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Qualitative Organic Acids Centre: United Kingdom Final Report 2021

prepared by Camilla Scott

Note: This annual report is intended for participants of the ERNDIM QLOU Sheffield 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 <u>www.erndim.org</u>.

1. Geographical distribution of participants

In 2021, 75 labs participated in the Qualitative Urine Organic Acid Scheme – Sheffield. For the first survey, 69 and second survey 66 laboratories submitted results.

Country	Number of participants	Country	Number of participants
Undefined country	3	New Zealand	2
Australia	6	Norway	1
Belgium	7	Pakistan	1
Finland	2	Poland	2
Hungary	1	Slovakia	2
Ireland	1	South Africa	2
Israel	1	Sweden	2
Japan	5	United Kingdom	16
Malaysia	3	United States of America	1
Mexico	18	Spain	1

2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Camilla Scott as Scientific Advisor and coordinated by CSCQ as scheme organiser (sub-contractor on behalf of ERNDIM), both appointed by and according to procedures laid down by the ERNDIM Board.

CSCQ dispatches QLOU EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports. Existing QLOU scheme participants can log on to the CSCQ results submission website at:

https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php

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

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: Normal.\<u>\gdrive\gdrive\shared\CLINICAL CHEMISTRY\Camilla +</u> Sharon\AppEV-AR-CS-QLOU\ardata\report\2021\QLOU\US\BaseAR-QLOU-US-2021 ER.docx -Staff donation

Patient B: AADC deficiency. -Dr Claus-Dieter Heidelberg scheme

Patient C: Primary Hyperoxaluria Type 1 (PH1) – Patient Donation

Patient D: 3-Hydroxyisobutyric aciduria. - Patient Donation

Patient E: Malonic aciduria. - Patient Donation

Patient F: No significant abnormality. – Staff Donation

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 qualitative organic acids.

4. Schedule of the scheme

- Feb 9th, 2021: shipment of samples of Survey 1 and Survey and of the clinical data by e-mail
- June 1st, 2021: deadline for result submission (Survey 1)
- Sep 7th, 2021: analysis of samples of the second survey
- Sep 27th, 2021: deadline for result submission (Survey 2)
- August 13th, 2021: report of Survey 1 by e-mail
- November 18th, 2021: report of Survey 2 by e-mail
- November 26th, 2021: SAB meeting (virtual)
- January 12th, 2022: annual report with scoring by e-mail.

5. Results

69 of 74 labs returned results for both surveys, mainly by the deadline.

	Survey 1	Survey 2
Receipt of results	75	74
No answer	1	2

6. Website reporting

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

- Results
 - Enter the key metabolites with the evaluation in the tables.
 - If the profile is normal: enter "Normal profile" in "Key metabolites".
 - Don't enter results in the "comments" window, otherwise your results may not be included in the evaluation program.
- Recommendations = advice for further investigation.
 - Scored together with the interpretative score.
 - Advice for treatment is not scored but may be taken into account particularly in cases of critical error assignment.

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		Correct results of the appropriate tests	2
		Analytical performance	Partially correct or non-standard methods	1
			Unsatisfactory or misleading	0
		Interpretative proficiency &	Good (diagnosis was established)	2
	1		Helpful but incomplete	1
		Recommendations	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: by the scientific advisor and the deputy scientific advisor. At the SAB meeting in November, 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 2021, the SAB decided that sample D has to be considered as a critical error for the labs who failed to identify an increase of 3-Hydroxyisobutyric acid. Non-identification of Malonic Acid in sample E has also been advised by the SAB for critical error. Sample B will be considered as education and the score will not be included for satisfactory performance of the increased vanillyl lactate.

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 2022 due to score and two performance support letters will be sent for critical error. 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%).

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

8. Results of samples and evaluation of reporting

8.1. Patient A

No significant abnormality.

Patient details provided to participants

Speech & language delay

Patient details

This sample was donated by an older child who is a relative of a member of staff and who has no known metabolic or other medical condition.

Analytical performance

The majority of participants found no abnormalities in this organic acid profile. Overall this sample demonstrated good analytical proficiency for a normal organic acid profile.

Diagnosis / Interpretative proficiency Interpretative proficiency

All but two laboratories interpreted this profile as normal and not suggestive of an organic acid disorder. Overall, the interpretative proficiency for this sample was good with the majority of laboratories recognising this as a normal profile.

Scoring

Two points were scored for no analytical findings and two points were scored for no evidence for an organic aciduria/no significant abnormality.

Overall impression

This was a high scoring survey with nearly all participants assigning this profile as a good example of a normal profile for organic acid analysis.

8.2. Patient B

Aromatic-L-Amino Acid Decarboxylase (AADC) Deficiency. A rare genetic disorder characterised by decreased activity of aromatic-l-amino acid decarboxylase. AADC is involved in the synthesis of dopamine and serotonin. Symptoms often develop early in life and include truncal muscular hypotonia, progressive extra pyramidal movement disorder and parkinson like dysotnia. A high index of suspicion when small amounts of vanilyl lactate are present in patients with suggestive clinical details warrants further more specific investigations including CSF neurotransmitters and associated metabolites of the biogenic amines. This patient was on TPN supplemented with N-Acetyl tyrosine at the time of sampling which accounted for the large peak of N-Acetvl tyrosine present in this sample.

Patient details provided to participants

8 year old boy with severe, predominantly truncal hypotonia and intermittent dystonic posturing. On treatment in ICU during sample collection.

Analytical performance

This was a challenging sample partly because of the large peak of N-Acetyl tyrosine and partly because of the relatively low concentration of vanillyl lactate. The majority of laboratories identified the N-Acetyl tyrosine and just over half also identified the increased vanillyl lactate. Participants were awarded one mark for identifying the N-Acetyl tyrosine and the full two marks for analytical performance if the vanilly lactate was identified as increased. Other metabolites associated with this disorder including vanillyl pyruvate and vanillyl alanine were also identified by some participants.



Ion spectrum for vanillyl lactate (RT on our column 23.5 minutes)



Ion spectrum for N-acetyl vanillyl alanine RT 25.5 mins

Diagnosis / Interpretative proficiency Interpretative proficiency

Forty-one participants identified the abnormal metabolites associated with AADC deficiency and reached the correct diagnosis as either the most likely or the alternative diagnosis. Two marks were awarded if AADC deficiency was considered as a diagnosis with the exception of when no significant abnormality or normal was stated the most likely abnormality in which case only 1 mark for interpretation was awarded if AADC was mentioned elsewhere in the report. No marks were given if AADC was not considered anywhere in the report. One mark was given if a non-specific neurotransmitter disorder was considered. Of those that did not reach the diagnosis, the majority identified the exogenous peak of N-Acetyl tyrosine and reported accordingly. The participants that did not reach AADC as a likely diagnosis attributed the profile to Total Parental Nutrition (TPN) supplementation or other possible metabolic conditions. Six participants suggested no significant abnormality or normal profile as the most likely diagnosis. It should be noted that N-Acetyl tyrosine is also a marker for AADC but in this case the peak was accentuated by the exogenous source.



Key considerations for identifying AADC from the organic acid profile:

- Presence of small of moderate peaks of vanillyl lactate.
- N-acetyl-vanillylalanine may also be present.
- Note the elevation is often mild.
- The VLA/VMA ratio by semi quantitative measurement has been described as a useful tool in the literature.

Recommendations

The most common recommendations included CSF neurotransmitter analysis, measurement of 3-O-methyl-dopa in plasma or blood spot, measurement of AADC enzyme activity in blood and genetic testing of the DDC gene. The clinical features for a neurotransmitter disorder are quite distinctive, and subsequently recommendations for investigation of the neurotransmitter disorders should be considered in a child with truncal hypotonia and dystonic posturing.

8.3. Patient C

Primary Hyperoxaluria type 1 (PH1). Primary hyperoxaluria type 1 is caused by a deficiency of the liver peroxisomal enzyme alanine:glyocylate aminotransferase (AGT) which catalyses the conversion of glycoxylate to glycine. If this enzyme is deficient the glycoylate is converted to oxalate which forms crystals that can deposit in the kidney and other organs. Presentation can be from infancy to adulthood typically with nephrolithiasis or reduced kidney function. Historically liver biopsy was obtained for enzymatic analysis but this is rarely perfomed now and genetic confirmation by mutational analysis of the AGXT gene is recommended.

Patient details provided to participants

Nephrocalcinosis

Patient details

This sample was donated from a patient with confirmed Primary Hyperoxaluria Type 1. **Overall impression**

Only three of the 73 participants that returned a submission for this survey did not conclude this sample was from a patient with Primary Hyperoxaluria type 1. All three that did not reach the correct diagnosis concluded that the oxalate was not significantly raised. Seventy participants provided Primary Hyperoxaluria as the most likely diagnosis. The most common alternative diagnosis was possible ethylene glycol poisoning.

This was a high scoring survey, with the vast majority of participants identifying both the increased oxalate and glycolate, and reaching the correct diagnosis of Primary Hyperoxaluria Type 1. The majority of the participants that correctly diagnosed Primary Hyerpoxaluria Type 1 suggested genetic analysis of the AGXT gene.

This sample has been distributed previously and the overall proficiency over the years has improved significantly.



8.4. Patient D

3-Hydroxyisobutyric aciduria due to Methylmalonate semialdehyde dehydrogenase deficiency.

Patient details provided to participants

Failure to thrive, recurrent ketoacidosis.

Patient details

3 Hydroxyisobutyric aciduria

Analytical & Interpretative performance

Only one participant failed to identify the 3 hydroxyisobutyric acid.

Ninety-seven percent of the participants identified the increased 3-Hydroxyisobutyric acid along with the slightly increased 3-hydroxypropionic acid. In all of these cases the interpretation of this profile was reported as consistent with 3-hydroxyisobutyric aciduria, most likely due to methylmalonate semialdehyde dehydrogenase (MMSDH) deficiency or 3-hydroxyisobutyric dehydrogenase deficiency (HIBADH).



Recommendations

ALDH6A1 gene for methylmalonate semialdehyde dehydrogenase deficiency was recommended by the majority of participants. HIBADH for 3-hydroxisobutyrate dehydrogenase deficiency was also recommended by several participants.

Overall impression

This was a high scoring survey in which all but one participant identified the 3-hydroxyisobutyric acid as significantly raised. All of these participants identified this as a case of 3-hydroxyisobutyric aciduria however the final diagnosis was divided between methylmalonate semialdehyde dehydrogenase deficiency and 3-hydroxisobutyrate dehydrogenase deficiency. The biochemical and clinical phenotype is highly variable and the organic acid profile for both disorders is very similar. Genetic and clinical correlation is required to reach the final diagnosis. The excretion of 3-hydroxisobutyric acid is heterogeneous for a number of defects with different underlying mechanisms. Identifying the abnormal profile by organic acids may only lead to a generic '3-hydroxyisobutytic aciduria' and the exact underlying defect should then be confirmed by molecular testing via the appropriate genetic panel. Failure to identify this condition was considered to be a critical error at the SAB Critical Errors meeting which took place in November 2021.

8.5. Patient E

Malonic aciduria due to Malonyl-CoA decarboxylase deficiency.

Patient details provided to participants

Intellectual disability, seizures

Patient details

This sample was donated by a patient with confirmed Malonic Aciduria.

Analytical & Interpretative performance

Sixty-nine participants returned a survey for this sample. Sixty-eight participants identified the increased malonic acid along with increased excretion of methylmalonic acid. Only one participant missed the large peak of malonic acid.

All of the participants that identified the correct metabolites reported the profile as diagnostic for either Malonic Aciduria or combined Methylmalonic/Malonic Aciduria. Seven participants opted for a combined Methylmalonic/Malonic aciduria and 62 participants opted for Malonic aciduria. The ratio of Malonic/MMA is a useful indicator for differentiation of the two disorders. In nearly all cases of combined Malonic/MMA the pattern of MMA>MA is consistent and can help distinguish between these two disorders (JIMD 2019 Jan;42(1):107-116)

Recommendations included urgent referral to a metabolic team and genetic analysis of the MLYCD gene.

This was a high scoring survey in which all but one of the participants that submitted a response identified the correct metabolites associated with Malonic Aciduria with the majority of participants opting for Malonic Aciduria as the most likely diagnosis. Failure to identify the increased Malonic acid in this sample was considered to be a critical error at the SAB meeting which took place in November 2021.



8.6. Patient F

Normal control sample with no significant abnormality in the organic acid profile.

Patient details provided to participants

ASD, ?recent regression

Patient details

This sample was donated from a healthy child relative of one of the laboratory staff.

Analytical & Interpretive performance

Five participants did not make a return and one participant experienced analytical problems with this sample. Of the remaining 68 participants only 49 opted for a clear no significant abnormality. However, of the 19 participants that identified mild increases in the organic acid profile there was no common theme for their interpretation.

9. Scores of participants

All data transfer, the submission of data as well as the request and viewing of reports proceed via the 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.

	Patient A Pat			Patient B	tient B Patient C					
Lab n°		Normal.		AAD	C deficien	cy.	Primar Ty	y Hyperox /pe 1 (PH1	caluria I)	
	Α	I	Total	Α	I	Total	Α	I	Total	Total
1	2	2	4	1	0	1	2	2	4	9
2	2	2	4	1	0	1	2	2	4	9
3	2	2	4	2	1	3	2	2	4	11
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	2	2	4	2	2	4	12
8	2	2	4	2	2	4	2	2	4	12
9										0
10	2	2	4	2	2	4	2	2	4	12
11	2	2	4	2	2	4	2	2	4	12
12	2	2	4	2	1	3	2	2	4	11
13	2	2	4	2	2	4	2	2	4	12
14	2	2	4	1	2	3	2	2	4	11
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	0	2	2	2	4	10
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	2	2	4	2	2	4	12
20	0	0	0	2	1	3	2	2	4	7
21	2	2	4	1	0	1	2	2	4	9
22	2	2	4	2	2	4	2	2	4	12
23	2	2	4	2	2	4	2	2	4	12
24	2	2	4	2	2	4	2	2	4	12
25	2	2	4	2	2	4	2	2	4	12
26	2	2	4	2	2	4	2	2	4	12

Detailed scores – Round 1

27	2	2	4	1	0	1	2	2	4	9
28	2	2	4	2	2	4	2	2	4	12
29	2	2	4	1	0	1	2	2	4	9
30	2	2	4	2	2	4	2	2	4	12
31	2	2	4	2	2	4	2	2	4	12
32	2	2	4	2	2	4	2	2	4	12
33	2	2	4	2	2	4	2	2	4	12
34	2	2	4	2	2	4	2	2	4	12
35	2	2	4	2	2	4	2	2	4	12
36	2	2	4	2	2	4	2	2	4	12
37	2	2	4	2	2	4	2	2	4	12
38	2	2	4	2	2	4	2	2	4	12
39	2	2	4	1	0	1	2	2	4	9
40	2	2	4	2	2	4	2	2	4	12
41	2	2	4	1	0	1	2	2	4	9
42	2	2	4	2	2	4	2	2	4	12
43	2	2	4	1	0	1	2	2	4	9
44	2	2	4	2	2	4	2	2	4	12
45	2	2	4	2	2	4	2	2	4	12
46	2	2	4	1	0	1	2	2	4	9
47	2	2	4	2	1	3	1	1	2	9
48	2	2	4	1	0	1	2	2	4	9
49	2	2	4	2	2	4	2	2	4	12
50	2	2	4	2	2	4	2	2	4	12
51	2	2	4	2	2	4	2	2	4	12
52	2	2	4	1	0	1	2	2	4	9
53	2	2	4	2	2	4	2	2	4	12
54	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0
57	2	2	4	1	0	1	2	2	4	9
58	2	2	4	1	0	1	0	0	0	5
59	2	2	4	2	2	4	2	2	4	12
60	2	2	4	2	2	4	2	2	4	12
61	2	2	4	2	2	4	2	2	4	12
62	2	2	4	1	0	1	2	2	4	9

63	2	2	4	2	1	3	2	2	4	11
64	2	1	3	1	0	1	0	0	0	4
65	0	0	0	1	0	1	1	0	1	2
66	2	2	4	2	2	4	2	2	4	12
67	2	2	4	2	2	4	2	2	4	12
68	2	2	4	1	0	1	2	2	4	9
69	2	2	4	1	0	1	2	2	4	9
70	2	2	4	1	0	1	2	2	4	9
71	2	2	4	0	0	0	2	2	4	8
72	2	2	4	2	2	4	2	2	4	12
73	2	2	4	1	1	2	2	2	4	10
74	2	2	4	1	0	1	2	2	4	9
75	2	2	4	1	0	1	2	2	4	9
76	2	2	4	1	0	1	1	1	2	7
77	2	2	4	2	2	4	2	2	4	12

Sample	Diagnosis	Overall Proficiency	Comment
Α	Normal	96%	
В	AADC	69%	Educational sample
С	Primary Hyperoxaluria	95%	
D	3 Hydroxyisobutyric Aciduria	97%	Critical error if missed
E	Malonic Aciduria	95%	Critical error if missed
F	Normal	81%	

Detailed scores – Round 2

Lab n°	3-Hyd	Patient D Iroxyisobut aciduria.	yric	Malo	Patient E onic acidur	ia.	No signi	Patient F ficant abno	ormality.	
	Α	I	Total	Α	I	Total	Α	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	2	2	4	12
5	2	2	4	2	1	3	2	2	4	11
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	2	2	4	2	2	4	2	2	4	12
12	2	2	4	2	2	4	2	2	4	12
13	2	2	4	2	2	4	2	2	4	12
14	2	2	4	2	2	4	2	2	4	12
15	2	2	4	2	2	4	2	2	4	12
16	2	2	4	2	2	4	2	2	4	12
17	2	2	4	2	2	4	2	2	4	12
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	2	2	4	2	2	4	12
20	2	2	4	2	2	4	0	0	0	8
21	2	2	4	2	2	4	2	2	4	12
22	2	2	4	2	2	4	2	2	4	12
23	2	2	4	2	2	4	2	2	4	12
24	2	2	4	2	2	4	2	2	4	12
25	0	0	0	0	0	0	0	0	0	0
26	2	2	4	2	2	4	1	2	3	11
27	2	2	4	2	2	4	2	2	4	12
28	2	2	4	2	2	4	2	2	4	12
29	2	2	4	2	2	4	2	2	4	12
30	2	2	4	2	2	4	2	2	4	12

31	2	2	4	2	2	4	0	0	0	8
32	2	2	4	2	2	4	2	2	4	12
33	2	2	4	2	2	4	2	2	4	12
34	2	2	4	2	2	4	1	2	3	11
35	1	0	1	2	2	4	2	2	4	9
36	2	2	4	2	2	4	0	1	1	9
37	2	2	4	2	2	4	2	2	4	12
38	2	2	4	2	2	4	1	2	3	11
39	2	2	4	2	1	3	0	1	1	8
40	2	2	4	2	2	4	2	2	4	12
41	2	2	4	2	2	4	2	2	4	12
42	2	2	4	2	2	4	0	0	0	8
43	2	2	4	2	1	3	2	2	4	11
44	2	2	4	2	2	4	0	0	0	8
45	2	2	4	2	2	4	2	2	4	12
46	2	2	4	2	2	4	2	2	4	12
47	2	2	4	2	2	4	2	2	4	12
48	2	2	4	2	2	4	2	2	4	12
49	2	2	4	2	2	4	0	0	0	8
50	2	2	4	2	2	4	2	2	4	12
51	2	2	4	2	2	4	2	2	4	12
52	2	2	4	2	1	3	0	0	0	7
53	2	2	4	2	2	4	2	2	4	12
54										0
55	2	2	4	2	2	4	2	2	4	12
56										0
57	2	2	4	2	2	4	1	1	2	10
58	2	2	4	2	1	3	2	2	4	11
59	2	2	4	2	2	4	2	2	4	12
60	2	2	4	2	2	4	2	2	4	12
61	2	2	4	2	2	4	2	2	4	12
62	2	2	4	2	2	4	2	2	4	12
63	2	2	4	2	2	4	2	2	4	12
64	0	0	0	0	0	0	0	0	0	0
65	2	0	2	2	2	4	0	0	0	6
66	2	2	4	2	2	4	2	2	4	12

67	2	2	4	2	2	4	2	2	4	12
68	2	2	4	0	0	0	2	2	4	8
69	2	2	4	2	2	4	2	2	4	12
70	2	2	4	2	2	4	2	2	4	12
71	2	2	4	2	1	3	0	0	0	7
72	2	2	4	2	2	4	2	2	4	12
73	2	2	4	2	2	4	2	2	4	12
74	2	2	4	2	2	4	2	2	4	12
75	2	2	4	2	2	4	0	0	0	8
76	2	2	4	2	1	3	2	2	4	11
77	2	2	4	2	2	4	2	2	4	12

Total scores

Lab n°	Α	В	С	D	E	F	Cumulative score	Cumulative score(%)	Critical error
1	4	1	4	4	4	4	21	88	
2	4	1	4	4	4	4	21	88	
3	4	3	4	4	4	4	23	96	
4	4	4	4	4	4	4	24	100	
5	4	4	4	4	3	4	23	96	
6	4	4	4	4	4	4	24	100	
7	4	4	4	4	4	4	24	100	
8	4	4	4	4	4	4	24	100	
9				4	4	4	12	50	
10	4	4	4	4	4	4	24	100	
11	4	4	4	4	4	4	24	100	
12	4	3	4	4	4	4	23	96	
13	4	4	4	4	4	4	24	100	
14	4	3	4	4	4	4	23	96	
15	4	4	4	4	4	4	24	100	
16	4	4	4	4	4	4	24	100	
17	4	2	4	4	4	4	22	92	
18	4	4	4	4	4	4	24	100	
19	4	4	4	4	4	4	24	100	
20	0	3	4	4	4	0	15	62	
21	4	1	4	4	4	4	21	88	
22	4	4	4	4	4	4	24	100	
23	4	4	4	4	4	4	24	100	
24	4	4	4	4	4	4	24	100	
25	4	4	4	0	0	0	12	50	
26	4	4	4	4	4	3	23	96	
27	4	1	4	4	4	4	21	88	
28	4	4	4	4	4	4	24	100	
29	4	1	4	4	4	4	21	88	
30	4	4	4	4	4	4	24	100	
31	4	4	4	4	4	0	20	83	
32	4	4	4	4	4	4	24	100	

33	4	4	4	4	4	4	24	100	
34	4	4	4	4	4	3	23	96	
35	4	4	4	1	4	4	21	88	
36	4	4	4	4	4	1	21	88	
37	4	4	4	4	4	4	24	100	
38	4	4	4	4	4	3	23	96	
39	4	1	4	4	3	1	17	71	
40	4	4	4	4	4	4	24	100	
41	4	1	4	4	4	4	21	88	
42	4	4	4	4	4	0	20	83	
43	4	1	4	4	3	4	20	83	
44	4	4	4	4	4	0	20	83	
45	4	4	4	4	4	4	24	100	
46	4	1	4	4	4	4	21	88	
47	4	3	2	4	4	4	21	88	
48	4	1	4	4	4	4	21	88	
49	4	4	4	4	4	0	20	83	
50	4	4	4	4	4	4	24	100	
51	4	4	4	4	4	4	24	100	
52	4	1	4	4	3	0	16	67	
53	4	4	4	4	4	4	24	100	
54	0	0	0				0	0	
55	0	0	0	4	4	4	12	50	
56	0	0	0				0	0	
57	4	1	4	4	4	2	19	79	
58	4	1	0	4	3	4	16	67	
59	4	4	4	4	4	4	24	100	
60	4	4	4	4	4	4	24	100	
61	4	4	4	4	4	4	24	100	
62	4	1	4	4	4	4	21	88	
63	4	3	4	4	4	4	23	96	
64	3	1	0	0	0	0	4	17	
65	0	1	1	2	4	0	8	33	
66	4	4	4	4	4	4	24	100	
67	4	4	4	4	4	4	24	100	
68	4	1	4	4	0	4	17	71	
I							1	1	

69	4	1	4	4	4	4	21	88	
70	4	1	4	4	4	4	21	88	
71	4	0	4	4	3	0	15	62	
72	4	4	4	4	4	4	24	100	
73	4	2	4	4	4	4	22	92	
74	4	1	4	4	4	4	21	88	
75	4	1	4	4	4	0	17	71	
76	4	1	2	4	3	4	18	75	
77	4	4	4	4	4	4	24	100	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 70 %)	67	91
Unsatisfactory performers (< 70 % adequate responses and/or critical error)	4	5
Partial and non-submitters	3	4

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

11. Tentative schedule and 2022

Sample distribution	2 nd February 2022
Start of analysis of Survey 2022/1 Website open	9 th May 2022
Survey 2022/1 - Results submission	30 th May 2022
Survey 2022/1 - Reports	June/July 2022
Start of analysis of Survey 2022/2	29 th August 2022
Survey 2022/2 – Results submission	19 th September 2022
Survey 2022/2 - Reports	October 2022
Annual Report 2022	January 2023

12. 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 QLOU scheme this certificate will indicate if results were submitted and whether satisfactory performance was achieved in the scheme.

Date of report, 2022-01-10 Name and signature of Scientific Advisor

CSall

Mrs C Scott and Miss S Colyer NHS Department of Clinical Chemistry and Newborn Screening The Children's Hospital Sheffield S10 2TH United Kingdom

APPENDIX 1.	Change log (changes since the last version)
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Version Number	Published	Amendments
1	29 April 2022	2021 annual report published

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