ERNDIM Quantitative Schemes Acylcarnitines 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 Acylcarnitines 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 129 datasets have been submitted, for 4 of them an annual report could not be generated due to insufficient data submission. 7 laboratories did not submit results at all.

3. *Design*

The Scheme has been designed, planned and coordinated by the scientific advisor Dr. P. Ruiz-Sala 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 lyophilised samples, all prepared from the same basic serum but enriched with various amounts of added analytes. The samples were identical two by two: the pairs, analytes and their source, as well as the added amounts are, in the table below. 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. Joined to the analytes, total carnitine has been added to the list to be measured. Total carnitine is not a spiked analyte.

[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

Table 1.

Analyte	Source:	Added Amounts (µmol/L)			
		Sample Pair 2025. 01 - 07	Sample Pair 2025. 02 - 08	Sample Pair 2025. 03 - 05	Sample Pair 2025. 04 - 06
Free carnitine (C0)	C0283 (Sigma)	58.8	10.0	40.0	0.0
Acetylcarnitine (C2)	11078 (AUMC)	15.0	0.0	10.0	25.0
Propionylcarnitine (C3)	9001873 (Sanbio)	2.0	15.0	0.0	8.0
Butyrylcarnitine (C4)	26542 (Sanbio)	5.0	1.0	3.0	0.0
3-OH-Butyrylcarnitine (C4-OH)	H830900 (Bio-Connect)	5.0	0.3	2.0	0.0
Tiglylcarnitine (C5:1)	HY-113408 (Sanbio)	0.3	2.0	0.0	1.0
Isovalerylcarnitine (C5)	26555 (Sanbio)	0.0	3.0	6.0	1.5
3-OH-Isovalerylcarnitine (C5-OH)	H943620 (TRC)	0.0	1.0	2.5	0.3
Hexanoylcarnitine (C6)	26554 (Sanbio)	1.0	0.0	0.6	2.0
Octanoylcarnitine (C8)	15048 (Sanbio)	0.8	6.0	0.0	1.5
Decanoylcarnitine (C10)	26549 (Sanbio)	0.0	2.0	5.0	0.5
Dodecanoylcarnitine (C12)	10194 (AUMC)	4.0	0.5	2.0	0.0
cis-5-Tetradecenoylcarnitine (C14:1)	T291425 (TRC)	1.0	0.0	0.3	1.8
Palmitoylcarnitine (C16)	26553 (Sanbio)	0.6	3.6	0.0	2.4
3-OH-Palmitoylcarnitine (C16-OH)	H943005 (TRC)	0.0	0.8	1.2	0.1
Oleoylcarnitine (C18:1)	O526700 (TRC)	0.9	0.0	0.4	1.4
Stearoylcarnitine (C18)	26566 (Sanbio)	1.4	0.2	0.7	0.0
3-OH-Stearoylcarnitine (C18-OH)	H953630 (TRC)	0.1	1.2	0.0	0.7
Malonylcarnitine (C3-DC)	M158150 (TRC)	0.0	0.7	1.2	0.1
Methylmalonylcarnitine (C4-DC)	M318900 (TRC)	0.7	0.0	0.1	1.2
Glutarylcarnitine (C5-DC)	G597600 (TRC)	3.0	0.5	1.5	0.0

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* on the 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 long-term 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 (168 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 aggregation has the Annual Report which summarises the performance of all analytes of 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 co-efficient of variation (CV) and relations between these parameters. 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.

4.1 Accuracy

A first approach to describe the accuracy is to compare 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 (C0) is 61.3 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 5.9% for total carnitine to 14.9% for Methylmalonylcarnitine (C4-DC). The overall precision of 10.4% is 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 octanoylcarnitine (C8) (0.997) and lowest for total carnitine (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 50% for 3-OH-butyrylcarnitine (C4-OH) to 134% for dodecanoylcarnitine (C12).

4.5 Inter-laboratory CV

For comparison of outcome for one patient in different hospitals and for use of shared reference intervals and / or the use of consensus target treatment ranges, it is important to have a high degree of harmonisation 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 free carnitine (C0) (124) whereas 76 labs submitted results for total carnitine. The Interlab CV ranges from 9.05% for total carnitine to 45.9% for methylmalonylcarnitine (C4-DC).

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.

4.7 Your performance: Flags

In order to easily judge performance of individual laboratories the annual report of an individual laboratory may include flags 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. 31% 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. However, it should be noted that not all laboratories return results for all analytes. Intensive discussion within the Scientific Advisory Board (SAB) resulted in a harmonised scoring scheme 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%	0%	3%
20 – 25%	2%	5%
15 – 20%	6%	11%
10 – 15%	8%	19%
5 – 10%	22%	41%
0 – 5%	28%	69%
0%	31%	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 analytes 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

It is observed that few participants mark the option of using certain deuterated standards. With regard to acylcarnitines with two or more possible isomers—such as added butyrylcarnitine (C4), which can be analyzed together with the isobutyrylcarnitine (C4, too) from the serum pool—distinct groups of results are observed. This may suggest that the names of the methods to be chosen in the scheme are not well defined or that the participants do not take them into account:

- FIA-methods (flow injection analysis methods) are those that dispense with the use of a chromatographic column, thus making it impossible to distinguish isomers by retention times.
- In contrast, LC (liquid chromatography) methods do use a chromatographic column and are the ones that could, in principle, distinguish isomers, such as butyryl- from isobutyrylcarnitine for C4.
- SID refers to the use of an acylcarnitine identical to the one being quantified, but containing stable isotopes in its composition.

5. Summary

The Annual Report deals with analytical performance in terms of accuracy, precision, linearity, recovery and interlab CV. All parameters (intralab CV, linearity, recovery, interlab CV and number of participating laboratories) demonstrate slightly better or equal performance when compared to 2024.

6. Preview Scheme 2026

The design of the 2026 scheme is similar to the 2025. We hope that the results obtained in 2025 will help the participants in 2026 to improve their results or confirm their good results.

7. Questions, Comments and Suggestions

If you have any questions, comments or suggestions please address to the scientific advisor of the scheme Dr. P. Ruiz-Sala 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/

Madrid, 17th February 2026

Dr. P. Ruiz-Sala
Scientific Advisor

Please note:
This annual report is intended for participants of the ERNDIM Acylcarnitines 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	12th March 2026	• 2025 annual report published

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