ERNDIM Administration Office
Manchester Centre for Genomic Medicine
6th floor, St Mary's Hospital
Oxford Road
Manchester
M13 9WL
UK

ERNDIM Administration Office	Scientific Coordination	Scheme Organisation
Manchester Centre for Genomic Medicine 6th floor, St Mary's Hospital Oxford Road Manchester M13 9WL UK Email: admin@erndim.org	Prof. Viktor Kozich, Petr Chrastina Department of Pediatrics and Adolescent Medicine General Faculty Hospital and Charles University 1st Faculty of Medicine Ke Karlovu 2 128 08 Prague 2 Czech Republic Tel: +420 224 947 161 or 224 967 679 Fax: +420 224 967 081 or 224 967 119	CSCQ (Quality Control Centre, Switzerland) Xavier Albe 2 chemin du Petit-Bel-Air 1225 Chêne-Bourg Switzerland, Tel: +41 22 305 52 36 Email: Xavier.Albe@hcuge.ch

Diagnostic Proficiency Testing
Centre: Czech Republic

Final Report 2018

prepared by
Prof. Viktor Kozich and 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.

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 14 countries have participated in the Diagnostic Proficiency Testing scheme in 2018, for details see the below table:

Country	Number of participants
Austria	1
Croatia	1
Cyprus	1
Czechia	1
Denmark	1
Finland	1
Germany	7
Latvia	1
Lithuania	1
Malaysia	1
Netherlands	1
Poland	1
Portugal	1
Slovakia	2

Version Number (& Date)	Amendments
[1] version 2 (19th July 2019)	• Page 15: Scientific Advisor signature added to authorization.

2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Viktor Kožich and Petr Chrastina as Scientific Advisors and coordinated by Xavier Albe as scheme organizer (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: All six urines were obtained from patients with known diagnoses. Five 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 our DPT center (distributed in all five DPT schemes).

In 2018 the samples have been heat-treated and 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 2018.

4. Schedule of the scheme

Sample distribution	February 5, Monday
Start of analysis of Survey 2018/1	February 26, Monday
Survey 2018/1 – results submission	March 19, Monday
Survey 2018/1 – report	May 28, Monday
Start of analysis of Survey 2018/2	May 28, Monday
Survey 2018/2 – results submission	June 18, Monday
Survey 2018/2 – report	August 20, Monday
Annual meeting of participants	September 4, Tuesday

5. Results

20 of 21 labs returned results for both surveys, mainly by the deadline.

	Survey 1	**Survey 2**
Receipt of results	20	20
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 2018 have been also scored by Dr Christine Vianey-Saban, from DPT France. At the SAB meeting in 29th October 2018, 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 2018, the SAB decided that sample D has to be considered as a critical error for the labs who failed to recognize abnormal excretion of 3-hydroxyglutarate and glutarate. Non-identification of uracil and thymine in sample A and the failure to recognize abnormal excretion of branched-chain 2-keto and 2-hydroxyacids and/or of branched-chain amino acids in sample F have also been advised by the SAB as a critical error.

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. Two performance support letters will be sent by the Scheme Advisor for 2018. Any partial submitters will receive a letter from the ERNDIM Executive Administrator, Sara Gardner.

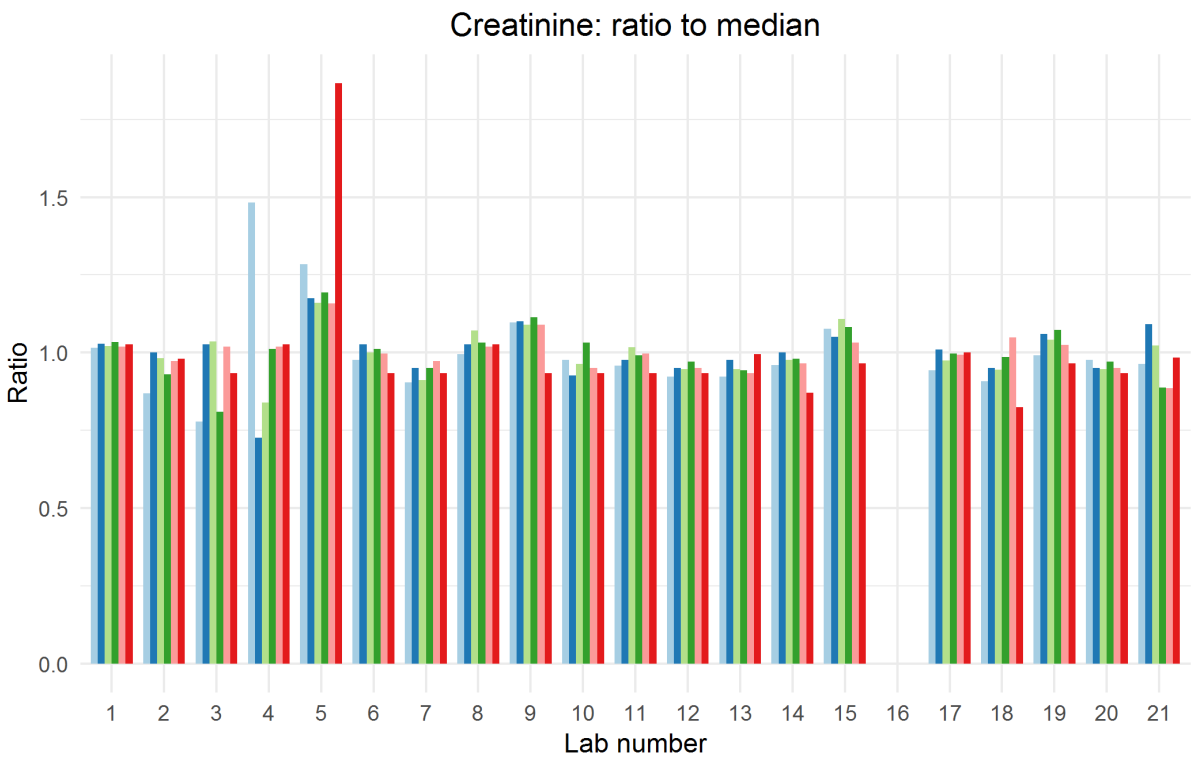
7.1. Score for satisfactory performance

Performance of the participant that obtained at least 15 points from the maximum of 24 (62%) and more within the calendar year and that did not receive "critical error" mark is considered satisfactory.

8. Results of samples and evaluation of reporting

8.1. Creatinine measurement for all samples

Creatinine determination was mostly satisfying. One lab had systematic high values (5). There were two outlier values. Creatinine values are expressed in the figure as the ratio of each measurement over the median of all labs. The interlab CV for sample A is < 12.7 %. This is still satisfying but much higher than the interlab CV for other sample (1.6 % – 3.3 %).



Sample	A	B	C	D	E	F
Mean	5.53	4.00	5.60	4.94	4.32	0.64
Median	5.37	4.02	5.55	4.91	4.30	0.61
SD	0.70	0.13	0.17	0.16	0.07	0.02

8.2. Patient A – dihydropyrimidine dehydrogenase deficiency

Patient details provided to participants
This female patient was referred at the age of 18 years with suspicion for multiple sclerosis based on MRI scan. Since the age of 5 years mental retardation and cognitive impairment was observed. Urine was collected at the age of 20 years.

Patient details
The sample was obtained from a woman with dihydropyrimidine dehydrogenase deficiency, diagnosis was confirmed by molecular genetic analysis.

Analytical performance
19 labs analyzed organic acids, only 14 labs performed analysis of purines and pyrimidines. All participants reported elevated excretion of thymine (1 point) and uracil (1 point). The analytical performance was excellent (100%).

Interpretative proficiency and recommendations
Dihydropyrimidine dehydrogenase deficiency was considered the correct diagnosis. Confirmation of diagnosis by enzyme assay of dihydropyrimidine dehydrogenase activity in fibroblasts or lymphocytes and/or mutation analysis of the *DPYD* gene was considered helpful. The interpretative proficiency score for this sample was excellent (100%).

Critical errors
No critical error for this sample. However, the failure to recognize abnormal excretion of uracil and thymine is considered by the ERNDIM SAB as a critical error which would prevent establishing the correct diagnosis.

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

8.3. Patient B – beta-mannosidosis

Patient details provided to participants
A 7 years old girl was referred for failure to thrive, short stature, psychomotor retardation, autistic features, speech impairment and hypotonia. The sample was collected at the age of 8 years; patient did not receive any therapy.

Patient details
The sample was obtained from a girl with beta-mannosidosis due to beta-mannosidase deficiency, diagnosis was confirmed by enzymatic analysis.

Analytical performance
17 labs performed OLS analysis. Only 6 labs reported a correct analytical finding "OLS profile characteristic for beta-mannosidosis", which was scored with 2 points. Abnormal OLS pattern suspected for other oligosaccharidoses or abnormal OLS pattern without specified diagnosis were considered partially correct and scored with 1 point. The analytical performance was poor (48%).

The typical disaccharide (mannosyl(1-4)-N-acetylglucosamine) coelutes with lactose. Different solvent systems for TLC separation is necessary to detect this disaccharide. Below, please, find examples of typical chromatograms.

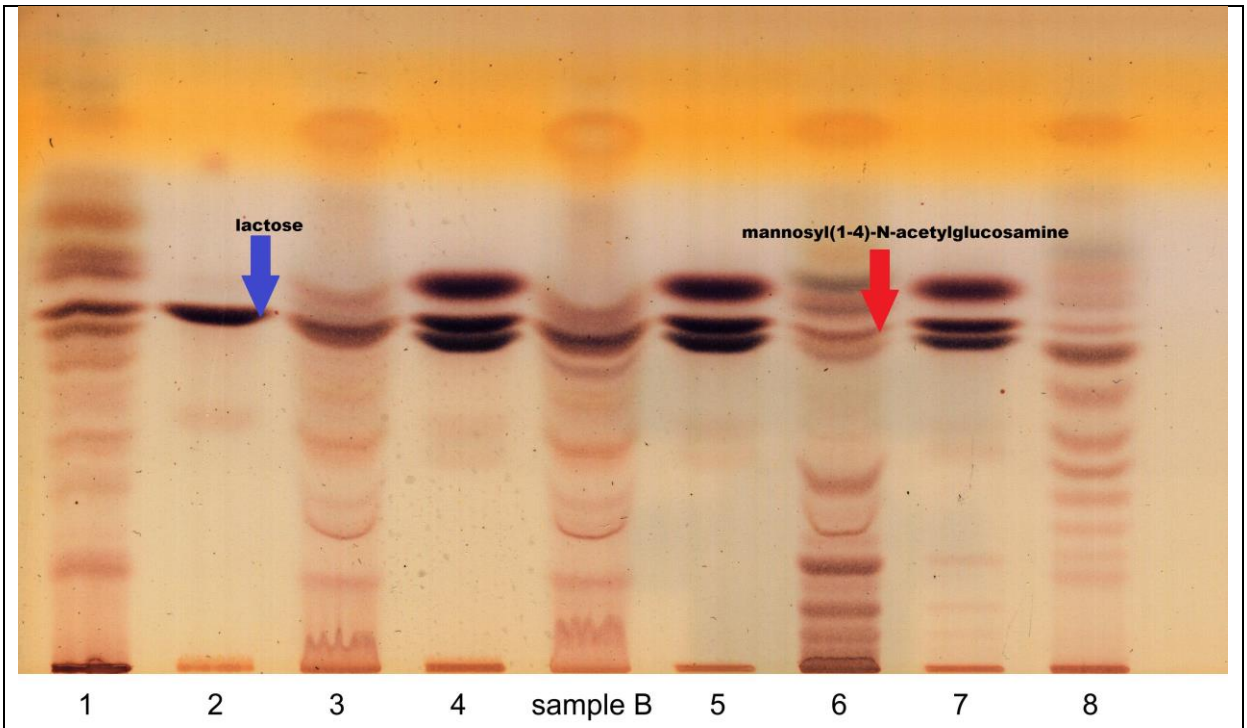


Figure 1: Oligosaccharides profile in the urine using standard solvent (75 ml butanol + 37.5 ml acetic acid + 37.5 ml water) and orcinol staining; 1 – GM1-gangliosidosis; 2 - lactose, 3 – GM2-gangliosidosis; 4,7 – sugars (glucose, lactose, raffinose); 5 – alfa-mannosidosis; 6 – beta-mannosidosis; 8 – healthy newborn.

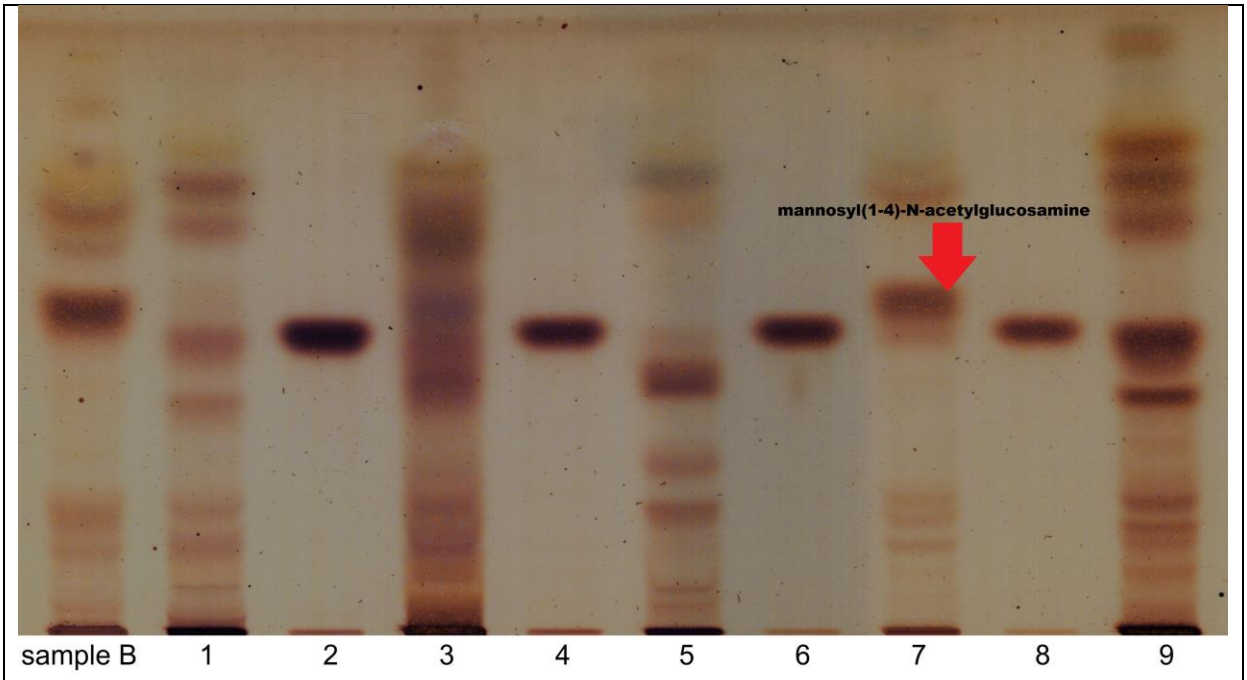


Figure 2: Oligosaccharides profile in the urine using special solvent (127.5 ml 1-propanol + 1.5 ml acetic acid + 22.5 ml water) and orcinol staining; 1 – GM1-gangliosidosis; 2,4,6,8 – lactose; 3 – GM2-gangliosidosis; 5 – alfa-mannosidosis; 7 – beta-mannosidosis; 9 – healthy newborn.

For improving performance in oligosaccharide analysis, we suggest consulting the ERNDIM protocol for qualitative TLC Oligosaccharide analysis (http://www.erndim.org/home/training.asp) and to consider purchasing an educational kit containing samples of 6 frequent oligosaccharidoses (http://cms.erndimqa.nl/Educational-Panels.aspx).

Interpretative proficiency and recommendations
The diagnosis of beta-mannosidosis due to beta-mannosidase deficiency was considered correct. Suspicion of other oligosaccharidoses was considered helpful but incomplete and scored with 1 point. Confirmation of diagnosis by enzyme assay of beta-mannosidase in leukocytes or cultured fibroblasts and/or mutation analysis of the *MANBA* gene was 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 poor (53%).

Critical errors
No critical error for this sample as the overall performance was very poor.

Overall impression
Difficult DPT sample with a poor total proficiency score (50%).

8.4. Patient C – Canavan disease

Patient details provided to participants
A 4 months old girl was admitted to hospital with bloody stools. The neurologist reported psychomotor retardation and nystagmus. The sample was collected at the age of 10 years; patient did not receive any therapy.

Patient details
The sample was obtained from a girl with Canavan disease due to aminoacylase 2 deficiency, diagnosis was confirmed by molecular genetic analysis.

Analytical performance
All labs analyzed organic acids and 18 labs reported elevated excretion of N-acetylaspartic acid, such analytical finding was considered correct and scored by 2 points. Elevated excretion of N-acetylasparagine (probably an incorrect nomenclature) were considered partially correct and scored with 1 point. The analytical performance was very good (98%).

Interpretative proficiency and recommendations
Canavan disease was considered the correct diagnosis. Confirmation of diagnosis by enzyme assay of aminoacylase 2 activity in fibroblasts or lymphocytes and/or mutation analysis of the *ASPA* gene were 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 a very good total proficiency score (99%).

8.5. Patient D – Glutaric aciduria type I

Patient details provided to participants
A 46 years old woman presented with choreodystonia and myoclonic jerks. The sample was obtained at the age of 46 years when the patient received a specific therapy.

Patient details
The sample was obtained from a woman with glutaric aciduria type I on dietary treatment, diagnosis was confirmed by molecular genetic analysis.

Analytical performance
All participants analyzed organic acids, 18 of them reported elevated excretion of 3-hydroxyglutarate and glutarate. Such analytical finding was considered correct result and scored by 2 points. The analytical performance for this easily detectable disease was suboptimal (90%).

Interpretative proficiency and recommendations

Glutaric aciduria type I was considered the correct diagnosis. Confirmation of diagnosis by enzymatic assay of glutaryl-CoA dehydrogenase and/or mutation analysis of *GCDH* gene were considered helpful. The proficiency score for this sample was good (90%).

Critical errors
The failure to recognize abnormal excretion of 3-hydroxyglutarate and glutarate is considered by the ERNDIM SAB as a critical error, which would prevent establishing the correct diagnosis; critical error was assigned to two participants in our scheme.

Overall impression
Typical DPT sample with good total proficiency score (90%) but two critical errors.

8.6. Patient E – Mucopolysaccharidosis type IV A

Patient details provided to participants
This boy was referred at the age of 6 years with short stature, kyphosis, chest deformity, genua valga and joint hypermobility. The sample was collected at the age of 6 years; patient did not receive any therapy.

Patient details
The sample was obtained from a boy with mucopolysaccharidosis type IV A due to deficiency of galactosamine-6-sulfate sulfatase, diagnosis was confirmed by molecular genetic analysis.

Analytical performance
Elevated excretion of glycosaminoglycans (1 point) and an increased proportion of keratan sulfate (1 point) were considered a correct analytical result. Increased excretion of GAGs or increased proportion of keratan sulfate only was scored as partially correct. Analytical performance was suboptimal (75%).

Interpretative proficiency and recommendations
The diagnosis of mucopolysaccharidosis type IV was considered correct. Confirmation of diagnosis by enzyme assay of galactosamine-6-sulfate sulfatase activity in fibroblasts/leucocytes and/or mutation analysis of the *GALNS* gene were considered helpful. The diagnosis of mucopolysaccharidosis type IV based on clinical information was scored with 1 point. Recommendation to carry out analysis of GAG fractionation for those participants that did not perform this analysis was considered also helpful. The proficiency score for this sample was very good (95%).

Critical errors
No critical error for this sample.

Overall impression
Typical DPT sample with good proficiency score (85%).

8.7. Patient F – Maple syrup urine disease

Patient details provided to participants
An 8 years old boy was admitted to hospital for second attack of vomiting with altered consciousness. The urinary sample was collected at the age of 8 years while he received specific treatment.

Patient details
The sample was obtained from a boy with maple syrup urine disease on dietary treatment, diagnosis was confirmed by molecular genetic analysis.

Analytical performance
All participants performed analysis of organic acids and observed the increased excretion of branched-chain 2-keto and 2-hydroxyacids - such analytical finding was considered correct and scored by 1 point. Sixteen participants reported analysis of amino acids, 15 of them detected mildly elevated excretion of branched-chain amino acids - such analytical finding was also considered correct and scored by 1 point. The scoring of analytical performance was ratified by the ERNDIM SAB. The analytical performance for this sample was good (88%).

Interpretative proficiency and recommendations
Maple syrup urine disease was considered correct diagnosis. Confirmation of diagnosis by enzyme assay of branched-chain keto acid dehydrogenase complex activity in fibroblasts/leucocytes and/or mutation analysis of the *BCKDHA*, *BCKDHB*, *DBT* and *DLD* genes were considered helpful. All participants concluded the correct diagnosis and thus the interpretative proficiency for this sample was excellent (100%).

Critical errors
No critical error for this sample. However, the failure to recognize abnormal excretion of branched-chain 2-keto and 2-hydroxyacids and/or of branched-chain amino acids, is considered by the ERNDIM SAB as a critical error, which would prevent establishing the correct diagnosis.

Overall impression
Typical DPT sample with a very good proficiency score (94%).

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 dihydropyrimidine dehydrogenase deficiency			Patient B beta-mannosidosis			Patient C Canavan disease			
	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	1	1	2	1	2	3	9
3	2	2	4	2	2	4	2	2	4	12
4	2	2	4	0	1	1	2	2	4	9
5	2	2	4	0	0	0	2	2	4	8
6	2	2	4	0	0	0	2	2	4	8
7	2	2	4	1	1	2	2	2	4	10
8	2	2	4	0	0	0	2	2	4	8
9	2	2	4	1	1	2	2	2	4	10
10	2	2	4	2	2	4	2	2	4	12
11	2	2	4	1	0	1	2	2	4	9
12	2	2	4	0	1	1	2	2	4	9
13	2	2	4	0	1	1	2	2	4	9
14	2	2	4	2	2	4	2	2	4	12
15	2	2	4	1	1	2	2	2	4	10
16	--	--	--	--	--	--	--	--	--	0
17	2	2	4	2	2	4	2	2	4	12
18	2	2	4	1	1	2	2	2	4	10
19	2	2	4	1	1	2	2	2	4	10
20	2	2	4	0	0	0	2	2	4	8
21	2	2	4	2	2	4	2	2	4	12

Detailed scores – Round 2

Lab n°	Patient D glutaric aciduria type I			Patient E mucopolysaccharidosis type IV A			Patient F maple syrup urine disease			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	2	2	4	2	2	4	2	2	4	12
3	2	2	4	1	2	3	2	2	4	11
4	2	2	4	1	2	3	2	2	4	11
5	2	2	4	2	2	4	1	2	3	11
6	2	2	4	2	2	4	1	2	3	11
7	2	2	4	1	2	3	2	2	4	11
8	2	2	4	2	2	4	2	2	4	12
9	2	2	4	1	2	3	2	2	4	11
10	2	2	4	2	2	4	2	2	4	12
11	0	0	0	2	2	4	2	2	4	8
12	2	2	4	0	1	1	2	2	4	9
13	2	2	4	1	1	2	2	2	4	10
14	2	2	4	1	2	3	2	2	4	11
15	2	2	4	2	2	4	2	2	4	12
16	--	--	--	--	--	--	--	--	--	0
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	1	2	3	11
20	2	2	4	1	2	3	1	2	3	10
21	0	0	0	1	2	3	1	2	3	6

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	2	3	4	4	4	21	88	
3	4	4	4	4	3	4	23	96	
4	4	1	4	4	3	4	20	83	
5	4	0	4	4	4	3	19	79	
6	4	0	4	4	4	3	19	79	
7	4	2	4	4	3	4	21	88	
8	4	0	4	4	4	4	20	83	
9	4	2	4	4	3	4	21	88	
10	4	4	4	4	4	4	24	100	
11	4	1	4	0	4	4	17	71	CE
12	4	1	4	4	1	4	18	75	
13	4	1	4	4	2	4	19	79	
14	4	4	4	4	3	4	23	96	
15	4	2	4	4	4	4	22	92	
16	--	--	--	--	--	--	0	0	
17	4	4	4	4	4	4	24	100	
18	4	2	4	4	4	4	22	92	
19	4	2	4	4	4	3	21	88	
20	4	0	4	4	3	3	18	75	
21	4	4	4	0	3	3	18	75	CE

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 60 % of adequate responses)	18	86
Unsatisfactory performers (< 60 % adequate responses and/or critical error)	2	10
Partial and non-submitters	1	5

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
Sample 2018-A	dihydropyrimidine dehydrogenase deficiency	100	100	100
Sample 2018-B	beta-mannosidosis	48	53	50
Sample 2018-C	Canavan disease	98	100	99
Sample 2018-D	glutaric aciduria type I	90	90	90
Sample 2018-E	mucopolysaccharidosis type IV A	75	95	85
Sample 2018-F	maple syrup urine disease	88	100	94

10. Annual meeting of participants

The annual meeting of participants of the Proficiency Testing Centre Czech Republic took place during the SSIEM Annual Symposium in Athens on 4th September 2018, 14 participants from 9 laboratories were represented. The following items were discussed during the annual meeting of our DPT centre:

1. Information
    - Prof Viktor Kožich stepped down as SA and Petr Chrastina, MSc. has taken over. Karolina Pešková, MSc. will be deputy since 2019.
    - ERNDIM is aiming at accrediting its activities
    - Calibration material for organic acids is available from the Metabolic Laboratory, Amsterdam UMC (https://www.vumc.com/branch/clinical-chemistry1/MetabolicLaboratory/OSL/Organic_acid_mixture)
    - New pilot schemes started (Cognitive amino acid and Special Assays in DBS)
2. Tests required for 2018
    - amino acids, organic acids, mucopolysaccharides, oligosaccharides and purines/pyrimidines
3. Discussion of results of samples A-F
    - scoring of 2018 results proposed by DPTC Czech Republic organizers has been subsequently evaluated by a second reviewer from an independent DPT center and SAB
        - Sample F: Scoring of analytical finding was discussed. Participants suggested that only presence of the branched-chain 2-keto and 2-hydroxyacids should be sufficient to diagnose MSUD and should be scored by 2 points without assessing

amino acids profile. This proposal of scoring was subsequently discussed by the ERNDIM SAB and was not ratified.

- Analytical difficulties in 2018 surveys
  - sample B: The typical disaccharide (mannosyl(1-4)-N-acetylglucosamine) coelutes with lactose. Different solvent systems for TLC separation is necessary to detect this disaccharide. Paticipants were recommended to consult the ERNDIM protocol for qualitative TLC Oligosaccharide analysis.
- Critical error in glutaric aciduria type I: Participants agreed that the failure to recognize abnormal excretion of 3-hydroxyglutarate and glutarate should be considered a critical error.

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 on Monday and Tuesday 29 and 30 April 2019 near Zurich. The program for biochemists includes:
    - Glycogen Storage Disorders
    - CDG Syndromes
    - Mitochondrial Disease
    - Neurotransmitters disorders
  - 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. Please, negotiate with scheme advisor the sample suitability to avoid duplication and overrepresentation of common diagnosis. 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 50 °C for 60 minutes. Make sure that this temperature is achieved in the entire urine sample, not only in the water bath. Then aliquot the sample in 10 ml plastic tubes (minimum 48 tubes), add stoppers and freeze. Be careful to constantly homogenize the urine while aliquoting the sample. Send the aliquots on dry ice by rapid mail or express transport to:

  Prof. Viktor Kozich, Petr Chrastina
  Department of Pediatrics and Adolescent Medicine
  General Faculty Hospital and
  Charles University 1st Faculty of Medicine
  Ke Karlovu 2
  128 08 Prague 2
  Czech Republic

Tel: +420 224 947 161 or 224 967 679
Fax: +420 224 967 081 or 224 967 119

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 2019

Sample distribution	February 5, Tuesday
Start of analysis of Survey 2019/1 Website open	March 4, Monday
Survey 2019/1 - Results submission	March 25, Monday
Survey 2019/1 - Reports	May 24, Friday
Start of analysis of Survey 2019/2	June 3, Monday
Survey 2019/2 – Results submission	June 24, Monday
Survey 2019/2 - Reports	August 23, Friday
Annual meeting of participants	September 3, Tuesday
Annual Report 2019	December 2019

The annual meeting of participants will take place on September 3rd, 2019 (in the morning session) during the SSIEM Annual Symposium in Rotterdam, Netherland.

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, 2019-03-11
Name and signature of Scientific Advisor

Prof. Viktor Kozich, Petr Chrastina
Department of Pediatrics and Adolescent Medicine
General Faculty Hospital and
Charles University 1st Faculty of Medicine
Ke Karlovu 2
128 08 Prague 2
Czech Republic
Tel: +420 224 947 161 or 224 967 679
Fax: +420 224 967 081 or 224 967 119