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Diagnostic Proficiency Testing

Centre: Switzerland

Final Report 2025

prepared by Déborah Mathis

Note: This annual report is intended for participants of the ERNDIM DPT Switzerland 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 ERNDIM Privacy Policy on www.erndim.org.

1. Geographical distribution of participants

In 2025, 21 labs participated to the Proficiency Testing Switzerland Scheme. 21 laboratories submitted results for both surveys.

Country	Number of participants
Australia	3
Austria	2
Canada	3
China	1
Estonia	2
France	1
Germany	3
Norway	1
Sweden	2
Switzerland	1
United States of America	2

2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Déborah Mathis as Scientific Advisor (SA) and coordinated by Alessandro Salemma and Nicola Braik as scheme organiser (sub-contractor on behalf of CSCQ), both appointed by and according to procedures laid down by the ERNDIM Board.

[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.

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 and Urine MPS 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 Samples used in 2025 have been provided by different centres: four samples by Inselspital Bern, Switzerland, one sample by Kinderspital Zürich, Switzerland and the common sample by DPT France.

Patient A: Mucopolysaccharidosis type VI (common sample)
Patient B: Barth syndrome, 3-methylglutaconic aciduria type II
Patient C: Thymidine phosphorylase deficiency; mitochondrial neurogastrointestinal encephalopathy syndrome (MNGIE)
Patient D: Mucopolysaccharidosis type IIIC
Patient E: Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency
Patient F: Multiple acyl-CoA dehydrogenase deficiency (MADD). Electron transfer flavoprotein-ubiquinone oxidoreducatse (ETF-QO) deficiency.

The samples have been heat-treated. They were analysed in our institute after 3 days 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.

3. Tests
Analyses of organic acids, glycosaminoglycans and purines/pyrimidines were required in 2025.

4. Schedule of the scheme
- Feb 05, 2025: shipment of samples of Survey 1 and 2
- March 17, 2025: analysis of samples of the first survey
- April 07, 2025: deadline for result submission (Survey 1)
- June 02, 2025: analysis of samples of the second survey
- June 23, 2025: deadline for result submission (Survey 2)
- October 09, 2025: annual meeting of participants, Madrid, Spain.

5. Results
21 of 21 labs returned results for both surveys by the deadline.

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 is 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 (correct diagnosis was indicated)	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 out by the scientific advisor as well as by a second assessor who changes every year. The results of DPT Switzerland 2025 have been also scored by Petr Chrastina, from the DPT CZ scheme. At the SAB meeting in November 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 a critical error has to be considered for sample A for the labs that did not consider lysosomal storage disorders at all. In DPT CH however, this applied to zero lab.
A certificate of participation will be issued for participation and it will be additionally notified whether the participant has received a performance support letter. A performance support letter is sent out if the performance is evaluated as unsatisfactory (low score or critical error). No performance support letter has been sent by the Scientific Advisor for 2025. Any partial submitters will receive a letter from the ERNDIM Executive Administrator.

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 (71%) is needed for satisfactory performance.

8. Results of samples and evaluation of reporting

8.1. Patient A

Diagnosis
Mucopolysaccharidosis type VI (OMIM #253200)

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

Analytical performance
Detection of increased dermatan sulfate or differentiation profile compatible with MPS type VI was scored two points (12/21 labs).
Detection of increased total MPS or differentiation profile indicative of an incorrect MPS type was scored one point (9/21 labs).

Interpretative proficiency
Mucopolysaccharidosis type VI as main diagnosis was scored two points (11/21 labs).
Other or unspecified types of mucopolysaccharidosis, or diagnosis based on clinical presentation, were scored one point (10/21 labs).

Overall impression
Analytical and interpretative proficiencies were 79% and 76%, respectively.
All laboratories reported MPS as the main diagnosis; however, only half correctly identified the specific MPS type. 4/21 laboratories did not perform MPS differentiation.

Multiple distributions of similar samples

	2008	2022
Analytical performance	65%	84%
Interpretative performance	72%	84%
Overall performance	69%	84%

8.2. Patient B

Diagnosis
3-Methylglutaconic aciduria in association with Barth Syndrome (OMIM 302060).

Patient details provided to participants
41-year-old man with cardiomyopathy; neutropenia in childhood.

Analytical performance
Detection of increased 3-methylglutaconic acid was scored 2 points (21/21 labs).

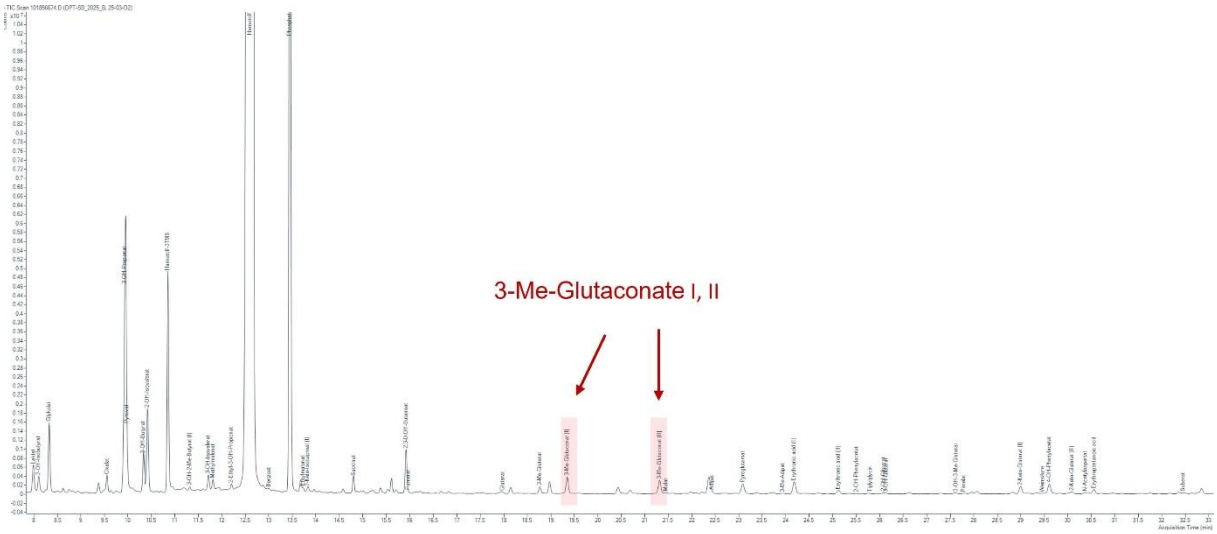


Figure 1: Organic acid analysis by gas chromatography mass spectrometry of sample B with clear peaks for 3-methyl-glutaconate.

Interpretative proficiency
Barth syndrome or 3-methylglutaconic aciduria was scored two points (21/21 labs).

Overall impression
Excellent analytical, interpretative and overall proficiency of 100%.

Multiple distributions of similar samples

	2013	2022
Analytical performance	68%	100%
Interpretative performance	68%	98%
Overall performance	68%	99%

8.3. Patient C

Diagnosis
Thymidine phosphorylase deficiency; mitochondrial neurogastrointestinal encephalopathy syndrome (MNGIE)

Patient details provided to participants
33-year-old male with leukoencephalopathy and muscular hypotonicity.
Further: The urine was obtained from a 33 year old patient with abnormal MRI scan, leukoencephalopathy, demyelinating neuropathy, muscular hypotonicity and wasted appearance. The diagnosis was confirmed by mutation analysis.

Analytical performance
Detection of increased thymidine and/or deoxyuridine was scored 2 points (17/21 labs).
Thymidine range: 14-50 mmol/mol creatinine.
Deoxyuridine range: 35-66 mmol/mol creatinine.
Detection of increased uracil and/or thymine was scored 1 point (4/21 labs)

Interpretative proficiency
Thymidine phosphorylase deficiency (MNGIE) as the main or alternative diagnosis was scored two points (17/21 labs). Diagnoses of dihydropyrimidine dehydrogenase deficiency (DPD) or dihydropyrimidinase deficiency (DHP) were scored one point (3/21 labs).

Overall impression
Overall, a mitigated proficiency of 81% was observed. Analytical proficiency was of 76% with 6 labs failing to detect one or both specific metabolites. Interpretative proficiency was of 86%. 4/21 labs concluded incorrectly to DPD or DHP deficiencies. One lab did not identify a specific diagnosis.

Multiple distributions of similar samples

	2010	2019
Analytical performance	50%	88%
Interpretative performance	50%	78%
Overall performance	50%	83%

8.4. Patient D

Diagnosis
Mucopolysaccharidosis type IIIC (OMIM #252930)

Patient details provided to participants
50-year-old woman with retinitis pigmentosa but otherwise in good general condition. Slight scoliosis.
Further: Genetically confirmed: compound-heterozygous for two variants in HGSNAT gene.

Analytical performance
Increased heparan sulfate or differentiation profile compatible with MPS III was scored two points (10/21 labs). Increased total MPS was scored one point (1 lab). Concentration of total MPS were reported to be normal by 6 labs and elevated by 7 labs. The other labs did not report any result for total MPS.

Interpretative proficiency
Mucopolysaccharidosis type III as main diagnosis was scored two points (10/21 labs). Other types of mucopolysaccharidosis or unspecified or diagnosis according to the clinical presentation were scored one point (1 lab).

Overall impression
Relatively poor overall proficiency with 50%. Only half of the labs detected increased heparan sulfate and concluded to MPS type III.

Multiple distributions of similar samples

	2008	2019
Analytical performance	65%	80%
Interpretative performance	70%	80%
Overall performance	67%	80%

8.5. Patient E

Diagnosis
Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency

Patient details provided to participants
35-year-old female patient with episode of hypoglycaemia after prolonged fasting at 23 years of age.
Further: Genetically confirmed with two pathogenic variants:
c.1102_1105delAGTT/p.(Ala396Leufs*18) and c.985A>G/p.(Lys329Glu) in ACADM gene.

Analytical performance
Increased concentration of at least one metabolite specific for MCAD deficiency (hexanoylglycine, suberylglycine or 3-phenylpropionylglycine) was scored two points (21/21 labs).

Hexanoylglycine: range: 2-5.5 mmol/mol creatinine.
Suberylglycine: range: 1-4.5 mmol/mol creatinine.
3-phenylpropionylglycine: range: 40-110 mmol/mol creatinine.

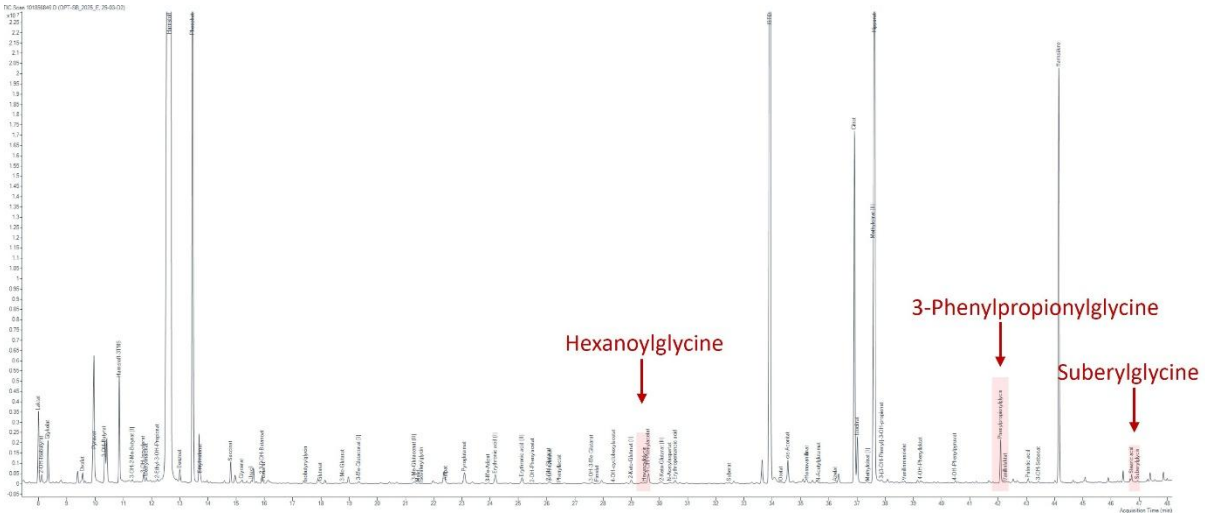


Figure 2: Organic acid analysis by gas chromatography mass spectrometry of sample E with typical metabolite abnormalities.

Interpretative proficiency
Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency as main diagnosis was scored two points (21/21 labs).

Overall impression
Excellent overall proficiency of 100%.

Multiple distributions of similar samples

	2006
Analytical performance	95%
Interpretative performance	95%
Overall performance	95%

8.6. Patient F

Diagnosis
Multiple acyl-CoA dehydrogenase deficiency (MADD). Electron transfer flavoprotein-ubiquinone oxidoreducatse (ETF-QO) deficiency.

Patient details
34-year-old female patient presented initially with Rey like syndrome. Currently under therapy, presenting mild ataxia but normal cognition.
Further: The therapy consist of fat-reduced diet combined with L-carnitine and riboflavin supplementation.

Analytical performance
Increased concentrations of at least three metabolites specific for MADD (ethylmalonic acid, glycine-conjugates, dicarboxylic acids) were scored two points (21/21 labs).

Ethylmalonate: range: 59-153 mmol/mol creatinine
Hexanoylglycine: range: 30-156 mmol/mol creatinine

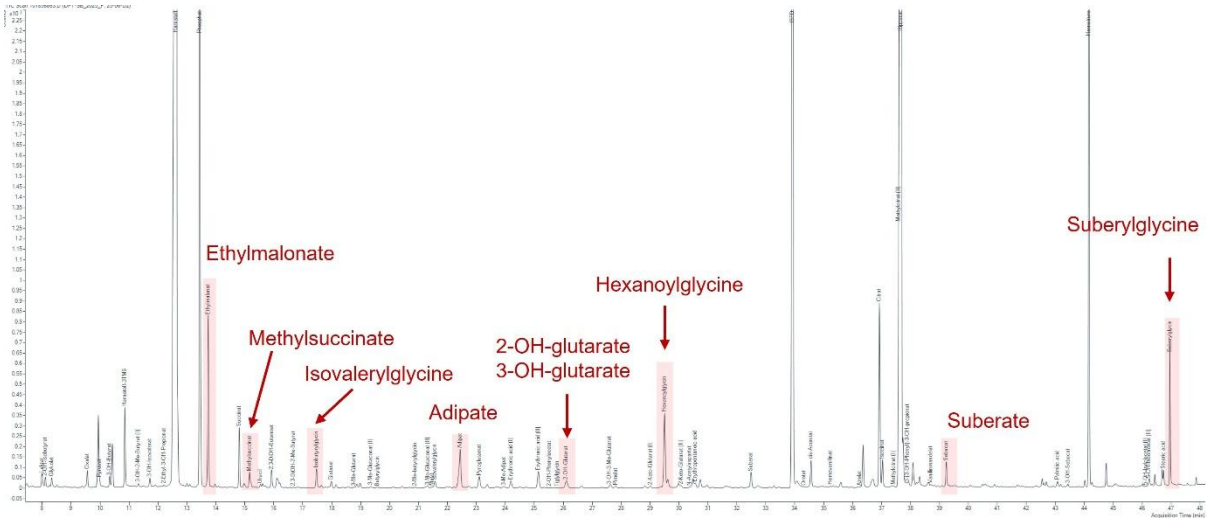


Figure 2: Organic acid analysis by gas chromatography mass spectrometry of sample F with typical metabolite abnormalities.

Interpretative proficiency
Multiple acyl-CoA dehydrogenase deficiency (MADD) as main diagnosis was scored two points (21/21 labs).

Overall impression
Excellent overall proficiency of 100%.

Multiple distributions of similar samples

	2023
Analytical performance	71%
Interpretative performance	71%
Overall performance	71%

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 MPS VI			Patient B Barth syndrome			Patient C MNGIE			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	1	1	2	2	2	4	2	1	3	9
3	2	1	3	2	2	4	1	1	2	9
4	2	2	4	2	2	4	2	2	4	12
5	2	1	3	2	2	4	1	1	2	9
6	2	2	4	2	2	4	2	2	4	12
7	1	2	3	2	2	4	2	2	4	11
8	2	2	4	2	2	4	2	2	4	12
9	1	1	2	2	2	4	2	2	4	10
10	2	2	4	2	2	4	2	2	4	12
11	1	1	2	2	2	4	2	2	4	10
12	2	2	4	2	2	4	2	2	4	12
13	1	1	2	2	2	4	1	0	1	7
14	2	2	4	2	2	4	2	2	4	12
15	2	2	4	2	2	4	2	2	4	12
16	1	1	2	2	2	4	2	2	4	10
17	1	1	2	2	2	4	2	2	4	10
18	1	1	2	2	2	4	2	2	4	10
19	2	2	4	2	2	4	1	2	3	11
20	2	2	4	2	2	4	2	2	4	12
21	1	1	2	2	2	4	2	2	4	10

Detailed scores – Round 2

Lab n°	Patient D MPS type IIIC			Patient E MCADD			Patient F MADD			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	0	0	0	2	2	4	2	2	4	8
3	0	0	0	2	2	4	2	2	4	8
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	2	2	4	2	2	4	12
7	1	0	1	2	2	4	2	2	4	9
8	0	1	1	2	2	4	2	2	4	9
9	0	0	0	2	2	4	2	2	4	8
10	2	2	4	2	2	4	2	2	4	12
11	0	0	0	2	2	4	2	2	4	8
12	0	0	0	2	2	4	2	2	4	8
13	2	2	4	2	2	4	2	2	4	12
14	0	0	0	2	2	4	2	2	4	8
15	0	0	0	2	2	4	2	2	4	8
16	2	2	4	2	2	4	2	2	4	12
17	0	0	0	2	2	4	2	2	4	8
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	2	2	4	2	2	4	12
20	0	0	0	2	2	4	2	2	4	8
21	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	4	4	4	24	100	
2	2	4	3	0	4	4	17	71	
3	3	4	2	0	4	4	17	71	
4	4	4	4	4	4	4	24	100	
5	3	4	2	4	4	4	21	88	
6	4	4	4	4	4	4	24	100	
7	3	4	4	1	4	4	20	83	
8	4	4	4	1	4	4	21	88	
9	2	4	4	0	4	4	18	75	
10	4	4	4	4	4	4	24	100	
11	2	4	4	0	4	4	18	75	
12	4	4	4	0	4	4	20	83	
13	2	4	1	4	4	4	19	79	
14	4	4	4	0	4	4	20	83	
15	4	4	4	0	4	4	20	83	
16	2	4	4	4	4	4	22	92	
17	2	4	4	0	4	4	18	75	
18	2	4	4	4	4	4	22	92	
19	4	4	3	4	4	4	23	96	
20	4	4	4	0	4	4	20	83	
21	2	4	4	4	4	4	22	92	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 70% of adequate responses)	21	100
Unsatisfactory performers (< 70% adequate responses and/or critical error)	0	0
Partial and non-submitters	0	0

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
DPT-SB-2025-A	MPS VI	**79**	**76**	**77**
DPT-SB-2025-B	Barth syndrome	**100**	**100**	**100**
DPT-SB-2025-C	MNGIE	**90**	**88**	**89**
DPT-SB-2025-D	MPS III	**50**	**50**	**50**
DPT-SB-2025-E	MCAD deficiency	**100**	**100**	**100**
DPT-SB-2025-F	MADD	**100**	**100**	**100**

10. Annual meeting of participants

This took place on October 9th in Madrid, Spain.

Participants: 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 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. Reminders

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

- Amino acids
- Organic acids
- Oligosaccharides
- Mucopolysaccharides
- Purine/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. 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 1st, 2026
Survey 2026/2 – Results submission deadline	June 22, 2026
Survey 2026/2 – Interim report available	July/August 2026
Annual meeting of participants	September/October, 2026
Annual Report 2026	January 2027

14. ERNDIM certificate of participation

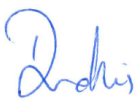
A combined certificate of participation covering all EQA schemes will be provided to all participants who take part in any ERNDIM scheme. For the DPT scheme this certificate will indicate if results were submitted and whether satisfactory performance was achieved in the scheme.

15. Questions, comments and suggestions

If you have any questions, comments or suggestions please address to the Scientific Advisor of the scheme, Déborah Mathis 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, 2025-01-21
Name and signature of Scientific Advisor



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

Version Number	Published	Amendments
1	01 April 2026	2025 annual report published

END