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Diagnostic Proficiency Testing

Centre: Switzerland

Final Report 2024

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 2024, 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	1
Germany	4
Norway	1
Sweden	2
Switzerland	1
United Kingdom	1
United States of America	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 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.
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 2024 have been provided by 2 different centres: Inselspital Bern, Switzerland and Kinderspital Zürich, Switzerland.

Patient A: Malonyl-CoA decarboxylase deficiency
Patient B: Citrullinemia type 1
Patient C: MPS type IVA
Patient D: Glutaraciduria type 1
Patient E: GM1 gangliosidosis
Patient F: Lesch-Nyhan syndrome

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.
Mailing: samples were sent by DHL; FedEx or the Swiss Post at room temperature.

3. Tests

Analyses of amino acids, organic acids, glycosaminoglycans and oligosaccharides were required in 2024.

4. Schedule of the scheme

- Feb 07, 2024: shipment of samples of Survey 1 and 2
- March 12, 2024: analysis of samples of the first survey
- March 26, 2024: deadline for result submission (Survey 1)
- June 03, 2024: analysis of samples of the second survey
- June 17, 2024: deadline for result submission (Survey 2)
- September 03, 2024: annual meeting of participants, Porto, Portugal.

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 2024 have been also scored by Christine Vianey-Saban, from the DPT F scheme. At the SAB meeting in November 2024, 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 2024, the SAB decided that a critical error has to be considered from sample C and E for the labs that did not consider lysosomal storage disorders at all.
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). One performance support letters has been sent by the Scientific Advisor for 2024. Any partial submitters will receive a letter from the ERNDIM Executive Administrator, Sara Gardner.

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
Malonyl-CoA decarboxylase deficiency (OMIM #248360)

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. Age at diagnosis: 3 years; current age 15 years.

Patient detailed information
Cognitive performance below average, mild learning disability. The patient is now integrated in special education. Patient overweighted, treated with precautionary measures to avoid catabolic state, on carnitine substitution.

Analytical performance
Detection of increased concentration of malonic acid in organic acid or C3DC-carnitine in acylcarnitine was scored 2 points (21/21 labs).

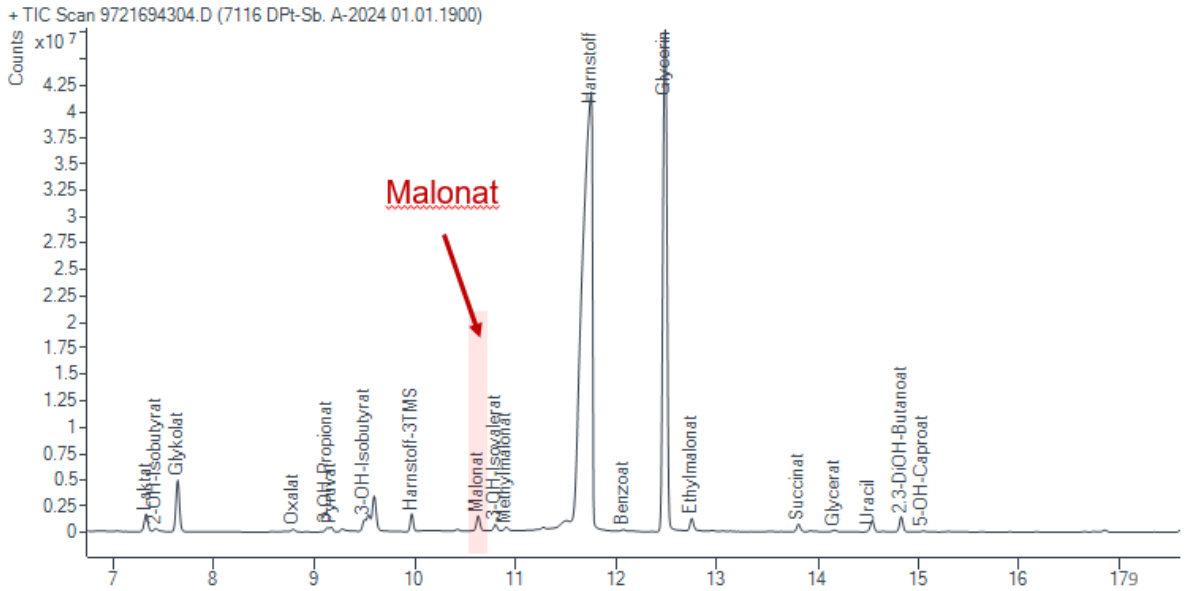

Figure 1: Organic acid analysis by GC-MS of sample A

Interpretative proficiency
Malonyl-CoA decarboxylase deficiency/malonic aciduria as main diagnosis was scored 2 points (17/21 labs). As alternative diagnosis it was scored 1 point (1 lab). CMAMMA as main or alternative diagnosis was scored 1 point (2 labs).

Appropriate further investigations
Analysis of acylcarnitine in blood. Confirmation of diagnosis by molecular analysis of MLCYD gene.

Overall impression
Very good overall proficiency of 98%. All labs detected and reported increased malonic acid, although the concentration was relatively low.

8.2. Patient B

Diagnosis
Citrullinemia type 1 (OMIM #215700)

Patient details provided to participants
Female patient on therapy, currently finishing normal school. Age at diagnosis: 9 months; current age 18 years.

Analytical performance
Detection of increased citrulline was scored 2 points (21/21 labs)

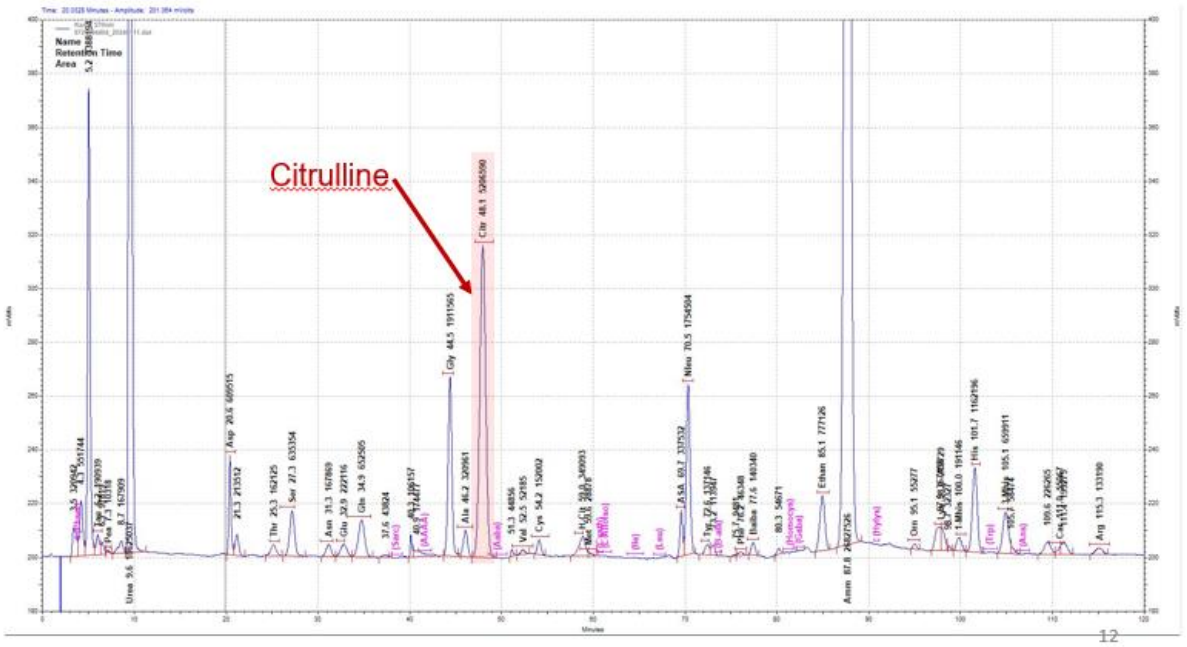

Figure 2: Amino acid analysis by ion-exchange chromatography of sample B

Interpretative proficiency
Citrullinemia type 1 as main or alternative diagnosis was scored with two points (19/21 labs).

Appropriate further investigations
Analysis of plasma ammonia and amino acids. Confirmation of diagnosis with enzymatic activity or genetic analysis of *ASS* gene.

Overall impression
Excellent analytical proficiency of 100%. Few labs interpreted increased citrulline as therapy and pointed towards OTC deficiency. ASL deficiency was also reported, as few labs detected slight increase in argininosuccinic acid. Very good overall proficiency of 95%.

Multiple distributions of similar samples

	2010	2013	2017
Overall performance	96%	97%	98%

8.3. Patient C

Diagnosis
Mucopolysaccharidosis type IVA (OMIM #253000)

Patient details provided to participants
Patient presented with short stature and pectus cranium carinatum but normal cognitive development. Age at diagnosis: 4 years; current age 21 years.

Analytical performance
Increased keratan sulfate or differentiation profile compatible with MPS IV was scored two points (11/21 labs). Increased total MPS was scored one point (16/21 labs).

Interpretative proficiency
Mucopolysaccharidosis type IVa as main diagnosis was scored two points (12/21 labs). Other types of mucopolysaccharidosis was scored one point (8/21 lab). One lab did not suggest lysosomal storage diseases at all.

Appropriate further investigations
Determination of enzyme activity of galactose-6-sulfatase and beta-galactosidase in leukocytes/fibroblasts. Molecular analysis of GALNS and GLB1 genes

Overall impression
Analytical proficiency of 74% is typical for MPS diagnosis as not all labs perform the differentiation of GAGs. Interpretation proficiency of 76% was very good, in part due to the specific clinical information given. Only one lab reported normal mucopolysaccharides. Overall proficiency was of 75%.

Multiple distributions of similar samples

	2014	2018
Overall performance	78%	72%

8.4. Patient D

Diagnosis
Glutaric aciduria type 1 (GA1); glutaryl-CoA dehydrogenase deficiency (OMIM #231670)

Patient details provided to participants
25 years old woman, who presented at age 2 with acute encephalopathy

Analytical performance
Increased excretion of glutaric acid and 3-OH-glutaric acid was scored 2 points (21/21 labs)

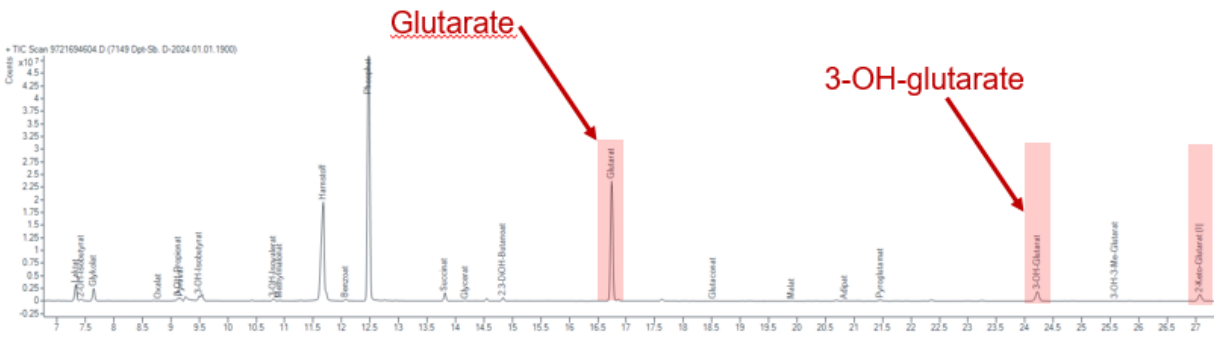

Figure 3: Organic acid analysis by GC-MS of sample D

Interpretative proficiency
Glutaric aciduria type 1 was scored 2 points (21/21 labs)

Appropriate further investigations
Analyse acylcarnitine in blood, confirm diagnosis with enzyme activity and/or genetic analysis of the GCDH gene.

Overall impression
Excellent proficiency with analytical and interpretation proficiency of 100%.

Multiple distributions of similar samples

	2015
Overall performance	90%

8.5. Patient E

Diagnosis
GM1 gangliosidosis, beta-galactosidase-1 deficiency.

Patient details provided to participants
15 months old boy with global developmental delay, dysmorphic features, enlarged liver. Diagnosis at 4 months of age.

Analytical performance
Abnormal pattern of oligosaccharides or mucopolysaccharides suggestive of GM1 was scored two points (17/21 labs). Recommendation to perform oligosaccharides or repeat analysis in fresh and more concentrated urine sample was scored 1 point (3/21 labs).

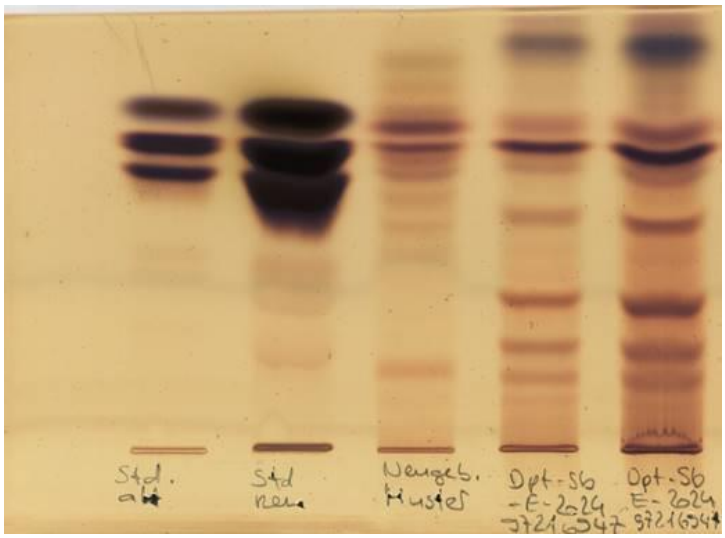

Figure 4: Qualitative TLC oligosaccharides of sample E

Interpretative proficiency
GM1-gangliosidosis as main diagnosis was scored 2 points (17/21 labs). Lysosomal storage disorders or wrong type of MPS was scored 1 point (3/21 labs).

Appropriate further investigations
Confirm diagnosis with enzyme activity and/or genetic analysis

Overall impression
Good performance with 88% proficiency in this sample with very low concentration of creatinine.

Multiple distributions of similar samples

	2006	2013	2018
Overall performance	66%	69%	65%

8.6. Patient F

Diagnosis
Lesch-Nyhan syndrome, HPRT deficiency (OMIM #300322)

Patient details
Patient with developmental delay and muscular hypotonia since 1 year of age. Later dystonia and irritability developed. Urine collected at 6 years on treatment with allopurinol.

Analytical performance
Increased excretion of xanthine and hypoxanthine was scored two points (18/21 labs).

Interpretative proficiency
Lesch-Nyhan syndrome as main diagnosis was scored 2 points (18/21 labs).

Appropriate further investigations
Confirm diagnosis with enzyme activity and/or genetic analysis of HPRT1 gene.

Overall impression
3 of 21 labs missed elevation of xanthine and hypoxanthine and thus the diagnosis resulting in an overall proficiency of 85%.

Multiple distributions of similar samples

	2014	2018
Overall performance	63%	76%

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 Malonic aciduria			Patient B Citrullinemia type 1			Patient C MPS IVa			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	1	2	3	11
2	2	2	4	2	2	4	1	1	2	10
3	2	1	3	2	2	4	2	2	4	11
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	2	2	4	1	2	3	11
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	2	2	4	2	2	4	12
8	2	2	4	2	2	4	2	2	4	12
9	2	2	4	2	2	4	1	1	2	10
10	2	2	4	2	0	2	2	2	4	10
11	2	2	4	2	2	4	1	1	2	10
12	2	2	4	2	2	4	2	2	4	12
13	2	2	4	2	2	4	2	2	4	12
14	2	2	4	2	2	4	2	2	4	12
15	2	2	4	2	2	4	2	2	4	12
16	2	2	4	2	2	4	2	2	4	12
17	2	2	4	2	2	4	1	1	2	10
18	2	2	4	2	0	2	1	1	2	8
19	2	2	4	2	2	4	0	0	0	8
20	2	2	4	2	2	4	1	2	3	11
21	2	1	3	2	2	4	1	1	2	9

Detailed scores – Round 2

Lab n°	Patient D GA1			Patient E GM1 gangliosidosis			Patient F Lesch-Nyhan syndrome			
	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	1	2	3	11
3	2	2	4	2	2	4	0	0	0	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	2	2	4	1	1	2	2	2	4	10
8	2	2	4	2	2	4	2	2	4	12
9	2	2	4	2	2	4	2	2	4	12
10	2	2	4	2	2	4	2	2	4	12
11	2	2	4	1	1	2	2	2	4	10
12	2	2	4	2	2	4	2	2	4	12
13	2	2	4	2	2	4	0	0	0	8
14	2	2	4	2	2	4	2	2	4	12
15	2	2	4	2	2	4	2	2	4	12
16	2	2	4	2	2	4	2	2	4	12
17	2	2	4	1	1	2	2	2	4	10
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	0	0	0	2	2	4	8
20	2	2	4	2	2	4	2	2	4	12
21	2	2	4	2	2	4	0	0	0	8

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	4	3	4	4	4	23	96	
2	4	4	2	4	4	3	21	88	
3	3	4	4	4	4	0	19	79	
4	4	4	4	4	4	4	24	100	
5	4	4	3	4	4	4	23	96	
6	4	4	4	4	4	4	24	100	
7	4	4	4	4	2	4	22	92	
8	4	4	4	4	4	4	24	100	
9	4	4	2	4	4	4	22	92	
10	4	2	4	4	4	4	22	92	
11	4	4	2	4	2	4	20	83	
12	4	4	4	4	4	4	24	100	
13	4	4	4	4	4	0	20	83	
14	4	4	4	4	4	4	24	100	
15	4	4	4	4	4	4	24	100	
16	4	4	4	4	4	4	24	100	
17	4	4	2	4	2	4	20	83	
18	4	2	2	4	4	4	20	83	
19	4	4	0	4	0	4	16	67	
20	4	4	3	4	4	4	23	96	
21	3	4	2	4	4	0	17	71	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 70% of adequate responses)	20	95
Unsatisfactory performers (< 70% adequate responses and/or critical error)	1	5
Partial and non-submitters	0	0

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
DPT-SB-2024-A	Malonic aciduria	**100**	**95**	**98**
DPT-SB-2024-B	Citrullinemia type 1	**100**	**90**	**95**
DPT-SB-2024-C	MPS IVa	**74**	**76**	**75**
DPT-SB-2024-D	Gluarciduria type 1	**100**	**100**	**100**
DPT-SB-2024-E	GM1-gangliosidosis	**88**	**88**	**88**
DPT-SB-2024-F	Lesch-Nyhan syndrom	**83**	**86**	**85**

10. Annual meeting of participants

This took place on September 03 in Porto, Portugal.

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

Urine samples: we remind you that each participant should endeavour to provide to the scheme organizer at least 300 ml of urine from a patient affected with an established inborn error of metabolism 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 over a short period of time from the same patient. Please don't send "normal" urine. Please send us an e-mail if you have such a sample and we will arrange the shipment.

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 2025

Sample distribution	February 5, 2025
Start of analysis of Survey 2025/1 (website open)	March 17, 2025
Survey 2025/1 - Results submission deadline	April 7, 2025
Survey 2025/1 – Interim report available	April/May 2025
Start of analysis of Survey 2025/2 (website open)	June 2, 2025
Survey 2025/2 – Results submission deadline	June 23, 2025
Survey 2025/2 – Interim report available	July/August 2025
Annual meeting of participants	September/October, 2025
Annual Report 2025	January 2026

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 (deborah.mathis@insel.ch) and/or to the ERNDIM Administration Office (admin@erndim.org)

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	21 January 2025	2024 annual report published

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