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Diagnostic Proficiency Testing
Centre: Czech Republic

Final Report 2020

prepared by
Petr Chrastina

Published: 17 February 2021[1]

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.

Note: Results of your laboratory are marked with arrows.

The fact that your laboratory participates in ERNDIM schemes is not confidential, however, the raw data and performance scores are confidential and will only be shared within ERNDIM for the purpose of evaluating your laboratories performance, unless ERNDIM is required to disclose performance data by a relevant government agency. For details please see the terms and conditions on page18 and the ERNDIM Privacy Policy on www.erndim.org.

1. Geographical distribution of participants

Twenty-one laboratories from 13 countries have participated in the Diagnostic Proficiency Testing scheme in 2019, for details see the below table:

Country	Number of participants	Country	Number of participants
Undefined country	1	Germany	6
Austria	1	Latvia	1
Croatia	1	Lithuania	1
Cyprus	1	Malaysia	1
Czech Republic	1	Poland	1
Denmark	1	Portugal	1
Finland	1	Slovakia	2

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 Xavier Albe 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

[1] If these scheme instructions are not Version 1 for this scheme year, go to APPENDIX 1 for details of the changes made since the last version of this document

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 France (distributed in all five DPT schemes).

In 2020 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 after 3 days at ambient temperature to mimic possible changes that might arise during transport). In all six samples prepared and checked by us the typical metabolic profiles were preserved after heat treatment and shipment from CSCQ.
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 2020.

4. Schedule of the scheme

Due to the disruption many labs are experiencing because of Covid-19, the March 2020 submission deadline have all been delayed until June 2020.

Sample distribution	February 11, Tuesday
Start of analysis of Survey 2020/1 Website open	March 9, Monday
Survey 2020/1 - Results submission	June 1, Monday
Survey 2020/1 - Reports	July 7, Tuesday
Start of analysis of Survey 2020/2	June 8, Monday
Survey 2020/2 – Results submission	June 29, Monday
Survey 2020/2 - Reports	August 10, Friday
Annual meeting of participants	September 2, Wednesday
Annual Report 2020	December 2020

5. Results

19 of 20 labs returned results for both surveys, mainly by the deadline.

	Survey 1	**Survey 2**
Receipt of results	20	20
No answer	0	0

6. Web site reporting

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

- Selection of tests: **don't select a test if you will not perform it**, otherwise the evaluation program includes it in the report.
- Results
  - Give quantitative data as much as possible.
  - Enter the key metabolites with the evaluation **in the tables** even if you don't give quantitative data.
  - If the profile is normal: enter "Normal profile" in "Key metabolites".
  - **Don't enter results in the "comments" window**, **otherwise your results will not be included in the evaluation program.**
- Recommendations = **advice for further investigation**.
  - Scored together with the interpretative score.
  - Advice for treatment are not scored.
  - **Don't give advice for further investigation in "Comments on diagnosis"**: it will not be included in the evaluation program.

7. Scoring and evaluation of results

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

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

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

Scoring and certificate of participation: scoring is carried by a second assessor who changes every year as well as by the scientific advisor. The results of DPT Czech Republic 2020 have been also scored by Joanne Croft, from DPT UK. At the SAB meeting in 19th October 2020, 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. There were no critical errors in 2020.

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 12 points from the maximum of 20 (60%) and more within the calendar year and that did not receive “critical error” mark is considered satisfactory.

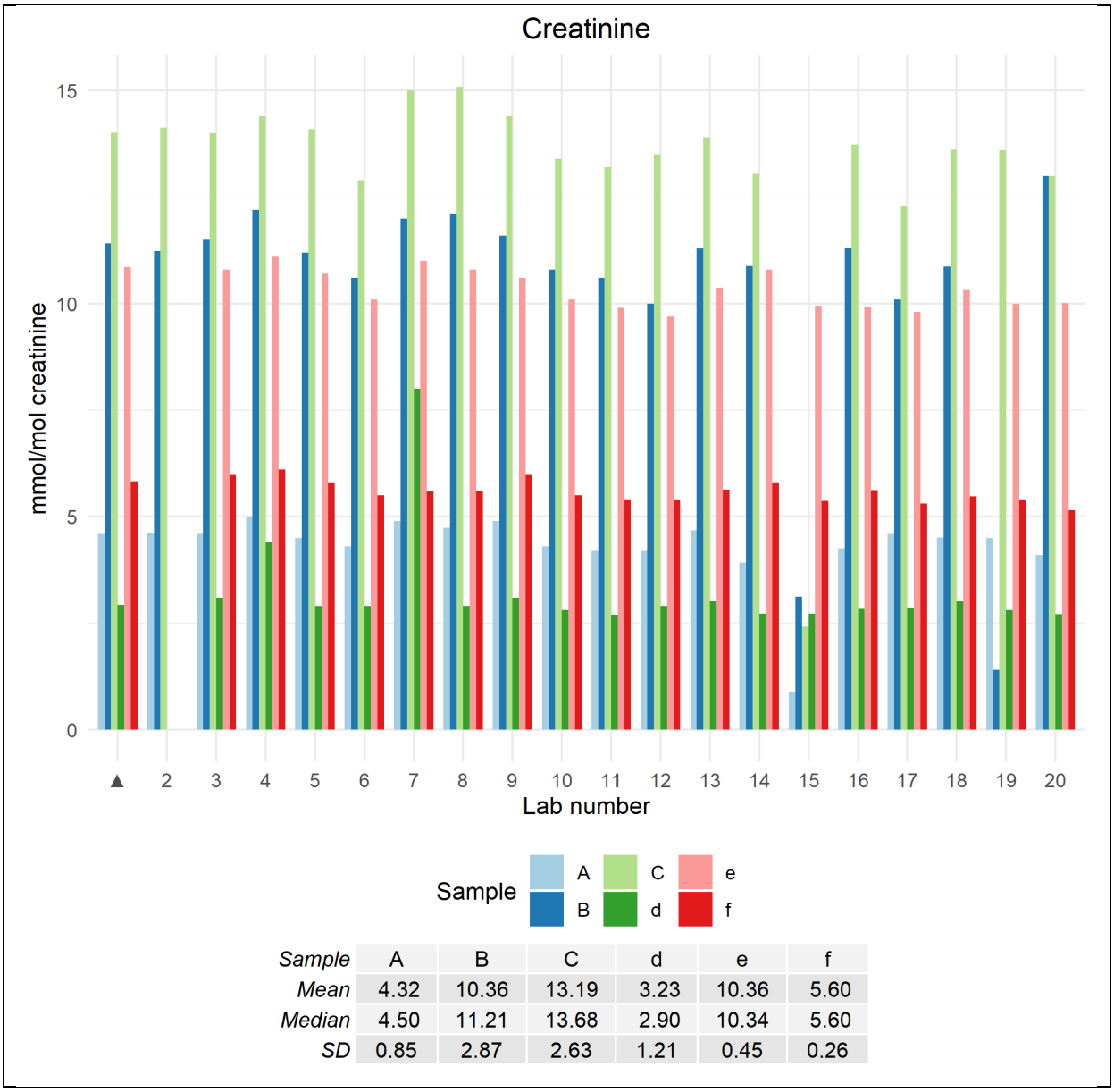
If your laboratory is assigned poor performance and you wish to appeal against this classification please email the ERNDIM Administration Office (admin@erndim.org), with full details of the reason for your appeal, within one month receiving your Performance Support Letter.

8. Results of samples and evaluation of reporting

8.1. Creatinine measurement for all samples

Creatinine determination was mostly satisfying. There were 4 outlier values. Creatinine values are expressed in the figure as the ratio of each measurement over the median of all labs.

Creatinine: ratio to median



Sample	A	B	C	d	e	f
Mean	4.32	10.36	13.19	3.23	10.36	5.60
Median	4.50	11.21	13.68	2.90	10.34	5.60
SD	0.85	2.87	2.63	1.21	0.45	0.26

8.2. Patient A

Phenylketonuria

Patient details provided to participants
Adult patient investigated due to spastic paraparesis, leukodystrophy and hemolytic uremic syndrome

Patient details
The sample was obtained from an untreated adult patient with phenylketonuria, diagnosis was confirmed by molecular genetic analysis.

Analytical performance
Eighteen participants analyzed urinary amino acids and reported high excretion of phenylalanine, such analytical finding was considered correct and scored by 1 point. All participants performed analysis of organic acids and observed the high excretion of the metabolites typical for PKU (phenyllactate, phenylpyruvate, 2-OH-phenylacetate etc.), such analytical finding was also considered correct and scored by 1 point. The analytical performance for this sample was very good (95%).

Interpretative proficiency and recommendation
Phenylketonuria was considered the correct diagnosis. Confirmation of diagnosis by mutation analysis 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 very good proficiency score (98%).

8.3. Patient B

Cystinuria

Patient details provided to participants
A 4 years old boy with kidney stones. The sample was collected at the age of 13 years; patient received specific therapy.

Patient details
The sample was obtained from a 13-years old boy with cystinuria. The diagnosis was established by molecular genetic analysis.

Analytical performance
All participants analyzed urinary amino acids. 19 participants reported presence of cystinuria and dibasic hyperaminoaciduria, such analytical finding was considered a correct analytical result and scored by 2 points. Dibasic hyperaminoaciduria only was scored as partially correct by 1 point. The analytical performance was very good (98%).

Interpretative proficiency and recommendation
Cystinuria was considered the correct diagnosis. Confirmation of diagnosis by mutation analysis 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 very good proficiency score (99%).

8.1. Patient C

alpha-mannosidosis

Patient details provided to participants

A 13 years old girl was referred for dysostosis multiplex and psychomotor retardation. The sample was collected at the age of 35 years; patient did not receive any therapy.

Patient details

This sample was obtained from a 35 years old woman with alpha-mannosidosis due to alpha-mannosidase deficiency, diagnosis was confirmed by molecular genetic analysis.

Analytical performance

17 labs performed OLS analysis and 16 of them reported a correct analytical finding "OLS profile characteristic for alpha-mannosidosis", which was scored with 2 points. The analytical performance was good (83%).

Interpretative proficiency and recommendation

The diagnosis of alpha-mannosidosis due to alfa-mannosidase deficiency was considered correct. Confirmation of diagnosis by enzyme assay of alfa-mannosidase activity in plasma/fibroblasts/leucocytes and/or mutation analysis of *MAN2B1* gene were considered helpful. Recommendation to carry out oligosaccharide analysis for those
participants who did not perform this analysis was considered also helpful and scored with 1 point. The interpretative proficiency score for this sample was very good (90%).

Critical errors

No critical error for this sample.

Overall impression

Typical DPT sample with good proficiency score (86%).

8.1. Patient D

Canavan disease

Patient details provided to participants

This boy was referred at the age of 8 months with severe psychomotor retardation, developmental delay and facial dysmorphia. The sample was collected at the age of 2 years; patient did not receive any therapy.

Patient details

The sample was obtained from a 2-years old boy with Canavan disease due to aspartoacylase deficiency. The diagnosis was confirmed by molecular genetic analysis.

Analytical performance

All participants performed analysis of organic acids and observed high excretion of N-acetylaspartate, such analytical finding was considered correct and scored by 2 points. The analytical performance for this sample was excellent (100%).

Interpretative proficiency and recommendation

Canavan disease was considered the correct diagnosis. Confirmation of diagnosis by mutation analysis of *ASPA* 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%).

8.1. Patient E

Adenylosuccinase deficiency

Patient details provided to participants
This male patient was referred at the age of 17 years with mild mental retardation. Since the age of 2 years developmental was observed. The sample was obtained at the age of 18 years; patient did not receive any therapy.

Patient details
The sample was obtained from an 18-years old man with adenylosuccinase deficiency. The diagnosis was established by molecular analysis.

Analytical performance
Only 11 participants analyzed urinary purines and pyrimidines. Seven participants reported accumulation of succinyladenosine (S-Ado) and/or succinylaminoimidazole carboxamide riboside (SAICAr), such analytical finding was considered a correct analytical result and scored by 2 points. The analytical performance was very poor (37%).

Interpretative proficiency and recommendation
Adenylosuccinase deficiency was considered the correct diagnosis. Confirmation of diagnosis by mutation analysis of *ADSL* gene was considered helpful. Suspicion of other disorders of purine and pyrimidine metabolism was considered helpful but incomplete and scored with 1 point. Recommendation to carry out purines and pyrimidines analysis for those participants who did not perform this analysis was considered also helpful and scored with 1 point. The proficiency score for this sample was poor (47%).

Critical errors
No critical error for this sample.

Overall impression
Typical DPT sample with poor proficiency score (42%).

8.1. Patient F

No IEM

Patient details provided to participants

A 45 years old man was referred for hematuria. The sample was obtained at the age of 45 years; patient did not receive any therapy.

Patient details

This sample was obtained from a 45 years old man without any evidence of an inherited metabolic disorder after extensive metabolic screening.

Analytical performance

18 participants analyzed minimally 3 of the 5 required methods. Normal profile and/or profile without specific finding were considered correct and scored by 2 points. One participant analyzed only urinary amino acids and urinary organic acids. Normal profile of these two methods was considered helpful and scored with 1 point. The analytical performance was excellent (97%).

Interpretative proficiency and recommendation

We considered the report of “no IEM” or “non-specific finding” a good diagnosis, which was scored with 2 points. The interpretative proficiency score for this sample was good (89%).

Critical errors

No critical error for this sample.

Overall impression

Typical DPT sample with very good proficiency score (93%).

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.

Detailed scores – **Round 1**

Lab n°	Patient A Phenylketonuria			Patient B Cystinuria			Patient C alpha-mannosidosis			
	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	0	0	0	8
3	2	2	4	2	2	4	2	2	4	12
4	1	2	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	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	2	2	4	12
10	2	2	4	2	2	4	0	0	0	8
11	2	2	4	2	2	4	0	1	1	9
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	0	0	0	8
16	2	2	4	2	2	4	2	2	4	12
17	2	2	4	2	2	4	2	2	4	12
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	2	2	4	2	2	4	12
20	1	2	3	1	2	3	2	2	4	10

Detailed scores – Round 2

Lab n°	Patient D Canavan disease			Patient E Adenylosuccinase deficiency			Patient F No IEM			
	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	0	0	0	0	0	0	0
3	2	2	4	2	0	2	2	2	4	10
4	2	2	4	0	0	0	2	2	4	8
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	0	0	0	2	2	4	8
7	2	2	4	2	2	4	2	2	4	12
8	2	2	4	0	0	0	2	2	4	8
9	2	2	4	2	2	4	2	2	4	12
10	2	2	4	0	0	0	2	2	4	8
11	2	2	4	0	1	1	2	2	4	9
12	2	2	4	0	1	1	1	0	1	6
13	2	2	4	0	1	1	2	2	4	9
14	2	2	4	0	0	0	2	2	4	8
15	2	2	4	0	0	0	2	2	4	8
16	2	2	4	0	1	1	2	2	4	9
17	2	2	4	0	1	1	2	0	2	7
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	2	2	4	2	2	4	12
20	2	2	4	0	1	1	2	2	4	9

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	0	0	0	0	8	33	
3	4	4	4	4	2	4	22	92	
4	3	4	4	4	0	4	19	79	
5	4	4	4	4	4	4	24	100	
6	4	4	4	4	0	4	20	83	
7	4	4	4	4	4	4	24	100	
8	4	4	4	4	0	4	20	83	
9	4	4	4	4	4	4	24	100	
10	4	4	0	4	0	4	16	67	
11	4	4	1	4	1	4	18	75	
12	4	4	4	4	1	1	18	75	
13	4	4	4	4	1	4	21	88	
14	4	4	4	4	0	4	20	83	
15	4	4	0	4	0	4	16	67	
16	4	4	4	4	1	4	21	88	
17	4	4	4	4	1	2	19	79	
18	4	4	4	4	4	4	24	100	
19	4	4	4	4	4	4	24	100	
20	3	3	4	4	1	4	19	79	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 60 % of adequate responses)	19	95
Unsatisfactory performers (< 60 % adequate responses and/or critical error)	1	5
Partial and non-submitters	0	0

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
DPT-CP-2020-A	Phenylketonuria	95	100	98
DPT-CP-2020-B	Cystinuria	98	100	99
DPT-CP-2020-C	alpha-mannosidosis	80	83	81
DPT-CP-2020-D	Canavan disease	95	95	95
DPT-CP-2020-E	Adenylosuccinase deficiency	35	45	40
DPT-CP-2020-F	No IEM	93	85	89

10. Annual meeting of participants

The annual meeting of participants of the Proficiency Testing Centre Czech Republic was held online on 2nd September 2020 instead of a face-to-face meeting as international travel restrictions were in place due to Covid-19. 28 participants from 10 laboratories were represented.

- This year we encountered one major analytical difficulty, namely purines and pyrimidines (P/P) analysis. Recommendation for P/P analysis is available on ERNDIM website.

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

- New **reference materials** are now provided by SKML: they are not related to EQA samples anymore. There are two concentration levels for each group of analytes. The most suitable low and high concentration levels are defined by the respective scientific advisors. Analytes and their concentrations will be approximately the same in consecutive batches of control material. These reference materials can be ordered through the ERNDIM website. Participants are encouraged to use them as internal control, but they cannot be used as calibrants. On the 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.

- A set of **organic acid mixtures** has been developed by Dr Herman ten Brink in Amsterdam, following request and advice from ERNDIM. The product is currently available at: HJ.tenBrink@VUmc.nl
- **Training**: SSIEM Academy training courses.
  - A 2 days course will be been organized in 2021 in Amsterdam. The program includes:
    - Aminoacidopathies
    - Hyperammonaemia
    - Urea Cycle Defects
  - The lectures will be available on the SSIEM website
- **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 60 minutes. Make sure that this temperature is achieved in the entire urine sample, not only in the water bath. Send the samples by rapid mail or express transport to:

  Petr Chrastina
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  General University Hospital in Prague
  Ke Karlovu 2
  128 08 Prague 2
  Czech Republic
  Tel: +420 224 947 161
  Email: petr.chrastina@vfn.cz

  Please send us an e-mail on the day you send the samples.

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 and fee in 2021

Sample distribution	February 9, Tuesday
Start of analysis of Survey 2021/1 Website open	March 8, Monday
Survey 2021/1 - Results submission	March 29, Monday
Survey 2021/1 - Reports	May 10, Monday
Start of analysis of Survey 2021/2	June 7, Monday
Survey 2021/2 – Results submission	June 28, Monday
Survey 2021/2 - Reports	August 9, Monday
Annual meeting of participants	October 20/21, Rome
Annual Report 2021	December 2021

Since there will be no SSIEM Symposium in 2021 (and ICIEM Symposium will take place in the Australia) the next Annual Meeting of the DPT Czech Republic will take place on September 20th and 21st in Rome, Italy.

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.

Date of report, 2020-12-09
Name and signature of Scientific Advisor

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

Version Number	Published	Amendments
1	18 January 2021	2020 annual report published
2	8th February 2021	Page 5, Poor Performance Policy, information for appeal of poor performance added.

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