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Diagnostic Proficiency Testing

Centre: The Netherlands

Final Report 2025

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

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The ERNDIM Diagnostic Proficiency Testing (DPT) Scheme is the ultimate external quality assessment scheme for biochemical genetics laboratories. In 2025, 18 labs participated in the Proficiency Testing Scheme NL.

1. Geographical distribution of participants

For both surveys, all 18 participants have submitted results.

Country	Number of participants
Australia	2
Belgium	6
Germany	1
Netherlands	5
New Zealand	1
South Africa	1
Switzerland	2

[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.

2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by George Ruijter as Scientific Advisor and coordinated by CSCQ, the Swiss organisation for quality assurance in medical laboratories, both appointed by and according to procedures laid down by the ERNDIM Board.

As a subcontractor of ERNDIM, 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 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 samples: Samples used in 2025 have been provided by:

- VKS, the Dutch IMD patient organisation
- Prof Kayserili, Koc University Hospital, Istanbul
- dr Vianey-Saban, scientific advisor of DPT-F
- Sheffield Childrens Hospital, UK
- Erasmus MC, Rotterdam, NL

Patient A: MPS VI (common sample provided by DPT F)
Patient B: BKT deficiency
Patient C: AGU
Patient D: cblC deficiency
Patient E: ADSL deficiency
Patient F: OAT deficiency

Sample pre-treatment (heat-treatment) was performed in the Scientific Advisor's laboratory, while aliquoting and dispatch of the samples was done by the Scheme organiser. Before dispatch to participants one set of samples was sent to the Scientific Advisor and checked for quality. In all six samples the typical metabolic profiles were preserved. The samples are stable for the duration of the scheme's submission calendar when stored under defined conditions.
Shipping: samples were sent by DHL, FedEx or the Swiss Post at room temperature.
The time allotted for submitting reports was 3 weeks after opening of the website. Clinical information on the samples was provided through the website.

3. Tests

The minimal required test panel for participation in any DPT scheme includes creatinine, dip stick, amino acids, organic acids, oligosaccharides, quantitative GAG screening and purines-pyrimidines. It is strongly recommended to have the following tests available for DPT-NL: GAG subtype analysis (by electrophoresis, TLC or LC-MS/MS), sialic acid, creatine-guanidinoacetate and polyols-sugars. Please note that in DPT schemes it is allowed to obtain results from partner laboratories when this is routine clinical practice. It is required to indicate in the report that results were obtained from a cluster lab.

4. Schedule of the scheme

- February 10, 2025: shipment of samples
- March 17, 2025: start analysis of samples of the first survey
- April 7, 2025: deadline for result submission (Survey 1)
- May 16, 2025: interim report with preliminary scores of Survey 1 published
- June 2, 2025: start analysis of samples of the second survey
- June 23, 2025: deadline for result submission (Survey 2)
- August 9, 2025: interim report with preliminary scores of Survey 2 published
- October 9, 2025: DPT meeting, ERNDIM symposium Madrid, Spain
- February 11, 2026: annual report with final scoring published

5. Results

All participants submitted results for both surveys on time.

	Survey 1	Survey 2
Receipt of results	18	18
No results submitted	0	0

6. Web site reporting

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

- Selection of tests: please **don't select a test if you do not intend to perform it**, otherwise the evaluation program will include it in the report.
- Results: please
  - Give quantitative data as much as possible.
  - Enter the key metabolites with interpretation **in the tables** even if you don't provide 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 investigations**)
  - Recommendations are scored together with interpretation.
  - Advice for treatment is not scored.
  - **Please don't give advice for further investigations in "Comments on diagnosis"**: it will not be included in the evaluation software.

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 aspects 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 the sum of these two aspects. The maximum score is 4 points per sample. The scores were calculated only for laboratories submitting results for both surveys.

Scoring and certificate of participation
Scoring is carried out by the scientific advisor and a second assessor from another DPT scheme. The second assessor changes every year. The results of DPT NL 2025 were additionally scored by Dr Vianey-Saban, from DPT F. At the SAB meeting in Leiden, November 27-28, 2025, the definitive scores have been set. 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. Details on critical errors in the 2025 samples are given in section 8 of this report.

ERNDIM provides a single certificate for all its schemes with details of participation and performance. In addition, performance support letters will be issued if the performance is evaluated as unsatisfactory. Two performance support letter will be sent by the Scheme Advisor for the scheme year 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

For DPT 2025 a total score of at least 17 points out of the maximum of 24 (71%) and absence of critical errors must be achieved for satisfactory performance.

8. Results of samples and evaluation of reporting

8.1. Creatinine measurement for all samples

Creatinine determination was good for all labs. No major systematic errors were observed. Creatinine values are provided in the Table below. CVs are <6 % for samples A, B, C, D and F, but slightly higher (11%) in sample E due to a relatively low creatinine concentration.

Sample	Median creatinine (mmol/L)	SD (mmol/L)	CV (%)	n
A	6.2	0.3	4.8	18
B	4.3	0.18	4.2	18
C	7.7	0.29	3.8	18
D	5.1	0.28	5.5	18
E	0.70	0.08	11.4	18
F	3.5	0.17	4.9	18

8.2. Patient A – MPS VI (Maroteaux-Lamy syndrome; OMIM 253200)

Patient details provided to participants
15-year-old boy. Dysmorphic features, scoliosis, size -1.5 SD, normal intellectual development. Under treatment.

Patient details
Pregnancy and delivery were normal. From 2 months to 6 years of age he had frequent upper airways infections. At 3 years, pectus carinatum was diagnosed. At 10 years, he had scoliosis with platyspondyly, dorsal kyphosis, narrow cervical canal and decrease in visual and hearing acuity. At 15 years, he was diagnosed with MPS VI by urine testing, which was confirmed by measurement of arylsulfatase B activity in leucocytes and mutation analysis of the ARSB gene. Since then, he is receiving enzyme replacement therapy every week.

Sample A was the common sample distributed to participants of all 5 DPT centres, was discussed during the ERNDIM participant meeting in Madrid, October 10, 2025 by dr Vianey-Saban from Lyon and summarised during the DPT meeting of DPT-NL. The presentation showing results and conclusions on this sample can be viewed on the ERNDIM website (erndim.org).

Analytical performance
Despite the moderate elevation of GAG, all 18 participants reported it to be elevated, and 17/18 specifically reported an abnormal DS level. Increasingly, laboratories report difficulties in purchasing good DMB batches that reliably distinguish normal controls from MPS urine samples. If this problem

persists, we advise to validate alternative methods using LC-MS/MS (see below).
Despite several methods for the LC-MS/MS analysis of GAG being described already 5-10 years ago, only few labs participating in DPT report using these (enzymatic GAG hydrolysis with LC-MS/MS of resulting disaccharides, Langereis et al PLoS One 2015 10:e0138622; methanolytic GAG hydrolysis with LC-MS/MS of disaccharides, Zhang et al Mol Genet Metab 2015 114:123-128 and LC-MS/MS of GAG-derived (oligo)saccharides, Saville et al Genet Med 2019 21:753-757). The majority of participants still use 1-dimensional electrophoresis to perform GAG subfraction analysis. In milder MPS presentations, MS-based methods are more sensitive to detect increased abnormal GAG species (data from the urine MPS scheme). Additionally, LC-MS/MS methods are an alternative for the traditional screening approach using DMB.
Oligosaccharides were reported normal by 10 participants and borderline/not specific by 2. Analytical proficiency was 97%.

Diagnosis / Interpretative proficiency
MPS VI was given as the most likely diagnosis by 14 participants, while another 2 mentioned MPS VI as a part of a small set of MPS, based on the GAG test results obtained. The two remaining labs gave MPS IV or MPS II as the most likely diagnosis. Among the alternative possible diagnoses, MPS I/II, MPS VII and MPS X were mentioned most frequently. All of these do show elevated DS, but along with HS or CS. An oligosaccharidosis was given as an alternative possible diagnosis by 2 labs, probably based on borderline oligosaccharide testing. Interpretive proficiency was 94%.

Recommendations
Many participants advised to measure the enzyme activity of arylsulfatase B (N-acetylgalactosamine-4-sulfatase), and/or molecular genetic testing of the corresponding gene ARSB. Enzyme replacement therapy was mentioned as a possibility, which, in fact, this patient already received.

Scoring
- Analytical results: elevated DS, score 2; elevated GAG screening without reporting GAG subtyping, score 1
- Interpretation of results: MPS VI mentioned, score 2; other/unspecified MPS or correct diagnosis without analytical results, score 1
- Critical error: none

Overall impression
Despite the moderate GAG elevation, all labs considered this sample to be an MPS. Overall proficiency was 96%.

Multiple distributions of similar samples
MPS VI has not been circulated since 2006.

8.3. Patient B – Beta-ketothiolase deficiency (mitochondrial acetyl-CoA acetyltransferase, ACAT; OMIM 203750)

Patient details provided to participants
Presented at age 1 y with vomiting and lethargy. Current age is 38 y.

Patient details
This patient was diagnosed with beta-ketothiolase (ACAT1) deficiency as an infant and always shows the typical pattern of organic acids in urine regardless of clinical condition. His development has been normal.

Analytical performance
The typical BKT deficiency metabolites were reported by most participants: tiglylglycine (17/18) and 2-methyl-3-hydroxy-butyric acid (15/18). Median concentrations were grossly elevated: tiglylglycine 366 mmol/mol and 2-methyl-3-hydroxy-butyric acid 663 mmol/mol. Elevated 2-methyl-acetoacetate was mentioned by 3 labs, while 2 participants reported this metabolite normal. 2-Methyl-acetoacetate decomposes during the heat treatment performed on DPT samples and it is not surprising that most participants did not detect it. Three labs mentioned elevated C5:1-carnitine. Analytical proficiency was 97%.

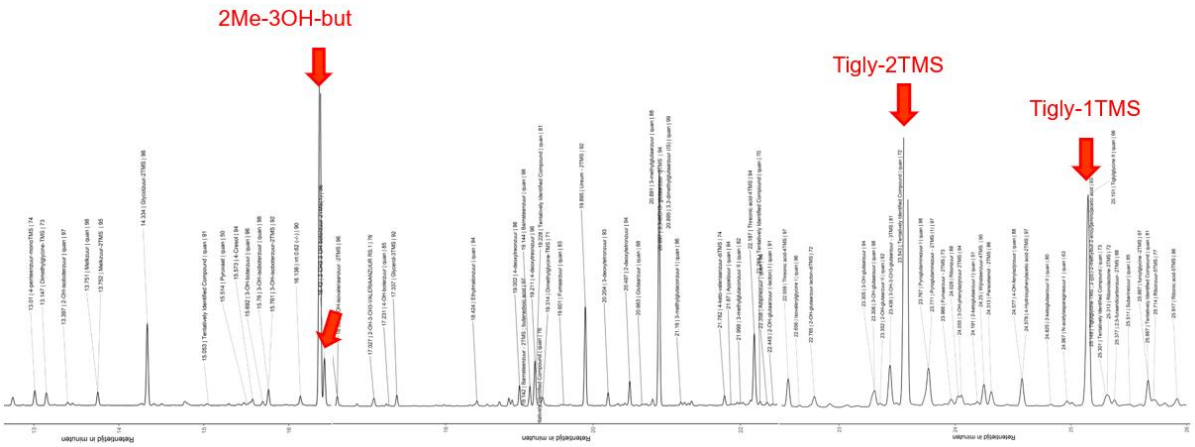

Fig. 1. Organic acid chromatogram of sample 2025-B with relevant metabolites indicated.

Diagnosis / Interpretative proficiency
Beta-ketothiolase deficiency was suggested as the most likely diagnosis by 14 labs (score 2), while 3 reported 2-methyl-3-hydroxy-butyryl-CoA dehydrogenase (MHBD) deficiency as the most likely diagnosis with BKT as the alternative possible diagnosis. Six participants reported MHBD deficiency as an alternative diagnosis, but 2 added that this was unlikely. MHBD deficiency is less likely based on: (1) clinical information, (2) the presence of 2 enantiomers (2 peaks) of 2-methyl-3-hydroxy-butyric acid, which is characteristic of BKT deficiency. In MHBD-deficient urine samples, only one enantiomer of 2-methyl-3-hydroxy-butyric acid is detected. The presence of tiglylglycine should trigger a suspicion of beta-ketothiolase deficiency in addition to MHBD and propionic acidemia. One participant concluded 3MCC deficiency, possibly due to misinterpretation of tiglylglycine-TMS. Propionic acdidaemia and MCT1 deficiency were mentioned as possible alternative diagnoses, but these do not fit the metabolite pattern.
It must be noted that, even during severe crises, some proven ACAT1 patients only show trace amounts of tiglylglycine and 2-methyl-3-hydroxybutyrate in their urinary organic acid profiles, while plasma C5-OH and C5:1 can be within normal range.
Interpretive proficiency was 92%.

Recommendations
Recommendations for further testing included plasma/DBS acylcarnitine analysis and genetic screening of the ACAT1 and HSD17B10 genes.

Scoring
- Analytical results: elevated 2-methyl-3-OH-butyric and elevated tiglylglycine were each scored 1 mark
- Interpretation of results: beta-ketothiolase deficiency as a first or alternative diagnosis, score 2
- Critical error: failure to report beta-ketothiolase as a diagnosis (n=1)

Overall impression
Clear beta-ketothiolase sample with overall proficiency of 94%.

Multiple distributions of similar samples
In a previous survey a different beta-ketothiolase sample was circulated (2007-L) with correct diagnoses by 19 out of 19 labs.

8.4. Patient C – Aspartylglucosaminuria (OMIM 208400)

Patient details provided to participants
A 6 year old male with dysmorphic features, delayed development, abnormal behaviour and frequent infections. Current age is 29 y.

Patient details
The diagnosis in this patient was confirmed by deficiency of aspartylglucosaminidase activity in WBC.

Analytical performance
Oligosaccharide analysis was performed and reported abnormal by all 18 labs. Several labs reported results from oligosaccharide analysis by LC-MS. Elevated aspartylglucosamine in amino acid analysis was reported by 11 participants (median value: 172 mmol/mol). Aspartylglucosamine elutes just before urea using Biochrom30 amino acid analysis. Analytical performance was 97%.

Diagnosis / Interpretative proficiency
Aspartylglucosaminuria was reported as the most likely diagnosis by 17 out of 18 participants. One participant concluded sialidosis. Interestingly 6 participants reported NGLY1 deficiency as a possible alternative diagnosis. NGLY1 is a congenital disorder of deglycosylation caused by a defective peptide:N-glycanase and shows an oligosaccharide pattern reminiscent of aspartylglucosaminuria (see Hall et al., Mol Genet Metab 2018, 124:82-86 and Hagemeijer et al, J Inherit Metab Dis 2023 46:206-219). Typically lower biomarker levels are observed in NGLY1 deficiency compared to aspartylglucosaminuria, requiring LC-MS tests for reliable detection. Interpretation proficiency was 97%.

Recommendations
Aspartylglucosaminidase activity testing in WBC/fibroblasts and AGA mutation testing was suggested by many participants.

Scoring
- Analytical results: elevated aspartylglucosamine and/or aspartylglucosaminuria oligosaccharide pattern, score 2; abnormal oligosaccharide pattern (incorrect/not specified), score 1
- Interpretation of results: aspartylglucosaminuria, score 2; other oligosaccharidosis, score 1
- Critical error: none

Overall impression
Surprisingly high overall proficiency, 97%, for this extremely rare disorder.

Multiple distributions of similar samples
Different samples obtained from the same patient were circulated in 2020, with proficiency 92%, in 2013 with proficiency 83% and in 2007 with proficiency 84%.

8.5. Patient D – Combined methylmalonic aciduria and homocystinuria due to cblC deficiency (OMIM 277400).

Patient details provided to participants
Boy aged 17 y. Slight anaemia and mild cognitive impairment.

Patient details
This patient was initially diagnosed with cblC deficiency by WES analysis (two MMACHC variants) which was subsequently confirmed by biochemical testing.

Analytical performance
All participants reported elevated methylmalonic acid (median value 321 mmol/mol), while 8 mentioned elevated methylcitric acid (median value 6 mmol/mol). A total of 15 labs reported elevated homocystine (median value 11 mmol/mol) and/or cysteinyl-homocysteine disulfide. When methylmalonic acid is clearly elevated, abnormalities in homocysteine or the disulfide must be checked. Analytical proficiency was 92%.

Diagnosis / Interpretative proficiency
Many different combinations of possible diagnoses were given. A differential diagnosis including B12 deficiency, a defect in B12 uptake or metabolism (cbl defect) was considered correct (reported in 'most likely' or 'alternative' diagnosis; scored with 2 p). In disorders of vitamin B12 absorption and transport, the symptoms are usually indistinguishable from those caused by dietary deficiency of vitamin B12. Cbl defects had to be mentioned to receive full score for interpretation and 17 participants did so. MMA (or MUT deficiency) and SUCLA2 deficiency were reported as a possible diagnosis by a number of participants, but are less likely with elevated homocystine. Seven participants reported cblC as the most likely diagnosis, which is correct, but can't be concluded from the analytical results alone and is probably assumed based on the clinical symptoms and the relatively high frequency of this defect among the various defects in B12 uptake or metabolism. NO2 abuse is another possible explanation of the

biochemical abnormalities, which was mentioned by 6 participants
Interpretive proficiency was 97%.

Recommendations
Recommendations for further testing included: analysis of B12, MMA, homocysteine, amino acids and acylcarnitines in plasma; sequencing of the MMACHC gene, and sequencing of genes involved in cobalamine metabolism by WES/WGS.

Scoring
- Analytical results: MMA elevated, 1 point; homocystine and/or mixed hcys-cys disulfide elevated, 1 point
- Interpretation of results: differential diagnosis minimally including a defect in B12 uptake or metabolism (and B12 deficiency), score 2; MMA with cbl not mentioned, score 1
- Critical error: none

Overall impression
Most participants have mentioned the correct differential diagnosis although some participants did not report elevated homocystine. Overall proficiency was 94%.

Multiple distributions of similar samples
Combined MMA-homocystinuria (cbl defects) have not been circulated since 2006.

8.6. Patient E – Adenylosuccinate lyase deficiency (OMIM 103050)

Patient details provided to participants
A 4 y old girl presenting with neuromotor regression, hypotonia and epilepsy.

Patient details
This 4 y-old girl suffered from neuromotor regression, hypotonia, drug-resistant epilepsy, no eye contact. Two variants were found in the ADSL gene upon WES analysis. Subsequent purine-pyrimidine analysis in plasma and urine showed elevated SAICAr and succinyladenosine and confirmed ADSL deficiency.

Analytical performance
SAICAr (median value 78 mmol/mol) and/or succinyladenosine (median value 144 mmol/mol) were detected by 14 out of the 18 participants. The range of SAICAr concentrations reported was 75-158 mmol/mol, which is a surprisingly narrow range. A SAICAr calibrator is now commercially available and may be used by participants. It is too expensive to include in the ERNDIM quantitative purine-pyrimidine (PPU) scheme, but AICAr, its product in purine biosynthesis, is included in the PPU scheme. S-Ado can be easily prepared from adenylosuccinate (succinyl-AMP, available from Sigma). Reference values of S-Ado are age-dependent. Urine from young children usually does contain some S-Ado, which makes quantitative analysis imperative to identify ADSL patients.
The Bratton-Marshall test to detect SAICAr was reported by one participant, with a negative result. Perhaps the SAICAr level (approx. 60 µmol/l in this sample) was too low to obtain a robust positive Bratton-Marshall test, although the test has been reported to have an LOD of 1 µmol/l. These results indicate that this screening test is not reliable and we recommend to perform quantitative purine analysis.
The creatinine concentration was rather low in the urine sample, but this did not preclude detection of the pathognomic metabolites. Many labs reported ketonuria and elevated taurine, which is possibly related to a ketogenic diet. We had no information with regard to treatment. Also 3-OH-propionic acid was elevated, but no other metabolites characteristic for propionic aciduria, such as methylcitric acid, were increased. 3-OH-propionic acid might be produced by gut bacteria .
Analytical proficiency was 78%.

Diagnosis / Interpretative proficiency
ADSL was concluded by all 14 labs that detected SAICAr and/or S-Ado. Four participants did not perform purine analysis, while this is required for participation in DPT, and missed the diagnosis. Other diagnoses reported were propionic acidaemia, SCOT deficiency and SCHAD deficiency. These incorrect diagnoses are likely based on the abnormalities that were observed in addition to elevated SAICAr and/or S-Ado. One participant concluded 'no diagnosis'. BKT, SCOT deficiency, creatine transporter deficiency, MCT1 deficiency and beta-alaninaemia were mentioned as possible alternative diagnoses. Again these are these are likely based on the abnormalities not related to the purine defect,

e.g. ketonuria. Creatin excretion was 1493 mmol/mol, a value which is not clearly elevated at age 4 y, besides the fact that this was a female patient. Beta-alaninaemia is considered a biochemical abnormality with questionable clinical significance.
Interpretive proficiency was 78%.

Recommendations
Mutation testing of the ADSL gene was recommended most frequently. Some labs suggested to measure ADSL activity in erythrocytes or cultured cells.

Scoring
- Analytical results: elevated SAICAr and/or SAdo: score 2
- Interpretation of results: ADSL deficiency: score 2
- Critical error: sample not eligible

Overall impression
Although this was a dilute urine sample (low creatinine), SAICAr and S-Ado were clearly elevated and all participants that analysed purines correctly established the diagnosis. Overall proficiency was 78%.

Multiple distributions of similar samples
Different ADSL samples were circulated in 2012 (2012-D) with overall proficiency 62% and in 2023 (2023-B) with overall proficiency 83%. Proficiencies in 2023 and 2025 are similar.

8.7. Patient F – Ornitine aminotransferase deficiency (gyrate atrophy; OMIM 258870)

Patient details provided to participants
A 10 year old male suffering from deteriorating visual acuity (on treatment).

Patient details
This boy presented with retinopathy and was diagnosed with gyrate atrophy (ornithine aminotransferase deficiency) by amino acid analysis in plasma. The urine sample was taken when he was on pyridoxine therapy.

Analytical performance
All but one participant detected elevated ornithine. Aminopiperidon is a cyclic derivative of ornithine (cyclic amide, beta-lactam). Detection may depend on the analytical system used. On Biochrom amino acid analysers it elutes close to 3-methyl-histidine/anserine (Fig 2). The ratio to ornithine is approximately 1/3. In MS analysis it may also appear as an in-source fragment (-H_2O).
Analytical proficiency was 94%.

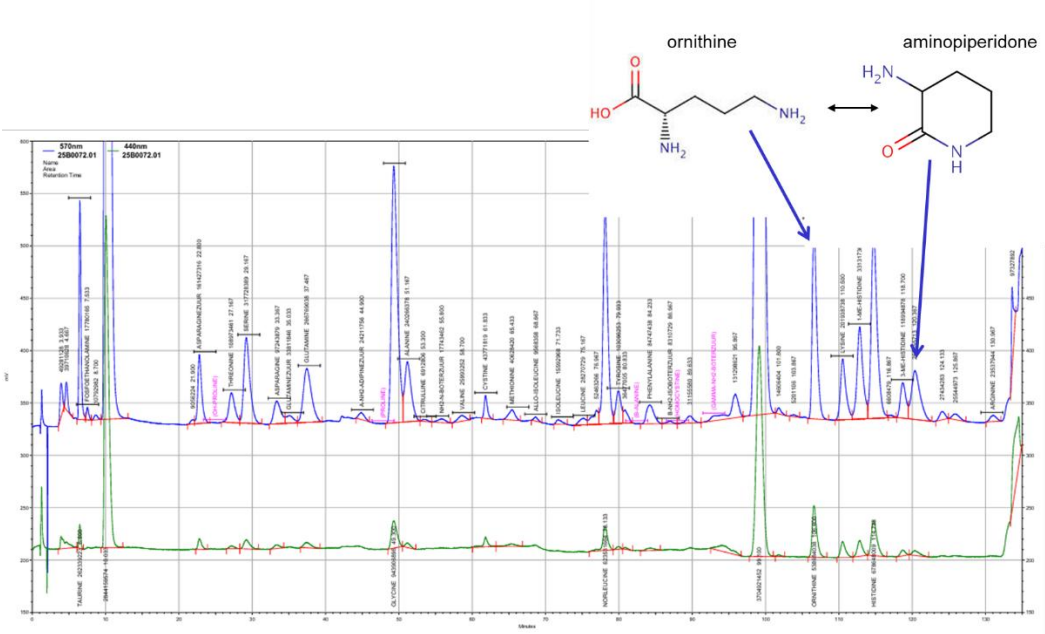

Fig. 2. Biochrom amino acid chromatogram of sample 2025-F with relevant metabolites indicated

Diagnosis / Interpretative proficiency
Seventeen participants correctly concluded OAT deficiency (or gyrate atrophy). One participant suggested a peroxisomal defect as the most likely diagnosis, but this would be hard to establish in urine with the panel of tests required in DPT. Several participants mentioned HHH syndrome or other urea cycle defects, LPI or cystinuria as alternative diagnoses. These possibilities, however, are unlikely based on biochemical findings (normal homocitrulline, glutamine, cystine, lysine, arginine, and orotic acid) as well as clinical symptoms. Interpretive proficiency was 94%.

Recommendations
Advice for further testing included plasma amino acid, creatine and guanidinoacetic acid analysis, sequencing of the OAT gene and OAT activity testing in cultured fibroblasts.

Scoring
- Analytical results: elevated ornithine: score 2
- Interpretation of results: ornithine aminotransferase deficiency (gyrate atrophy): score 2
- Critical error: failure to report ornithine aminotransferase deficiency as a diagnosis (n=1)

Overall impression
Clear OAT sample with high proficiency: 94%

Multiple distributions of similar samples
The same sample was circulated in 2013 (2013-D) with a similar overall proficiency of 92%

9. Scores of participants

All data transfer, i.e. submission of results as well as viewing and downloading of reports proceed via the DPT-CSCQ results website. The results of participants are confidential and only accessible using username and password on the CSCQ website. Anonymised scores of all laboratories are provided in the annual report. Your results are indicated by an arrow 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 MPS VI			Patient B BKT deficiency			Patient C AGU			
	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	1	1	2	2	2	4	2	2	4	10
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	1	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	1	1	2	10
15	2	2	4	1	2	3	2	2	4	11
16	2	2	4	2	2	4	2	2	4	12
17	2	1	3	2	0	2	2	2	4	9
18	2	2	4	2	2	4	2	2	4	12

Detailed scores – Round 2

Lab n°	Patient D cblC deficiency			Patient E ADSL deficiency			Patient F OAT deficiency			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	2	2	4	2	2	4	2	2	4	12
3	2	2	4	2	2	4	2	2	4	12
4	2	1	3	2	2	4	2	2	4	11
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	2	2	4	2	2	4	12
7	1	2	3	0	0	0	2	2	4	7
8	2	2	4	2	2	4	2	2	4	12
9	2	2	4	2	2	4	2	2	4	12
10	1	2	3	2	2	4	2	2	4	11
11	2	2	4	2	2	4	0	0	0	8
12	2	2	4	0	0	0	2	2	4	8
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	1	2	3	2	2	4	2	2	4	11
17	2	2	4	0	0	0	2	2	4	8
18	2	2	4	0	0	0	2	2	4	8

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	4	4	4	4	4	24	100	
2	4	4	4	4	4	4	24	100	
3	4	4	4	4	4	4	24	100	
4	4	4	4	3	4	4	23	96	
5	4	4	4	4	4	4	24	100	
6	4	4	4	4	4	4	24	100	
7	4	4	4	3	0	4	19	79	
8	2	4	4	4	4	4	22	92	
9	4	4	4	4	4	4	24	100	
10	4	4	4	3	4	4	23	96	
11	4	3	4	4	4	0	19	79	CE
12	4	4	4	4	0	4	20	83	
13	4	4	4	4	4	4	24	100	
14	4	4	2	4	4	4	22	92	
15	4	3	4	4	4	4	23	96	
16	4	4	4	3	4	4	23	96	
17	3	2	4	4	0	4	17	71	CE
18	4	4	4	4	0	4	20	83	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 17 points and no critical errors)	16	89
Unsatisfactory performers (< 17 points and/or critical error)	2	11
Partial and non-submitters	0	0

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
DPT-NL-2025-A	MPS VI	97	94	96
DPT-NL-2025-B	BKT deficiency	97	92	94
DPT-NL-2025-C	AGU	97	97	97
DPT-NL-2025-D	cblC deficiency	92	97	94
DPT-NL-2025-E	ADSL deficiency	78	78	78
DPT-NL-2025-F	OAT deficiency	94	94	94

10. Annual meeting of participants

The annual DPT meeting was organised on October 9, 2025 during the ERNDIM symposium in Madrid, Spain
Representatives from many participating labs were present and actively participated in the discussions.

Please note 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 critical review of all results with a discussion on interpretation of results and, if possible, to reach a consensus on best practice.

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 aminoa cids 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 300 ml of urine from a patient affected with an established inborn error of metabolism, accompanied by a short clinical report. If possible, please collect 1500 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. Tentative schedule in 2026

Sample distribution	February 4, 2026
Start of analysis of Survey 2026/1 (website open)	March 17, 2026
Survey 2026/1 - Results submission deadline	April 7, 2026
Survey 2026/1 – Interim report available	April/May 2026
Start of analysis of Survey 2026/2 (website open)	June 1, 2026
Survey 2026/2 – Results submission deadline	June 22, 2026
Survey 2026/2 – Interim report available	July/August 2026
Annual meeting of participants	August 25, 2026 (Helsinki)
Annual Report 2026	January 2027

13. 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.

14. Questions, Suggestions and Complaints

If you have any questions, comments or suggestions please address to the Scientific Advisor of the scheme, George Ruijter 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, 2026-02-12

Name and signature of Scientific Advisor

APPENDIX 1. Change log (changes since the last version)

Version Number	Published	Amendments
1	February 12 2026	2025 annual report published

END