ERNDIM Quantitative Schemes Amino Acids(serum)

ANNUAL REPORT 2025

Scheme Organiser	Scientific Advisor	Website for reporting results	Administration office
Dr. R.M. Schoeman Streekziekenhuis Koningin Beatrix MCA Laboratory Beatrixpark 1 7101 BN Winterswijk The Netherlands e-mail: mca.office@skbwinterswijk.nl	Dr. Rachel Carling Biochemical Sciences,Synnovis 4th Floor, North Wing St Thomas' Hospital London SE1 7EH United Kingdom **Deputy Scientific Advisor** Dr. Zoe Barclay Biochemical Sciences,Synnovis 4th Floor, North Wing St Thomas' Hospital London SE1 7EH United Kingdom e-mail: admin@erndim.org	Mrs. Irene 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 Office, Third Floor, ICE Building 3 Exchange Quay, Salford, M5 3ED United Kingdom e-mail: admin@erndim.org

Published: London-Winterswijk, 12th February 2026[1]

1. *Purpose*

The purpose of the ERNDIM External Quality Assurance Scheme for Quantitative Amino Acids is the monitoring of the analytical quality of the quantitative assay of amino acids in plasma in laboratories involved in the screening and diagnosis of patients with inherited metabolic disorders. For details see www.erndim.org / www.ERNDIMQA.nl

2. *Participants*

A total of 299 datasets were submitted. Due to insufficient data submission, it has not been possible to generate annual reports for 11 of them. Six laboratories did not submit any results.

3. *Design*

The scheme has been designed, planned and coordinated by the scientific advisors, Dr. Rachel Carling and Dr. Zoe Barclay, and Dr. R.M. Schoeman as scheme organiser (on behalf of the MCA Laboratory), each appointed by and according to procedures laid down by the ERNDIM Board. The design includes special attention to sample content and to the layout of reports. Samples are produced with amino acids at concentration ranges seen in healthy controls and/or patients with inborn errors of metabolism although the patterns of amino acid levels may not reflect those in real life. Low levels of amino acids are sometimes included to mimic those seen in treated patients. As a sub-contractor 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.

[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 consisted of 8 lyophilised samples, all prepared from the same basic human serum which has been treated to remove most of the amino acids present and to which various amounts of analytes are added. As can be seen from Table 1 the added quantities were identical in pairs of the samples. The nature, source and the added amounts of the analytes are also summarised in table 1. 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. Pair identification, source and amounts of added analytes.

		Added quantities (micromol/L)			
Analyte	**Source**	**Sample pair 2025. 01-07**	**Sample pair 2025. 02-05**	**Sample pair 2025. 03-06**	**Sample pair 2025. 04-08**
2-aminobutyric acid	Sigma A1879	31.0	10.6	40.8	19.8
Alanine	Sigma 44526	298	50.7	902	149
Alloisoleucine	Sigma I8754	15.5	0.0	75.2	5.4
Arginine	Sigma 90538	61.3	540	20.0	180
Argininosuccinic acid	Sigma A5707	55.6	14.5	112	27.7
Asparagine	Sigma 51363	45.0	15.3	60.2	29.9
Aspartic acid	Sigma 51572	30.4	59.8	25.0	45.0
Citrulline	Sigma 1133842	150	5.1	748	14.9
Cystine	Sigma 49603	45.9	0.0	59.8	30.1
Glutamic acid	Sigma 95436	120	29.7	360	60.1
Glutamine	Sigma 76523	363	1450	121	725
Glycine	Sigma 76524	365	1450	122	724
Histidine	Sigma 73767	75.7	300	25.2	150
Hydroxyproline	Sigma PHR1939	19.9	60.4	0.0	40.1
Isoleucine	Sigma 56241	360	1440	73.0	720
Leucine	Sigma 76526	360	1440	71.9	721
Lysine	Sigma 67448	300	30.0	599	59.7
Methionine	Sigma 39496	79.8	8.0	159	15.5
Ornithine	Sigma O2375	360	18.2	719	36.0
Phenylalanine	Sigma 40541	125	1250	12.3	375
Proline	Sigma 93693	300	30.0	601	60.5
Sarcosine	Sigma S7672	14.7	6.0	29.3	9.8
Serine	Sigma 54763	62.1	14.9	89.8	30.2
Sulphocysteine	TRC S789483	16.3	0.0	160	7.9
Taurine	Sigma 93019	116	461	58.0	229
Threonine	Sigma 61506	115	459	58.5	230
Tryptophan	Sigma 51145	32.7	110	10.7	76.7
Tyrosine	Sigma 91515	300	15.2	600	60.0
Valine	Sigma 50848	301	30.5	601	59.6

All amino acids used are of the highest purity that is commercially available. Concentrations < 100 micromol/L are given to one decimal place. Samples have been tested for stability and homogeneity according to ISO 13528 in which requirements for regulatory purposes of quality management systems for medical devices are described.

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 both short- 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 different levels of detail of results which allows individual laboratories the choice of fully detailed and/or summarised reports. The “Analyte in Detail” is the most detailed report and shows results of a specific analyte in a specific sample. Thus, for the 29 amino acids in the 2025 cycle, 232 (8 x 29) Analyte-in-Detail-reports can be requested. A more condensed report is the “Cycle Review” which summarises the performance of all analytes in a specific sample (eight such Cycle Reviews can be requested in 2025). The Annual Report summarises all results giving an indication of overall performance for all analytes in all eight samples.

Depending on the responsibilities within the laboratory, participants can choose to review the annual report (e.g. Quality Managers) or the 232 detailed reports (e.g. scientific staff).

Analyte	Accuracy (mean)		Precision (CV% duplicates)		Linearity (r)		Recovery (%added analyte)		Data all labs	
	Your Lab	All labs	Your Lab	All labs	Your Lab	All labs	Your Lab	All labs	n	Interlab cv
2-Aminobutyric acid	32.0	28.9	8.5%	5.8%	0.990	0.980	168%	120%	195	10.7%
Alanine	372	355	0.9%	4.2%	1.000	0.999	99%	98%	280	9.55%
Alloisoleucine		24.3		9.1%		0.998		100%	220	16.6%
Arginine	226	216	1.9%	5.5%	1.000	0.998	99%	94%	282	9.82%
Argininosuccinic acid		30.4		17.2%		0.971		71%	157	31.9%
Asparagine	39.6	39.5	3.4%	7.6%	0.996	0.989	109%	101%	259	15.2%
Aspartic Acid	33.1	40.0	3.7%	7.6%	0.987	0.969	51%	75%	264	14.3%
Citrulline	250	229	1.3%	5.1%	1.000	1.000	110%	99%	278	12.8%
Cystine	31.6	27.5	5.5%	10.8%	0.984	0.984	88%	79%	254	14.9%
Glutamic acid	165	159	1.9%	5.2%	1.000	0.998	106%	98%	278	9.98%
Glutamine	667	660	1.6%	6.2%	1.000	0.998	97%	98%	277	10.3%
Glycine	661	659	1.0%	4.9%	1.000	0.998	98%	97%	279	9.37%
Histidine	135	134	1.8%	6.0%	1.000	0.997	96%	94%	272	9.86%
Hydroxyproline	31.5	30.1	11.6%	9.4%	0.986	0.991	111%	98%	233	17.9%
Isoleucine	641	628	1.0%	5.2%	1.000	0.998	96%	95%	283	9.14%
Leucine	OR	634	OR	5.1%	OR	0.998	OR	97%	284	9.52%
Lysine	267	258	0.9%	4.9%	1.000	0.999	106%	101%	282	9.91%
Methionine	67.9	66.8	3.1%	5.3%	1.000	0.999	103%	100%	286	11.8%
Ornithine	301	287	0.5%	5.2%	1.000	0.999	105%	100%	280	10.9%
Phenylalanine	436	429	1.4%	5.1%	1.000	0.999	97%	95%	290	10.9%
Proline	233	248	1.2%	5.2%	1.000	0.999	96%	99%	270	10.7%
Sarcosine		15.9		11.3%		0.980		110%	147	19.9%
Serine	56.9	53.8	2.2%	6.0%	1.000	0.995	108%	101%	279	9.64%
Sulfocysteine		29.7		11.8%		0.998		63%	103	29.6%
Taurine	232	218	1.5%	5.2%	1.000	0.998	106%	99%	265	9.40%
Threonine	228	217	1.2%	4.7%	1.000	0.998	104%	99%	278	7.81%
Tryptophan	75.4	84.0	7.6%	7.2%	0.992	0.988	81%	91%	236	13.2%
Tyrosine	251	242	0.6%	4.9%	1.000	0.999	102%	97%	290	9.01%
Valine	266	251	2.6%	4.4%	1.000	0.999	107%	99%	287	9.89%
Overall	237	217	2.8%	6.8%	0.997	0.994	102%	95%	255	12.9%

Above is an example of an annual report. The explanation of the flags can be found in the General information section (Use Website / Explanation Annual Report)

4. Discussion of Results in the Annual Report 2025

In this part the results as seen in the annual report 2025 will be discussed. Please keep at hand your annual report from the website when you follow the various aspects below and keep in mind that we only discuss the results of “all labs”. It is your responsibility to inspect and interpret the results of your own laboratory.

4.1 Accuracy

A first approach to evaluating your performance in terms of accuracy is comparison of your mean values for each amino acid in the eight samples with those of all laboratories. This is shown in the columns "Your Lab" and "All Labs" under the heading "Accuracy". For example, for alanine, the mean for all laboratories is 355 micromol/litre. with which you can compare the mean of your lab.

It is important to recognise that using ERNDIM QTAS 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 the analytical performance of a laboratory and is addressed in the schemes’ design. Samples provided in pairs can be regarded as duplicates from which CVs can be calculated. The column “Precision” in the annual report shows your CVs for the respective amino acids in comparison to median values for all laboratories. Precision ranges from 4.2% for alanine to 17.2 % for argininosuccinic acid. 17 amino acids demonstrated good performance with CVs < than 6%. The average intra-laboratory CV is 7%.

4.3 *Linearity*

Linearity over the whole relevant analytical range is another important parameter for analytical quality and is also examined within the schemes. A comparison of the added quantities on the x-axis and your measured quantities on the y-axis allows calculation of the coefficient of regression (**r**). The column “Linearity” in the annual report shows your **r** values for the respective amino acids in comparison to the median **r** values for all laboratories. Ideally the **r** value is close to 1.000 and ranges from aspartic acid (0.969) to 8 amino acids that give an excellent r value (r = 0.999). It must be remembered that only a limited concentration range is tested in this scheme.

4.4 *Recovery*

A second approach to describe performance is the percentage recovery of added analyte. In this approach the amounts of weighed quantities added to the samples are the assumed target values after adjustment for blank values. The correlation between weighed amounts (on the x-axis) and your measured quantities (on the y-axis) has been calculated. The slope of the resulting relation (a in y = ax + b) in this formula multiplied by 100% is your recovery of the added amounts. The outcome for your lab in comparison to the median outcome of all laboratories is shown in the column “Recovery”. The recovery is generally acceptable with 25 analytes having a recovery of between 91 - 120%. Poor recovery is evident for four analytes: sulphocysteine (63%). argininosuccinic acid (71%), aspartic acid (75%) and cystine (79%).

4.5 *Inter-laboratory CV*

For comparison of amino acid levels for diagnosis and monitoring of treatment for one patient in different hospitals, and to facilitate the use of shared reference intervals, it is essential to have a high degree of harmonisation. Part of the schemes' design is to monitor this by calculating the inter-laboratory variation. This, along with the number of laboratories that submitted results, is shown in the column "Data all labs" in the annual report. Agreement between laboratories is reasonable for most amino acids with 13 amino acids having an inter-laboratory CV of <10% and ten amino acids having an inter-laboratory CV between 10 and 15%. However, six amino acids have a CV >15% with argininosuccinic acid having the greatest CV, at 31.9%.

4.6 Number of Participating Laboratories and submitted results

For 21 of the individual amino acids results were submitted in at least 255 datasets (85% of the 299 datasets).

4.7 Inter-relationships between quality parameters

The various parameters described above often have an inter-relationship: usually more than one parameter points in the same direction towards either good or bad analytical performance.

For example, for alanine all parameters indicate good performance: precision (CV = 4.2%). linearity (r = 0.999). recovery (98%) and inter-lab variation (inter-lab CV 9.55%) with the majority of laboratories (n=280 datasets) submitting results.

4.8 Your performance: Flags

In order to easily judge performance of individual laboratories. the annual report may include flags in case of poor performance for accuracy, precision, linearity and recovery. Amino acids 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 amino acid. Criteria for flags can be found in the general information on the website (on this website under general information; interactive website, explanation annual report).

4.9 Poor Performance Policy

A wide dispersion in the overall performance of individual laboratories is evident. Table 2 shows the percentage of red flags observed. 35% 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 this will be ratified by the SAB. A letter pointing out failure to achieve these levels will be issued 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 laboratories 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 Red Flags

% Red Flags seen in Annual Report	Percentage Labs In this Category	Cumulative Percentage Of Labs
>25%	4%	4%
25%	1%	5%
20 – 25%	3%	8%
15 – 20%	5%	13%
10 – 15%	8%	21%
5 – 10%	15%	36%
0 – 5%	35%	71%
0%	29%	100%

4.10 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 amino acids 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.

4.11 Additional Specific Remarks of the Scientific Advisor

The scheme results are consistent with those seen in previous years. Argininosuccinic acid and sulphocysteine continue to be the two poorest performing analytes with inter-laboratory variation of approximately 30%, and significant under recovery. Performance of alloisoleucine, asparagine, aspartic acid, cystine and sarcosine could be improved. All other analytes demonstrated good overall performance.

5. Summary of performance

General comments

The results obtained this year are comparable to those seen previously. discrepancies with calculated recoveries are evident for a few amino acids.

Quantitative comparisons (see table 3).

The overall performance evaluated by comparing intra-laboratory variation (imprecision) with inter-laboratory variation for each amino acid reveals three main groups. There are thirteen amino acids with good intra- and inter-laboratory precision (<10%). Ten amino acids show acceptable intra- and inter-laboratory precision (intra-lab precision <10% and inter-lab precision between 10-15) and there are six amino acids for which performance is poor, with inter-laboratory CVs > 15% (range 15.2-32%).

Taking all parameters into account there is a group of 23 well-established amino acids for which there is good overall performance reflected by satisfactory values for all five analytical quality parameters (acceptable precision and inter-laboratory CV, linearity exceeding 0.9, recovery between 90 and 110%, and a high percentage of submitted results). There is also a group of six analytes where performance is less than satisfactory; allo-isoleucine; argininosuccinic acid; asparagine; aspartic acid; cystine; sulphocysteine.

Table 3. Summary of results of all laboratories

Analyte	Accuracy (mean µmol/L)	Precision (CV% duplicates)	Linearity (r)	Recovery (%added analyte)	Data all labs	
	All labs	All labs	All labs	All labs	n	Inter-lab CV
2-aminobutyric acid	28.9	5.8%	0.980	120%	195	10.7%
Alanine	355	4.2%	0.999	98%	280	9.55%
Alloisoleucine	24.3	9.1%	0.998	100%	220	16.6%
Arginine	216	5.5%	0.998	94%	282	9.82%
Argininosuccinic acid	30.4	17.2%	0.971	71%	157	31.9%
Asparagine	39.5	7.6%	0.989	101%	259	15.2%
Aspartic acid	40.0	7.6%	0.969	75%	264	14.3%
Citrulline	229	5.1%	1.000	99%	278	12.8%
Cystine	27.5	10.8%	0.984	79%	254	14.9%
Glutamic acid	159	5.2%	0.998	98%	278	9.98%
Glutamine	660	6.2%	0.998	98%	277	10.3%
Glycine	659	4.9%	0.998	97%	279	9.37%
Histidine	134	6.0%	0.997	94%	272	9.86%
Hydroxyproline	30.1	9.4%	0.991	98%	233	17.9%
Isoleucine	628	5.2%	0.998	95%	283	9.14%
Leucine	634	5.1%	0.998	97%	284	9.52%
Lysine	258	4.9%	0.999	101%	282	9.91%
Methionine	66.8	5.3%	0.999	100%	286	11.8%
Ornithine	287	5.2%	0.999	100%	280	10.9%
Phenylalanine	429	5.1%	0.999	95%	290	10.9%
Proline	248	5.2%	0.999	99%	270	10.7%
Sarcosine	15.9	11.3%	0.980	110%	147	19.9%
Serine	53.8	6.0%	0.995	101%	279	9.64%
Sulphocysteine	29.7	11.8%	0.998	63%	103	29.6%
Taurine	218	5.2%	0.998	99%	265	9.40%
Threonine	217	4.7%	0.998	99%	278	7.81%
Thryptophan	84.0	7.2%	0.988	91%	236	13.2%
Tyrosine	242	4.9%	0.999	97%	290	9.01%
Valine	251	4.4%	0.999	99%	287	9.89%
Mean	217	6.8%	0.994	95%	255	12.9%

6. *Preview of the Scheme for 2026*

Our policy is to include the same common amino acids in each year's samples as well as the occasional unusual one which are selected year to year. The design of the 2026 scheme is essentially the same as in 2025.

7. *Questions. Comments and Suggestions*

If you have any questions. comments or suggestions in addition to specific user comments please address these to the scientific advisors of the scheme. Dr. Rachel Carling (Rachel.Carling@synnovis.co.uk) and Dr. Zoe Barclay, and/or 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, 10/02/2026

Dr. Rachel Carling
Scientific Advisor

Please note:
This annual report is intended for participants of the ERNDIM Amino Acids (serum). 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 february 2026	• 2025 annual report published

END