ERNDIM
Quantitative Schemes
Special Assays in dried blood spots

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 dried blood spots is the monitoring of the analytical quality of the quantitative assay of a range of analytes in dried blood spots 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 131 datasets have been submitted. For one of them an annual report could not be generated due to insufficient data submission.

3. *Design*

The scheme has been designed, planned and coordinated by the scientific advisors, Dr. Rachel Carling and Professor Stuart Moat, and Dr. R.M. Schoeman as scheme organiser (on behalf of the MCA Laboratory), all three 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 sub-contractor of ERNDIM, the MCA Laboratory prepares and distributes the EQA samples 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

Each year, eight dried blood spots, comprising four identical pairs, are distributed to participants. All samples were prepared from the same basic whole blood but were enriched with varying amounts of the analytes. Blood was depleted to create low concentrations but not to a zero level. Thus, the final concentration of each sample is the remaining physiological concentration plus the spiked amount. The analytes and their source, as well as the added amounts, are shown in the table below for each pair. 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:**	**Added Amounts (µmol/L)**			
		Sample Pair 2025. 01 & 03	**Sample Pair 2025. 02 & 08**	**Sample Pair 2025. 04 & 06**	**Sample Pair 2025. 05 & 07**
Allo-isoleucine	Sigma I8454	10.1	0.0	50.0	4.9
Free Carnitine	Sigma C0283	73.0	0.0	123.0	23.0
Total Homocysteine	Sigma H6010	36.0	76.0	1.0	16.0
Isoleucine	Roth 3922.1	243.9	1024.6	0.0	504.7
Leucine	Roth 3984.1	433.0	0.0	911.7	192.1
Methionine	Sigma 64319	39.9	15.0	139.9	64.9
NTBC	Sigma PHR1731	65.0	13.0	130.0	26.0
Phenylalanine	Sigma 78019	651.4	36.3	1326.9	96.9
Succinylacetone	Sigma D1415	7.0	0.0	14.0	3.5
Tyrosine	Sigma 93829	44.2	0.0	629.2	11.0
Valine	Roth 4879.1	27.3	105.8	0.0	64.9

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 review 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 annual report is discussed below.

A second important characteristic of the website is the different levels of detail of results which allows individual laboratories the choice of fully detailed and/or summarised 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 (88 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 (16 such Cycle-Review-Reports can be requested in 2025). The most comprehensive report is the Annual Report which summarises the performance of all analytes in each of the four pairs of 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 accuracy is to compare the mean outcome of the eight samples from your lab with the mean outcome from all labs. This is done in the first column of the annual report. It can be seen that the all laboratory mean concentration for alloisoleucine is 16.0 µmol/L.

It is important to recognise that using the ERNDIM Quantitative DBS 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 such, 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 are prepared in pairs and each pair can be regarded as duplicates from which CV's can be calculated (intra-laboratory CV as an indicator of reproducibility). Outcome for your lab in comparison to the median of all labs is shown in column "Precision" of the Annual Report. The all laboratory mean imprecision ranges from 5.8% for leucine to 13.2% for succinylacetone.

4.3 Linearity

Linearity over the 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 for phenylalanine is 0.997.

4.4 Recovery

A second approach to describe accuracy is the percentage recovery of added analyte. In this approach, recovery is measured relative to the weighed amount of analyte used to enrich the sample. The correlation between the weighed quantities 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 laboratory in comparison to median outcome of all laboratories is shown in the column "Recovery" in the Annual Report. The all laboratory mean recovery ranges from 25% for succinylacetone to 94% for valine.

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 inter-laboratory harmonisation. Part of the schemes' design is to monitor this by calculating the inter-laboratory CV. This, along with the number of laboratories who submitted results, is shown in the column "Data all Labs" in the Annual Report. Most laboratories (n = 104) submitted results for phenylalanine whereas only fifteen labs submitted results for NBTC. The mean inter-laboratory CV ranges from 17.9% for isoleucine to 39.5% for succinylacetone.

4.6 Cross Sectional Relations

The various parameters as described above often have an inter-relation: more than one parameter directs towards good or poor analytical performance.

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

It is evident that there is considerable variation in the overall performance of individual laboratories. Table 2 shows the percentage of flags observed. 53% of the laboratories have no flag at all and thus have attained excellent overall performance. In contrast, at the other extreme, 4% of laboratories have 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%	4%	4%
25%	5%	9%
20 – 25%	3%	12%
15 – 20%	2%	14%
10 – 15%	8%	22%
5 – 10%	15%	37%
0 – 5%	10%	47%
0%	53%	100%

4.9 Certificates

Overall performance (as is 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 scheme results, which are consistent with those seen in previous years, highlight the poor performance of NTBC, total homocysteine and succinyl acetone. Although only a relatively small number of laboratories return results on these analytes, n=15, 35 and 38 respectively, there is evidently a need to improve performance of these analytes. We are in the process of retrospectively reviewing data from the SADB scheme and aim to circulate any findings to participants in 2026.

5. Summary

The Annual Report deals with analytical performance in terms of accuracy, precision, linearity, recovery and inter-lab CV. For most analytes performance parameters were broadly comparable to those seen in 2024. A notable exception was succinyl acetone, where a reduction in both intra- and inter-laboratory variation was evident, although performance of this analyte remains an issue: the mean inter-laboratory variation was 25.2%, ranging from 17.9% for isoleucine, to 39.5% for succinylacetone.

6. Preview Scheme 2026

The design of the 2026 scheme is essentially the same as in 2025.

7. Questions, Suggestions and Complaints

If you have any questions, comments or suggestions please address to the scientific advisor of the scheme Dr. Rachel Carling 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/

London, 26/01/2026

Dr. Rachel Carling
Scientific Advisor

Please note:
This annual report is intended for participants of the ERNDIM Special Assays in dried blood spots 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	5th February 2026	• 2025 annual report published

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