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Diagnostic Proficiency Testing

Centre: Czech Republic

Final Report 2019

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.

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 15 countries have participated in the Diagnostic Proficiency Testing scheme in 2019, for details see the below table:

Country	Number of participants
Austria	1
Croatia	1
Cyprus	1
Czechia	1
Denmark	1
Finland	1
France	1
Germany	6
Latvia	1
Lithuania	1
Malaysia	1
People's Republic of	1

Version Number (& Date) Amendments
version 7 (07 August 2020) Page 16 : Scientific Advisor signature added

8.1. Patient E

Formiminoglutamic aciduria

Patient details provided to participants

A 19 years old man was referred for hepatomegaly, abdominal pain and dyskinesia. The sample was obtained at the age of 19 years; patient did not receive any therapy.

Patient details

The sample was obtained from a 19 years old man with formiminoglutamic aciduria due to deficiency of glutamate formiminotransferase, diagnosis was confirmed by molecular genetic analysis.

Overall impression

All participants analyzed organic acids, only 6 of them reported elevated excretion of hydantoin-5-propionic acid. The Scientific Advisory Board classed this sample as 'educational', since the metabolite pattern in this sample was particularly challenging.

Figure 1: Organic acids profile (GC/MS) in urine

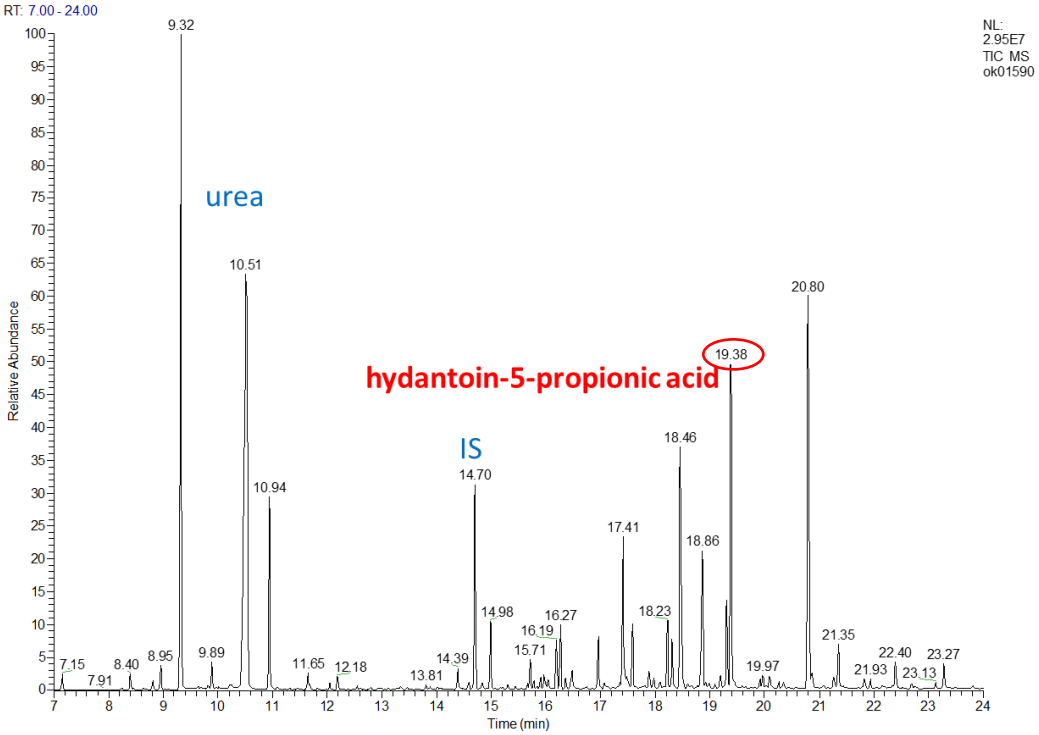
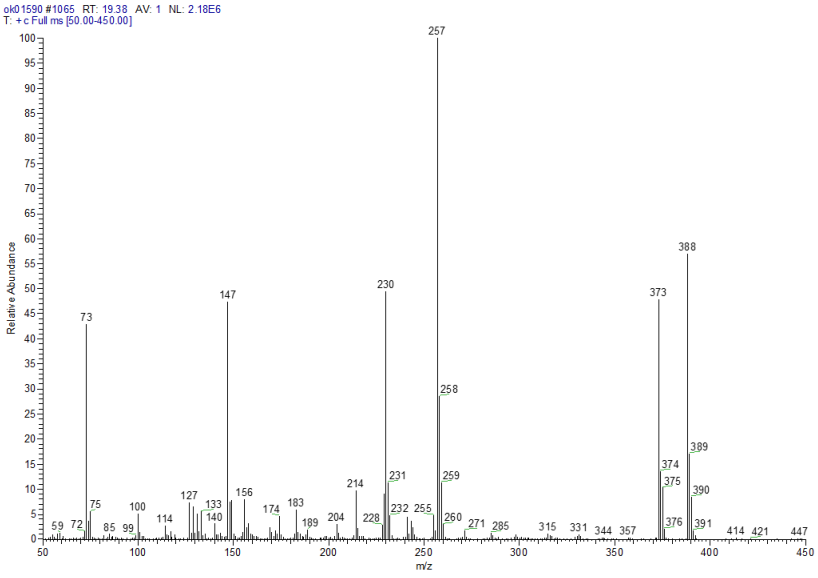


Figure 2: Mass spectrum of hydantoin-5-propionic acid (3tms)



8.1. Patient F

Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome

Patient details provided to participants

This boy was referred at the age of 14 months with developmental delay, liver dysfunction and increased ammonia. The sample was collected at the age of 9 years; patient received specific therapy.

Patient details

The sample was obtained from a 9-year old boy with hyperornithinemia-hyperammonemia-homocitrullinuria (HHH) syndrome. The diagnosis was confirmed by molecular genetic analysis.

Analytical performance

All participants performed analyses of amino acids. Only 3 participants observed increased excretion of homocitrulline, such analytical finding was considered correct and scored by 1 point. 20 participants detected elevated excretion of orotic acid, such analytical finding was also considered correct and scored by 1 point. Elevated excretion of uracil was considered partially correct and scored with 1 point. The analytical performance was poor (55%).

	Urinary AA (patient on treatment)							Orotic acid
IEM	**Orn**	**Cit**	**Hcit**	**ASA**	**Arg**	**Cys**	**Lys**	
NAGS/CPS1 deficiency		N-↑			N-↑			**N**
OTC deficiency		N-↑			N-↑			↑
Citrullinemia I	↑	↑↑↑	↑		↑	N-↑	↑	↑
Citrin deficiency	↑	↑↑			↑	N-↑	↑	↑
Argininosuccinic aciduria		↑	↑	↑↑↑	N-↑			↑
Arginase deficiency	↑	↑	↑	↑	↑↑↑	↑	↑	N-↑
LPI	↑	↑	↑		↑	↑	↑↑↑	↑
HHH syndrome	↑	↑	↑↑		↑	N-↑	N-↑	↑
Gyrate atrophy	↑↑↑				↑	↑	↑	N
Cystinuria	↑				↑	↑↑↑	↑	N

Interpretative proficiency and recommendations

The diagnosis of HHH syndrome was considered correct while suspicion for other urea cycle disorder with exception of argininosuccinic aciduria was considered helpful but incomplete. Confirmation of diagnosis by mutation analysis was considered helpful. The proficiency score for this sample was poor (55%).

Critical errors

The failure to recognize abnormal excretion of orotate and homocitrulline is considered by the ERNDIM SAB as a critical error, which would prevent establishing the correct diagnosis; critical error was assigned to one participant in our scheme.

Overall impression

Typical DPT sample with poor proficiency score (55%).

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 Adenine phosphoribosyltransferase deficiency			Patient B No IEM			Patient C Sialidosis type I due to neuraminidase deficiency			
	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	2	2	4	2	2	4	12
4	2	2	4	2	2	4	1	2	3	11
5	2	2	4	2	2	4	1	1	2	10
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	2	2	4	12
11	--	--	--	--	--	--	--	--	--	0
12	0	1	1	2	2	4	0	1	1	6
13	0	0	0	2	2	4	2	2	4	8
14	0	1	1	2	2	4	2	2	4	9
15	0	0	0	2	2	4	2	2	4	8
16	0	1	1	2	2	4	2	2	4	9
17	0	0	0	2	2	4	2	2	4	8
18	2	2	4	2	2	4	2	2	4	12
19	0	0	0	2	2	4	2	2	4	8
20	0	0	0	0	0	0	0	0	0	0
21	0	0	0	1	0	1	2	2	4	5

Detailed scores – Round 2

Lab n°	Patient D Mucopolysaccharidosis type II			Patient E Formiminoglutamic aciduria			Patient F Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome			
	A	**I**	**Total**	**A**	**I**	**Total**	**A**	**I**	**Total**	**Total**
1	2	2	4	--	--	--	1	2	3	7
2	2	2	4	--	--	--	1	1	2	6
3	2	2	4	--	--	--	1	2	3	7
4	2	2	4	--	--	--	1	1	2	6
5	2	2	4	--	--	--	1	1	2	6
6	2	2	4	--	--	--	1	1	2	6
7	2	2	4	--	--	--	1	1	2	6
8	2	2	4	--	--	--	1	1	2	6
9	2	2	4	--	--	--	1	0	1	5
10	2	2	4	--	--	--	2	2	4	8
11	1	1	2	--	--	--	1	1	2	4
12	0	1	1	--	--	--	1	1	2	3
13	2	2	4	--	--	--	2	1	3	7
14	2	2	4	--	--	--	1	1	2	6
15	2	2	4	--	--	--	2	2	4	8
16	2	1	3	--	--	--	1	0	1	4
17	2	2	4	--	--	--	1	2	3	7
18	2	2	4	--	--	--	1	1	2	6
19	2	2	4	--	--	--	1	1	2	6
20	0	1	1	--	--	--	0	0	0	1
21	2	1	3	--	--	--	1	1	2	5

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	4	4	4	--	3	19	95	
2	4	4	4	4	--	2	18	90	
3	4	4	4	4	--	3	19	95	
4	4	4	3	4	--	2	17	85	
5	4	4	2	4	--	2	16	80	
6	4	4	4	4	--	2	18	90	
7	4	4	4	4	--	2	18	90	
8	4	4	4	4	--	2	18	90	
9	4	4	4	4	--	1	17	85	
10	4	4	4	4	--	4	20	100	
11	--	--	--	2	--	2	4	20	
12	1	4	1	1	--	2	9	45	
13	0	4	4	4	--	3	15	75	
14	1	4	4	4	--	2	15	75	
15	0	4	4	4	--	4	16	80	
16	1	4	4	3	--	1	13	65	
17	0	4	4	4	--	3	15	75	
18	4	4	4	4	--	2	18	90	
19	0	4	4	4	--	2	14	70	
20	0	0	0	1	--	0	1	5	CE
21	0	1	4	3	--	2	10	50	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 60 % of adequate responses)	17	81
Unsatisfactory performers (< 60 % adequate responses and/or critical error)	4	19
Partial and non-submitters	1	5

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
DPT-CP-2019-A	Adenine phosphoribosyltransferase deficiency	55	63	59
DPT-CP-2019-B	No IEM	93	90	91
DPT-CP-2019-C	Sialidosis type I due to neuraminidase deficiency	85	90	88
DPT-CP-2019-D	Mucopolysaccharidosis type II	88	88	88
DPT-CP-2019-E	Formiminoglutamic aciduria	--	--	--
DPT-CP-2019-F	Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome	55	55	55

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 Rotterdam on 3rd September 2019, 13 participants from 8 laboratories were represented.

- Analytical difficulties in 2019 surveys
  - sample E: elevated excretion of hydantoin-5-propionic acid in organic acids profile is typical founding for formiminoglutamic aciduria.
  - sample F: Homocitrulline coelutes with methionine in ion exchange chromatography.
- Critical error in HHH syndrome: Participants agreed that the failure to recognize abnormal excretion of homocitrulline and orotic acid 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 20 and 21 April 2020 near Amsterdam. The program for biochemists 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 50 °C for 20 minutes. Make sure that this temperature is achieved in the entire urine sample, not only in the water bath. Send the sample on dry ice by rapid mail or express transport to:

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  General Faculty Hospital and
  Charles University 1st Faculty of Medicine
  Ke Karlovu 2
  128 08 Prague 2
  Czech Republic
  Tel: +420 224 947 161
  Fax: +420 224 967 081

  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
- Purines/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 and fee in 2020

Sample distribution	February 11, Tuesday
Start of analysis of Survey 2020/1 Website open	March 9, Monday
Survey 2020/1 - Results submission	March 30, Monday
Survey 2020/1 - Reports	May 29, Friday
Start of analysis of Survey 2020/2	June 8, Monday
Survey 2020/2 – Results submission	June 29, Monday
Survey 2020/2 - Reports	August 28, Friday
Annual meeting of participants	September 1, Tuesday
Annual Report 2020	December 2020

The annual meeting of participants will take place on September 1st, 2020 (in the morning session) during the SSIEM Annual Symposium in Freiburg, Germany.

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, 2019-12-23
Name and signature of Scientific Advisor 

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