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Qualitative Organic Acids

Centre: Germany

Final Report 2024

prepared by
Dr. J. Janda

Note: This annual report is intended for participants of the ERNDIM Qualitative Organic Acids in urine 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 patients with confirmed diagnoses to enable laboratories to gain or maintain experience to identify organic acid disorders. The scheme is organised by Dr Joachim Janda (Metabolic Center Heidelberg) in conjunction with Centre Suisse de Contrôle de Qualité (CSCQ, the Swiss organisation for quality assurance in medical laboratories) both appointed by and according to procedures laid down the ERNDIM Board.
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.

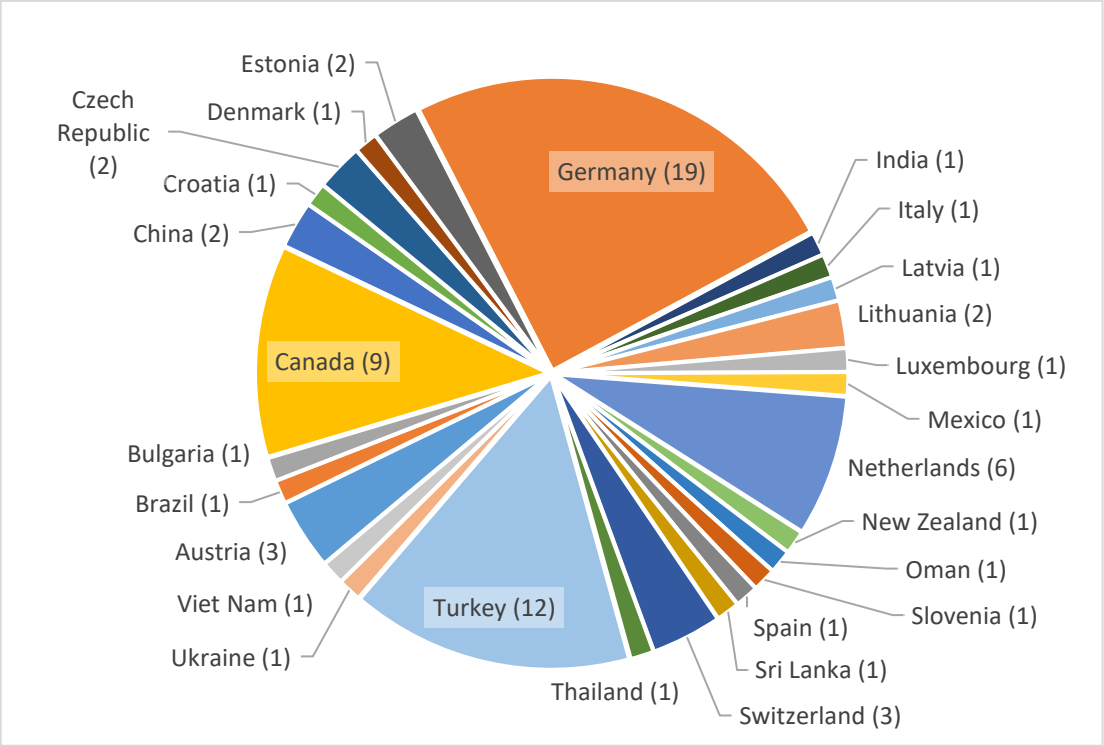
2. Geographical distribution of participants

In 2024, seventy-four laboratories from many different countries participated in the QLOU Heidelberg scheme. There was one educational participant in 2024 (none in 2023). Educational participants take part in all aspects of the scheme and receive interim reports with scores. However, performance is not indicated on the ERNDIM certificate for them.
Participants and new applicants are 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.

[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
Austria	3
Brazil	1
Bulgaria	1
Canada	9
China	2
Croatia	1
Czech Republic	2
Denmark	1
Estonia	2
Germany	19
India	1
Italy	1
Latvia	1
Lithuania	2

Country	Number of participants
Luxembourg	1
Mexico	1
Netherlands	6
New Zealand	1
Oman	1
Slovenia	1
Spain	1
Sri Lanka	1
Switzerland	3
Thailand	1
Turkey	12
Ukraine	1
Viet Nam	1



3. Design and logistics of the scheme including sample information

As usual, the samples used in 2024 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.
In 2024, CSCQ dispatched the QLOU EQA samples to the scheme participants and provides a website for online submission of results and access to scheme reports. Existing QLOU, ACDB, DPT and Urine MPS scheme participants can log on to the CSCQ results submission website at:
https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php

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 2024 ERNDIM QLOU Heidelberg scheme.

	1st Submission Round	2nd Submission Round
Sample IDs	QLOU-DH-2024-**A** QLOU-DH-2024-**B** QLOU-DH-2024-**C**	QLOU-DH-2024-**D** QLOU-DH-2024-**E** QLOU-DH-2024-**F**
Shipment of samples	07 February 2024	
Start of analysis (clinical data available)	07 May 2024	19 August 2024
Reminder for result submission	21 May 2024	02 September 2024
Results submission deadline	28 May 2024	09 September 2024
Interim reports available on CSCQ website	14 August, 2024	21 October, 2024

Samples included in the 2024 ERNDIM QLOU Heidelberg scheme.

Survey	Sample	Diagnosis
24-05-OUH	QLOU-DH-2024-A	Aromatic L-amino acid decarboxylase deficiency
	QLOU-DH-2024-B	Isovaleryl-CoA dehydrogenase deficiency
	QLOU-DH-2024-C	Ornithine transcarbamylase deficiency
24-08-OUH	QLOU-DH-2024-D	Alkaptonuria (Homogentisate1,2-dioxygenase deficiency)
	QLOU-DH-2024-E	Normal control sample
	QLOU-DH-2024-F	Methylmalonic aciduria due to deficient cobalamin adenosyltranferase

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:	AADCD	Metabolic Center Heidelberg
Patient B:	IVA	
Patient C:	OTC	
Patient D:	AKU	
Patient E:	Normal	
Patient F:	MMA cblB type	

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 2024 ERNDIM QLOU Heidelberg scheme

	Survey 1	Survey 2
Receipt of results	77	74
No answer	0	3

6. Web site reporting

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

- **Selection of tests**
  Do not select a test if you will not perform it, otherwise the evaluation program includes 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 do not 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.
- **Diagnosis**
  Do not enter the diagnosis in the “comments” window, otherwise it will not be included in the evaluation program.
- **Recommendations (= advice for further investigation).**
  - Scored together with the interpretative score.
  - Advice for treatment will not be 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 samples were scored using the criteria given below. These criteria have been set by the Scientific Advisor, approved by the ERNDIM Scientific Advisory Board (SAB). A second evaluation of this year's results was carried out by Mrs. Camilla Scott, scientific advisor of the QLOU Sheffield scheme. The final decision on the scoring in the scheme was made by the SAB at its autumn meeting (28 November 2024).

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’ (CE) 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 are sufficient according to the requirement set by the SAB. The classification of samples to be judged for critical error was undertaken at the SAB meeting held on 18 November 2024.

Score for satisfactory performance
At least 17 points out of a maximum of 24 (71%) are required for satisfactory performance.

The ERNDIM Annual Certificate covers all ERNDIM schemes in which a laboratory has participated during the scheme year. For the ‘Qualitative Organic Acids in Urine’ scheme, “participation” is defined as requiring full returns for both surveys during the year. Failure to meet this requirement will result in the certificate of participation showing ‘non-submitter’ or ‘partial submitter’ rather than ‘satisfactory’ or ‘unsatisfactory’.

8. Results of samples and evaluation of reporting

8.1. Patient A

Aromatic L-amino acid decarboxylase deficiency

The sample originates from a boy with genetically confirmed AADC deficiency who received intracerebral gene therapy. The sample was collected in PICU while he was treated for a hyperkinetic status. At the time of urine sampling, he received intravenous parenteral nutrition including fat and amino acids. He received various medications including benzodiazepines, steroids, GABAergic substances, and other sedative drugs.

GC-MS analysis of the sample reveals an elevated concentration of vanillactic acid (VLA) while vanillylmandelic acid (VMA) is in the lower normal concentration range. The diagnostic ratio VLA/VMA is grossly elevated (compare: Brennenstuhl et al., Mol. Genet. Metab. 131 (2020) 163–170, doi 10.1016/j.ymgme.2020.07.001)
High concentrations of N-acetyltyrosine can be found due to i.v. amino acid supplementation. Secondary metabolites such as 4-hydroxyphenyllactic and 4-hydroxyphenylacetic acids are also detectable with prominent peaks. Metabolites of pharmaceuticals are present because of medical treatment.

Patient details provided to participants

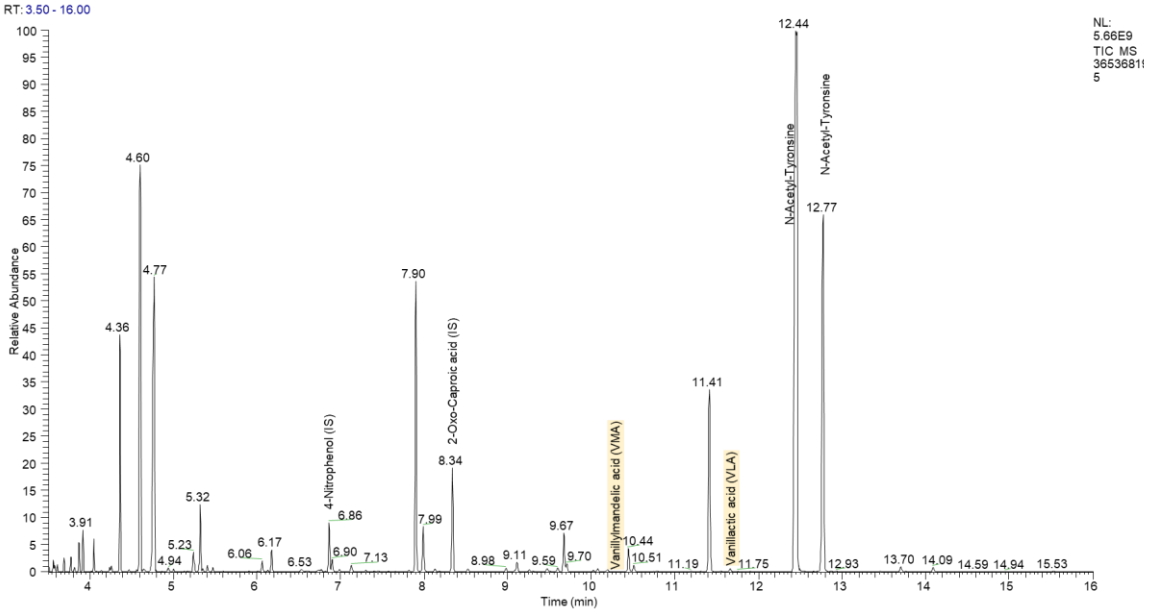
10-year-old boy with severe psychomotor retardation and truncal hypotonia and hypertonia of extremities. On treatment while the sample was taken.

Analytical performance

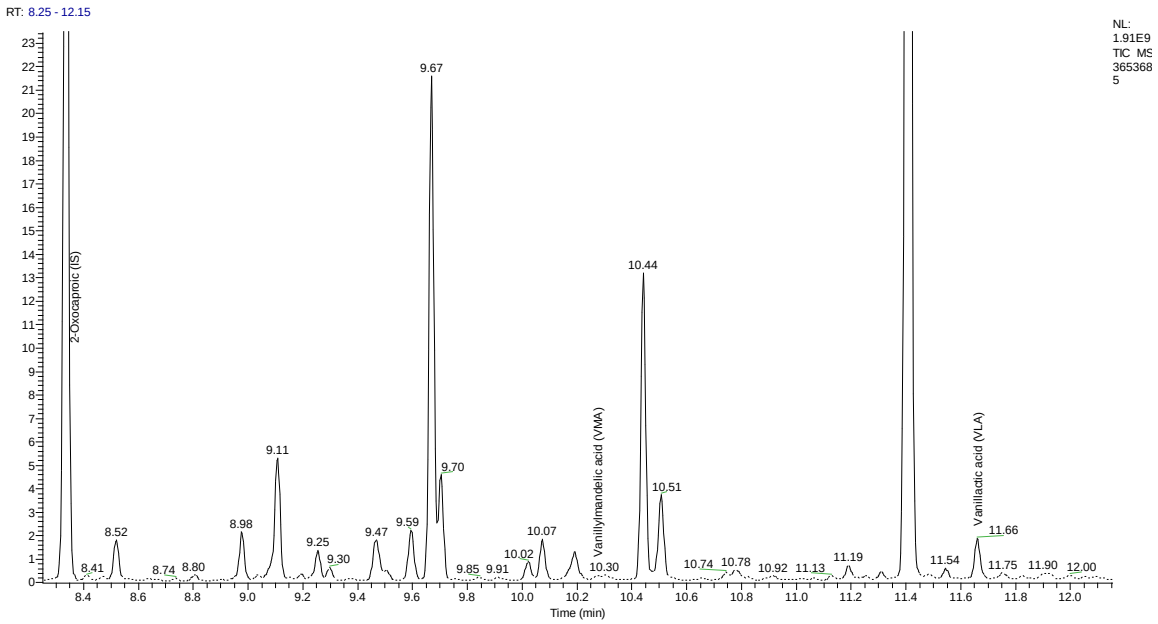
VLA was reported in at least elevated concentrations by 45 participants (58%; elevated n=44, grossly elevated n=1). Two participants rated this metabolite concentration as normal and one characterized the VLA level as low. Only four participants reported results on VMA concentrations and rated them as low (n=3, also ‘not detectable’) or normal (n=1).

N-acetyltyrosine, as a predominant peak in the chromatogram was reported by most participants as grossly elevated (n=62, 81%) or elevated (n=5, 7%). Accordingly, concentrations of the metabolites 4-hydroxyphenyllactic (n=28, 37%) and/or 4-hydroxyphenylacetic acid (n=23, 30%) were also frequently reported as elevated.

Evaluation criteria: Two points were awarded for reporting elevated or grossly elevated levels of VLA.



Example chromatogram for sample A (4-Nitrophenol is internal standard).



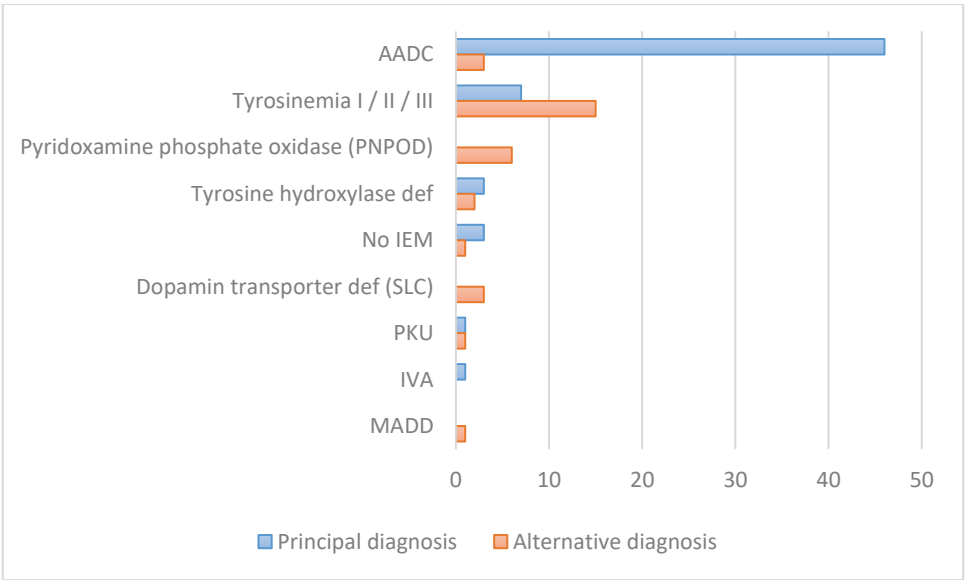
Sample A chromatogram section focussing on the key metabolites. VLA is a small but detectable peak.

Diagnosis / Interpretative proficiency

AADC was reported by 49 (64%) participants. Tyrosinemia (all types combined, n=22 or 29%) was the second most frequently reported diagnosis. Five laboratories considered tyrosine hydroxylase and three participants opted for a normal profile not representing an inborn error of metabolism.

Evaluation criteria: Two points were given for reporting AACD as diagnosis. Mentioning neurotransmitter disorders were given one point.

In 2021, for the first in a long time, an AADC sample was distributed in QLOU-DH, which was treated as an educational sample. This time, the AADC sample was scored but not used for the assessment of critical errors. However, it is noticeable that many laboratories have probably not yet included VLA in their scope of investigation or are not actively looking for it. This is expressly encouraged.



Most frequently reported diagnoses for sample A.

Recommendations

Further laboratory tests recommended by the participants were determination of pterins in CSF (n=37), molecular genetic analyses (n=48), measuring enzymatic activity (n=26), or analysis of plasma amino acids (n=24). Seventeen labs specifically referred to 3-OMD analysis in CSF or dried blood spots.

Overall impression
This sample was difficult for many participants. The analytical and interpretative proficiencies were 60% and 67%, respectively. Compared to the last circulation of an AADC sample in 2021, this is an improvement, however.

8.2. Patient B

Isovaleryl-CoA dehydrogenase deficiency

The sample originates from a patient with confirmed IVA. IVA was diagnosed after metabolic decompensation at the second day of life by organic acid analysis and later confirmed by enzyme analysis in fibroblasts and molecular analysis.
The organic acids profile of this sample is dominated by characteristic isovalerylglycine peaks.

Patient details provided to participants

Man of 35 years with muscular hypotonia in infancy. Further normal development.

Analytical performance

All participants but one reported on isovalerylglycine and characterized its concentration as grossly elevated (n=73) or elevated (n=3). The 3-hydoxyisovaleric acid concentration was reported as elevated by two (2.6%), normal by 20 (26%) participants, and low by one (1.3%) participant. One lab reported a grossly elevated 3-methylglutaconic acid concentration.

Evaluation criteria: Two points are awarded, if isovalerylglycine is reported as elevated or grossly elevated.

Diagnosis / Interpretative proficiency

Isovaleric aciduria was reported by almost all labs as the primary diagnosis. Alternative diagnoses mentioned occasionally were multiple acyl-CoA dehydrogenase (n=4) or short-chain acyl-CoA dehydrogenase deficiencies (n=3). One lab opted for 3-methylglutaconic aciduria as principal diagnosis.

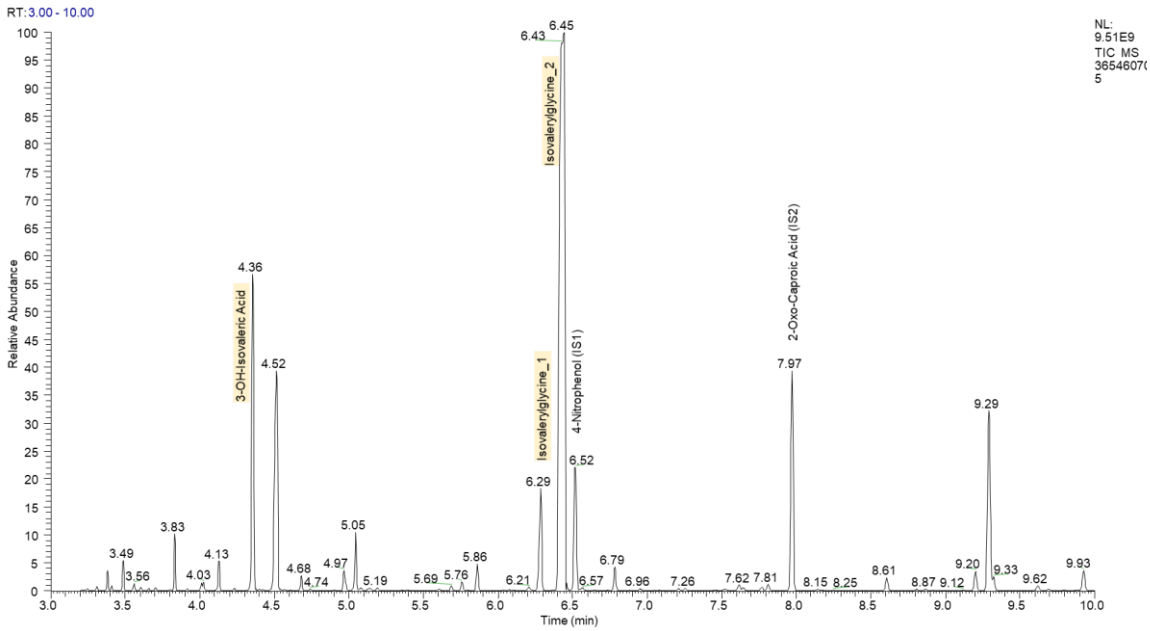
Evaluation criteria: Two points are assigned if IVA is given as principal diagnosis or if given as an alternative including a recommendation allowing for a correct differentiation.

Recommendations

In their recommendations, the participants focussed on tests to support and confirm their proposed diagnoses, e. g., analysis of acylcarnitines in plasma or urine (n=56), molecular genetic testing (n=60), and/or measurement of enzymatic activity (n=22).

Overall impression

This sample was straightforward for the participants to handle and resulted in excellent performance of 99% for both analysis and diagnosis.



Example chromatogram for sample B highlighting important metabolites.

8.3. Patient C

Ornithine transcarbamylase deficiency

The sample comes from a girl with multiple malformations. She was born with a lumbar spina bifida and Arnold-Chiari-Malformation and had several surgical interventions without clinical signs of hyperammonemic decompensations. Owing to neurological deterioration, metabolic examinations were performed at the age of 11 years which revealed hyperammonemia (248 µmol/l), elevated glutamine and orotic acid. OTC deficiency was confirmed by molecular analysis. The sample was taken while on scavenger therapy with sodium benzoate, sodium phenylbutyrate and L-citrulline.

The key metabolite, orotic acid, is clearly detectable in elevated concentration (69 mmol/mol creatinine) by GC-MS analysis, as well as uracil as a further helpful metabolite. However, signals of active substances and secondary metabolites resulting from therapeutic treatment with sodium benzoate and phenylbutyrate are more prominent in the chromatogram. Furthermore, increased lactate and pyruvate levels due to impaired mitochondrial energy metabolism are detectable.

Patient details provided to participants

10-year-old girl with spina bifida, Arnold-Chiari malformation and severe psychomotor retardation.

Analytical performance

All 77 participating labs sent results for this sample. Of these, only 66% reported orotic acid to be in elevated (N=29, 37%) or grossly elevated (N=22, 29%) concentration. Benzoic acid or its metabolite hippuric acid were reported more frequently and in abnormally high concentrations by 71% and 58%, respectively. Other metabolites frequently mentioned as in increased levels were phenylacetic (58%), lactic (31%), and 4-OH-phenylacetic acids (30%).

Evaluation criteria: Reporting orotic acid at least as elevated is awarded 2 pts. The indication of benzoic / hippuric acid as a result of benzoate treatment yields 1 pt.

Diagnosis / Interpretative proficiency

OTC was reported as primary diagnosis by 26 participants (34%) and by six participants (8%) as alternative. 58% of the participating laboratories mentioned urea cycle disorders (UCDs) in general, with orotidine-5-monophosphate decarboxylase deficiency, uridine monophosphate synthase deficiency and argininosuccinate synthase deficiency being mentioned frequently. Ten participants stated that the profile does not correspond to an IEM and ten participants considered PKU as primary diagnosis or alternative.

Evaluation criteria: Two points are awarded for reporting OTC as diagnosis. One point is given for other urea cycle disorders. Recommendations for follow-up tests appropriate to clarify the diagnosis, e. g. amino acids in plasma or molecular genetics, are considered when UCDs are indicated.

Recommendations

Frequent recommendations for supporting or confirmatory analyses were measurement of plasma amino acids (n=56), molecular genetic testing (n=47), determination of ammonia in plasma (n=22), or quantification of orotic acid in plasma. Eight recommendations each were given for repetition of urinary organic acids, measurement of enzymatic activity, acylcarnitines in plasma or urine, and determination of purines and pyrimidines.

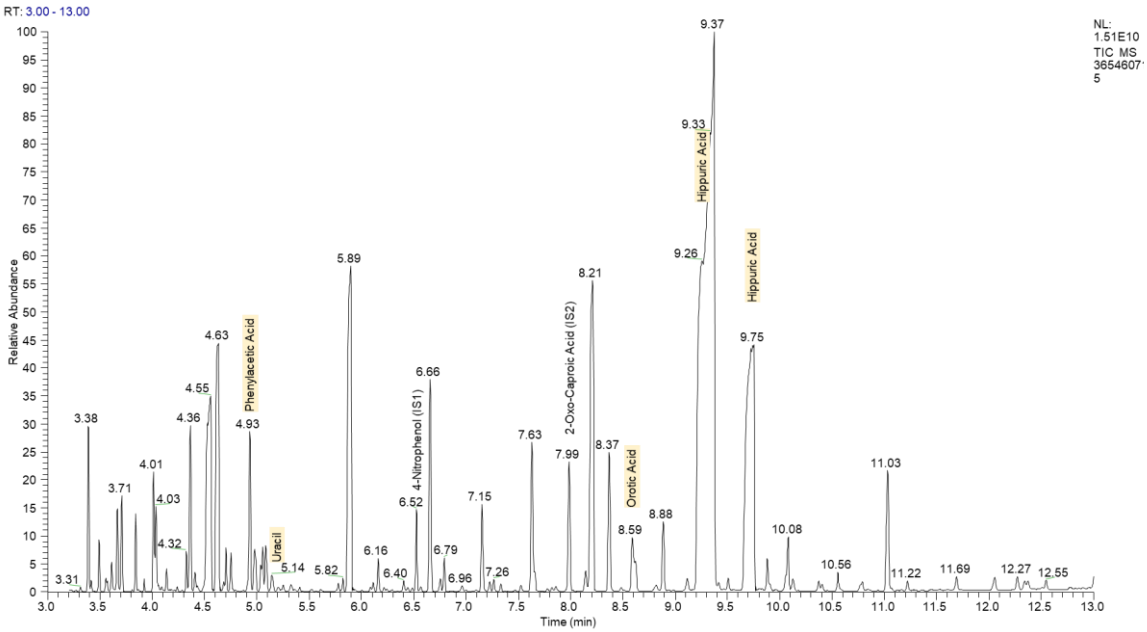
Overall impression

This was a challenging sample due to the patient's complex history, resulting in an analytical proficiency of 78% and an interpretative proficiency of 69%.
Compared to the last circulation of an OTC sample, it is remarkable that this time fewer laboratories were able to detect the elevated key metabolite, orotic acid (last result: 80% of participants), although it was present in a similar concentration.

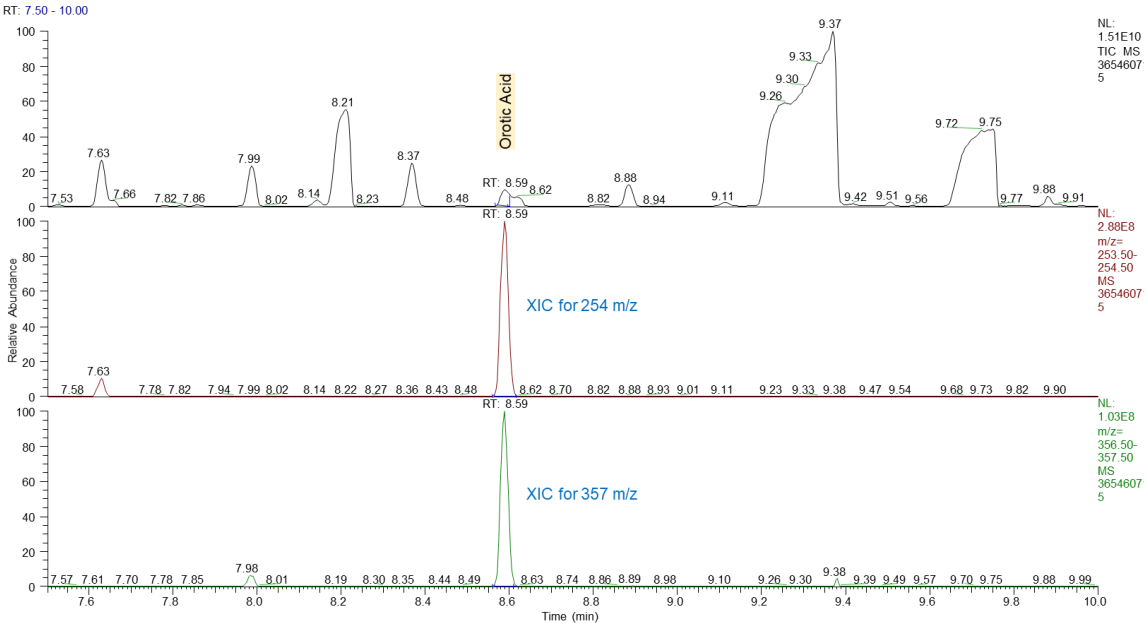
Overall, it is striking that more than 30% of this scheme's participants did not consider OTC or a UCD, which is likely related to the poor detection of orotic acid in this sample. However, the concentration of this key metabolite is high enough here to show a clearly detectable peak, if the corresponding masses are extracted from the total ion chromatogram (TIC), even if it is not prominently displayed in the TIC at first glance (compare figures below).

The results should therefore be understood as an indication or reminder that **important metabolites are not always the most prominent ones**, but that in certain cases it is necessary to actively search for key metabolites on the basis of known, method-specific (and lab-internal) characteristics (i. e., detector response, retention time, …).

Compared to earlier OTC samples the clinical description given of this sample was less revealing for the distributed diagnosis. For this reason and in light of the heterogeneous interpretations, the SAB decided to exclude this sample from critical error evaluation.



Example chromatogram for sample C highlighting important metabolites.



Total ion chromatogram section (top) for orotic acid of the scanning GC-MS analysis above and two extracted ion chromatograms (XIC) of the mass-to-charge ratios specific for the tri-TMS derivatised orotic acid.

8.4. Patient D

Alkaptonuria (Homogentisate1,2-dioxygenase deficiency)

The sample originates from a 60-year-old man with biochemically confirmed alkaptonuria. In infancy the parents noticed dark urine in the diapers, in young adulthood dark sclerae and pinnae were seen. The patient has arthropathy of shoulders, knees and lumbar spine. The distributed sample was taken before treatment with Nitisinone was started.
Organic acid analysis reveals a grossly elevated concentration of homogentisic acid (720 mmol/mol creatinine), the distinctive metabolite for alkaptonuria.

Patient details provided to participants

Man aged 45 years with severe back pain.

Analytical performance

Seventy-seven participants were registered in this year's QLOU-DH scheme. In the second survey, 74 of them submitted results. Homogentisic acid was characterized as elevated by two labs, while 67 labs classified its concentration as grossly elevated. Other compounds that were sporadically reported as elevated or even grossly elevated were 4-OH-phenylacetic (10 labs) or -lactic acids (9 labs), glycolic and lactic acids (6 labs both).

Evaluation criteria: Two points were awarded for reporting an elevated or grossly elevated homogentisic acid concentration.

Diagnosis / Interpretative proficiency

The vast majority of participants clearly identified alkaptonuria as the diagnosis (n=70). Two laboratories that reported elevated malonic acid levels concluded their results to indicate malonic aciduria, while two other laboratories reported a normal organic acid profile for the sample.

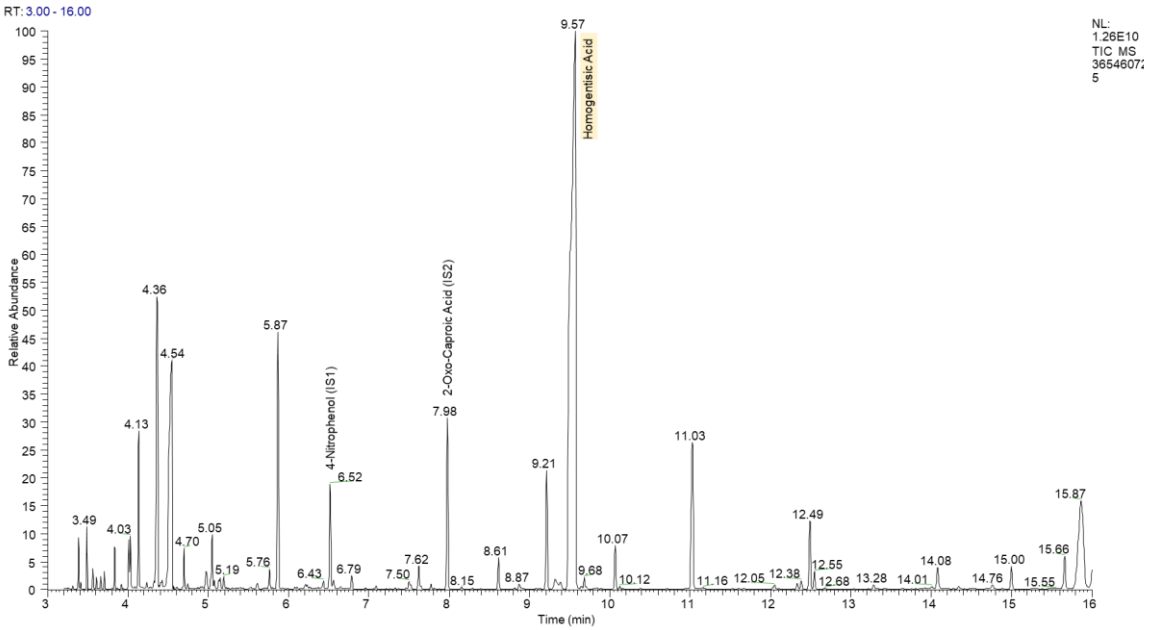
Evaluation criteria: Two points were given for reporting alkaptonuria as diagnosis.

Recommendations

In their recommendations, the participants focused on confirmatory analyses, i. e., molecular genetic testing (n=61), plasma amino acids (n=7), or measuring enzymatic activity in fibroblasts (n=6).

Overall impression

This sample was not challenging for most participants. The analytical and interpretative proficiencies were 93% and 95%, respectively.



Example chromatogram for sample D highlighting the key metabolite, homogentisic acid.

8.5. Patient E

Normal control sample

The sample originates of an individual not known to have a metabolic disorder. The analysis of the organic acids by GC-MS showed no substantial abnormalities.

Patient details provided to participants

21-year-old man with febrile seizures in childhood

Analytical performance

Seventy-seven participants were registered in this year's QLOU-DH scheme. In the second survey, 74 of them provided results, and 70 of them considered that the sample did not represent a metabolic disorder.

Evaluation criteria: Full points are awarded for reporting a normal profile.

Diagnosis / Interpretative proficiency

While 70 laboratories characterized the sample as normal, two participants who detected elevated concentrations of vanillactic acid concluded that the result indicated AADC deficiency. One laboratory opted for an autism spectrum disorder and another reported 'MADD, orotic aciduria or MMA' as interpretation.

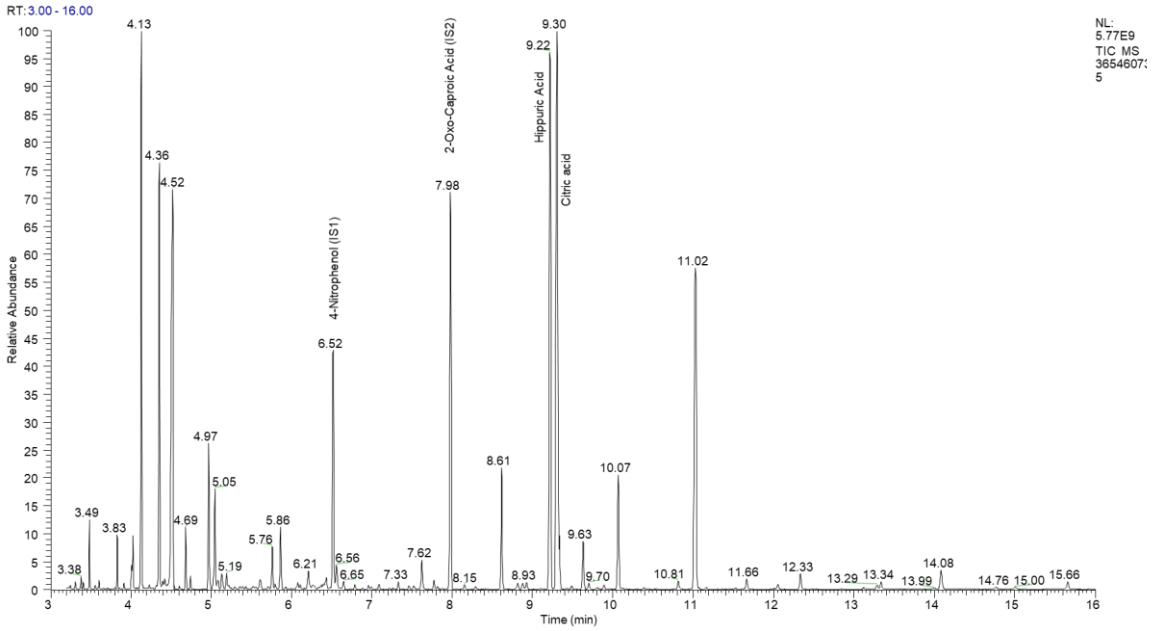
Evaluation criteria: Full points are awarded for reporting a normal profile.

Recommendations

Most participants expressed their recommendations for further testing as optional in case a metabolic disorder is still suspected. The most common recommendation was an extended metabolic workup - preferably with samples obtained during a crisis.

Overall impression

The participants performed well in identifying the normal control resulting in an overall proficiency of 93% for both analysis and diagnosis.



Example chromatogram for sample E. A largely normal profile.

8.6. Patient F

Methylmalonic aciduria due to deficient cobalamin adenosyltranferase

The sample comes from a patient with a diagnosis of methylmalonic aciduria after neonatal metabolic decompensation. Later on, a homozygous variant in *MMAB* was identified, confirming MMA cblB type.

The key metabolite, methylmalonic acid, is prominent in this sample in high concentration (3650 mmol/mol creatinine). Besides this, GC-MS analysis also reveals elevated concentrations of other metabolites typically seen in MMA cblB, i. e. methylcitric acid, 3-hydroxypropionic acid, and propionylglycine.

Patient details provided to participants

23-year-old male with dystonia, scoliosis and mental retardation.

Analytical performance

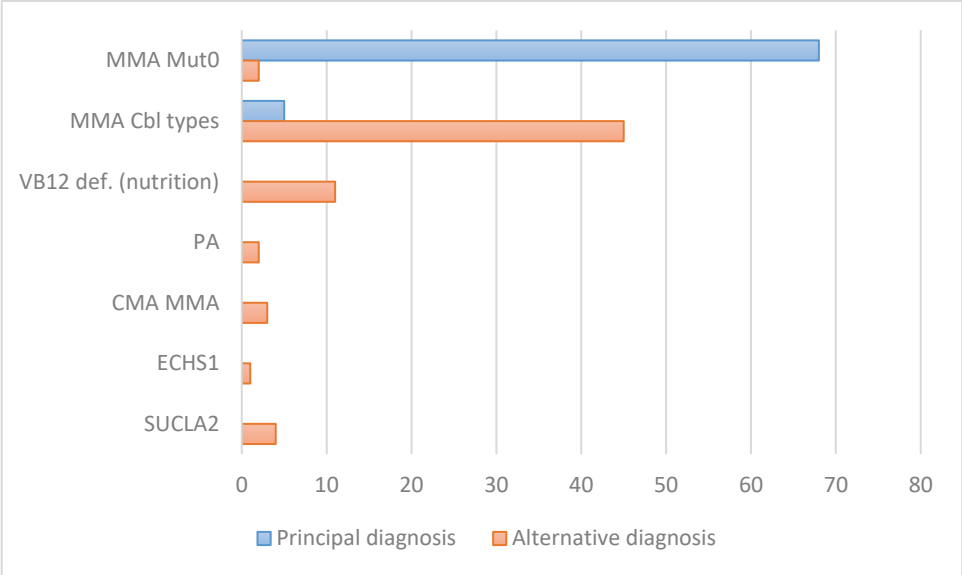
Seventy-seven participants were registered in this year's QLOU-DH scheme. In the second survey, 74 of them submitted results. Of these, 73 participants reported at least elevated concentrations of methylmalonic acid. The most frequently reported other metabolites were methylcitric acid (n=60), 3-hydroxypropionic acid (n=39), and propionylglycine (n=17).

Evaluation criteria: One point is awarded for reporting elevated or grossly elevated methylmalonic acid. One more point is awarded for reporting at least one more relevant metabolite (i. e., methylcitric acid, 3-hydroxypropionic acid, propionylglycine) as at least elevated.

Diagnosis / Interpretative proficiency

Methylmalonic acid was reported by 73 of the 74 participants, with 47 participants differentiating between different forms of MMA in their interpretation. Eleven laboratories also considered a nutritional deficiency of vitamin B_{12}. Depending on their analytical findings, several laboratories also mentioned further diagnoses as alternative, such as SUCLA2, CMAMMA, PA, or ECHS1.

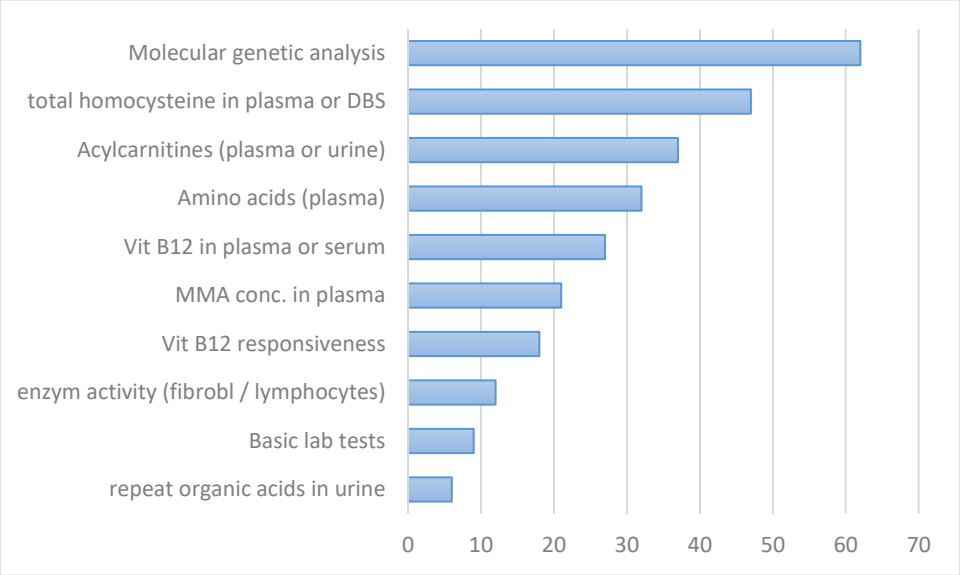
Evaluation criteria: One point is given for MMA as principal and/or alternative diagnosis. One or more recommendations allowing for differentiation, i. e. specifying the CblB type, yield one more point.



Most frequently reported diagnoses for sample F.

Recommendations

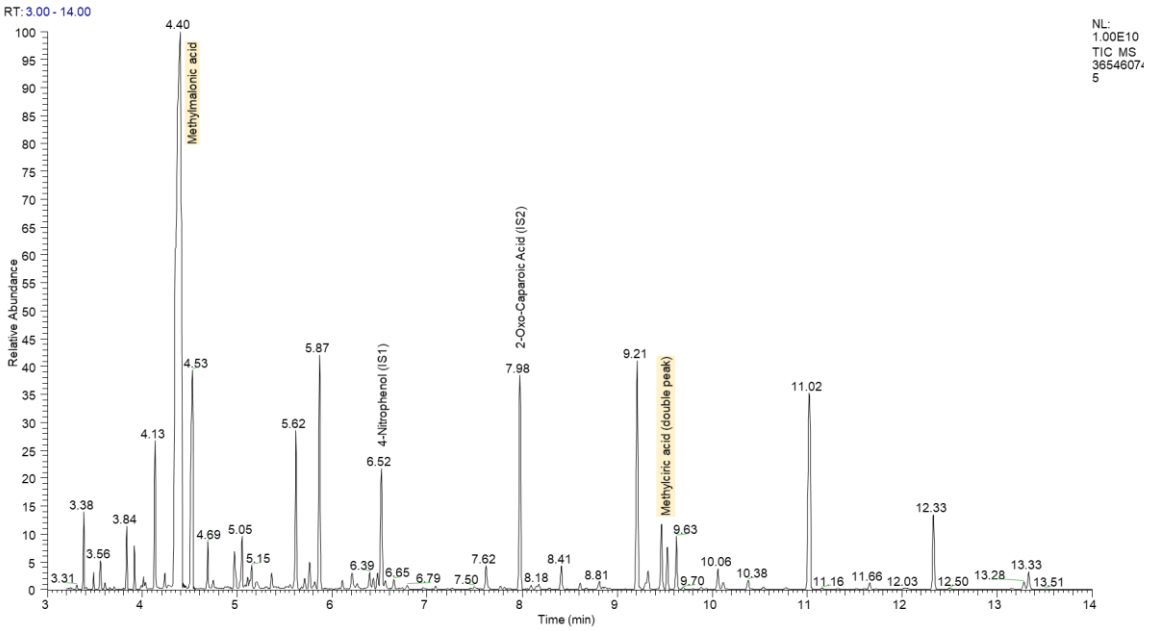
Most participants reported recommendations for further analyses to differentiate and confirm their proposed diagnoses. Most frequently reported tests were determination of homocysteine (n=47), amino acids (n=32), cobalamin (n=27), and/or methylmalonic acid (n=21) in serum or plasma besides basic haematologic investigations. Eighteen labs suggested to test the vitamin B_{12} responsiveness. Molecular genetic confirmation was advised by 62 participants where the best option was to suggest a panel covering multiple types of MMA.



Numbers of given recommendations for further testing.

Overall impression

For most participants, it was not a challenge to conclude MMA from their analysis results. However, not all participants considered further differentiation in their recommendations. The analytical and interpretive proficiencies were 93% and 96%, respectively.



Example chromatogram for sample F highlighting important metabolites.

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.

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.

9.1. Round 1

Lab n°	Patient A AADCD			Patient B IVA			Patient C OTC			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	0	0	0	2	2	4	2	2	4	8
3	2	2	4	2	2	4	0	0	0	8
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	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	1	3	2	2	4	2	1	3	10
14	0	0	0	2	2	4	2	2	4	8
15	0	0	0	2	2	4	2	2	4	8
16	2	2	4	2	2	4	0	0	0	8
17	2	2	4	2	2	4	2	2	4	12
18	2	2	4	2	2	4	2	2	4	12
19	0	0	0	2	2	4	2	2	4	8
20	2	2	4	2	2	4	2	2	4	12
21	0	0	0	2	2	4	0	0	0	4
22	2	2	4	2	2	4	2	2	4	12
23	0	0	0	2	2	4	2	2	4	8
24	2	2	4	2	2	4	2	2	4	12
25	2	2	4	2	2	4	2	2	4	12

Lab n°	Patient A AADCD			Patient B IVA			Patient C OTC			
	A	I	Total	A	I	Total	A	I	Total	Total
26	2	2	4	2	2	4	1	0	1	9
27	0	0	0	2	2	4	2	2	4	8
28	2	1	3	2	2	4	2	2	4	11
29	2	2	4	2	2	4	1	0	1	9
30	2	2	4	2	2	4	2	2	4	12
31	2	2	4	2	2	4	0	0	0	8
32	0	0	0	2	2	4	2	2	4	8
33	2	2	4	2	2	4	0	0	0	8
34	2	2	4	2	2	4	2	2	4	12
35	0	0	0	2	2	4	2	2	4	8
36	2	2	4	2	2	4	2	2	4	12
37	2	2	4	2	2	4	2	2	4	12
38	0	0	0	2	2	4	2	2	4	8
39	0	2	2	2	2	4	1	0	1	7
40	0	0	0	2	2	4	2	2	4	8
41	2	2	4	2	2	4	1	0	1	9
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	0	2	2	1	0	1	7
45	0	0	0	2	2	4	1	0	1	5
46	2	2	4	2	2	4	1	0	1	9
47	0	1	1	2	2	4	1	0	1	6
48	0	0	0	2	2	4	2	2	4	8
49	2	2	4	2	2	4	2	2	4	12
50	0	0	0	2	2	4	2	2	4	8
51	2	2	4	2	2	4	2	0	2	10
52	2	2	4	2	2	4	0	0	0	8
53	0	1	1	2	2	4	1	0	1	6
54	2	2	4	2	2	4	2	2	4	12
55	2	2	4	2	2	4	0	0	0	8
56	2	2	4	2	2	4	2	2	4	12
57	0	0	0	2	2	4	2	2	4	8
58	2	2	4	2	2	4	1	0	1	9

Lab n°	Patient A AADCD			Patient B IVA			Patient C OTC			
	A	I	Total	A	I	Total	A	I	Total	Total
59	2	2	4	2	2	4	2	2	4	12
60	0	0	0	2	2	4	2	2	4	8
61	2	2	4	2	2	4	2	2	4	12
62	0	2	2	2	2	4	1	0	1	7
63	0	2	2	2	2	4	1	2	3	9
64	0	1	1	2	2	4	2	2	4	9
65	0	0	0	2	2	4	2	2	4	8
66	0	0	0	2	2	4	1	0	1	5
67	0	0	0	2	2	4	2	2	4	8
68	2	2	4	2	2	4	2	2	4	12
69	0	0	0	2	2	4	2	2	4	8
70	2	2	4	2	2	4	2	2	4	12
71	1	2	3	2	2	4	1	2	3	10
72	0	0	0	2	0	2	1	0	1	3
73	0	0	0	2	2	4	2	0	2	6
74	2	2	4	2	2	4	1	2	3	11
75	0	2	2	2	2	4	1	0	1	7
76	0	0	0	2	2	4	0	0	0	4
77	2	2	4	2	2	4	1	2	3	11

9.2. Round 2

Lab n°	Patient D AKU			Patient E Normal			Patient F MMA cblB 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	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	0	0	0	2	2	4	8
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

Lab n°	Patient D AKU			Patient E Normal			Patient F MMA cblB type			
	A	I	Total	A	I	Total	A	I	Total	Total
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	1	2	3	11
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
31	2	2	4	2	2	4	2	2	4	12
32	2	2	4	2	2	4	2	2	4	12
33	2	2	4	2	2	4	2	2	4	12
34	2	2	4	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	1	2	3	11
38	0	0	0	2	2	4	2	2	4	8
39	0	2	2	2	2	4	1	2	3	9
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

Lab n°	Patient D AKU			Patient E Normal			Patient F MMA cblB type			
	A	I	Total	A	I	Total	A	I	Total	Total
44	2	2	4	2	2	4	1	1	2	10
45	2	2	4	2	2	4	1	2	3	11
46	2	2	4	2	2	4	1	2	3	11
47	2	2	4	2	2	4	2	2	4	12
48	0	0	0	0	0	0	0	0	0	0
49	2	2	4	2	2	4	2	2	4	12
50	0	0	0	2	2	4	2	1	3	7
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	1	2	3	11
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	1	2	3	11
60	2	2	4	2	2	4	2	2	4	12
61	2	2	4	2	2	4	2	2	4	12
62	2	2	4	2	2	4	1	2	3	11
63	2	2	4	2	2	4	2	2	4	12
64	2	2	4	0	0	0	2	2	4	8
65	2	2	4	2	2	4	2	2	4	12
66	0	0	0	0	0	0	0	0	0	0
67	2	2	4	2	2	4	2	2	4	12
68	2	2	4	2	2	4	2	2	4	12
69	0	0	0	0	0	0	0	0	0	0
70	2	2	4	2	2	4	2	2	4	12
71	2	2	4	2	2	4	2	2	4	12
72	0	0	0	0	0	0	0	0	0	0
73	2	2	4	2	2	4	2	2	4	12
74	2	2	4	2	2	4	2	1	3	11
75	2	2	4	2	2	4	1	1	2	10
76	0	0	0	0	0	0	2	2	4	4

Lab n°	Patient D AKU			Patient E Normal			Patient F MMA cblB type			
	A	I	Total	A	I	Total	A	I	Total	Total
77	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 in %	Critical error
1	4	4	4	4	4	4	24	100	
2	0	4	4	4	4	4	20	83	
3	4	4	0	4	4	4	20	83	
4	4	4	4	4	4	4	24	100	
5	4	4	4	4	4	4	24	100	
6	4	4	4	4	0	4	20	83	
7	4	4	4	4	4	4	24	100	
8	4	4	4	4	4	4	24	100	
9	4	4	4	4	4	4	24	100	
10	4	4	4	4	4	4	24	100	
11	4	4	4	4	4	4	24	100	
12	4	4	4	4	4	4	24	100	
13	3	4	3	4	4	4	22	92	
14	0	4	4	4	4	4	20	83	
15	0	4	4	4	4	4	20	83	
16	4	4	0	4	4	4	20	83	
17	4	4	4	4	4	4	24	100	
18	4	4	4	4	4	4	24	100	
19	0	4	4	4	4	4	20	83	
20	4	4	4	4	4	4	24	100	
21	0	4	0	4	4	3	15	62	
22	4	4	4	4	4	4	24	100	
23	0	4	4	4	4	4	20	83	
24	4	4	4	4	4	4	24	100	
25	4	4	4	4	4	4	24	100	
26	4	4	1	4	4	4	21	88	
27	0	4	4	4	4	4	20	83	
28	3	4	4	4	4	4	23	96	

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score in %	Critical error
29	4	4	1	4	4	4	21	88	
30	4	4	4	4	4	4	24	100	
31	4	4	0	4	4	4	20	83	
32	0	4	4	4	4	4	20	83	
33	4	4	0	4	4	4	20	83	
34	4	4	4	4	4	4	24	100	
35	0	4	4	4	4	4	20	83	
36	4	4	4	4	4	4	24	100	
37	4	4	4	4	4	3	23	96	
38	0	4	4	0	4	4	16	67	CE
39	2	4	1	2	4	3	16	67	
40	0	4	4	4	4	4	20	83	
41	4	4	1	4	4	4	21	88	
42	4	4	4	4	4	4	24	100	
43	4	4	4	4	4	4	24	100	
44	4	2	1	4	4	2	17	71	
45	0	4	1	4	4	3	16	67	
46	4	4	1	4	4	3	20	83	
47	1	4	1	4	4	4	18	75	
48	0	4	4	0	0	0	8	33	CE
49	4	4	4	4	4	4	24	100	
50	0	4	4	0	4	3	15	62	CE
51	4	4	2	4	4	4	22	92	
52	4	4	0	4	4	4	20	83	
53	1	4	1	4	4	3	17	71	
54	4	4	4	4	4	4	24	100	
55	4	4	0	4	4	4	20	83	
56	4	4	4	4	4	4	24	100	
57	0	4	4	4	4	4	20	83	
58	4	4	1	4	4	4	21	88	
59	4	4	4	4	4	3	23	96	
60	0	4	4	4	4	4	20	83	
61	4	4	4	4	4	4	24	100	

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score in %	Critical error
62	2	4	1	4	4	3	18	75	
63	2	4	3	4	4	4	21	88	
64	1	4	4	4	0	4	17	71	
65	0	4	4	4	4	4	20	83	
66	0	4	1	0	0	0	5	21	
67	0	4	4	4	4	4	20	83	
68	4	4	4	4	4	4	24	100	
69	0	4	4	0	0	0	8	33	
70	4	4	4	4	4	4	24	100	
71	3	4	3	4	4	4	22	92	
72	0	2	1	0	0	0	3	12	
73	0	4	2	4	4	4	18	75	
74	4	4	3	4	4	3	22	92	
75	2	4	1	4	4	2	17	71	
76	0	4	0	0	0	4	8	33	CE
77	4	4	3	4	4	4	23	96	

9.4. Performance

	Number of labs	% total labs
Satisfactory performers (≥ 71 % of adequate responses)	67	87
Unsatisfactory performers (< 71 % adequate responses and/or critical error)	7	9
Partial and non-submitters	3	4

9.5. Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
QLOU-DH-2024-A	AADCD	60	67	64
QLOU-DH-2024-B	IVA	99	99	99
QLOU-DH-2024-C	OTC	78	68	73
QLOU-DH-2024-D	AKU	93	95	94
QLOU-DH-2024-E	Normal	95	95	95
QLOU-DH-2024-F	MMA cblB type	92	96	94

10. Tentative 2025 schedule

Sample distribution	5th February 2025
Start of analysis of Survey 2025/1 Website open	6th May 2025
Survey 2025/1 - Results submission	27th May 2025
Survey 2025/1 - Reports	June 2025
Start of analysis of Survey 2025/2 Website open	18th August 2025
Survey 2025/2 – Results submission	8th September 2025
Survey 2025/2 - Reports	September/October 2025
Annual Report 2025	January-March 2026

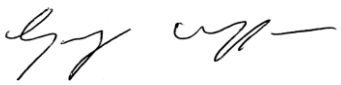
11. ERNDIM certificate of participation

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.

12. Questions, Comments and Suggestions

If you have any questions, comments or suggestions please address to the Scientific Advisor of the scheme, Dr. Joachim Janda (Joachim.Janda@med.uni-heidelberg.de) and/or to the ERNDIM Administration Office (admin@erndim.org).
To be able to continue this scheme, we need a steady supply of new patient samples. Several laboratories have donated urine samples to the 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.
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.

Date of report, 2025-03-03
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 QLOU 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	29.04.2025	2024 annual report published

END