Congenital Disorders of Glycosylation (CDG)

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2024 First Round Interim Report

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Please Note:

- This interim report is intended for participants of the ERNDIM CDG scheme. The contents should not be used for any publication without permission of the Scientific Advisor.
- This is an interim report and it includes provisional scores only. All scores are subject to change following moderation at the Scientific Advisory Board meeting in autumn of this year. For final scores and performance data the ERNDIM CDG Annual Report should be referred to.
- The fact that your laboratory participates in this scheme 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 ERNDIM Privacy Policy on www.erndim.org.

1. Results Submission

Results were submitted to the online results website (cscq.hcuge.ch/cscq/ERNDIM/) which is hosted and maintained by CSCQ. The submission deadline for the first round (samples CDG-PP-2024-A, -B and -C) was 13th May 2024.

55 laboratories registered for the 2024 CDG scheme, of these 54 labs (98.2%) submitted results for the first round.

2. Scoring scheme

In agreement with ERNDIM rules, we applied a scoring system of 2+2:

Technical aspects: 1 point for identification of an abnormal profile and 1 point for correct identification of the profile as type I or II.

Diagnostic suggestions: This section should be filled for scoring. Just referring to a specialised lab is insufficient. If required, advice can be obtained from a reference laboratory or in collaboration with a clinical colleague. For normal profiles 2 points are scored. For abnormal profiles, comments should be made on the possibility of the presence of a secondary cause in light of the clinical indication. In addition, the right suggestions should be made for the next step in the diagnostic process that eventually will lead to the genetic defect. Scoring for this part is not so straightforward, but we tried to keep it as consistent as possible.

[1] **If this Annual Report is not Version 1 for this scheme year, go to APPENDIX 2 (page 5) for details of the changes made since the last version of this document.**

The maximum score achievable with full submission for all samples is 24, while a maximum of 12 points are available for labs that only submitted results for the first or second round. The level for satisfactory performance is 17 points.

For the 2022 scheme onwards labs that only submit results for 3 or fewer samples in a scheme year will be classed as partial submitters and their performance will not be evaluated. This information is included in the CDG scheme instructions for 2022 onwards. Partial submitters receive a formal Non-submitter letter notifying them of this status and their certificate of participation shows them as not submitting results for the relevant scheme. As the number of participants in the CDG scheme are limited due to the nature of the EQA samples, ERNDIM reserves the right to exclude participants that are classed as partial/non-submitters for 2 out of 3 registered years (i.e., persistent partial and non-submitters) from the scheme.

For the 2014 scheme onwards, another criterion for satisfactory performance is the absence of any "critical error", which is defined as an error resulting from seriously misleading analytical findings and/or interpretations with serious clinical consequences for the patient. For the 2024 CDG scheme, any critical errors will be agreed at the meeting of the Scientific Advisory Board on 28th and 29th November 2024, and details of these will be included in the 2024 CDG Annual Report.

a. Appeals

If your laboratory is classed as having poor performance at the end of the 2024 scheme and you wish to appeal against this classification, please use the link given in the Performance Support letter you will be sent, to submit your appeal request. The online form should be completed with full details of the reason for your appeal and submitted within one month of receiving your Performance Support Letter. Please note that only appeals submitted using the online response form will be considered.

3. Results of samples and evaluation of reporting

The shipped samples were from (CDG) patients and from controls. The final results of the three first round samples with respect to CDG are summarised in Table 1 below.

Table 1: Samples in the first-round of the 2024 scheme

Sample	Clinical Information	Sex	Age	Diagnosis
CDG-PP-2024-A	Hepatomegaly, intellectual disability, epilepsy	M	8 years	Normal profile
CDG-PP-2024-B	Strabismus, axial hypotonia, deep venous thrombosis	F	10 years	Type 1 - PMM2-CDG
CDG-PP-2024-C	Nephrotic syndrome, hypertrophic cardiomyopathy, osteoporosis	M	5 years	Transferrin variant

All submitted results are treated as confidential information and are only shared with ERNDIM approved persons for evaluation and reporting purposes.

For the laboratories that reported their method (54/54), Isofocusing was the method employed most often (17/54), followed by HPLC (13/54), CE (13/54), Mass Spectrometry (8/54) and Other (3/54).

Table 2: Scoring of the first-round samples in the 2024 scheme

Sample	No of returns	Technical Aspects (%)	Diagnostic Suggestions (%)	Total (%)
CDG-PP-2024-A	54	97.2	97.2	97.2
CDG-PP-2024-B	54	95.4	89.8	92.6
CDG-PP-2024-C	54	92.6	88.0	90.3

The full anonymised results for all labs that submitted results are given in APPENDIX 1 on page 4 of this report.

3.1. CDG-PP-2024-A: Control sample

Almost all laboratories reported this sample as normal, resulting in a proficiency score of 97.2%.

3.2. CDG-PP-2024-B: Type 1 – PMM2-CDG

All labs reported this sample as abnormal and nearly all centers correctly assigned this profile as type I profile. The profile was rather mild with elevation of disialotransferrin and some participants reported a slight elevation of asialotransferrin as well. The age and clinical presentation could hint in the direction of PMM2-CDG. The advice for further diagnostics should include the option of PMM2-CDG as most frequent CDG-I subtype.

3.3. CDG-PP-2024-C: Transferrin variant

Most labs using IEF or CE reported an abnormal profile of transferrin, either directly suggesting a protein polymorphism or an abnormal type II profile, resulting in a total proficiency score of 90.3%. It is important to note that the polymorphism was only detected by IEF or CE, and not by HPLC, WB, and mass spectrometry. Several laboratories performed neuraminidase incubation to confirm a polymorphism. The presence of a polymorphism is clinically without any complication, but this could complicate the interpretation of the profile type.

4. Questions, Comments and Suggestions

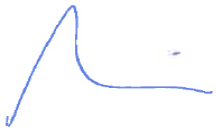
If you have any questions, comments or suggestions in addition to specific user comments please contact the ERNDIM Administration Office (admin@erndim.org).

5. Confidentiality Statement

This interim report is intended for participants of the ERNDIM Congenital Disorders of Glycosylation scheme. The contents of this report or data derived from the use or analysis of ERNDIM EQA materials must not be used in written publications or oral presentations unless the explicit prior consent of ERNDIM has been granted.

Dr Dulce Quelhas

Scientific Advisor



Blai Morales

Deputy Scientific Advisor

APPENDIX 1. **Detailed scores for submitting laboratories**

Sample ID / Average score / Lab ID	Technical				Advice				Total score (Max 12)
	A	B	C	Total	A	B	C	Total	
1	2	2	2	**6**	2	2	2	**6**	**12**
2	2	2	2	**6**	2	2	2	**6**	**12**
3	2	2	2	**6**	2	2	2	**6**	**12**
4	2	2	2	**6**	2	2	2	**6**	**12**
5	2	2	2	**6**	2	2	2	**6**	**12**
6	2	2	2	**6**	2	2	2	**6**	**12**
7	2	2	2	**6**	2	2	2	**6**	**12**
8	2	2	2	**6**	2	2	2	**6**	**12**
9	0	2	1	**3**	0	2	0	**2**	**5**
10	2	2	2	**6**	2	2	2	**6**	**12**
11	2	2	1	**5**	2	1	1	**4**	**9**
12	2	2	2	**6**	2	2	2	**6**	**12**
13	2	2	2	**6**	2	2	2	**6**	**12**
14	2	2	2	**6**	2	2	2	**6**	**12**
15	2	2	2	**6**	2	2	2	**6**	**12**
16	2	2	2	**6**	2	2	2	**6**	**12**
17	2	2	2	**6**	2	2	2	**6**	**12**
18	2	2	2	**6**	2	2	2	**6**	**12**
19	2	2	2	**6**	2	1	1	**4**	**10**
20	2	1	2	**5**	2	1	2	**5**	**10**
21	2	1	2	**5**	2	2	2	**6**	**11**
22	2	1	2	**5**	2	1	1	**4**	**9**
23	2	2	2	**6**	2	2	2	**6**	**12**
24	2	2	1	**5**	2	2	2	**6**	**11**
25	2	2	2	**6**	2	2	2	**6**	**12**
26	2	2	2	**6**	2	1	2	**5**	**11**
27	2	2	2	**6**	2	2	2	**6**	**12**
28	2	2	2	**6**	2	2	2	**6**	**12**
29	2	2	2	**6**	2	1	2	**5**	**11**
30	2	2	2	**6**	2	2	2	**6**	**12**
31	2	1	2	**5**	2	0	2	**4**	**9**
32	2	2	2	**6**	2	2	2	**6**	**12**
33	2	2	2	**6**	2	2	2	**6**	**12**
34	2	2	2	**6**	2	2	2	**6**	**12**
35	2	2	2	**6**	2	2	2	**6**	**12**
36	2	2	2	**6**	2	2	1	**5**	**11**
37	2	2	0	**4**	2	1	0	**3**	**7**
38	2	2	2	**6**	2	2	2	**6**	**12**
39	2	2	0	**4**	2	1	0	**3**	**7**
40									**No results submitted**
41	2	2	2	**6**	2	2	2	**6**	**12**
42	2	2	2	**6**	2	1	1	**4**	**10**

Sample ID / Average score / Lab ID	Technical				Advice				Total score (Max 12)
	A	B	C	Total	A	B	C	Total	
43	2	2	2	**6**	2	2	2	**6**	**12**
44	2	2	2	**6**	2	2	2	**6**	**12**
45	2	2	2	**6**	2	2	2	**6**	**12**
46	2	2	2	**6**	2	2	2	**6**	**12**
47	2	2	2	**6**	2	2	2	**6**	**12**
48	2	1	1	**4**	2	2	0	**4**	**8**
49	2	2	2	**6**	2	2	2	**6**	**12**
50	2	2	2	**6**	2	2	2	**6**	**12**
51	1	2	2	**5**	1	2	2	**5**	**10**
52	2	2	2	**6**	2	2	2	**6**	**12**
53	2	2	2	**6**	2	2	2	**6**	**12**
54	2	2	2	**6**	2	2	2	**6**	**12**
55	2	2	2	**6**	2	2	2	**6**	**12**

APPENDIX 2. Change log (changes since the last version)

Version Number	Published	Amendments
1	27 September 2024	• 2024 First round interim report published

END OF REPORT