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Acylcarnitine DBS scheme

ACDB-IR -Scheme- Rome-Italy

Annual Report 2022

prepared by
Cristiano Rizzo

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, a subcontractor of ERNDIM.
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 2022 49 laboratories from many different countries participated in the ACDB Rome scheme.
There was one educational participant in 2022 (one in 2021). 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.
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.

[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.

Country	Number of participants	Country	Number of participants
Belgium	6	Portugal	2
Bulgaria	1	Saudi Arabia	1
Croatia	1	Singapore	1
Czechia	2	Slovakia	1
Germany	1	Slovenia	1
Greece	1	Spain	9
Israel	3	Switzerland	2
Lebanon	1	Taiwan	1
Lithuania	2	Turkey	2
Malaysia	3	United Kingdom	1
Morocco	1	United States of America	6

3. Design and logistics of the scheme including sample information

As usual, the samples used in 2022 were authentic human blood spot samples, 5 from affected patients and one from a healthy individual.
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 2022 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 2022 ERNDIM ACDB Rome scheme.

Scheme Year:	2022	
ACDB Centre:	Rome	
CSCQ Sample dispatch date: ***(please give date)***	02 February 2022	
	1st Submission Round	**2nd Submission Round**
Sample ID's:	ACDB-IR-2022-**A** ACDB-IR-2022-**B** ACDB-IR-2022-**C**	ACDB-IR-2022-**D** ACDB-IR-2022-**E** ACDB-IR-2022-**F**
Please give dates for:		
Analysis start & Website submission availability*: ***(suggested date of 3 weeks before results submission deadline)***	14 March 2022	06 June 2022
Reminder for result submission*: ***(1 week before deadline)***	28 March 2022	21 June 2022
Results submission deadline*: ***(suggested a Monday at midnight CET)***	04 April 2022	28 June 2022
Scientific Advisor to upload previous database (1 week after deadline)	11 April 2022	05 July 2022
Availability of results to Scientific Advisor: ***(2 weeks after submission deadline)***	19 April 2022	13 July 2022

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 2022 ERNDIM ACDB Rome scheme.

Survey	Sample no.	Diagnosis
Survey 1	ACDB-IR-2022-A	**3-hydroxy-3-methylglutaryl-CoA lyase deficiency**
	ACDB-IR-2022-B	**Ethylmalonic encephalopathy (ETHE1)**
	ACDB-DH-2022-C	**Very long Chain Acyl-CoA Dehydrogenase deficiency**
Survey 2	ACDB-DH-2022-D	**Combined methylmalonic aciduria and homocystinuria type cblC**
	ACDB-DH-2022-E	**Normal profile**
	ACDB-DH-2022-F	MCAD

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 urine samples have been provided by the scheme organizers

5. Results

Returned results in the 2022 ERNDIM ACDB Rome scheme.

	Survey 1	**Survey 2**
Receipt of results	47	41
No answer	3	6

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 2022 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 23th, 2022).
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 19th, 2020.

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 reportin

8.1. Patient A

Clinical information: Patient admitted for vomiting, diarrhea, hypoglycemia and metabolic acidosis. In treatment with carnitine

34/47 (72%) respondents considered 3-hydroxy-3methylglutaryl-CoA lyase deficiency, 11 respondents considered 3-methyl-Crotonyl-CoA carboxylase deficiency, 1 respondents suggested multiple carboxylase deficiency , 1 respondents suggested 3-methylglutaconic acidemia as the most likely diagnosis

The alternative differential diagnosis suggested by respondents included:
3-hydroxy-3methylglutaryl-CoA lyase deficiency (HMGCLD) (n=15)
Beta-Ketothiolase deficiency (n= 20)
2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency (2M3HBA) (n=18)
3-methylglutaconic aciduria (3MGA) (n=20)
Biotinidase deficiency (n= 13)
Multiple carboxylase deficiency (MCD) (n=26)
3-methylcrotonyl-CoA carboxylase 2 deficiency (MCC2D) (n=16)
3-hydroxyisobutyric aciduria (HIBADH) (n=2)
Mitochondrial DNA depletion syndrome 9 (ENCEPHALOMYOPATHIC TYPE WITH METHYLMALONIC ACIDURIA); MTDPS9; (n=1)
Succinate-CoA Ligase, Alpha subunit (SUCGL1) (n=2)
Neurodegeneration infantile-onset, Biotin-responsive (NERIB) 1
Treatment with valproic acid (N=2)

Suggested follow up test to confirm the diagnosis or guide further investigation were: organic acid analysis on urine (n=46), genetic analysis of the different genes (36 respondents suggest molecular study to look for mutation in the HMGCL gene) linked to C5OH–carnitine elevation, plasma carnitine/acylcanitines analysis (n=9), biotinidase assay (n=5), 3-hydroxy-3methylglutaryl-CoA-lyase enzymatic activity in fibroblasts

The implementation of appropriate dietary management was mentioned by 4 respondents. Referral to a metabolic physician was mentioned by 5 respondents.

Definitive diagnosis: 3-hydroxy-3-methylglutaryl-CoA lyase deficiency

8.2. Patient B

Clinical information: Patient admitted for encephalopathy, acrocyanosis and petechiae

Ethylmalonic encephalopathy (EE) is an autosomal recessive severe metabolic disorder of infancy affecting the brain, gastrointestinal tract and peripheral vessels. EE is caused by mutations in the ETHE1 gene, which encodes a mitochondrial sulphur dioxygenase involved in the catabolism of hydrogen sulphide. The diagnosis of EE is suggested by clinical findings and laboratory findings of increased blood lactate levels, plasma thiosulphate, C4-C6 carnitines in blood and increased excretion of ethylmalonic acid (EMA) in urine, where also methylsuccinic acid and C4-C6-acylglycines may be found.
Increased C4 and C5 together would indicate ethylmalonic encephalopathy

22/47 (47%) respondents considered Ethylmalonic encephalopathy (EE),15 respondents suggested short-chain-acyl-CoA dehydrogenase deficiency (SCADD), 4 respondents suggested Multiple dehydrogenase deficiency (MADD-Glutaric acidemia type 2), 4 respondents suggested Isobutyryl-Dehydrogenase deficiency (IBDD) deficiency as the most likely diagnosis.

The alternative differential diagnosis suggested by respondents included:
a) Multiple dehydrogenase deficiency (Glutaric academia type 2) (n=18)
b) Short-Chain Acyl-CoA dehydrogenase deficiency (SCAD) (n=12)
c) Isovaleryl-CoA dehydrogenase deficiency (n=3)
d) Isobutyryl-CoA dehydrogenase deficiency (n=23)
e) 2-Methylbutyryl-CoA dehydrogenase (n=1)
f) Ethylmalonic encephalopathy (EE) (n=10)
g) riboflavin transporters deficency (n=3)
h) pivalic contamination (n=2)
i) Formiminoglutamic aciduria (FIGLU) (n=3)

Suggested follow up test to confirm the diagnosis or guide further investigation were: mutation analysis of of ETHE1 gene (n=25), ACADS gene (n=14), ETFA/ETFB/ETFDH genes (n=8), ACAD8 gene (n=8), genetic analysis not specified (n=8), urinary organic acids (n=32), plasma and urine thiosulphate (n=5), plasma carnitine/acylcanitines analysis (n=7), lactate (n=4).

Definitive diagnosis: Ethylmalonic encephalopathy (ETHE1)

8.1. Patient C

Clinical information: Patient admitted for nonketotic hypoglycemia hepatomegaly, rhabdomyolysis with exercise. In treatment

46/47 (98%) respondents considered Very long Chain Acyl-CoA Dehydrogenase deficiency (VLCADD),1 respondent suggested normal profile deficiency as the most likely diagnosis

The alternative differential diagnosis suggested by respondents included:

a) Carnitine-acylcarnitine translocase (CACT) deficiency (n=3),
b) Carnitine Palmitoyl transferase type 2 (CPT2) deficiency (n=3)
c) Mitochondrial trifunctional protein (MTP) deficiency/long-chain 3-Hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency/long-chain 3-Ketoacyl-CoA Thiolase (LCKAT) deficiency (n=2)

Suggested follow up test to confirm the diagnosis or guide further investigation were: mutation analysis of ACADVL gene (n=39), urinary organic acids (n=23), VLCAD activity in fibroblasts and lymphocytes (n=13), plasma carnitine/acylcanitines analysis (n=15)

Definitive diagnosis: Very long Chain Acyl-CoA Dehydrogenase deficiency (VLCADD)

8.1. Patient D

Clinical information: Patient admitted for low vision with maculopathy and hypovitaminosis D
49 partecipants. 5 participants did not provide a response
43/44 (98%) respondents considered a disorders of intracellular cobalamin metabolism, 1 respondent suggested multiple carboxylase deficency as the most likely diagnosis.

Suggested follow up test to confirm the diagnosis or guide further investigation were: genetic analyses of genes related to elevation of C3-carnitine (panel including MMACHC gene and other genes involved in the absorption, transport and intracellular metabolism of cobalamins and propionic pathway disorders) (n=31), urinary organic acids (n=38), plasma total Hcys (n=35), serum Vit. B12 (n=27), plasma aminoacids (n=15), plasma methylmalonate (n=12), cblC complementation studies in fibroblasts (n=7), plasma carnitine/acylcanitines analysis (n=6), plasma SAM and SAH (n=2), plasma S-adenosylcobalamin (n=1)

Definitive diagnosis: Combined methylmalonic aciduria and homocystinuria type cbl

8.1. Patient E

Clinical information: Patient admitted for autistic feature
49 partecipants. 5 participants did not provide a response

34/44 (77%) respondents considered a normal profile, 6 respondents suggested primary carnitine deficiency, 2 respondents suggested CPT2 deficiency, 2 respondents suggested trimethyllysine hydroxylase deficiency (TMLHE) as the most likely diagnosis

Definitive diagnosis: Normal profile

8.1. Patient F

Clinical information: no symptoms, good weight gain

49 partecipants. 5 participants did not provide a response
44/44 (100%) respondents considered Medium chain Acyl-CoA dehydrogenase deficiency as the most likely diagnosis
Suggested follow up test to confirm the diagnosis or guide further investigation were: ACADM mutation analysis (n=38), urinary organic acids (n=33), plasma carnitine/acylcanitines analysis (n=15), MCAD enzyme assay in leucocytes (n=10)
10 respondents suggest as treatment: carnitine supplementation, high carbohydrates low fat diet, avoidance of fasting.

Definitive diagnosis: Medium chain Acyl-CoA dehydrogenase deficiency

9. Scores of participants

All data transfer, the submission of data as well as the request and viewing of reports proceed via the QLOU-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 HMGCLD			Patient B (EE); ETHE1			Patient C VLCADD			
	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	2	2	4	2	2	4	12
5	2	2	4	1	2	3	2	2	4	11
6	1	2	3	2	2	4	2	2	4	11
7	2	2	4	1	2	3	2	2	4	11
8	2	2	4	2	2	4	2	2	4	12
9	2	2	4	1	2	3	2	2	4	11
10	2	2	4	2	2	4	2	2	4	12
11	1	2	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	1	2	3	2	2	4	11
16	2	2	4	2	1	3	2	2	4	11
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	1	2	3	11
21	2	2	4	1	2	3	2	2	4	11
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
27	2	2	4	2	2	4	2	2	4	12

28	2	2	4	1	2	3	2	2	4	11
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	2	2	4	12
32	2	2	4	1	0	1	2	2	4	9
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	1	2	3	2	2	4	11
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	1	2	3	2	2	4	11
39	2	2	4	2	0	2	2	2	4	10
40	2	2	4	2	2	4	2	2	4	12
41	2	2	4	2	2	4	2	2	4	12
42	--	--	--	--	--	--	--	--	--	0
43	2	2	4	1	2	3	2	2	4	11
44	2	2	4	2	2	4	2	2	4	12
45	2	2	4	2	2	4	2	2	4	12
46	--	--	--	--	--	--	--	--	--	0
47	2	2	4	1	2	3	0	0	0	7
48	2	2	4	2	1	3	2	2	4	11
49	2	1	3	2	2	4	2	2	4	11

Detailed scores – Round 2

Lab n°	Patient D cblC			Patient E Normal			Patient F MCAD			
	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	2	2	4	2	2	4	12
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	2	0	2	2	2	4	10
7	--	--	--	--	--	--	--	--	--	0
8	2	2	4	2	2	4	2	2	4	12
9	2	2	4	2	0	2	2	2	4	10
10	2	2	4	2	2	4	2	2	4	12
11	--	--	--	--	--	--	--	--	--	0
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	0	2	2	2	4	10
17	2	1	3	2	2	4	2	2	4	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	1	2	3	11
21	2	2	4	2	2	4	2	2	4	12
22	2	2	4	2	0	2	2	2	4	10
23	2	2	4	2	0	2	2	2	4	10
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
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	0	2	2	2	4	10
30	1	2	3	2	0	2	2	2	4	9

31	--	--	--	--	--	--	--	--	--	0
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	0	2	2	2	4	10
38	2	2	4	2	0	2	2	2	4	10
39	2	2	4	2	2	4	2	2	4	12
40	2	2	4	2	0	2	2	2	4	10
41	2	2	4	2	2	4	2	2	4	12
42	--	--	--	--	--	--	--	--	--	0
43	2	2	4	2	2	4	2	2	4	12
44	2	2	4	2	2	4	2	2	4	12
45	2	2	4	2	2	4	2	2	4	12
46	--	--	--	--	--	--	--	--	--	0
47	2	2	4	2	0	2	2	2	4	10
48	2	2	4	2	2	4	2	2	4	12
49	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	4	24	100	
2	4	4	4	4	4	4	24	100	
3	4	4	4	4	4	4	24	100	
4	4	4	4	4	4	4	24	100	
5	4	3	4	4	4	4	23	96	
6	3	4	4	4	2	4	21	88	
7	4	3	4	--	--	--	11	46	
8	4	4	4	4	4	4	24	100	
9	4	3	4	4	2	4	21	88	
10	4	4	4	4	4	4	24	100	
11	3	4	4	--	--	--	11	46	
12	4	4	4	4	4	4	24	100	
13	4	4	4	4	4	4	24	100	
14	4	4	4	4	4	4	24	100	
15	4	3	4	4	4	4	23	96	
16	4	3	4	4	2	4	21	88	
17	4	4	4	3	4	4	23	96	
18	4	4	4	4	4	4	24	100	
19	4	4	4	4	4	4	24	100	
20	4	4	3	4	4	3	22	92	
21	4	3	4	4	4	4	23	96	
22	4	4	4	4	2	4	22	92	
23	4	4	4	4	2	4	22	92	
24	4	4	4	4	4	4	24	100	
25	4	4	4	4	4	4	24	100	
26	4	4	4	4	4	4	24	100	
27	4	4	4	4	4	4	24	100	
28	4	3	4	4	4	4	23	96	
29	4	4	4	4	2	4	22	92	
30	4	4	4	3	2	4	21	88	
31	4	4	4	--	--	--	12	50	
32	4	1	4	4	4	4	21	88	CE
33	4	4	4	4	4	4	24	100	

34	4	4	4	4	4	4	24	100	
35	4	3	4	4	4	4	23	96	
36	4	4	4	4	4	4	24	100	
37	4	4	4	4	2	4	22	92	
38	4	3	4	4	2	4	21	88	
39	4	2	4	4	4	4	22	92	CE
40	4	4	4	4	2	4	22	92	
41	4	4	4	4	4	4	24	100	
42	--	--	--	--	--	--	0	0	
43	4	3	4	4	4	4	23	96	
44	4	4	4	4	4	4	24	100	
45	4	4	4	4	4	4	24	100	
46	--	--	--	--	--	--	0	0	
47	4	3	0	4	2	4	17	71	CE
48	4	3	4	4	4	4	23	96	
49	3	4	4	4	4	4	23	96	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 60 % of adequate responses)	41	84
Unsatisfactory performers (< 60 % adequate responses and/or critical error)	6	12
Partial and non-submitters	5	10

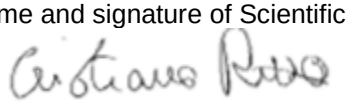
Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total(%)
ACDB-IR-2022-A	HMGCLD	98	99	98
ACDB-IR-2022-B	(EE); ETHE1	88	94	91
ACDB-IR-2022-C	VLCADD	97	98	97
ACDB-IR-2022-D	cblC	99	99	99
ACDB-IR-2022-E	Normal	100	75	88
ACDB-IR-2022-F	MCAD	99	100	99

10. 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.

Date of report, 2023-05-31
Name and signature of Scientific Advisor



Dr. Cristiano Rizzo
Scientific Advisor

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

Version Number	Published	Amendments
1	14 July 2023	2022 annual report published

END