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Diagnostic Proficiency Testing

Centre: United Kingdom

Final Report 2018

prepared by
Mrs Joanne Croft

Note: This annual report is intended for participants of the ERNDIM DPT UK 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 on page18 and the ERNDIM Privacy Policy on www.erndim.org.

In 2018, 21 labs participated to the Diagnostic Proficiency Testing Scheme United Kingdom.

1. Geographical distribution of participants

For the first survey 21 and for the second survey 20 laboratories submitted results.

Country	Number of participants
Australia	1
Ireland	1
Malaysia	1
New Zealand	2
Spain	1
United Kingdom	15

2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Joanne Croft 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

Origin of patients: all urine samples have been provided by the scheme organizers.

Patient A: Dihydropyrimidine dehydrogenase deficiency – Common sample sent to all the labs participating in the DPT scheme. Provided by Petr Chrastina, DPT scheme, Czech Republic.
Patient B: Aspartylglucosaminuria – Provided by George Ruijter, DPT scheme, Netherlands.
Patient C: Sample from a healthy child with no suspected inborn error of metabolism. – Provided by Joanne Croft, DPT scheme, UK.
Patient D: HHH syndrome (Hyperammonaemia, hyperornithinaemia, homocitrullinaemia)– Provided by Brian Fowler, DPT scheme, Switzerland.
Patient E: Argininosuccinic aciduria (ASA) - Provided byJoanne Croft, DPT scheme, UK.
Patient F: Gyrate atrophy (ornithine aminotransferase deficiency) – Provided by Joanne Croft, DPT scheme, UK.

The samples have been heat-treated. They were pre-analysed in our laboratory after 2 weeks incubation at room 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, mucopolysaccharides and oligosaccharides were required in 2018. If you are not performing one of these analyses you can send the sample to another laboratory for analysis, but you are responsible for the results.

4. Schedule of the scheme

- February 5th 2018: shipment of samples of Survey 1 and Survey 2 by CSCQ
- Feb 26th 2018: clinical data available on CSCQ website and start analysis of samples (Survey 1)
- March 12th 2018: reminder for website submission
- March 19th 2018: deadline for result submission (Survey 1)
- May 28th 2018: clinical data available on CSCQ website and start analysis of samples (Survey 2)
- June 11th 2018: reminder for website submission
- June 18th 2018: deadline for result submission (Survey 2)
- July 9th 2018: interim reports for both Surveys available on CSCQ website
- Nov 29th 2018: SAB meeting - definition of critical errors
- March 2019: Annual Report with definitive scoring sent by e mail

5. Results

20 of 21 labs returned results for both surveys, with 1 lab not returning results for the second survey.

	Survey 1	**Survey 2**
Receipt of results	21	20
No answer	0	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 UK 2018 have been also scored by Petr Chrastina from DPT Czech Republic. At the SAB meeting in November 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 A has to be considered as a critical error for the labs who failed to identify thymine and uracil. For sample E failure to identify orotic acid AND argininosuccinic acid was deemed to be a critical error. Failure to detect increased ornithine was deemed to be a critical error for sample F.

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. Four 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.

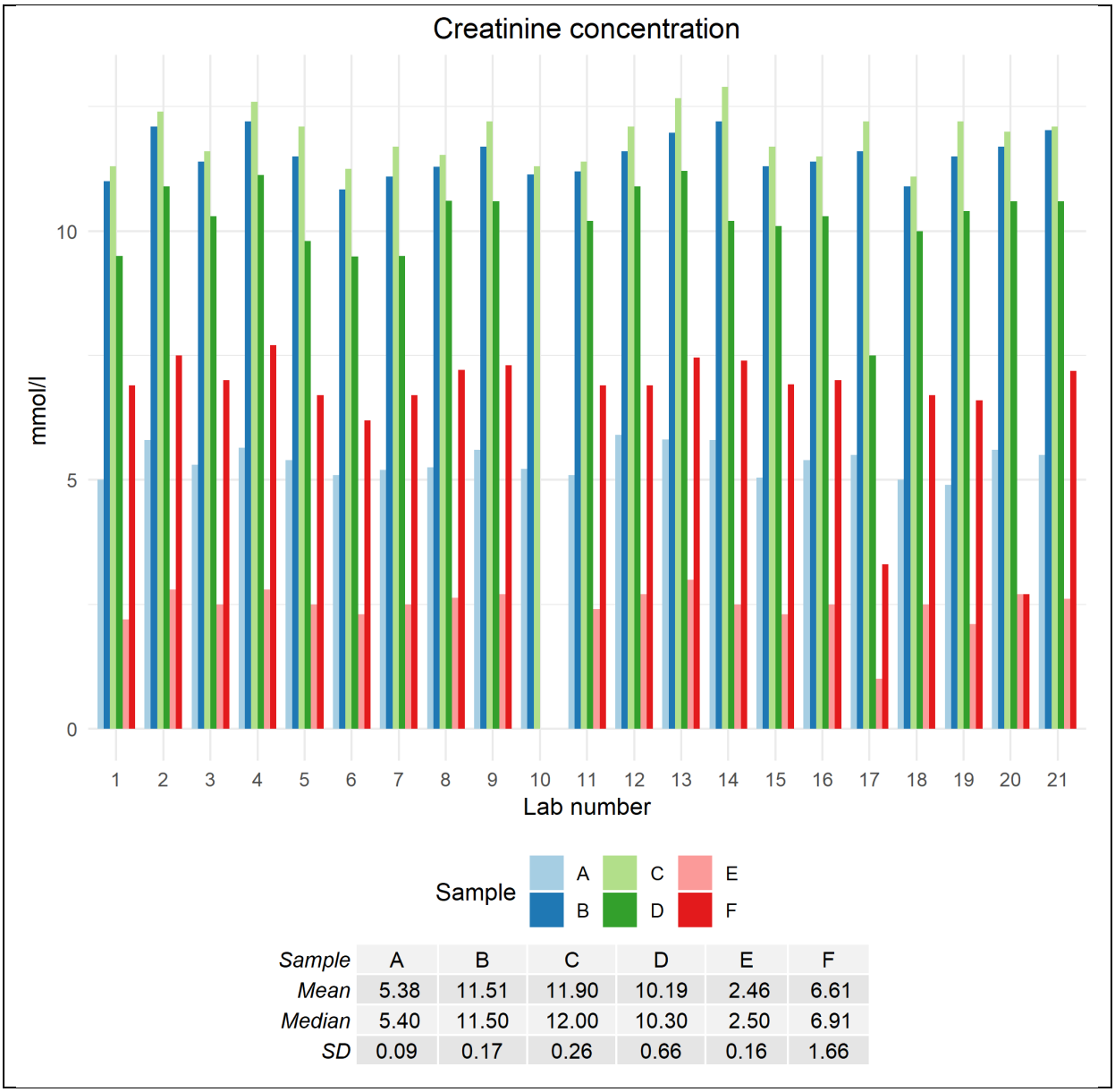
7.1. Score for satisfactory performance

At least 15 points from the maximum of 24 (62%). However, in 2018 it was decided at the SAB meeting that Sample B (aspartylglucosaminuria) will be classed as an educational sample and will not be scored. This sample will be distributed again within the next few years but will not be eligible to be classed as educational again.
Therefore a satisfactory performance for 2018 is 12 from the maximum of 20 (60%).

8. Results of samples and evaluation of reporting

8.1. Creatinine measurement for all samples

Creatinine concentration, as determined by each laboratory, is shown in the graph below along with the mean, median and standard deviations for each sample. Agreement between laboratories is good.



Sample	A	B	C	D	E	F
Mean	5.38	11.51	11.90	10.19	2.46	6.61
Median	5.40	11.50	12.00	10.30	2.50	6.91
SD	0.09	0.17	0.26	0.66	0.16	1.66

8.2. Patient A – Dihydropyrimidine dehydrogenase deficiency. Diagnosis has been confirmed by enzymatic and genetic testing. Sample sent as the common sample by the Czech DPT scheme scientific advisor.

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 diagnosis of dihydropyrimidine dehydrogenase deficiency has been confirmed by enzymatic and genetic testing. The sample was sent as the common sample to all the DPT scheme participants. Details have been presented by Petr Chrastina (DPT Czech Republic) during the ERNDIM workshop on September 4th 2018 (available on ERNDIM website).

Scoring

- Analytical results: increase of uracil (score 1), increase of thymine (score 1)
- Interpretation of results: dihydropyrimidine dehydrogenase deficiency as first or alternative diagnosis (score 2)

Analytical performance
The analytical performance for this sample was very good with 20 out of 21 participants scoring 2 marks for analysis (1 mark for detecting increased excretion of uracil, 1 mark for detecting increased excretion of thymine). Of these, only 4 participants provided quantitative results. The remaining laboratory failed to detect either of these metabolites. It was agreed at the Scientific Advisory Board (SAB) meeting held in November 2018 that failure to detect these metabolites should be classed as a critical error.

Diagnosis / Interpretative proficiency

All those laboratories who scored 2 marks for analysis also scored 2 marks for interpretation giving dihydropyrimidine dehydrogenase deficiency as the most likely diagnosis, with the remaining laboratory scoring 0 marks overall for Sample A.

7 participants also provided other possible diagnoses:
Dihydropyrimidinase deficiency (4/7)
Ureidopropionase deficiency (2/7)
Thymidine phosphorylase deficiency (1/7)

Recommendations

13/20 participants who correctly diagnosed this patient as having dihydropyrimidine dehydrogenase deficiency suggested quantitation of purines/pyrimidines. 16/20 suggested genetic analysis. Perhaps the most important point to be made is the potential for 5-Flurouracil toxicity in this group of patients (potentially fatal outcome), although only 6/20 mentioned this.

Overall impression

- Analytical performance 95%
- Interpretative performance 95%
- Overall performance 95%

8.3. Patient B – This sample came from a patient with Aspartylglucosaminuria. This sample was kindly provided by George Ruijter, scientifc advisor of the Netherlands DPT scheme. The sample was obtained with the help of VKS (the Dutch patient organisation).

Patient details provided to participants
Delayed speech, hyperactive behaviour. Frequent infections of ears and upper respiratory tract.

Scoring

Please note that this Sample has been deemed to be Educational by the SAB; therefore the scores for Sample B are not included in this year's scheme. This has not affected any laboratories overall performance.

- Analytical results: 2 marks were awarded for performing oligosaccharide analysis, seeing an abnormal profile and diagnosing aspartylglucosaminuria, or for detecting aspartylglucosamine by amino acid analysis.1 mark was awarded for performing oligosaccharide analysis, seeing an abnormal profile and diagnosing another oligosaccharide disorder.
- Interpretation of results: Correct diagnosis of aspartylglucosaminuria (2 marks). Suggesting doing oligosaccharide analysis if not already done or for giving another oligosaccharide disorder as the diagnosis (1 mark).

Analytical performance

8/21 participants scored 2 marks for analysis.

- 5/8 detected aspartylglucosamine by amino acid analysis.
- 4/8 correctly identified the abnormal oligosaccharides
- 1/8 identified both markers

2/21 participants scored 1 mark for analysis

- Oligosaccharide analysis performed, abnormal pattern, gave another disorder

11/21 participants scored 0 marks for analysis

Diagnosis / Interpretative proficiency

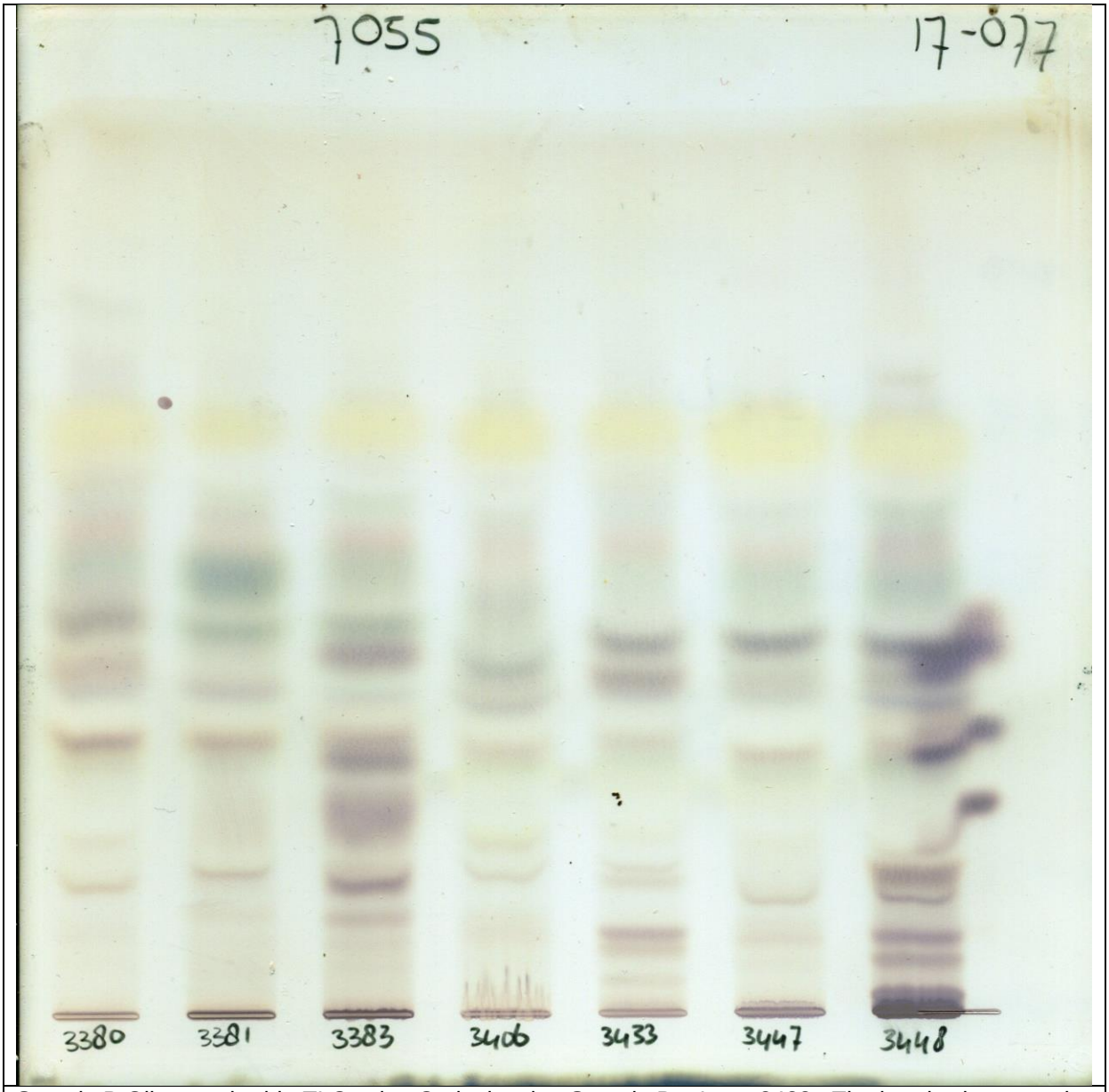
8/21 scored 2 marks for interpretation (gave aspartylglucosamiuria as the primary or alternative diagnosis)
4/21 scored 1 mark for interpretation
9/21 scored 0 marks for interpretation

Recommendations

4/21 – oligosaccharide analysis (if not already done)
7/21 – enzyme analysis
5/21 – genetic testing
2/21 – referral (to specialist)

Overall impression

This sample caused a few problems analytically for many of the participants. For this reason, sample B is to be classed as educational this year. This means that the scores from this sample will not be taken into account i.e. the maximum score available this year is 20 marks, instead of 24, and an acceptable score is 12 or more. After taking off the marks for this sample, the participants who did not obtain an adequate score did not change compared to including the marks for sample B.
This sample will be used again in a future year to assess whether analytical and interpretative performance has improved. When used again, this sample will not be eligible as an educational sample.



Sample B Oligosaccharide TLC using Orcinol stain. Sample B = Lane 3433. The bands closest to the application site are the characteristic ones. Image provided by George Ruijter.

Also please refer to the ERNDIM website for an image of Oligosaccharide TLC showing the patterns of oligosaccharides in urine from patients with different oligosaccharide disorders (http://www.erndim.org/home/training.asp#3).

8.1. Patient C – Sample from a healthy child with no suspected inborn error of metabolism. Sample donated by a child of member of laboratory staff.

Patient details provided to participants
Learning difficulties.

Patient details

This urine was donated by a healthy child of a member of our laboratory staff. There is no suspected inborn error of metabolism.

Scoring

- Analytical results: Performing 3 analyses (not including pre-investigations) and finding no significant abnormality was scored with 2 marks.
- Interpretation of results: No significant abnormality (2 marks)

Analytical performance

20/21 participants scored 2 marks. The remaining participant was scored with 1 mark for analysis. This laboratory found increased 3 hydroxy glutarate on organic acids, and gave Glutaric Aciduria Type 1 as their primary diagnosis. This was not reported by any of the other participants. However, it was decided by the SAB that this was not a critical error as they had suggested a repeat urine for organic acid analysis.

Diagnosis / Interpretative proficiency

19/21 participants scored 2 marks for interpretation.
2/21 participants scored 0 marks for interpretation. 1 of these was the laboratory who diagnosed GA1 deficiency. The other did not put any information into the interpretation section. When this occurred in previous years I was told by other DPT scientific advisors that I had been too lenient in still giving a score. External quality assurance samples should be treated in the same fashion as real patient samples for which you would never not give a comment.

Recommendations

6/21 – no further recommendations provided
6/21 – further investigations dependent on further clinical details
6/21 – plasma amino acids
3/21 - ? Carnosinase
1/21 – next generation based screening
1/21 – GCMS of organic acids (this participant performed organic acid screening)

Overall impression

- Analytical performance 98%
- Interpretative performance 88%
- Overall performance 93%

Analytical performance for this sample was very good. However, interpretation was not as good with marks being lost for not completing all the required fields.

8.1. Patient D – HHH syndrome (Hyperammonaemia, hyperornithinaemia, homocitrullinaemia). This sample was kindly provided by Brian Fowler, scientific advisor for the Swiss DPT scheme, and was used as the common sample in the 2014 DPT scheme. The diagnosis has been confirmed genetically.

Patient details provided to participants
Mild hypotonia at 6 months of age. At 14 months presented with developmental delay and failure to thrive. Sample collected while receiving specific treatment.

Patient details

Following an uneventful pregnancy and birth this male child showed mild hypotonia at 6 months of age. At 14 months he presented with developmental delay and failure to thrive with liver dysfunction when increased ammonia (200 µmol/L), increased ornithine, orotic acid and a mild increase in homocitrulline was found leading to the diagnosis of HHH. Sample collected while receiving specific treatment. Diagnosed at 14 months of age. Sample collected at 8 years of age.

Scoring

- Analytical results: increased orotic acid (1 mark); increased homocitrulline (1 mark)
- Interpretation of results: HHH syndrome as either primary diagnosis or alternate diagnosis (2 marks). Other urea cycle disorder (2 marks). (This was due to the difficulties in detecting the homocitrulline).

Analytical performance

Results were received from 20/21 participants.

19/20 participants scored 1 mark for analysis (for detecting orotic acid). The remaining participant scored 2 marks as they also detected the homocitrulline using ion exchange chromatography).

9/20 provided a quantitative result for orotic acid – mean value 34 µmol/mmol creatinine.

Diagnosis / Interpretative proficiency

19/20 participants scored 2 marks for interpretation. The remaining participant scored 1 mark as they gave Orotic aciduria as the diagnosis with no mention of performing plasma amino acids or ammonia.

Recommendations

15/20 – plasma amino acids
11/20 – plasma ammonia
12/20 – mutation analysis (though the gene depended on diagnosis given)
11/20 – refer to metabolic team
7/20 – family testing
2/20 – enzyme studies

Overall impression

- Analytical performance 53%
- Interpretative performance 98%
- Overall performance 75%

Detection of homocitrulline appears to be an ongoing issue. When used in 2014, only 3/21 participants in the UK DPT scheme identified the homocitrulline in this sample.
Identification of homocitrulline is the key to getting this diagnosis. It is accepted that the fact this patient was on treatment makes EQA samples particularly difficult. Homocitrulline absence by current methods does not rule out HHH syndrome.

Multiple distributions of similar samples

This sample was previously used as the common sample in 2014, when 3/21 participants in the UK DPT scheme detected the homocitrulline.

8.1. Patient E – Argininosuccinic aciduria (ASA). This sample had been used previously in 2012 and 2015.

Patient details provided to participants
Failure to thrive. Sample taken while on specific treatment

Patient details

This female patient was diagnosed at 3 years of age. The sample was collected at 16 years of age while on specific treatment.

Scoring

- Analytical results: increased argininosuccinic acid (1 mark); orotic acid (1 mark)
- Interpretation of results: Argininosuccinic aciduria (ASA) (2 marks); Other urea cycle disorder (1 mark)

Analytical performance

Results were received from 20/21 participants.

17/20 scored 2 marks for analysis.
3/20 scored 0 marks for analysis. These laboratories failed to detect orotic acid and the argininosuccinic acid.

8/17 participants who detected orotic acid provided a quantitative result. Mean value = 19.3 µmol/mmol creatinine.

17/20 participants also commented on the finding of increased malonic acid in this sample. Participants who interpreted this as malonic aciduria, but who also detected the orotic acid/ASA, were not scored down. This finding of malonic acid remains unexplained.

Diagnosis / Interpretative proficiency

17/20 participants scored 2 marks for interpretation (correctly diagnosed ASA either as the primary or alternative diagnosis).
3/20 participants scored 0 marks (those participants who did not detect the orotic acid and the ASA).

Recommendations

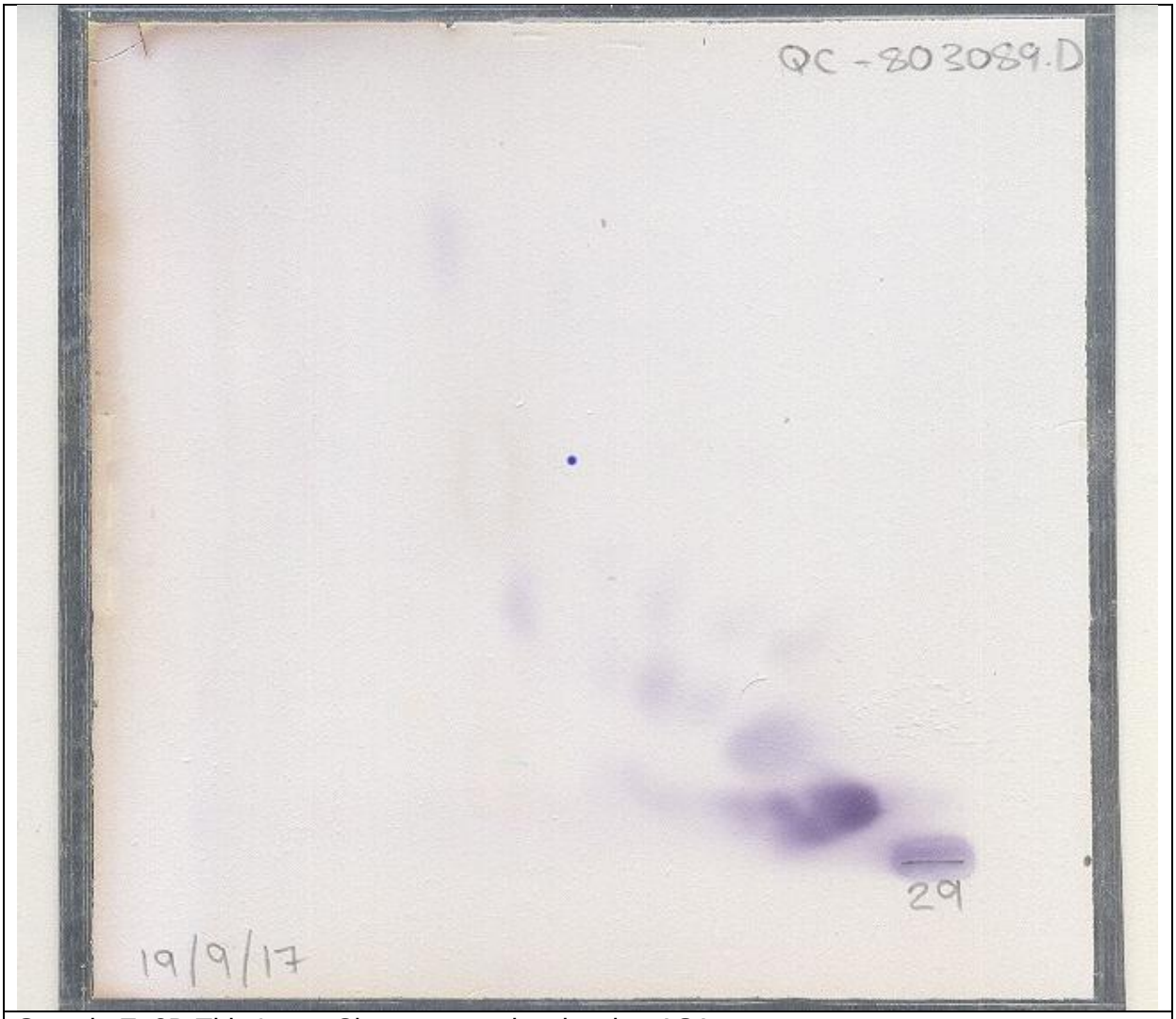
14/20 – plasma amino acids
8/20 – acylcarnitine profile
11/20 – refer to metabolic team

14/20 - mutation analysis
ASL gene – 3/14
MLCYD gene – 6 /14
Both ASL and MLCYD genes – 2/14
Gene not stated – 3/14

Overall impression

- Analytical performance 85%

- Interpretative performance 85%
- Overall performance 85%



Sample E. 2D Thin Layer Chromatography showing ASA spot.

Multiple distributions of similar samples

This sample was also distributed in 2015. Failure to detect both ASA and orotic acid was deemed to be a critical error by the SAB. Again for 2018, failure to detect both these metabolites is classed as a critical error.

This sample has been used twice previously.

In 2012:
17/20 (85%) of participants identified increased ASA
10/20 (50%) of participants identified orotic acid

In 2015:
19/23 (83%) of participants identified increased ASA
18/23 (78%) of participants identified orotic acid

In 2018:
17/20 (85%) of participants identified increased ASA

17/20 (85%) of participants identified orotic acid

No improvement in detecting ASA
Clear improvement in detecting orotic acid

8.1. Patient F – Gyrate atrophy (ornithine aminotransferase deficiency).

Patient details provided to participants
Retinopathy

Patient details

This sample was obtained from a female patient with ornithine aminotransferase deficiency (gyrate atrophy). Diagnosis was made at 10 years of age. Sample was collected at 11 years of age.

Scoring

- Analytical results: detection of increased ornithine (2 marks)
- Interpretation of results: Gyrate atrophy or ornithine aminotransferase deficiency as either primary or alternative diagnosis (2 marks)

Analytical performance

Results were received from 20 of 21 participants.

18/20 participants scored 2 marks for analysis. The remaining 2 participants both scored 0 marks for analysis. Both performed amino acid analysis, 1 by 2D-thin layer chromatography (2D-TLC) and 1 by ion exchange chromatography.
The mean concentration of ornithine was 271 µmol/mmol creatinine (16/20 participants provided a quantitative result). It was agreed at the SAB meeting that failure to detect the increased ornithine would be classed as a critical error.

Diagnosis / Interpretative proficiency

18/20 participants scored 2 marks for interpretation, with the remaining 2 participants scoring 0 marks (these were the labs who did not detect the increased ornithine).

Recommendations

15/20 – plasma amino acids
17/20 – mutation studies
5/20 – plasma ammonia
7/20 – family testing
2/20 – trial of pyridoxine

Overall impression

- Analytical performance 90%
- Interpretative performance 90%
- Overall performance 90%

Performance for this sample was good with the majority of participants identifying the abnormal metabolite and giving the correct diagnosis.

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 Aspartylglucosaminuria			Patient C Sample from a healthy child with no suspected inborn error of metabolism.			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	--	--	--	2	2	4	8
2	2	2	4	--	--	--	2	2	4	8
3	2	2	4	--	--	--	2	2	4	8
4	2	2	4	--	--	--	2	2	4	8
5	2	2	4	--	--	--	2	2	4	8
6	2	2	4	--	--	--	2	0	2	6
7	2	2	4	--	--	--	1	0	1	5
8	2	2	4	--	--	--	2	2	4	8
9	2	2	4	--	--	--	2	2	4	8
10	2	2	4	--	--	--	2	2	4	8
11	2	2	4	--	--	--	2	2	4	8
12	2	2	4	--	--	--	2	2	4	8
13	2	2	4	--	--	--	2	2	4	8
14	2	2	4	--	--	--	2	1	3	7
15	2	2	4	--	--	--	2	2	4	8
16	2	2	4	--	--	--	2	2	4	8
17	2	2	4	--	--	--	2	2	4	8
18	2	2	4	--	--	--	2	2	4	8
19	2	2	4	--	--	--	2	2	4	8
20	2	2	4	--	--	--	2	2	4	8
21	0	0	0	--	--	--	2	2	4	4

Detailed scores – Round 2

Lab n°	Patient D HHH syndrome (Hyperammonaemia, hyperornithinaemia, homocitrullinaemia)			Patient E Argininosuccinic aciduria (ASA)			Patient F Gyrate atrophy (ornithine aminotransferase deficiency)			
	A	**I**	**Total**	**A**	**I**	**Total**	**A**	**I**	**Total**	**Total**
1	1	2	3	2	2	4	2	2	4	11
2	1	2	3	2	2	4	2	2	4	11
3	1	2	3	2	2	4	2	2	4	11
4	1	2	3	2	2	4	2	2	4	11
5	2	2	4	2	2	4	2	2	4	12
6	1	1	2	2	2	4	2	2	4	10
7	1	2	3	2	2	4	2	2	4	11
8	1	2	3	2	2	4	2	2	4	11
9	1	2	3	0	0	0	0	0	0	3
10	--	--	--	--	--	--	--	--	--	0
11	1	2	3	0	0	0	2	2	4	7
12	1	2	3	2	2	4	2	2	4	11
13	1	2	3	2	2	4	2	2	4	11
14	1	2	3	2	2	4	2	2	4	11
15	1	2	3	2	2	4	2	2	4	11
16	1	2	3	2	2	4	0	0	0	7
17	1	2	3	2	2	4	2	2	4	11
18	1	2	3	2	2	4	2	2	4	11
19	1	2	3	2	2	4	2	2	4	11
20	1	2	3	2	2	4	2	2	4	11
21	1	2	3	0	0	0	2	2	4	7

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	--	4	3	4	4	19	95	
2	4	--	4	3	4	4	19	95	
3	4	--	4	3	4	4	19	95	
4	4	--	4	3	4	4	19	95	
5	4	--	4	4	4	4	20	100	
6	4	--	2	2	4	4	16	80	
7	4	--	1	3	4	4	16	80	
8	4	--	4	3	4	4	19	95	
9	4	--	4	3	0	0	11	55	CE
10	4	--	4	--	--	--	8	40	
11	4	--	4	3	0	4	15	75	CE
12	4	--	4	3	4	4	19	95	
13	4	--	4	3	4	4	19	95	
14	4	--	3	3	4	4	18	90	
15	4	--	4	3	4	4	19	95	
16	4	--	4	3	4	0	15	75	CE
17	4	--	4	3	4	4	19	95	
18	4	--	4	3	4	4	19	95	
19	4	--	4	3	4	4	19	95	
20	4	--	4	3	4	4	19	95	
21	0	--	4	3	0	4	11	55	CE

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 60 % of adequate responses)	16	76
Unsatisfactory performers (< 60 % adequate responses and/or critical error)	5	24
Partial and non-submitters	1	5

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
Sample 2018-A	Dihydropyrimidine dehydrogenase deficiency	95	95	95
Sample 2018-B	Aspartylglucosaminuria	--	--	--
Sample 2018-C	Sample from a healthy child with no suspected inborn error of metabolism.	98	88	93
Sample 2018-D	HHH syndrome (Hyperammonaemia, hyperornithinaemia, homocitrullinaemia)	53	98	75
Sample 2018-E	Argininosuccinic aciduria (ASA)	85	85	85
Sample 2018-F	Gyrate atrophy (ornithine aminotransferase deficiency)	90	90	90

10. Annual meeting of participants

This took place in Athens on September 4th 2018 from 9.00 to 10.30, before the SSIEM Meeting.

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

- 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. 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 urine by first class post to:

  Mrs Joanne Croft
  Dept of Clinical Chemistry
  Sheffield Children’s NHS Foundation
  Trust, Western Bank
  Sheffield, S10 2TH
  United Kingdom
  Tel: +44(0)114 271 7000 Ext 17267
  Fax: +44(0)114 276 6205
  Email: Joanne.Croft@sch.nhs.uk

  Please send either Joanne Croft or Claire Hart (Claire.Hart@sch.nhs.uk) 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	5 February 2019
Start of analysis of Survey 2019/1 Website open	March 4
Survey 2019/1 - Results submission	March 25
Survey 2019/1 - Reports	April
Start of analysis of Survey 2019/2	June 3
Survey 2019/2 – Results submission	June 24
Survey 2019/2 - Reports	July
Annual meeting of participants	Sept 3 Rotterdam SSIEM
Annual Report 2019	December

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, 2019-03-06
Name and signature of Scientific Advisor
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