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Diagnostic Proficiency Testing
Centre: France
Final Report 2025

Prepared by
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Note: This annual report is intended for participants of the ERNDIM DPT France scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

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

1. Geographical distribution of participants

In 2025, 20 labs registered to DPT France. One lab could not submit results to the first survey because they did not pay the 2024 fees. Finally, 19 labs submitted results for the first survey, and 20 labs for the second survey.

Country	Number of participants
Czech Republic	1
France	8
Italy	4
Portugal	2
Spain	5

[1] If this report is not Version 1 for this scheme year, go to 0 for details of the changes made since the last version of this document.

2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Christine Vianey-Saban and Cécile Acquaviva as Scientific Advisors and coordinated by Alessandro Salemma and Rose Defossez (erndim.survey@cscq.ch) as scheme organizer (sub-contractors on behalf of CSCQ), both appointed by and according to procedures laid down the ERNDIM Board.

CSCQ dispatches DPT EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports. Existing DPT scheme participants can log on to the CSCQ results submission website at:
https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php

2 surveys	Round 1: patients A, B and C
	Round 2: patients D, E and F

Origin of patients: urine samples have been provided by Dr Joachim Janda (QLOU scheme, Heidelberg, Germany), Dr Cristiano Rizzo (ACDB, Rome, Italy), Dr Anne-Frédérique Dessein (CHU Lille, France), and the Scientific Advisors.

Patient A: Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome, arylsulfatase B deficiency, *ARSB* gene)
Patient B: Maple syrup urine disease (MSUD), deficiency of branched-chain 2-ketoacid dehydrogenase complex
Patient C: Hawkinsinuria, autosomal dominant deficiency of 4-hydroxyphenylpyruvate dioxygenase (gene *HPD*)
Patient D: GM1 gangliosidosis (beta-galactosidase deficiency, *GLB1* gene)
Patient E: Primary hyperoxaluria type II (glyoxylate reductase / hydroxypyruvate reductase deficiency - *GRHPR* gene)
Patient F: Glutaric aciduria type I, low excretor (glutaryl-CoA dehydrogenase deficiency, *GCDH* gene)

The samples have been heat-treated. They were pre-analysed in our institute after 2 weeks incubation at ambient temperature (to mimic possible changes that might arise during transport). In all six samples the typical metabolic profiles were preserved after this process. The samples are stable for the duration of the scheme's submission calendar when stored under defined conditions.
Mailing: samples were sent by DHL, FedEx or the Swiss Post at room temperature. For Spain and Italy, due to custom problems in 2024, the samples have been sent by MCA, NL.

3. Tests

Analyses of amino acids, organic acids, mucopolysaccharides, oligosaccharides and purines / pyrimidines are mandatory.

4. Schedule of the 2025 scheme

- February 5: shipment of samples of Survey 1 and Survey 2
- March 17: clinical data available on CSCQ website and start analysis of samples of the first survey
- April 7: deadline for result submission (Survey 1)
- June 2: clinical data available on CSCQ website and start analysis of samples of the second survey
- June 23: deadline for result submission (Survey 2)
- July 1: interim report of Survey 1 on CSCQ website (sent by the SA to CSCQ on May 1)
- August 4: interim report of Survey 2 on CSCQ website (sent by the SA to CSCQ on July 31)
- October 9: meeting of participants in Madrid
- November 28: definition of critical errors during the SAB meeting
- February 2026: Personalized annual report available on CSCQ website

5. Results

	Survey 1	Survey 2
Receipt of results	19	20
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 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 don't give quantitative data.
  - If the profile is normal: enter "Normal profile" in "Key metabolites".
  - **Don't enter results in the "comments" window**, **otherwise your results will not be included in the evaluation program.**
- Recommendations = **advice for further investigation**.
  - Scored together with the interpretative score.
  - Advice for treatment are not scored.
  - **Don't give advice for further investigation in "Comments on diagnosis"**: it will not be included in the evaluation program.

7. Scoring and evaluation of results

Information regarding procedures for establishment of assigned values, statistical analysis, interpretation of statistical analysis etc. can be found in generic documents on the ERNDIM website.
The scoring system has been established by the International Scientific Advisory Board of ERNDIM. Two criteria are evaluated: 1) analytical performance, 2) interpretative proficiency also considering recommendations for further investigations.

A	Analytical performance	Correct results of the appropriate tests	2
		Partially correct or non-standard methods	1
		Unsatisfactory or misleading	0
I	Interpretative proficiency & Recommendations	Good (diagnosis was established)	2
		Helpful but incomplete	1
		Misleading or wrong diagnosis	0

The total score is calculated as a sum of these two criteria. The maximum to be achieved is 4 points per sample. The scores were calculated only for laboratories submitting results.

Scoring and certificate of participation: scoring is carried by a second assessor who changes every year as well as by the scientific advisor. The results of DPT France 2025 have been also scored by Dr Joanne Croft, from DPT United Kingdom. At the SAB meeting in Leiden on November 27, 2025, the definitive scores have been finalized. The concept of critical error was introduced in 2014. A critical error is defined as an error resulting from seriously misleading analytical findings and /or interpretations with serious clinical consequences for the patient. Thus, labs failing to make a correct diagnosis of a sample considered as eligible for this category will be deemed not to have reached a satisfactory performance even if their total points for the year exceed the limit set at the SAB. For 2025, the SAB decided that sample C has to be considered as a critical error for the lab that did not identify metabolites diagnostic of MSUD (amino acids or organic acids). The failure to propose glutaric aciduria type I as main or alternative diagnosis in sample F has also been advised by the SAB as a critical error.

A certificate of participation will be issued for participation, and it will be additionally notified whether the

participant has received a performance support letter. This performance support letter is sent out if the performance is evaluated as unsatisfactory. Two performance support letters will be sent by the Scheme Advisor for 2025. Any partial submitters will receive a letter from the ERNDIM Executive Administrator, Sara Gardner.

For further information, please refer to the Framework for Assessment and Education for Qualitative Schemes on our website (https://eqa.erndim.org/information/view/14)

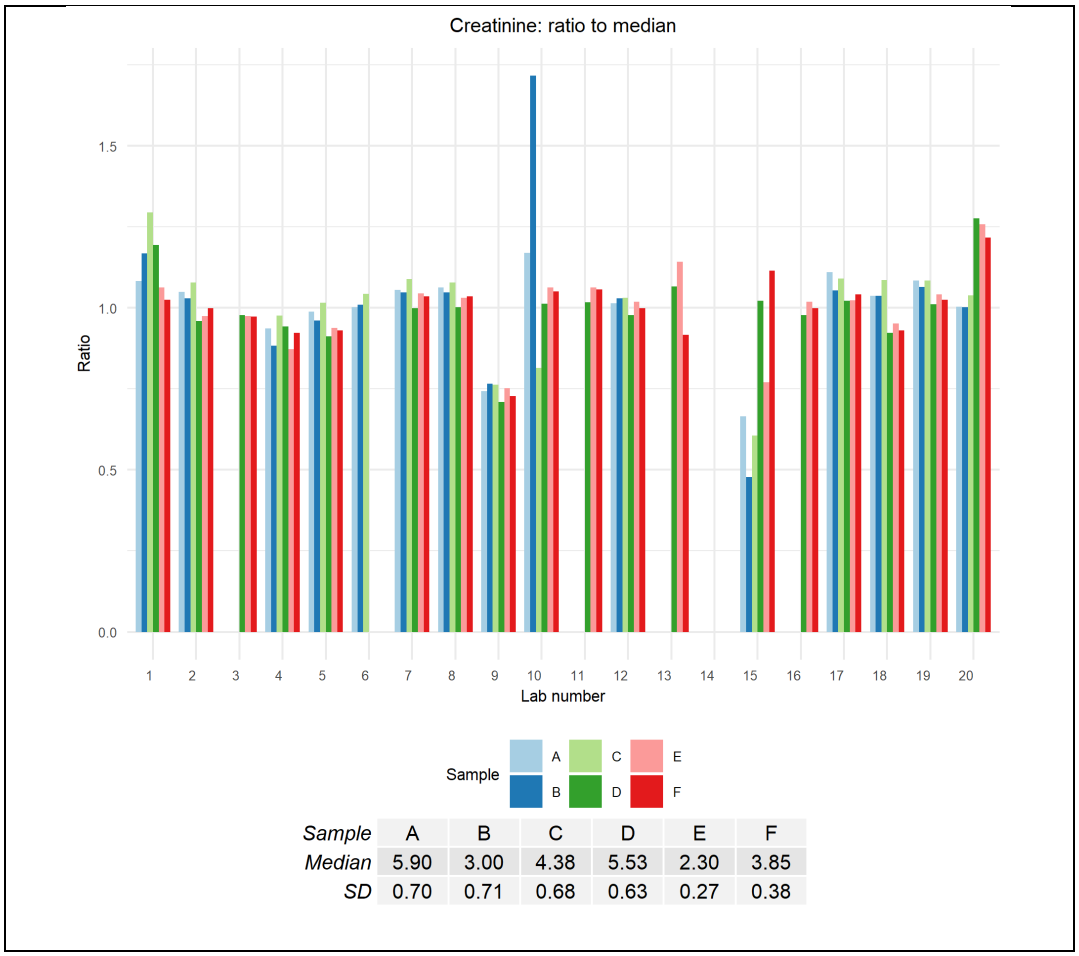
7.1. Score for satisfactory performance

At least 17 points from the maximum of 24 (70%).
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 determination was satisfying for most labs. Lab 10 and lab 15 had scattered results. Lab 9 had low values. Creatinine values are expressed in the figure as the ratio of each measurement over the median of all labs.
After exclusion of 2 wrong values for sample B and 1 wrong value for sample C, CV varied between 10% and 12.5% but samples had relatively low creatinine. This is higher than the interlab CV 2024 for Special Assays in Urine (5.5%, n = 128).



Sample	A	B	C	D	E	F
Median	5.90	3.00	4.38	5.53	2.30	3.85
SD	0.70	0.71	0.68	0.63	0.27	0.38

8.2. Patient A

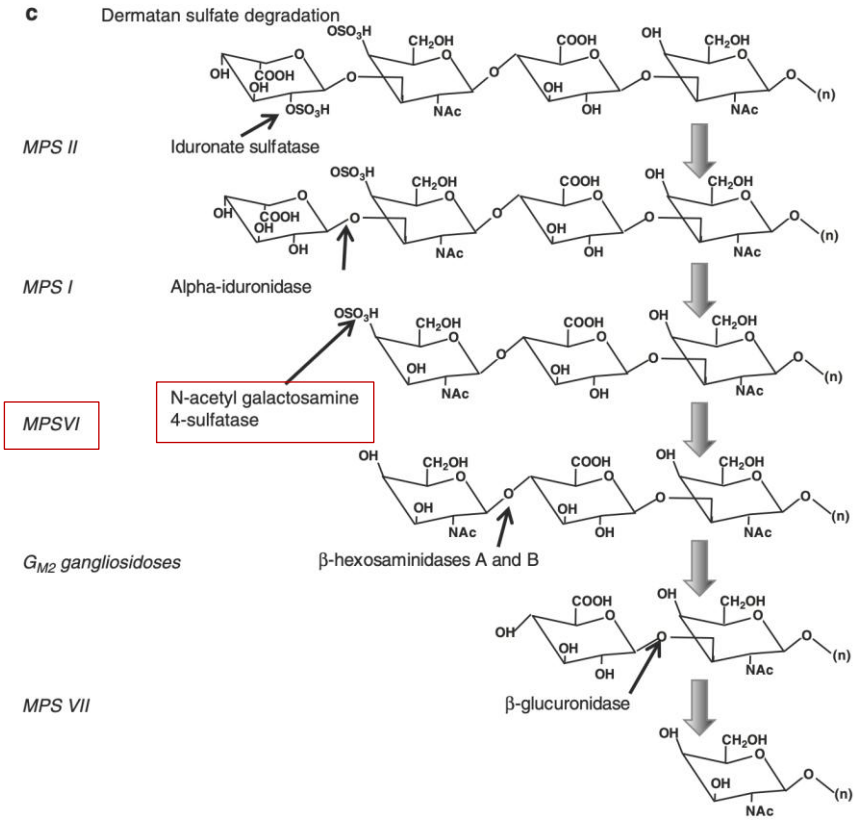
Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome, arylsulfatase B deficiency, *ARSB* gene)

Patient details provided to participants

15-year-old boy. Dysmorphic features, scoliosis, size -1.5 SD, normal intellectual development. Under treatment.

Patient details

It is the common sample distributed to all DPT centres. A separate presentation is available on ERNDIM website. The patient is a 15-year-old boy, born after a normal pregnancy and delivery. From 2 months to 6 years of age, he had frequent upper airways infections. His height at 1 year of age was +3 SD. Pectus carinatum was noted at 3 years of age. At 10 years of age, he presented with scoliosis with platyspondyly, dorsal kyphosis, a narrow cervical canal and decreased visual and hearing acuity. At 15 years of age, his intellectual development is normal, and his height is -1.5 SD. He underwent back surgery with arthrodesis of T10 to T12. At that time, urinary MPS analysis was requested because of spine abnormalities and dysmorphic features. Diagnosis of MPS VI was confirmed by measuring arylsulfatase B activity in leucocytes. Since then, he has received weekly enzyme replacement therapy.



From Physician's Guide to the Diagnosis, Treatment and Follow-up of Inherited Metabolic Diseases, 2023.

Mucopolysaccharidosis type VI, also called Maroteaux-Lamy syndrome, is a rare autosomal recessive lysosomal storage disorder due to arylsulfatase B deficiency (*ARSB* gene). Patients present with a wide phenotypic spectrum (S Jones, F Wijburg, Inborn Metabolic Diseases – Diagnostic & Treatment, 2016):

- Usual signs: short stature, dysostosis multiplex, degenerative joint disease
- Frequent signs: cardiac valve disease, hearing loss, obstructive sleep apnoea, corneal, clouding, carpal tunnel disease, and inguinal or umbilical hernia
- Possible signs: cervical cord compression, communicating hydrocephalus, optic nerve atrophy and blindness

Arylsulfatase B (also called N-acetylgalactosamine 4-sulfatase) is a lysosomal enzyme which removes 4-sulfate groups from the non-reducing end of chondroitin 4-sulfate and dermatan sulfate and thereby regulates their degradation.

Analytical performance

Seventeen out of 19 participants performed **GAGs quantification**. Fifteen of them reported an increased excretion, whereas 2 mentioned a normal excretion (one using DMB assay and the other using harmine assay). **GAGs fractionation** was also performed by 17 labs. They reported an increase in:

- **Dermatan sulfate**: **13 labs**
- Chondroitin sulfate: 9 labs
- Heparan sulfate: 6 labs
- Keratan sulfate: 1 lab

Among the 11 participants who performed oligosaccharides, 9 reported a normal profile and 2 a slight increase in sialyl-oligosaccharides.

Diagnosis / Interpretative proficiency

Most likely diagnosis

Mucopolysaccharidosis type VI	**8**
MPS I, MPS II or **MPS VI**	**1**
Mucopolysaccharidosis type IV	8
Mucopolysaccharidosis	2

Alternative diagnosis

MPS VI or MPS VII	**2**
MPS I, MPS II, **MPS VI** or MPS VII	**2**
MPS I or MPS II	1
MPS IV	1
Oligosaccharidosis	1

Scoring

- **Analytical performance**
  - Increase in dermatan sulfate (score 2)
  - Increase in GAGs quantification (score 1)
- **Interpretation of results**
  - MPS VI as first or alternative diagnosis (score 2)
  - Other or wrong MPS type, diagnosis of MPS VI according to clinical signs (score 1)
- **Critical error:** failure to diagnose or suspect a mucopolysaccharidosis. Number of occurrences: 0

Multiple distributions of similar samples

A similar urine samples have been distributed in 2006 and 2015: the overall performance was slightly better.

	2006	2015	**2025**
Analytical performance	**84 %**	**87 %**	**79 %**
Interpretative performance	**82 %**	**89 %**	**82 %**
Overall performance	**84 %**	**88 %**	**80 %**

8.3. Patient B

Hawkinsinuria, autosomal dominant deficiency of 4-hydroxyphenylpyruvate dioxygenase (gene *HPD*)

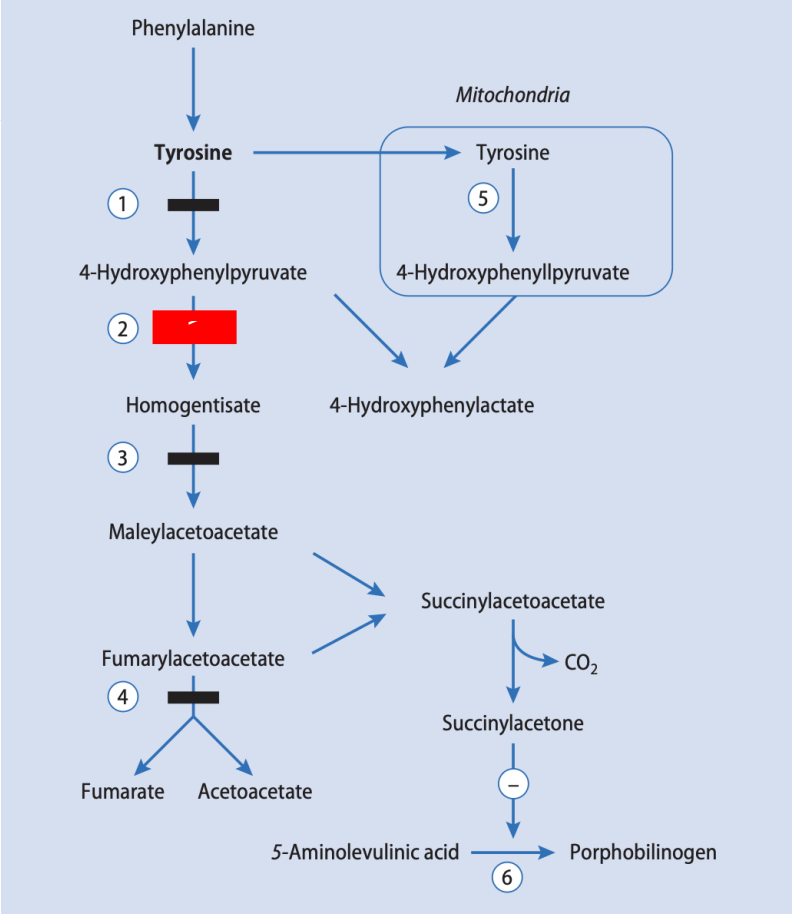
Patient details provided to participants

Adult female. Feeding difficulties and failure to thrive in infancy. Evaluation at the age of 12 months revealed mild developmental delay and metabolic acidosis. Today well.

Patient details

This 21-year-old female patient presented feeding difficulties and failure to thrive in infancy. An evaluation at the age of 12 months revealed a mild developmental delay and metabolic acidosis, but she is well today. At the time of sample collection, the patient was pregnant.

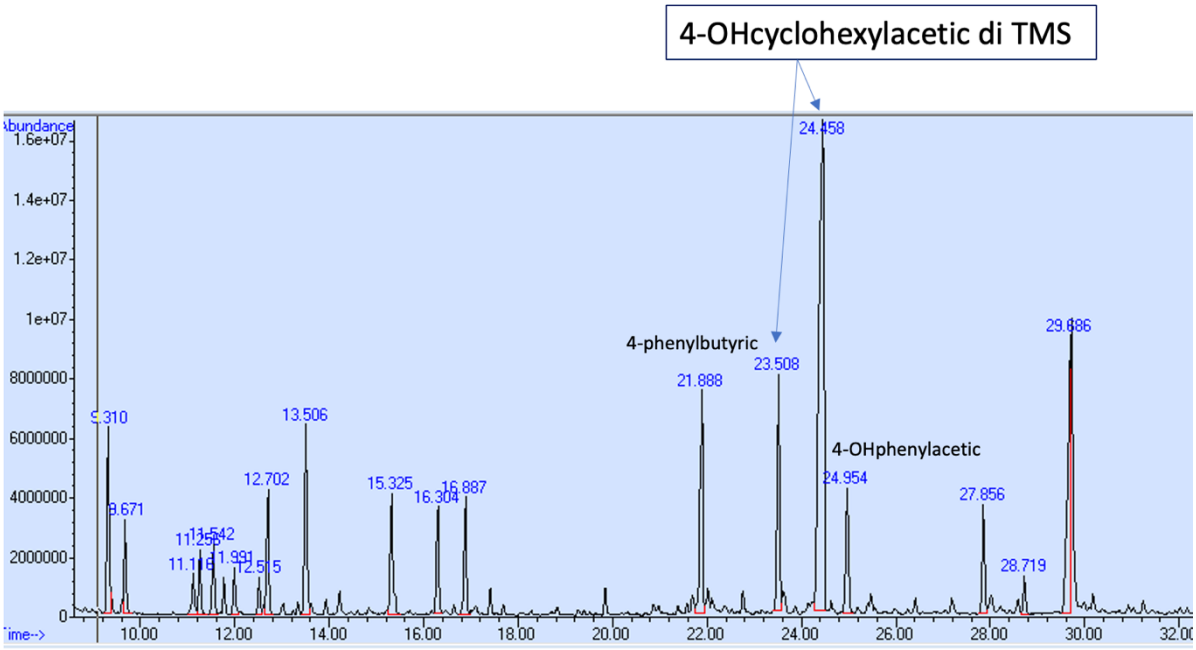
Hawkinsinuria is a very rare autosomal dominant IEM, not completely understood. Patients can present with failure to thrive and acidosis in the first year of life, but this does not occur in all affected infants. Symptoms normalise after the first year of life. The biochemical diagnosis relies on plasma amino acid analysis with the identification of Hawkinsin (2-cystenyl-1, 4-dihydroxycyclohexenylacetate - eluted between urea and threonine using IEC) and a slight increase in tyrosine (only in infancy), and on urinary organic acids with the identification of Hawkinsin (2-cystenyl-1, 4-dihydroxycyclohexenylacetate) at any time, of 4-hydroxycyclohexylacetatic acid (cis and trans - appear after infancy), and the increase of 4-hydroxyphenylacetate, 4-hydroxyphenyllactate, and 4-hydroxyphenylpyruvate (in infancy).
The disease is due to gain-of-function variants of 4-hydroxyphenylpyruvate dioxygenase gene (*HPD)*, the same gene in than tyrosinemia type III. Hawkinsin and 4-hydroxycyclohexylacetate are thought to derive from incomplete conversion of 4-hydroxyphenylpyruvate to homogentisate.

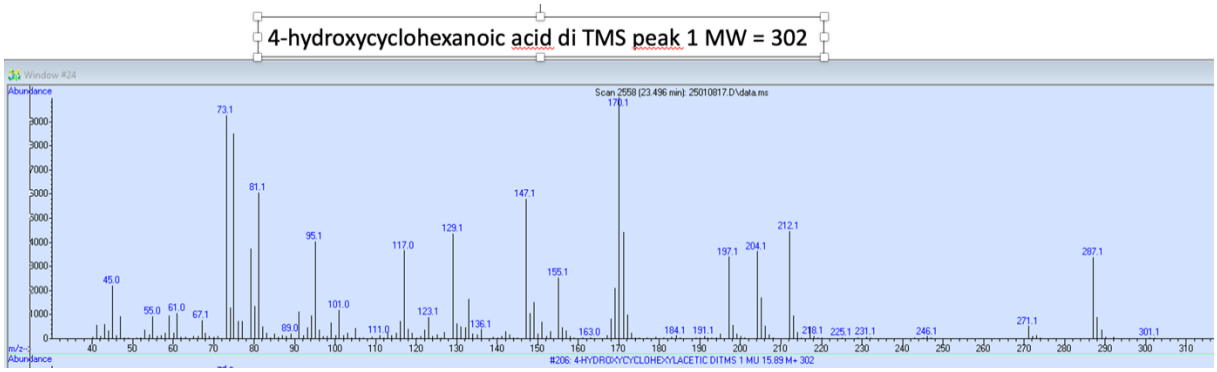


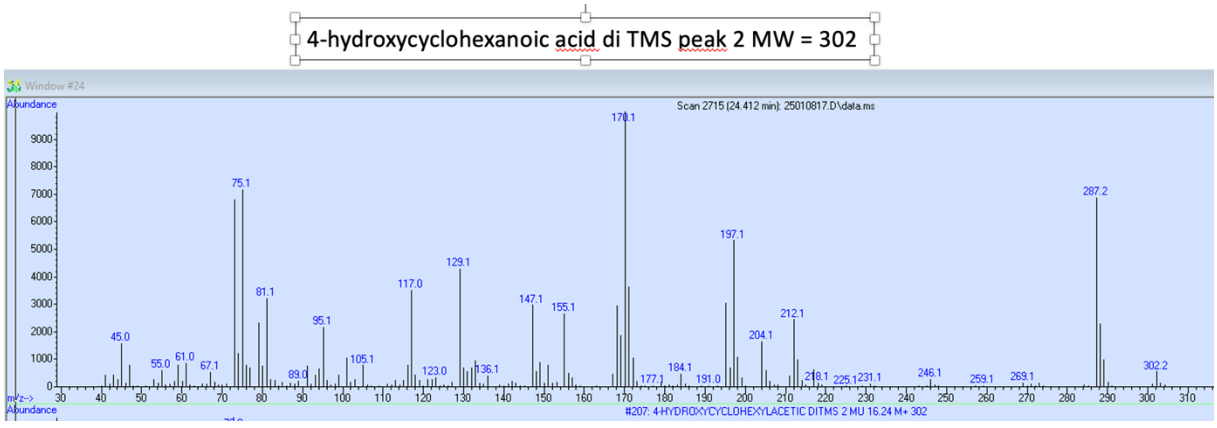
From Inborn Metabolic Diseases. Diagnosis & Treatment, 6th Edition

All participants performed organic acid analysis and 16 of them reported the identification of **4-hydroxycyclohexylacetic acid** (cis and/or trans) (562 ; 660 mmol/mol creatinine ; n = 2). Three mentioned that there was no increase in 4-hydroxyphenyllactic and 4-hydroxyphenylacetic acids, and one in 4-hydroxyphenylacetic acid.

Cis and trans-4-hydroxycyclohexylacetic acid are eluted between 4-phenylbutyric acid (the internal standard) and 4-hydroxyphenylactic acid (see below).



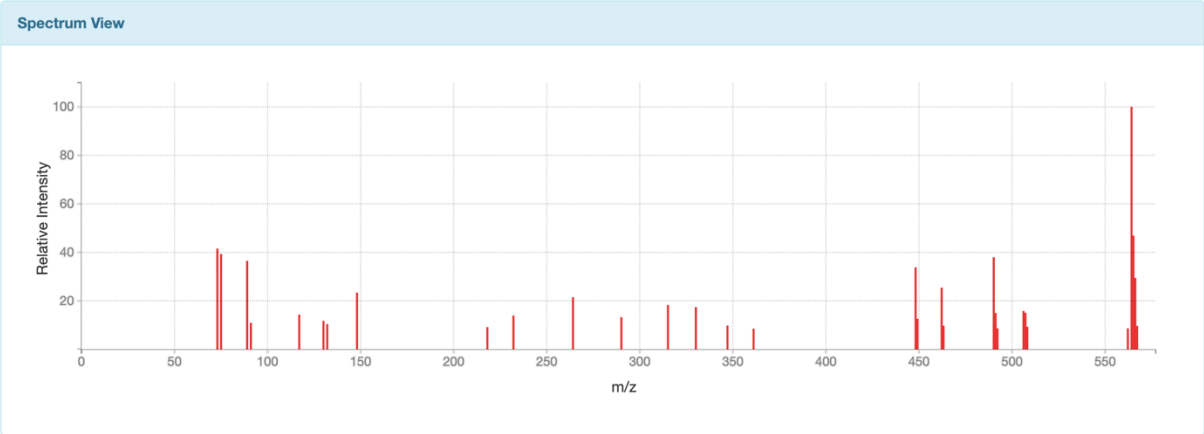




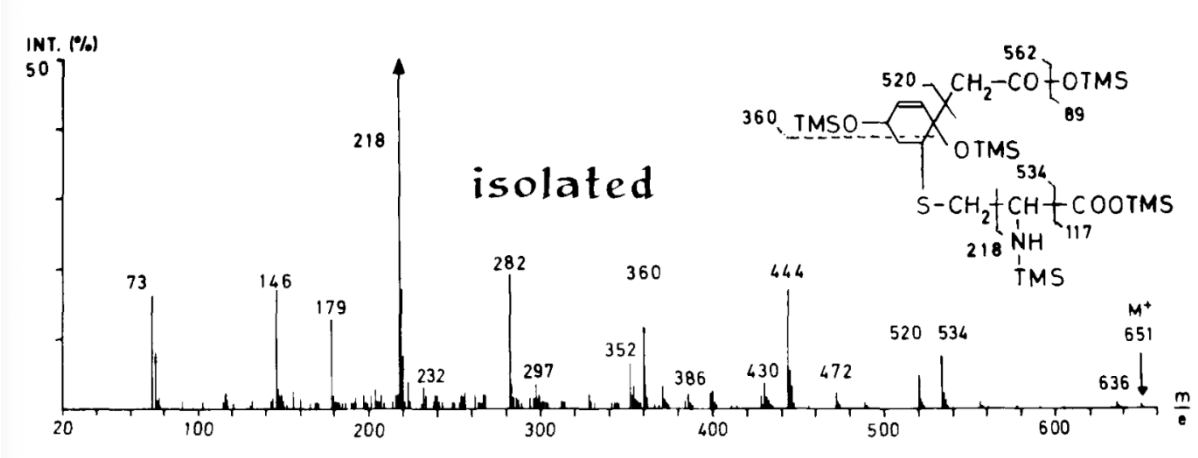
Trans-4-hydroxycyclohexylacetic is excreted in large amounts in hawkinsinuria. However, it has been detected in a few different foods such as duck, chicken and pig and therefore it could be a potential biomarker for the consumption of these foods.
https://foodb.ca/compounds/FDB022313#:~:text=trans%2D4%2DHydroxycyclohexylacetic%20acid%2C,Next

None of the participants reported an increase in hawkinsin (2-cystenyl-1, 4-dihydroxycyclohexenylacetate) in the organic acid profile. We failed to identify this compound. Its theoretical mass spectrum is:

Hawkinsin 4 TMS (2-cystenyl-1, 4-dihydroxycyclohexenylacetatic acid) putative spectrum, MW = 579.
From: **https://foodb.ca/spectra/c_ms/38384**



Hawkinsin 5 TMS, MW = 651
From Niederwiser et al. Clin Chim Acta 1977, 76:345-356



Diagnosis / Interpretative proficiency

Most likely diagnosis

Hawkinsinuria	**14**
Tyrosinemia type III	2
Iminoglycinuria	2
3HMG-CoA lyase deficiency	1

Alternative diagnosis

Hyperprolinemia type I	2
Serine biosynthesis disorder	1

Scoring

- **Analytical performance**
  - Identification of 4-hydroxycyclohexylacetic acid (cis or trans) or Hawkinsin (2-cysteinyl-1,4-dihydroxycyclohexenylacetic acid) (score 2)

- **Interpretation of results**

- Hawkinsinuria as main or alternative diagnosis (score 2)
- Tyrosinemia type III (score 1)

- **Critical error:** sample not eligible

Multiple distributions of similar samples

This is the first time that such a urine sample has been distributed. The overall proficiency was satisfying.

	2025
Analytical performance	**84 %**
Interpretative performance	**79 %**
Overall performance	**82 %**

8.4. Patient C

Maple syrup urine disease (MSUD), deficiency of branched-chain 2-ketoacid dehydrogenase complex.

Patient details provided to participants

25-year-old girl. Coma at 9 days of life with seizures treated by anticonvulsant drugs and peritoneal dialysis. Poor compliance to treatment. Waiting for liver transplant.

Patient details

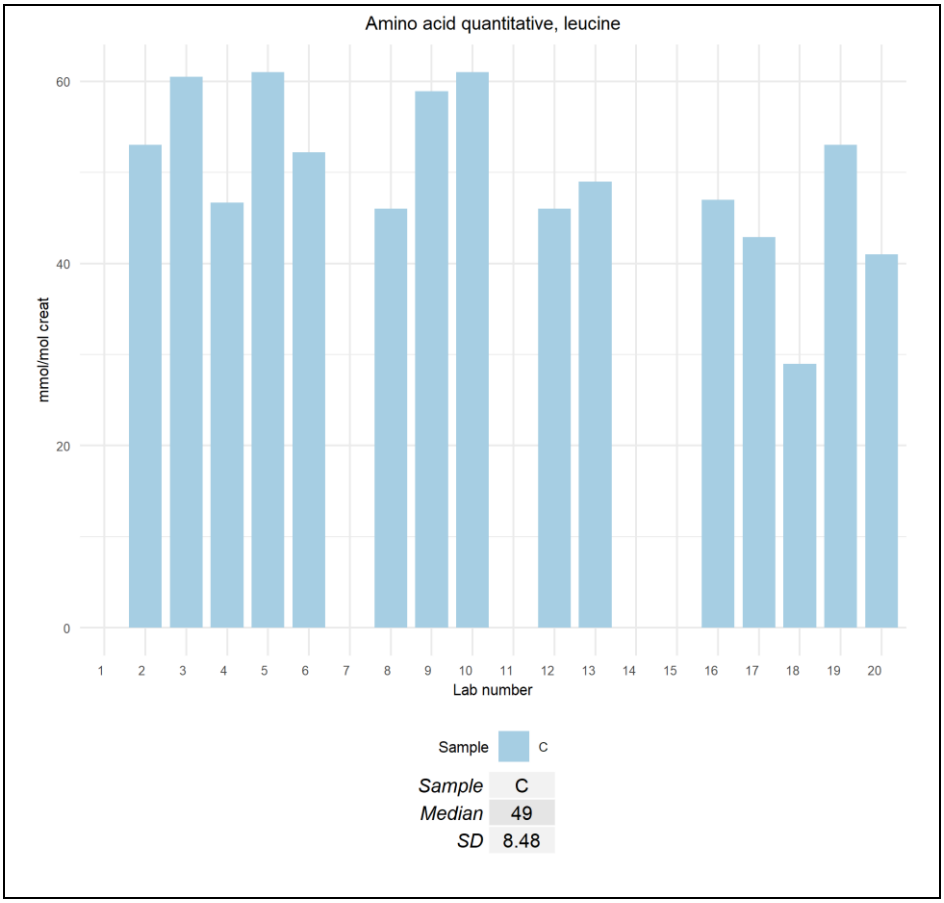
The patient is a 25-year-old adult woman. The disease was revelated by digestive and neurological signs leading to a coma with seizures at 9 days of life, treated by phenobarbital, phenytoin and peritoneal dialysis. The management has always been difficult since the patient has never accepted the low protein diet, leading to feeding difficulties. A gastrostomy was placed at the age of 3 years. The course of the disease was marked by numerous episodes of decompensation and the subsequent development of slight mental retardation. She is waiting for liver transplant.

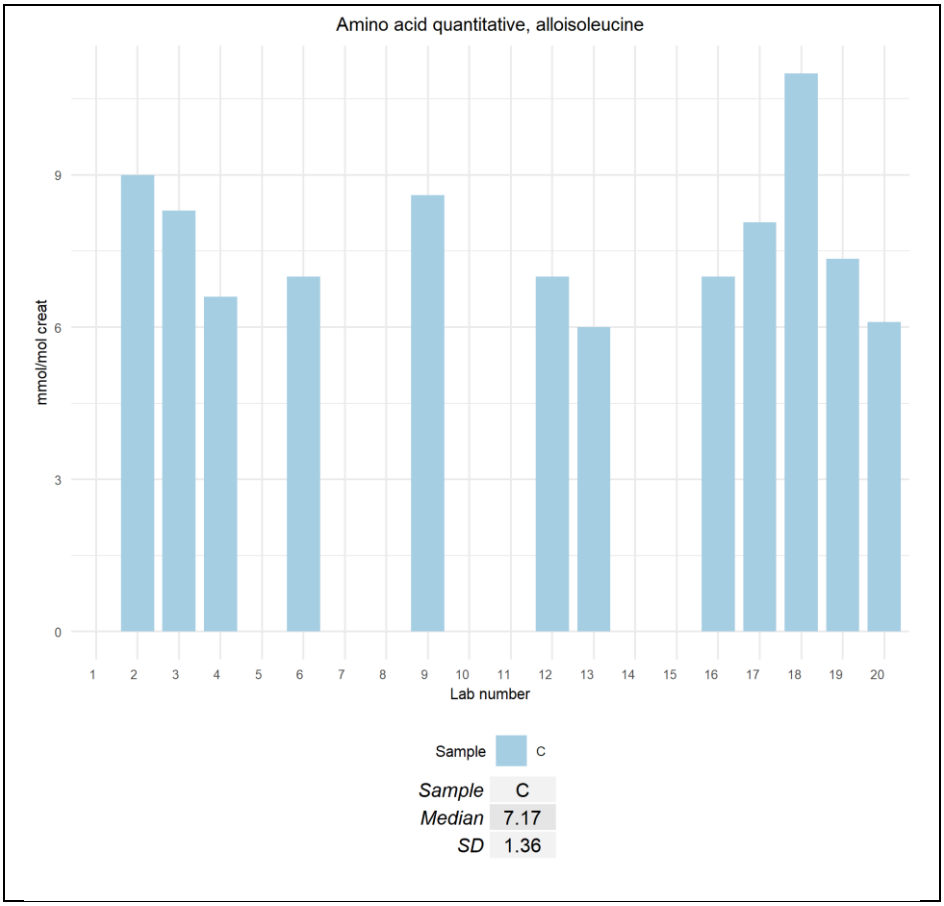
Analytical performance

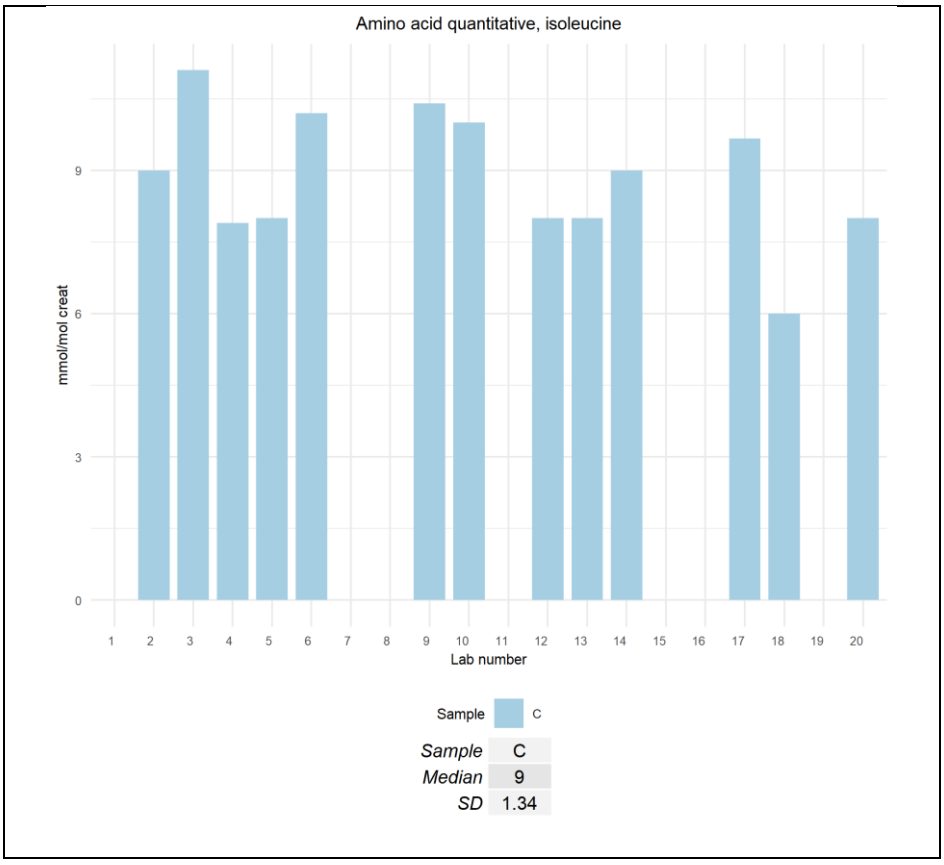
All participants but one performed **amino acids** (18/19). They reported an increase in:

- **Leucine** **15**
  (median = 49 mmol/mol creatinine; range : 29.0 – 61.0 ; n = 15)
- **Alloisoleucine** **14**
  (median = 7.2 mmol/mol creatinine; range : 6.0 – 11.0 ; n = 12)
- **Isoleucine** **13**
  (median = 9 mmol/mol creatinine; range : 6.0 – 11.1 ; n = 15)
- **Valine** **12**
  (median = 14.4 mmol/mol creatinine; range : 1.0 – 17.9 ; n = 12)

But 2 labs reported a normal profile, using IEC.




Amino acid quantitative, alloisoleucine
mmol/mol creat
0
3
6
9
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Lab number
Sample C
Sample C
Median 7.17
SD 1.36


Amino acid quantitative, isoleucine
mmol/mol creat
0
3
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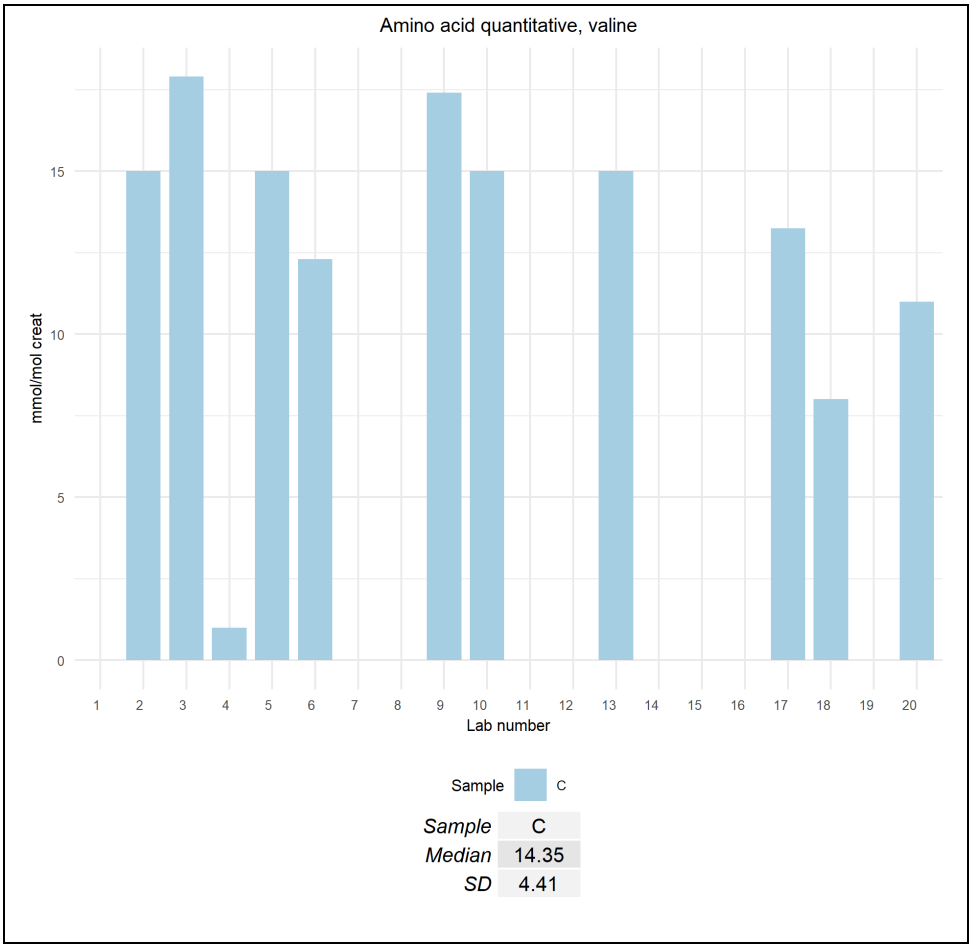
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Lab number
Sample C
Sample C
Median 9
SD 1.34



The coefficient of variation for the measurement of these amino acids varied between 15 and 31%.

All participants performed **organic acids** (19/19), and mentioned an increase in:

- **2-ketoisocaproic acid** **13**
  (12 ; 38 ; 120 mmol/mol creatinine ; n = 3)
- **2-keto-3-methylvaleric** **9**
  (28 ; 90 mmol/mol creatinine ; n = 2)
- **2-ketoisovaleric acid** **6**
  (35 mmol/mol creatinine ; n = 1)
- **2-hydroxyisovaleric acid** **16**
  (median = 96 mmol/mol creatinine; range : 76 – 140 ; n = 4)
- **2-hydroxyisocaproic acid** **9**
  (4 ; 40 mmol/mol creatinine ; n = 2)
- **2-hydroxy-3-methylvaleric acid** **9**

One participant reported an isolated increase in 3-hydroxyisovaleric acid.

Diagnosis / Interpretative proficiency

Most likely diagnosis

Maple Syrup Urine disease	18
(leucinosis, branched-chain 2-ketoacid dehydrogenase complex def.)	
Isovaleric aciduria	1

Alternative diagnosis

E3 deficiency	2
(dihydrolipoamide dehydrogenase deficiency)	

Scoring

- **Analytical performance**
  - Elevation of at least four diagnostic metabolites among branched-chain amino acids (alloisoleucine, leucine, isoleucine, valine), branched-chain 2-keto and 2-hydroxyacids (2-ketoisocaproic, 2-ketoisovaleric, 2-keto-3-methylvaleric, 2-hydroxyisocaproic, 2-hydroxyisovaleric, 2-hydroxy-3-methylvaleric acids) (score 2)

- **Interpretation of results**
  - MSUD as main diagnosis (score 2)

- **Critical error:** failure to diagnose MSUD. Number of occurrences: 1

Multiple distributions of similar samples

A similar urine sample has been distributed in 2003: the overall performance was similar.

	2003	2025
Analytical performance	**87 %**	**95 %**
Interpretative performance	**100 %**	**95 %**
Overall performance	**95 %**	**95 %**

8.5. Patient D

GM1 gangliosidosis (beta-galactosidase deficiency, *GLB1* gene)

Patient details provided to participants

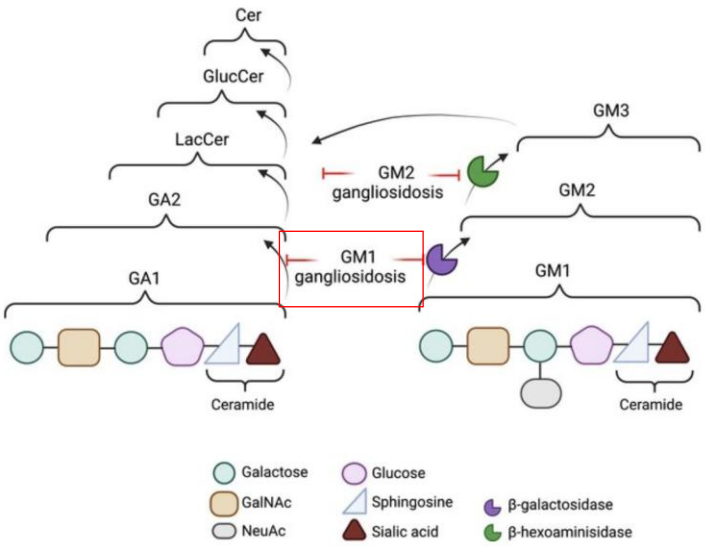
Female, 9-year-old. Mild intellectual disability, language disorder, hypotonia, facial dysmorphia, minor limb anomalies, walking difficulties.

Patient details

This 9-year-old girl is born from unrelated parents. She presented with mild intellectual disability, language disorder, hypotonia, facial dysmorphia, minor limb anomalies and walking difficulties. The diagnosis was confirmed enzymatically (beta-galactosidase activity in leukocytes reduced by 99%) and genetically (compound heterozygosity for 2 missense variants in *GLB1* gene) at 9 years of age. The results were compatible with the pathological phenotype of the patient and the diagnosis of GM1 gangliosidosis type II (late infantile/juvenile).

GM1 gangliosidosis can have different clinical presentations:

- Severe **neonatal form**, with cardiomyopathy. It can also be a cause of ***hydrops fetalis***,
- **Early infantile form** (type I): the more frequent, with early developmental delay, and neurological disease, hepatosplenomegaly, coarse features, Hurler-like bone changes. Death occurs by 1-2 years of age,
- **Late infantile variant** (type II): a slower course with loss of developmental milestones,
- **Adult form** (type III): very rare, cerebellar dysfunction.



Caption

Catabolism of GM1 and GM2 gangliosides and other sphingolipids. GM1 ganglioside is metabolized to GM2 ganglioside by β-galactosidase and, subsequently, GM2 is converted to GM3 by β-hexosaminidase and/or GM2 activator protein (not pictured). Deficiencies in these enzymes lead to accumulation in these sphingolipids leading to GM1 or GM2 based on enzyme defect. Abbreviations: GalNAc, N-acetylgalactosamine; NeuAc, N-acetylneuraminic acid; GM1, GM1 ganglioside; GM2, GM2 ganglioside; GM3, GM3 ganglioside; GA1, GA1 ganglioside; GA2, GA2 ganglioside; LacCer, lactosylceramide; GlucCer, glucosylceramide; Cer, ceramide.

Diagnosis / Interpretative proficiency

Most likely diagnosis

GM1 gangliosidosis (GM1 type I, II or III, beta-galactosidase deficiency)	**13**
Aspartylglucosaminuria	2
Hyperphenylalaninaemia	2
Mucopolysaccharidosis type I, II or VI	1
Creatine transporter deficiency	1
No abnormality detected	1

Alternative diagnosis

MPS IVB (Morquio B)	4
Galactosialidosis	2
Another oligosaccharidosis	1
Hyperphenylalaninaemia	2

GAMT deficiency	1
Creatine transporter deficiency	1

Scoring

- **Analytical performance**
  - Oligosaccharide profile evocative of GM1 gangliosidosis (score 2)
  - Oligosaccharide profile evocative of aspartylglucosaminuria (score 1)

- **Interpretation of results**
  - GM1 gangliosidosis (score 2)
  - Aspartylglucosaminuria (score 1)

- **Critical error:** sample not eligible

Multiple distributions of similar samples

Two similar urine samples have been distributed in 2015 and 2017: the overall performance was previously better.

	2015	2017	**2025**
Analytical performance	**78 %**	**84 %**	**70 %**
Interpretative performance	**80 %**	**92 %**	**70 %**
Overall performance	**79 %**	**88 %**	**70 %**

8.6. Patient E

Primary hyperoxaluria type II (glyoxylate reductase / hydroxypyruvate reductase deficiency - GRHPR gene)

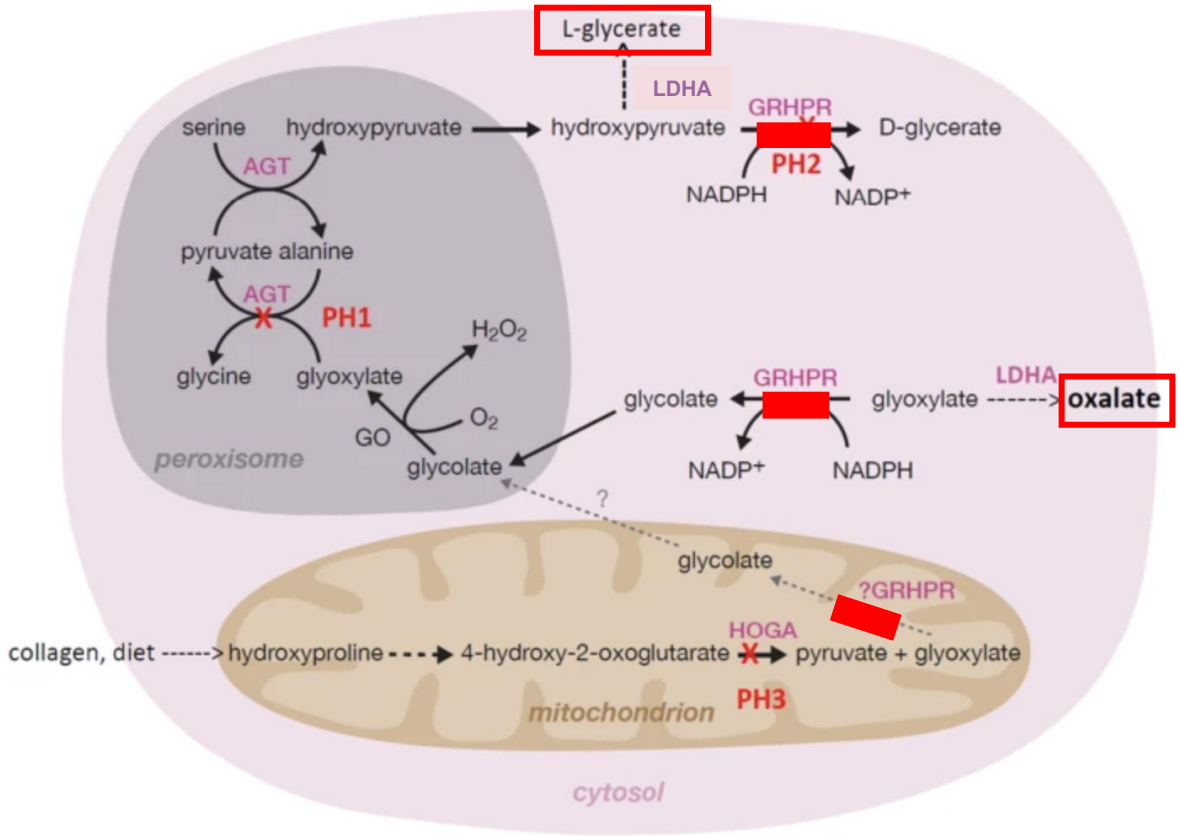
Patient details provided to participants

6-year-old boy. Antenatal bilateral pyelectasis. At birth, hyperechogenic kidneys and nephrocalcinosis. First episode of haematuria at 8 months of age. Today well under treatment.

Patient details

The patient is a 6-year-old boy. He presented antenatal bilateral pyelectasis, and, at birth, hyperechogenic kidneys and nephrocalcinosis. At 8 months of age, he had a first episode of haematuria. An elevated oxalic acid excretion was documented at 13 months of age: oxalic acid = 445 mmol/mol creat (controls: <120), but glycolic acid excretion was normal. A gene panel for hyperoxalurias was performed at 15 months of age and diagnosed a compound heterozygosity for 2 variants in *GRHPR* gene. The high increase in glyceric acid (organic acids) confirmed the pathogenicity of the variants. A treatment with potassium citrate and hyperhydration was initiated and completed at 4 years of age by the introduction of stiripentol, an antiepileptic drug which has been shown to inhibit neuronal lactate dehydrogenase and to reduce hepatic oxalate production. Today he is well under this treatment.

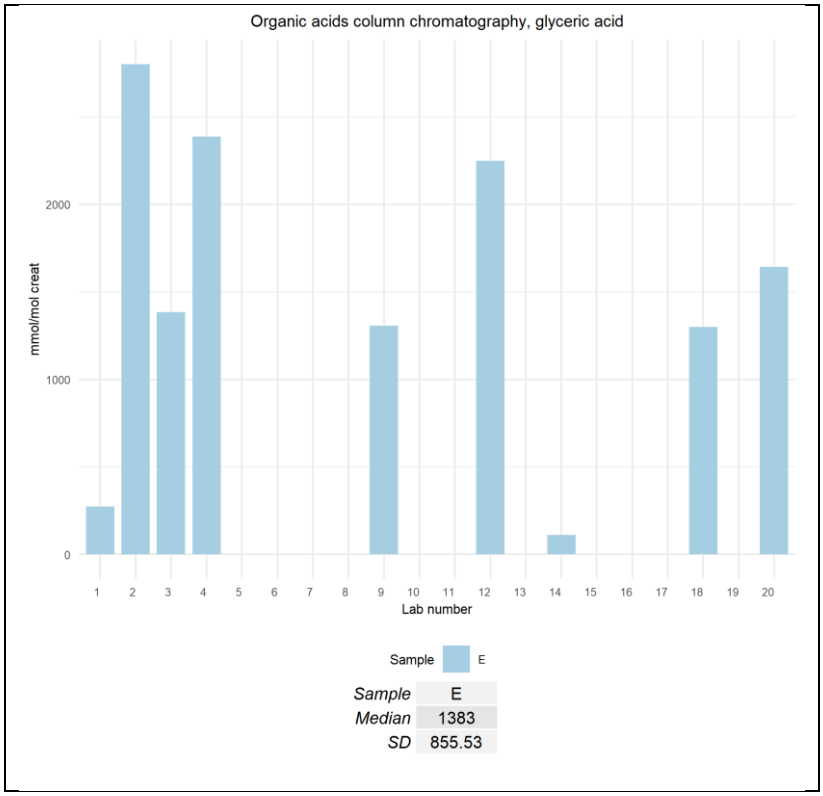
Primary hyperoxaluria type II is rare autosomal recessive disorder. The clinical course is comparable but generally less severe as compared to primary hyperoxaluria type I, and includes nephrocalcinosis, nephrolithiasis, renal colic. Chronic kidney disease (CKD) and end stage renal failure (ESRF) occur less frequently: they have not been reported in childhood but affects about 50% of adult patients. It is due to a defect in the glyoxylate reductase / hydroxypyruvate reductase (GR/HPR) activity (*GRHPR* gene), a cytosolic enzyme. Lack of GR/HPR leads to an accumulation of glyoxylate and hydroxypyruvate, which are both metabolized by lactate dehydrogenase A to oxalate and L-glycerate, respectively. A single nucleotide deletion, c.103delG, accounts for 31–35% of mutant alleles in hyperoxaluria type II, mainly restricted to those of Caucasian descent.

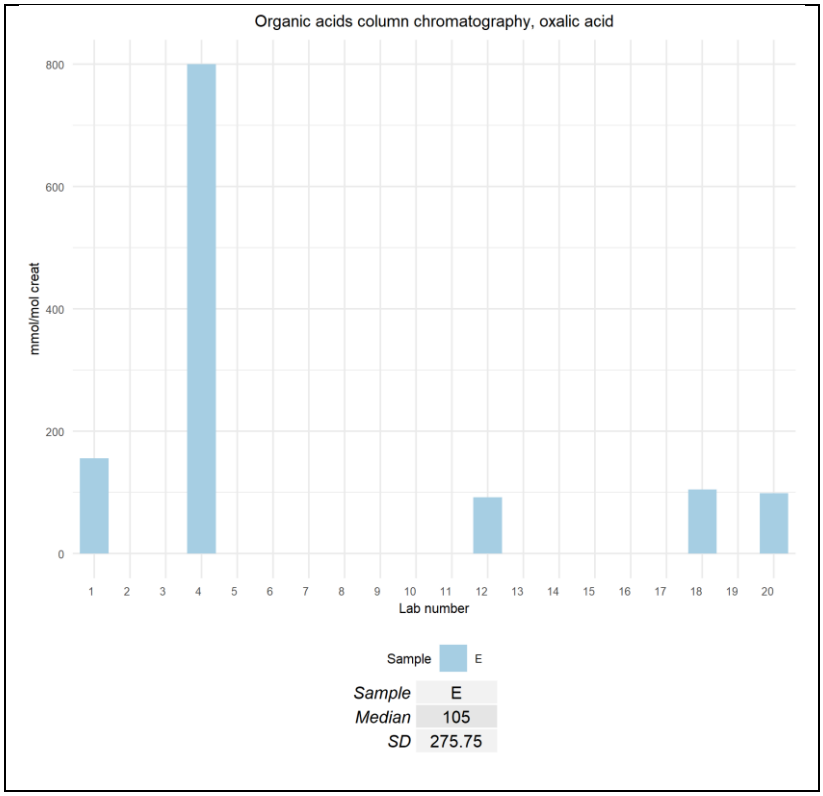


From PMID: 35695965

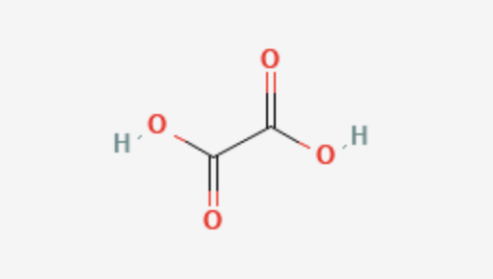
Analytical performance

All labs performed **organic acids** (20/20) and reported an increase in **glyceric acid** (median = 1383 mmol/mol creatinine; range: 110 – 2800 ; n = 9), but only 9 of them reported an increase in **oxalic acid** (99 ; 105 ; 109.5 ; 156 ; 800 mmol/mol creatinine ; n = 4). Height participants mentioned that glycolic acid excretion (median = 42.5 mmol/mol creatinine; range: 28 – 169 ; n = 4) was normal, and 4 specified that oxalic acid excretion was normal.





No participant performed a **specific measurement of oxalic acid**. Before sending the urine samples, the scientific advisors measured oxalic acid excretion using GC/MS with stable isotope dilution. It was significantly elevated = 277 mmol/mol creat (controls: 17 – 100).
Oxalic acid is a polar compound that is poorly extracted by organic solvents such as ethylacetate. In addition, in urine it occurs mainly as calcium oxalate and precipitates at alkaline pH. Therefore, for an accurate measurement of oxalic acid, urines must be acidified prior to extraction to solubilize oxalic acid, and a stable isotope of oxalic acid must be added as internal standard, to normalize experimental variables such as extraction. This probably explains why most labs did not report an increase in oxalic using a standard organic acid analysis.



Diagnosis / Interpretative proficiency

Most likely diagnosis

Hyperoxaluria type II	19
(L-glyceric aciduria, glyoxalate/hydroxypyruvate reductase def.)	
Hyperoxaluria type I	1

Alternative diagnosis

D-glyceric aciduria	4
Double compound hyperoxaluria type II & III	1

Recommendations

The recommendation to perform specific oxalic acid quantification was important for this sample.

Scoring

- **Analytical performance**
  - Increase in glyceric acid (score 1)
  - Increase in oxalic acid or recommendation to perform specific oxalic acid quantification (score 1)

- **Interpretation of results**
  - Hyperoxaluria type II (score 2)
  - Primary hyperoxaluria type I (score 1)

- **Critical error:** failure to detect an increase in glyceric or oxalic acids. Number of occurrences: 0

Multiple distributions of similar samples

This is the first time that such a urine sample has been distributed, and the overall performance was quite good.

	2025
Analytical performance	**90 %**
Interpretative performance	**98 %**
Overall performance	**94 %**

8.7. Patient F

Glutaric aciduria type I, low excretor (glutaryl-CoA dehydrogenase deficiency, *GCDH* gene)

Patient details provided to participants

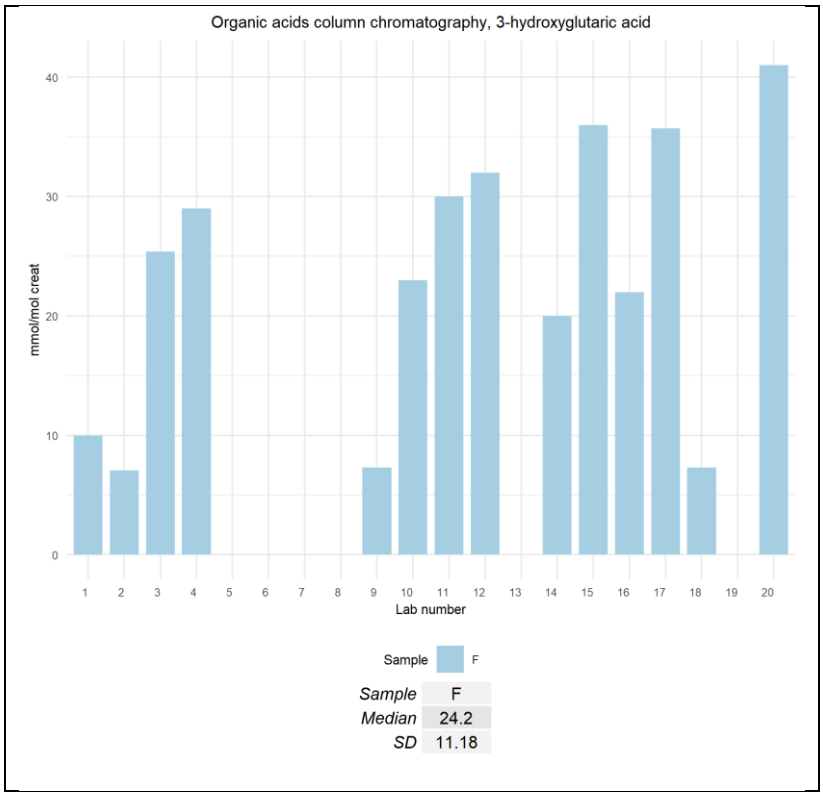
57-year-old women, born from consanguineous parents. Has been complaining for many years of fatigue, balance problems, and recently of reduced walking perimeter. Abnormal brain MRI and electroneuromyogram.

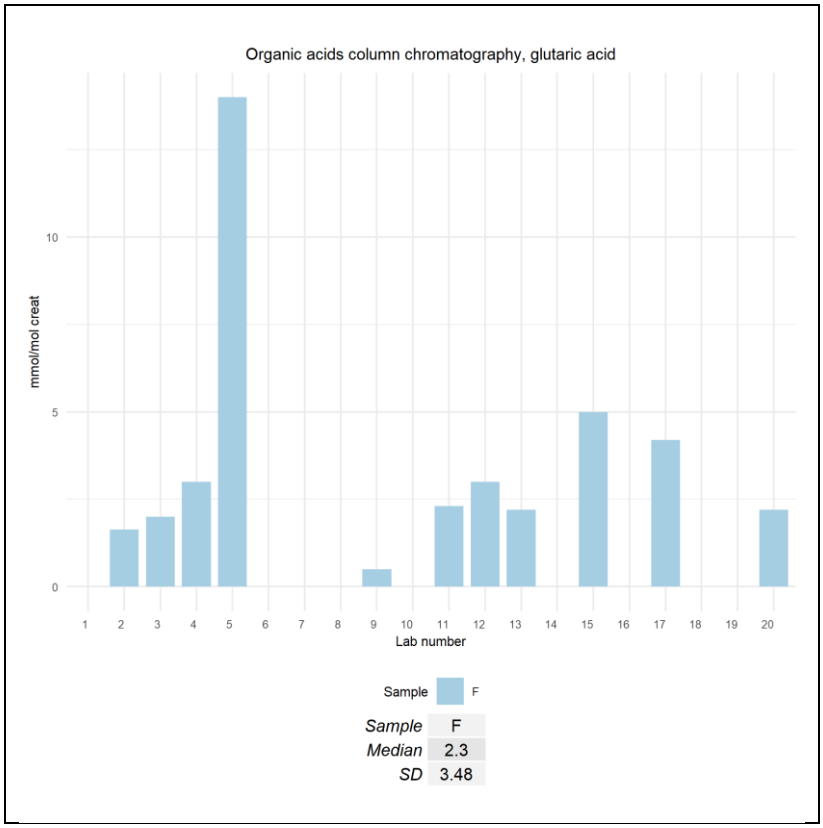
Patient details

This 57-year-old women is born from consanguineous parents. She has been complaining for many years of fatigue, dyspnea, balance problems, and recently of reduced walking perimeter, and cognitive problems. Brain MRI and electroneuromyogram were abnormal (no details provided). DBS acylcarnitine profile, performed as part of a broader etiological assessment, revealed an increase in glutarylcarnitine. Urinary organic acids showed an isolated increase in 3-hydroxyglutaric acid. The diagnosis of glutaric aciduria type I, low excretor, was confirmed by mutation analysis of *GCDH* gene (homozygosity for a deleterious variant).

Analytical performance

All participants performed **organic acids** (20/20) and reported an increase in **3-hydroxyglutaric acid** (median = 24.2 mmol/mol creatinine; range: 7.06 – 41 ; n=14). Only one reported an increase in glutaric acid (no quantification), whereas 13 of them mentioned a normal excretion (median = 2.3 mmol/mol creatinine; range: 0.5 – 14.0 ; n=11).





We tried to compare the excretion of 3-hydroxyglutaric acid in the different conditions:

- Glutaric aciduria type I, low excretors of glutaric acid (Busquets, Merinero et al, Pediatric Research 2000;48: 315–322): results from 17 patients.

mmol/mol creat	Range	Median	Mean	Controls
3-hydroxyglutarate	**18 - 571**	**101**	**160**	**2 – 14**
Glutarate	2 - 84	10	21	2 – 10

- SCHAD deficiency (*Vilarinho et al, Mol Genet Metab 2012;106:277, **Martins et al, JIMD 2011;34:835, ***Patient from Centre de Biologie Est)

	1*	2**	3**	4**	5**	8***
Plasma C4OH acylcarnitine (µmol/L)	1.22			0.5 - 0.6	0.7	0.7 - 1.6
Urinary 3-hydroxy glutarate (mmol/mol creat)	**113**	**12 - 45**	**22 - 45**	**33 - 114**	**55**	**13 - 31**

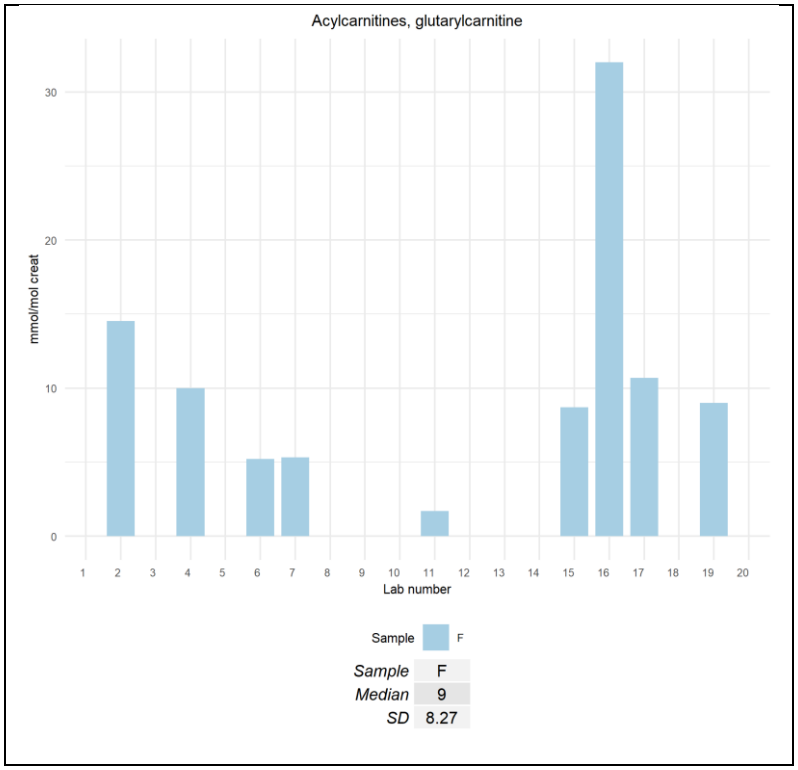
- CPT I deficiency (Korman et al, Mol Genet Metab 2005;86:337)

mmol/mol creat	Patient 1	Patient 2	Patient 3	Controls
Age	14 months	3 years	23 months	
3-hydroxyglutarate	**9.8**	**24.7**	**14.7**	0.88 – 4.5
Glutarate	3.4	1.2	2.3	0.5 – 10.8
Dicarboxylic acids	C6 – C12	C6 – C12	C6 – C12	

- Ketotic states: <10 mmol/mol creat (in our experience)

Therefore, it seems that 3-hydroxyglutarate excretion is higher in glutaric aciduria type I than in SCHAD deficiency, with even lower excretion in CPT I deficiency and ketotic states.

The 11 labs that performed **acylcarnitines (11/20)** reported an increase in **glutarylcarnitine** (median = 9 mmol/mol creatinine; range: 1.7 – 32 ; n=9).



It may seem unusual to perform urinary acylcarnitines. In 2005, Tortorelli et al. investigated 14 GA-I patients (5 of them had a normal glutaric acid excretion and 9 a normal plasma acylcarnitine profile) and 54 subjects with glutaric aciduria secondary to other causes (16-7509 mmol/mol creatinine; reference range: <15) but a normal excretion of 3-hydroxyglutaric acid. They demonstrated that the excretion of glutarylcarnitine was significantly elevated in the 14 GA-I patients (14-522 mmol/mol creatinine; reference range: <5.2), whereas it was normal in the 54 "control" subjects with glutaric aciduria secondary to other causes. They concluded: "Urinary excretion of **glutarylcarnitine is a specific biochemical marker of glutaric aciduria type I** which could be particularly useful in the work up of patients with suggestive clinical manifestations but without glutaric aciduria and with normal plasma acylcarnitine profiles".

(Tortorelli S, Hahn SH, Cowan TM, Brewster TG, Rinaldo P, Matern D. The urinary excretion of glutarylcarnitine is an informative tool in the biochemical diagnosis of glutaric acidemia type I. Mol Genet Metab. 2005;84(2):137-43)

Diagnosis / Interpretative proficiency

Most likely diagnosis

Glutaric aciduria type I (GAI low excretor, glutaryl-CoA dehydrogenase def.)	18
Pompe disease	2

Alternative diagnosis

Glutaric aciduria type I, late onset	1
Glutaric aciduria type II	2
CPT I, SCHAD def.	1

Scoring

- **Analytical performance**
  - Increase in 3-hydroxyglutaric acid and/or glutarylcarnitine (score 2)

- **Interpretation of results**
  - Glutaric aciduria type I as main diagnosis (score 2)

- **Critical error:** failure to propose glutaric aciduria type I as first or alternative diagnosis. Number of occurrences: 1

Multiple distributions of similar samples

A similar urine sample (low excretor) has been distributed in 2018: the analytical performance is perfect in both samples, but the overall performance was better in the 2018 sample, probably because 3-hydroxyglutaric acid excretion was higher.

	2018	**2025**
Analytical performance	**100 %**	**100 %**
Interpretative performance	**100 %**	**93 %**
Overall performance	**100 %**	**96 %**

9. Scores of participants

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

Detailed scores – Round 1

Lab n°	Patient A Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome, arylsulfatase B deficiency, *ARSB* gene)			Patient B Maple syrup urine disease (MSUD), deficiency of branched-chain 2-ketoacid dehydrogenase complex			Patient C Hawkinsinuria, autosomal dominant deficiency of 4-hydroxyphenylpyruvate dioxygenase (gene *HPD*)			
	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	1	1	2	2	2	4	2	2	4	10
6	1	1	2	2	2	4	2	2	4	10
7	0	1	1	2	1	3	0	0	0	4
8	1	1	2	2	1	3	2	2	4	9
9	2	2	4	0	0	0	2	2	4	8
10	2	2	4	2	2	4	2	2	4	12
11	--	--	--	--	--	--	--	--	--	--
12	1	1	2	2	2	4	2	2	4	10
13	1	1	2	2	2	4	2	2	4	10
14	2	2	4	2	2	4	2	2	4	12
15	1	1	2	2	2	4	2	2	4	10
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	0	0	0	2	2	4	8
19	2	2	4	0	0	0	2	2	4	8
20	2	2	4	2	2	4	2	2	4	12

Detailed scores – Round 2

Lab n°	Patient D GM1 gangliosidosis (beta-galactosidase deficiency, *GLB1* gene)			Patient E Primary hyperoxaluria type II (glyoxylate reductase / hydroxypyruvate reductase deficiency - *GRHPR* gene)			Patient F Glutaric aciduria type I, low excretor (glutaryl-CoA dehydrogenase deficiency, *GCDH* gene)			
	A	**I**	**Total**	**A**	**I**	**Total**	**A**	**I**	**Total**	**Total**
1	0	0	0	2	2	4	2	2	4	8
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	0	0	0	2	2	4	2	2	4	8
6	2	2	4	1	1	2	2	2	4	10
7	2	2	4	2	2	4	2	2	4	12
8	2	2	4	2	2	4	2	2	4	12
9	1	1	2	2	2	4	2	1	3	9
10	2	2	4	1	2	3	2	2	4	11
11	2	2	4	2	2	4	2	2	4	12
12	0	0	0	1	2	3	2	2	4	7
13	2	2	4	2	2	4	2	2	4	12
14	2	2	4	2	2	4	2	2	4	12
15	0	0	0	1	2	3	2	2	4	7
16	2	2	4	2	2	4	2	2	4	12
17	0	0	0	2	2	4	2	2	4	8
18	1	1	2	2	2	4	2	0	2	8
19	2	2	4	2	2	4	2	2	4	12
20	2	2	4	2	2	4	2	2	4	12

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	4	4	0	4	4	20	83	
2	4	4	4	4	4	4	24	100	
3	4	4	4	4	4	4	24	100	
4	4	4	4	4	4	4	24	100	
5	2	4	4	0	4	4	18	75	
6	2	4	4	4	2	4	20	83	
7	1	3	0	4	4	4	16	67	CE
8	2	3	4	4	4	4	21	88	
9	4	0	4	2	4	3	17	71	
10	4	4	4	4	3	4	23	96	
11	--	--	--	4	4	4	12	50	
12	2	4	4	0	3	4	17	71	
13	2	4	4	4	4	4	22	92	
14	4	4	4	4	4	4	24	100	
15	2	4	4	0	3	4	17	71	
16	4	4	4	4	4	4	24	100	
17	4	4	4	0	4	4	20	83	
18	4	0	4	2	4	2	16	67	CE
19	4	0	4	4	4	4	20	83	
20	4	4	4	4	4	4	24	100	

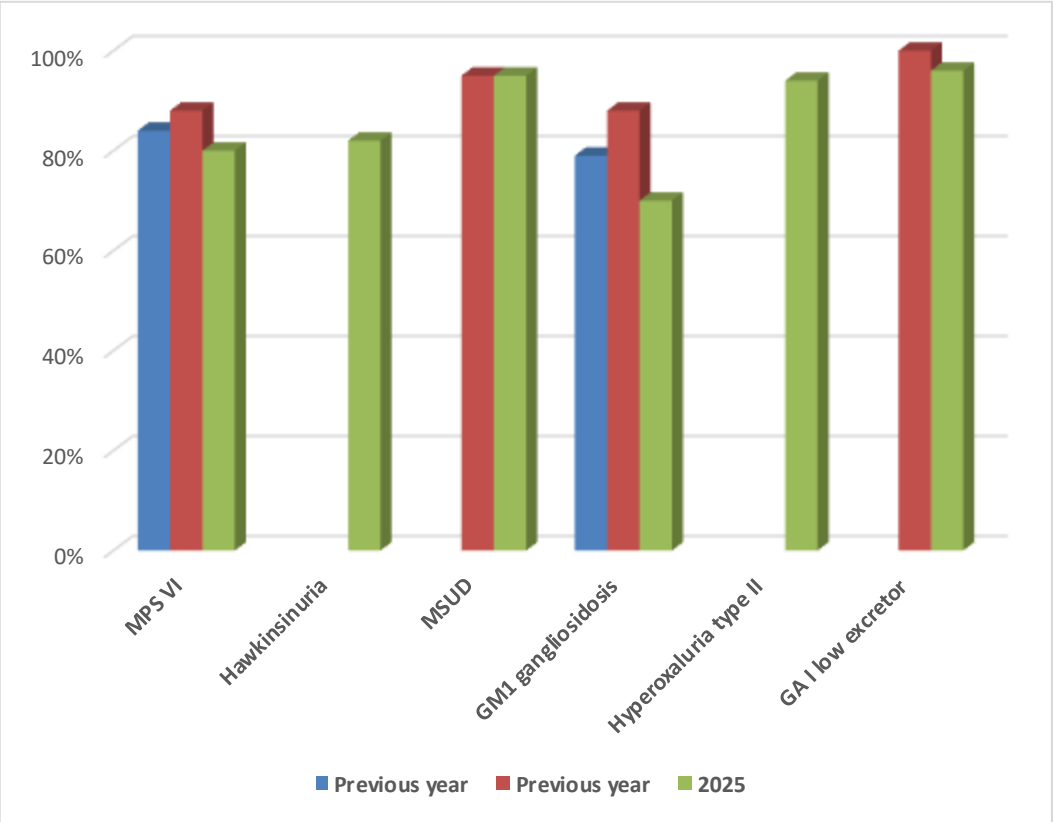
Performance

	Number of labs	% total labs
Satisfactory performers (≥ 17 points and no critical errors)	17	85
Unsatisfactory performers (< 17 points and/or critical error)	2	10
Partial and non-submitters	1	5

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
DPT-FL-2025-A	Mucopolysaccharidosis type VI	79	82	80
DPT-FL-2025-B	Maple syrup urine disease (MSUD)	84	79	82
DPT-FL-2025-C	Hawkinsinuria	95	95	95
DPT-FL-2025-D	GM1 gangliosidosis	70	70	70
DPT-FL-2025-E	Primary hyperoxaluria type II	90	98	94
DPT-FL-2025-F	Glutaric aciduria type I, low excretor	100	93	96

Improvement DPT France



10. Annual meeting of participants

This took place in Madrid on October 4th, 2025, from 17.30 to 19.00, during the ERNDIM 2025 Symposium.

Participants

The annual DPT meeting was organized on October 9, 2025 during the ERNDIM symposium in Madrid, Spain. 13 people from 9 labs were present and actively participated in the discussions.

We remind you that attending the annual meeting is an important part of the proficiency testing. The goal of the program is to **improve** the competence of the participating laboratories, which includes the critical review of all results with a discussion about improvements.

11. Information from the Executive Board and the Scientific Advisory Board

- Following 2 years as a pilot scheme, **'Lipids In Serum' (LIS)** will be organised as a full scheme starting in 2026 in collaboration with MCA laboratory. The scientific advisors of this scheme are Dr Susan Goorden (Rotterdam, NL) and Dr Marie van Dijk (Amsterdam, NL). LIS is a quantitative scheme in which several lipids relevant to IMD diagnostics are included. Some of the lipids included in LIS are new, while others have been in the Special Assays Serum scheme for some years already. Some lipids will be removed from SAS in 2026 (see details in the ERNDIM scheme catalogue.
- **Control materials** are provided by SKML/MCA laboratory since a few years. These are no longer related to EQA materials and have been produced separately. Two concentration levels for each group of analytes are available. The most suitable low and high concentration levels are defined by the scientific advisors of the schemes. Analytes and their concentrations will be similar in consecutive batches of control material. These reference materials can be ordered at MCA laboratory (https://www.erndimqa.nl/). Participants are encouraged to use them as internal control

samples, but they cannot be used as calibrators. On the ERNDIMQA website a new section for data management completes the ERNDIM internal Quality Control System. Laboratories have the option to submit results and request reports showing their result in the last run in comparison to defined acceptance limits, their own historical data and the mean of all laboratories using the same batch control material. Control materials for cystine in leukocytes are being tested, while amino acids in urine and CSF are under development. Control materials for neurotransmitters in CSF have been discontinued due to stability issues.

- **Training**:

  After successful webinars on amino acids, acylcarnitines, organic acids and purines-pyrimidines in 2024 and 2025 ERNDIM will organise two additional workshops on special assays in 2026. These workshops will focus on technical aspects of measuring metabolites. Dates of these workshops will be announced by email and on the ERNDIM website and registration will be required.

  An SSIEM Academy training course will be organised in 2026. Detail will be available on the SSIEM website

- **Urine samples**: To be able to continue this scheme we need a steady supply of new and interesting patient samples. Several laboratories have donated samples in the past, for which they are gratefully acknowledged. If you have one or more samples available and are willing to donate these to the scheme, please contact us at admin@erndim.org

  For the DPT scheme, we need at least 250 ml of urine from a patient affected with an established inborn error of metabolism, accompanied by a short clinical report. If possible, please collect 1250 ml of urine: this sample can be used as the common sample and be circulated to all labs participating to the DPT schemes. Each urine sample must be collected from a single patient. Please don't send a pool of urines, except if urine has been collected during a short period of time from the same patient.

  When a donated sample is used, the participating lab donating the sample will have a 20% discount on the DPT scheme fee in the next scheme year.

12. Reminders

We remind you that to participate to the DPT-scheme, you must perform at least:

- Amino acids
- Organic acids
- Oligosaccharides
- Mucopolysaccharides
- Purines & pyrimidines

If you are not performing one of these assays, you can send the samples to another lab (cluster lab) but you are responsible for the results.
Please send quantitative data for amino acids and, as much as possible, for organic acids.

13. DPT-France 2026 schedule

Sample distribution	4 February 2026
Start of analysis of Survey 2026/1 Website open	March 17
Survey 2026/1 - Results submission	April 7
Survey 2026/1 - Reports	April
Start of analysis of Survey 2026/2	June 1
Survey 2026/2 – Results submission	June 22
Survey 2026/2 - Reports	July
Annual meeting of participants	August 25 Helsinki SSIEM
Annual Report 2026	December

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

15. Questions, Suggestions and Complaints

If you have any questions, comments or suggestions please address to the Scientific Advisor of the scheme, Christine Vianey-Saban and/or to the ERNDIM Administration Office (admin@erndim.org).

Most complaints received by ERNDIM consist of minor misunderstandings or problems with samples, which can usually be resolved via direct contact with the ERNDIM administrative staff. If you wish to file a formal complaint, please email your complaint with details of your issue to admin@erndim.org or contact us through our website at https://www.erndim.org/contact-us/

Date of report, 2026-02-16
Name and signature of Scientific Advisor

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APPENDIX 1

DIAGNOSTIC PROFICIENCY TESTING (DPT) FRANCE

URINE SAMPLES ALREADY SENT

• 1998 : 1	P1	OCT
	P2	Propionic acidemia
• 1999 : 1	P1	MPS I or II
	P2	Cystinuria (common sample)
• 1999 : 2	P3	CblC
	P4	HMG-CoA lyase deficiency
• 2000 : 1	P1	Iminodipeptiduria (common sample)
	P2	Glutathion synthetase
• 2001 : 1	P1	Mevalonate kinase deficiency
	P2	L-2-OH glutaric
• 2001 : 2	P3	Methylmalonic (common sample)
	P4	MPS IIIA San Fillippo
• 2002 : 1	P1	LCHAD deficiency
	P2	Sulphite oxidase deficiency
• 2002 : 2	P3	Biotinidase deficiency (common sample)
	P4	MPS I
• 2003:1	P1	Tyrosinemia type I
	P2	SC-BCAD deficiency
	P3	Argininosuccinic aciduria
• 2003:2	P4	3-methylcrotonyl-CoA carboxylase deficiency
	P5	Sialidosis (common sample)
	P6	MSUD
• 2004:1	P1	Tyrosinemia type I, treated patient
	P2	Propionic acidemia
	P3	Non metabolic disease, septic shock
• 2004:2	P4	Mevalonic aciduria (common sample)
	P5	Fucosidosis
	P6	Alkaptonuria
• 2005:1	P1	Isovaleric acidemia
	P2	Tyrosinemia type II (common sample)
	P3	Disorder of peroxysome biogenesis
• 2005:2	P4	Multiple acyl-CoA dehydrogenase deficiency
	P5	Alpha-mannosidosis
	P6	4-hydroxybutyric aciduria
• 2006:1	P1	Aromatic amino acid decarboxylase deficiency
	P2	Hyperoxaluria type I
	P3	Mucopolysaccharidosis type VI
• 2006:2	P4	Hypophosphatasia (common sample)
	P5	Lysinuric protein intolerance
	P6	MCAD deficiency

• 2007:1	P1	Mitochondrial acetoacetyl-CoA thiolase
	P2	Homocystinuria due to CBS deficiency
	P3	Hyperlysinemia (common sample)
• 2007:2	P4	Aspartylglucosaminuria
	P5	Phenylketonuria
	P6	SCAD deficiency
• 2008:1	P1	Cbl C/D
	P2	Mucopolysaccharidosis type III (common sample)
	P3	2-hydroxyglutaric aciduria
• 2008:2	P4	Glycerol kinase deficiency
	P5	□-mannosidosis
	P6	3-methylcrotonyglycinuria
• 2009:1	P1	Mucopolysaccharidosis type III
	P2	Salla disease (common sample)
	P3	No metabolic disorder
• 2009:2	P4	Glutaric aciduria type I
	P5	Iminodipetiduria
	P6	Multiple acyl-CoA dehydrogenase deficiency
• 2010:1	P1	Mevalonic aciduria
	P2	Aminoacylase I deficiency
	P3	No metabolic disorder
• 2010:2	P4	Sialidosis type I (common sample)
	P5	Glutaric aciduria type I
	P6	Aspartylglucosaminuria
• 2011:1	A	Molybdenum cofactor deficiency
	B	GAMT deficiency (common sample)
	C	Methylmalonic semialdehyde dehydrogenase def.
• 2011:2	D	Mucopolysaccharidosis type IVA (Morquio)
	E	Phenylketonuria
	F	Citrullinemia type I
• 2012:1	A	Intermittent MSUD (common sample)
	B	HHH syndrome
	C	Mucopolysaccharidosis type I
• 2012:2	D	“RedBulluria”
	E	CblC
	F	SCAD deficiency
• 2013:1	A	NFU1 deficiency
	B	MNGIE syndrome (educational)
	C	Lysinuric protein intolerance (common sample)
• 2013:2	D	Mitochondrial acetoacetyl-CoA thiolase deficiency
	E	Morquio disease (MPS IV)
	F	Glycerol kinase deficiency
• 2014:1	A	Iminodipeptiduria
	B	HHH syndrome (common sample)
	C	4-hydroxybutyric aciduria

• 2014:2	D	Fucosidosis
	E	L-2-hydroxyglutaric aciduria
	F	SCHAD deficiency
• 2015:1	A	Combined malonic & methylmalonic aciduria
	B	Homocystinuria-CBS deficiency (common sample)
	C	Mucopolysaccharidosis type VI
• 2015:2	D	N-acetylaspartic aciduria
	E	D-2-hydroxyglutaric aciduria type II
	F	GM1 gangliosidosis
• 2016:1	A	Primary hyperoxaluria type II (common sample)
	B	Methionine S-adenosyltransférase (MAT) def.
	C	Glycerol kinase deficiency
• 2016:2	D	Ethylmalonic encephalopathy (*ETHE1* gene)
	E	Mucopolysaccharidosis type IVA
	F	Argininosuccinic aciduria
• 2017:1	A	Citrullinaemia type I (common sample)
	B	MNGIE
	C	Formiminoglutamic aciduria
• 2017:2	D	GM1 gangliosidosis
	E	No IEM
	F	Imerslund-Gräsbeck
• 2018:1	A	DPD deficiency (common sample)
	B	MPS VII
	C	SCHAD deficiency
• 2018:2	D	Glutaric aciduria type I (low excretor)
	E	OAT deficiency
	F	Dihydropyrimidine dehydrogenase (DPD) deficiency
• 2019:1	A	APRT deficiency (common sample)
	B	Beta-mannosidosis
	C	Hyperprolinaemia type II
• 2019:2	D	Multiple acyl-CoA dehydrogenase deficiency (MADD)
	E	MPS II
	F	Argininaemia
• 2020:1	A	PKU (common sample)
	B	Alkaptonuria
	C	MPS IVA
• 2020:2	D	Citrullinaemia type I
	E	Iminodipeptiduria
	F	GAMT deficiency
• 2021:1	A	Alpha-mannosidosis (common sample)
	B	Alpha-mannosidosis
	C	MAT deficiency (beta-ketothiolase)
• 2021:2	D	CBS deficiency
	E	4-hydroxybutyric aciduria
	F	Hyperprolinaemia type II

• 2022:1	A	Barth syndrome (common sample)
	B	Propionic acidaemia
	C	MPS IVA
• 2022:2	D	No IEM
	E	3-methylcrotonyl-CoA carboxylase deficiency
	F	Aromatic amino acid decarboxylase deficiency
• 2023:1	A	Argininosuccinic aciduria (common sample)
	B	2-methylbutyryl-CoA dehydrogenase deficiency
	C	Isovaleric acidemia
• 2023:2	D	Combined MCAD and OCTN2 deficiency
	E	Fucosidosis
	F	Phenylketonuria
• 2024:1	A	Malonyl-CoA decarboxylase deficiency
	B	L-2-hydroxyglutaric aciduria
	C	Citrullinaemia type I
• 2024:2	D	Adenylosuccinate lyase (ADSL) deficiency
	E	No IEM
	F	Multiple acyl-CoA dehydrogenase deficiency (MADD)

APPENDIX 2. Change log (changes since the last version)

Version Number	Published	Amendments
1	16 February 2026	2025 annual report published

END