SLEIMPN

Programa de control externo de calidad ERNDIM; esquemas cualitativos

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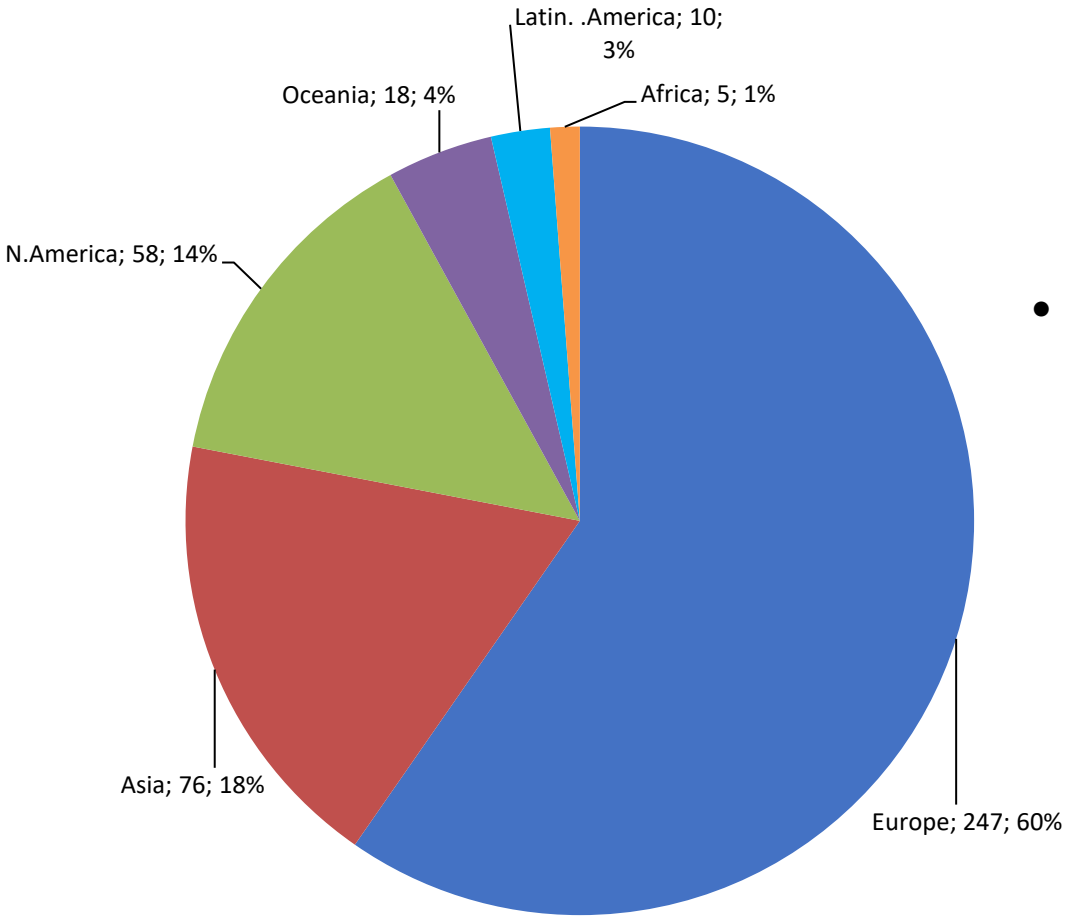
Abril 26, 2023

Participantes



www.erndim.org

2022 (n = 414)
(4.3% ↑ 2017)

- Países = 62

EQA: esquemas

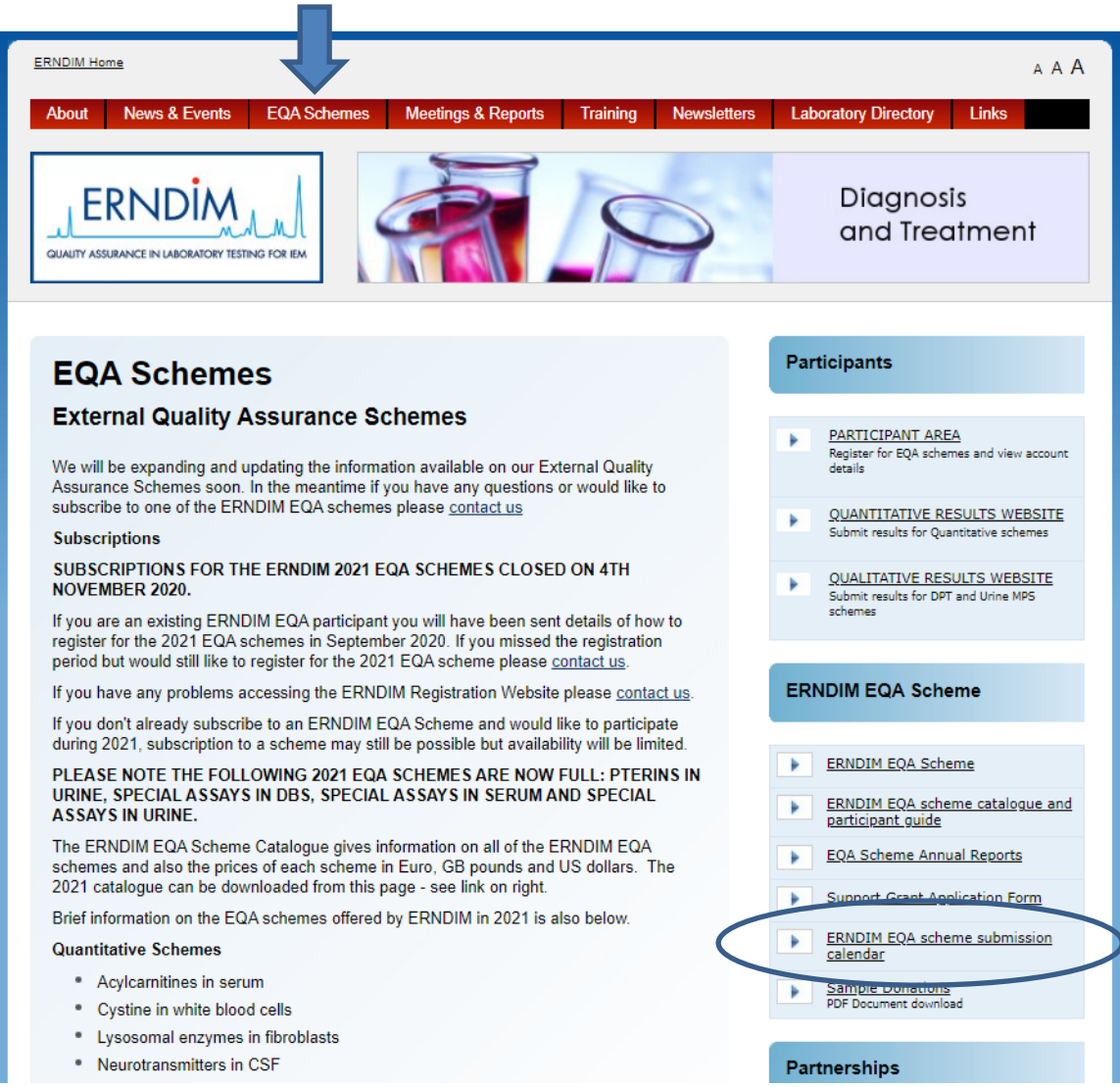
Cuantitativos
Amino acids (serum)
Acylcarnitines (serum)
Organic acids (urine)
Purines-Pyrimidines (urine)
Special assays serum
Special assays urine
Special assays DBS

Cualitativos
Diagnostic Proficiency Testing (urine)
Organic acids (urine)
Acycarnitines (DBS)
Mucopolysaccharides (urine)
CDG (serum)

Híbridos	Interpretación/puntuación
Lysosomal enzymes (Fib)	Yes
Cystine (WBC)	Yes
Pterins (urine)	Yes
Neurotransmitters (CSF)	Yes

Aminoácidos: esquema interpretativo

EQA Web


ERNDIM Home
A A A
About
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ERNDIM
QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM
Diagnosis and Treatment
EQA Schemes
External Quality Assurance Schemes
We will be expanding and updating the information available on our External Quality Assurance Schemes soon. In the meantime if you have any questions or would like to subscribe to one of the ERNDIM EQA schemes please contact us
Subscriptions
SUBSCRIPTIONS FOR THE ERNDIM 2021 EQA SCHEMES CLOSED ON 4TH NOVEMBER 2020.
If you are an existing ERNDIM EQA participant you will have been sent details of how to register for the 2021 EQA schemes in September 2020. If you missed the registration period but would still like to register for the 2021 EQA scheme please contact us.
If you have any problems accessing the ERNDIM Registration Website please contact us.
If you don't already subscribe to an ERNDIM EQA Scheme and would like to participate during 2021, subscription to a scheme may still be possible but availability will be limited.
PLEASE NOTE THE FOLLOWING 2021 EQA SCHEMES ARE NOW FULL: PTERINS IN URINE, SPECIAL ASSAYS IN DBS, SPECIAL ASSAYS IN SERUM AND SPECIAL ASSAYS IN URINE.
The ERNDIM EQA Scheme Catalogue gives information on all of the ERNDIM EQA schemes and also the prices of each scheme in Euro, GB pounds and US dollars. The 2021 catalogue can be downloaded from this page - see link on right.
Brief information on the EQA schemes offered by ERNDIM in 2021 is also below.
Quantitative Schemes
Acylcarnitines in serum
Cystine in white blood cells
Lysosomal enzymes in fibroblasts
Neurotransmitters in CSF
Participants
PARTICIPANT AREA
Register for EQA schemes and view account details
QUANTITATIVE RESULTS WEBSITE
Submit results for Quantitative schemes
QUALITATIVE RESULTS WEBSITE
Submit results for DPT and Urine MPS schemes
ERNDIM EQA Scheme
ERNDIM EQA Scheme
ERNDIM EQA scheme catalogue and participant guide
EQA Scheme Annual Reports
Support Grant Application Form
ERNDIM EQA scheme submission calendar
Sample Donations
PDF Document download
Partnerships

Reuniones científicas

- Meeting Oct 2021. Organising committee: Cristiano Rizzo, Carlo Dionisi-Vici, CVS, Nenad Blau, GR, with JBa representing the AO. Online meeting with pre-recorded presentations (Total of 472 registrations)

Continent	Symposium attendees	2021 EQA participants (number of labs
Europe	273 (65%)	239 (59%)
Asia	71 (17%)	73 (18%)
North America	26 (6%)	57 (14%)
Oceania	20 (5%)	19 (5%)
South America	17 (4%)	10 (2%)
Africa	16 (4%)	6 (2%)

Next virtual meeting → November 2023

ERNDIM - SSIEM Academy

Otras actividades

Control interno de calidad

- Amino acids
- Organic acids
- Purines/pyrimidines
- Acylcarnitines
- SAS and SAU
- Homocysteine,
- Pterins
- Neurotransmitters

produced separate from EQA materials

Paneles educacionales

- Oligosaccharide kit

All supplied by MCA laboratory

Nuevos esquemas EQA

Nuevas ideas → programas piloto

1. Lipids/sterols in serum: 4th special assays scheme

Currently in SAS: C22, C24, C26, phytanic acid, pristanic acid, 7-Dehydrocholesterol, 7-Ketocholesterol, Cholestane-3b,5a,6b-triol, Cholestanol, Glucosylsphingosine, Lyso Gb3, Lysosphingomyelin, coenzyme Q10..

2. Metabolomics in plasma/serum Qualitative scheme?

3. Lysosomal enzymes in DBS Depends on sample availability

4. Qualitative bile acids?

5. Individual metabolites

Encuesta anual para valorar nuevas ideas

ESQUEMAS cualitativos

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

Funciones asesor científico:

1. Scheme information
2. Recolección de muestras: 6 muestras de orina de pacientes anuales
3. Resultados en WebSite
4. Evaluación de cada laboratorio, con la ayuda del software CSCQ
5. Reports (2 intermedioas y 1 anual), con la ayuda del software CSCQ
6. Enviar cartas a laboratorios, por bajo rendimiento, errores críticos, a laboratorios que envían datos parciales o no envían resultados, con ayuda de aplicativo con la oficina del ERNDIM; segundo revisor
7. Participar en las reuniones anuales con los otros asesores científicos para discutir los resultados del esquema

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

1. Scheme information

Table 1: Scheme Information

Scheme Year:	2023	
QLOU Centre:	Barcelona	
CSCQ Sample dispatch date: *(please give date)*	08 February 2023	
	1st Submission Round	**2nd Submission Round**
Sample ID's:	QLOU-EB-2023-**A** QLOU-EB-2023-**B** QLOU-EB-2023-C	QLOU-EB-2023-**D** QLOU-EB-2023-**E** QLOU-EB-2023-**F**
Please give dates for:		
Analysis start & Website submission availability*: *(suggested date of 3 weeks before results submission deadline)*	09 May 2023	29 August 2023
Reminder for result submission*: *(1 week before deadline)*	23 May 2023	12 September 2023
Results submission deadline*: *(suggested a Monday at midnight CET)*	30 May 2023	19 September 2023
Scientific Advisor to upload previous database *(1 week after deadline)*	07 June 2023	27 September 2023
Availability of results to Scientific Advisor: *(2 weeks after submission deadline)*	13 June 2023	03 October 2023

Table 2: Sample Information **

Sample ID	Clinical Information	Sex	Patient Age
QLOU-EB-2023-**A**	Patient under treatment, currently well and diagnosed by newborn screening.	M	13 years
QLOU-EB-2023-**B**	Autistic features. Actually pregnant	F	34 years
QLOU-EB-2023-C	Urine sample collected at 21 years old under treatment. Since the age of 2,5 years the patient began to experience recurrent episodes oh headache, hypotonia, vomiting, axial ataxia and vegetative symptoms.	M	21 years
QLOU-EB-2023-**D**	Female diagnosed at 8 months of age when she had a severe viral infection, diarrhoea, vomiting, metabolic acidosis and hypoglycemia. At present she is under treatment.	F	22 years
QLOU-EB-2023-**E**	Female that at 4 years of age presented with development delay, mild mental retardation, tremor and ataxia. Diagnosed at 43 years of age.	F	53 years
QLOU-EB-2023-**F**	Male with developmental delay, hiperamonemia episodes. Currently under treatment and MRI and physical examination were normal.	M	28 yeras

Table 3: Sample preparation for ERNDIM survey

Bulk ID	Sample ID	Total volume (ml)	Volume of each individual sample (ml)	Number of samples to be prepared *
	QLOU-EB-2023-**A**	Sending by Camilla	2	86
	QLOU-EB-2023-**B**	250	2	86
	QLOU-EB-2023-C	210	2	86
	QLOU-EB-2023-**D**	300	2	86
	QLOU-EB-2023-**E**	250	2	86
	QLOU-EB-2023-**F**	210	2	86

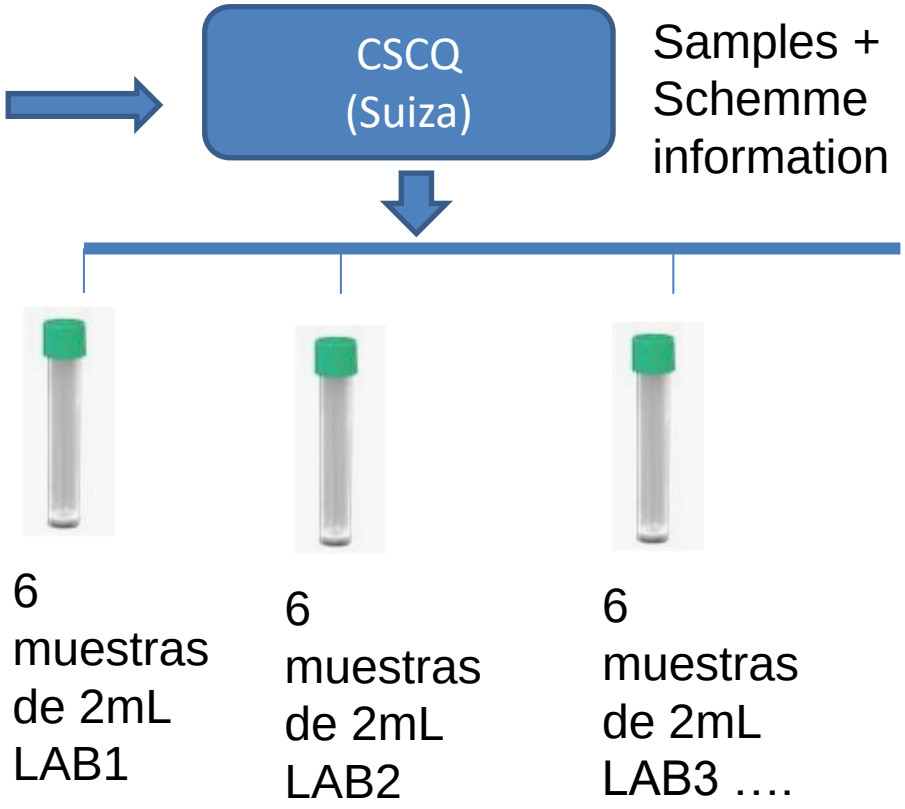
*No. of participants per QLOU centre (80) plus 4 spare sets & max of 2 sets for the scheme organiser (see table 4).

Please note: the number of spare samples for the 2023 common sample should be 3 x 4 = 12 sets

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

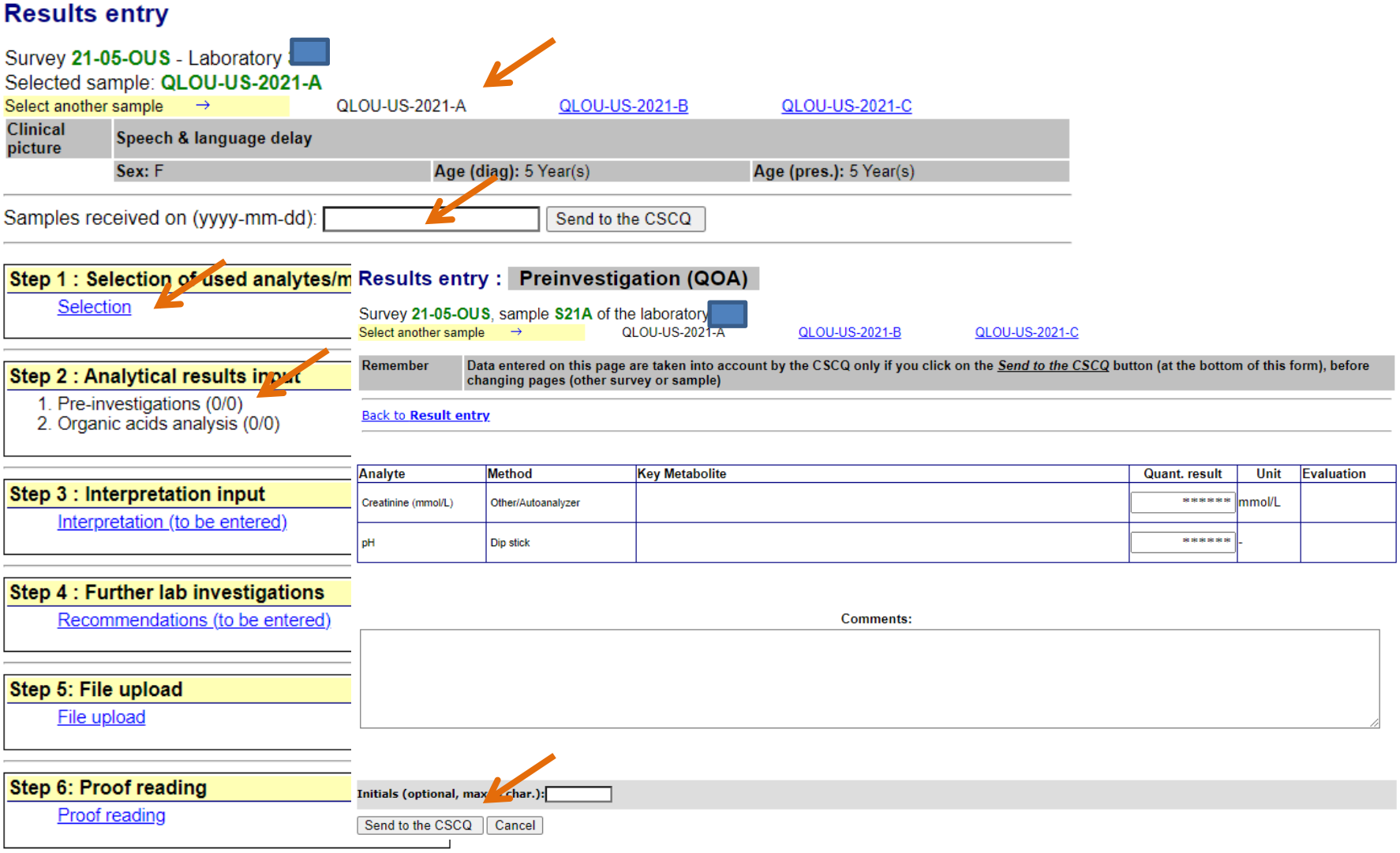
2. Recolección de las muestras

Para 75 laboratorios
2mL min/laboratorio
Total : 200 mL X 6 individuos:
-5/6 muestras patológicas (intercalar entidades conocidas y nuevas)
-1/0 controles



QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

3. Results in the website https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.ph



Results entry

Survey 21-05-OUS - Laboratory

Selected sample: QLOU-US-2021-A

Select another sample → QLOU-US-2021-A QLOU-US-2021-B QLOU-US-2021-C

Clinical picture	Speech & language delay		
	Sex: F	Age (diag): 5 Year(s)	Age (pres.): 5 Year(s)

Samples received on (yyyy-mm-dd): Send to the CSCQ

Step 1 : Selection of used analytes/m
Selection

Step 2 : Analytical results input
1. Pre-investigations (0/0)
2. Organic acids analysis (0/0)

Step 3 : Interpretation input
Interpretation (to be entered)

Step 4 : Further lab investigations
Recommendations (to be entered)

Step 5: File upload
File upload

Step 6: Proof reading
Proof reading

Results entry : Preinvestigation (QOA)

Survey 21-05-OUS, sample S21A of the laboratory

Select another sample → QLOU-US-2021-A QLOU-US-2021-B QLOU-US-2021-C

Remember: Data entered on this page are taken into account by the CSCQ only if you click on the *Send to the CSCQ* button (at the bottom of this form), before changing pages (other survey or sample)

Back to Result entry

Analyte	Method	Key Metabolite	Quant. result	Unit	Evaluation
Creatinine (mmol/L)	Other/Autoanalyzer		*******	mmol/L	
pH	Dip stick		*******	-	

Comments:

Initials (optional, max char.):

Send to the CSCQ Cancel

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

3. Results in the website https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.ph

Results entry

Survey **21-05-OUS** - Laboratory [redacted]
Selected sample: **QLOU-US-2021-A**
Select another sample → QLC

Clinical picture	Speech & language delay
	Sex: F

Samples received on (yyyy-mm-dd):

Step 1 : Selection of used analytes/me
Selection

Step 2 : Analytical results input
1. Pre-investigations (0/0)
2. Organic acids analysis (0/0)

Step 3 : Interpretation input
Interpretation (to be entered)

Step 4 : Further lab investigations
Recommendations (to be entered)

Step 5: File upload
File upload

Step 6: Proof reading
Proof reading

changing pages (other survey or sample)

Back to **Result entry**

Analyte	Method	Key Metabolite	Quant. result	Unit	Evaluation
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Normal profile	******	mmol/mol creat	Normal
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	3-hydroxypropionate	100	mmol/mol creat	Elevated
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	methylcitric acid	2	mmol/mol creat	Normal
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered
Organic acids column chromatography	Method 1/GC-MS ; Ethylacetate ; No ; Silylation	Please specify key metabolite	******	mmol/mol creat	To be entered

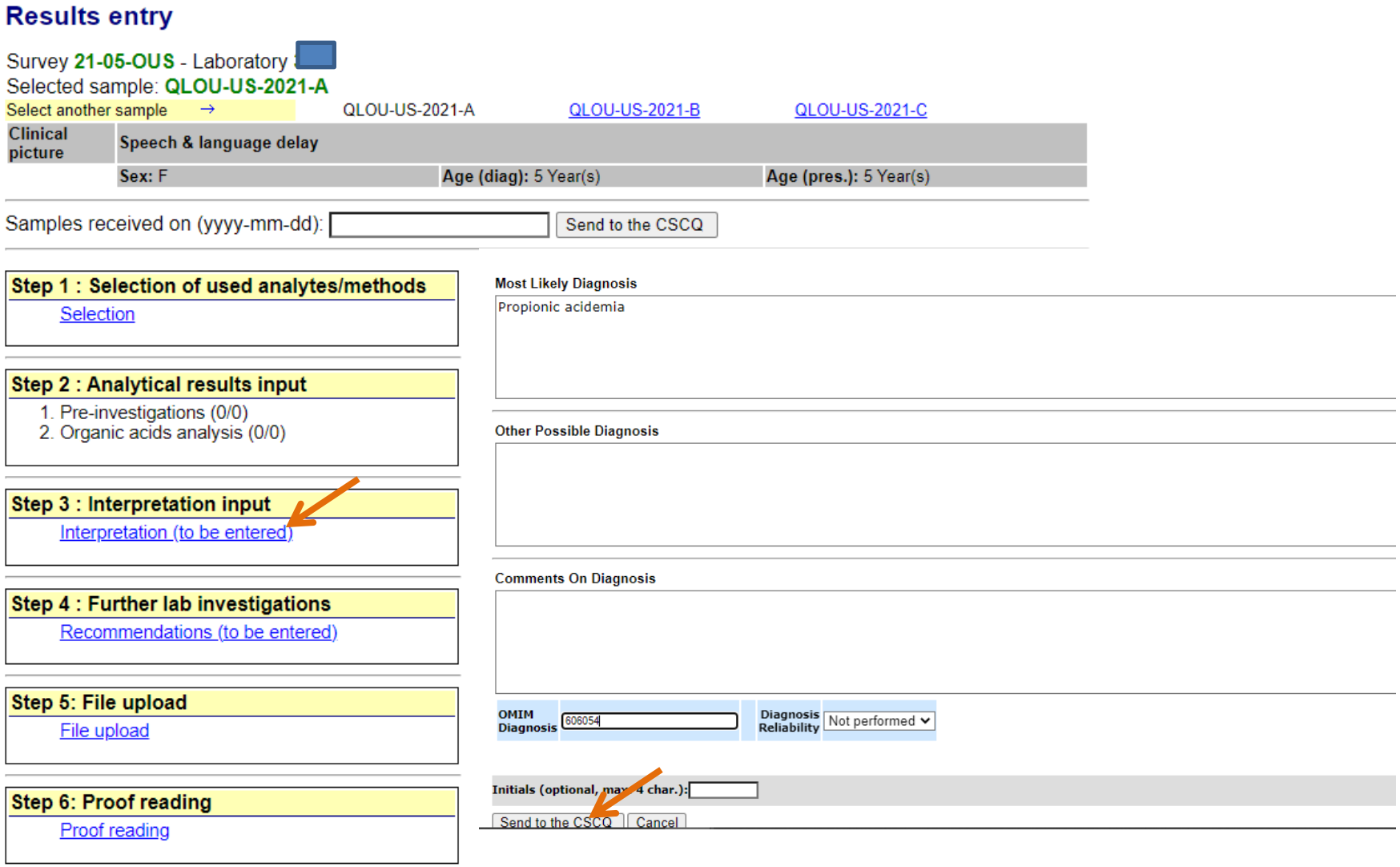
Comments:

Initials (optional, max. 4 char.):

Send to the CSCQ | Cancel

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

3. Results in the website https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.ph



QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

3. Results in the website https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.ph

Results entry

Survey **21-05-OUS** - Laboratory [redacted]
Selected sample: **QLOU-US-2021-A**

Select another sample → QLOU-US-2021-A QLOU-US-2021-B QLOU-US-2021-C

Clinical picture	Speech & language delay		
	Sex: F	**Age (diag):** 5 Year(s)	**Age (pres.):** 5 Year(s)

Samples received on (yyyy-mm-dd): [ ] Send to the CSCQ

Step 1 : Selection of used analytes/methods
Selection

Step 2 : Analytical results input
1. Pre-investigations (0/0)
2. Organic acids analysis (0/0)

Step 3 : Interpretation input
Interpretation (to be entered)

Step 4 : Further lab investigations
Recommendations (to be entered)

Step 5: File upload
File upload

Step 6: Proof reading
Proof reading

Back to **Result entry**

Recommendations

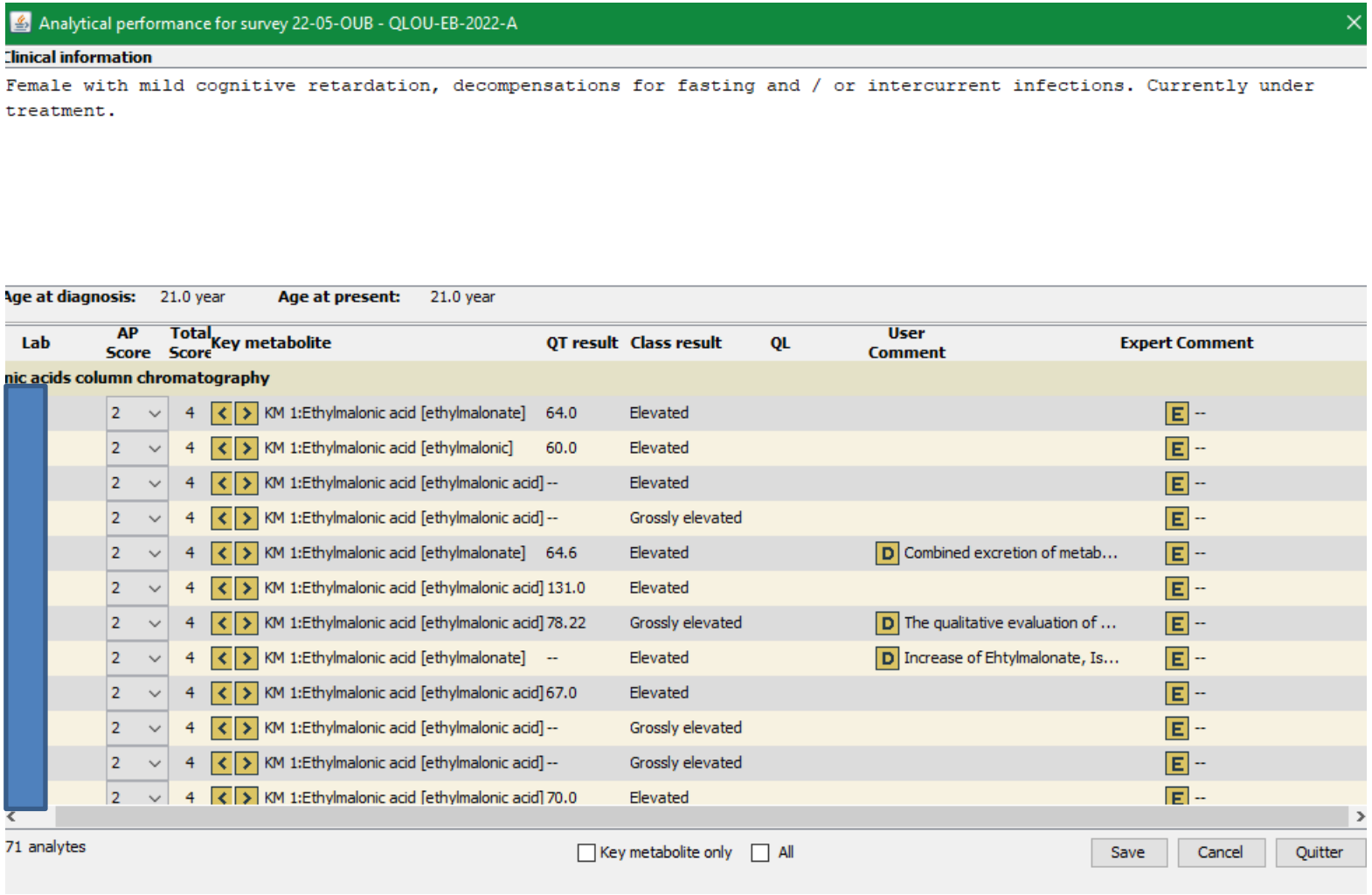
Acylcarnitines and aminoacids in plasma
Molecular studies in PPCA and PCCB genes

Initials (optional, max. 4 char.): [ ]

Send to the CSCQ | Cancel

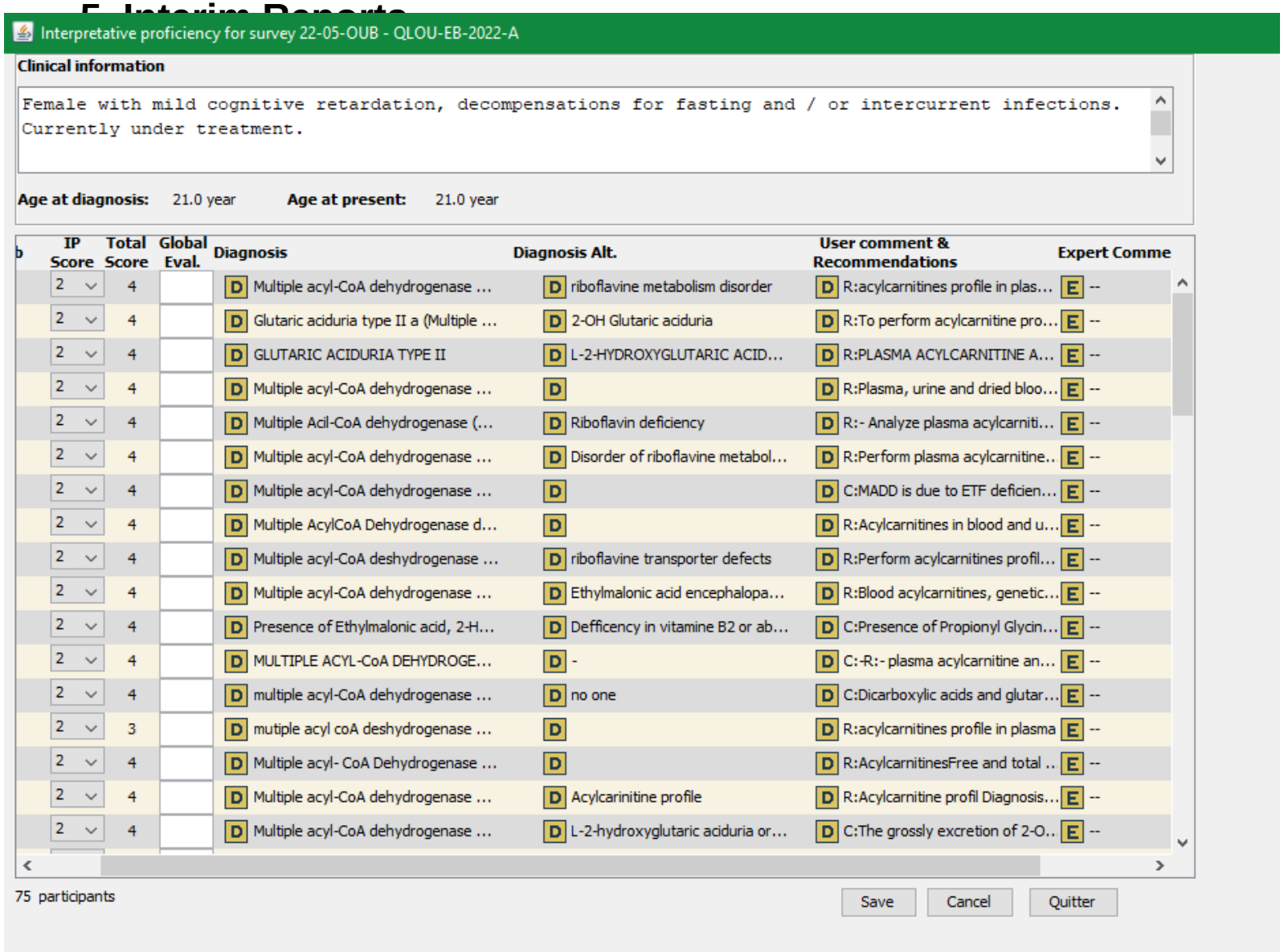
QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

4. Evaluación /Interim Reports



QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

5. Interim Reports



Report elements for survey 22-05-OUB - QLOU-EB-2022-A

Clinical information

Female with mild cognitive retardation, decompensations for fasting and / or intercurrent infections. Currently under treatment.

Age at diagnosis: 21.0 year **Age at present:** 21.0 year

Report input

- Patient detailed information
- General comment on analytical performance (all participants)
- General comment on interpretative proficiency (all participants)
- General comment on recommendations (all participants)
- Overall impression on the survey
- Definitive diagnosis (detailled)
- Definitive diagnosis (short)
- Definitive recommendations

Attached documents

- Manage attached documents

Report display and PDF generation

Key	Lab	IP Score	Total Score	Proof reading	Report	
4703	6	2	4	Display	Display	PDF
4706	13	2	4	Display	Display	PDF
4496	14	2	4	Display	Display	PDF
4499	27	2	4	Display	Display	PDF
4502	33	2	4	Display	Display	PDF
4505	36	2	4	Display	Display	PDF
4508	38	2	4	Display	Display	PDF
4511	41	2	4	Display	Display	PDF
4514	43	2	4	Display	Display	PDF
4517	44	2	4	Display	Display	PDF
4520	46	2	4	Display	Display	PDF

75 participants

All PDF | Scores | Save | Cancel | Qui

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

4. Evaluación /Interim Reports

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	Analytical performance	Correct results of the appropriate tests	2
		Partially correct or non-standard methods	1
		Unsatisfactory or misleading	0
I	Interpretative proficiency & Recommendations	Good (diagnosis was established)	2
		Helpful but incomplete	1
		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.

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

4. Interim report

21-05-OUB

QLOU-EB-2021-C Isovaleric acidemia or isovaleryl-CoA dehydrogenase deficiency **Total score: 4**

Patient details

Male patient diagnosed of isovaleric acidemia at 8 years old presenting feeding refusal, lethargy and developmental delay. Currently he is 44 years old and is under treatment with hypoporteic diet and carnitine supplementation.

Analytical performance

-The key metabolites were isovalerylglycine and isovalerylglutamate, which are increased. The 3-hydroxy-isovaleric acid in this sample was not increased.
-66 laboratories of 73 active participants submitted results for sample C.
-All the laboratories, except one, 65 (98%), reported correctly the increase of isovalerylglycine. One lab did not put anything in the analytical results, but with correct diagnosis.
-Only 18 (27%) participants detected the increase of isovalerylglutamate. In the sample of isovaleric aciduria circulated in 2018 only the 19% detected high amounts of isovalerylglutamate.

SCORE: 2 points are given for the detection of isovalerylglycine.

Interpretative proficiency

All laboratories, 66 (100%), reported the isovaleric acidemia as correct diagnosis.

SCORE: 2 points are given for the diagnosis of isovaleric acidemia or isovaleryl-CoA dehydrogenase deficiency.

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

4. Interim report

21-05-OUB

QLOU-EB-2021-C Isovaleric acidemia or isovaleryl-CoA dehydrogenase deficiency

Total score: 4

Recommendations

- The majority of the participants recommend plasma or DBS acylcarnitine analysis and molecular analysis of IVD gene.
-Some participants also recommended plasma aminoacid analysis and detemination of isovaleryl CoA dehydrogenase activity in white bllod cells or fibroblasts.

Overall impression

The overall performance was 99%.

Investigations

Organic acids column	n (quant)	n (qual)	Median value	SD	Your results (quant) mmol/mol creat	Your results (qual)
isovalerylglycine	23	70	1675,00	2269,98	461.0	Grossly elevated
Isovalerylglutamate	2	18	42,00	18,00	--	--
3-hydroxyisovaleric acid	9	24	3,00	114,02	--	--

Interpretation

Your result: Isovaleric aciduria

Your score for interpretation: 2

Your total score: 4

Recommendations for further tests

Your result: Continue the medical, dietetic and biological monitoring

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

5. Annual Report

ERNDiM

Quality Assurance in Laboratory Testing for IEM

ERNDIM Administration Office
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E-mail: admin@erndim.org

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Telephone (+)34 93 2275672
Fax (+)34 93 2275668
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Scheme Organisation
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Email: **1)** Alessandro.Salemma@hcuge.ch; **2)** Nicola.Braik@hcuge.ch

Published: 29 April 2022[1]

Qualitative Organic Acids

Centre: Spain

Final Report 2021

prepared by
Dr. Judit García Villoria and Dr. Antònia Ribes Rubió

1. Introduction

The ERNDIM Qualitative Organic Acids in urine scheme offers urine samples obtained from confirm patients with confirmed diagnoses to enable laboratories to gain or maintain experience to identify organic acid disorders. The scheme is organised by Judit Garcia Barcelona Scheme 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 t 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 identifyir a profile as normal can avoid unnecessary further investigation and distress to the patient and famil

2. Participants

In 2020 seventy five laboratories from many different countries participated in the QLOU *Barcelona* scheme. One laboratory was educational participants in 2020 (2 in 2019). They take part in all aspe 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 Barcelona, Heidelberg and Sheffield qualitative urinary organic acid schemes which are run separately. The three organising laboratorie each participate in the other's scheme by rotation.

Table 1: Geographical distribution of participants

Country	*Number of laboratories*	*Country*	*Number of laboratories*
ARGENTINA	4	ITALY	14
BRAZIL	2	KINGDOM OF SAUDIA ARABIA	1
CHILE	1	LEBANON	1
CHINA	2	PHILIPPINES	1
COLOMBIA	1	PORTUGAL	2
CYPRUS	1	QATAR	1
FRANCE	21	REPUBLIC OF SINGAPORE	1
GERMANY	1	SPAIN	10

3. Design of the scheme and logistics

As usual, the samples used in 2020 were authentic human urine samples, 6 from affected patients and 3 from healthy individuals.
All samples selected by the Scientific Advisor have been heat-treated and were tested for suitability in the Scientific Advisor's laboratory.
In 2020 CSCQ dispatched the QLOU 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 chromatograms can be uploaded on the CSCQ website.

4. Schedule of the scheme

Scheme Year:	2023	
QLOU Centre:	Barcelona	
CSCQ Sample dispatch date: *(please give date)*	08 February 2023	
	1st Submission Round	**2nd Submission Round**
Sample ID's:	QLOU-EB-2023-**A** QLOU-EB-2023-**B** QLOU-EB-2023-**C**	QLOU-EB-2023-**D** QLOU-EB-2023-**E** QLOU-EB-2023-**F**
Please give dates for:		
Analysis start & Website submission availability*: *(suggested date of 3 weeks before results submission deadline)*	09 May 2023	29 August 2023
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Scientific Advisor to upload previous database *(1 week after deadline)*	07 June 2023	27 September 2023
Availability of results to Scientific Advisor: *(2 weeks after submission deadline)*	13 June 2023	03 October 2023

To be able to continue this scheme we need a steady supply of new patient samples. Several laboratories have donated samples to the Urine QLOU 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 QLOU scheme in the following year.

Table 3: Samples included in the 2020 ERNDIM QLOU *Barcelona* scheme.

Survey	Sample no.	Diagnosis
20-05-OUB	QLOU-EB-2020-A	Normal
	QLOU-EB-2020-B	2-hydroxyglutaric aciduria
	QLOU-EB-2020-C	Ornithine transcarbamylase deficiency
20-07-OUB	QLOU-EB-2020-D	3-hydroxy-3-methylglutaryl-CoA lyase deficiency
	QLOU-EB-2020-E	Tyrosinemia type I
	QLOU-EB-2020-F	Normal

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

5. Annual Report

8.4. Patient C

Isovaleric acidemia or isovaleryl-CoA dehydrogenase deficiency

Patient details provided to participants

44 year-old male, diagnosed at 8 years when presenting with developmental delay, feeding refusal and lethargy. At present under treatment.

Patient details

Male patient diagnosed of isovaleric acidemia at 8 years old presenting feeding refusal, lethargy and developmental delay. Currently he is 44 years old and is under treatment with hypoporteic diet and carnitine supplementation.
Pathological excretion of isovalerylglycine and isovalerylglutamate were detected.

Analytical performance

-The key metabolites were isovalerylglycine and isovalerylglutamate, which are increased. The 3-hydroxy-isovaleric acid in this sample was not increased.

-66 laboratories of 73 active participants submitted results for sample C.

-All the laboratories, except one, 65 (98%), reported correctly the increase of isovalerylglycine. One lab did not put anything in the analytical results, but with correct diagnosis.

-Only 18 (27%) participants detected the increase of isovalerylglutamate. In the sample of isovaleric aciduria circulated in 2018 only the 19% detected high amounts of isovalerylglutamate.

Diagnosis / Interpretative proficiency

All laboratories, 66 (100%), reported the isovaleric acidemia as correct diagnosis.

Recommendations

- The majority of the participants recommend plasma or DBS acylcarnitine analysis and molecular analysis of IVD gene. -Some participants also recommended plasma amino acid analysis and determination of isovaleryl CoA dehydrogenase activity in white blood cells or fibroblasts.

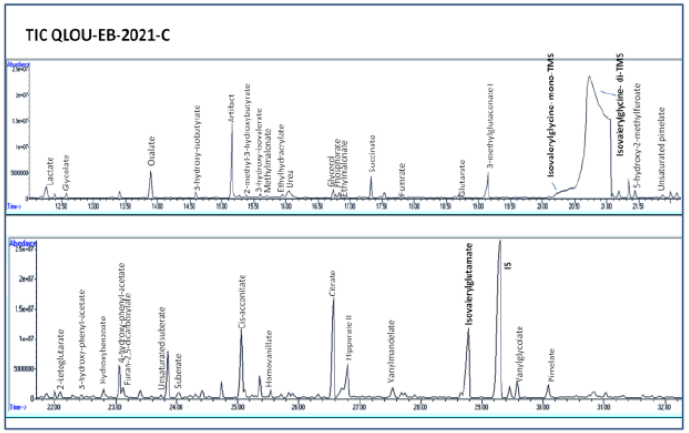
Scoring

- Analytical results: 2 points are given for the detection of isovalerylglycine.
- Interpretation of results: 2 points are given for the diagnosis of isovaleric acidemia or isovaleryl-CoA dehydrogenase deficiency.

Overall impression

The overall performance was 99%.

Chromatogram sample C and isovalerylglutamate ion spectrum:



Total ion chromatogram sample QLOU-EB-2021-C

QLOU: QUALITATIVE ORGANIC ACIDS SCHEME

5. Annual Report

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).

Lab number in the above table:«23»

Detailed scores

Lab no	A	B*)	C	Sum	D	E	F	Sum	Total score	% of total	Performance
1	4		4	8	4	4	4	12	20	100	
2	4		4	8	4	4	4	12	20	100	Educational Participant
3	4		4	8	4	4	4	12	20	100	
4	4		4	8	4	4	4	12	20	100	
5				0				0	0	0	NO RETURN
6	4		4	8	4	4	4	12	20	100	
7	4		4	8	4	4	4	12	20	100	
8	4		4	8	4	4	4	12	20	100	
9	4		4	8	4	4	4	12	20	100	NO RETURN
10	4		4	8	4	4	4	12	20	100	PP, CE
11	4		4	8	4	4	4	12	20	100	

Total score 2020:«32»

PP: Poor performance < 71% proficiency

CE: critical error- error en diagnóstico

Cartas a los participantes

Overall Proficiency

Sample ID	Diagnosis	Proficiency (%)
QLOU-EB-2021-A	Normal profile	100%
QLOU-EB-2021-B	Aromatic l-amino acid decarboxylase (AADC) deficiency (QLOU common sample) - **Educational sample**	62%
QLOU-EB-2021-C	Isovaleric aciduria	99%
QLOU-EB-2021-D	Phenylketonuria	99%
QLOU-EB-2021-E	Glutaric aciduria type 1 low excretor	95%
QLOU-EB-2021-F	Normal profile	97%

Acylcarnitines in dried blood spots

deberes del asesor científico:
1) proporcionar 6 muestras patológicas a los centros participantes en un año (recolectar 3 ml de sangre para cada muestra y ponerlo en dbs (spot de 30 microlitro); depende de los numerod de participantes) y proporcionar datos clínicos resumidos
2) evaluar los resultados y elaborar los dos informes intermedios en los plazos preestablecidos, con la ayuda del software CSCQ
3) proporcionar el informe anual con la ayuda del software CSCQ
4) enviar cartas a laboratorios, por bajo rendimiento, errores críticos, a laboratorios que envían datos parciales o no envían resultados; segundo revisor
5) participar en las reuniones anuales con los otros asesores científicos para discutir los resultados del esquema

22-06-ACL / ACDB-UL-2022-D [redacted] **Lab 88**

Clinical picture
Patient sex : M Age at diagnosis : 1 Month(s) Age present : 1 Month(s)
Hypoglycaemia, hypotonia

1. Analytical Results [redacted]

Acylcarnitine (ACDB) **ACDB-UL-2022-D Lab 88**

Analyte	Method	Key metabolite	Evaluation	Quant.	Unit	Lower Lim.	Upper Lim.
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C0	Low/decreased	5.82	umol/L	9	56
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C2	Low/decreased	4.52	umol/L	11	47
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C14:1	Grossly elevated	0.68	umol/L	0.01	0.3
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C14	Grossly elevated	0.63	umol/L	0.01	0.35
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C16:1	Grossly elevated	0.84	umol/L	0.01	0.35
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C16:1-OH	Elevated	0.29	umol/L	0.01	0.1
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C16-OH	Grossly elevated	1.17	umol/L	0.01	0.08
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C18:1-OH	Grossly elevated	1.69	umol/L	0.01	0.09
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C18-OH	Grossly elevated	1.08	umol/L	0.01	0.07
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	C20-OH	Elevated	0.12	umol/L	0.01	0.04
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	ratio C16-OH/C16	Grossly elevated	0.44	umol/L		0.05
Acylcarnitines	Method 1/MS-MS/Precursor ion scan/Derivatised kit	ratio C14:1/C16	Elevated	0.25	umol/L		0.16

2. Interpretation [redacted]
User Initials : USR1 **Lab 88**
Most Likely Diagnosis
LCHAD
Other Possible Diagnosis
mitochondrial trifunctional protein (TFP) deficiency; VLCAD
Comments On Diagnosis
OMIN Diagnosis : Diagnosis Reliability : -2

3. Recommendations [redacted]
User Initials : USR1 **Lab 88**
Organic acid in urine; lactate; ammonia; Fibroblast acylcarnitine profiling; enzyme assay of LCHAD and long-chain 3-ketothiolase activity; mutation in the alpha and beta subunit of the hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase (HADHA and HADHB); Then mutation in ACADVL

criterios de evaluación similares para ácidos orgánicos y acilcarnitinas DBS

Table 5: 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 (Table 4)	1
	Incorrect: minimally required results not reported	0
Diagnostic proficiency	Correct according to criteria set for the sample (Table 5)	2
	Partially correct	1
	Unsatisfactory or misleading	0
	Maximum total score	**4**

Table 7: Overall proficiencies of the 2019 surveys.

Sample ID	Sample type	Proficiency (%)
ACDB-DH-2019-A	propionyl-CoA carboxylase deficiency (propionic acidaemia)	98
ACDB-DH-2019-B	3-methylcrotonyl-CoA carboxylase (3-MCC) deficiency	85
ACDB-DH-2019-C	normal	83
ACDB-DH-2019-D	isovaleric acidaemia	95
ACDB-DH-2019-E	multiple acyl-CoA dehydrogenase (MAD) deficiency	88
ACDB-DH-2019-F	long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency	88

10. Scores of participants

Table 8 presents detailed scores and performance data for all participants.

Scores and performance data were confirmed by the Scientific Advisory Board meeting in Nove 2019.

The anonymous data are accessible to all participants. Individual data are only visible to your laboratory

Lab no	A	B	C	sum	D	E	F	sum	Total score	Performance
1										Educational
2	4	4	4	12	4	4	4	12	24	
3	4	4	4	12	4	4	4	12	24	
4	4	4	3	11	4	4	4	12	23	
5	4	4	4	12	4	3	4	11	23	
6	4	4	4	12	4	4	4	12	24	
7										non-submitter
8	4	4	4	12	4	4	4	12	24	
9	4	4	4	12	4	4	4	12	24	
10	4	4	4	12	4	3	4	11	23	
11	4	4	3	11	3	4	4	11	22	
12	4	2	3	9	4	4	4	12	21	
13	4	4	4	12	4	4	4	12	24	
14	4	4	4	12	4	4	4	12	24	
15	4	4	4	12	4	4	4	12	24	
16	4	1	3	8	4	4	4	12	20	
17	4	4	4	12	4	4	4	12	24	
18	4	4	4	12	4	4	0	8	20	CE
19	4	4	4	12	4	4	4	12	24	

Programa de Interpretación de aminoácidos
(Interpretative-Cognitive Scheme)

El **objetivo** es educar y evaluar la capacidad de los laboratorios para detectar enfermedades metabólicas hereditarias que dan como resultado perfiles característicos de aminoácidos en **plasma u otro tipo de muestra**.

Los laboratorios participantes deben interpretar de los datos de un análisis de aminoácidos ya realizado (no se envía ninguna muestra, no se analiza ninguna muestra sino que se interpreta una muestra ya analizada).

Junto con los datos de cuantificación de aminoácidos, los participantes reciben información clínica y valores cuantitativos de aminoácidos en plasma, orina y LCR (con rangos de referencia).

Información enviada a los participantes:

COGNITIVE SCHEME for Amino Acids

CASE 2019-01

Clinical information

Sex/Age	Female, 14y
Pregnancy	normal
Birth	uneventful
Family History	normal
Previous history	
Initial symptoms	Metabolic decompensation at 8 months of age, hyperammonaemia,
Follow-up	Multiple episodes of metabolic decompensation, poor growth but normal intelligence. Nutritional monitoring.
Treatment	Specific treatment including benzoic acid
Miscellaneous	

Laboratory Results:

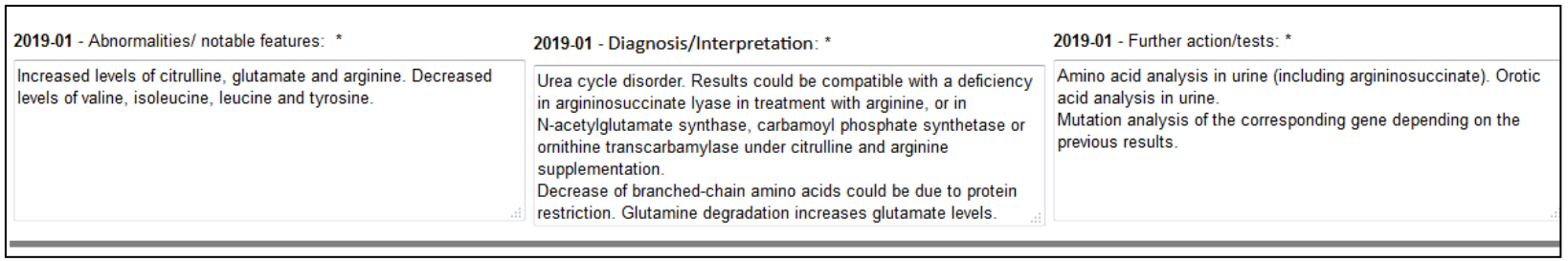
Plasma Amino acids	Value (µmol/L)	Reference interval	comments
Taurine	57	10-162	
Aspartate	16	4-28	
Threonine	124	72-192	
Serine	78	75-175	
Asparagine	22	32-64	
Glutamate	135	11-59	
Glutamine	455	396-740	
Proline	120	75-307	
Glycine	151	148-324	
Alanine	500	192-508	
Citrulline	226	17-49	
a-aminobutyrate	7	10-38	
Valine	103	142-278	
Cystine	18	32-64	
Methionine	31	16-36	
Isoleucine	14	38-94	
Leucine	31	76-168	
Tyrosine	24	40-92	
Phenylalanine	48	38-78	
Ornithine	66	20-84	
Lysine	212	105-221	
Histidine	104	58-106	
Arginine	191	45-125	

Éste sería un ejemplo de caso a estudiar

Breve resumen de la historia clínica

Resultado del análisis de aminoácidos que incluye los valores normales

Respuesta enviada por los participantes al Asesor Científico:



2019-01 - Abnormalities/ notable features: *	**2019-01** - Diagnosis/Interpretation: *	**2019-01** - Further action/tests: *
Increased levels of citrulline, glutamate and arginine. Decreased levels of valine, isoleucine, leucine and tyrosine.	Urea cycle disorder. Results could be compatible with a deficiency in argininosuccinate lyase in treatment with arginine, or in N-acetylglutamate synthase, carbamoyl phosphate synthetase or ornithine transcarbamylase under citrulline and arginine supplementation. Decrease of branched-chain amino acids could be due to protein restriction. Glutamine degradation increases glutamate levels.	Amino acid analysis in urine (including argininosuccinate). Orotic acid analysis in urine. Mutation analysis of the corresponding gene depending on the previous results.

Programa de Interpretación de aminoácidos
(Interpretative-Cognitive Scheme)

Los deberes del asesor científico son:

Para comenzar el programa:

1) proporcionar los datos de cuantificación aminoácidos de 6 muestras a los centros participantes junto con un breve resumen de la historia clínica o cualquier otro dato que pueda ser relevante

Una vez que los participantes han enviado sus resultados:

2) evaluar los resultados y elaborar dos informes intermedios en los plazos preestablecidos.

3) proporcionar el informe anual más extenso

4) enviar cartas a laboratorios, por bajo rendimiento, errores críticos, a laboratorios que envían datos parciales o no envían resultados; segundo revisor

5) participar en las reuniones anuales con los otros asesores científicos para discutir los resultados del esquema

Informe de los resultados enviado por el asesor científico a los participantes

Case 2019-1

Treated urea cycle defect, ornithine carbamoyltransferase deficiency.
Plasma amino acid concentrations together with the laboratories reference ranges were provided.

The results provided were from a 14 year old girl who exhibited multiple episodes of metabolic decompensation since the age of 8 months and has shown poor growth but is mentally normal.
Current treatment comprises low protein intake plus essential amino acid mixture (equivalent to 0.8 g/kg/day), sodium benzoate, citrulline and arginine.
The diagnosis was confirmed by mutation analysis.

Correct findings / abnormalities:
Increases of plasma citrulline and arginine (1 point) and mention of the very low levels of essential amino acids were considered necessary for full points.

Correct Diagnosis:

Since it is very difficult to identify the true defect due to treatment the correct diagnosis was considered to be a urea cycle defect (2 points). Unjustified specific defects were scored with 1 point-
An example of a good evaluation is as follows:
Most likely CPS1 or OTC deficiency on supplements of citrulline or citrulline+ arginine
Alternative diagnosis of citrullinaemia with arginine supplements less likely as citrulline usually much higher in that disorder.
Low branched chain amino acids most likely secondary to sodium phenylbutyrate therapy.

Further tests:

Measurement of blood ammonia and / or urine orotic acid, the need to review the diet and appropriate genetic testing were each scored with one point to a maximum of 2 points. Regarding genetic testing it is important that mention is made of a specific gene that is appropriate to the findings and suggested diagnosis.

Informe de los resultados enviado por el asesor científico a los participantes

Puntuaciones

Lab I.D.	Sample 2019-1-Scores				Sample 2019-2-Scores				Sample 2019-3-Scores				
	Abnormal 2 pts	Diag 2 pts	Tests 2 pts	**Total**	Abnormal 2 pts	Diag 2 pts	Tests 2 pts	**Total**	Abnormal 2 pts	Diag 2 pts	Tests 2 pts	**Total**	**Total**
1	2	2	2	**6**	1.5	2	2	**5.5**	2	2	2	**6**	**17.5**
2	2	2	2	**6**	1.5	2	2	**5.5**	2	2	1	**5**	**16.5**
3	2	1	2	**5**	1.5	2	2	**5.5**	2	2	2	**6**	**16.5**
4	2	1	1	**4**	1.5	2	2	**5.5**	2	2	1	**5**	**14.5**
5	2	2	2	**6**	1.5	2	2	**5.5**	2	2	2	**6**	**17.5**
6	2	2	2	**6**	1.5	2	2	**5.5**	2	2	2	**6**	**17.5**
7	2	2	2	**6**	2	1	1	**4**	2	2	2	**6**	**16**
8	2	2	2	**6**	2	2	2	**6**	2	2	2	**6**	**18**
9	2	2	2	**6**	1.5	2	2	**5.5**	2	2	2	**6**	**17.5**
10	1	2	2	**5**	1.5	2	2	**5.5**	2	2	2	**6**	**16.5**
11	2	1	2	**5**	1.5	1	1	**3.5**	2	2	2	**6**	**14.5**
12	1	1	0	**2**	1.5	2	2	**5.5**	2	2	2	**6**	**13.5**
13	2	1	1	**4**	2	1	1	**4**	2	2	2	**6**	**14**
14	2	1	1	**4**	1.5	2	2	**5.5**	2	2	2	**6**	**15.5**
15	2	2	2	**6**	1.5	2	2	**5.5**	2	2	1	**5**	**16.5**

CONCLUSIONES

- SLEIMPN: Fomentar participación: número de laboratorios potencialmente interesados
- Evitar solapamientos
- Centros y ”Scientific Advisors” en latinoamérica (preferible de tres países distintos)
- ERNDIM ayuda en la fase de desarrollo y será posible utilizar la plataforma CSCQ de evaluación de los resultados.
- Para un futuro, ERNDIM averigua con MCA (empresa que fabrica material de control) si es posible preparar muestra cuantitativas para futuros esquemas.

ERNDiM

Gracias!!