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Qualitative Organic Acids

Centre: Germany

Final Report 2021

prepared by
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Note: This annual report is intended for participants of the ERNDIM Qualitative Organic Acids (QLOU) Heidelberg scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

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1. Introduction

The ERNDIM Qualitative Organic Acids in urine scheme offers urine samples obtained from confirmed patients with confirmed diagnoses to enable laboratories to gain or maintain experience to identify organic acid disorders. The scheme is organised by The scheme is organised by Dr. Claus-Dieter Langhans and Dr. Joachim Janda (metabolic centre Heidelberg) 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. 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 seventy-four laboratories from many different countries participated in the QLOU Heidelberg scheme. There were no educational participants in 2021 (none in 2020). Educational participants take

[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.

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 Barcelona, Heidelberg and Sheffield qualitative urinary organic acid schemes which are run separately. The three organising laboratories each participate in the other's scheme by rotation.

Country	Number of participants
Undefined country	4
Austria	3
Bulgaria	1
Canada	10
Croatia	1
Czechia	2
Denmark	1
Egypt	1
Estonia	2
Germany	17
India	1
Italia	1
Latvia	1
Lithuania	1
Luxembourg	1
Mexico	1
Netherlands	8
People's Republic of China	2
Philippines	1
Slovenia	1
Sri Lanka	1
Switzerland	3
Thailand	1
Turkey	9
Viet Nam	1

3. Design and logistics of the scheme including sample information

As usual, the samples used in 2021 were authentic human urine samples, five from affected patients and one from a healthy individual.

All samples selected by the Scientific Advisor have been heat-treated and were tested for suitability in the Scientific Advisor's laboratory.

The scheme has been designed and planned by Claus-Dieter Langhans and Joachim Janda as Scientific Advisors and coordinated by CSCQ as scheme organiser (sub-contractor on behalf of ERNDIM), both appointed by and according to procedures laid down by the ERNDIM Board.

CSCQ dispatched the QLOU EQA samples to the scheme participants and provided 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 chromatograms can be uploaded on the CSCQ website.

4. Schedule of the scheme

Time schedule in the 2021 ERNDIM QLOU Heidelberg scheme.

	1st Submission Round	2nd Submission Round
Sample IDs:	QLOU-DH-2021-A QLOU-DH-2021-B QLOU-DH-2021-C	QLOU-DH-2021-D QLOU-DH-2021-E QLOU-DH-2021-F
Shipment of samples	February 09th, 2021	
Start of analysis (clinical data available)	May 11th, 2021	September 7th, 2021

	1st Submission Round	2nd Submission Round
Reminder for result submission	May 25th, 2021	September 20th, 2021
Results submission deadline:	June 1st, 2021	September 27th, 2021
Interim reports available on CSCQ website	October 25th, 2021	November 29th, 2021

To be able to continue this scheme we need a steady supply of new patient samples. Several laboratories have donated samples to the Urine QLOU scheme in the past, for which they are gratefully acknowledged. If you are able to collect one or more samples 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 QLOU scheme in the following year.

Samples included in the 2021 ERNDIM QLOU Heidelberg scheme.

Survey	Sample no.	Diagnosis
21-05-OUH	QLOU-DH-2021-A	SCEH or ECHS 1 deficiency
	QLOU-DH-2021-B	AADC deficiency
	QLOU-DH-2021-C	Alkaptonuria
21-09-OUH	QLOU-DH-2021-D	3-MCC deficiency
	QLOU-DH-2021-E	normal
	QLOU-DH-2021-F	MCAD deficiency

The scheme format was kept identical to those of previous years. Samples were shipped by regular mail. Details regarding stability of samples are provided in the sample package.

Interim reports were generated by the evaluation program developed by CSCQ.

Origin of patients: all urine samples have been provided by the scheme organizers or specified participants.

Patient A:	SCEH or ECHS 1 deficiency	Metabolic centre Heidelberg
Patient B:	AADC deficiency	Metabolic centre Heidelberg
Patient C:	Alkaptonuria	Metabolic centre Heidelberg
Patient D:	3-MCC deficiency	Metabolic centre Heidelberg
Patient E:	normal	Metabolic centre Heidelberg
Patient F:	MCAD deficiency	Metabolic centre Heidelberg

5. Results

Returned results in the 2021 ERNDIM QLOU Heidelberg scheme

	Survey 1	Survey 2
Receipt of results	74	75
No answer	1	0

6. Web site reporting

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

- Selection of tests: **don't select a test if you will not perform it**, otherwise the evaluation programme will include it in the report.
- 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".

- **Do not enter results 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.
  - **Do not 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 25th, 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' 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 19th, 2021.

Samples eligible for critical errors in the 2021 ERNDIM QLOU Heidelberg scheme.

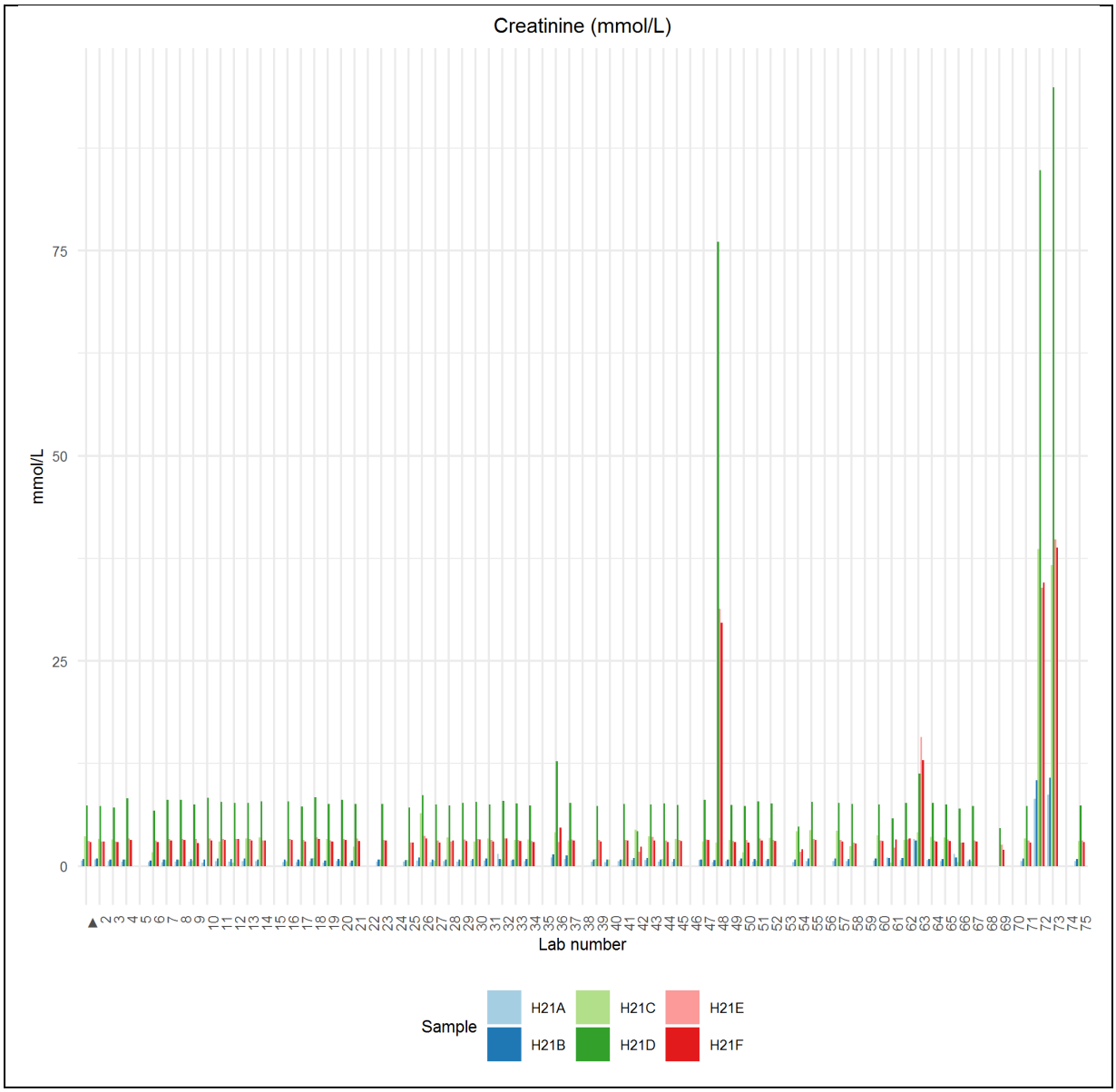
QLOU-DH-2021-A
QLOU-DH-2021-C
QLOU-DH-2021-D
QLOU-DH-2021-F

Score for satisfactory performance
For satisfactory performance at least 17 points from the maximum of 24 points (71%) are required.
For the Annual Certificate of Participation covering all ERNDIM programmes, the term "participation" for this scheme (QLOU) is defined as meaning that at least two returns are required during the year. If this requirement is not met, the certificate of participation will state "non-submitter" instead of "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. Creatinine measurement for all samples

Creatinine: ratio to median



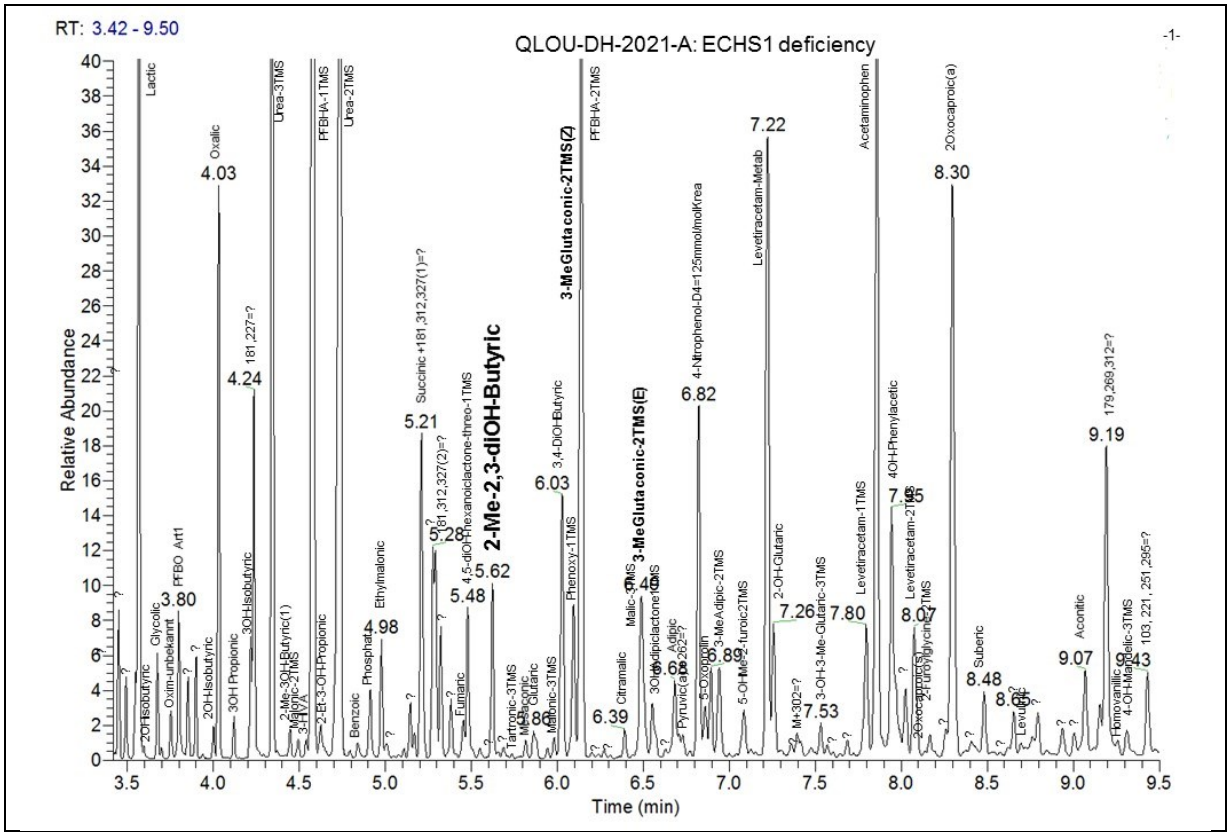
8.2. Patient A

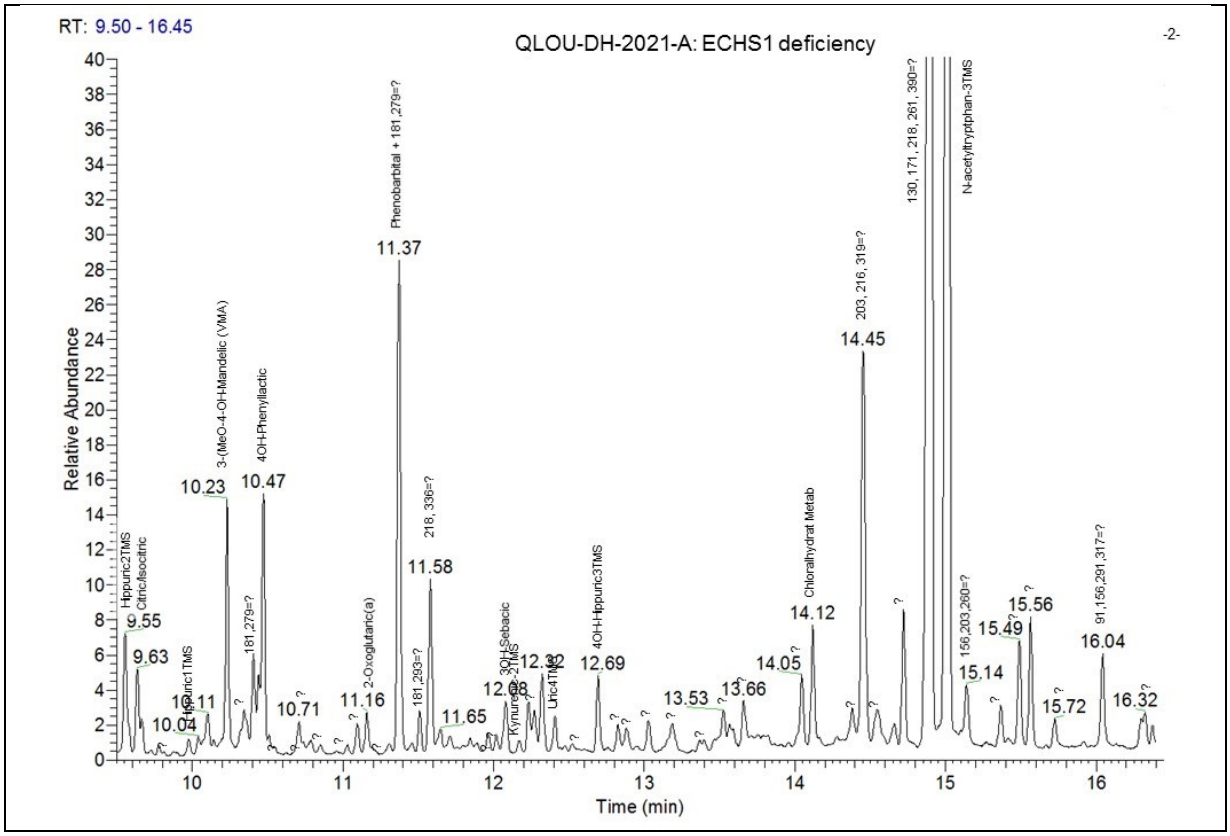
Short-chain enoyl-CoA hydratase deficiency

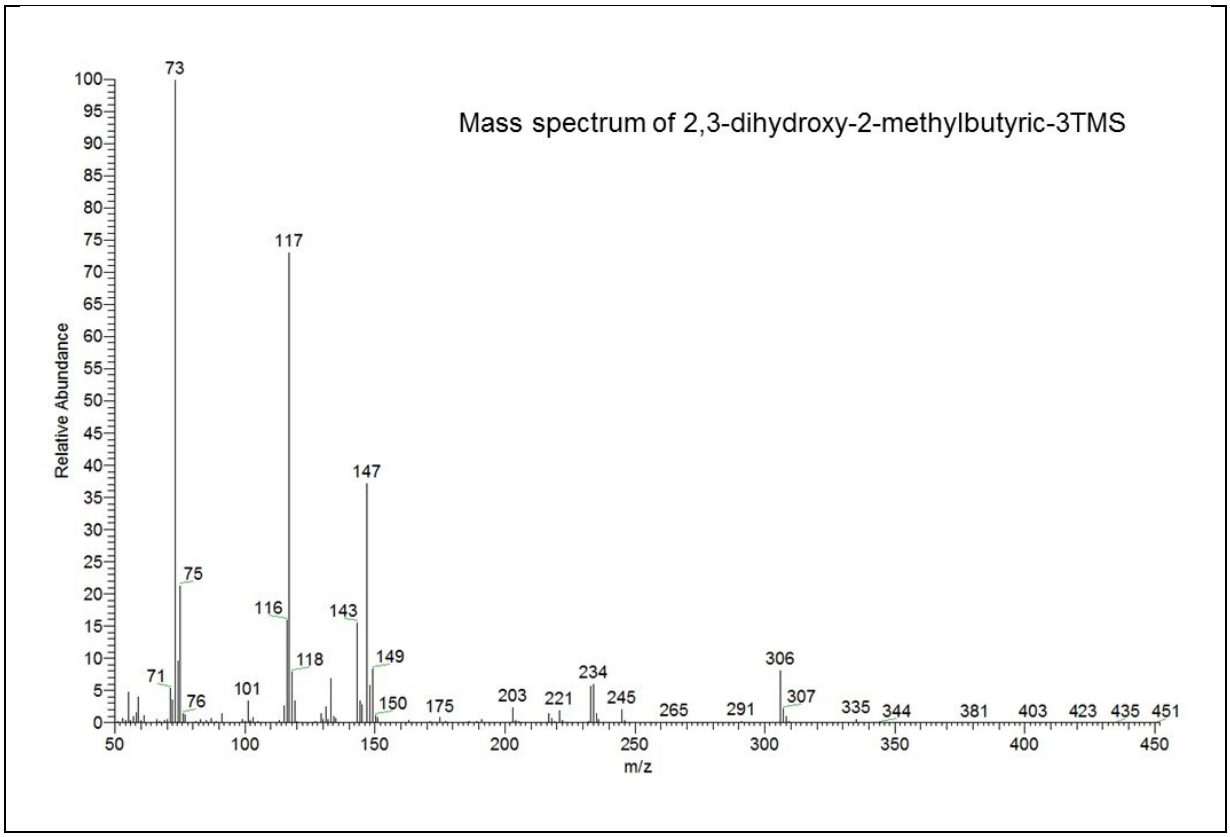
Patient details provided to participants
14-month-old girl with developmental regression, elevated plasma lactate and abnormal brain MRI

Patient details
Elevated amounts of 2,3-dihydroxy-2-methylbutyric acid and 3-methylglutaconic acid.
Drug metabolites detectable.

Analytical performance
2,3-dihydroxy-2-methylbutyric acid was reported by thirty participants (42%) whereas 3-methyl-glutaconic acid was found by fifty-eight laboratories (81%).
Analytical performance was only 62%.







Diagnosis / Interpretative proficiency

Most participants indicated mitochondrial dysfunction, but short-chain enoyl-CoA hydratase (SCEH/ECHS 1) deficiency or 3-hydroxyisobutyryl-CoA hydrolase (HIBCH) deficiency was specifically suggested by only thirty-four participants (47%).

Diagnostic performance was 72%.

Scoring
The two main metabolites were used to evaluate analytical performance.
Two points were awarded for detecting 2,3-dihydroxy-2-methylbutyric acid and only one point for 3-methylglutaconic acid.
For diagnostic proficiency, only the mention of ECHS1 deficiency was rewarded with two points, whereas mitochondrial diseases gave only one point.

Overall impression
In order to get a specific indication of ECHS1 via the organic acid profile, it is essential to identify the key metabolite 2,3-dihydroxy-2-methylbutyric acid. The recommendation for laboratories is to extend their laboratory mass spectra libraries by this metabolite, if not already done.
Furthermore, it can be noted that unfortunately a few laboratories still have problems identifying 3-methylglutaconic acid.

Overall performance was 67%.

A urine from a patient with ECHS1 deficiency was sent for the third time in 2021 after 2016 and 2018. Forty-nine participants (68%) were active in the Heidelberg scheme in all three years.
Of these, thirteen participants (26%) found the sample normal in 2016 and fourteen (29%) diagnosed 3-methylglutaconic aciduria (or a subset). ECHS1 was not mentioned by any of these laboratories.
In 2018, there were only nine laboratories (18%) that gave a normal diagnosis. Three participants (1%) diagnosed 3-MGA and twenty-six (53%) gave the correct diagnosis.
In the current sample 2021, performance still improved somewhat. Now twenty-eight participants (57%) diagnosed ECHS1/HIBCD, five (10%) diagnosed 3-MGA, and only one lab considered the profile normal.

This sample was considered by the SAB to be eligible for critical error, as is the case for two participants who reported "normal" without adequate further recommendations.

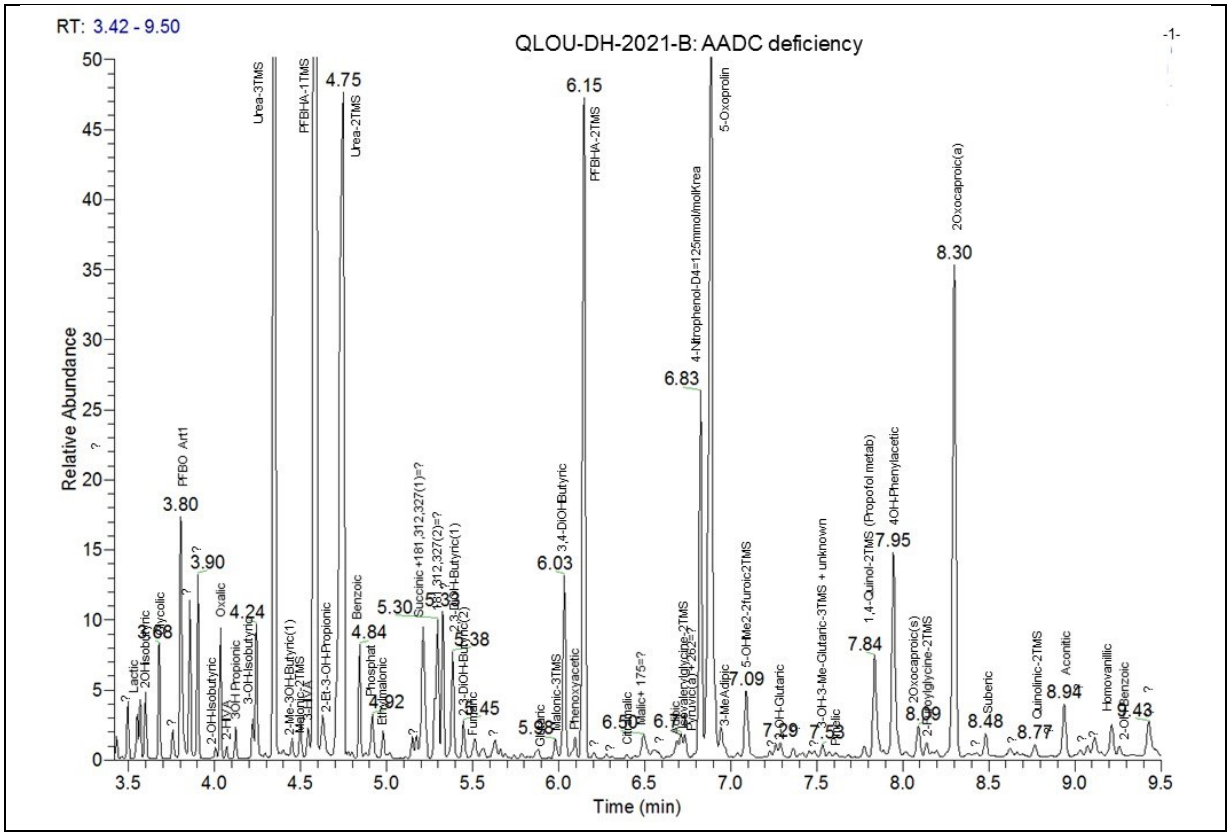
8.3. Patient B

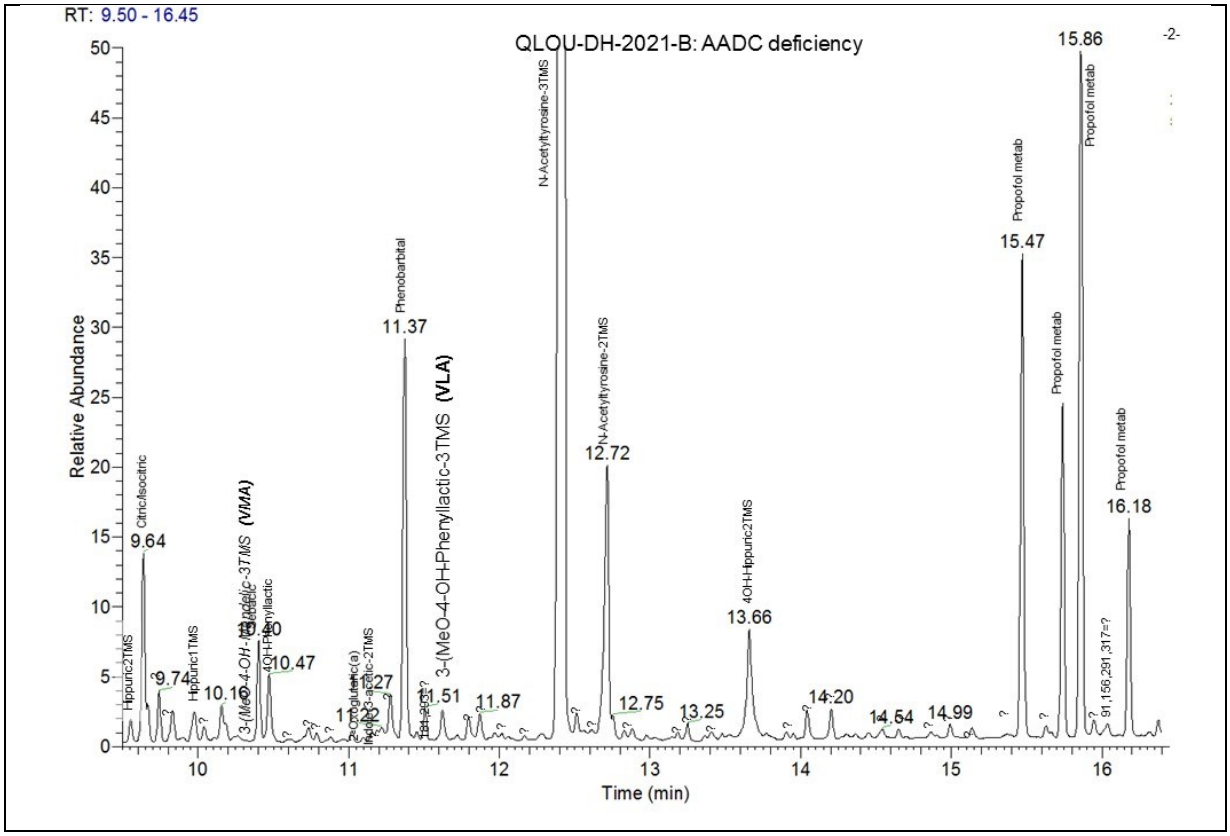
Aromatic l-amino acid decarboxylase deficiency

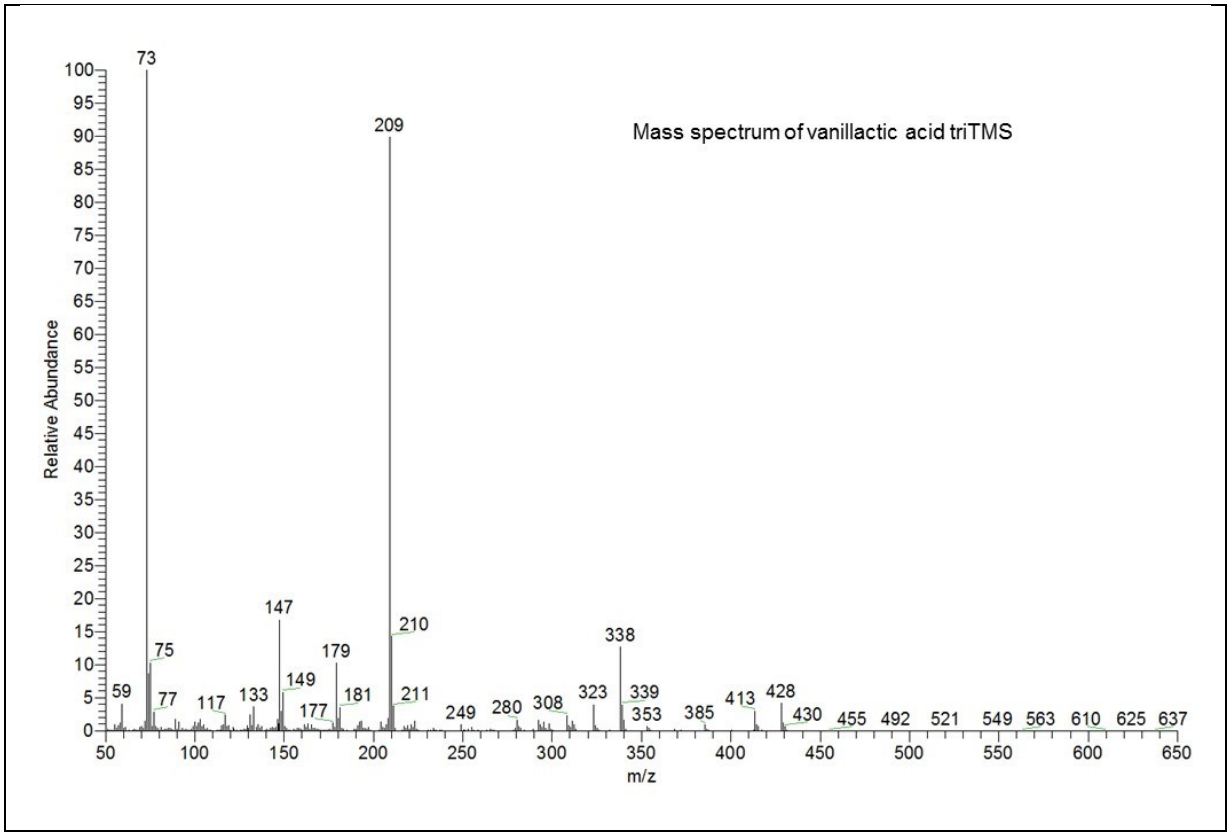
Patient details provided to participants
8-year-old boy with severe, predominantly truncal hypotonia and intermittent dystonic posturing. On treatment during sample collection in ICU.

Patient details
The patient initially presented at the age of 2 months with global muscular hypotonia and dystonic movements. Neurotransmitter analysis in CSF at the age of six month showed reduced homovanillic acid and 5-hydroxyindoleacetic acid. 3-OMD, L-DOPA and 5-hydroxytryptophane were significantly increased. Pterine analysis gave a normal result.
Diagnosis was confirmed by enzyme analysis of AADC activity.
The current urine was collected at the age of eight years while he was being fed parenterally in the intensive care unit.
The sample showed increased concentration of vanillactic acid (VLA) with very low amounts of vanilmandelic acid (VMA), resulting in a significantly increased VLA/VMA ratio.
The very high concentration of N-acetyltyrosine primarily results from artificial nutrition.

Analytical performance
The key metabolite vanillactic acid (VLA) was reported by only twenty-nine participants (40%).
However, sixty participants (83%) reported elevated N-acetyltyrosine, for which we awarded one point.
Therefore, the analytical proficiency was 64%.


RT: 3.42 - 9.50
QLOU-DH-2021-B: AADC deficiency
-1-
Relative Abundance
Time (min)
Urea-3TMS
PFBHA-1TMS
4.75
Urea-2TMS
6.15
PFBHA-2TMS
5-Oxoprolin
4-Nitrophenol-D4=125mmol/molKrea
6.83
2Oxocaproic(a)
8.30
3.80
PFBO_Art1
3.90
4.24
5.30
4.84
6.03
3,4-DiOH-Butyric
7.84
7.95
4OH-Phenylacetic
7.09
5-OH-Me2-2furoic2TMS
1,4-Quinol-2TMS (Propofol metab)
2Oxocaproic(s)
8.09
8.48
Suberic
8.77
8.94
Quinolinic-2TMS
Aconitic
Homovanillic
2-OH-Benzoic
8.43


RT: 9.50 - 16.45
QLOU-DH-2021-B: AADC deficiency
-2-
Relative Abundance
Time (min)
Hippuric2TMS
Citric/Isocitric
9.64
9.74
Hippuric1TMS
10.10
3-(MeO-4-OH-Phenyl)lactic-3TMS (VMA)
10.47
4OH-Phenyllactic
11.22
11.27
3-(MeO-4-OH-Phenyllactic-3TMS (VLA)
11.37
Phenobarbital
11.51
11.87
N-Acetyltyrosine-3TMS
N-Acetyltyrosine-2TMS
12.72
12.75
13.25
4OH-Hippuric2TMS
13.66
14.20
14.54
14.99
15.47
Propofol metab
15.86
Propofol metab
16.18
Propofol metab
91,156,291,317=?



Diagnosis / Interpretative proficiency
Only thirty-four participants (47%) diagnosed AADC deficiency.
Fourteen submitters (19%) gave a normal diagnosis.
Tyrosinaemia was suggested by nine participants (12%).
Two points were given for the correct diagnosis and one point for suggesting a neurotransmitter disorder.
Diagnostic proficiency was 51%

Scoring

This sample was considered by the SAB to be an educational sample.
Scores are not to be taken into account in evaluating overall performance.

Overall impression

A large number of laboratories seemed to have difficulty in detecting VLA, resulting in the very low overall proficiency of 58% for this sample.

Some laboratories may not be aware of the mass spectrum of VLA, or the peak height may have been incorrectly estimated. A semi-quantitative estimation of the concentration via peak area could be helpful in such cases.

This was a common sample and was sent from all three QLOU centres.

The scientific advisors from both Barcelona and Sheffield reported comparable proficiencies, all around 50-60%.

Although the determination of organic acids is not the first choice to diagnose AADC deficiency, laboratories should pay more attention to this metabolite.

8.4. Patient C

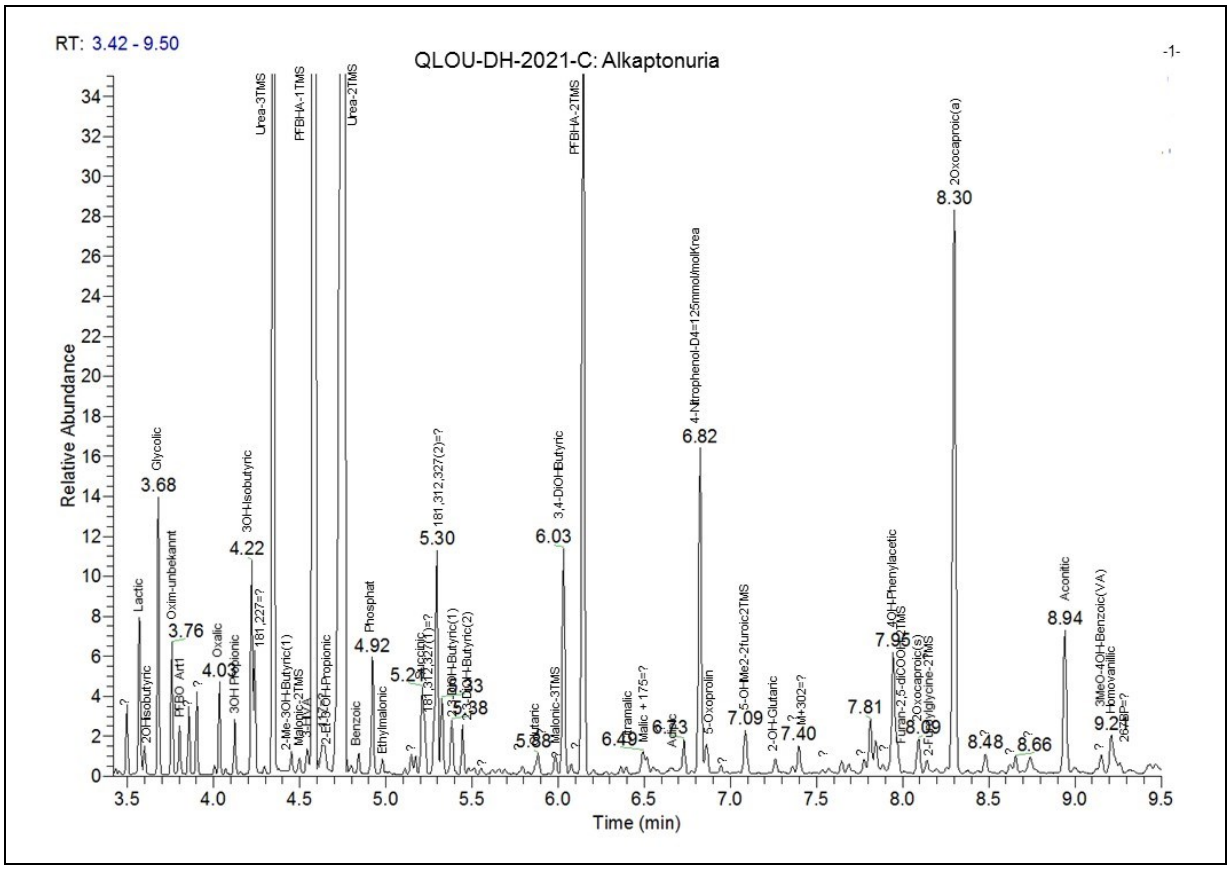
Alkaptonuria

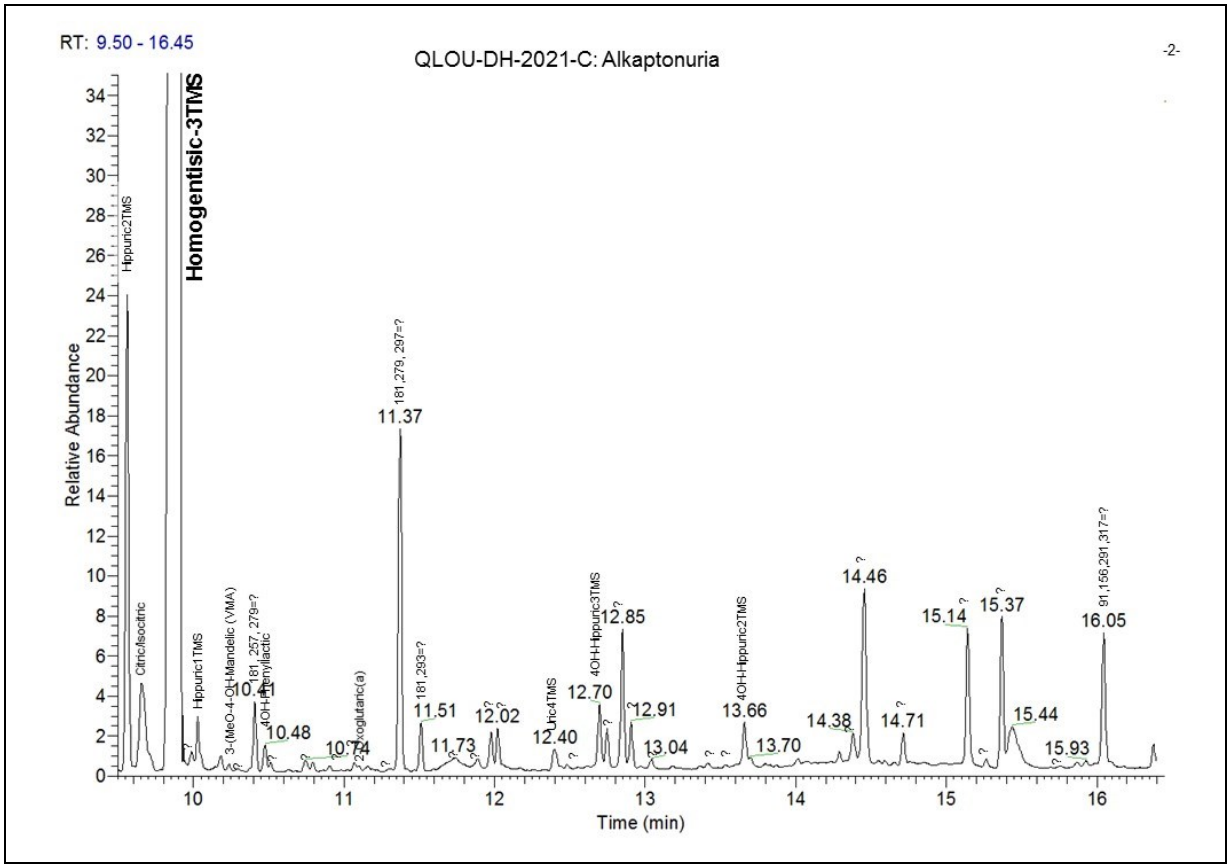
Patient details provided to participants
45-year-old male with a history of pain mainly of the large joints

Patient details

The chromatogram of this sample is dominated by a huge peak of homogentisic acid, the pathognomonic marker of alkaptonuria.

Analytical performance.
The vast majority of participants had no problems detecting homogentisic acid.
The analytical performance was high at 93%.





Diagnosis / Interpretative proficiency
The correct diagnosis was given by almost all participants (69/72).
Interpretative proficiency was high at 93%.

Overall impression
This was not a very challenging sample. Both the analytics and the interpretation were excellent for the most part.
The overall proficiency was 93%.

Critical error

As alkaptonuria is a treatable condition, the SAB has decided that it is a critical error not to find this diagnosis.

This concerns two participants.

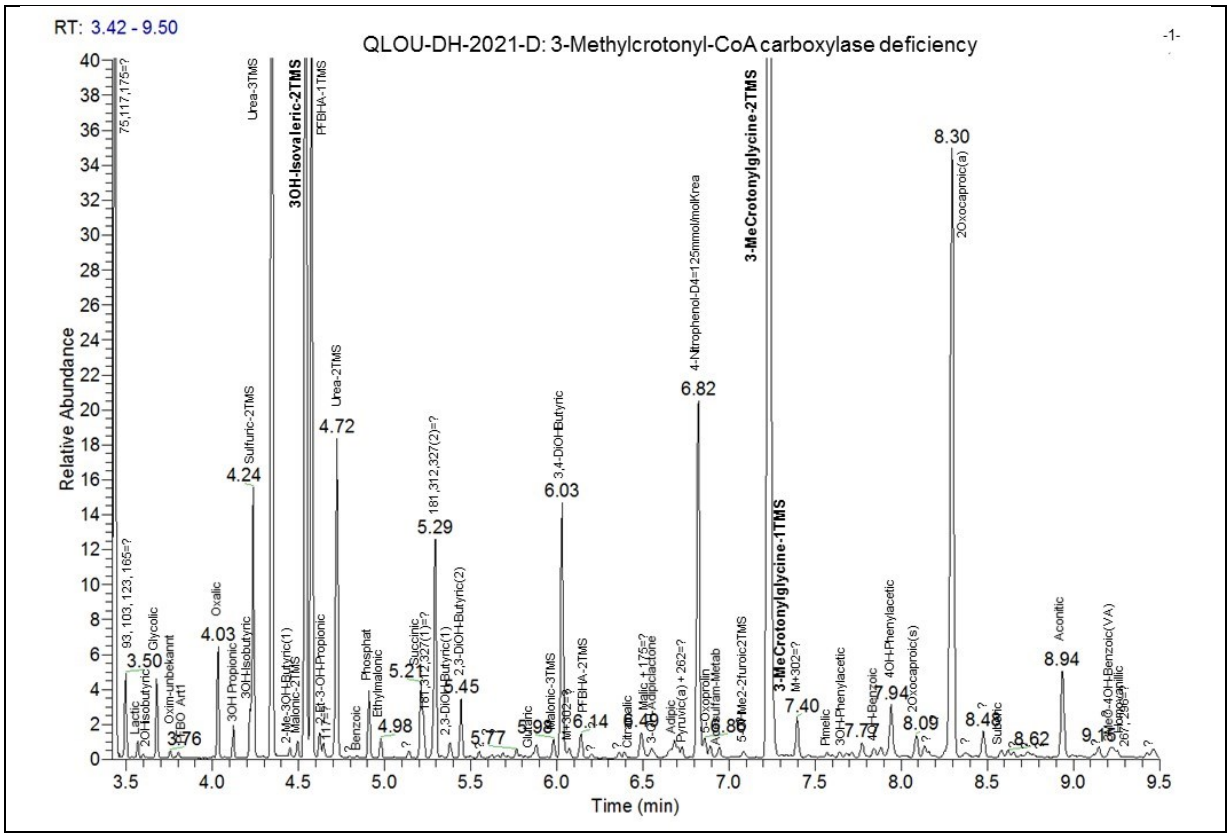
8.5. Patient D

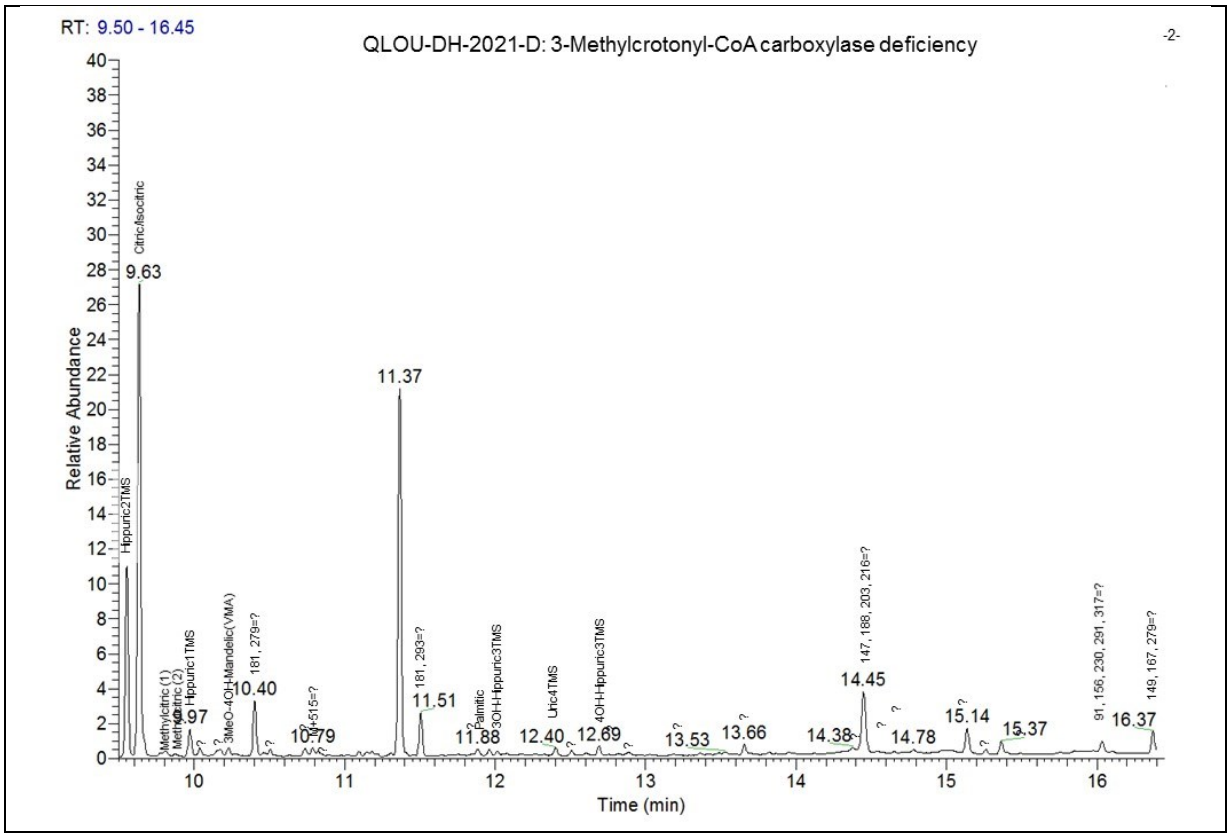
3-methylcrotonyl-CoA carboxylase deficiency

Patient details provided to participants
16-year-old boy with muscular hypotonia

Patient details
The chromatogram of this sample shows clearly elevated 3-hydroxyisovaleric acid (3-HIVA) and 3-methylcrotonylglycine (3-MCG).

Analytical performance
The analytical performance was very high at 98%.
Sixty-nine participants (97%) reported increased 3-methylcrotonylglycine and sixty-five participants (92%) increased 3-hydroxyisovaleric acid.
Because we gave two points for increased 3-MCG and one point for 3-HIVA alone, the analytical performance was 93%





Diagnosis / Interpretative proficiency

The interpretation of the analytical findings was not a problem for most participants, so that the correct diagnosis of 3-methylcrotonylglycinuria or 3-methylcrotonyl-CoA carboxylase deficiency was clear.

Only three participants suggested other diagnoses. These were isovaleric aciduria, beta-ketothiolase deficiency and a normal profile.
Therefore, the diagnostic performance was 91%.

Overall impression
Due to the clear profile the overall performance was very good at 92%.

Critical error

Also, for this sample, the SAB decided that an incorrect diagnosis is to be considered a critical error.
Two participants were assigned a critical error.

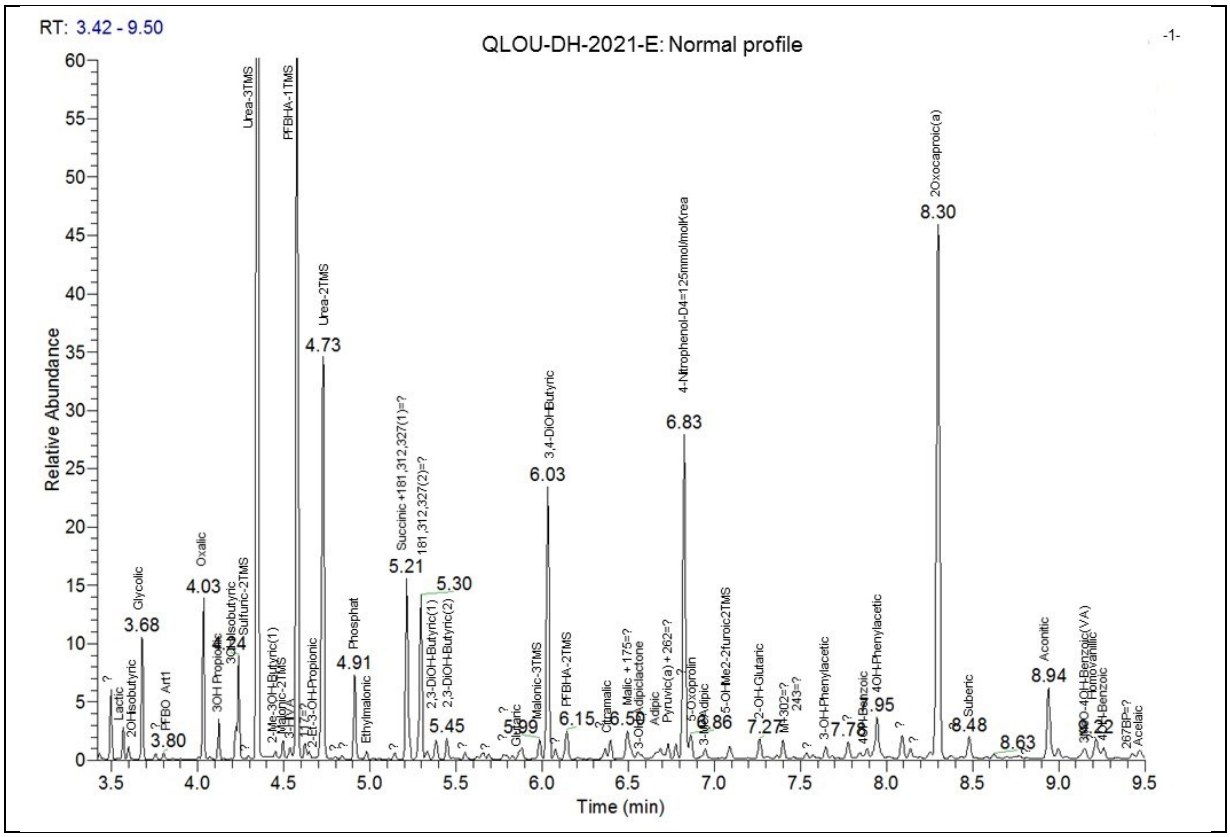
8.6. Patient E

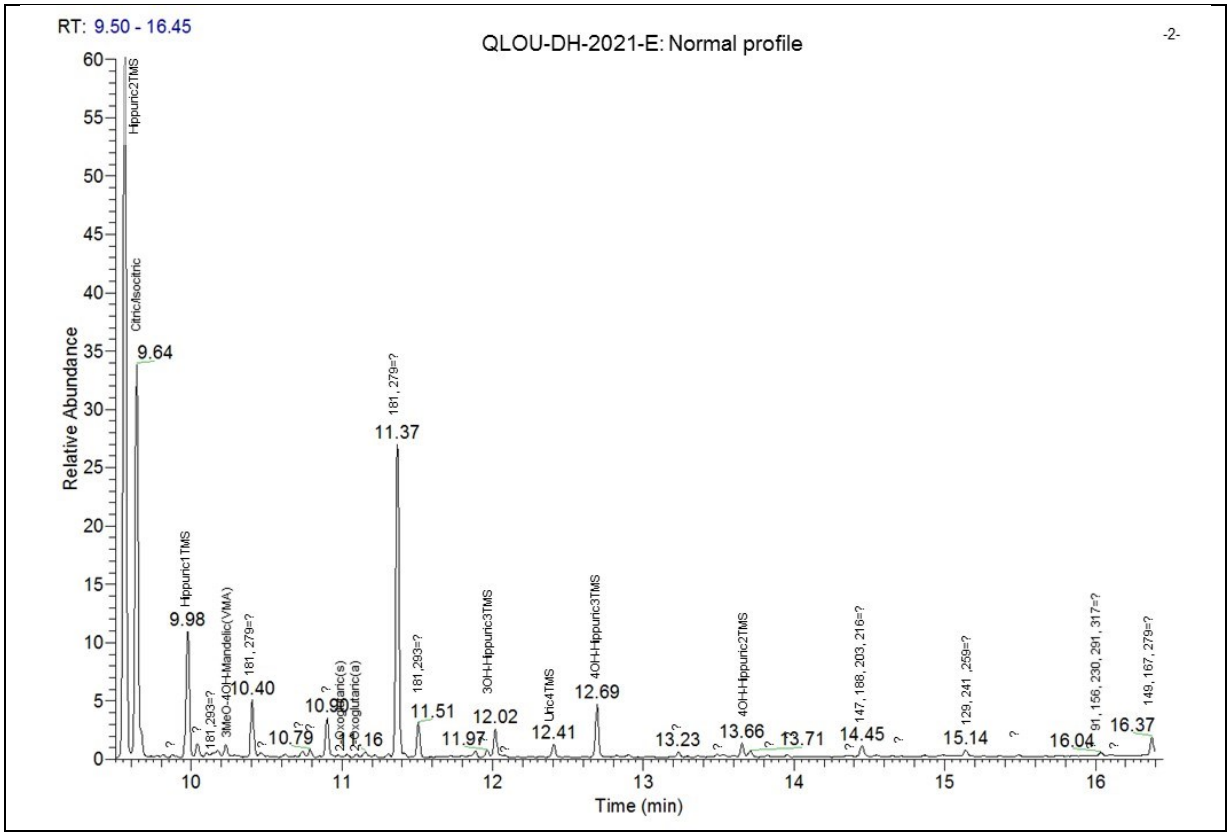
Normal control

Patient details provided to participants
7-year-old girl with acute attacks of ataxia

Patient details
This urine was collected from a healthy boy. The chromatogram shows no relevant abnormalities.

Analytical performance
Most laboratories found no noticeable changes in the organic acid profile.
Only a few participants reported some metabolites like 3-(3-hydroxyphenyl)-3-hydroxypropanoic acid, 3-hydroxyphenylacetic acid, succinic acid, hippuric acid or 4-hydroxyphenylacetic acid that they found elevated and lost a few points.
Therefore, the analytical performance was 87 %.





Diagnosis / Interpretative proficiency
The majority of participants (63/71) diagnosed a normal sample.
In contrast, few senders suggested different diagnoses.
In detail, ethylmalonic aciduria, glutaric aciduria type I, 3-methylglutaconic aciduria, short/branched-chain acyl-CoA dehydrogenase deficiency or OTC deficiency were named, but also autism and dysbiosis in colon microbiota.
If we felt that these suggestions were too far from reality, we deducted points.

Overall impression
Presumably based on the provided clinical description, some laboratories were very cautious and partly overinterpreted their analytical results.
The overall proficiency was therefore “only” 85%.

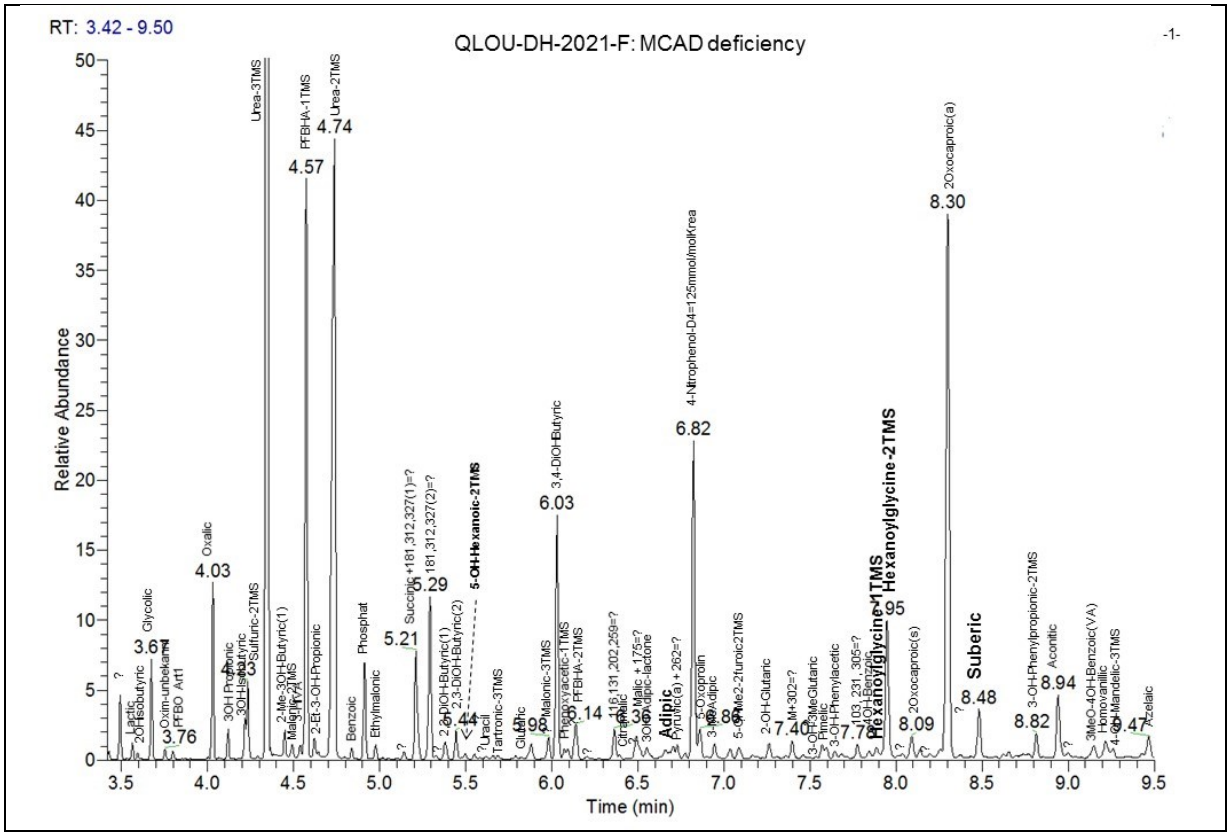
8.7. Patient F

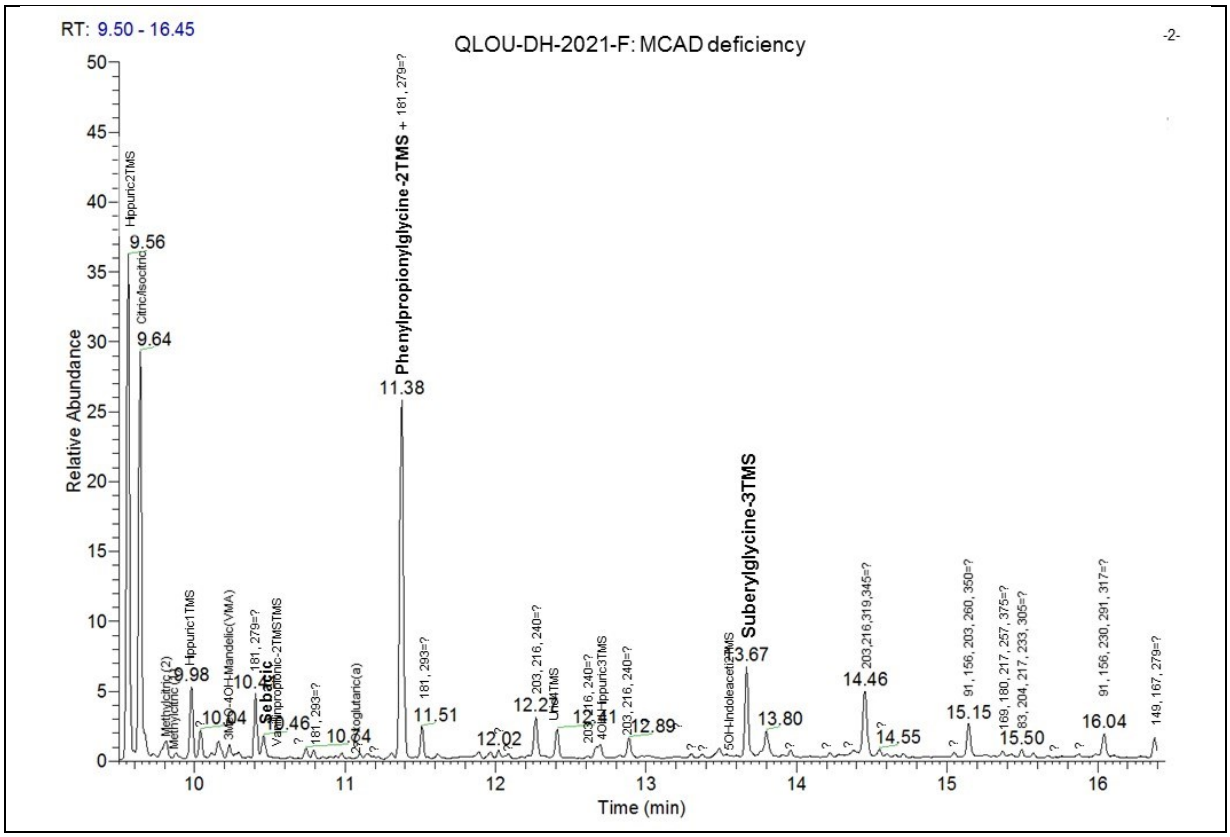
Medium-chain acyl-CoA dehydrogenase deficiency

Patient details provided to participants
2-year-old boy admitted due to hypoglycaemia

Patient details
The organic acid profile showed clearly elevated hexanoylglycine, phenylpropionylglycine and suberylglycine.

Analytical performance
The key to correct diagnosis is the detection of hexanoylglycine, suberylglycine and phenylpropionylglycine. Sixty-five participants (92%) reported these metabolites, whereas five did not.
Analytical performance was 92%





Diagnosis / Interpretative proficiency

Sixty-six participants (93%) diagnosed the sample as MCAD deficiency or fatty acid oxidation defect. However, four participants gave a normal diagnosis.

The diagnostic performance was also 92%.

Overall impression
The overall performance of all laboratories was 92% this year.
A urine sample from another MCAD patient was sent in 2018. At that time, the performance was only 79%. So overall, one can see an improvement of the labs here.
Of the sixty laboratories active in the Heidelberg scheme in both years, eleven participants gave a normal diagnosis in 2018 but only three in 2021.
In detail, nine participants improved, but one did not. One lab gave the correct diagnosis in 2018 but not in 2021. Another participant who suspected MCT supply in 2018 gave a normal diagnosis in 2021.

Critical error

The ERNDIM SAB considered it a critical failure if the relevant glycine conjugates have not been identified, as this mistake makes correct diagnosis impossible.

Critical errors were assigned to five participants.

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.

9.1. Detailed scores – Round 1

Lab n°	Patient A SCEH or ECHS 1 deficiency			Patient B AADC deficiency			Patient C Alkaptonuria			
	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	0	1	1	--	--	--	2	2	4	5
4	2	2	4	--	--	--	2	2	4	8
5	0	0	0	--	--	--	0	0	0	0
6	0	2	2	--	--	--	2	2	4	6
7	2	2	4	--	--	--	2	2	4	8
8	1	1	2	--	--	--	2	2	4	6
9	2	2	4	--	--	--	2	2	4	8
10	1	1	2	--	--	--	2	2	4	6
11	2	2	4	--	--	--	2	2	4	8
12	2	2	4	--	--	--	2	2	4	8
13	2	2	4	--	--	--	2	2	4	8
14	0	1	1	--	--	--	2	2	4	5
15	1	2	3	--	--	--	2	2	4	7
16	1	0	1	--	--	--	2	2	4	5
17	2	2	4	--	--	--	2	2	4	8
18	1	1	2	--	--	--	2	2	4	6

Lab n°	Patient A SCEH or ECHS 1 deficiency			Patient B AADC deficiency			Patient C Alkaptonuria			
	A	I	Total	A	I	Total	A	I	Total	Total
19	2	2	4	--	--	--	2	2	4	8
20	2	2	4	--	--	--	2	2	4	8
21	1	1	2	--	--	--	2	2	4	6
22	1	2	3	--	--	--	2	2	4	7
23	2	2	4	--	--	--	2	2	4	8
24	0	0	0	--	--	--	2	2	4	4
25	1	1	2	--	--	--	2	2	4	6
26	1	0	1	--	--	--	2	0	2	3
27	0	0	0	--	--	--	2	2	4	4
28	2	2	4	--	--	--	2	2	4	8
29	2	2	4	--	--	--	2	2	4	8
30	2	2	4	--	--	--	2	2	4	8
31	1	1	2	--	--	--	2	2	4	6
32	0	1	1	--	--	--	2	2	4	5
33	2	2	4	--	--	--	2	2	4	8
34	1	1	2	--	--	--	2	2	4	6
35	2	2	4	--	--	--	2	2	4	8
36	2	2	4	--	--	--	2	2	4	8
37	2	2	4	--	--	--	2	2	4	8
38	0	0	0	--	--	--	0	0	0	0
39	1	1	2	--	--	--	0	2	2	4
40	1	1	2	--	--	--	2	2	4	6
41	1	1	2	--	--	--	2	2	4	6
42	1	1	2	--	--	--	2	2	4	6
43	2	2	4	--	--	--	2	2	4	8
44	2	2	4	--	--	--	0	0	0	4
45	0	2	2	--	--	--	2	2	4	6
46	1	1	2	--	--	--	2	2	4	6
47	1	1	2	--	--	--	2	2	4	6
48	1	2	3	--	--	--	2	2	4	7
49	1	1	2	--	--	--	2	2	4	6
50	1	1	2	--	--	--	0	0	0	2

Lab n°	Patient A SCEH or ECHS 1 deficiency			Patient B AADC deficiency			Patient C Alkaptonuria			
	A	I	Total	A	I	Total	A	I	Total	Total
51	2	2	4	--	--	--	2	2	4	8
52	1	2	3	--	--	--	2	2	4	7
53	2	2	4	--	--	--	2	2	4	8
54	1	2	3	--	--	--	2	2	4	7
55	2	2	4	--	--	--	2	2	4	8
56	2	2	4	--	--	--	2	2	4	8
57	2	2	4	--	--	--	2	2	4	8
58	2	2	4	--	--	--	2	2	4	8
59	0	0	0	--	--	--	2	2	4	4
60	2	2	4	--	--	--	2	2	4	8
61	1	1	2	--	--	--	2	2	4	6
62	2	2	4	--	--	--	2	2	4	8
63	1	1	2	--	--	--	2	2	4	6
64	2	2	4	--	--	--	2	2	4	8
65	2	2	4	--	--	--	2	2	4	8
66	0	1	1	--	--	--	2	2	4	5
67	1	1	2	--	--	--	2	2	4	6
68	--	--	--	--	--	--	--	--	--	0
69	1	2	3	--	--	--	2	2	4	7
70	0	2	2	--	--	--	2	2	4	6
71	1	1	2	--	--	--	2	2	4	6
72	0	0	0	--	--	--	2	2	4	4
73	1	1	2	--	--	--	2	2	4	6
74	1	1	2	--	--	--	2	2	4	6
75	1	1	2	--	--	--	2	2	4	6

9.2. Detailed scores – Round 2

Lab n°	Patient D 3-MCC deficiency			Patient E normal			Patient F MCAD deficiency			
	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	0	2	2	2	4	10
4	2	2	4	2	2	4	2	2	4	12
5	0	0	0	0	0	0	0	0	0	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	2	2	4	2	2	4	2	2	4	12
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	2	2	4	2	2	4	2	2	4	12
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
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 n°	Patient D 3-MCC deficiency			Patient E normal			Patient F MCAD deficiency			
	A	I	Total	A	I	Total	A	I	Total	Total
31	2	2	4	2	2	4	2	2	4	12
32	2	2	4	2	2	4	2	2	4	12
33	2	2	4	2	2	4	2	2	4	12
34	0	0	0	0	0	0	0	0	0	0
35	2	2	4	2	2	4	2	2	4	12
36	2	2	4	0	0	0	2	2	4	8
37	1	0	1	2	2	4	0	0	0	5
38	0	0	0	0	0	0	0	0	0	0
39	2	2	4	2	2	4	2	2	4	12
40	0	0	0	0	0	0	0	0	0	0
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	2	2	4	2	0	2	2	2	4	10
46	2	2	4	2	2	4	2	2	4	12
47	2	2	4	2	2	4	2	2	4	12
48	2	2	4	2	2	4	2	2	4	12
49	2	2	4	2	2	4	2	2	4	12
50	2	2	4	2	2	4	0	0	0	8
51	2	2	4	2	2	4	2	2	4	12
52	2	2	4	2	2	4	2	2	4	12
53	2	2	4	2	2	4	2	2	4	12
54	2	2	4	2	2	4	2	2	4	12
55	2	2	4	2	2	4	2	2	4	12
56	2	2	4	2	2	4	2	2	4	12
57	2	2	4	2	2	4	2	2	4	12
58	2	2	4	2	2	4	2	2	4	12
59	2	2	4	2	2	4	2	2	4	12
60	2	2	4	2	2	4	1	2	3	11
61	2	2	4	2	2	4	2	1	3	11
62	2	2	4	2	2	4	2	2	4	12
63	2	2	4	0	0	0	2	2	4	8

Lab n°	Patient D 3-MCC deficiency			Patient E normal			Patient F MCAD deficiency			
	A	I	Total	A	I	Total	A	I	Total	Total
64	2	2	4	2	2	4	2	2	4	12
65	2	2	4	2	2	4	2	2	4	12
66	2	2	4	1	0	1	0	0	0	5
67	2	2	4	1	0	1	2	2	4	9
68	0	0	0	0	0	0	0	0	0	0
69	2	2	4	2	2	4	2	2	4	12
70	2	2	4	0	0	0	2	2	4	8
71	2	2	4	2	2	4	2	2	4	12
72	2	0	2	2	2	4	2	2	4	10
73	2	2	4	2	2	4	0	0	0	8
74	2	2	4	1	0	1	2	2	4	9
75	2	2	4	2	2	4	2	2	4	12

9.3. Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	--	4	4	4	4	20	100	
2	4	--	4	4	4	4	20	100	
3	1	--	4	4	2	4	15	75	
4	4	--	4	4	4	4	20	100	
5	0	--	0	0	0	0	0	0	
6	2	--	4	4	4	4	18	90	
7	4	--	4	4	4	4	20	100	
8	2	--	4	4	4	4	18	90	
9	4	--	4	4	4	4	20	100	
10	2	--	4	4	4	4	18	90	
11	4	--	4	4	4	4	20	100	
12	4	--	4	4	4	4	20	100	
13	4	--	4	4	4	4	20	100	
14	1	--	4	4	4	4	17	85	
15	3	--	4	4	4	4	19	95	
16	1	--	4	4	4	4	17	85	
17	4	--	4	4	4	4	20	100	

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
18	2	--	4	4	4	4	18	90	
19	4	--	4	4	4	4	20	100	
20	4	--	4	4	4	4	20	100	
21	2	--	4	4	4	4	18	90	
22	3	--	4	4	4	4	19	95	
23	4	--	4	4	4	4	20	100	
24	0	--	4	4	4	4	16	80	
25	2	--	4	4	4	4	18	90	
26	1	--	2	4	4	4	15	75	
27	0	--	4	4	4	4	16	80	CE
28	4	--	4	4	4	4	20	100	
29	4	--	4	4	4	4	20	100	
30	4	--	4	4	4	4	20	100	
31	2	--	4	4	4	4	18	90	
32	1	--	4	4	4	4	17	85	
33	4	--	4	4	4	4	20	100	
34	2	--	4	0	0	0	6	30	CE
35	4	--	4	4	4	4	20	100	
36	4	--	4	4	0	4	16	80	
37	4	--	4	1	4	0	13	65	CE
38	0	--	0	0	0	0	0	0	
39	2	--	2	4	4	4	16	80	
40	2	--	4	0	0	0	6	30	
41	2	--	4	4	4	4	18	90	
42	2	--	4	4	4	4	18	90	
43	4	--	4	4	4	4	20	100	
44	4	--	0	4	4	4	16	80	CE
45	2	--	4	4	2	4	16	80	
46	2	--	4	4	4	4	18	90	
47	2	--	4	4	4	4	18	90	
48	3	--	4	4	4	4	19	95	
49	2	--	4	4	4	4	18	90	
50	2	--	0	4	4	0	10	50	CE
51	4	--	4	4	4	4	20	100	

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
52	3	--	4	4	4	4	19	95	
53	4	--	4	4	4	4	20	100	
54	3	--	4	4	4	4	19	95	
55	4	--	4	4	4	4	20	100	
56	4	--	4	4	4	4	20	100	
57	4	--	4	4	4	4	20	100	
58	4	--	4	4	4	4	20	100	
59	0	--	4	4	4	4	16	80	CE
60	4	--	4	4	4	3	19	95	
61	2	--	4	4	4	3	17	85	
62	4	--	4	4	4	4	20	100	
63	2	--	4	4	0	4	14	70	
64	4	--	4	4	4	4	20	100	
65	4	--	4	4	4	4	20	100	
66	1	--	4	4	1	0	10	50	CE
67	2	--	4	4	1	4	15	75	
68	--	--	--	0	0	0	0	0	
69	3	--	4	4	4	4	19	95	
70	2	--	4	4	0	4	14	70	
71	2	--	4	4	4	4	18	90	
72	0	--	4	2	4	4	14	70	
73	2	--	4	4	4	0	14	70	CE
74	2	--	4	4	1	4	15	75	
75	2	--	4	4	4	4	18	90	

9.4. Performance

	Number of labs	% total labs
Satisfactory performers (≥ 60 % of adequate responses)	63	84
Unsatisfactory performers (< 60 % adequate responses and/or critical error)	12	16
Partial and non-submitters	1	1

9.5. Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
QLOU-DH-2021-A	SCEH or ECHS 1 deficiency	62	72	67
QLOU-DH-2021-B	AADC deficiency	--	--	--
QLOU-DH-2021-C	Alkaptonuria	93	93	93
QLOU-DH-2021-D	3-MCC deficiency	93	91	92
QLOU-DH-2021-E	normal	87	83	85
QLOU-DH-2021-F	MCAD deficiency	87	87	87

10. Preview of the scheme in 2022

There will be no changes in the structure and design of the QLOU scheme in 2022.
However, from 2022 onwards, Dr Joachim Janda from the metabolic centre Heidelberg will replace Dr Claus-Dieter Langhans as the new scientific advisor for QLOU Heidelberg.

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

Date of report, 2022-05-24
Name and signature of Scientific Advisor

Dr C. D. Langhans
Scientific Advisor
Laboratory of Metabolic Diseases

Dr J. Janda
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Prof. Dr. G. F. Hoffmann
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APPENDIX 1. **Change log (changes since the last version)**

Version Number	Published	Amendments
1	24 May 2022	2021 annual report published

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