ERNDiM
Quality Assurance in Laboratory Testing for IEM

ERNDIM Quantitative Schemes Pilot Lipids in Serum

ANNUAL REPORT 2024

Scheme Organiser	Scientific Advisor	Website for reporting results	Administration office
Dr. C.W. Weykamp Streekziekenhuis Koningin Beatrix MCA Laboratory Beatrixpark 1 7101 BN Winterswijk The Netherlands e-mail: mca.office@skbwinterswijk.nl	S. Goorden, PhD Erasmus Medical Center Department Clinical Genetics P.O. Box 2040 3000 CA Rotterdam Netherlands e-mail: s.goorden@erasmusmc.nl **Deputy Scientific Advisor** M. van Dijk, PhD Amsterdam UMC Dept. Genetic Metabolic Diseases Meibergdreef 9 1105 AZ Amsterdam Netherlands Email: m.vdijk@amsterdamumc.nl	Ms I. de Graaf Streekziekenhuis Koningin Beatrix MCA Laboratory Beatrixpark 1 7101 BN Winterswijk The Netherlands e-mail: i.degraaf@skbwinterswijk.nl	ERNDIM Administration Office c/o EMQN CIC, Unit 4, Enterprise House, Manchester Science Park Pencroft Way Manchester M15 6SE United Kingdom. e-mail: admin@erndim.org

Published: Rotterdam-Winterswijk, 14th February 2025[1]

1. *Purpose*

The ERNDIM External Quality Assurance Scheme for Quantitative Pilot Lipids in Serum monitors the analytical performance of laboratories providing screening and diagnosis of patients with inherited metabolic disorders. For details see www.erndim.org / www.ERNDIMQA.nl

2. *Participants*

46 laboratories ordered 49 sets of samples. 44 sets of data were submitted.

3. *Design*

The Scheme has been designed, planned and coordinated by the scientific advisors Dr. Susanna Goorden and Dr Marie van Dijk, and Dr. C.W. Weykamp 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 provides a website for on-line submission of results and access to scheme reports.

[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.

Samples

The scheme works with 4 pairs of lyophilised samples. The compounds included in the scheme are added at 3 levels and at basal levels, resulting in 4 concentration levels. All samples are prepared from the same native serum sample. The compounds, their source and the amounts added are listed in Table 1 below. The compounds reported are referred to as analytes. The samples were tested for stability and homogeneity according to ISO 13528.

Tabel 1.

Analyte	Source:	Units	Added Amounts			
			Sample Pair 2024. 01 - 08	Sample Pair 2024. 02 - 05	Sample Pair 2024. 03 - 07	Sample Pair 2024. 04 – 06
7-dehydrocholesterol (7-DHC)	Sigma 30800	µmol/L	74.2	8.99	0.0	169
7-ketocholesterol (7-KC)	Sigma C2394	µmol/L	0.47	0.94	0.09	1.57
C26:0-lysophospatidylcholine (C26:0-lysoPC)	Sigma 855810P	µmol/L	0.10	0.15	0.49	0.99
Cholestane-3ß. 5α. 6ß-triol	Merck 7000054P	µmol/L	0.75	0.30	0.0	0.45
Cholestanol	Sigma D6128	µmol/L	13.3	68.1	0.0	93.4
Desmosterol	Merck D6513	µmol/L	0.0	10.3	107	428
Glucosylsphingosine	Sigma 43659	nmol/L	545	954	0.0	409
Lyso-globotriaosylceramide (Lyso-Gb3)	Sigma G9534	nmol/L	100	9.60	0.0	49.6
Lyso-monosialoganglioside 1 (Lyso-GM1)	Sanbio 24837	nmol/L	4.85	0.0	19.9	80.0
Lyso-monosialoganglioside 2 (Lyso-GM2)	Sanbio 33073	nmol/L	79.8	4.99	0.0	19.94
Lyso-sphingomyelin (Lyso-SM)	Sanbio 10007947	nmol/L	5009	406	0.00	812
N-palmitoyl-O-phosphocholineserine (PPCS)	Bioconnect P347920	nmol/L	0.0	49.5	396	2003
Sitosterol	Merck 567152	µmol/L	796	0.0	20.2	200

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 three 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 21 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.

The second important feature of the website is the aggregation of results, allowing the participant to choose between detailed reports or an overview of overall performance. "Analyte in Detail" is the most detailed report available as it shows the result of a specific

analyte in a sample. "Cycle Review" is a more condensed report summarising the performance of all analytes in a particular sample. Eight such reports are available. The 'Annual Report' is a single report summarising the performance of all eight samples. Depending on the level of detail you require, you can choose to review only the Annual Report or delve into the detailed reports.

4. Discussion of Results in the 2024 Annual Report

In this part, we discuss information that the 2024 annual report provides, and regard accuracy, precision, linearity, recovery, inter-laboratory CV and cross-sectional relations. Please keep your annual report at hand when you go through the “guided tour” below. Do remember we only discuss the results of “all labs”; it is up to you to inspect and interpret the results of your own laboratory.

4.1 Accuracy

A first approach to assessing accuracy is to compare your average result over 8 samples with the mean of all laboratories. This is shown in the 'Your lab' and 'All labs' columns under the 'Accuracy' heading. For example, the mean of all laboratories for Cholestanol is 43.2 µmol/litre. You can compare your laboratory's mean to this collective mean.

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 quality parameter, and the scheme is designed to assess the intra-laboratory coefficient of variation (CV) as an indicator. The sample pairs can be considered as duplicates and used to calculate intra-laboratory CVs. The precision column shows how your results compare to the mean of all participants. The precision ranges from 6.6% for C:26-lysoPC to 50.1% for Lyso-GM2. The overall intra-laboratory CV is 17.8%.

4.3 Linearity

Linearity over the relevant analytical range is another important parameter for analytical quality. This is also included in the scheme design. With the weighted quantities on the x-axis and your measured quantities on the y-axis, the coefficient of regression (r) is calculated. In the linearity column you can see how your results compare with the mean of all participants. The mean r ranges from 0.855 for 7-KC to 0.997 for Sitosterol.

4.4 Recovery

A second way of assessing accuracy is to determine recovery. Recovery is the amount of analyte measured relative to the amount of the same analyte added. This approach assumes that the weighted amount is the target amount. The correlation between the weighted amounts added (on the x-axis) and your measured amounts (on the y-axis) has been calculated. The slope of the correlation curve multiplied by 100% is your recovery. In the Recovery column you can see how your results compare to the average of all participants. The mean recovery ranges from 30% for Lyso-GM2 to 115% for 7-KC. The overall recovery is 82%.

4.5 Inter-lab CV

A high degree of harmonisation between analytical results from different laboratories is very important for patient care and the use of common reference values. It should be

irrelevant in which laboratory the analytical results were obtained. The scheme is also designed to monitor inter-laboratory CV. The column "Data All Labs" shows the number of participants who submitted results per analyte. Most laboratories submitted results for Cholestanol (30), whereas only 7 laboratories measured 7-KC. The inter-laboratory CV ranges from 16.2% for Glucosylsphingosine to 791% for 7-KC. The mean inter-laboratory CV for all analytes is 103%.

4.6 Cross Sectional Relations

The various parameters discussed above are often interrelated. Often several parameters point to good or poor analytical control. In the Lipids pilot scheme several non-analytic factors contributed to high variation, such as submitted concentrations in wrong units (most notable for 7-KC).

4.7 Your performance: Flags

The Annual Report includes flags to help you easily assess your performance. The flags have different colours to indicate poor performance for accuracy, precision, linearity and recovery. Compounds with satisfactory performance in at least 3 out of 4 parameters (no or one flag) are marked with a green flag. Thus, a green flag indicates satisfactory analytical performance. The criteria for flagging can be found in the General Information section of the website.

4.8 Poor Performance Policy

There is a wide variation in the overall performance of individual laboratories. Table 2 shows the percentage of flags scored. 36% of the laboratories have no flags at all and have achieved excellent overall performance. At the other extreme, 12% of the participants scored more than 25% of flags. However, as the Lipids scheme is in a pilot phase, there is not yet a poor performance policy in place.

Table 2. Percentage flags

% Red flags seen in annual report	Percentage labs in this category	Cumulative percentage of labs
>25%	12%	12%
25%	4%	16%
20 – 25%	0%	16%
15 – 20%	14%	30%
10 – 15%	9%	39%
5 – 10%	14%	53%
0 – 5%	11%	64%
0%	36%	100%

4.9 Interpretation

In this scheme we also requested the interpretation of test results. Table 3 shows the interpretation frequency for the respective sample pairs. The correct interpretation is marked with a green box. Interpretation is in most cases correct, with exception of the sample pair 03-07. This is possibly due to the fact that this concentration was close to the upper limit of the reference range for PPCS.

Table 3.

Description	Pair 2023. 01-08	Pair 2023. 02-05	Pair 2023. 03-07	Pair 2023. 04-06
PPCS lower than our reference interval	4 – 1	0 – 3	2 - 2	0 – 0
PPCS within our reference interval	12 - 14	13 – 13	5 – 4	3 - 3
PPCS higher than our reference interval	5 - 4	7 – 5	12 – 12	17 - 19

4.10 Certificates

As the Lipids scheme is a pilot no certificate of participation will be provided.

4.11 Additional Specific Remarks of the Scientific Advisor

During the pilot it became clear that asking for interpretation of PPCS values was not clear for all participants; some labs filled this out while not submitting any PPCS values. The interpretation part will therefore not be continued in the 2025 scheme. It was also noted that for some labs, desmosterol and 7-DHC could not be separated leading to incorrect values. This problem will be solved in the 2025 pilot scheme. Finally, some labs commented on the fact that the lyso-sphingomyelin levels were far above the concentrations found in patients. This will also be adjusted in the 2025 scheme.

5. *Summary*

Overall, the pilot Lipids scheme ran successfully. The issues mentioned above will be addressed in the 2025 scheme.

6. *Preview 2025 Scheme*

The design of the scheme in 2025 will be essentially the same as the 2024 scheme, with the addition of Coenzyme Q10 and Lathosterol. The scheme will run another year as a pilot.

7. Questions, Comments, and Suggestions

If you have any questions, comments or suggestions, please contact the scientific advisor Dr. Susanna Goorden (s.goorden@erasmusmc.nl) or the scheme organiser D. C.W. Weykamp (mca.office@skbwinterswijk.nl).

Rotterdam, 6th January 2025

Dr. S. Goorden
Scientific Advisor

Please note:
This annual report is intended for participants of the ERNDIM Lipids in Serum Pilot scheme. The content may not be used for any publication without permission of the scheme advisor.

The fact that your laboratory takes part in ERNDIM schemes is not confidential. However, the raw data and performance scores are confidential and will be shared only within ERNDIM to evaluate your laboratory's 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	14th February 2025	• 2024 annual report published

END