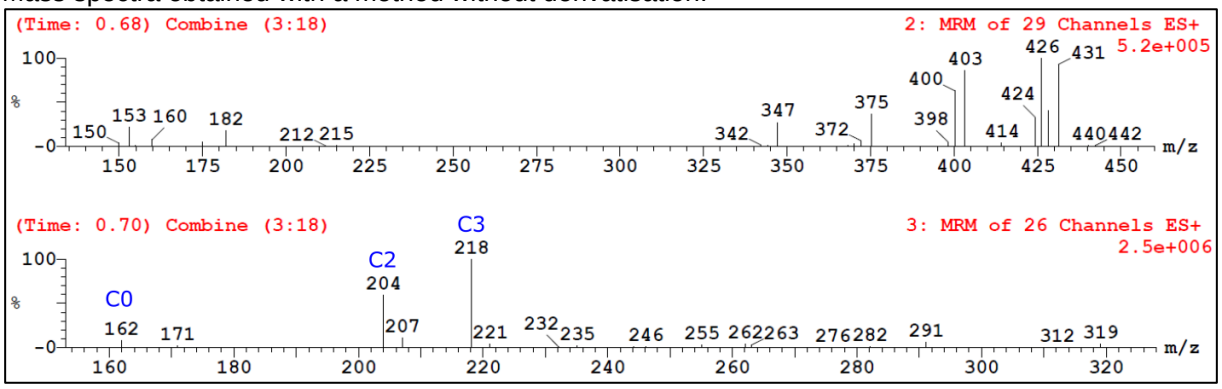
Male patient, presented as newborn with progressive lethargy and muscular hypotonia

The sample originated from a patient with mut(0) type methylmalonic aciduria (MMA) in therapy.

Analytical performance

The AC profile is dominated by largely increased C3 signal. Elevated levels can also be determined for C4DC carnitine and the diagnostic ratios C3/C2 and C3/C0.

Mass spectra obtained with a method without derivatisation.



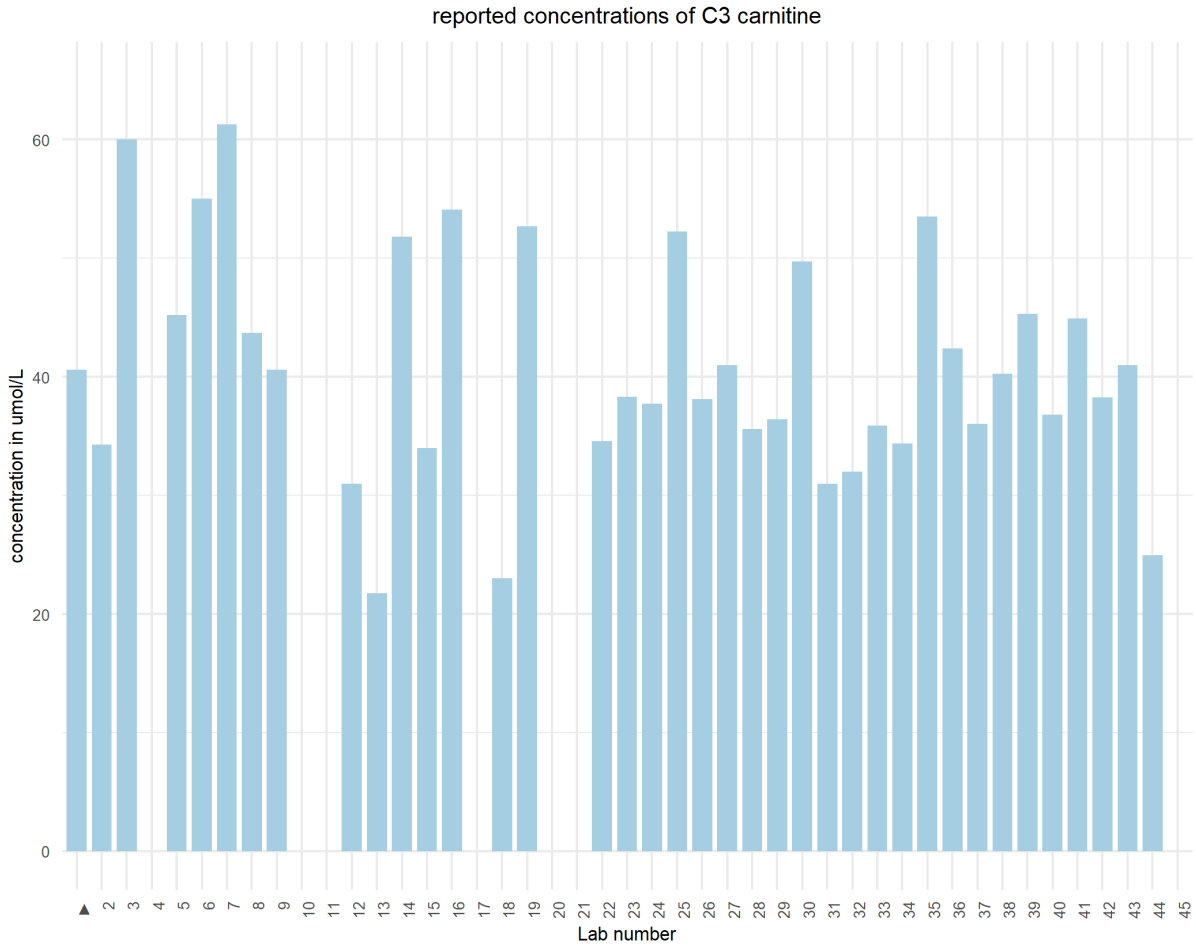
All laboratories submitting results for this sample (40/45) reported either grossly elevated (n=37) or elevated (n=3) C3 carnitine levels. The majority of labs (n=31) also described C4DC carnitine levels to be either grossly elevated (n=15), elevated (n=14) or normal (n=2). Free carnitine was reported as normal by 18 participants and as elevated by four. In addition, participants accounted for diagnostic ratios: Elevated or grossly elevated C3/C2 was stated by 19 labs (47.5%), as well as C3/C0 or C3/C16 by eight labs each (20%). C2 carnitine was also occasionally listed in the participants' results as grossly elevated (n=1), elevated (n=8) or normal (n=3). Eleven laboratories reported additional results for C5OH carnitine, however, it was not evident whether methods were used that distinguished C4DC from C5OH. Only one laboratory explicitly reported such results as butyl esters. Other ACs were reported less frequently and included C4 (normal: n=1, low: n=1), C4OH (elevated: n=2), C5 (elevated: n=4), C5:1 (grossly elevated: n=1, elevated: n=7), C8 (normal: n=2), C18:1 (elevated: n=2) and C18:2 carnitines (elevated: n=2). Moreover, two participants also reported results obtained with a second-tier method.

Diagnosis / Interpretative proficiency

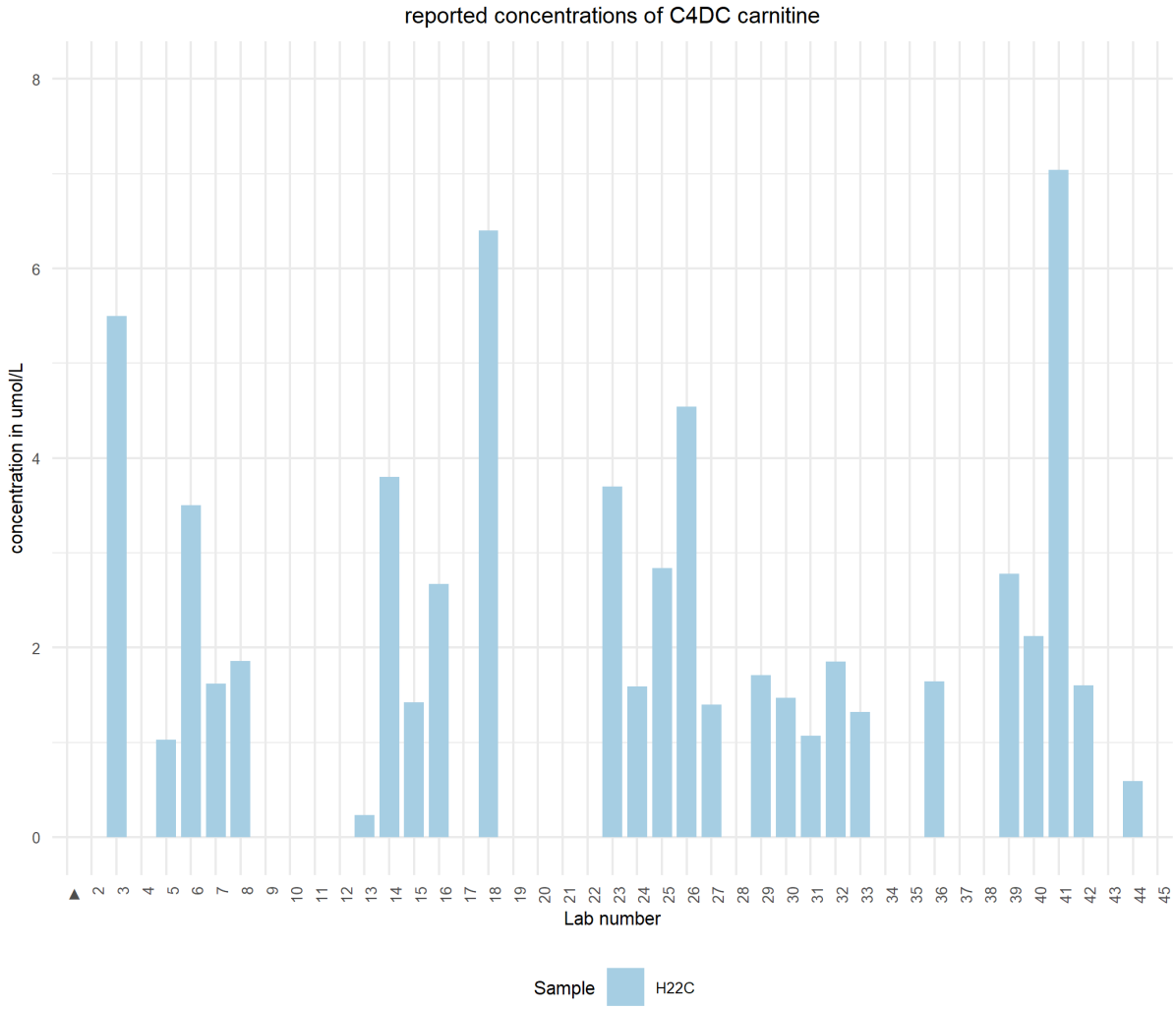
All participants, who submitted results but one gave methylmalonic acidaemia as primary (n=31) or alternative (n=8) diagnosis. For primary diagnosis, propionic acidaemia (PA) was suggested second most (n=6), followed by holocarboxylase synthase (HCS) deficiency (n=2) and a cobalamin-related disorder (n=1). Interpretative results other than MMA MCM type given as alternative diagnoses included PA (n=19), cobalamine-related deficiencies (n=14), multiple carboxylase deficiency (n=3) and HCS deficiency (n=2).

Recommendations

In their recommendations, most laboratories concentrated on differentiation. Analysis of organic acids in urine was mentioned most frequently (n=39), followed my molecular genetic testing (n=31). Plasma analyses were also suggested for determination of total homocysteine (n=16), amino acids (n=15), methylmalonic acid (n=8) and/or ACs (n=7). Seven laboratories advocated for measurement of enzymatic activity, four advised to determine the vitamin B_{12} status and two suggested to perform a cobalamin-responsiveness test. Treatment suggestions were given by 14 participants.



Sample	H22C
Mean	40.77
Median	39.27
SD	9.43



Sample	H22C
Mean	2.6
Median	1.78
SD	1.83

Scoring

Analytical: Two points are awarded when reporting C3 as elevated or grossly elevated.

Interpretational: MMA has to be reported either as the primary diagnosis or as an alternative diagnosis to achieve two points. In the latter case, a method suitable for finding the correct diagnosis must also to be recommended.

Overall impression

Participants demonstrated a superb performance in the analytical (100%) and interpretative (98.2%) identification of MMA.

8.4. Patient D

3-Hydroxy-3-methy-glutaryl-CoA lyase deficiency (HMG CLD)

Patient details provided to participants

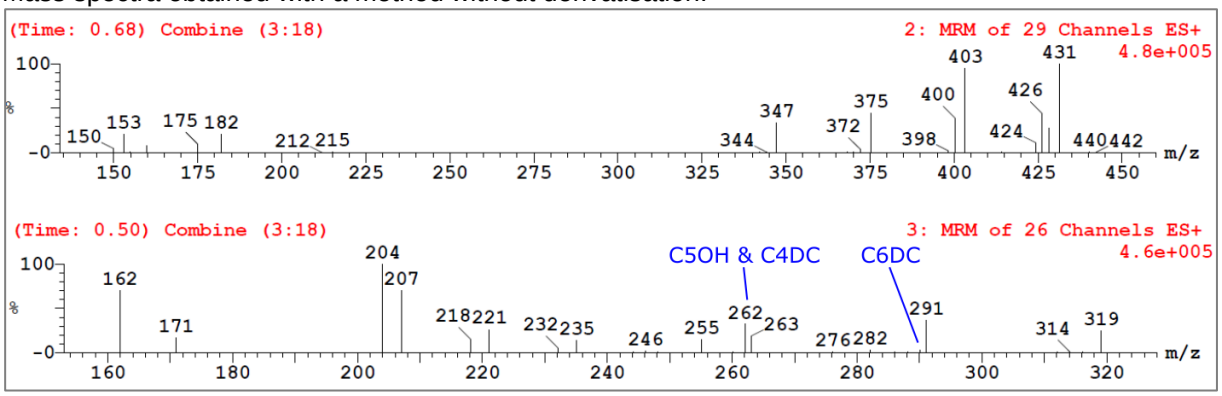
6-year-old girl with hypoglycemia and metabolic acidosis

The sample originated from a patient with confirmed HMG CLD and was kindly provided by the Department of Paediatrics and Inherited Metabolic Disorders of the General University Hospital in Prague.

Analytical performance

Diagnostic markers for HMG CLD are the C6-DC and C5-OH carnitines, which can have isobaric analytes depending on the method applied (e. g. underivatized / butylated). For this sample, 36 out of 45 labs reported results.

Mass spectra obtained with a method without derivatisation.



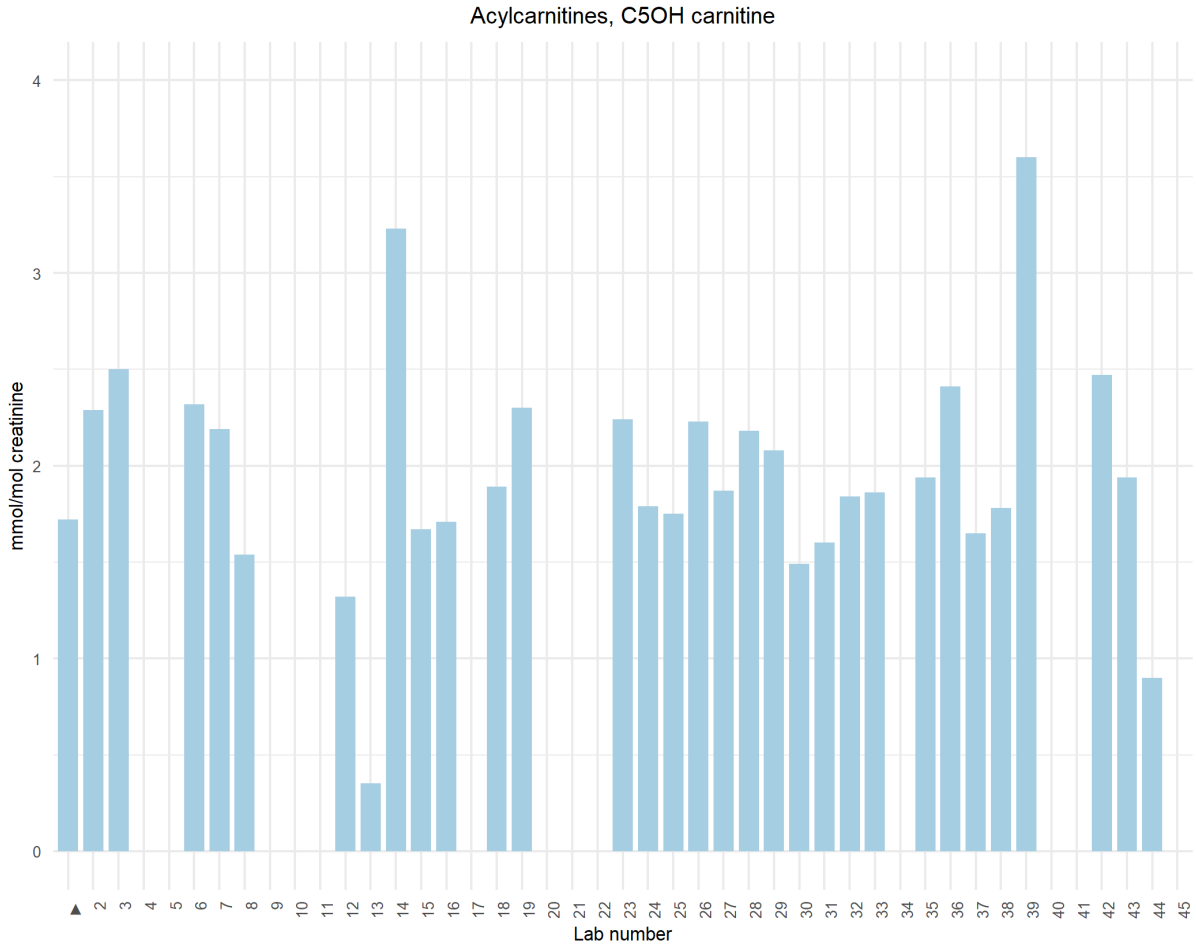
Of these, 33 classified C5-OH carnitine as elevated or grossly elevated (91.7%). Twenty-four of them rated C6-DC as elevated or grossly elevated (66.7%). In addition, free carnitine was mentioned to be normal by 15 labs or present in elevated concentrations by nine labs.
As C5-OH can be indicative for multiple metabolic disorders, several participants reported certain analytes as normal to rule out particular deficiencies, e. g. tiglyl (C5:1; n=8) or propionyl (C3; n=5) carnitine.

Diagnosis / Interpretative proficiency

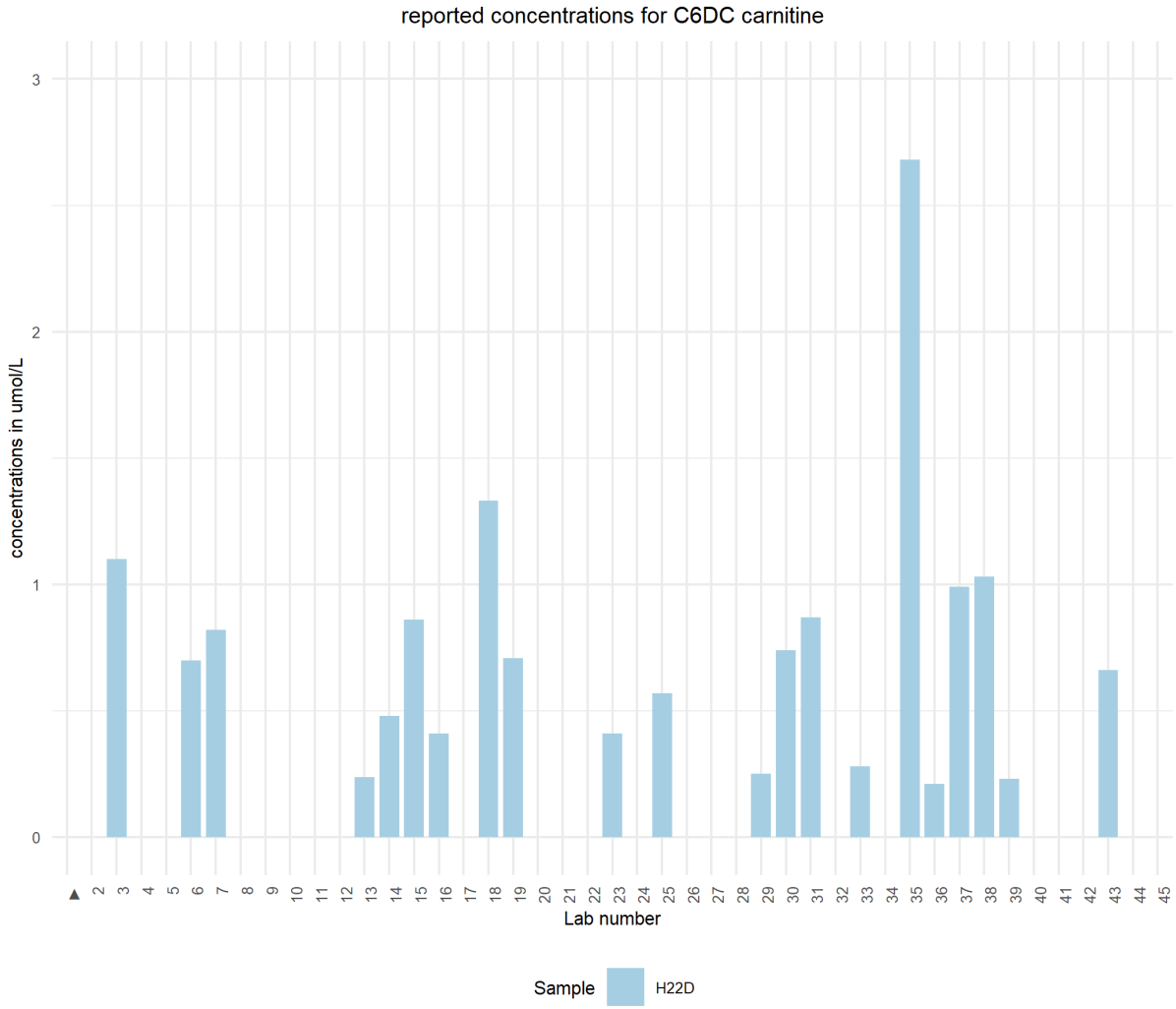
Of the 36 laboratories reporting results, 27 diagnosed HMG CLD. Two participants opted for a different primary diagnosis but mentioned HMG CLD as an alternative. The most frequently mentioned other primary diagnosis was 3-methylcrotonyl-CoA carboxylase deficiency (n=5), which was also named most frequently as an alternative diagnosis (n=19). Other metabolic defects often considered as alternatives were 3-methylglutaconic aciduria type I (MGA, n=13), multiple carboxylase deficiency (MCD, n=10), biotinidase deficiency (BIOT, n=7), or beta-ketothiolase deficiency (MAT, n=7).
Three laboratories failed to find either C5-OH or C6-DC to be elevated which led to incorrect diagnoses; one of them detected elevated C5-DC and opted for multiple acyl-CoA dehydrogenase deficiency, one lab reported grossly elevated C4-DC and diagnosed succinate-CoA ligase deficiency, one participant reported grossly elevated tyrosine instead and interpreted the results indicative for carnitine palmitoyltransferase I deficiency. Another laboratory interpreted the sample as not representative for a metabolic disease, although it had found both analytes, C6-DC and C5-OH, elevated.

Recommendations

In their recommendations, the participants focused on confirmation of their findings or on differentiation. Additional lab tests mostly mentioned were determination of organic acids in urine (n=34), molecular genetic testing (n=30), and measurement of enzymatic activity (n=9). Seven participants gave recommendations on therapeutic treatment.



Sample	H22D
Mean	2.02
Median	1.87
SD	0.97



Sample	H22D
Mean	0.71
Median	0.68
SD	0.54

Scoring
Evaluation criteria: Reporting of C5-OH gives 2 points.
Please note that in future samples of HMG CLD, it will be required also to report on C6-DC in order to receive the full score, as already mentioned for the common sample (A) of this year's report.

For interpretation, two points were awarded for either reporting HMG CLD as primary or secondary diagnosis – in the latter case, a method suitable to find the correct diagnosis must be given in the recommendations.

For this sample, reported results led to critical errors in two cases: One lab detected elevated C5DC carnitine and reported MAD deficiency as the primary diagnosis, another lab detected elevated free carnitine, decreased C2 carnitine and reported CPT1a deficiency.

Overall impression
Achieving an analytical proficiency of 93.1%, this result was slightly less as for sample A (also HMG CLD) of this year, but still excellent. The interpretative proficiency was 84.7% for this sample, which is very good, but underlines certain difficulties compared to sample A.

8.5. Patient E

Propionyl-CoA carboxylase deficiency

Patient details provided to participants

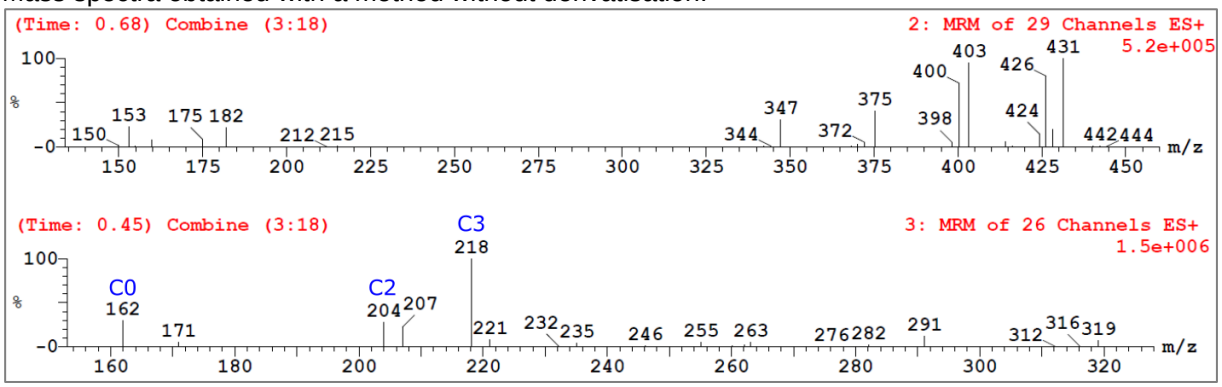
3-year old girl with feeding difficulties and recurrent vomiting

The sample originated from a patient with confirmed propionic aciduria (PA) under treatment.

Analytical performance

The diagnostic marker for PA is propionyl carnitine (C3) which is dominating the MS spectrum below. Several ratios such as C3/C2 are commonly used as secondary identifiers were elevated too.

Mass spectra obtained with a method without derivatisation.



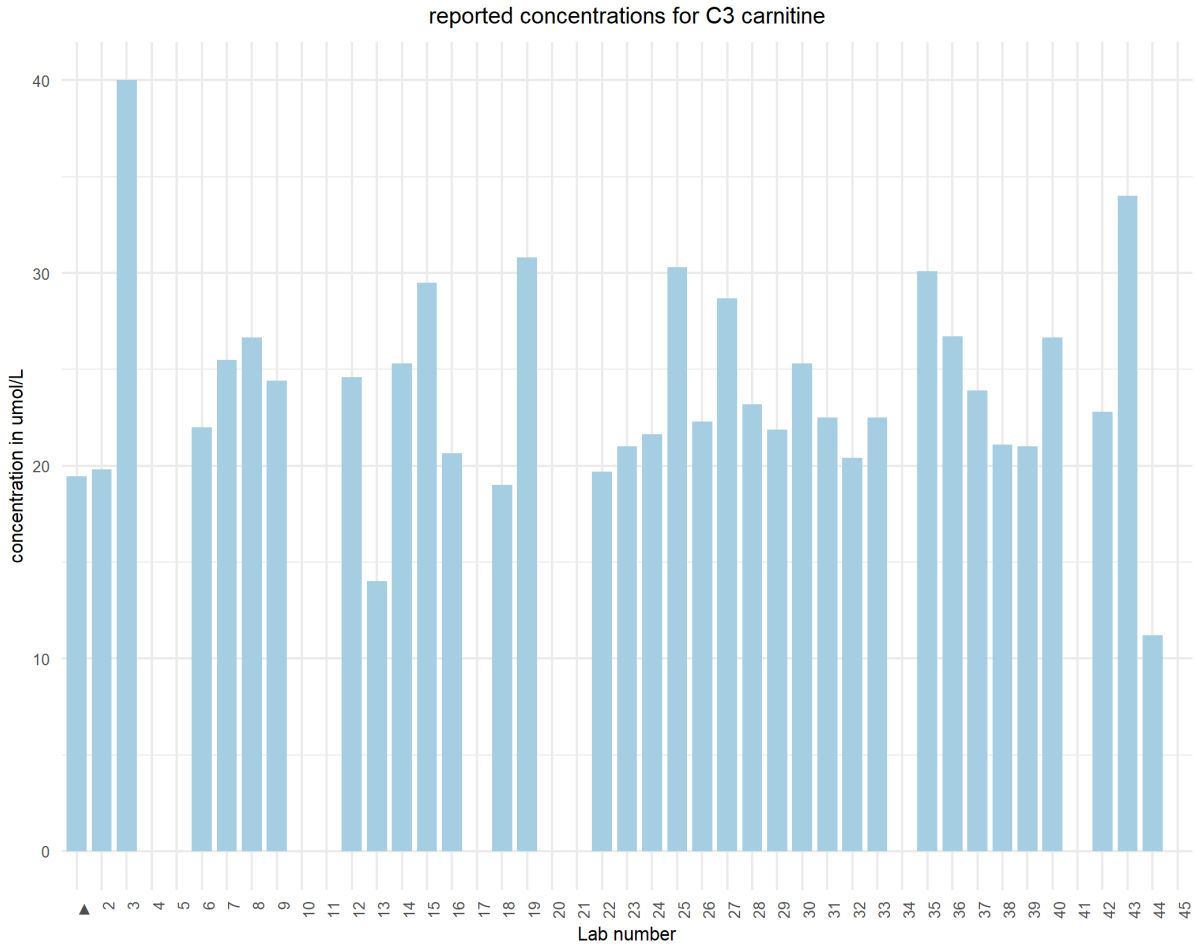
Thirty-six participants out of 45 submitted results for this sample and reported C3 either as elevated or grossly elevated. Free carnitine was also frequently reported to be grossly elevated (n=4), elevated (n=20) or normal (n=4). The majority of submitting laboratories additionally stated methylmalonyl/succinyl carnitine (C4DC) to be in normal concentrations (n=19). Moreover, many labs reported diagnostic ratios as elevated or grossly elevated, in particular C3/C2 (n=17), C3/C16 (n=8), or C3/C0 (n=6).

Diagnosis / Interpretative proficiency

The majority of participants reported PA as the primary diagnosis (n=32) and four labs as an alternative diagnosis. The latter opted for either methylmalonic aciduria (MMA) or disorders of cobalamin metabolism as primary diagnosis. MMA was also the most frequently mentioned alternative (n=25).

Recommendations

The most frequently recommended laboratory tests for diagnostic follow-up were chromatographic determination of organic acids in urine (n=35), molecular genetic testing (n=28), measuring amino acids in plasma (n=14), enzymatic activity in fibroblasts (n=13), or homocysteine in plasma (n=11).



Sample	H22E
Mean	23.96
Median	22.8
SD	5.29

Scoring
Two points are awarded when reporting C3 as elevated or grossly elevated for the analytical score. PA must be reported either as the primary diagnosis or as an alternative diagnosis to achieve two points for interpretation. In the latter case, a method suitable for finding the correct diagnosis must also to be recommended.

Overall impression
This sample appeared not to be difficult for the participants. Analytical as well as interpretative proficiency are 100%!

8.6. Patient F

No diagnosis (normal control sample)

Patient details provided to participants

63-year-old female with mild muscle weakness and occasional pain

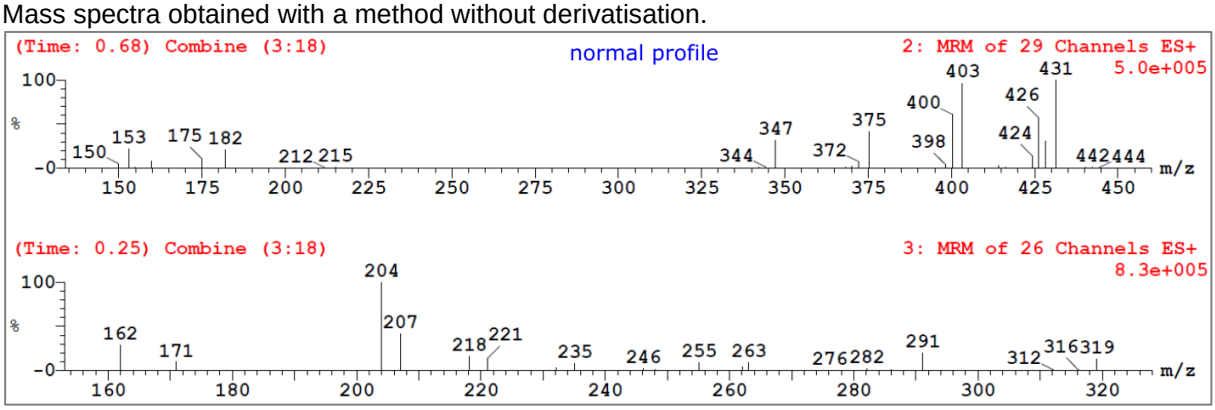
Patient details

The sample originates from a colleague, who is not known to have a metabolic disorder.

Analytical performance

Of the 45 participants taking part in this ACDB scheme, 36 reported results for this sample. All of them stated the AC profile to be normal or at least not representative of a metabolic disorder.

Mass spectra obtained with a method without derivatisation.



Due to the way the results for this sample have been reported by many laboratories, we again refer to section 4.5 in the scheme instructions, which describes how a normal AC profile should be reported. Submissions are difficult to evaluate, when comment fields are used instead of the results tables.

Diagnosis / Interpretative proficiency

All participants referred to the normal profile and gave no specific diagnosis. In addition, some participants gave assessments concerning the clinical description and provided additional recommendations for further examinations.

Recommendations

Some labs advised to continue the metabolic workup and e. g. to perform investigation of urinary organic acids (n=15), repeat AC analysis with a plasma sample (n=9), analyse plasma amino acids (n=7), or to perform basic blood tests.

Scoring

Evaluation criteria: Two points are awarded, when a “normal profile” is reported.
Evaluation criteria: Two points are given, when there is no diagnosis entered or it is referred to the normal AC profile.

Overall impression

The participants performed excellently identifying the normal control sample with 100% analytical and 100% interpretative proficiency.

9. Scores of participants

All data transfer, the submission of data as well as the request and viewing of reports proceed via the ACDB results website hosted by CSCQ. 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, your laboratory is labelled in the leftmost column.

Detailed scores – Round 1

Lab no.	Patient A Hydroxymethylglutaric aciduria (HMG CLD)			Patient B Glutaric acidemia type 1 (GA-I)			Patient C Methylmalonic aciduria, mut(0) type			
	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	--	--	--	--	--	--	--	--	--	0
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	2	2	4	2	1	3	7
10	--	--	--	--	--	--	--	--	--	0
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	--	--	--	--	--	--	--	--	--	0
18	2	2	4	0	0	0	2	2	4	8
19	2	2	4	2	2	4	2	2	4	12
20	2	2	4	2	2	4	2	2	4	12
21	2	2	4	--	--	--	--	--	--	4
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
27	2	2	4	2	2	4	2	2	4	12

Lab no.	Patient A Hydroxymethylglutaric aciduria (HMG CLD)			Patient B Glutaric acidemia type 1 (GA-I)			Patient C Methylmalonic aciduria, mut(0) type			
	A	**I**	**Total**	**A**	**I**	**Total**	**A**	**I**	**Total**	**Total**
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	2	2	4	2	2	4	12
32	2	1	3	2	2	4	2	2	4	11
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	1	3	2	2	4	2	2	4	11
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

Detailed scores – Round 2

Lab no	Patient D Hydroxymethylglutaric aciduria (HMG CLD)			Patient E Propionic acidemia (PA)			Patient F Normal profile			
	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	--	--	--	--	--	--	--	--	--	0
5	--	--	--	--	--	--	--	--	--	0
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	2	2	4	2	2	4	8
10	--	--	--	--	--	--	--	--	--	0
11	--	--	--	--	--	--	--	--	--	0
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	0	2	2	2	4	2	2	4	10
16	2	2	4	2	2	4	2	2	4	12
17	--	--	--	--	--	--	--	--	--	0
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	2	2	4	2	2	4	12
20	2	1	3	2	2	4	2	2	4	11
21	--	--	--	--	--	--	--	--	--	0
22	2	2	4	2	2	4	2	2	4	12
23	2	2	4	2	2	4	2	2	4	12
24	0	0	0	2	2	4	2	2	4	8
25	2	2	4	2	2	4	2	2	4	12
26	2	2	4	2	2	4	2	2	4	12
27	2	2	4	2	2	4	2	2	4	12
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

Lab no	Patient D Hydroxymethylglutaric aciduria (HMG CLD)			Patient E Propionic acidemia (PA)			Patient F Normal profile			
	A	**I**	**Total**	**A**	**I**	**Total**	**A**	**I**	**Total**	**Total**
31	2	2	4	2	2	4	2	2	4	12
32	2	1	3	2	2	4	2	2	4	11
33	2	2	4	2	2	4	2	2	4	12
34	--	--	--	--	--	--	--	--	--	0
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	0	0	0	2	2	4	2	2	4	8
41	--	--	--	--	--	--	--	--	--	0
42	2	2	4	2	2	4	2	2	4	12
43	2	2	4	2	2	4	2	2	4	12
44	2	1	3	2	2	4	2	2	4	11
45	--	--	--	--	--	--	--	--	--	0

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	4	4	4	4	4	24	100	
2	4	4	4	4	4	4	24	100	
3	4	4	4	4	4	4	24	100	
4	--	--	--	--	--	--	0	0	
5	4	4	4	--	--	--	12	50	
6	4	4	4	4	4	4	24	100	
7	4	4	4	4	4	4	24	100	
8	4	4	4	4	4	4	24	100	
9	0	4	3	0	4	4	15	62	CE
10	--	--	--	--	--	--	0	0	
11	4	4	4	--	--	--	12	50	
12	4	4	4	4	4	4	24	100	
13	4	4	4	4	4	4	24	100	
14	4	4	4	4	4	4	24	100	
15	4	4	4	2	4	4	22	92	
16	4	4	4	4	4	4	24	100	
17	--	--	--	--	--	--	0	0	
18	4	0	4	4	4	4	20	83	CE
19	4	4	4	4	4	4	24	100	
20	4	4	4	3	4	4	23	96	
21	4	--	--	--	--	--	4	17	
22	4	4	4	4	4	4	24	100	
23	4	4	4	4	4	4	24	100	
24	4	4	4	0	4	4	20	83	
25	4	4	4	4	4	4	24	100	
26	4	4	4	4	4	4	24	100	
27	4	4	4	4	4	4	24	100	
28	4	4	4	4	4	4	24	100	
29	4	4	4	4	4	4	24	100	
30	4	4	4	4	4	4	24	100	
31	4	4	4	4	4	4	24	100	
32	3	4	4	3	4	4	22	92	
33	4	4	4	4	4	4	24	100	

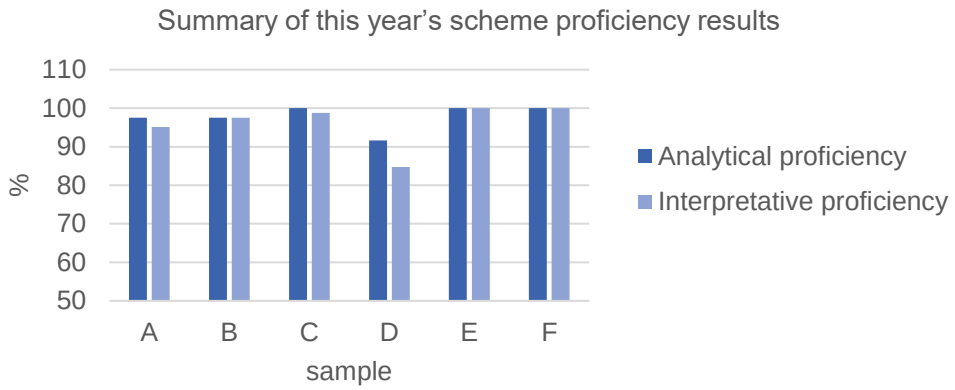
Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
34	4	4	4	--	--	--	12	50	
35	4	4	4	4	4	4	24	100	
36	4	4	4	4	4	4	24	100	
37	4	4	4	4	4	4	24	100	
38	4	4	4	4	4	4	24	100	
39	4	4	4	4	4	4	24	100	
40	3	4	4	0	4	4	19	79	CE
41	4	4	4	--	--	--	12	50	
42	4	4	4	4	4	4	24	100	
43	4	4	4	4	4	4	24	100	
44	4	4	4	3	4	4	23	96	
45	--	--	--	--	--	--	0	0	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 71 % of adequate responses)	33	73
Unsatisfactory performers (< 71 % adequate responses and/or critical error)	3	7
Partial and non-submitters	9	20

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
ACDB-DH-2022-A	Hydroxymethylglutaric aciduria (HMG CLD)	98	95	96
ACDB-DH-2022-B	Glutaric acidemia type 1 (GA-I)	98	98	98
ACDB-DH-2022-C	Methylmalonic aciduria, mut(0) type	100	99	99
ACDB-DH-2022-D	Hydroxymethylglutaric aciduria (HMG CLD)	92	85	88
ACDB-DH-2022-E	Propionic acidemia (PA)	100	100	100
ACDB-DH-2022-F	Normal profile	100	100	100



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

Date of report, 2023-05-08
Name and signature of Scientific Advisor

Dr J. Janda
Scientific Advisor
Laboratory of Metabolic Diseases

Prof. Dr. G. F. Hoffmann
Director
Department of General Paediatrics

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	14 July 2023	2022 annual report published

END