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Diagnostic Proficiency Testing Centre: Czech Republic

Final Report 2024

prepared by
Petr Chrastina

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

1. Geographical distribution of participants

Seventeen laboratories from 13 countries have participated in the Diagnostic Proficiency Testing scheme in 2024, for details see the below table:

Country	Number of participants
Austria	1
Croatia	1
Cyprus	1
Czech Republic	1
Denmark	1
Finland	1
Germany	5
Latvia	1
Lithuania	1
Malaysia	1
Portugal	1
Slovakia	1
Switzerland	1

[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 Petr Chrastina as Scientific Advisor and coordinated by Alessandro Salemma as scheme organiser (sub-contractor 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 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: All six urines were obtained from patients with known diagnoses. Four urine samples have been provided by the scheme organizers and one sample has been provided by Department of Clinical Biochemistry of University Children's Hospital in Bratislava. The common sample was from DPT Center Switzerland (distributed in all five DPT schemes).

In 2024 the samples have been heat-treated and apart from the common sample A were re-analyzed in our department after receiving the samples from CSCQ (samples were shipped via courier at ambient temperature to mimic possible changes that might arise during transport). In all five samples prepared and checked by us the typical metabolic profiles were preserved after heat treatment.
Mailing: samples were sent by DHL; FedEx or the Swiss Post at room temperature.

3. Tests

Analyses of amino acids, organic acids, mucopolysaccharides, oligosaccharides and purines/pyrimidines were required in 2024.

4. Schedule of the scheme

Sample distribution by CSCQ	07 February 2024
Start of analysis of Survey 2024/1	12 March 2024
Survey 2024/1 – results submission	02 April 2024
Survey 2024/1 – report	14 May 2024
Start of analysis of Survey 2024/2	03 June 2024
Survey 2024/2 – results submission	01 July 2024
Survey 2024/2 – report	05 August 2024
Annual meeting of participants	03 September 2024
Annual report 2024	January 2025

5. Results

16 of 17 labs returned results for both surveys by the deadline.

	Survey 1	**Survey 2**
Receipt of results	16	16
No answer	1	1

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 Czech Republic 2024 have been also scored by Joanne Croft, from DPT UK. At the SAB meeting on 28th November 2024, the definitive scores have been finalized.

ERNDIM is now applying the concept of 'critical error' in the scoring of results. In principle this is a category of error that would be unacceptable to the majority of labs and would have a serious adverse effect on patient management.

Examples of such errors could be:

a) Failure to recognise a pre-defined set of diagnoses.
b) Missing a diagnosis when proficiency for that EQA sample is >95% (where proficiency for an EQA sample is the percentage of EQA participants that correctly identified the diagnosis of the sample).
c) Failure to perform a relevant test.
d) Identifying a 'normal' sample as having an IEM when it is clear that the sample was obtained from a patient not suspected of having an IEM and the findings reported were not identified by the rest of the participants and this diagnosis could potentially result in treatment that is harmful for the patient.

When a critical error is established for one or more samples, performance is not acceptable in that year, regardless of the number of points assigned. A critical error needs to be ratified by the ERNDIM Scientific Advisory Board. In 2024, critical error was established for sample B.
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. Any partial submitters will receive a letter from the ERNDIM Executive Administrator, Sara Gardner.

7.1. Score for satisfactory performance

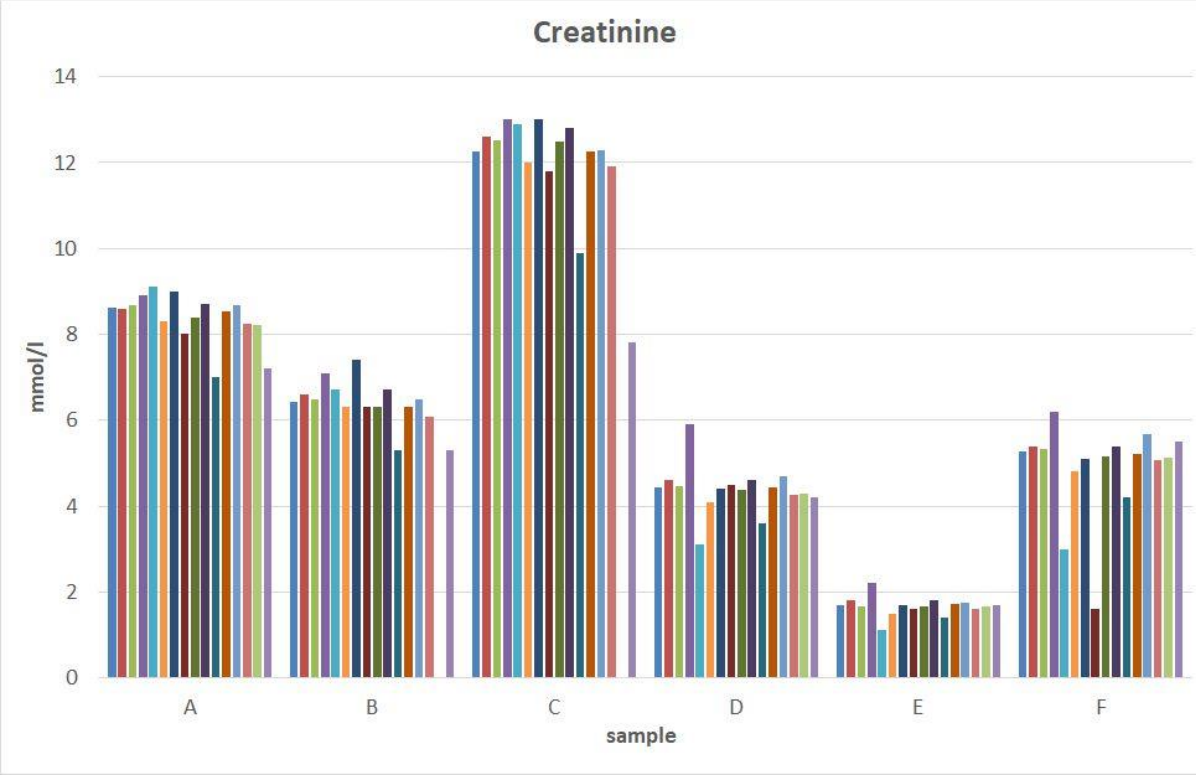
Performance of the participant that obtained at least 17 points from the maximum of 24 (71%) and more within the calendar year and that did not receive "critical error" mark is considered satisfactory.

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.

8. Results of samples and evaluation of reporting

8.1. Creatinine measurement for all samples

Creatinine determination was mostly satisfying with some outliers.



Sample	A	B	C	D	E	F
mean	8,39	6,39	11,97	4,37	1,66	4,88
median	8,57	6,43	12,28	4,42	1,69	5,18
SD	0,58	0,55	1,38	0,57	0,23	1,12

8.2. Patient A

malonyl-CoA decarboxylase deficiency

Patient details provided to participants

Diagnosed by family screening after sudden infant death of brother at 5 months of age in the context of an intercurrent viral infection. Dilated cardiomyopathy, normal development.

Patient details

The sample was obtained from a 15-years old boy with malonyl-CoA decarboxylase deficiency.

Analytical performance

All participants analyzed organic acids and 14 of them reported increased malonic acid excretion. Such an analytical finding was considered a correct result and scored 2 points. The analytical performance for this sample was good (88%).

Interpretative proficiency and recommendation

The diagnosis of malonyl-CoA decarboxylase deficiency as the most likely diagnosis was considered appropriate and scored 2 points. Confirmation of the diagnosis by enzymatic assay and/or mutation analysis of the *MLYCD* gene was considered helpful. Suspicion of combined malonic and methylmalonic

aciduria was considered helpful but incomplete. In this disorder, the excretion of methylmalonic acid is higher than the excretion of malonic acid. Combined malonic and methylmalonic aciduria as the most likely diagnosis received 1 point. The diagnosis of malonyl-CoA decarboxylase deficiency as another possible diagnosis was scored as 1 point. The proficiency score for this sample was good (88%).

Critical errors
No critical error for this sample.

Overall impression
Typical DPT sample with good proficiency score (88%).

8.3. Patient B

alpha-mannosidosis due to alpha-mannosidase deficiency

Patient details provided to participants
This girl was referred at the age of 1 year for facial dysmorphia. The sample was collected at the age of 5 years.

Patient details
The sample was obtained from a 5-year-old girl with alpha-mannosidosis due to alpha mannosidase deficiency. The diagnosis was confirmed by molecular genetic analysis.

Analytical performance
Fifteen laboratories performed OLS analysis and 12 of them reported a correct analytical result "OLS profile characteristic for alpha-mannosidosis", which was scored 2 points. The analytical performance was slightly suboptimal (75%).

Interpretative proficiency and recommendation
The diagnosis of alpha-mannosidosis due to alpha-mannosidase deficiency was considered correct and scored 2 points. Confirmation of the diagnosis by enzyme assay of alfa-mannosidase activity in plasma/fibroblasts/leukocytes and/or mutation analysis of the *MAN2B1* gene was considered helpful. The recommendation to perform oligosaccharide analysis for those participants who did not perform this analysis was also considered helpful and scored 1 point. The interpretation proficiency score for this sample was slightly suboptimal (78%).

Critical errors
The failure to recognize abnormal oligosaccharides profile is considered by the ERNDIM SAB as a critical error, which would prevent establishing the correct diagnosis; critical error was assigned to 3 participants.

Overall impression
Typical DPT sample with slightly suboptimal proficiency score (77%).

Over the years, the success rate of diagnosing alpha-mannosidosis has remained low.
To improve your performance in oligosaccharide analysis, we recommend that you consult the ERNDIM protocol for qualitative TLC oligosaccharide analysis (https://www.erndim.org/resources/) and consider purchasing a training kit containing samples of 6 common oligosaccharidoses (https://www.erndimqa.nl/Information.aspx?I=1068).

8.4. Patient C

mucopolysaccharidosis type VI due to arylsulfatase B deficiency

Patient details provided to participants
A 44-year-old man was referred for spinal stenosis and mild dysmorphy. The sample was collected at the age of 46 years; patient did not receive any therapy.

Patient details
The sample was obtained from a 46-years old man with mucopolysaccharidosis type VI due to arylsulfatase B deficiency. The diagnosis was confirmed by molecular genetic analysis.

Analytical performance
Twelve participants analyzed glycosaminoglycans (GAG) in urine and 13 participants performed GAG fractionation. Elevated excretion of glycosaminoglycans without report on chondroitin sulfate and/or dermatan sulfate elevation was considered as partially correct and scored with 1 point. Increased proportion of chondroitin sulfate and/or dermatan sulphate was scored as correct analytical result with 2 points. The analytical performance for this sample was slightly suboptimal (75%).

Interpretative proficiency and recommendation
The diagnosis of mucopolysaccharidosis type VI was considered correct (2 points), while suspicion for MPS (other types of MPS or non-specified MPS) was considered helpful but incomplete (1 point). Confirmation of the diagnosis by measurement of arylsulfatase B in leukocytes/fibroblasts and/or mutation analysis of the *ARSB* gene was considered helpful. Recommendation to perform GAG fractionation for those participants who did not perform this analysis was also considered helpful (1 point). The proficiency score for this sample was good (81%).

Critical errors
No critical error for this sample.

Overall impression
Typical DPT sample with slightly suboptimal proficiency score (78%).

8.5. Patient D

hyper-IgD syndrome due to mevalonate kinase deficiency

Patient details provided to participants
This boy was referred at the age of 16 years for repeated febrile illness. The sample was collected at the age of 25 years during a febrile illness.

Patient details
This sample was obtained from a 25-year-old man with hyper-IgD syndrome due to mevalonate kinase deficiency. The diagnosis was confirmed by molecular genetic analysis.

Analytical performance
All participants analyzed organic acids and only 11 of them reported increased excretion of mevalonolactone or mevalonic acid. Such an analytical finding was considered a correct result and scored 2 points. The proficiency score for this sample was slightly suboptimal (69%).

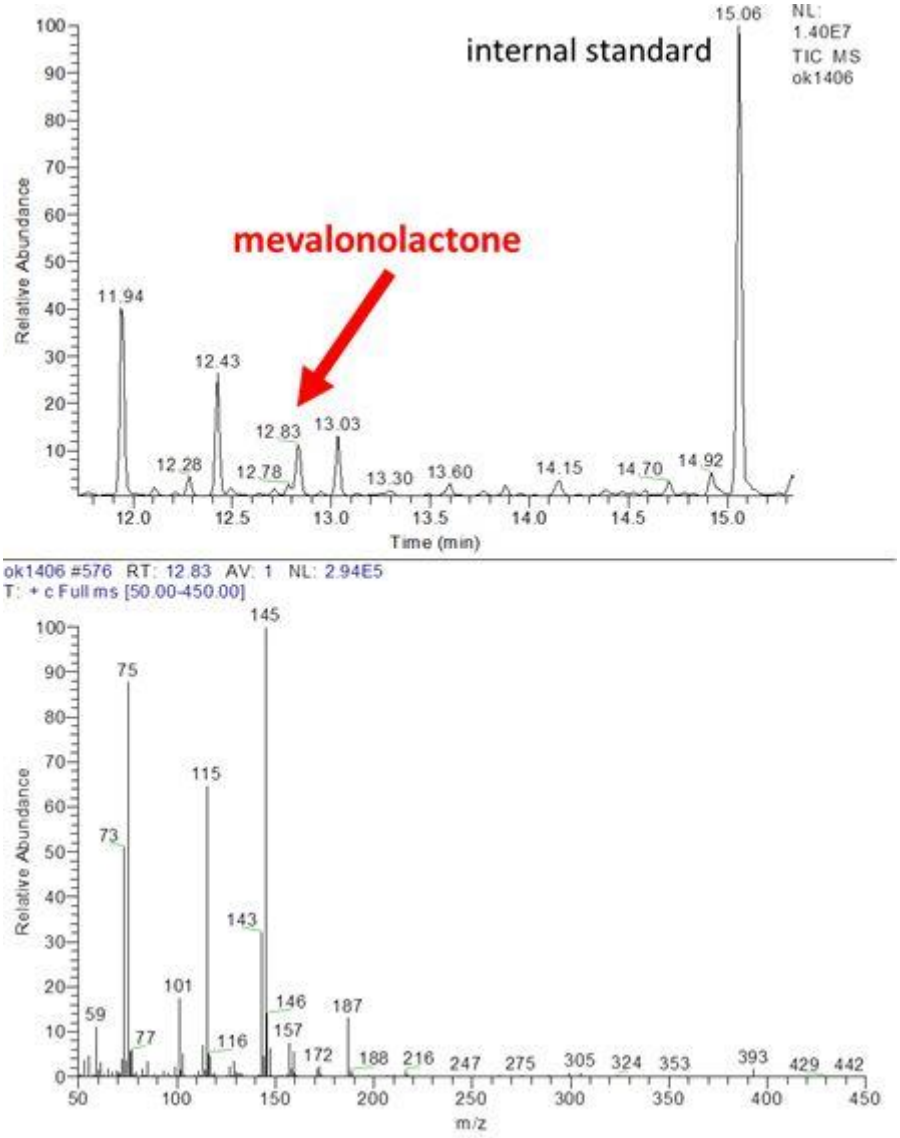
Interpretative proficiency and recommendation
Hyper-IgD syndrome or mevalonate kinase deficiency was considered a correct diagnosis and scored 2 points. The diagnosis of hyper-IgD syndrome based on clinical information was worth 1 point. Confirmation of the diagnosis by mutation analysis of the *MVK* gene was considered helpful. The proficiency score for this sample was slightly suboptimal (75%).

Critical errors
No critical error for this sample.

Overall impression
Typical DPT sample with slightly suboptimal proficiency score (72%).

The lack of annotation of increased excretion of mevalonic acid or mevalonolactone was a major analytical difficulty this year. Below, please, find examples of typical chromatogram for Sample D.

Figure 1: peak of mevalonolactone (GC/MS) in urine of patient 2024D (heat-treated urine after 3 days at RT) and mass spectrum of mevalonolactone



8.6. Patient E

methylmalonic aciduria due to methylmalonyl-CoA mutase deficiency

Patient details provided to participants

This boy was referred at the age of 3 days for hyperammonemia and metabolic acidosis. The sample was collected at the age of 4 years on the specific treatment.

Patient details

The sample was obtained from a 4-year-old boy with methylmalonic aciduria due to methylmalonyl-CoA mutase deficiency, diagnosis was confirmed by molecular genetic analysis.

Analytical performance

All participants analyzed organic acids and reported increased excretion of methylmalonic acid, such an analytical finding was considered correct and scored 1 point. All participants also reported increased excretion of methylcitric acid, such an analytical finding was also considered correct and scored 1 point. The analytical performance for this sample was excellent (100%).

Interpretative proficiency and recommendation

The diagnosis of methylmalonic aciduria due to methylmalonyl-CoA mutase deficiency was considered appropriate and scored 2 points. Confirmation of the diagnosis by mutation analysis of the *MMUT* gene was considered helpful. The proficiency score for this sample was excellent (100%).

Critical errors
No critical error for this sample.

Overall impression
Easy DPT sample with excellent proficiency score (100%).

8.7. Patient F

4-hydroxybutyric aciduria due to succinic semialdehyde dehydrogenase deficiency

Patient details provided to participants
This boy was referred at the age of 4 years for speech delay, moderate mental retardation, and frequent hyperactivity. The sample was collected at the age of 10 years.

Patient details
The sample was obtained from a 10-years old male patient with 4-hydroxybutyric aciduria due to succinic semialdehyde dehydrogenase deficiency. The diagnosis was confirmed by molecular genetic analysis.

Analytical performance
All participants analyzed organic acids and reported increased excretion of 4-hydroxybutyric acid, such an analytical finding was considered correct and scored 2 points. The analytical performance for this sample was excellent (100%).

Interpretative proficiency and recommendation
The diagnosis of 4-hydroxybutyric aciduria due to succinic semialdehyde dehydrogenase deficiency was considered appropriate and scored 2 points. Confirmation of the diagnosis by mutation analysis of the *ALDH5A1* gene was considered helpful. The proficiency score for this sample was excellent (100%).

Critical errors
No critical error for this sample.

Overall impression
Easy DPT sample with excellent proficiency score (100%).

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 malonyl-CoA decarboxylase deficiency			Patient B alpha-mannosidosis			Patient C mucopolysaccharidosis type VI			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	0	1	1	2	2	4	2	2	4	9
3	2	2	4	2	2	4	1	1	2	10
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	0	0	0	2	2	4	8
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	0	0	0	2	2	4	8
8	2	2	4	2	2	4	2	2	4	12
9	0	0	0	2	2	4	0	1	1	5
10	2	2	4	0	1	1	0	1	1	6
11	2	2	4	2	2	4	1	1	2	10
12	2	2	4	2	2	4	0	0	0	8
13	2	2	4	2	2	4	2	2	4	12
14	2	1	3	2	2	4	2	2	4	11
15	2	2	4	2	2	4	2	2	4	12
16	2	2	4	0	0	0	2	2	4	8
17	--	--	--	--	--	--	--	--	--	0

Detailed scores – Round 2

Lab n°	Patient D hyper-IgD syndrome			Patient E methylmalonic aciduria			Patient F 4-hydroxybutyric aciduria			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	0	0	0	2	2	4	2	2	4	8
3	2	2	4	2	2	4	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	0	1	1	2	2	4	2	2	4	9
7	2	2	4	2	2	4	2	2	4	12
8	2	2	4	2	2	4	2	2	4	12
9	0	0	0	2	2	4	2	2	4	8
10	2	2	4	2	2	4	2	2	4	12
11	2	2	4	2	2	4	2	2	4	12
12	2	2	4	2	2	4	2	2	4	12
13	0	0	0	2	2	4	2	2	4	8
14	2	2	4	2	2	4	2	2	4	12
15	2	2	4	2	2	4	2	2	4	12
16	0	1	1	2	2	4	2	2	4	9
17	--	--	--	--	--	--	--	--	--	0

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	1	4	4	0	4	4	17	71	
3	4	4	2	4	4	4	22	92	
4	4	4	4	4	4	4	24	100	
5	4	0	4	4	4	4	20	83	CE
6	4	4	4	1	4	4	21	88	
7	4	0	4	4	4	4	20	83	CE
8	4	4	4	4	4	4	24	100	
9	0	4	1	0	4	4	13	54	
10	4	1	1	4	4	4	18	75	
11	4	4	2	4	4	4	22	92	
12	4	4	0	4	4	4	20	83	
13	4	4	4	0	4	4	20	83	
14	3	4	4	4	4	4	23	96	
15	4	4	4	4	4	4	24	100	
16	4	0	4	1	4	4	17	71	CE
17	--	--	--	--	--	--	0	0	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 70 % of adequate responses)	12	71
Unsatisfactory performers (< 70 % adequate responses and/or critical error)	4	24
Partial and non-submitters	1	6

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
DPT-CP-2024-A	malonyl-CoA decarboxylase deficiency	88	88	88
DPT-CP-2024-B	alpha-mannosidosis	75	78	77
DPT-CP-2024-C	mucopolysaccharidosis type VI	75	81	78
DPT-CP-2024-D	hyper-IgD syndrome	69	75	72
DPT-CP-2024-E	methylmalonic aciduria	100	100	100
DPT-CP-2024-F	4-hydroxybutyric aciduria	100	100	100

10. Annual meeting of participants

The annual meeting of participants of the Proficiency Testing Centre Czech Republic was held during SSIEM Annual Symposium on 3rd September 2024 in Porto, Portugal.

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

- **Urine samples**: we remind you that every year, each participant must provide to the scheme organizer at least 300 ml of urine from a patient affected with an established inborn error of metabolism or “normal” urine, together with a short clinical report. If possible, please collect 1500 ml of urine: this sample can be sent to all labs participating to one of the DPT schemes. Each urine sample must be collected from a single patient (don’t send urine spiked with pathological compounds). Please don’t send a pool of urines, except if urine has been collected on a short period of time from the same patient. For “normal” urine, the sample must be collected from a symptomatic patient (don’t send urine from your kids!). As soon as possible after collection, the urine sample must be heated at 56 °C for 30 minutes. Make sure that this temperature is achieved in the entire urine sample, not only in the water bath. Please send us an e-mail about possible samples and we will organize transport with your cooperation.

12. Reminders

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

- Amino acids
- Organic acids
- Oligosaccharides
- Mucopolysaccharides

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 2025

Sample distribution	07 February 2025
Start of analysis of Survey 2025/1	17 March 2025
Survey 2025/1 – results submission	07 April 2025
Survey 2025/1 – report	20 May 2025
Start of analysis of Survey 2025/2	02 June 2025
Survey 2025/2 – results submission	23 June 2025
Survey 2025/2 – report	04 August 2025
Annual meeting of participants	to be determined by the ERNDIM SAB
Annual report 2025	January 2026

Since there will be no SSIEM Symposium in 2025 (and ICIEM Symposium will take place in the Japan) it is at present unclear when and where the next Annual Meeting of the DPT Czech Republic will be organized. Time and place will be decided by ERNDIM SAB.

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, Petr Chrastina (petr.chrastina@vfn.cz) and/or to the ERNDIM Administration Office (admin@erndim.org)

Date of report, 2025-01-23
Name and signature of Scientific Advisor

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

Version Number	Published	Amendments
1	24 January 2025	2024 annual report published

END