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# Acylcarnitine DBS scheme

# ACDB-IR -Scheme- Rome-Italy

# Annual Report 2023

prepared by
Cristiano Rizzo

**Note**: This annual report is intended for participants of the ERNDIM ACDB scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

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## 1. Introduction

The ERNDIM Acylcarnitine in dried blood spots scheme offers dried blood spots obtained from confirmed patients with confirmed diagnoses to enable laboratories to gain or maintain experience to identify organoacidopathies and fatty acid β-oxidation defects. The scheme is organised by Dr Cristiano Rizzo (metabolic center Rome) in conjunction with CSCQ, the Swiss organisation for quality assurance in medical laboratories.
As in previous years, samples were sent out to cover the spectrum of what is typically observed in the metabolic laboratory. A mix of clearly diagnostic profiles and some more challenging profiles were provided. As in previous years normal profiles were also sent out. The requirement to interpret a normal profile, as such, is as important as correctly identifying abnormal profiles. Correctly identifying a profile as normal can avoid unnecessary further investigation and distress to the patient and family.

## 2. Geographical distribution of participants

In 2023 47 laboratories from many different countries participated in the ACDB Rome scheme.
There was one educational participant in 2023. Educational participants take part in all aspects of the scheme and receive interim reports with scores, but performance is not indicated on the ERNDIM certificate of performance.

[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.

Participants and new applicants will distributed between the Heidelberg, London and Rome acylcarnitine in dried blood spots schemes which are run separately. The three organising laboratories each participate in the other's scheme by rotation.

| Country | Number of participants |
|---|---|
| Belgium | 6 |
| Bulgaria | 1 |
| Croatia | 1 |
| Czechia | 2 |
| Greece | 1 |
| India | 1 |
| Israel | 3 |
| Lebanon | 1 |
| Lithuania | 2 |
| Malaysia | 3 |
| Morocco | 1 |
| Portugal | 2 |
| Saudi Arabia | 1 |
| Singapore | 1 |
| Slovakia | 1 |
| Slovenia | 1 |
| Spain | 8 |
| Switzerland | 2 |
| Taiwan | 1 |
| Turkey | 1 |
| United Kingdom | 2 |
| United States of America | 5 |

## 3. Design and logistics of the scheme including sample information

As usual, the samples used in 2023 were authentic human blood spot samples, 5 from affected patients and one from a healthy individual.

The scheme has been designed and planned by Cristiano Rizzo as Scientific Advisor and coordinated by CSCQ, the Swiss organisation for quality assurance in medical laboratories, both appointed by and according to procedures laid down by the ERNDIM Board

All samples selected by the Scientific Advisor are prepared from 30-50µl of lithium heparin anticoagulated whole blood on Whatman (Schleicher & Schuell) 903™ paper. All samples are obtained following local ethical and consent guidelines.

In 2023 CSCQ dispatched the ACDB EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports. Existing QLOU, ACDB, 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
Labelled copies of scan/chromatograms can be uploaded on the CSCQ website.

## 4. Schedule of the scheme

Time schedule in the 2023 ERNDIM ACDB Rome scheme.

| | | |
|---|---|---|
| **Scheme Year:** | 2023 | |
| **ACDB Centre:** | Rome | |
| **CSCQ Sample dispatch date:** ***(please give date)*** | 08 February 2023 | |
| | **1st Submission Round** | **2nd Submission Round** |
| **Sample ID's:** | ACDB-IR-2023-**A**<br>ACDB-IR-2023-**B**<br>ACDB-IR-2023-**C** | ACDB-IR-2023-**D**<br>ACDB-IR-2023-**E**<br>ACDB-IR-2023-**F** |
| **Please give dates for:** | | |
| **Analysis start & Website submission availability*:** ***(suggested date of 3 weeks before results submission deadline)*** | 13 March 2023 | 05 June 2023 |
| **Reminder for result submission*:** ***(1 week before deadline)*** | 27 March 2023 | 19 June 2023 |
| **Results submission deadline*:** ***(suggested a Monday at midnight CET)*** | 03 April 2023 | 26 June 2023 |
| **Scientific Advisor to upload previous database (1 week after deadline)** | 11 April 2023 | 04 July 2023 |
| **Availability of results to Scientific Advisor:** ***(2 weeks after submission deadline)*** | 17 April 2023 | 10 July 2023 |

***To be able to continue this scheme we need a steady supply of new patient samples. Several laboratories have donated samples to the ACDB scheme in the past, for which they are gratefully acknowledged. If you have one or more samples available and are willing to donate these to the scheme, please contact us at*** admin@erndim.org.
***Laboratories which donate samples that are used in the scheme are eligible for a 20% discount on their participation in the ACDB scheme in the following year.***

Samples included in the 2023 ERNDIM ACDB Rome scheme.

| Survey | Sample no. | Diagnosis |
|---|---|---|
| Survey 1 | ACDB-IR-2023-A | **Glutaryl-CoA dehydrogenase deficiency (glutaric acidemia type I)** |
| | ACDB-IR-2023-B | **2-Methylbutyryl-CoA Dehydrogenase Deficiency (Short/Branched-Chain Acyl-CoA Dehydrogenase Deficiency)** |
| | ACDB-DH-2023-C | **Carnitine Palmitoyltransferase 1 Deficiency** |
| Survey 2 | ACDB-DH-2023-D | **Multiple Acyl-CoA Dehydrogenase Deficiency (glutaric aciduria type II)** |
| | ACDB-DH-2023-E | **Isobutyryl-CoA Dehydrogenase Deficiency** |
| | ACDB-DH-2023-F | **Normal profile** |

The scheme format was kept identical to those of previous years. Samples were shipped by regular mail. Details regarding stability of samples are provided in the sample package. Interim reports were generated by the evaluation program developed by CSCQ.

**Origin of patients**: All samples have been provided by the scheme organisers.

## 5. Results

Returned results in the 2023 ERNDIM ACDB Rome scheme.

| | **Survey 1** | **Survey 2** |
|---|---|---|
| Receipt of results | 47 | 47 |
| No answer | 3 | 2 |

## 6. Web site reporting

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

- 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.**
- ***Diagnosis***
  - **Don't enter the diagnosis 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

A scoring system was developed in 2012 and approved by the ERNDIM Scientific Advisory Board. Similar to other qualitative (proficiency testing) ERNDIM schemes, the maximum score for a sample is 4 points.
Qualitative results and diagnostic proficiency of the 2023 samples were scored using the criteria given below. These criteria have been set by the Scientific Advisor, approved by the Scientific Advisory Board. The final decision about scoring of the scheme is made in the Scientific Advisory Board (SAB) during the Autumn meeting (November 30th, 2023).
General criteria used to score results

| Item | Description of scoring criteria | Score |
|---|---|---|
| Quantitative results | Correct classification of quantitative results (i.e. normal or increased) according to reference values | 1 |
| | Incorrect classification of quantitative results | 0 |
| Qualitative results | Correct results according to criteria set for the sample | 1 |
| | Incorrect: minimally required results not reported | 0 |
| Diagnostic proficiency | Correct according to criteria set for the sample | 2 |
| | Partially correct | 1 |
| | Unsatisfactory or misleading | 0 |
| | **Maximum total score** | **4** |

Starting with the 2014 schemes the concept of 'critical error' is introduced to the assessment of the qualitative schemes. Labs failing to make a correct diagnosis of a sample considered eligible for this category will be deemed not to have reached a satisfactory performance even if their total points for the year is sufficient according to the requirement set by the SAB. The classification of samples to be judged for critical error was undertaken at the SAB meeting held on November 23th, 2023.

### 7.1 Score for satisfactory performance

At least 17 points from the maximum of 24 (70%).
We are required to define "Participation" for the purpose of the ERNDIM Annual Certificate which covers all ERNDIM schemes. For this acylcarnitine in dried blood spots scheme we have defined "Participation" as requiring two returns during the year. Failure to meet this requirement will result in the certificate of participation showing 'non-submitter' rather than 'satisfactory' or 'unsatisfactory'.

## 8. Results of samples and evaluation of reporting

### 8.1 Sample A

Clinical information: 30-year-old man presented in infancy with macrocephaly and dystonia. Today under treatment.

47 laboratories who were registered with the Rome section of the Scheme. Results were returned by 44 labs (93%).
44/44 (100%) respondents considered glutaryl-CoA dehydrogenase deficiency (glutaric acidemia type I) as the most likely diagnosis.
Suggested follow up test to confirm the diagnosis or guide further investigation were mutation analysis of glutaryl-CoA dehydrogenase (GCDH) gene (n=39), urinary organic acids (n=38), enzyme assay in cultured fibroblast (n=16), plasma carnitine/acylcanitines analysis (n=12), urinary glutarylcarnitine (n=2)
The implementation of appropriate dietary management (carnitine supplementation, lysine restricted diet) was mentioned by 16 respondents. Referral to a metabolic physician was mentioned by 13 respondents.

Glutaric acidemia type 1 (GA1) is an autosomal recessive neurometabolic disorder caused by glutaryl-CoA dehydrogenase (GCDH) deficiency (GDD) due to mutations in the GCDH gene (19p13.2). GCDH is involved in L-lysine, L-hydroxylysine and L-tryptophane catabolic pathways. Normal levels of glutarylcarnitine (C5DC) in DBS or plasma do not rule out GA1.
A positive MS/MS screening result should be confirmed by one or more alternative techniques, including:
1) Urinary organic acids (glutaric acid and 3-hydroxy-glutaric acid) by GC/MS. GA1 is divided into two arbitrarily defined biochemical subtypes: high excreters of urinary glutaric acid (GA) and low excreters. Urinary organic acid analysis suggests GA1 if it reveals 3-OH-glutaric aciduria with or without increased glutaric acid
2)plasma carnitine/acylcarnitine analysis
3) urinary quantification of glutarylcarnitine
4) The diagnosis is confirmed by identification of biallelic pathogenic variants in GCDH gene or, when molecular genetic test results are uncertain, by detection of significantly reduced activity of the enzyme glutaryl-CoA dehydrogenase (GCDH) in cultured fibroblasts or leukocytes.
Treatment includes: dietary management with carnitine supplementation and lysine restricted diet

**Definitive diagnosis: Glutaryl-CoA dehydrogenase deficiency (glutaric acidemia type I)**

### 8.2 Sample B

Clinical information: Patient asymptomatic on a free diet

47 laboratories who were registered with the Rome section of the Scheme. Results were returned by 44 labs (93%). 5 laboratories repoted normal C5-carnitine levels
33/44 (75%) respondents considered 2-Methylbutyryl-CoA Dehydrogenase Deficiency (Short/Branched-Chain Acyl-CoA Dehydrogenase Deficiency; SBCADD) or Isovaleryl-CoA Dehydrogenase Deficiency (Isovaleric acidemia; IVA) as the most likely diagnosis. 10/44 (23%) respondents considered normal the acylcarnitine profile.
22/44 (50%) respondent suggested in addition, the possibility of false positives due to contamination by pivalate-containing drugs or cosmetic products containing neopentanoate
Suggested follow up test to confirm the diagnosis or guide further investigation were mutation analysis of Short/Branched-Chain Acyl-CoA dehydrogenase (ACADSB) or/and Isovaleryl-CoA Dehydrogenase (IVD) genes (n=31), urinary organic acids (n=34), enzyme assay in cultured fibroblast (n=4), plasma carnitine/acylcanitines analysis (n=5).
3 respondents performed a II tier test which provided the chromatographyc separation of the C5 isomers (isovalerylcarnitine, 2-methylbutyrilcarnitine, pivaloylcarnitine, valerylcarnitine) on the blood spot.
The implementation of appropriate dietary management (carnitine supplementation, protein restricted diet) was mentioned by 4 respondents. Referral to a metabolic physician was mentioned by 2 respondents.

2-methylbutyryl-CoA dehydrogenase or short/branched-chain acyl-CoA dehydrogenase (SBCAD) deficiency is an autosomal recessive metabolic disorder of impaired isoleucine degradation. It is most often ascertained via newborn screening and is usually clinically asymptomatic, although some patients have been reported to have delayed development and neurologic signs.
Isovaleric acidemia can present with severe neonatal ketoacidosis leading to death, but can in milder cases present recurrent episodes of ketoacidosis of varying degree occuring later in infancy and childhood.

**Definitive diagnosis: 2-Methylbutyryl-CoA Dehydrogenase Deficiency (Short/Branched-Chain Acyl-CoA Dehydrogenase Deficiency)**

### 8.3 Sample C

Clinical information: Patient presented episodes of hypoglycaemic coma at 3 and 6 months. Currently has episodes of myalgia in the legs. On a diet.

47 laboratories who were registered with the Rome section of the Scheme. Results were returned by 44 labs (93%).
44/44 (100%) respondents reported a Carnitine Palmitoyl Transferase I Deficency. 5 respondents considered as alternative diagnosis supplementation with carnitine, 3 respondents CPT2, 2 respondents COASY Protein-Associated Neurodegeneration (CoPAN), 1 respondent Very long Chain Acyl-CoA dehydrogenase deficiency, 1 respondent Medium Chain Acyl-CoA dehydrogenase deficiency, 1 respondent HMG.
41 respondents suggested these follow up test to confirm the diagnosis: 40 respondents suggested the CPT1A mutation analysis, 21 respondents suggested enzyme assay in cultured fibroblasts, 10 respondents suggested plasma carnitine/acylcanitines analysis, 3 respondents suggested urinary carnitine analysis, 9 respondent suggested organic acid analysis, 3 respondents suggested ammonia, 9 respondents liver enzymes and CPK assay. The implementation of appropriate dietary management to avoiding fasting (carbohydrate rich diet, low fat diet supplement with MCT and essential fatty acids) was mentioned by 10 respondents.
Carnitine palmitoyltransferase 1 (CPT1) deficiency is an autosomal recessive disorder of long-chain fatty acid oxidation, characterised by severe episodes of hypoglycemia usually occuring after fasting or illness. Onset is in infancy or early childhood .
CPT1 deficiency is caused by mutations in the CPT1A gene (11q13), that codes for the liver isoform of the CPT1. During metabolic crises hypoketotic hypoglycemia, elevated levels of plasma carnitine, liver transaminases and mild hyperammonemia can be detected. Diagnosis is suspected from the elevation of free carnitine (C0) with low levels of long-chain acylcarnitine, elevated ratio (C0/C16+C18) is highly specific for the disorder. Molecular analysis of the CPT1A gene and evidence of enzyme deficiency by CPT-1A assay in cultured liver, lymphocytes, and fibroblasts confirm the diagnosis.
Treatment consists mainly of avoiding fasting. Additional measures such as overnight meals with raw cornstarch throughout childhood and/or a low-fat diet supplemented with medium-chain triglycerides that can be metabolized by mitochondria independently of the carnitine cycle may be considered.
Recently, mutations in CoA synthase (COASY) have been identified as a cause of a novel neurodegeneration with brain iron accumulation subtype (COASY Protein-Associated Neurodegeneration, CoPAN) characterized by elevation of free carnitine (C0) with low levels of long-chain acylcarnitine and elevated ratio (C0/C16+C18). CoPAN has to be considered as differential diagnosis with CPT1 deficency
Ref. Christina Evers et al. Am J Med Genet A 2017 Jul;173(7):1878-1886. doi: 10.1002/ajmg.a.38252

**Definitive diagnosis: Carnitine Palmitoyltransferase 1 Deficiency**

## 8.4 Sample D

Clinical information: Patient presented episodes of asthenia, hypotonia, hypertransanimasemia and elevated CPK at 6 months of age. She is currently on carnitine and riboflavin treatment. On a free diet.

47 laboratories were registered in Rome section of the Scheme. Results were turned by 45 labs (96%).
1 laboratory reported no alterations in the acylcarnitine profile
The acylcarnitine pattern with increased medium-chain and long chain acylcarnitines (C6, C8, C10, C12, C14, C14:1, C14:2, C18:1 and C18:2) in combination with the clinical presentation is highly suggestive for MADD.
The suggested alternative diagnoses were: defects in FAD synthase, riboflavin transporters or the mitochondrial flavin adenine dinucleotide transporter (MTF) (13 respondents); Medium chain Acyl-CoA deficiency (8 respondents); Carnitine palmitoyltransferase II (4 respondents); Mitochondrial trifunctional protein deficiency (2 respondents); Carnitine-acylcarnitine translocase deficiency (1 respondent); unspecified mitochondrial disorder (1 respondent); autosomal recessive polycystic kidney disease (1 respondent), Zellweger syndrome (1 respondent), alterations in sterol biosynthesis (1 respondent).
Suggested follow up test to confirm the diagnosis or guide further investigation were mutation analysis of ETFA, ETFB, ETFDH, FLAD1 SLC52A1, SLC52A2 SLC52A3, SLC25A32 genes (n=40), urinary organic acids (n=41), enzyme assay in cultured fibroblast (n=5), plasma acylcarnitines analysis (n=5).
It is important for patients with MADD to strictly avoid fasting to prevent hypoglycemia and crises of metabolic acidosis.
The implementation of appropriate dietary management and therapy (riboflavin, carnitine, coenzyme Q10, glycine supplementation, triheptanoine, protein and fat restricted diet and high carbohydrate, ketogenic diet) was mentioned by 10 respondents. Referral to a metabolic physician was mentioned by 3 respondents.
The significant elevations of medium and long chain acylcarnitines on treatment with riboflavin suggest that there is only partial riboflavin responsiveness or a lack of adherence to the treatment

**Definitive diagnosis: Multiple Acyl-CoA Dehydrogenase Deficiency (glutaric aciduria type II)**

## 8.5 Sample E

Clinical information: Patient presented with headache episodes at 11 years old.

47 laboratories were registered in Rome section of the Scheme. Results were turned by 45 labs (96%).
1 laboratory reported no alterations in the acylcarnitine profile
The acylcarnitine pattern with increased C4-carnitine and the clinical presentation is highly suggestive for SCADD or IBDD.
32/45 (71%) respondents considered Short Chain Acyl-CoA Dehydrogenase Deficiency (SCADD; OMIM 201470) ,11/45 (24%) respondents considered Isobutyryl-CoA Dehydrogenase Deficiency (IBDD; OMIM 611283) 1 respondent considered Urea Cycle disorders, 1 respondent considered Propionic acidemia or Methylmalonic acidemia as the most likely diagnosis.
The suggested alternative diagnoses were: IBD (19 respondents); SCAD(10 respondents); Ethylmalonic encephalopathy(9 respondents); glutaric aciduria type II(3 respondents); formimino glutamic acidemia (FIGLU)(3 respondents); ackee fruit intoxication 2 respondents); unspecified mitochondrial disorder(2 respondent); MSUD (1 respondent).
Suggested follow up test to confirm the diagnosis or guide further investigation were mutation analysis of ACADS, ACAD8, ETHE1 genes (n=37), urinary organic acids (n=40), enzyme assay in cultured fibroblast (n=7), plasma acylcarnitines analysis (n=11), urine acylcarnitines analysis (n=3), plasma aminoacids (n=2).
Referral to a metabolic physician was mentioned by 3 respondents
Short-chain acyl-CoA dehydrogenase deficiency (SCADD) is an inborn error of mitochondrial fatty acid oxidation caused by mutations in ACADS gene. It is characterised by increased butyrylcarnitine in plasma/DBS and ethylmalonic acid (EMA) and butyrylglicine (C4) concentrations in urine.
Isobutyryl-CoA dehydrogenase deficiency (IBDD) is an inborn error of valine metabolism, is caused by mutations in ACAD8 gene. It is characterised by elevated isobutyrylcarnitine (iso-C4) in blood/DBS and isobutyrylglycine in the urine.
Urinary organic acid analysis and resolution between butyrylcarnitine and isobutyrylcarnitine using the second-tier LC-MS/MS method in DBS are required to further establish the diagnosis. The final confirmation is by molecular-genetic testing. The majority of infants with SCADD or IBDD detected by expanded newborn screening remain asymptomatic. There are no generally accepted recommendations for treatment and diet.
Analysis of DBS using the second-tier LC-MS/MS method distinguished C4-carnitines and due to the elevated isobutyrylcarnitine, it is evident that this case is Isobutyryl-CoA Dehydrogenase Deficiency.

**Definitive diagnosis: Isobutyryl-CoA Dehydrogenase Deficiency (IBDD)**

### 8.6 Sample F

Clinical information: patient with a heart conduction disorder.

47 laboratories who were registered with the Rome section of the Scheme. Results were returned by 45 labs (96%).
38/45 (84%) respondents considered a normal acylcarnitine profile, 1 respondent considered primary carnitine deficiency, 2 respondents considered LCHAD/MTP deficiency,1 respondent considered CPT2, 1 respondent considered propionic acidemia, 1 respondent considered MHTFR as the most likely diagnosis
The suggested alternative diagnoses were: CPT2 (4 respondents), SCAD (3 respondents), VLCAD (3 respondents), primary carnitine deficiency (1 respondent), Homocystinuria (1 respondent), vitamin B12 deficency (1 respondent), CblE (1 respondent), CblG (1 respondent).
Suggested follow up test to confirm the diagnosis or guide further investigation were mutation analysis of ACADS, HADHA, ACADS genes (n=4), urinary organic acids (n=7), plasma acylcarnitines analysis (n=4), plasma aminoacids (n=2).

**Definitive diagnosis: Normal acylcarnitine profile**

## 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.

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.

**Detailed scores** – **Round 1**

| Lab n° | Sample A GA1 | | | Sample B 2MBD or SBCADD | | | Sample C CPT1 | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | A | I | Total | A | I | Total | A | 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 | 0 | 0 | 0 | 2 | 2 | 4 | 8 |
| **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 | 0 | 0 | 0 | 1 | 2 | 3 | 7 |
| **9** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| **10** | 2 | 2 | 4 | 2 | 1 | 3 | 2 | 2 | 4 | 11 |
| **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 | 0 | 2 | 2 | 2 | 4 | 10 |
| **15** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| **16** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **17** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **18** | 2 | 1 | 3 | 2 | 2 | 4 | 2 | 2 | 4 | 11 |
| **19** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **20** | 1 | 2 | 3 | 1 | 0 | 1 | 1 | 1 | 2 | 6 |
| **21** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **22** | 2 | 2 | 4 | 2 | 1 | 3 | 2 | 2 | 4 | 11 |
| **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 | 1 | 3 | 2 | 2 | 4 | 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 | 0 | 0 | 0 | 2 | 2 | 4 | 8 |
| **31** | 2 | 2 | 4 | 0 | 1 | 1 | 2 | 2 | 4 | 9 |
| **32** | 2 | 2 | 4 | 2 | 1 | 3 | 2 | 2 | 4 | 11 |
| **33** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **34** | 2 | 2 | 4 | 2 | 0 | 2 | 2 | 2 | 4 | 10 |
| **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 | 1 | 3 | 2 | 1 | 3 | 10 |
| **39** | 2 | 2 | 4 | 0 | 0 | 0 | 2 | 2 | 4 | 8 |
| **40** | 2 | 2 | 4 | 0 | 1 | 1 | 2 | 2 | 4 | 9 |
| **41** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **42** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **43** | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0 |
| **44** | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0 |
| **45** | 2 | 1 | 3 | 2 | 0 | 2 | 2 | 2 | 4 | 9 |
| **46** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **47** | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0 |

**Detailed scores – Round 2**

| Lab n° | Sample D MADD | | | Sample E IBDD | | | Sample F Normal | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | A | I | Total | A | I | Total | A | I | Total | Total |
| **1** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 0 | 2 | 10 |
| **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 | 1 | 2 | 3 | 2 | 2 | 4 | 11 |
| **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** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **10** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **11** | 2 | 1 | 3 | 2 | 2 | 4 | 2 | 2 | 4 | 11 |
| **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 | 0 | 2 | 10 |
| **19** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **20** | 2 | 2 | 4 | 1 | 2 | 3 | 2 | 2 | 4 | 11 |
| **21** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **22** | 2 | 2 | 4 | 2 | 1 | 3 | 2 | 0 | 2 | 9 |
| **23** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **24** | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0 |
| **25** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **26** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **27** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **28** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **29** | 2 | 1 | 3 | 2 | 2 | 4 | 2 | 2 | 4 | 11 |
| **30** | 2 | 1 | 3 | 2 | 2 | 4 | 2 | 2 | 4 | 11 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **31** | 2 | 1 | 3 | 2 | 2 | 4 | 2 | 2 | 4 | 11 |
| **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** | 1 | 2 | 3 | 0 | 0 | 0 | 2 | 0 | 2 | 5 |
| **39** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **40** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 0 | 2 | 10 |
| **41** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 0 | 0 | 8 |
| **42** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **43** | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0 |
| **44** | -- | -- | -- | -- | -- | -- | -- | -- | -- | 0 |
| **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 |

## Total scores

| Lab n° | A | B | C | D | E | F | Cumulative score | Cumulative score ( % ) | Critical error |
|---|---|---|---|---|---|---|---|---|---|
| **1** | 4 | 4 | 4 | 4 | 4 | 2 | 22 | 92 | |
| **2** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **3** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **4** | 4 | 0 | 4 | 4 | 3 | 4 | 19 | 79 | |
| **5** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **6** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **7** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **8** | 4 | 0 | 3 | 4 | 4 | 4 | 19 | 79 | |
| **9** | 4 | 4 | 3 | 4 | 4 | 4 | 23 | 96 | |
| **10** | 4 | 3 | 4 | 4 | 4 | 4 | 23 | 96 | |
| **11** | 4 | 4 | 4 | 3 | 4 | 4 | 23 | 96 | |
| **12** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **13** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **14** | 4 | 2 | 4 | 4 | 4 | 4 | 22 | 92 | |
| **15** | 4 | 4 | 3 | 4 | 4 | 4 | 23 | 96 | |
| **16** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **17** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **18** | 3 | 4 | 4 | 4 | 4 | 2 | 21 | 88 | |
| **19** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **20** | 3 | 1 | 2 | 4 | 3 | 4 | 17 | 71 | |
| **21** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **22** | 4 | 3 | 4 | 4 | 3 | 2 | 20 | 83 | |
| **23** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **24** | 4 | 4 | 4 | -- | -- | -- | 12 | 50 | |
| **25** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **26** | 4 | 3 | 4 | 4 | 4 | 4 | 23 | 96 | |
| **27** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **28** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **29** | 4 | 4 | 4 | 3 | 4 | 4 | 23 | 96 | |
| **30** | 4 | 0 | 4 | 3 | 4 | 4 | 19 | 79 | |
| **31** | 4 | 1 | 4 | 3 | 4 | 4 | 20 | 83 | |
| **32** | 4 | 3 | 4 | 4 | 4 | 4 | 23 | 96 | |
| **33** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **34** | 4 | 2 | 4 | 4 | 4 | 4 | 22 | 92 | |
| **35** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **36** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **37** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **38** | 4 | 3 | 3 | 3 | 0 | 2 | 15 | 62 | |
| **39** | 4 | 0 | 4 | 4 | 4 | 4 | 20 | 83 | |
| **40** | 4 | 1 | 4 | 4 | 4 | 2 | 19 | 79 | |
| **41** | 4 | 4 | 4 | 4 | 4 | 0 | 20 | 83 | |
| **42** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **43** | -- | -- | -- | -- | -- | -- | 0 | 0 | |
| **44** | -- | -- | -- | -- | -- | -- | 0 | 0 | |
| **45** | 3 | 2 | 4 | 4 | 4 | 4 | 21 | 88 | |
| **46** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **47** | -- | -- | -- | 4 | 4 | 4 | 12 | 50 | |

**Performance**

| | **Number of labs** | **% total labs** |
|---|---|---|
| **Satisfactory performers (≥ 70 % of adequate responses)** | 43 | 91 |
| **Unsatisfactory performers (< 70 % adequate responses and/or critical error)** | 2 | 4 |
| **Partial and non-submitters** | 4 | 9 |

**Overall Proficiency**

| **Sample** | **Diagnosis** | **Analytical (%)** | **Interpretation (%)** | **Total (%)** |
|---|---|---|---|---|
| **ACDB-IR-2023-A** | GA1 | 99 | 98 | 98 |
| **ACDB-IR-2023-B** | 2MBD or SBCADD | 85 | 74 | 80 |
| **ACDB-IR-2023-C** | CPT1 | 95 | 98 | 97 |
| **ACDB-IR-2023-D** | MADD | 99 | 95 | 97 |
| **ACDB-IR-2023-E** | IBDD | 95 | 97 | 96 |
| **ACDB-IR-2023-F** | Normal | 98 | 86 | 92 |

## 10. Tentative 2024 schedule

| | |
|---|---|
| Sample distribution | 8th February 2024 |
| Start of analysis of Survey 2024/1 Website open | 13th March 2024 |
| Survey 2024/1 - Results submission | 2rd April 2024 |
| Survey 2024/1 - Reports | April/May 2024 |
| Start of analysis of Survey 2024/2 Website open | 5th June 2024 |
| Survey 2024/2 – Results submission | 19th June 2024 |
| Survey 2024/2 - Reports | July/August 2024 |
| Annual Report 2024 | January 2025 |

## 11. 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 ACDB scheme this certificate will indicate if results were submitted and whether satisfactory performance was achieved in the scheme.

## 12. Questions, Comments and Suggestions

If you have any questions, comments or suggestions please address to the Scientific Advisor of the scheme, Dr. Cristiano Rizzo (cristiano.rizzo@opbg.net) and/or to the ERNDIM Administration Office (admin@erndim.org)

Date of report, 2024-02-28
Name and signature of Scientific Advisor

Dr. Cristiano Rizzo
Scientific Advisor

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

| Version Number | Published | Amendments |
|---|---|---|
| 1 | 29 February 2024 | 2023 annual report published |
| 2 | 18 March 2024 | Removed duplicated section 10, and updated text regarding the activities of subcontractors in section 3 |
| | | |

**END**