Congenital Disorders of Glycosylation (CDG)

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2023 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-2023-A, -B and -C) was 15th May 2023.

55 laboratories registered for the 2023 CDG scheme, of these 53 labs (96.4%) 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. 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

[1] **If this Annual Report is not Version 1 for this scheme year, go to APPENDIX 2 (page 7) for details of the changes made since the last version of this document.**

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 2023 CDG scheme, any critical error will be agreed at the meeting of the Scientific Advisory Board on 30th November and 1st December 2023.

a. Appeals

If your laboratory is classed as having poor performance at the end of the 2023 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 and from a confirmed individual with alcohol abuse. 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 2023 scheme

Sample	Clinical Information	Sex	Age	Diagnosis
CDG-PP-2023-A	Hepatic fibrosis, gamma-glutamyl transferase (GGT)	F	21 years	Alcohol Abuse sample
CDG-PP-2023-B	Polycystic kidney disease, hyperinsulinemic hypoglycemia	M	2 years	Normal sample
CDG-PP-2023-C	Mild intellectual disability, pigmentary retinopathy and slurred speech.	F	17 years	PMM2-CDG

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 (53/53), Isofocusing was the method employed most often (17/53), followed by HPLC (13/53), CE (11/53), Mass Spectrometry (7/53) and Other (5/53).

Table 2: Scoring of the first-round samples in the 2023 scheme

Sample	No of returns	Technical Aspects (%)	Diagnostic Suggestions (%)	Total (%)
CDG-PP-2023-A	53	95.3	88.7	92.0
CDG-PP-2023-B	53	98.1	69.8	84.0
CDG-PP-2023-C	53	98.1	98.1	98.1

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

CDG-PP-2023-A: alcohol abuse

Many laboratories reported this sample as abnormal and indicated a mild type I profile. However, in some cases (due to mild sialic acid loss), a CDG-II and mixed profile was indicated. This sample is from an individual with chronic alcohol use. This is known as a secondary cause for (mild) CDG-I profiles. The clinical indication of an adult patient could also fit very well with an adult case of PMM2-CDG or MPI-CDG, since several case reports have been published with near-normal transferrin glycosylation and abnormal liver enzymes. It is unclear if the clinical condition of the current individual was related to the alcohol abuse or was unrelated. The Total Proficiency score was **92%,** representing a stabilised result compared to the former year's score.

CDG-PP-2023-B: Control

Most laboratories reported this sample as normal, resulting in a Technical proficiency score of **98,1%.** Although, this sample was from a PMM2-CDG patient with Polycystic kidney disease with hyperinsulinaemic hypoglycaemia (HIPKD). It is a recently described disease caused by a single nucleotide variant, c.-167G>T, in the promoter region of *PMM2* (encoding phosphomannomutase 2), either in homozygosity or compound heterozygosity with a pathogenic coding variant in *trans*. A relevant number of participants suggested the correct diagnosis, taking into account the highly suggestive clinical phenotype.

CDG-PP-2023-C: PMM2-CDG

A type 1 profile was identified and interpreted as abnormal by most laboratories, resulting in a proficiency score of **98.1%.** The pattern was a classical type 1 pattern, and no significant differences were noticed when comparing

the performance of different methods. The clinical symptoms are, however, somewhat suggestive of PMM2-CDG. Therefore, in case of interpretation of a profile as type 1, a diagnosis of PMM2-CDG should be advised in this situation.

Identification of the profile as abnormal and indicating PMM2-CDG as a possible diagnosis should be included for total scoring.

4. Questions, Comments and Suggestions

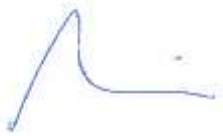
If you have any questions, comments or suggestions in addition to specific user comments please contact the ERNDIM Administration Office (admin@erndim.org).

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

Your laboratory's anonymised lab number in the table below is: 28

Sample ID / Lab ID	Technical				Advice				Total score (Max 12)
	A	B	C		A	B	C		
Average score	1.91	1.96	1.96	Total	1.77	1.40	1.96	Total	
1	2	2	2	**6**	2	2	2	**6**	**12**
2	2	2	2	**6**	1	0	2	**3**	**9**
3	2	2	2	**6**	2	2	2	**6**	**12**
4	2	2	2	**6**	1	0	2	**3**	**9**
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	0	2	**4**	**10**
9	1	2	2	**5**	2	2	2	**6**	**11**
10	2	2	2	**6**	2	0	2	**4**	**10**
11	2	2	2	**6**	2	2	2	**6**	**12**
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**	1	0	2	**3**	**9**
15	2	2	2	**6**	1	2	2	**5**	**11**
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	1	2	**5**	**11**
19	2	2	2	**6**	2	0	0	**2**	**8**
20	2	2	2	**6**	2	2	2	**6**	**12**
21	2	0	2	**4**	1	2	2	**5**	**9**
22	2	2	2	**6**	2	2	2	**6**	**12**
23	2	2	2	**6**	2	**2**	2	**6**	**12**
24	2	2	2	**6**	2	0	2	**4**	**10**
25	2	2	2	**6**	1	2	2	**5**	**11**
26	2	2	2	**6**	1	0	2	**3**	**9**
27	2	2	2	**6**	2	2	2	**6**	**12**
28	2	2	2	**6**	2	0	2	**4**	**10**
29	2	2	2	**6**	1	0	2	**3**	**9**
30	2	2	2	**6**	2	2	2	**6**	**12**
31	2	2	2	**6**	1	2	2	**5**	**11**
32	2	2	2	**6**	2	2	2	**6**	**12**
33									**No results submitted**
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	2	**6**	**12**
37	2	**2**	0	**4**	2	2	2	**6**	**10**
38	2	2	2	**6**	2	2	2	**6**	**12**
39	0	**2**	2	**4**	2	2	2	**6**	**10**
40									**No results submitted**

Sample ID / Average score / Lab ID	Technical				Advice				Total score (Max 12)
	A	B	C		A	B	C		
	1.91	1.96	1.96	Total	1.77	1.40	1.96	Total	
41	2	2	2	**6**	2	2	2	**6**	**12**
42	2	2	2	**6**	2	2	2	**6**	**12**
43	0	2	2	**4**	1	**0**	2	**3**	**7**
44	2	2	2	**6**	2	2	2	**6**	**12**
45	2	2	2	**6**	2	0	2	**4**	**10**
46	2	2	2	**6**	2	2	2	**6**	**12**
47	2	2	2	**6**	2	0	2	**4**	**10**
48	2	2	2	**6**	2	1	2	**5**	**11**
49	2	2	2	**6**	1	2	2	**5**	**11**
50	2	2	2	**6**	2	0	2	**4**	**10**
51	2	2	2	**6**	1	1	2	**4**	**10**
52	2	2	2	**6**	2	1	2	**5**	**11**
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	07 November 2023	• 2023 First round interim report published

END OF REPORT