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Message from the Chair



Dear Colleagues,

2016 has been a special year for ERNDIM, because the first steps to establish ERNDIM were taken 25 years ago. In 1991 a group of enthusiastic Doctors and Biochemists applied to the European community for a grant concentrating on a Quality Assurance Programme for laboratory testing in IEM. This first application was not granted, but a subsequent application was successful and the ERNDIM group began its work in May 1994. The BIOMED-I grant supported the successful establishment of Quality Control schemes for Quantitative Amino Acids, Qualitative Organic Acids, Quantitative Organic Acids and Special Metabolite Assays. On September 5th 1994 the ERNDIM Foundation was formally registered at the Dutch



ERNDIM's Scientific Advisory Board, Leiden, November 2016

Photo courtesy of Ms Alice Brockway

chamber of commerce in Maastricht. As many as 162 laboratories were involved in one or more schemes in the first years.

Since these early years much progress has been made and ERNDIM has evolved into a successful organisation with increases in the number of EQA schemes, as well as other activities, such as the SSIEM Academy, and a strong increase in our number of participants. Last year we had 393 participants from 59 countries. This has all been possible owing to the efforts of dedicated Scientific Advisors, the ERNDIM office team, Board members and our partner organisations, SKML and CSCQ, but in particular thanks to your confidence in ERNDIM shown by being participants in our EQA schemes. I would like to thank you for your support.

In 2016 we introduced a new scheme: Neurotransmitters in CSF, after a successful pilot stage. Novel schemes in 2017 will be Pterins in urine (Scientific Advisor: Prof Nenad Blau) and



**Dr George Ruijter, Chair,
Executive Committee**

Quantitative Acylcarnitines in serum (Scientific Advisor: Dr Pedro Ruiz Sala; see item on page 4). Currently, we are planning a pilot scheme for Special Assays in dried blood spots (page 4) alongside the very successful Special Assays schemes in serum and urine.

Dr Cas Weykamp and his team have successfully modified the ERNDIMQA website so that more detail is provided about performance in the annual report (page 3). Also, we are gradually increasing our activities with CSCQ, e.g. by moving more qualitative schemes to the CSCQ website.

The process of accreditation of ERNDIM is slowly, but steadily, taking shape. Dr Sara Gardner, Executive Administrator of ERNDIM, has nearly completed description of management requirements. We hope to move forward faster once we have appointed a new Scientific Administrator in 2017 (page 2).

Very best wishes for 2017

George Ruijter

On behalf of the ERNDIM
Executive Committee

Change to performance assessment for qualitative schemes

Proficiency testing (PT) schemes (Qualitative Organic Acids, Acylcarnitines in dried blood spots, CDG, Urine MPS and DPT) are scored on the basis of analytical performance, interpretation and recommendations for further testing.

The maximum score for each sample is 4. Across the different PT schemes, the score required for satisfactory performance is 60% of the total maximum score of a scheme year (range 60 to 63% due to rounding of scores to the nearest integer).

One of ERNDIM's aims is to provide education to participants, for instance by including interesting and challenging

samples in the PT schemes, which hopefully results in improved detection of inborn errors of metabolism. Indeed we have shown, by repeated circulation of a sample or different samples of the same disease, that proficiency has improved over the years, e.g. in Qualitative Organic Acids (Peters et al., *J Inher Metab Dis* 2016, 39, 683-687). To the laboratory, the 60% cut-off value for satisfactory proficiency may be realistic, but we must realise that from the patient perspective a missed diagnosis is a nightmare. In our continuous efforts to improve IEM diagnostics we feel that now is the time to slowly 'raise the bar'. Therefore, the Scientific Advisory board (SAB) has decided

that the level required for satisfactory performance will be increased to 70% of the total maximum score of a scheme year in the 2018 Qualitative Organic Acids and Acylcarnitines in dried blood spots schemes.

In these schemes proficiency is generally high and by this change we do not expect a strong increase in the number of participants with unsatisfactory performance.

Where appropriate, similar increases will be applied to other PT schemes in the future. Ratification of such increases will always be done by the SAB and will be communicated to participants at an early stage.

“the level required for satisfactory performance will be increased to 70% ... in the 2018 qualitative organic acids and acylcarnitines in dried blood spots schemes”



Accreditation Progress

We are still making steady progress towards applying for accreditation. In the past year we have:

- Made changes to the EQA Scheme Calendar to allow the certificates of participation to be produced earlier than previously.
- Made progress in harmonising the schedules of the Qualitative schemes.
- Enhanced the quantitative results website to improve the evaluation of results (see 'Changes to SKML results website', page 3).
- Updated the scoring policies for Qualitative and Quantitative schemes.
- Agreed a policy and procedure for introducing new schemes.
- Formalised many of the administration procedures for the Administration Office.
- Continued progress on formalising our relationships with our subcontractors.
- Recruited a new Scientific Administrator to improve the resilience of the Administration Office (see below).

National Representatives

The ERNDIM National Representatives are key members of ERNDIM and assist the ERNDIM Management Committees in disseminating the activities of the network to laboratories in their country. National Representatives are selected by ERNDIM, where possible, following nominations by the National Society. The list of National Representatives is currently being reviewed. Please contact brian.fowler@ukbb.ch for further details.

Expansion of the Administration Office

We are very grateful for support from SSIEM in funding an expansion of the Administration Office in Manchester, UK.

The funding will allow us to recruit a Scientific Administrator to help with

the management of the EQA schemes and progress towards applying for accreditation. This post is important as it will improve the resilience of the Administration Office, which currently relies on a very

small number of staff.

Our long term aim is to be able to fund this post sustainably and, with this in mind, the 2017 participation fees were increased (details on page 2).

Changes to SKML results website (www.ernidmqa.nl)

We have made some changes to the results website for the quantitative EQA schemes (www.ernidmqa.nl), with the aim of improving the differentiation between outliers and non-submissions.

Previously in the individual online annual reports 'N/A' was shown in the boxes for the analytical parameters (accuracy, precision, linearity and recovery) if either 1) no results were submitted; 2) only a few results were submitted; 3) some results were classed as outliers; or 4) a combination of few submitted results and some results classed as outliers. Poor results were not highlighted but if performance for an individual analyte was satisfactory the analyte name was shown in a green box.

Name of 'flag'	Definition	Shown in the parameter field as:	
		Text	Colour
No results	No results submitted		white
Few results	<6 out of 8 results submitted	FR	white
Outlying results	2 or more outliers	OR	purple
Outlying results and Few results	6 results from which at least one is an outlier	ORFR	yellow
Missing pair	Both results for a sample pair are missing or classed as an outlier	MP	amber
Poor result	Result in 5% of worst performances for all labs	Value of result	red
No flag	Satisfactory result	Value of result	white

The changes to the website mean that instead of 'N/A' there will now be a range of different possible 'flags' shown for the analytical parameters depending on the reason for the missing or poor result. The details of the 'flags' are given in the table above.

These different categories of 'flag' will allow a more transparent

evaluation of performance for the quantitative schemes.

Other recent changes to the website are the inclusion of z-scores in the cycle reviews (from 2016 scheme year onwards) and an update to allow multiple datasets for the quantitative schemes to be shown on the certificates of participation for the 2016 scheme year onwards.



“changes to the results website....with the aim of improving the differentiation between outliers and non-submissions”

CSCQ Results Website

CSCQ are continuing to work on expanding the Results website for the qualitative schemes. We had hoped that the CDG and Qualitative Organic Acids scheme would move to the CSCQ results website last year but unfortunately the development work has taken

longer than expected. However, the aim is for online results submission for both these schemes to begin later this year with the Acylcarnitines scheme moving to online results submission the following year.

We are very grateful for support from SSIEM in funding the

development of these CSCQ website extensions which will allow a more rapid transition to online results submission for these schemes than would otherwise have been possible.

If you have any queries or concerns please contact admin@ernidm.org.

Participation Costs

Jörgen Bierau, Honorary Treasurer, Executive Committee

As you have noticed there has been a significant increase in the scheme prices for 2017 participation. The Board of Trustees ratified an approximate cumulative 20% increase in the scheme prices over the next 4 years. This increase is necessary to secure the continuity of our Manchester Office. SSIEM have generously committed to temporarily fund the costs for a second scientific administrator giving ERNDIM time to secure the

sustainability of these costs. To ensure independence, ERNDIM have opted for an increase in fees as opposed to external sponsorship.

ERNDIM have also changed their policy on mailing costs. In 2016 a symbolic €11 mailing costs was charged to non-European participants meaning that effectively, ERNDIM has been paying for almost all the mailing costs. Starting 2017 we have begun to charge every participant

a €25 per scheme contribution for mailing costs and for 2018 we will introduce realistic costs for postage and packaging.

I do realise that these increases are inconvenient, but they are necessary to sustain ERNDIM and allow it to continue to evolve into the organisation that our community of metabolic laboratories needs and treasures.



Changes to EQA calendar



To date ERNDIM schemes are usually not completely finalised until July/August in the year following the scheme year (7-8 months after the end of the schemes) with the distribution of the certificates of participation. This situation is not ideal, e.g. EQA results cannot, or only partially, be included in management reviews held by participant labs. The Executive Committee has therefore decided to change the EQA calendar and finalise

schemes much earlier. The ultimate aim is to finalise schemes in October of the scheme year. The discussion of poor performance and critical error of the qualitative schemes will be undertaken during the November meeting of the Scientific Advisory Board so that the annual reports and performance support letters can be sent in December/January. Certificates of participation will then be issued in the first quarter of the next year. In

order to achieve this, the organisation of schemes needs to be changed. For some schemes, particularly those struggling to acquire samples, this is a challenging task. We will therefore need a transition period of 1-2 years and will hopefully be able to implement our plans for the 2018 scheme year. Your help, by providing patients samples, is crucial to achieve this.

“The ultimate aim is to finalise schemes in October of the scheme year..... Certificates of participation will then be issued in the first quarter of the next year”

New EQA Schemes

There are two new EQA schemes running in 2017:

- Acylcarnitines in serum (Scientific Advisor: Dr Pedro Ruiz-Sala)
- Pterins in Urine (Scientific Advisor: Prof Nenad Blau)

Unfortunately it was not possible to continue the Pterins/DHPR in DBS pilot which ran in conjunction with the Pterins in urine pilot.

In 2017 we will also be launching a new centre for

the Acylcarnitines in DBS scheme. Dr Ralph Fingerhut (Zurich) will be the Scientific Advisor for the new centre. Having 3 organising centres for this scheme will mean fewer participants per centre. This will allow each centre to use clinical samples of smaller volume for the EQA materials, and should mean that suitable samples will be easier to obtain.

Future Pilot Schemes

Cognitive Amino Acids

The introduction of the pilot scheme for the Cognitive amino acids, described in detail in last year's newsletter has been held back until later this year, mainly due to the need to fit the provision of online submission into the busy schedule of similar developments ongoing with CSCQ. Thus we will begin with offline submission, reporting and evaluation. About 25 labs that participate in the Quantitative Amino Acid scheme from selected countries will be invited to take part in the pilot and we aim to distribute the first cases to them at the end of June.

Special Assays in DBS

After the very positive response in the 2016 Participant Survey (see page 5), detailed plans for the scheme are being developed with the aim of launching the pilot in late 2017.

SKML will organise the scheme and results submission will be via the SKML quantitative results website.

Laboratory Directory

(www.erndim.org/home/laboratories.asp)

The laboratory directory remains available for all laboratories providing services for IEM, both as providers and users. It has been updated to include the latest versions of database programmes and website administration tools to increase ease of administration and robustness. As before we encourage present laboratories to validate and if necessary update their

details, new laboratories to join and of course we hope this will be more and more useful to users of services. We remind participating labs that if a particular assay is not present in the drop down menu it can be added to the list just by contacting us. To underpin this we plan a publicity move to promote provider lab participation and to increase awareness among practicing Physicians.



Participant Survey 2016

We would like to thank everyone who responded to the Participant Survey in June 2016. We received responses from 268 participants from 238 centres in 51 countries; giving a response rate, by centres, of 62%!

The results from the annual survey help us to continue to improve the quality and efficiency of the ERNDIM schemes and also the service that we offer you so your input is very important to us.

[A full report on the Survey Results is on the website](#) but briefly 7 out of 12 of the schemes had the same overall scores as

last year with 3 schemes (Quantitative Organic Acids, Cystine in WBC & Urine MPS) having slightly improved scores. The best scores for individual aspects were for 'Frequency of samples', 'Adequacy of the report' and 'Billing Arrangements'; while the most improved scores of the whole survey were for the Cystine in WBC (Adequacy of the report, Website display & billing arrangements) and CDG schemes (Website display & Value for money).

The responses to the questions which assess the overall

performance of ERNDIM were very positive with the overwhelming majority of respondents rating the quality of services provided by ERNDIM as 'excellent' or 'good', and having 'complete' or 'a lot' of confidence that ERNDIM can deliver the service required by participants.

We also asked if you would be interested in participating in a Quantitative special assays in dried blood spots scheme and 95 centres answered 'Yes'! Plans for this scheme are now being developed - see 'Future pilot schemes' on page 4.

“The results from the annual survey help us to continue to improve the quality and efficiency of the ERNDIM schemes and also the service that we offer you”

Use of EQA data in publications

Mick Henderson, Quality Lead, Executive Committee

We would like to remind our participants that it is our policy that ERNDIM must be acknowledged in any written or oral presentation that quotes data obtained from the use of our EQA materials. Permission to use this data must be sought from the ERNDIM Administration office before any documents are submitted for publication. In the case of quantitative schemes the office will seek permission from the relevant scheme scientific

advisor or scheme organiser. In the case of qualitative schemes, which use samples from clinical cases, in addition to the consent of the Scientific Advisor and / or Scheme organiser, permission to use any data derived from the EQA materials will only be granted if ERNDIM can confirm with the donating clinician/organisation that appropriate consent was obtained from the patient / patient's guardian. A standard text

acknowledgement will then be supplied. After the data has been published a copy of the publication, with full reference/citation information, should be sent to the ERNDIM office.

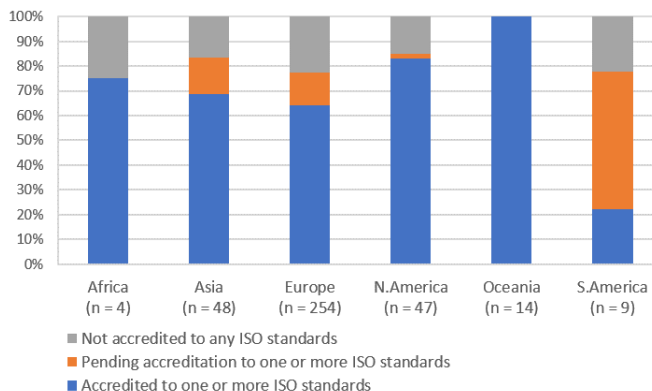
Can I emphasise that this is not just good practice but it is also good for ERNDIM to be advertised in this way. And in addition it provides a protection for the authors of the paper.

Accreditation Status of ERNDIM Participants

During registration for the 2017 EQA schemes labs were asked to complete a short survey asking for details of the ISO standards they are accredited to.

95% of the labs that registered for the 2017 EQA schemes (376/397) completed the survey which asked if labs were accredited to ISO 9001, ISO 15189, ISO 17025 or another ISO standard.

254/376 labs (68%) replied that they were accredited to one or more ISO standards, with 50 of these labs (13%) stating they were accredited to more than one ISO standard. A further 47/376 labs



(13%) reported that their accreditation to one or more ISO standards is pending, while 75/376 labs (20%) stated that their lab

was not accredited (or had any pending applications) for any of the specified ISO standards.





MetabERN

As you probably are aware, the European Commission has put out a call for the establishment of European Reference Networks (ERNs). The goal of the ERN programme is to improve care for patients with rare diseases that require concentration of resources and expertise, i.e. by ensuring that European centres use the same treatment protocols and diagnostic procedures and establish best practice. The goal of ERNDIM is to reach a consensus among European

biochemical genetics laboratories on reliable and standardised procedures for diagnosis and monitoring of inherited metabolic diseases by providing external quality assurance schemes and by educational activities. This very much corresponds to the goal of ERNs and the ERNDIM Executive Committee has therefore contacted Prof Maurizio Scarpa, who has successfully applied with a proposal 'MetabERN', a network of health care providers active in



European
Reference
Networks

inborn errors of metabolism. ERNDIM and MetabERN have agreed to collaborate in order to ensure the highest possible quality of laboratory services within participating health care providers. ERNDIM will not financially support MetabERN, but will be represented in the Advisory Board of MetabERN by Dr Victor Kožich. The role of ERNDIM within MetabERN is expected to develop in 2017-2018.

“ERNDIM offers a small number of Training Support Grants each year”

Training Support Grants

As part of our aim to help improve standards in biochemical genetic testing ERNDIM offers a small number of Training Support Grants each year.

This grant is designed for trainees, in a permanent laboratory position, to gain experience and knowledge in a European ERNDIM approved laboratory in order to develop or introduce new methods to their own laboratory.

Funds can be applied for to cover the travel and accommodation costs incurred by such visits and a maximum of 6 grants will be awarded each year, subject to the approval of the Executive

Committee. Full application criteria are given in the application form which can be found on the ERNDIM website under [TrainingGrants](#).

In 2016 one training support grant was awarded:

- Dr Zekušić from University Hospital Centre Zagreb, Croatia visited Prof Bonham's Laboratory at Sheffield Children's Hospital in the UK to increase her understanding of the analysis and interpretation of acylcarnitine profiles in plasma.

You can read Dr Zekušić's report on her visit on the website under [TrainingTravel Grant Reports](#).

Chromatogram Library

Work on the the ERNDIM chromatogram Library has been held up somewhat since the student helping on the project finished her time with us last April. Nevertheless work has continued on finalising the initial phase of the project and we hope to go online for all ERNDIM participants later in the year. When it is complete the library will catalogue the resources available in the Qualitative scheme annual reports and our contributions to the SSIEM academy and will be accessible from www.erndim.org.



ESHG EuroGentest Quality Subcommittee



The ESHG – EUGT Quality sub-committee met twice in 2016. The main items the committee is dealing with currently are:

- The presentation of the EQA providers' annual reports focussing on overall

performance of labs.

- Attempts to bring on board non-EUGT schemes by inviting them to join us in performance evaluation and to participate in a workshop.
- A scheme for EQA of genetic counselling will become an official scheme in 2017.
- As an initial move in relation

to quality issues in Newborn screening, we will monitor current practice in information and support given to parents.

The current Chair, Ros Hastings is standing down and we are looking for a successor together with the Board of the ESHG.

ERNDIM Management Committees

Scientific Advisory Board (SAB)

During 2016 there were a number of changes to the membership of the SAB:

- DPT UK: Prof Jim Bonham stepped down as Scientific Advisor (SA) and Mrs Joanne Croft has taken over.
- Quantitative Amino Acids: Dr Rachel Carling has taken over as SA from Prof Brian Fowler.
- Quantitative Organic Acids: Dr Geert Martens stepped down as SA and Mme Clothilde Roux has taken over.

Changes for 2017:

- Acylcarnitines in DBS - Dr Ralph Fingerhut is joining this scheme as the SA for a new organising centre in Zurich.
- Acylcarnitines in serum - Dr Pedro Ruiz-Sala is the SA for this new scheme.
- Cystine in WBC - Dr Daniel Herrera has taken over as SA from Dr Mick Henderson.
- Pterins in Urine - Prof Nenad Blau is the SA for this new scheme.

Executive Committee & Board of Trustees

There were no changes to the Executive Committee or Board of Trustees in 2016.

Full details of the members of the Board of Trustees, the Executive Committee and the Scientific Advisory Board are on the website ([About](#), [Organisation and Key Persons](#)).

SSIEM Academy



ERNDIM collaborated with ETAC to organise the two day training meeting that was held in Freiburg on the 18th and 19th April 2016.

The course was heavily oversubscribed; 132 applications were received and 41 scientists and 37 clinicians attended.

The topics of the Academy were Amino acids, Hyperammonemia, Urea cycle defects and Metabolic liver disease.

The joint clinical and lab workshops proved very popular and the feedback was positive with over 98% of the returned evaluation forms agreeing or strongly agreeing that “The programme was relevant to current practice” and that “The academy was relevant to my educational needs”.



The topics for the 2017 Academy (24th-25th April 2017, Lyon) were organic acidemias, fatty acid oxidation defects and cardiomyopathy.

Registration was in November 2016 and all available places were filled as 123 applications were received for the 80 places.

As usual, the feedback was very positive with all the joint lectures and workshops scoring very well for both clarity and educational value and 100% of the returned evaluation forms agreeing or strongly agreeing that “The programme was relevant to current practice” and that “The academy was relevant to my educational needs”.

Information on future Academies will be posted on the ERNDIM website under [News & Events](#).

“100% of returned evaluation forms agreed that the academy was relevant to my educational needs”

Participants' Meeting 2017

The annual ERNDIM participant meeting, including the workshops of the five diagnostic proficiency testing schemes is usually held at the annual symposium of the SSIEM. This year there will be no SSIEM meeting and we expect that not very many ERNDIM participants will be able to attend the ICIEM meeting in Rio de Janeiro. Therefore the ERNDIM Board decided to hold a separate meeting to include the DPT

discussions and scientific workshops. This will be similar to the very successful meeting we held in Basel in 2009.

The meeting will take place November 21st and 22nd, 2017 in Manchester. The scientific programme of Nov 21st, contains a session on Novel diagnostic approaches and treatment of Lysosomal Storage Diseases. On Nov 21st the Diagnostic Proficiency Testing schemes meetings will also be held and we

will organise a social dinner. On Nov 22nd workshops on lysosomal enzyme testing, neurotransmitters in CSF, acylcarnitines in DBS and organic acids will be organised as well as a session on current and future developments in Biochemical Genetics testing and external quality assurance.

A detailed scientific programme, venue and fees will be announced soon by email and on the ERNDIM website.



Website update (www.erndim.org)

Documents added in the last year

• [Newsletters](#)

- Newsletter 2017

[EQA Schemes](#)

- EQA scheme calendar
- Information on how to donate samples

Meetings & Reports

• [Meetings](#)

- Presentations, ERNDIM meeting, Rome, Sept. 2016

• [Reports](#)

- Report on the 2016 Participant Survey
- 2015 & 2016 EQA scheme annual reports
- Critical Errors in the 2015 Qualitative EQA schemes

Training & Education

• [Travel Grant Reports](#)

- Travel Grant Report by Dr Zekušić

• [Educational Documents](#)

- Methods for White cell cystine assay

Registration Website (www.erndim.org/qa)

Under the Participant Information tab which is only accessible if you log into the Registration Website:

• [General Information](#)

- ERNDIM participants' Guide
- ERNDIM Registration Website manual
- Educational Participation Application forms
- Link to Repeat Sample Request form

• [EQA Schemes](#)

Scheme specific information will be uploaded here,

Meeting of ERNDIM's Scientific Advisory Board, Leiden, November 2016 [photo on page 1]

Left hand side, from front: Prof Brian Fowler, Dr Christine Vianey-Saban, Dr Kees Schoonderwoerd, Dr Claus-Dieter Langhans, Dr Cas Weykamp (SKML), Dr George Ruijter, Dr Pedro Ruiz-Sala, Dr Begoña Merinero,

Dr Simon Pope, Mrs Irene de Graaf (SKML), Dr Sara Gardner.

Right hand side, from front: Dr Charles Turner, Dr Jörgen Bierau, Dr Dirk Lefeber, Mme Clothilde Roux, Dr Geert Martens,

Mrs Jane Dalley, Dr Xavier Albe (CSCQ), Dr Daniel Herrera, Ms Katie Sheils, Dr Marie Jackson, Dr Mick Henderson, Dr Joanne Croft.

Photo courtesy of Ms Alice Brockway



“Working towards a consensus between Biochemical Genetics Centres on reliable and standardised procedures for diagnosis, treatment and monitoring of inherited metabolic diseases”

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