ERNDIM
Quantitative Schemes
Special Assays in Serum

ANNUAL REPORT 2025

Scheme Organiser	Scientific Advisor	Website for reporting results	Administration office
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1. *Purpose*

The purpose of the ERNDIM External Quality Assurance Scheme for Special Assays in Serum is the monitoring of the analytical quality of the quantitative assay of a range of analytes in serum in laboratories involved in the diagnosis of patients with inherited metabolic disorders. For details see www.erndim.org / www.ERNDIMQA.nl

2. *Participants*

A total of 290 datasets (243 labs) have been submitted, for 4 of them an annual report could not be generated due to insufficient data submission. 3 laboratories did not submit results at all.

3. *Design*

The Scheme has been designed, planned and coordinated by the scientific advisor (Dr. Rafael Artuch) and Dr. R.M. Schoeman as scheme organiser (on behalf of MCA Laboratory), both appointed by and according to the procedure of the ERNDIM Board. The design includes samples and reports to provide information with a balance between short-term and long-term reports and between detailed and aggregated information. As a subcontractor of ERNDIM, the MCA Laboratory prepares and distributes the EQA samples to the scheme participants and provide a website for on-line submission of results and access to scheme reports.

Samples

The scheme consisted of 8 lyophilized samples, all prepared from the same basic serum but with various amounts of added analytes. The samples were identical two by two: the pairs analytes, their source, and the added amounts are in the table below

[1] If this Annual 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.

except for biotinidase activity, NEFA and total cholesterol concentrations which are endogenous. Samples have been tested for stability and homogeneity according to ISO 13528, and are stable for the duration of the scheme's submission calendar when stored under defined conditions.

Table 1.

Analyte	Source:	Units	Added Amounts			
			Sample Pair 2025. 01 - 08	Sample Pair 2025. 02 - 05	Sample Pair 2025. 03 - 07	Sample Pair 2025. 04 – 06
3-OH-Butyric Acid	Sigma 298360	mmol/L	2.44	0.94	0.00	3.94
7-Dehydrocholesterol	Sigma 30800	µmol/L	73.54	168.78	0.00	9.02
7-Ketocholesterol	Sigma C2394	µmol/L	0.50	1.50	0.10	1.00
Biotinidase	Endogenous	nmol/min/ ml serum				
C22:0 Behenic acid	Sigma 216941	µmol/L	55.91	15.90	0.00	35.92
C24:0 Lignoceric acid	Sigma L6641	µmol/L	46.13	30.96	1.06	11.00
C26:0 Cerotic acid	Sigma H0388	µmol/L	1.04	9.13	0.00	4.14
C26:0 LPC	Sigma 855810P	µmol/L	1.46	0.78	0.14	0.30
Carnitine Free	Sigma C0283	µmol/L	102.56	62.10	0.00	11.93
Cholestane-3b. 5a. 6b-triol	Merck 700054P	µmol/L	0.80	0.50	0.05	0.30
Cholestanol	Sigma D6128	µmol/L	13.02	93.03	0.00	68.06
Cholesterol	Endogenous	mmol/L				
Coenzyme Q10	Sigma C9538	µmol/L	4.02	2.01	0.00	1.00
Creatine	Sigma C3630	µmol/L	42.43	23.13	0.00	63.07
Galactose	Sigma G0750	µmol/L	1199.98	1899.93	50.33	500.07
Glucosylsphingosine	Sigma 43659	nmol/L	599.94	402.16	0.00	1002.10
Guanidino acetic acid	Sigma G11608	µmol/L	12.97	6.47	1.22	19.10
Homocysteine	Sigma H6010	µmol/L	200.24	40.34	0.00	15.08
Lactic Acid	Sigma L7022	mmol/L	2.19	6.49	0.00	4.19
Lyso Gb3	Sigma G9534	nmol/L	99.90	50.00	0.00	9.80
Lysoshpingomyelin	Cayman Chem. 100079475	nmol/L	400.20	39.90	0.00	20.30
Methylmalonic acid	Sigma M54058	µmol/L	400.02	50.02	0.00	2.14
NEFA	Endogenous	µmol/L				
Phytanic acid	Sigma P4060	µmol/L	7.03	22.01	0.00	15.00
Pipecolic Acid	Sigma P2519	µmol/L	20.33	8.27	0.00	38.25
Pristanic acid	Bioconnect SC281137	µmol/L	7.15	4.96	0.00	1.97
Pyruvic Acid	Sigma B8574	mmol/L	0.20	0.15	0.05	0.10
Succinylacetone	Sigma D1415	µmol/L	4.06	1.64	0.00	0.81

Reports

All data-transfer, the submission of data, and the request and viewing of reports proceed via the interactive website www.erndimqa.nl which can also be reached through the ERNDIM website (www.erndim.org). The results of your laboratory are confidential and only accessible to you (with your name and password). The anonymised mean results of all labs are accessible to all participants. Statistics of the respective reports are explained in the general information section of the website.

An important characteristic of the website is that it supplies short-term and long-term reports. Short-term reports associated with the four individual specimens are available

two weeks after the submission deadline and provide up-to-date information on analytical performance. Although it is technically possible to produce reports immediately, there is a delay of 14 days to enable the scientific advisor to inspect the results and add comments to the report when appropriate.
The annual report is based on the design-anchored connection between samples which enables a range of analytical parameters (accuracy, precision, linearity, recovery and inter-lab dispersion) to be reported once the annual cycle has been completed.

A second important characteristic of the website is the wide range in aggregation of results which permits labs to make an individual choice for detailed and/or aggregated reports. The most detailed report which can be requested from the website is the "Analyte in Detail" which shows results of a specific analyte in a specific sample (224 such Analyte-in-Detail-reports can be requested in the 2025 cycle). A more condensed report is the "Cycle Review" which summarises the performance of all analytes in a specific sample (8 such Cycle-Review-Reports can be requested in 2025). The highest degree of data aggregation can be found in the Annual Report which summarises the performance of all analytes from all 8 samples (one such Annual-Report can be requested in 2025).

4. Discussion of Results in the Annual Report 2025

In this section the results of the annual report 2025 are summarised in terms of accuracy, precision, linearity, recovery, inter-laboratory CV, and cross sectional relations. Please keep at hand your Annual Report from the Interactive Website when you read the "guided tour" below and keep in mind that we only discuss the results of "all labs": it is up to you to inspect and interpret the specific results of your laboratory.

Biotinidase, cholesterol and NEFA

Due to the absence of spiking, recovery and linearity data are unavailable for these analytes. Therefore, they are excluded from the annual report. However, we have retained these analytes within the scheme, particularly for participant laboratories' accreditation requirements.

4.1 Accuracy

A first approach to describe the accuracy is to compare the mean outcome in your lab of the eight samples with the mean outcome of all labs. This is done in the first columns of the annual report. It can be seen that the mean outcome for all labs for free Carnitine free is 73.8 µmol/L.
It is important to recognise that using ERNDIM Quantitative EQA material to establish bias is potentially a limitation. The bias of the method has been determined by comparing results to a derivation of the ERNDIM all laboratory trimmed mean, not a true target value. As the materials produced by the scheme are not reference materials, the bias determined is not a measure of absolute accuracy and is simply a measure of performance relative to other laboratories.

4.2 Precision

Reproducibility is an important parameter for quality in the laboratory and is encountered in the schemes' design. Samples come in pairs which can be regarded as duplicates from which CV's can be calculated (Intra laboratory CV as indicator for reproducibility). Outcome for your lab in comparison to the median of all labs is shown in column "Precision" of the Annual Report. Precision ranges from 3.4% for lactic acid to 20.8% for Coenzyme Q10. The overall precision of 9.5% is quite satisfying.

4.3 Linearity

Linearity over the whole relevant analytical range is another important parameter for analytical quality. Again, this is encountered in the Schemes' design. With weighed quantities on the x-axis and your measured quantities on the y-axis the coefficient of regression (r) has been calculated. Outcome for your lab in comparison to the median of all labs is in the column "Linearity" of the annual report. It can be seen that the coefficient of regression is best for Homocysteine and Methylmalonic acid (0.999) and lowest for Coenzyme Q10 (0.947).

4.4 Recovery

A second approach to describe accuracy is the percentage recovery of added analyte. In this approach it is assumed that the recovery of the weighed quantities is the target value. The correlation between weighed quantities as added to the samples (on the x-axis) and your measured quantities (on the y-axis) has been calculated. The slope of the correlation multiplied by 100% is your recovery of the added amounts. Outcome for your lab in comparison to median outcome of all labs is shown in the column "Recovery" in the Annual Report. For all labs the recovery ranges from 51% for Coenzyme Q10 and Phytanic acid to 103% for Creatine. The overall recovery was 86%.

4.5 Interlab CV

For comparison of outcome for one patient in different hospitals and for use of shared reference values it is relevant to have a high degree of harmonization between results of various laboratories. Part of the schemes' design is to monitor this by calculating the Interlaboratory CV. This, along with the number of laboratories who submitted results, is shown in the column "Data all Labs" in the Annual Report. It can be seen that most laboratories submitted results for 3-hydroxybutyric acid (n=120) whereas only 9 labs submitted results for 7-Ketocholesterol. The Inter-laboratory CV ranges from 6.10% for Lactic Acid to 47.7% for Lysosphingomyelin.

4.6 Cross Sectional Relations

The various parameters as described above often have an interrelation: more than one parameter directs towards good or bad analytical control.
A typical example of good analytical control is lactic acid: many (84) datasets submitted results, the reproducibility within the labs is good (precision of 3.4%), the interlab CV is good (6.1%), linearity is good (0.997) as is the recovery (96%).

4.7 Your performance: Flags

In order to easily judge performance of individual laboratories the annual report of an individual laboratory may include flags with different colours in case of poor performance for accuracy, precision, linearity and recovery. Analytes with satisfactory performance for at least three of the four parameters (thus no or only one flag) receive a green flag. Thus, a green flag indicates satisfactory performance for analysis of that particular analyte. Criteria for flags can be found in the general information on the website (on this website under general information; interactive website, explanation annual report).

4.8 Poor Performance Policy

A wide dispersion in the overall performance of individual laboratories is evident. Table 2 shows the percentage of flags observed. 58% of the laboratories have no flag at all and thus have attained excellent overall performance. In contrast, at the other extreme there are also 3% of laboratories with more than 25% red flags. Intensive discussion within the Scientific Advisory Board (SAB) has resulted in a harmonised scoring system that has been in place for the quantitative schemes for more than ten years; Likewise, there has been agreement as to what constitutes satisfactory performance. Both

parameters are checked annually and, if necessary, re-evaluated. For further information, please refer to the Framework for Assessment and Education for Quantitative Schemes on our website (https://eqa.erndim.org/information/view/14). The ERNDIM Board has decided that the Scientific Advisor will judge the performance of the individual laboratories based on these levels of satisfactory performance and issue a letter of advice of failure to achieve satisfactory performance to those laboratories which do not achieve satisfactory performance. The letter is intended to instigate dialogue between the EQA scheme organiser and the participating laboratory in order to solve any particular analytical problems in order to improve quality of performance of labs in the pursuit of our overall aim to improve quality of diagnostic services in this field.

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.

Table 2. Percentage Flags

% Red Flags seen in Annual Report	Percentage Labs In this Category	Cumulative Percentage Of Labs
>25%	3%	3%
25%	8%	11%
20 – 25%	2%	13%
15 – 20%	5%	18%
10 – 15%	7%	25%
5 – 10%	7%	32%
0 – 5%	10%	42%
0%	58%	100%

4.9 Certificates

Overall performance (as indicated by red/green flags in each laboratories annual report) is summarised in the annual participation certificate. The certificate lists the total number of special assays in the scheme, the number for which results have been submitted, and the number for which satisfactory performance has been achieved. It is important to bear in mind that the certificate should be viewed in conjunction with the individual annual report in the case of internal or external auditing.

4.10 Additional Specific Remarks of the Scientific Advisor

The Annual Report dealing with analytical performance in terms of accuracy, precision, linearity, recovery and inter-laboratory CV, shows in general a good overall performance. 15 metabolites displayed a CV < 15%, 4 between 15-20% and 6>20%.
19 out 25 analytes showed an interlab CV below 20%, 4/25 between 20-30%. CoQ has improved (Interlab CV = 28%) when compared with previous year.
The worst performance in terms of interlab CV was observed for Lysosphingomyelin (47%) and succinylacetone (43%).
Galactose and pyruvate issues seems solved with the antibiotics added to the matrix.

5. Summary

The Annual Report dealing with analytical performance in terms of accuracy, precision, linearity, recovery and inter-laboratory CV shows a performance with similarities to previous years. For some analytes the performance is good, while for others there is still something to do to achieve sufficient intra- and inter-laboratory quality.

6. *Preview Scheme 2026*

For 2026, several lipids (7-Ketocholesterol, C26:0 LPC, Cholestane-3b,5a,6b-triol, Coenzyme Q10, Glucosylsphingosine, Lyso Gb3 and Lysosphingomyeline) will be moved to the new Lipids in Serum (LIS) scheme (for further information, please view the 2026 EQA Scheme catalogue on the ERNDIM website). In 2026, FGF21 and GDF15 are non-scoring analytes newly added to SAS.

7. *Questions, Comments and Suggestions*

If you have any questions. comments or suggestions please address to the scientific advisor of the scheme Dr. Rafael Artuch and/or to the scheme organiser Dr. R.M. Schoeman (mca.office@skbwinterswijk.nl).

Most complaints received by ERNDIM consist of minor misunderstandings or problems with samples, which can usually be resolved via direct contact with the ERNDIM administrative staff. If you wish to file a formal complaint, please email your complaint with details of your issue to admin@erndim.org or contact us through our website at https://www.erndim.org/contact-us/

Barcelona, 17th March 2026

Mr. Rafael Artuch
Scientific Advisor

Please note:
This annual report is intended for participants of the ERNDIM Special Assays in Serum scheme. The contents should not be used for any publication without permission of the scheme advisor.

The fact that your laboratory participates in ERNDIM schemes is not confidential. However. the raw data and performance scores are confidential and will be shared within ERNDIM for the purpose of evaluating your laboratory performance. unless ERNDIM is required to disclose performance data by a relevant government agency. For details. please see the terms and conditions in the ERNDIM Privacy Policy on www.erndim.org.

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

Version Number	Published	Amendments
1	17th March 2026	• 2025 annual report published

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