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Qualitative Organic Acids in Urine

Centre: Heidelberg-Germany

Final Report 2023

prepared by
Dr. J. Janda

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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 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.

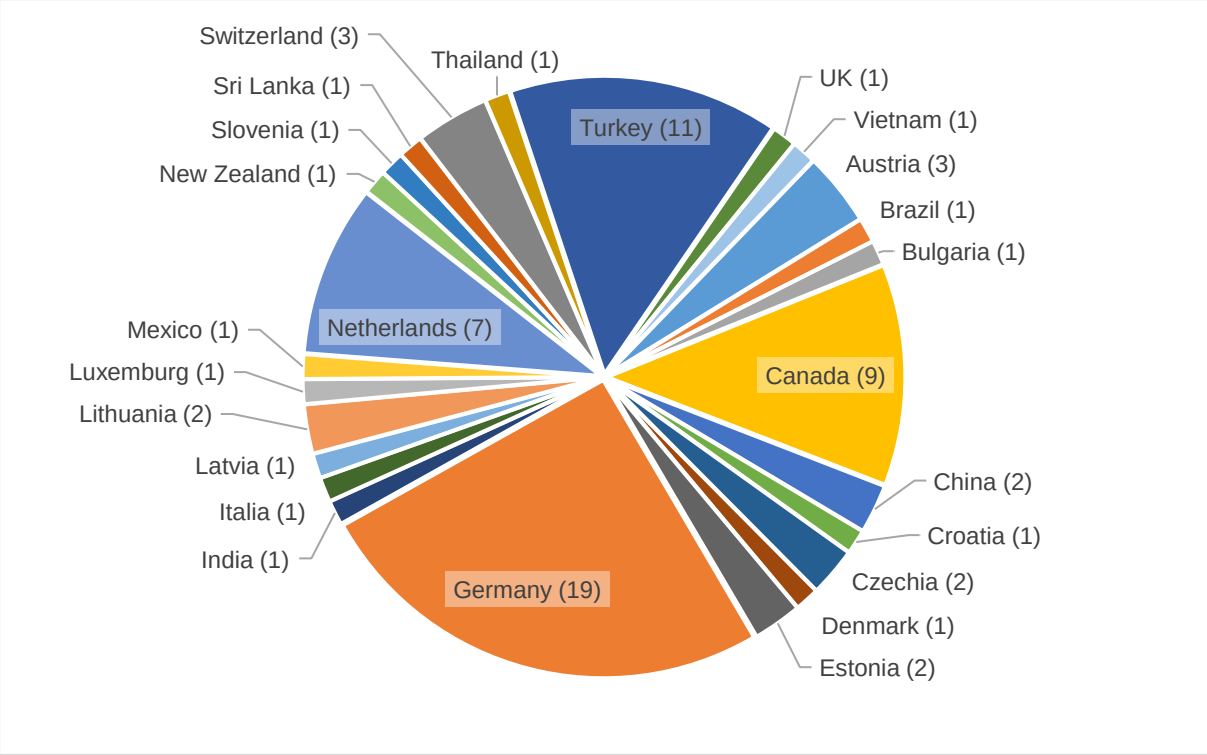
2. Geographical distribution of participants

In 2023, seventy-four laboratories from many different countries participated in the QLOU Heidelberg scheme. There were no educational participants in 2023 (none in 2022) - those take part in all aspects of the scheme and receive interim reports with scores. However, performance is not indicated on the ERNDIM certificate for educational participants.
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
Croatia	1
Czechia	2
Denmark	1
Estonia	2
Germany	19
India	1
Italia	1
Latvia	1
Lithuania	2

Country	Number of participants
Luxembourg	1
Netherlands	7
New Zealand	1
People's Republic of China	1
Slovenia	1
Sri Lanka	1
Switzerland	3
Thailand	1
Turkey	11
United Kingdom	1
Mexico	1
Viet Nam	1



3. Design and logistics of the scheme including sample information

As usual, the samples used in 2023 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 2023, 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 2023 ERNDIM QLOU Heidelberg scheme.

	1st Submission Round	2nd Submission Round
Sample IDs	QLOU-DH-2023-A QLOU-DH-2023-B QLOU-DH-2023-C	QLOU-DH-2023-D QLOU-DH-2023-E QLOU-DH-2023-F
Shipment of samples	February 08, 2023	
Start of analysis (clinical data available)	May 09, 2023	August 29, 2023
Reminder for result submission	May 23, 2023	September 12, 2023
Results submission deadline	May 30, 2023	September 19, 2023
Interim reports available on CSCQ website	August 30, 2023	October 20, 2023

Samples included in the 2023 ERNDIM QLOU Heidelberg scheme.

Survey	Sample	Diagnosis
23-05-OUH	QLOU-DH-2023-A	Propionic aciduria
	QLOU-DH-2023-B	HMG CLD
	QLOU-DH-2023-C	MSUD
23-08-OUH	QLOU-DH-2023-D	normal
	QLOU-DH-2023-E	PKU
	QLOU-DH-2023-F	HWKS

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:	Propionic aciduria	Metabolic Center Heidelberg
Patient B:	HMG CLD	
Patient C:	MSUD	
Patient D:	normal	
Patient E:	PKU	
Patient F:	HWKS	

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 2023 ERNDIM QLOU Heidelberg scheme

	Survey 1	Survey 2
Receipt of results	71	73
No answer	3	1

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 2023 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 (November 30, 2023).

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 November 13, 2023.

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

Propionyl-CoA carboxylase deficiency

The sample originates from a patient with biochemically confirmed propionic acidemia (PA). Recurrent metabolic decompensations. The sample was collected while on PICU after metabolic and cardiac decompensation.
GC-MS analysis of the sample reveals clearly elevated concentrations of methylcitric acid and tiglylglycine. Slight elevations of supportive metabolites such as 2-methylbutyryl- and 3-methylcrotonyl glycines can also be found. Depending on the lab's reference ranges, the concentration of 3-hydroxypropionic acid may be borderline or even normal. Propionylglycine is within the normal range.

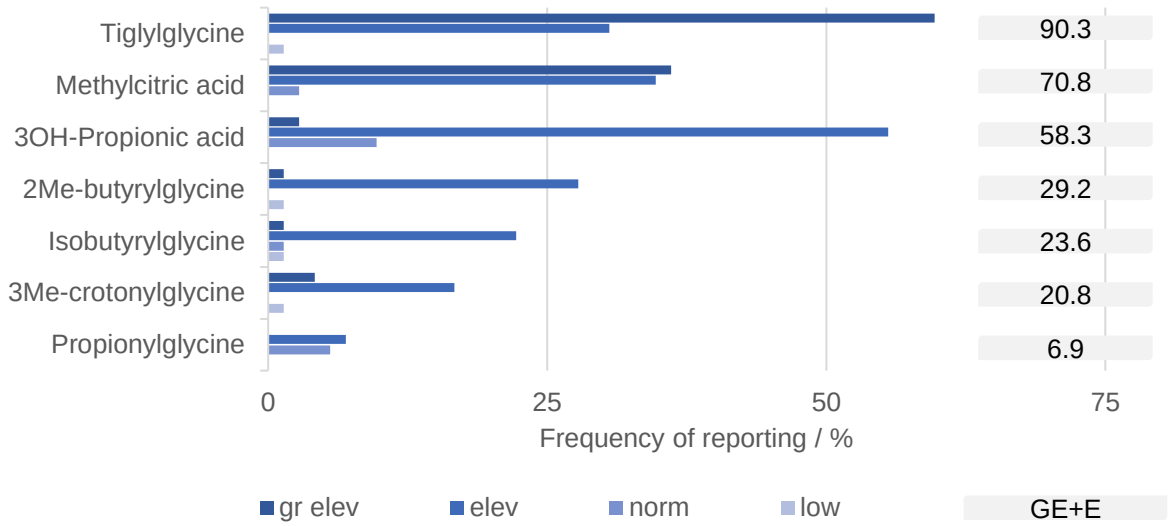
Patient details provided to participants

16-year-old boy with dystonia, optic atrophy and hypertrophic cardiomyopathy, currently under medication

Analytical performance

In this survey, 72 of 75 participants reported results. The metabolites most frequently reported as elevated or even grossly elevated were tiglylglycine (90% of labs reporting results) and methylcitric acid (71%), followed by 3-OH-propionic acid (58%), hippuric acid (47%), 2-methylbutyryl- (29%), isobutyryl- (24%), and 3-methylcrotonylglycine (21%).
Five participants reported elevated propionylglycine, while four reported normal concentrations for this metabolite.

Evaluation criteria: Two points are given for reporting methylcitric acid and tiglylglcine at least as elevated. Missing one of these analytes can be compensated by additionally reporting other relevant metabolites, however.

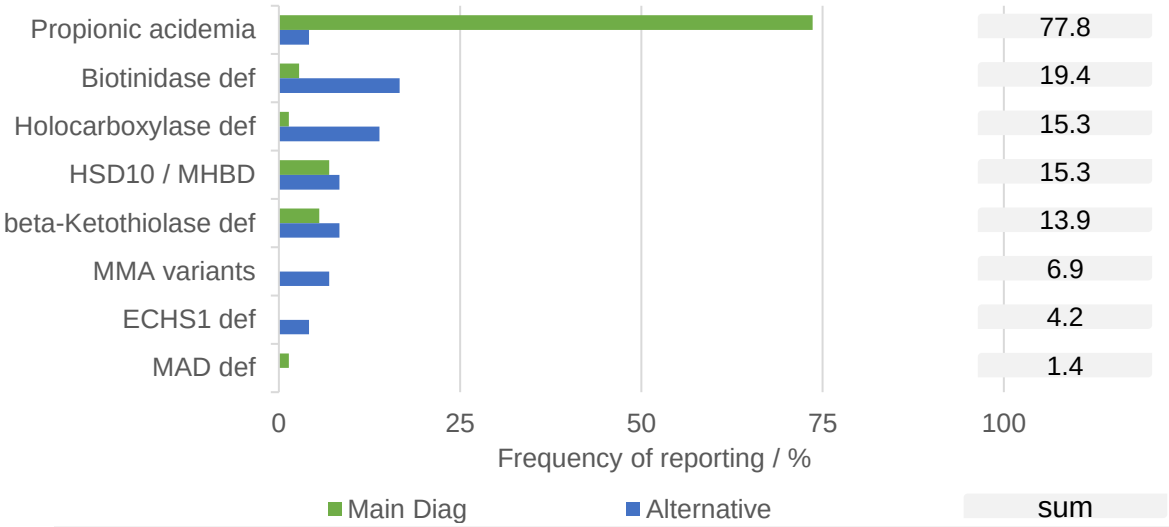


Most frequently reported metabolites relevant for sample A. Additionally, hippuric acid was reported by a high number of labs.

Diagnosis / Interpretative proficiency

PA was reported as the principal diagnosis by 53 participants and three considered it as an alternative diagnosis. Other IEMs repeatedly reported as primary diagnosis were 2-methyl-3-hydroxybutyryl-CoA dehydrogenase (n=5), beta-ketothiolase (n=4), or biotinidase (n=2) deficiencies, which were also most frequently considered as alternative diagnoses.
Two labs found the organic acid profiles to be normal. Due to the difficulty of this sample, no evaluation of critical errors was carried out.

Evaluation criteria: Stating PA as the principal diagnosis is scored as two points. If PA is indicated as an alternative diagnosis, the recommendations must also specify a method enabling to find the correct diagnosis.



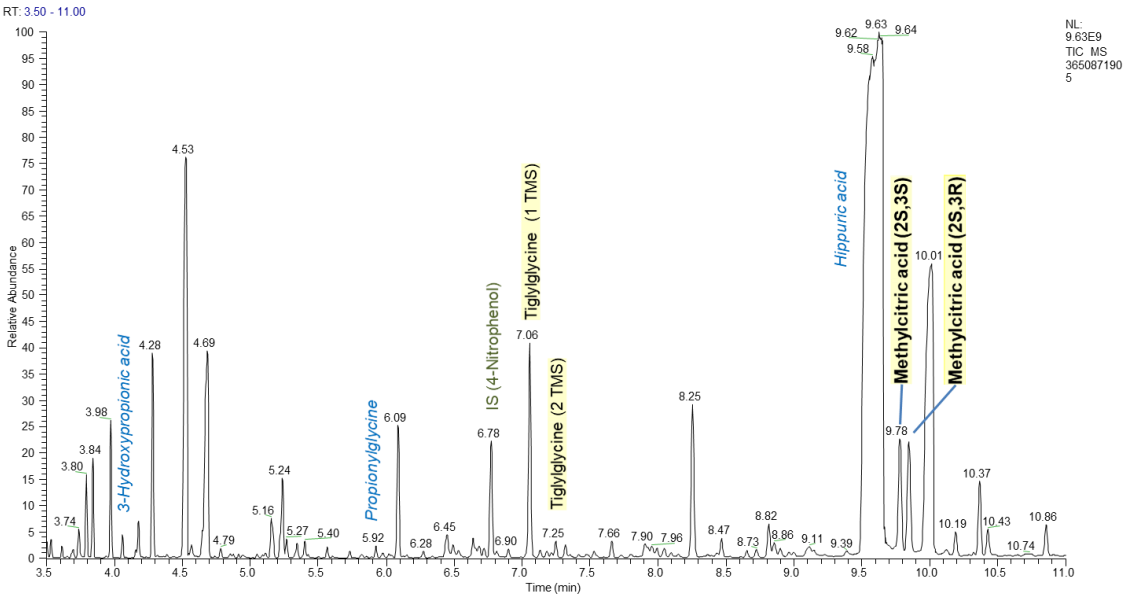
Most frequently reported diagnoses for sample A.

Recommendations

In their recommendations, the participants focused on differentiation mostly by analysis of plasma or blood acylcarnitines (n=40) and confirmation by molecular genetics (n=52) or enzyme assays (n=23). Plasma amino acids were also frequently recommended (n=23). Ten participants gave advice on further treatment.

Overall impression

Compared to previous distributions of PA samples, this one seemed more challenging for some participants. Although analytical performance was good at 91%, only 77% diagnostic proficiency was achieved.



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

8.2. Patient B

3-hydroxy-3-methylglutaryl-CoA lyase deficiency

The sample was taken from a patient with confirmed HMG CLD, who was diagnosed biochemically at the age of 5 months because of metabolic decompensation after vaccination. He has had frequent metabolic decompensations in early childhood.

The organic acids profile of this sample gained by GC-MS analysis shows clearly elevated signals for the characteristic metabolites 3-hydroxy-3-methylglutaric, 3-methylglutaric, 3-methylglutaconic, and 3-

hydroxyisovaleric acids. In addition, other metabolites that may occur in HMG CLD are also present in elevated concentrations, such as medium-chain dicarboxylic acids or 3-methylcrotonylglycine.

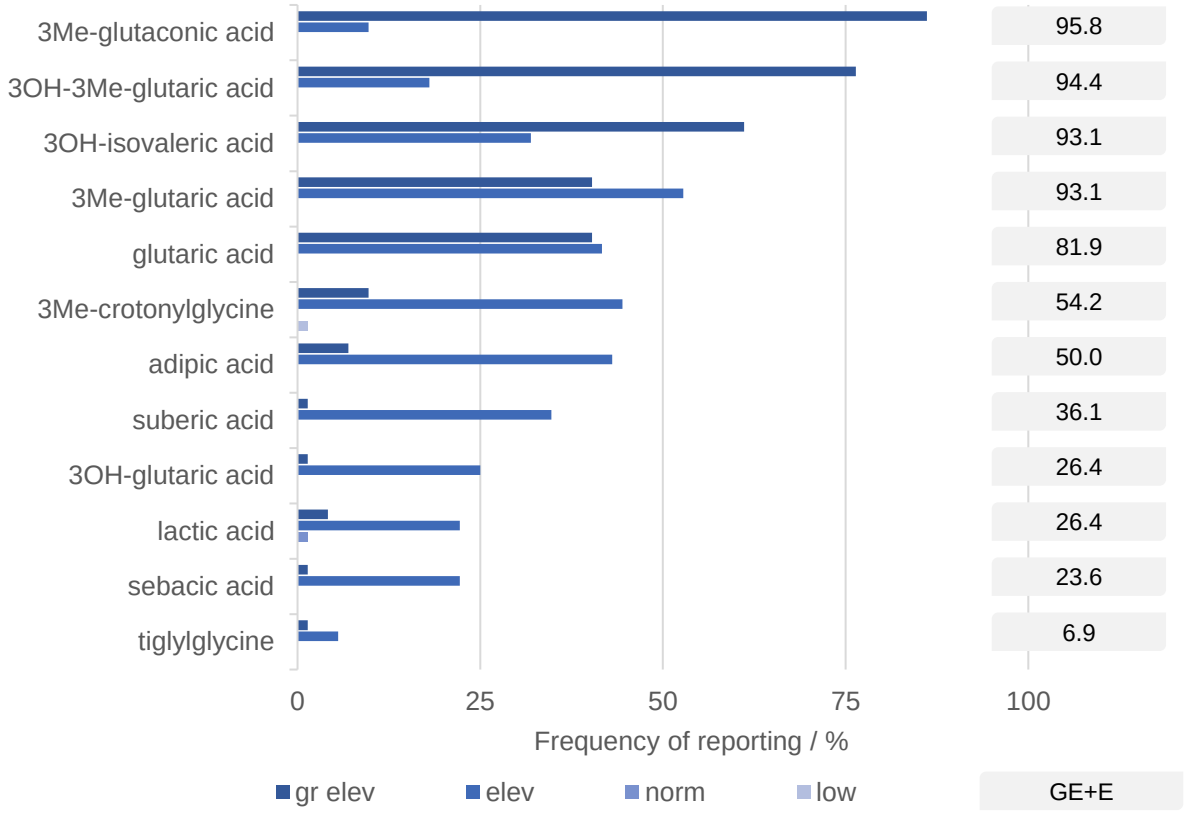
Patient details provided to participants

30-year-old man with mild hepatomegaly and kidney stones.

Analytical performance

Seventy-two participants reported results for this sample. The metabolites most frequently reported as elevated or grossly elevated were 3-methylglutaconic acid (94% of result reporting labs), 3-hydroxy-3-methylglutaric acid (93%), 3-methylglutaric acid (93%), 3-hydroxyisovaleric acid (92%), glutaric acid (81%), 3-methylcrotonylglycine (54%), adipic (50%), suberic (36%), and sebacic (24%) acids. Some participants also mentioned elevated lactate (24%) and/or 3-hydroxyglutaric acid (26%) concentrations.

Evaluation criteria: Two points are awarded, if at least three of the four signature metabolites 3-hydroxy-3-methylglutaric, 3-methylglutaric, 3-methylglutaconic, or 3-hydroxyisovaleric acid are reported as elevated or grossly elevated.

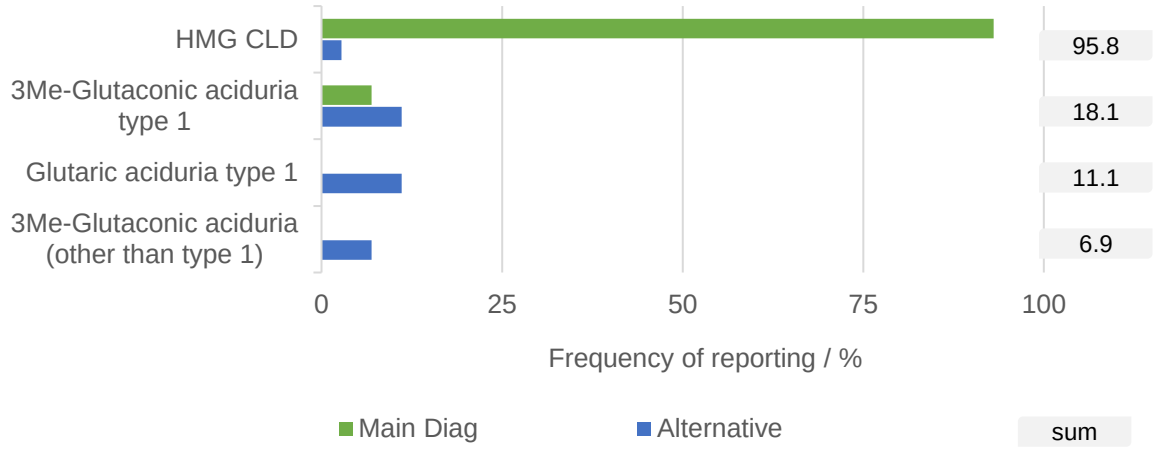


Most frequently reported metabolites for sample B.

Diagnosis / Interpretative proficiency

Sixty-seven of the participants submitting results reported HMG CLD as diagnosis, while two labs mentioned it as alternative. 3-Methylglutaconic aciduria type 1 was the second-most reported primary diagnosis (n=5) and also frequently given as alternative (n=8). Other IEMs mentioned as alternatives were glutaric aciduria type 1 (n=8) and other types of glutaconic aciduria (n=5).

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



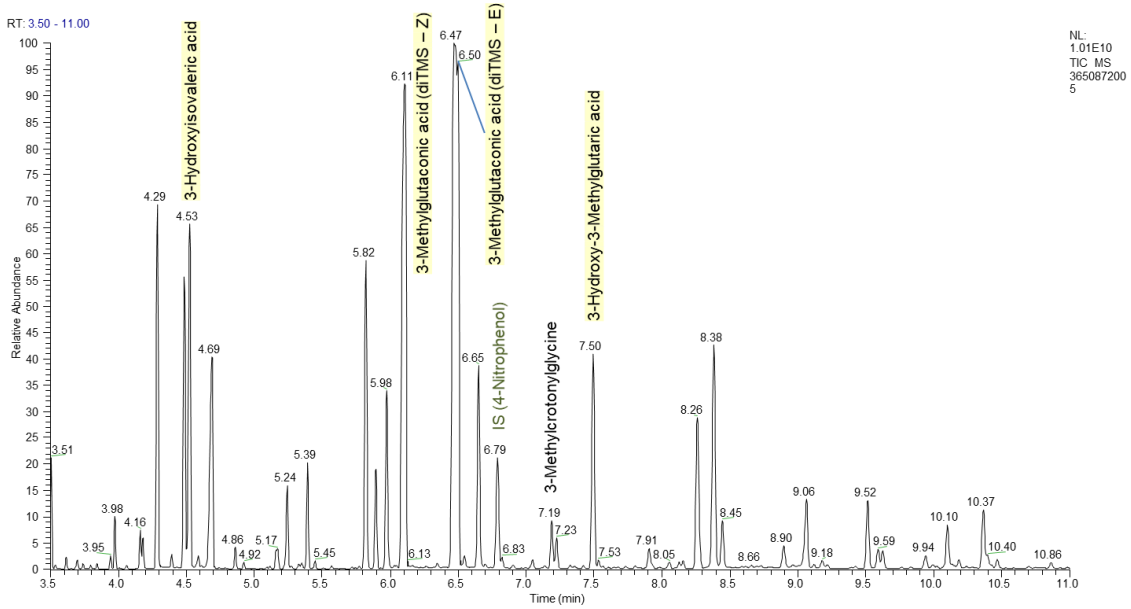
Most frequently reported diagnoses for sample B.

Recommendations

The method most commonly recommended for differentiation was analysis of acylcarnitines in plasma or blood (n=37). For differentiation, the participants opted for molecular genetic analysis (n=58) and/or determination of enzymatic activity (n=21).

Overall impression

The participants performed very well with this sample, both from an analytical (97%) and diagnostic (95%) perspective.



Example chromatogram for sample B.

8.3. Patient C

Maple syrup urine disease

The sample comes from a child with a family history of MSUD (two affected older sisters). Elevated leucine and alloisoleucine were seen on the second day of life confirming maple syrup urine disease. The patient had recurrent metabolic decompensations. The circulated sample was taken in decompensated state.

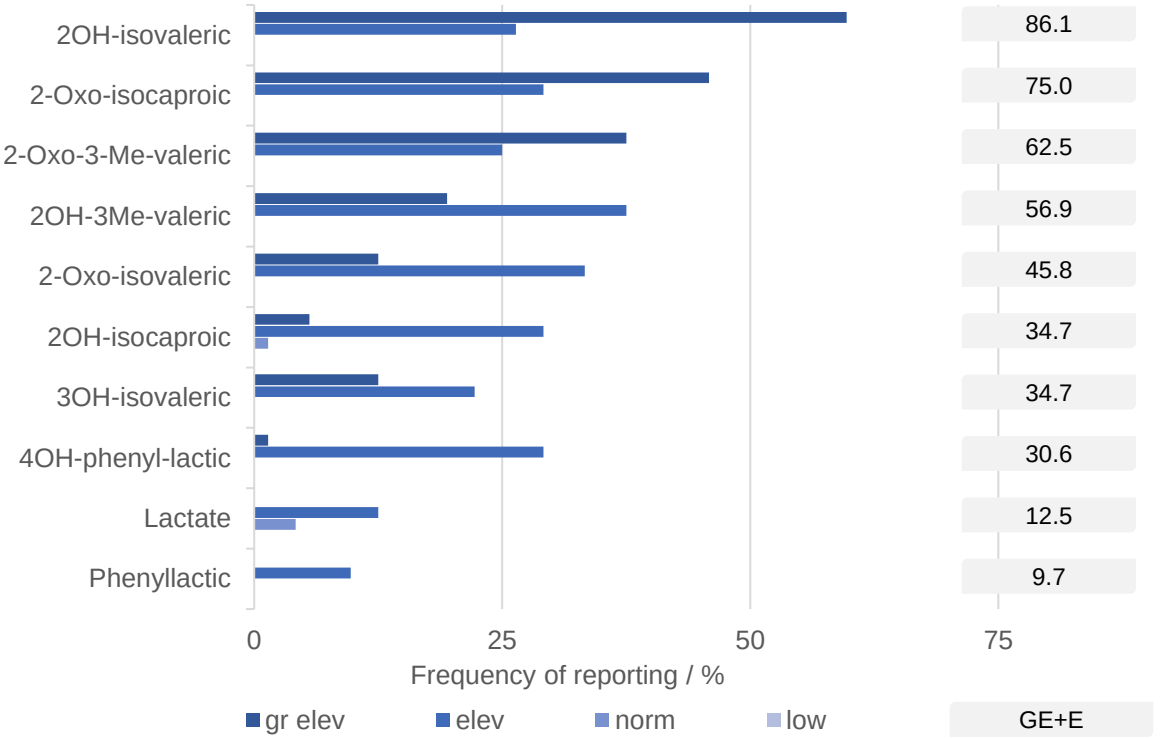
GC-MS analysis of organic acids reveals a profile representative for MSUD with elevated concentrations of the typical branched chain alpha-keto acids, 2-oxoisovaleric acid, 2-oxoisocaproic acid, 2-oxo-3-methylvaleric acid, and their hydroxy-analogues.

Patient details provided to participants

Four-year-old girl with episodic vomiting and hypotonia. Currently under treatment.

Analytical performance
The 72 participants submitting results for this sample mostly reported 2-hydroxyisovaleric acid (86% of participants), 2-oxo-isocaproic (75%), 2-oxo-3-methylvaleric (63%), 2-hydroxy-3-methyl-valeric (57%), 2-oxo-isovaleric (46%), and/or 2-hydroxy-isocaproic (35%) acids. Other metabolites referred to in the reports were 3-hydroxy-isovaleric (35%), 4-hydroxy-phenyllactic (31%), lactic (13%), and phenyllactic (10%) acids.

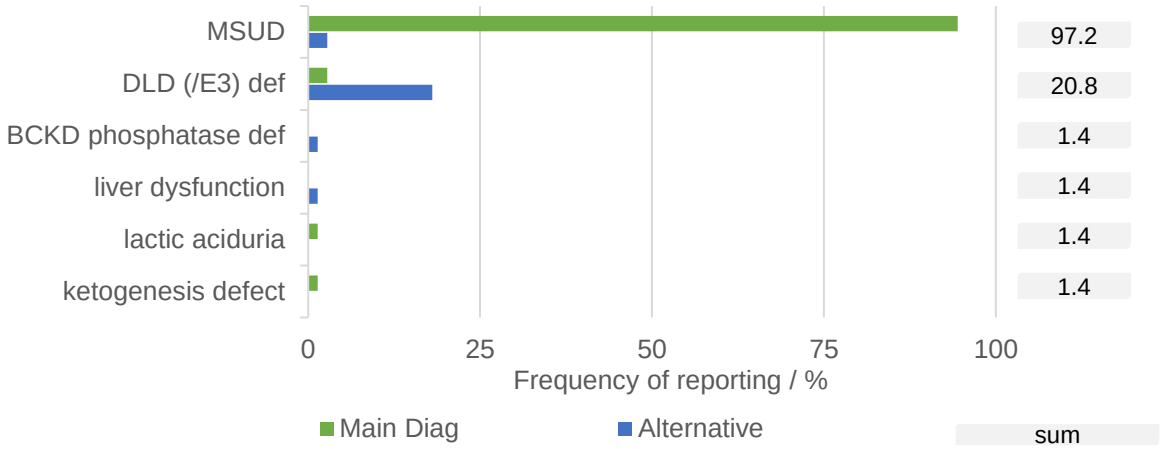
Evaluation criteria: Two points are given for reporting at least two of the key metabolites 2-oxoisovaleric acid, 2-oxoisocaproic acid, 2-oxo-3-methylvaleric acid, or the corresponding 2-hydroxy-metabolites.



Most frequently reported metabolites for sample C.

Diagnosis / Interpretative proficiency
Sixty-eight of the participants who reported results diagnosed MSUD in this sample. Two participants suggested MSUD as an alternative and selected dihydrolipoyl dehydrogenase deficiency as the primary diagnosis. This was also the most frequently mentioned alternative diagnosis by participants overall (n=13). One participant suggested a ketogenesis defect as principal diagnosis, another lab reported lactic aciduria (although both labs managed to find two key metabolites each) - both diagnoses were considered a critical error by the SAB.

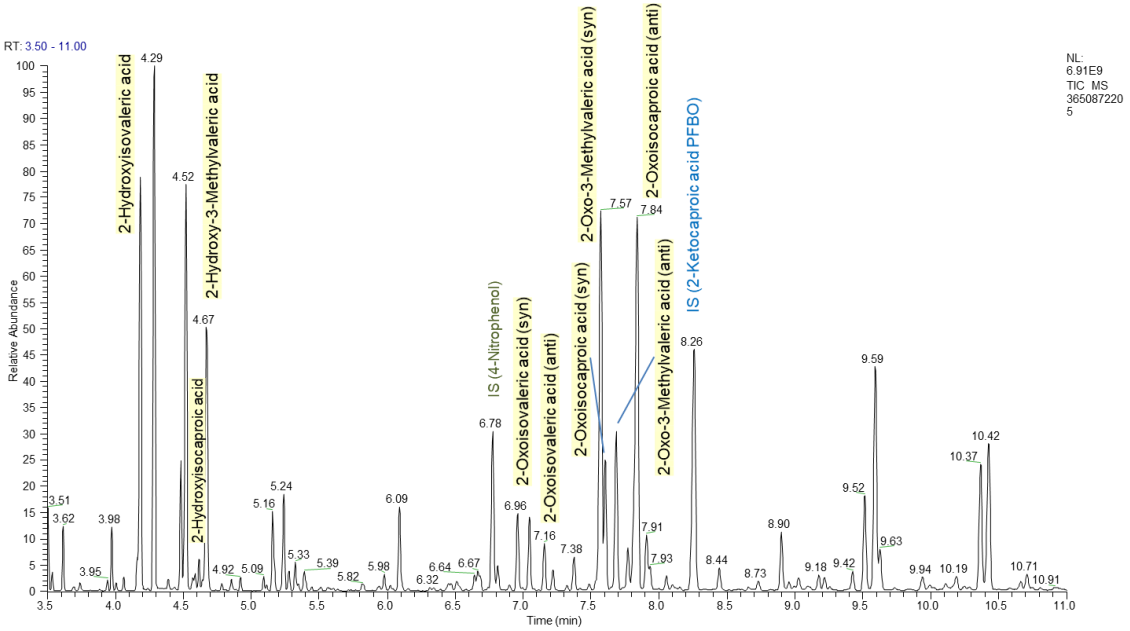
Evaluation criteria: Reporting of MSUD as principal diagnosis is awarded with two points. If given as alternative diagnosis, an additional recommendation suitable to find the correct diagnosis is required to achieve this score.



Most frequently reported diagnoses for sample C.

Recommendations
The analysis of amino acids in plasma was mostly recommended by the participants to support their findings (n=47) and molecular genetic analysis (n=54) and/or enzymatic activity tests (n=17) were suggested for confirmation. 17 participants gave recommendations for further treatment.

Overall impression
This sample was not complicated for most participants. They achieved 98% analytical and 97% diagnostic proficiency, respectively.



Example chromatogram for sample C

8.4. Patient D

Normal control

The sample originated from a male adolescent with no known metabolic disease.

Patient details provided to participants
Nine-year-old boy with myoclonic epilepsy.

Analytical performance
Seventy-four laboratories were participating and 73 of them submitted results for this sample. A normal profile without findings relevant for an inborn error of metabolism (IEM) was stated by 69 participants.

Four laboratories did not mention a normal profile. Instead, elevated concentrations of metabolites such as glycerol, 5-oxoproline, 3-OH-propionic, vanillylmandelic, homovanillic, and ethylmalonic acids were reported.

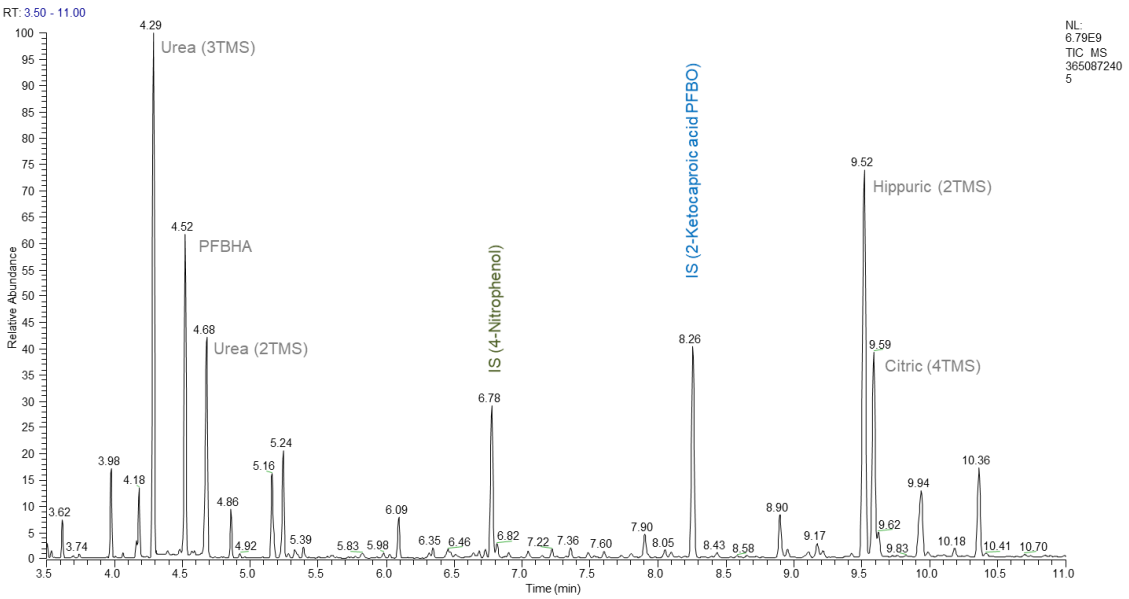
Evaluation criteria: Two points are given for reporting a normal profile.

Diagnosis / Interpretative proficiency
Sixty-nine participants (94,5%) reported that the sample was not representative for a metabolic disorder. One participant considered glycerol kinase deficiency, 5-oxoprolinase deficiency was mentioned by another. Two other participants reported neuroblastoma or ethylmalonic encephalopathy as their diagnoses.

Evaluation criteria: Two points are given for reporting a normal profile or the absence of a metabolic disorder.

Recommendations
Many participants recommended further investigations to narrow down the reasons for the mentioned epilepsy.

Overall impression
With 95% analytical and 96% interpretative proficiency, the participants performed well in recognizing the normal control sample.



Example chromatogram for sample D. Typically occurring signals are marked in grey.

8.5. Patient E

Phenylketonuria

The sample originates of a patient with a genetically confirmed classical phenylketonuria (PKU), who had terminated his phenylalanine-reduced diet in adulthood. Phe concentration at the time of sampling was 1300 µmol/L.

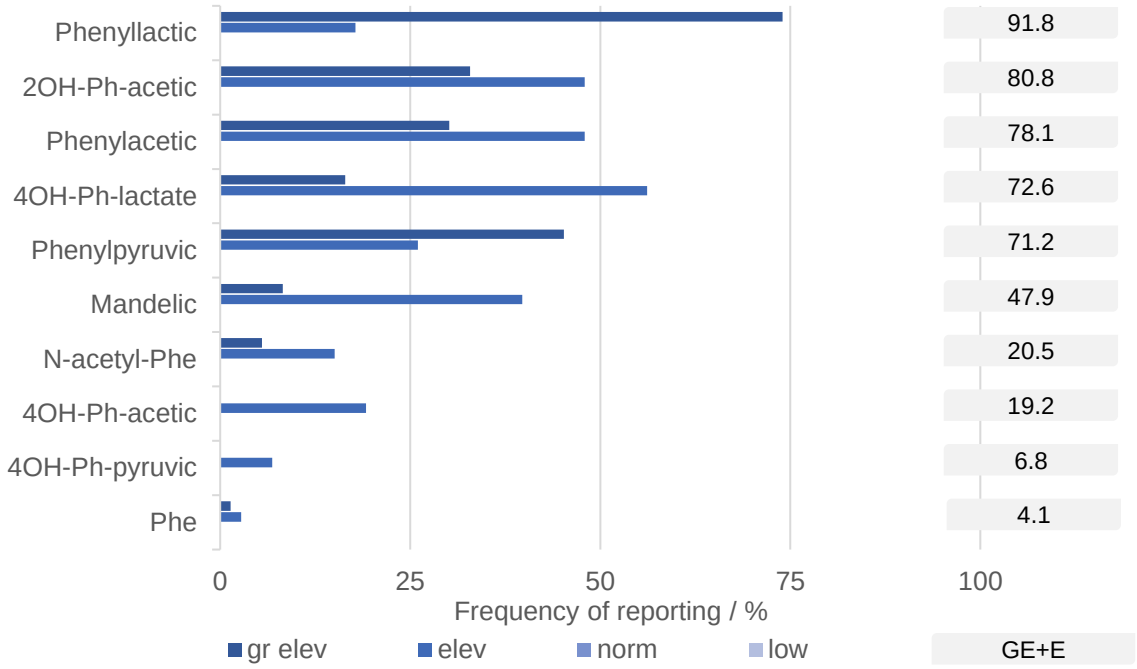
The analysis of organic acids in this sample reveals clearly elevated concentrations of the characteristic metabolites phenylacetic acid, 2-OH-phenylacetic acid, phenyllactic acid, and mandelic acid.

Patient details provided to participants
39-year-old male on vegetarian diet.

Analytical performance
Seventy-three participants reported results for this sample. The metabolites which were most frequently reported as elevated or even grossly elevated were phenyllactic acid (92%), 2-OH-phenylacetic acid (81%), phenylacetic acid (78%), 4-OH-phenyllactic acid (73%), phenylpyruvic acid (71%), and mandelic

acid (48%). Some participants also reported N-acetyl-phenylalanine (19%) or glycolic acid (n=3) in elevated concentrations.

Evaluation criteria: Typical key metabolites for PKU are phenylacetic, 2-OH-phenylacetic, phenyllactic, phenylpyruvic, and mandelic acids. Two points are given for reporting three or more of these as at least elevated, one point for reporting one or two of them.

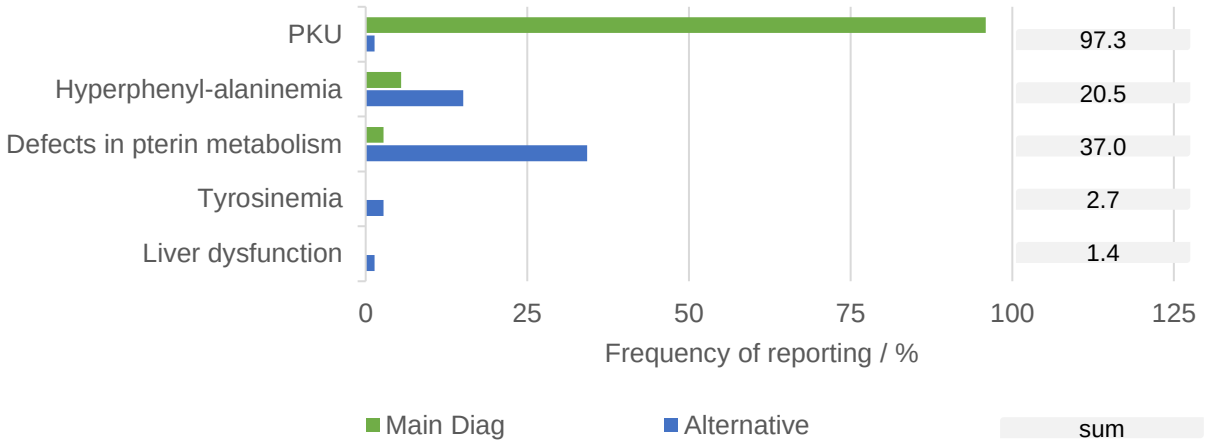


Most frequently reported metabolites for sample E.

Diagnosis / Interpretative proficiency

Seventy participants stated PKU as their principal diagnosis and one participant considered it as alternative diagnosis. Pterin metabolism disorders such as tetrahydrobiopterin (BH_4) deficiency were also considered as principal or alternative diagnoses. One participant reporting only on elevated lactic acid, mentioned lactic acidemia with possible pyruvate dehydrogenase phosphatase deficiency. This was considered a critical error.

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

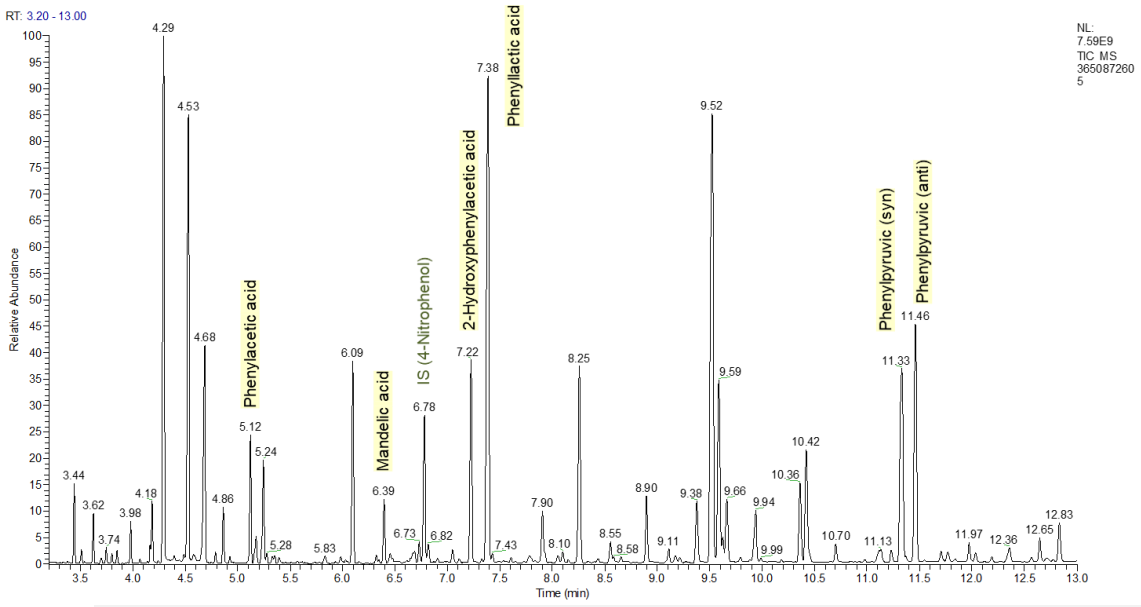


Most frequently reported diagnoses for sample E. PKU and hyperphenylalaninemia were reported jointly by several participants.

Recommendations

To support their findings or to differentiate, the participants recommended to perform further tests such as amino acids in plasma or blood (n=60), molecular genetic analysis (n=55 and mostly referring to the PAH gene) determination of pterins in urine or plasma (n=31), or conduct a BH_4 loading test (n=15). Twenty-one participants mentioned recommendations for treatment.

Overall impression
The participants performed very well with this sample, achieving 95% analytical and 99% diagnostic proficiency.



Example chromatogram for sample E

8.6. Patient F

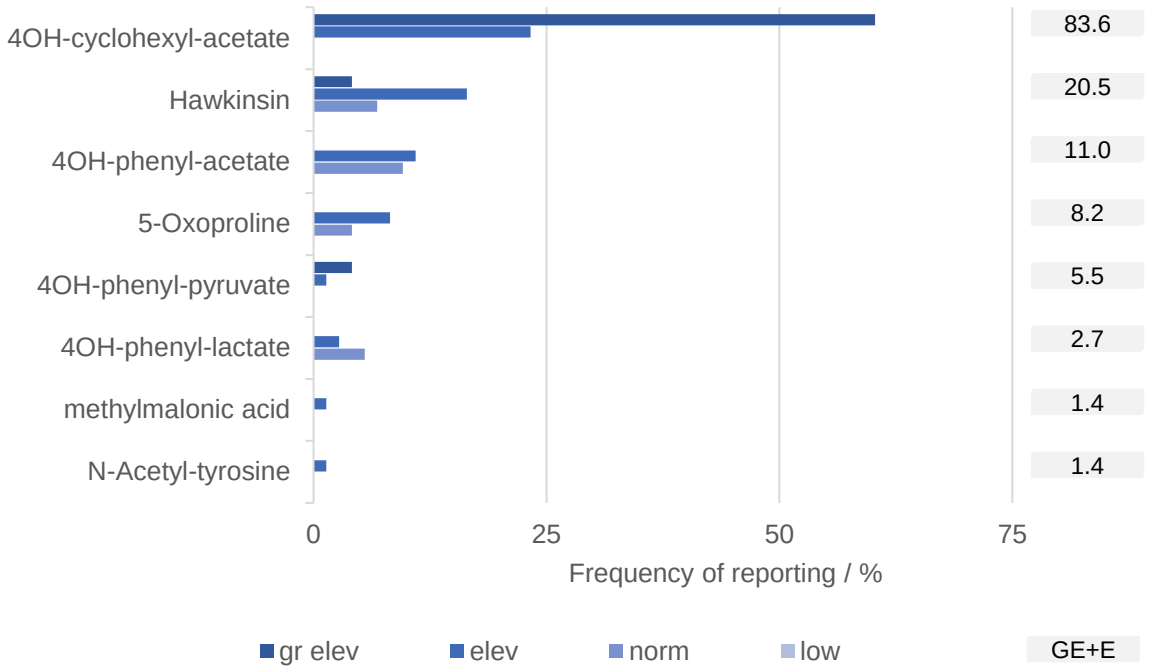
Hawkinsinuria

The sample originated from a female teenager. At the age of 12 months, developmental delay was apparent and metabolic acidosis and anaemia prompted further metabolic evaluation. Hawkinsinuria was diagnosed biochemically and confirmed by molecular analysis (Asn241Ser in *HPD*).
The organic acids chromatogram is dominated by a large peak representing 4-OH-cyclohexylacetic acid isomers, which are paramount for hawkinsinuria. 4-OH-phenylacetic, -lactic, and -pyruvic acids were not elevated in this sample as it is typical for this disorder beyond infancy.

Patient details provided to participants
12-year-old girl, who presented at 7 months of age with failure to thrive and metabolic acidosis.

Analytical performance
The 73 participants submitting results for this sample most frequently reported on 4-hydroxycyclohexylacetic acid. It was rated as elevated 17 times and 44 times as grossly elevated. Some participants also reported on hawkinsin ((2-Cystein-S-yl-1,4-dihydroxycyclohex-5-en-1-yl)acetic acid, 3x grossly elevated, 12x elevated). 4-OH-phenylacetic acid, 4-OH-phenyllactic acid, 4-OH-phenylpyruvic acid, or 5-oxoproline were mentioned less frequently (n=4 to 15) and were in some cases stated to be in normal concentrations.

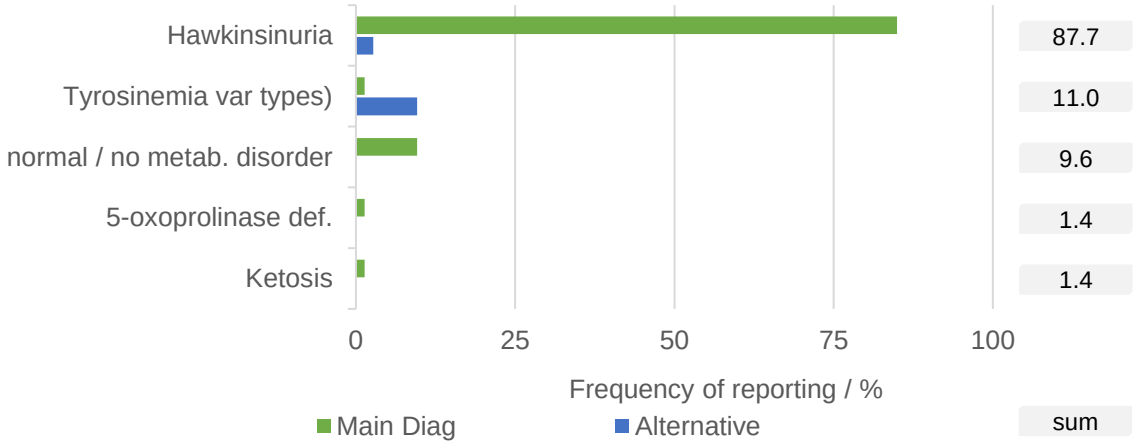
Evaluation criteria: Reporting one or both of the key metabolites hawkinsin and 4-OH-cyclohexylacetic acid as at least elevated is awarded with 2 pts. One point is given for reporting on 4-OH-phenylacetic acid, 4-OH-phenyllactic acid, 4-OH-phenylpyruvic acid, and/or 5-oxoproline.



Most frequently reported metabolites for sample F.

Diagnosis / Interpretative proficiency
In most cases (62/73), hawkinsinuria was reported as principal diagnosis and two participants considered it as alternative diagnosis. Other alternatives considered by the participants were different types of tyrosinemia. Seven participants found the organic acids profile non-representative for an IEM and reported a normal sample.

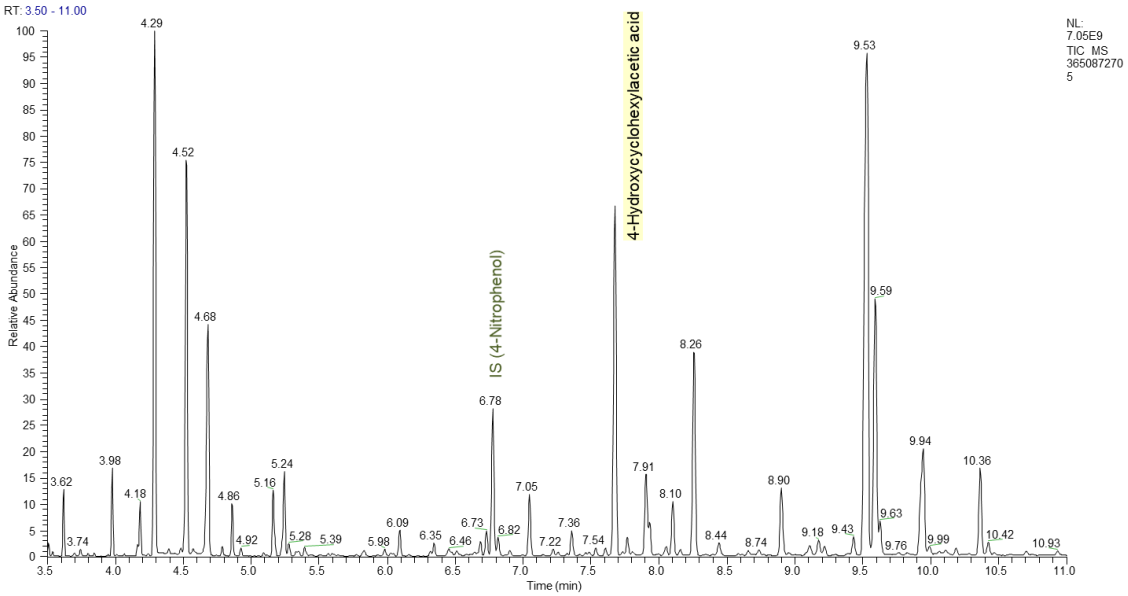
Evaluation criteria: Reporting of hawkinsinuria as principal diagnosis is awarded with two points. If given as alternative diagnosis, an additional recommendation suitable to find the correct diagnosis is required to achieve this score.



Most frequently reported diagnoses for sample F.

Recommendations
Further laboratory tests often recommended by the participants to support their suggested diagnoses were genetic testing (n=52, mostly focussing the HPD gene), determination of amino acids in general or (n=31) specifically referring to hawkinsin in urine (n=22).

Overall impression
The participants achieved 90% analytical and 88% diagnostic proficiency, respectively, which is an improvement compared to the last circulation of a HWKS sample (QLOU-DH-2018-A: 76% overall proficiency).



Example chromatogram for sample F

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. Detailed scores – Round 1

Lab n°	Patient A Propionic aciduria			Patient B HMG CLD			Patient C MSUD			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	2	1	3	2	2	4	2	2	4	11
3	2	2	4	2	2	4	2	2	4	12
4	2	2	4	2	2	4	2	2	4	12
5	2	0	2	2	2	4	2	2	4	10
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	2	2	4	2	2	4	12
8	1	0	1	2	2	4	2	2	4	9
9	2	2	4	2	2	4	2	2	4	12
10	2	2	4	2	2	4	2	2	4	12
11	2	0	2	2	2	4	2	2	4	10
12	2	2	4	2	2	4	2	2	4	12

Lab n°	Patient A Propionic aciduria			Patient B HMG CLD			Patient C MSUD			
	A	I	Total	A	I	Total	A	I	Total	Total
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	1	2	3	11
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	0	2	2	2	4	10
25	2	2	4	2	0	2	2	2	4	10
26	2	2	4	2	2	4	2	2	4	12
27	2	0	2	2	0	2	2	2	4	8
28	2	2	4	2	2	4	2	2	4	12
29	2	2	4	2	2	4	2	2	4	12
30	2	2	4	2	2	4	2	2	4	12
31	2	2	4	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	0	2	2	2	4	2	2	4	10
35	2	1	3	2	2	4	2	2	4	11
36	2	2	4	2	2	4	2	2	4	12
37	2	2	4	2	2	4	2	2	4	12
38	2	2	4	2	2	4	2	2	4	12
39	2	2	4	2	2	4	2	2	4	12
40	2	2	4	2	2	4	2	2	4	12
41	2	2	4	2	2	4	2	2	4	12
42	1	2	3	2	2	4	2	2	4	11
43	2	0	2	2	2	4	2	2	4	10
44	2	2	4	2	2	4	2	2	4	12
45	1	2	3	2	2	4	2	2	4	11

Lab n°	Patient A Propionic aciduria			Patient B HMG CLD			Patient C MSUD			
	A	I	Total	A	I	Total	A	I	Total	Total
46	0	0	0	0	2	2	1	2	3	5
47	2	0	2	2	2	4	2	2	4	10
48	2	0	2	2	2	4	2	2	4	10
49	2	2	4	2	2	4	2	2	4	12
50	2	2	4	2	2	4	2	0	2	10
51	2	2	4	2	2	4	2	2	4	12
52	2	2	4	2	2	4	2	2	4	12
53	0	0	0	2	2	4	2	2	4	8
54	1	2	3	2	2	4	2	2	4	11
55	2	2	4	2	2	4	2	2	4	12
56	2	2	4	2	2	4	2	2	4	12
57	1	0	1	2	2	4	2	2	4	9
58	2	2	4	2	2	4	2	2	4	12
59	--	--	--	--	--	--	--	--	--	0
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	2	2	4	12
63	1	0	1	2	1	3	2	0	2	6
64	1	2	3	2	2	4	2	1	3	10
65	0	0	0	1	2	3	1	2	3	6
66	2	0	2	2	2	4	2	2	4	10
67	2	2	4	2	2	4	2	2	4	12
68	2	2	4	2	2	4	2	2	4	12
69	2	2	4	2	2	4	2	2	4	12
70	2	0	2	2	2	4	2	2	4	10
71	--	--	--	--	--	--	--	--	--	0
72	2	2	4	2	2	4	2	2	4	12
73	--	--	--	--	--	--	--	--	--	0
74	1	0	1	2	2	4	2	2	4	9

9.2. Round 2

Lab n°	Patient D normal			Patient E PKU			Patient F HWKS			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	2	2	4	2	2	4	2	2	4	12
3	2	2	4	2	2	4	2	2	4	12
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	2	2	4	2	2	4	12
8	2	2	4	2	2	4	2	2	4	12
9	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	1	2	3	2	2	4	11
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	1	1	2	2	2	4	0	0	0	6
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	1	2	3	2	2	4	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

Lab n°	Patient D normal			Patient E PKU			Patient F HWKS			
	A	I	Total	A	I	Total	A	I	Total	Total
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	0	0	0	8
40	2	2	4	2	2	4	1	0	1	9
41	2	2	4	2	2	4	0	0	0	8
42	2	2	4	2	2	4	2	2	4	12
43	2	2	4	1	2	3	2	0	2	9
44	2	2	4	2	2	4	2	2	4	12
45	2	2	4	2	2	4	0	0	0	8
46	2	2	4	2	2	4	2	2	4	12
47	2	2	4	2	2	4	1	0	1	9
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	0	0	0	1	2	3	2	2	4	7
53	2	2	4	2	2	4	2	2	4	12
54	0	0	0	2	2	4	2	2	4	8
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	0	0	0	0	0	0	2	2	4	4
60	2	2	4	1	2	3	2	2	4	11
61	2	2	4	2	2	4	0	0	0	8
62	2	2	4	2	2	4	2	2	4	12
63	2	2	4	2	2	4	2	2	4	12
64	2	2	4	2	2	4	2	2	4	12
65	2	2	4	2	2	4	2	2	4	12

Lab n°	Patient D normal			Patient E PKU			Patient F HWKS			
	A	I	Total	A	I	Total	A	I	Total	Total
66	2	2	4	2	2	4	2	2	4	12
67	2	2	4	2	2	4	2	2	4	12
68	2	2	4	2	2	4	2	2	4	12
69	2	2	4	2	2	4	2	2	4	12
70	2	2	4	2	2	4	2	2	4	12
71	2	2	4	2	2	4	2	2	4	12
72	2	2	4	2	2	4	1	2	3	11
73	--	--	--	--	--	--	--	--	--	0
74	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	3	4	4	4	4	4	23	96	
3	4	4	4	4	4	4	24	100	
4	4	4	4	4	4	4	24	100	
5	2	4	4	4	4	4	22	92	
6	4	4	4	4	4	4	24	100	
7	4	4	4	4	4	4	24	100	
8	1	4	4	4	4	4	21	88	
9	4	4	4	4	4	4	24	100	
10	4	4	4	4	4	4	24	100	
11	2	4	4	4	3	4	21	88	
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	3	2	4	0	17	71	
16	4	4	4	4	4	4	24	100	
17	4	4	4	4	4	4	24	100	
18	4	4	4	4	4	4	24	100	
19	4	4	4	4	4	4	24	100	
20	4	4	4	4	4	4	24	100	

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score in %	Critical error
21	4	4	4	4	3	4	23	96	
22	4	4	4	4	4	4	24	100	
23	4	4	4	4	4	4	24	100	
24	4	2	4	4	4	4	22	92	
25	4	2	4	4	4	4	22	92	
26	4	4	4	4	4	4	24	100	
27	2	2	4	4	4	4	20	83	
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	4	4	4	4	4	4	24	100	
33	4	4	4	4	4	4	24	100	
34	2	4	4	4	4	4	22	92	
35	3	4	4	4	4	4	23	96	
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	0	20	83	
40	4	4	4	4	4	1	21	88	
41	4	4	4	4	4	0	20	83	
42	3	4	4	4	4	4	23	96	
43	2	4	4	4	3	2	19	79	
44	4	4	4	4	4	4	24	100	
45	3	4	4	4	4	0	19	79	
46	0	2	3	4	4	4	17	71	
47	2	4	4	4	4	1	19	79	
48	2	4	4	4	4	4	22	92	
49	4	4	4	4	4	4	24	100	
50	4	4	2	4	4	0	18	75	CE
51	4	4	4	4	4	4	24	100	
52	4	4	4	0	3	4	19	79	
53	0	4	4	4	4	4	20	83	

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score in %	Critical error
54	3	4	4	0	4	4	19	79	
55	4	4	4	4	4	4	24	100	
56	4	4	4	4	4	4	24	100	
57	1	4	4	4	4	4	21	88	
58	4	4	4	4	4	4	24	100	
59	--	--	--	0	0	4	4	17	CE
60	4	4	4	4	3	4	23	96	
61	4	4	4	4	4	0	20	83	
62	4	4	4	4	4	4	24	100	
63	1	3	2	4	4	4	18	75	CE
64	3	4	3	4	4	4	22	92	
65	0	3	3	4	4	4	18	75	
66	2	4	4	4	4	4	22	92	
67	4	4	4	4	4	4	24	100	
68	4	4	4	4	4	4	24	100	
69	4	4	4	4	4	4	24	100	
70	2	4	4	4	4	4	22	92	
71	--	--	--	4	4	4	12	50	
72	4	4	4	4	4	3	23	96	
73	--	--	--	--	--	--	0	0	
74	1	4	4	4	4	4	21	88	

9.4. Performance

	Number of labs	% total labs
Satisfactory performers (≥ 71 % of adequate responses)	69	93
Unsatisfactory performers (< 71 % adequate responses and/or critical error)	2	3
Partial and non-submitters	3	4

9.5. Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
QLOU-DH-2023-A	Propionic aciduria	90	76	83
QLOU-DH-2023-B	HMG CLD	98	95	96
QLOU-DH-2023-C	MSUD	98	96	97
QLOU-DH-2023-D	normal	95	95	95
QLOU-DH-2023-E	PKU	95	99	97
QLOU-DH-2023-F	HWKS	90	88	89

10. Tentative 2024 schedule

Sample distribution	8th February 2024
Start of analysis of Survey 2024/1 Website open	7th May 2024
Survey 2024/1 - Results submission	28th May 2024
Survey 2024/1 - Reports	June 2024
Start of analysis of Survey 2024/2 Website open	19th August 2024
Survey 2024/2 – Results submission	9th September 2024
Survey 2024/2 - Reports	September/October 2024
Annual Report 2024	January 2025

11. ERNDIM certificate of participation

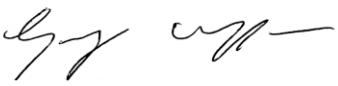
A combined certificate of participation covering all EQA schemes will be provided to all participants who take part in any ERNDIM scheme. For the QLOU scheme this certificate will indicate if results were submitted and whether satisfactory performance was achieved in the scheme.

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, 2024-03-22
Name and signature of Scientific Advisor





Dr. J. Janda Scientific Advisor Laboratory of Metabolic Diseases	Prof. Dr. V. Peters 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	26 March 2023	2023 annual report published

END