



Quality Assurance in Laboratory Testing for IEM

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Diagnostic Proficiency Testing

Centre: United Kingdom

Final Report 2022

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 page 18 and the ERNDIM Privacy Policy on www.erndim.org.

1. Geographical distribution of participants

In 2022, 20 labs participated in the Diagnostic Proficiency Testing Scheme UK. For both surveys, all 20 participating laboratories submitted results.

| Country | Number of participants |
|----------------|------------------------|
| Australia | 1 |
| Ireland | 1 |
| New Zealand | 1 |
| Spain | 1 |
| Switzerland | 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 Claire Hart as Deputy Scientific Advisor and coordinated by Alessandro Salemma as Scheme Organiser (sub-contractor on behalf of CSCQ), both appointed by and according to procedures laid down the ERNDIM Board.

¹ If this report is not Version 1 for this scheme year, go to APPENDIX 1 for details of the changes made since the last version of this document.

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 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 or specified participants.

Patient A: Barth syndrome – Sheffield Children’s NHS Foundation Trust. This was the common sample sent to all DPT scheme participants.
 Patient B: Hyperammonaemia, hyperornithinaemia, homocitrullinuria (HHH) syndrome – Sheffield Children’s NHS Foundation Trust
 Patient C: Mitochondrial neuro-gastro intestinal encephalopathy (MNGIE) – Dr Ruijter, Rotterdam Centre de Biologie Est, Lyon
 Patient D: MPS 3B – Sheffield Children’s NHS Foundation Trust
 Patient E: Primary Hyperoxaluria Type 1 – Sheffield Children’s NHS Foundation Trust
 Patient F: AADC deficiency – Dr Claus Dieter Langhans, Heidelberg

The samples have been heat-treated. They were pre-analysed in our institute after 3 days incubation at ambient temperature (to mimic possible changes that might arise during transport). In all six samples the typical metabolic profiles were preserved after this process.
 Mailing: samples were sent by DHL, FedEx or the Swiss Post at room temperature.

3. Tests

Analysis of amino acids, organic acids, mucopolysaccharides, oligosaccharides and purines/pyrimidines were required in 2022.

4. Schedule of the scheme

- Feb 2, 2022: shipment of samples of Survey 1 and Survey 2
- Mar 14, 2022: analysis start of samples, clinical details and website submission availability for the first survey
- Apr 4, 2022: deadline for result submission (Survey 1)
- May, 2022: interim report of Survey 1 by e-mail
- June 6, 2022: analysis start of samples, clinical details and website submission availability for the second survey
- June 28, 2022: deadline for result submission (Survey 2)
- August, 2022: interim report of Survey 2 by e-mail
- November 14, 2022: on line meeting of the qualitative scheme scientific advisors to discuss and confirm critical errors
- November 24/25, 2022: SAB meeting in Rome
- January 2023: annual report published

5. Results

20 of 20 labs returned results for both surveys, all 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 UK 2022 have been also scored by Petr Chrastina, from DPT Czech Republic. At the SAB meeting in November 2022 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. One laboratory will receive a critical error this year.

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 laboratories will receive a performance support letter from the Scheme Advisor for 2022, one for critical error and one for poor score. Any partial submitters will receive a letter from the ERNDIM Executive Administrator, Sara Gardner.

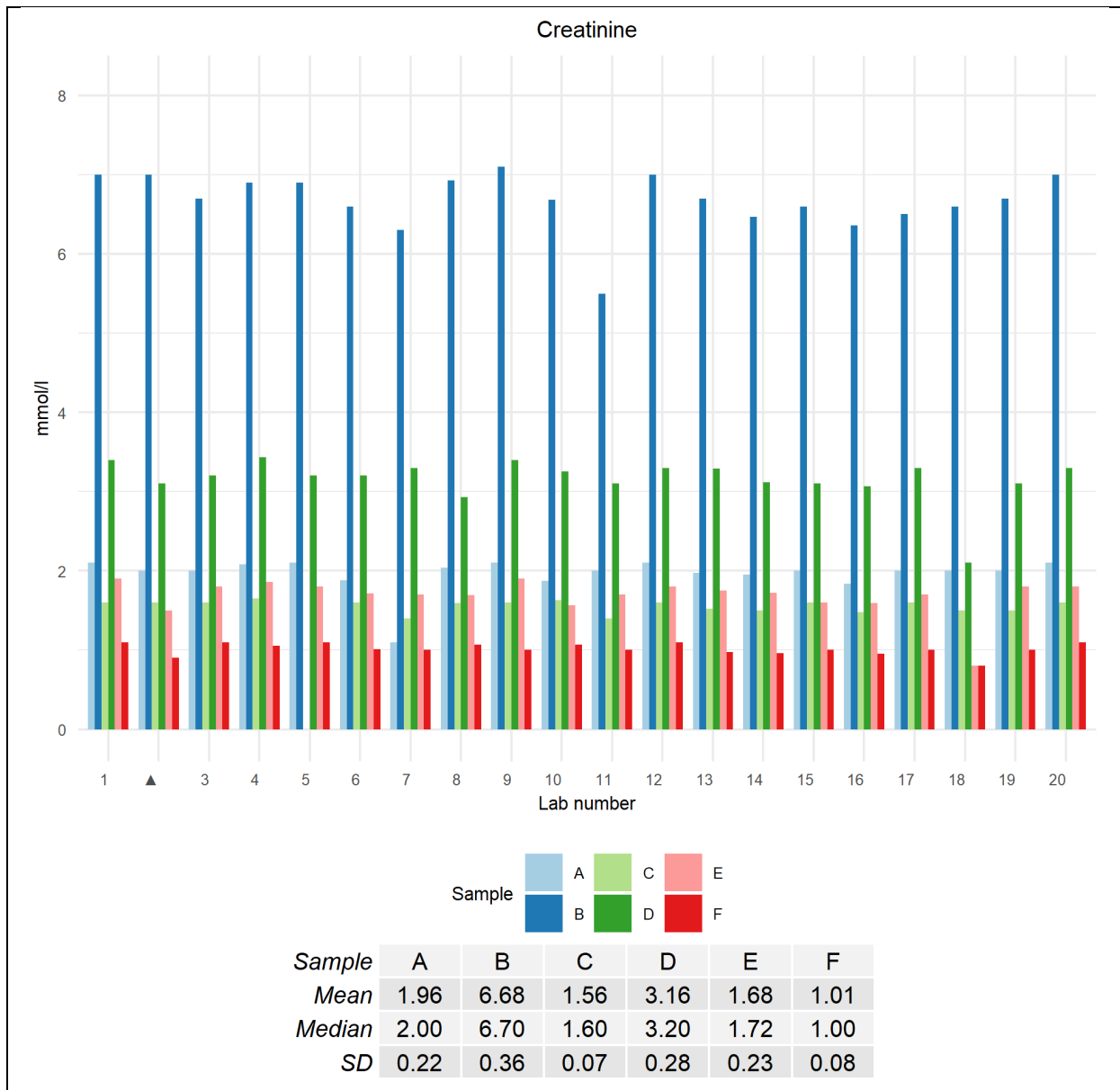
7.1. Score for satisfactory performance

At least 17 points from the maximum of 24 (70.8%). This has increased from a minimum of 15 out of 24.

8. Results of samples and evaluation of reporting

8.1. Creatinine measurement for all samples

There was good agreement for the creatinine concentrations for all 6 samples. Only 1 creatinine value was not provided by 1 laboratory (Lab 5 for Sample C).



8.2. Patient A

3 methylglutaconic aciduria due to Barth syndrome

Patient details provided to participants

Pre-natal growth concerns. Monitored throughout life for poor growth. Presented at 4 years of age due to lips going blue during exercise.

Patient details

This sample was donated by a 14 year old male patient who had been picked up prenatally due to growth concerns. He presented at the age of 4 years due to his lips turning blue during exercise and obtained a diagnosis at the age of 14 years when genome sequencing became available. The genetic result was confirmed by bloodspot cardiolipin analysis.

Analytical performance

All 20 participants scored 2 marks for analysis, by detecting and reporting the increased concentration of 3 methyl glutaconate.

Diagnosis / Interpretative proficiency

Giving Barth syndrome as either the primary or alternative diagnosis was scored with 2 marks. 19 of 20 participants therefore scored the full 4 marks available for this sample. The remaining participant scored 1 mark for interpretation as they diagnosed this as a 3 methylglutaconic aciduria.

Recommendations

Those given are as follows (for the UK scheme participants):

Cardiolipin: 17

General genetics: 10

TAZ gene: 15

Full Blood Count: 8

Refer to metabolic: 16

Refer to cardiology: 5

Repeat organic acids: 6

Genetic counselling/sibling testing etc.: 6

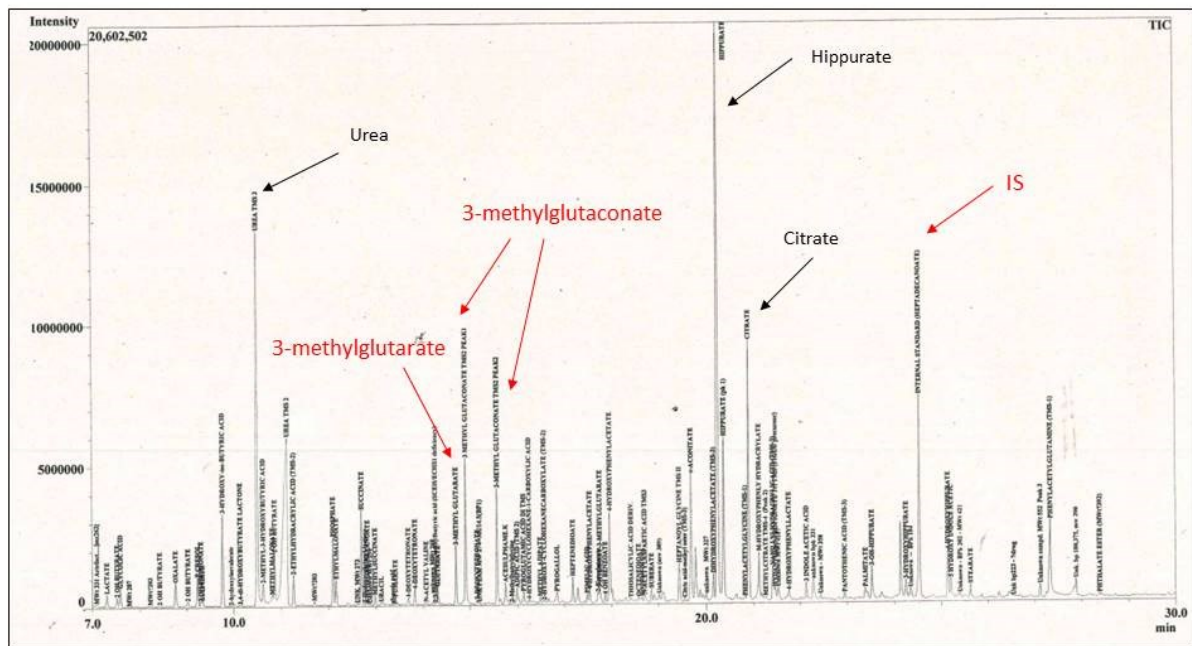
Scoring (as used by all the DPT scheme organisers for this sample)

- Analytical:
 - Detecting increased concentration of 3 methyl glutaconate: 2 marks
- Interpretation:
 - Barth syndrome (as primary or alternate diagnosis): 2 marks
 - Any secondary 3 methylglutaconic aciduria (as primary or alternate diagnosis): 2 marks
 - Primary 3 methylglutaconic acidurias (either HMG CoA lyase or 3 methylglutaconyl CoA hydratase deficiency) with no mention of Barth syndrome: 1 mark only
 - 3 methylglutaconic aciduria as diagnosis only (i.e. no mention of primary or secondary): 1 mark only

The primary 3 methylglutaconic acidurias are distinguishable from each other and from secondary causes due to the presence of other metabolites on the organic acid profile (increased 3 hydroxy 3 methylglutarate and usually 3 hydroxy isovaleric acid in HMG CoA lyase deficiency and increased 3 hydroxyisovaleric acid in 3 methylglutaconyl CoA hydratase deficiency).

Overall impression

Proficiency for this sample was excellent and was the same as or even better than the proficiency seen in the other DPT schemes (this was the common sample).



Sample A Organic acid chromatogram

8.3. Patient B

This sample was donated by a patient with Hyperammonaemia, hyperornithinaemia, homocitrullinuria (HHH) syndrome

Patient details provided to participants

Ataxia and liver failure.

Patient details

This sample came from a 12 year old female who was diagnosed at the age of 4.5 years.

Analytical performance

16/20 participants scored 2 marks for analysis

1/20 participants scored 1 mark for analysis (detected the increased ornithine but did not positively identify the homocitrulline)

3/20 scored 0 marks for analysis

Diagnosis / Interpretative proficiency

16/20 scored 2 marks for interpretation (gave HHH as the primary diagnosis)

1/20 scored 1 mark for interpretation

3/20 scored 0 marks for interpretation

Recommendations

Blood ammonia: 16

Plasma amino acids: 18

Mutation analysis of the SLC25A15 gene – 11

Refer to metabolic team: 14

Investigate siblings: 5

Scoring

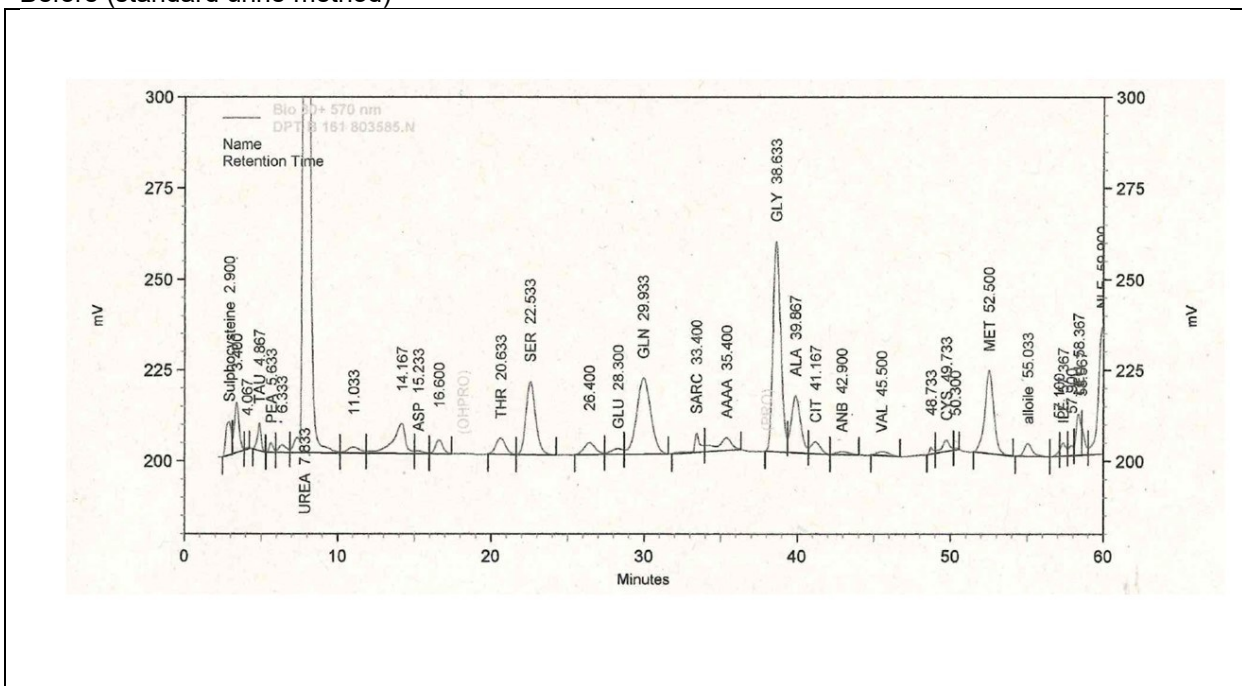
- Analytical:
 - Detecting increased ornithine – 1 mark
 - Positive identification of homocitrulline – 1 mark
- Interpretation:
 - HHH syndrome – 1 marks
 - Other urea cycle defect – 1 mark

Overall impression

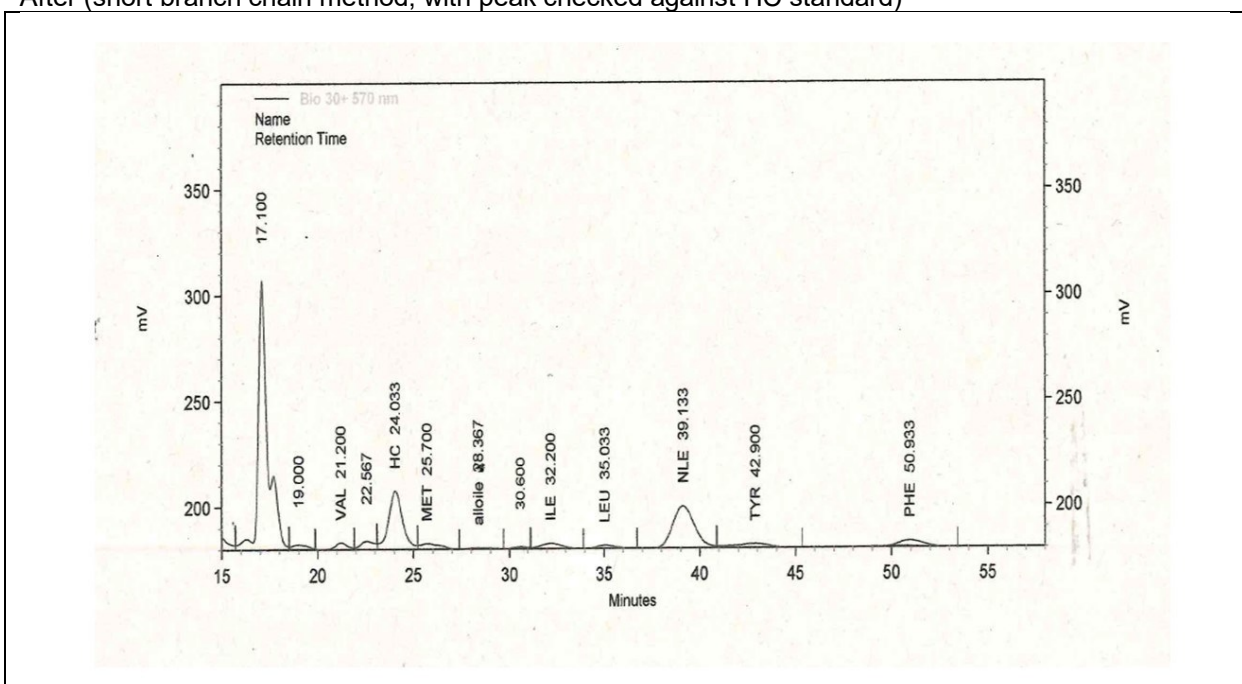
Overall proficiency for this sample was good, although 2 laboratories scored 0 marks and 1 scored 1 mark.

Some participants mentioned the problem with ion exchange chromatography as a method for positively identifying homocitrulline as there is no clear separation between this and methionine. We use a different programme on our analyser which gives the required separation.

Before (standard urine method)



After (short branch chain method, with peak checked against HC standard)



8.4. Patient C

Thymidine phosphorylase deficiency aka Mitochondrial neuro-gastro intestinal encephalopathy (MNGIE)

Patient details provided to participants

Psychomotor retardation, myopathy and severe cachexia (weight 26 kg). MRI revealed leukodystrophy.

Patient details

This sample was donated by a 16 year old female who had been diagnosed at the age of 14 years. The sample was given to the UK DPT scheme by Dr George Ruijter.

Analytical performance

10/20 scored 2 marks
6/20 scored 1 mark
4/20 scored 0 marks

Those that scored 2 marks either did purine and pyrimidine analysis or sent sample to a referral laboratory.

Those that scored 1 mark picked up the thymine and uracil on the organic acids.

Diagnosis / Interpretative proficiency

14/20 scored 2 marks
4/20 scored 1 mark
2/20 scored 0 marks

Those that scored 2 marks either had the purine and pyrimidine results or recognised the potential significance of thymine and uracil along with clinical details.

Those that scored 1 mark tended to be suggesting 'mitochondriopathy' on basis of other findings such as increased lactate.

Recommendations

Purine/pyrimidine analysis (or repeat if already done) – 8

Mutation analysis – 3

Specifically mentioned mutation analysis of the TYMP gene – 11

Thymidine phosphorylase enzyme analysis – 4

Referral to metabolic team - 13

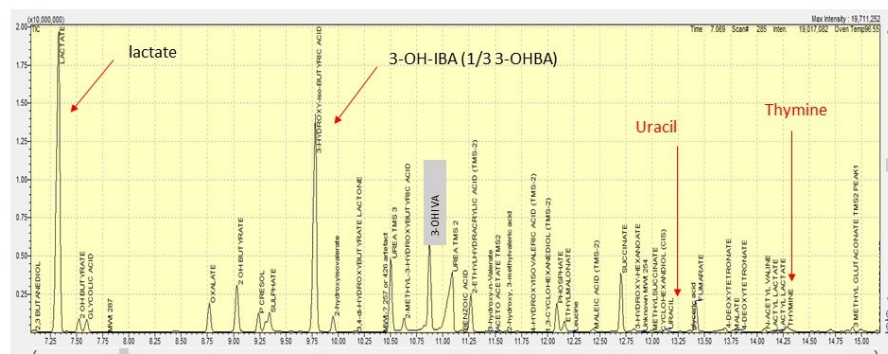
Scoring

- Analytical:
 - Detecting increased thymidine and/or deoxyuridine (and thymine, uracil) – 2 marks
 - Detecting increased thymidine and/or uracil (without mentioning thymidine and deoxyuridine) – 1 mark
- Interpretation:
 - MNGIE – 2 marks
 - Mitochondriopathy – 1 mark

Overall impression

Proficiency for this sample was the lowest of the 6 samples sent out in 2022 with 10/20 laboratories scoring 4 marks.

Sample C - Organic Acid Chromatogram



8.5. Patient D

MPS 3B (Sanfilippo syndrome) due to alpha-N-acetylglucosaminidase deficiency (NAGLU gene)

Patient details provided to participants

Early developmental delay and conductive hearing loss.

Patient details

Sample obtained from a 3.5 year old male presenting with early developmental delay and conductive hearing loss.

Analytical performance

18/20 – 2 marks

2/20 – 1 mark (only do quantitative analysis of GAGs)

Diagnosis / Interpretative proficiency

17/20 – 2 marks

3/20 – 1 mark

Of the 3 laboratories who scored 1 mark, 2 were the participants who did not provide a qualitative result who therefore could not be specific. The other was a laboratory who identified heparin sulphate as the main GAG species but put MPS1/2 as the most likely diagnosis.

Recommendations

19/20 – enzymology to determine subtype (A-D)

16/20 – genetic confirmation

12/20 – refer to metabolic consultant/screen siblings

5/20 – mentioned excluding heparin treatment as a cause of the findings

4/20 – qualitative analysis by 2D electrophoresis or LC-MS/MS (labs who had not done or who had done 1D but not 2D)

Scoring

- Analytical:
 - Identifying raised GAG/creatinine ratio and that Heparan sulphate was the major component – 2 marks
 - Identifying raised GAG/creatinine ratio but specifying no further – 1 mark

- Interpretation:
 - MPS3 (Sanfilippo syndrome) – 2 marks
 - An unspecified MPS disorder or other MPS disorder – 1 mark

Overall impression

Very good proficiency for this sample. The GAG concentration was high in this sample (18 participants provided a quantitative result, values are in g/mol creatinine).

Mean = 61.4

Median = 57.4

S.D = 24.33

Min value = 23, max value = 112.7

8.6. Patient E

Primary Hyperoxaluria Type 1 due to alanine:glyoxylate aminotransferase deficiency (AGT gene)

Patient details provided to participants

Renal stones

Patient details

This sample was obtained from a 6 year old male presenting with renal stones.

Analytical performance

20/20 participants scored 2 marks

Diagnosis / Interpretative proficiency

20/20 participants scored 2 marks

All correctly gave the most likely diagnosis as Hyperoxaluria type 1.

Recommendations

17/20 – quantitative oxalate

18/20 – confirmation of diagnosis by genetic mutation (ART gene)

13/20 – clinical referral (11/13 suggesting renal rather than metabolic)

10/20 – quantitative glycolate

2/20 – 2,4 dihydroxyglutarate (PH3 metabolite)

2/20 – confirmation of diagnosis by enzymology (needs a liver biopsy!)

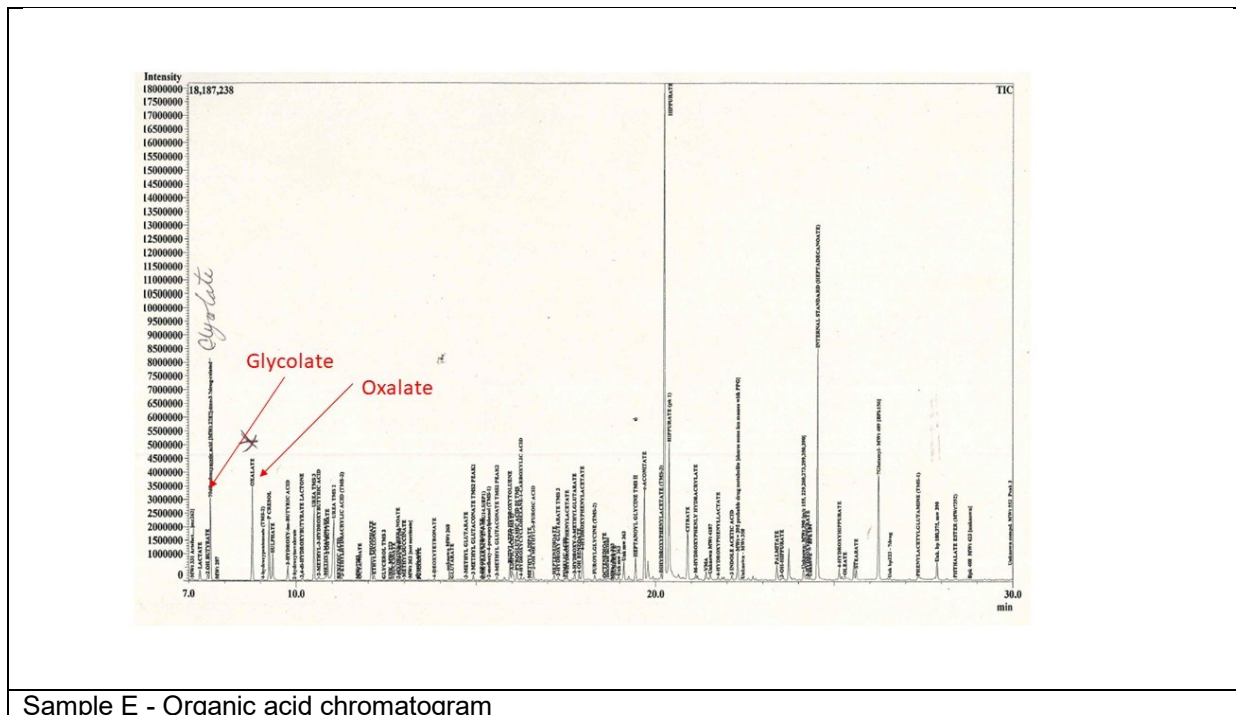
Others – revolved around ruling out other possible causes of renal stones e.g. purines and pyrimidines for APRT deficiency.

Scoring

- Analytical:
 - Increased glycolate and oxalate – 2 marks
 - Increased glycolate and indicating the need to measure oxalate to confirm increase – 2 marks
- Interpretation:
 - Primary Hyperoxaluria type 1 – 2 marks
 - Other hyperoxaluria/recommending appropriate investigations that would have lead to recognition of hyperoxaluria – 1 mark
 -

Overall impression

Excellent proficiency.



8.7. Patient F

Aromatic L-amino acid decarboxylase deficiency (DDC gene) with administration of TPN containing N-acetyl tyrosine.

Patient details provided to participants

Global muscular hypotonia with dystonic movements. Sample collected whilst on treatment in ICU.

Patient details

This sample was donated by a male patient who was diagnosed with aromatic L-amino acid decarboxylase deficiency at the age of 6 months. The sample was collected while the patient was on treatment on ICU at the age of 8 years. This sample was kindly provided by Dr Claus Dieter Langhans.

Analytical performance

18/20 scored 2 marks

1/20 scored 1 mark

1/20 scored 0 marks

The laboratory that scored 1 mark did not identify increased vanillyl-lactate but did identify the raised N-acetyltyrosine.

The laboratory that scored 0 marks did not enter any organic acid results.

Diagnosis / Interpretative proficiency

18/20 scored 2 marks

2/20 scored 1 mark

1/20 scored 0 marks

Of the 2 laboratories that scored 1 mark, the laboratory who did not identify the increased vanillyl-lactate but who did identify the raised N-acetyltyrosine did not suggest AADC but did recommend CSF neurotransmitters as further investigation for dystonia. The other did indicate that vanillyl-lactate was raised in the analytical section only put AADC as the alternative diagnosis (with a completely different diagnosis as the primary diagnosis) with no recommendation to do CSF neurotransmitters.

The laboratory that scored 0 marks did not complete the interpretation/recommendation section (this was the laboratory that did not enter any organic acid results).

Recommendations

18/20 – CSF neurotransmitters

15/20 – mutational analysis (14/15 specified AADC)

12/20 – refer to metabolic/neurology

9/20 – enzymology of AADC

8/20 – 3-O-methyldopa (plasma/DBS)

8/20 – patient history. Particularly whether they were on total parenteral nutrition at the time the sample was collected

3/20 – plasma amino acids (2 laboratories noted slightly increased orotic acid)

2/20 – serum prolactin

2/20 - ? on L-Dopa (increased HVA would usually give that away)

Other recommendation were around following up slightly increased orotic acid or acylglycines identified by a few labs

Only 1 laboratory mentioned PNPO deficiency (suggested CSF amino acids) - ? due to clinical details or lack of familiarity)

Scoring

• Analytical:

- Identifying raised vanilyl-lactate and N-acetyltyrosine – 2 marks
- Identifying raised vanilyl-lactate – 2 marks
- Identifying raised N-acetyltyrosine – 1 mark

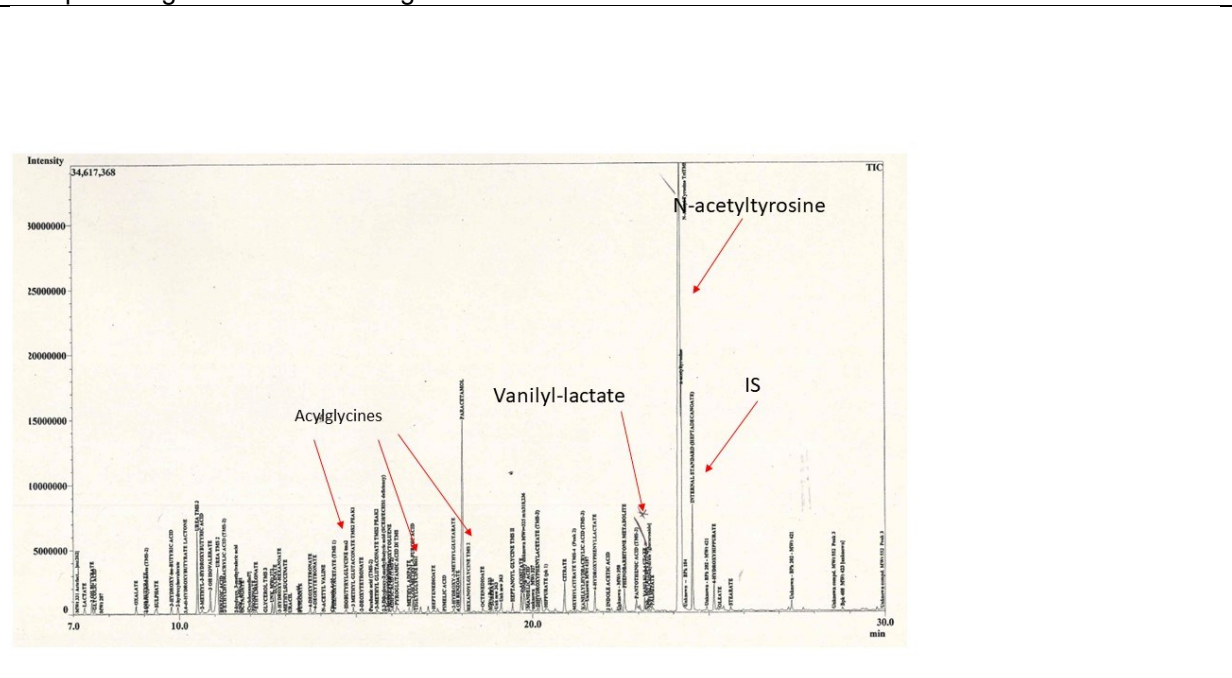
• Interpretation:

- AADC as the most likely diagnosis – 2 marks
- AADC as the alternative diagnosis but without recommendation for CSF neurotransmitters – 1 mark
- NSA/other diagnosis but with a recommendation for CSF neurotransmitters – 1 mark

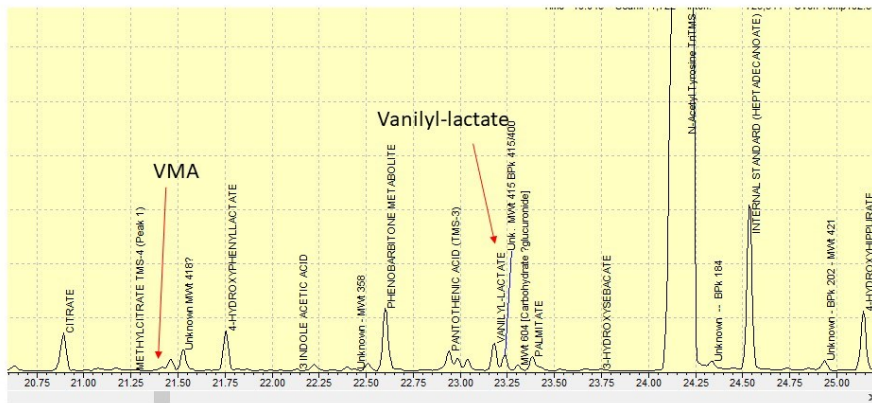
Overall impression

Proficiency for this sample was very good – perhaps the fact it had also recently been used in the qualitative organic acid scheme meant that laboratories who subscribe to both schemes had come across this disorder and knew the key metabolites to look out for.

Sample F Organic acid chromatogram



Sample F Organic acid chromatogram 'close up'



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 Barth syndrome | | | Patient B Hyperammonaemia, hyperornithinaemia, homocitrullinuria (HHH) syndrome | | | Patient C Mitochondrial neuro- gastro intestinal encephalopathy (MNGIE) | | | Total |
|--------|-----------------------------|---|-------|---|---|-------|--|---|-------|-------|
| | A | I | Total | A | I | Total | A | I | Total | |
| 1 | 2 | 2 | 4 | 1 | 2 | 3 | 0 | 0 | 0 | 7 |
| 2 | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| 3 | 2 | 1 | 3 | 2 | 2 | 4 | 2 | 2 | 4 | 11 |
| 4 | 2 | 2 | 4 | 2 | 0 | 2 | 1 | 2 | 3 | 9 |
| 5 | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| 6 | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| 7 | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| 8 | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 2 | 2 | 10 |
| 9 | 2 | 2 | 4 | 0 | 0 | 0 | 1 | 2 | 3 | 7 |
| 10 | 2 | 2 | 4 | 0 | 0 | 0 | 2 | 2 | 4 | 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 | 1 | 2 | 3 | 11 |
| 14 | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| 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 | 1 | 1 | 2 | 10 |
| 20 | 2 | 2 | 4 | 0 | 1 | 1 | 0 | 1 | 1 | 6 |

Detailed scores – Round 2

| Lab n° | Patient D MPS 3B | | | Patient E Primary Hyperoxaluria Type 1 | | | Patient F AADC deficiency | | | Total |
|--------|---------------------|---|-------|--|---|-------|------------------------------|---|-------|-------|
| | A | I | Total | A | I | Total | A | I | 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 | 2 | 2 | 4 | 12 |
| 5 | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| 6 | 1 | 1 | 2 | 2 | 2 | 4 | 2 | 2 | 4 | 10 |
| 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 | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 1 | 2 | 10 |
| 12 | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| 13 | 2 | 1 | 3 | 2 | 2 | 4 | 2 | 2 | 4 | 11 |
| 14 | 1 | 1 | 2 | 2 | 2 | 4 | 2 | 2 | 4 | 10 |
| 15 | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| 16 | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| 17 | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 1 | 3 | 11 |
| 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 | 2 | 2 | 4 | 0 | 0 | 0 | 8 |

Total scores

| Lab n° | A | B | C | D | E | F | Cumulative score | Cumulative score (%) | Critical error |
|--------|---|---|---|---|---|---|------------------|------------------------|----------------|
| 1 | 4 | 3 | 0 | 4 | 4 | 4 | 19 | 79 | |
| 2 | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| 3 | 3 | 4 | 4 | 4 | 4 | 4 | 23 | 96 | |
| 4 | 4 | 2 | 3 | 4 | 4 | 4 | 21 | 88 | |
| 5 | 4 | 4 | 3 | 4 | 4 | 4 | 23 | 96 | |
| 6 | 4 | 4 | 4 | 2 | 4 | 4 | 22 | 92 | |
| 7 | 4 | 4 | 3 | 4 | 4 | 4 | 23 | 96 | |
| 8 | 4 | 4 | 2 | 4 | 4 | 4 | 22 | 92 | |
| 9 | 4 | 0 | 3 | 4 | 4 | 4 | 19 | 79 | |
| 10 | 4 | 0 | 4 | 4 | 4 | 4 | 20 | 83 | |
| 11 | 4 | 4 | 1 | 4 | 4 | 2 | 19 | 79 | |
| 12 | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| 13 | 4 | 4 | 3 | 3 | 4 | 4 | 22 | 92 | |
| 14 | 4 | 4 | 3 | 2 | 4 | 4 | 21 | 88 | |
| 15 | 4 | 4 | 0 | 4 | 4 | 4 | 20 | 83 | CE |
| 16 | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| 17 | 4 | 4 | 4 | 4 | 4 | 3 | 23 | 96 | |
| 18 | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| 19 | 4 | 4 | 2 | 4 | 4 | 4 | 22 | 92 | |
| 20 | 4 | 1 | 1 | 4 | 4 | 0 | 14 | 58 | |

Performance

| | Number of labs | % total labs |
|---|----------------|--------------|
| Satisfactory performers (≥ 60 % of adequate responses) | 18 | 90 |
| Unsatisfactory performers (< 60 % adequate responses and/or critical error) | 2 | 10 |
| Partial and non-submitters | 0 | 0 |

Overall Proficiency

| Sample | Diagnosis | Analytical (%) | Interpretation (%) | Total (%) |
|---------------|--|----------------|--------------------|-----------|
| DPT-UK-2022-A | Barth syndrome | 100 | 98 | 99 |
| DPT-UK-2022-B | Hyperammonaemia, hyperornithinaemia, homocitrullinuria (HHH) syndrome | 83 | 83 | 83 |
| DPT-UK-2022-C | Mitochondrial neuro-gastro intestinal encephalopathy (MNGIE) | 58 | 83 | 70 |
| DPT-UK-2022-D | MPS 3B | 95 | 93 | 94 |
| DPT-UK-2022-E | Primary Hyperoxaluria Type 1 | 100 | 100 | 100 |
| DPT-UK-2022-F | AADC deficiency | 93 | 90 | 91 |

10. Annual meeting of participants

This took place in Freiburg, Germany, before the SSIEM 2022 Meeting.

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. We understand that attending these meetings in person is not always possible and requests for a hybrid meeting (in person and on-line) are being discussed for feasibility by the Executive Board.

Please note that details for the Annual meeting of participants in 2023 have yet to be confirmed.

11. Information from the Executive Board and the Scientific Advisory Board

- **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!).

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. Schedule for 2023

| | |
|---|------------------|
| Sample distribution | 8 February 2023 |
| Start of analysis of Survey 2023/1 Website open | 13 March 2023 |
| Survey 2023/1 - Results submission | 3 April 2023 |
| Survey 2023/1 – Interim Report | May/June 2023 |
| Start of analysis of Survey 2023/2 | 5 June 2023 |
| Survey 2023/2 – Results submission | 26 June 2023 |
| Survey 2023/2 – Interim Report | July/August 2023 |
| Annual meeting of participants | TBC |
| Annual Report 2023 | December 2023 |

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, 2023-01-15

Name and signature of Scientific Advisor



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

| Version Number | Published | Amendments |
|----------------|-----------------|------------------------------|
| 1 | 17 January 2023 | 2022 annual report published |
| | | |
| | | |

END