QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

ERNDIM Administration Office
Manchester Centre for Genomic Medicine
6th Floor, St Mary's Hospital, Oxford Road,
Manchester M13 9WL, United Kingdom.
Tel: +44 161 276 6741
Fax: +44 161 850 1145
Email: admin@erndim.org

Qualitative Blood Spot Acylcarnitine Scheme

Scientific Advisor/Scheme Organiser
Mr Charles Turner
WellChild Laboratory, Arctic (1st Floor),
Evelina London Children's Hospital,
London SE1 7EH, UK
Tel: +44 20 718 80159
Fax: +44 20 718 84702
Email: chas.turner@kcl.ac.uk

Deputy Scientific Advisor/Scheme Organiser
Prof Neil Dalton
WellChild Laboratory, Arctic (1st Floor),
Evelina London Children's Hospital,
London SE1 7EH, UK
Tel: +44 20 718 80159
Fax: +44 20 718 84702
Email: neil.dalton@kcl.ac.uk

Annual Report London 2017

Date of publication: 27 Mar 2018

1. **Scheme Design**
   The scheme has been designed and planned by Dr Charles Turner and Prof Neil Dalton as Scientific Advisor/Scheme Organiser and deputy Scientific Advisor/Scheme Organiser, respectively, both appointed by and according to procedures laid down by the ERNDIM Board.

2. **Samples**
   All EQA materials are 30-50µl of lithium heparin anticoagulated whole blood dried as blood spots on Perkin Elmer (Ahlstrom) 226 paper. All samples are obtained following local ethical and consent guidelines.

3. **Shipment**
   Two circulations of 3 samples each (2017.A-C and 2017.D-F) were sent out to the 42 laboratories from 14 countries worldwide assigned to the London centre of the ERNDIM dried blood spot acylcarnitine scheme. The first circulation was sent out in June, with a return date of 21st July 2017 and the second in October with a return date of 8th December 2017.

4. **Receipt of results**
   Returns for circulation 2017.A-C were received from 41 (98%); 36 of these arrived by the initial due date. For circulation 2017.D-F valid returns were received from 40 (95%); 34 of these arrived before the due date.

   There were no laboratories who failed to make a return on both circulations. Two laboratories reported on circulation 2017.A-C only, and one on circulation 2017.D-F only.

5. **Scoring scheme**
   In the process of working towards accreditation for ERNDIM there is a need for harmonization of performance assessment within the qualitative schemes (see ERNDIM 'Newsletter Spring 2013' at www.erndim.org). In 2013 we changed the scoring system from the former scale (-2, -1, 0, +1, +2) to the four point system (+1, +2, + 3, +4) which is used also in the DPT schemes. In this system a maximum of two points is given each for analytical results and interpretation, with the latter including suggestions for further testing/actions. The total score achievable for a single circulation of three samples is twelve and twenty four for the whole sample set of six samples per year. To obtain satisfactory performance a score of 16 or more should be achieved on two returns. This will increase to 17/24 for 2018. In 2017 an acceptable score was defined as 16/24. Laboratories that participate only in one circulation are treated as non-submitters.

   From the 2014 scheme onwards another criterion for satisfactory performance is the absence of any "critical error" which is defined as an error resulting from seriously misleading analytical findings and /or interpretations with serious clinical consequences for the patient.

6. Results of samples and evaluation of reporting

All submitted results are treated as confidential information and are only shared with ERNDIM approved persons for the purposes of evaluation and reporting.

Participants were asked to respond via email using a supplied report template, and to send a scan and/or table of quantitative results if possible. All laboratories responded by email.

Most laboratories provided a suggested/differential diagnosis. Most suggested some form of appropriate follow-up testing to confirm a putative diagnosis. A summary of the samples sent, and the number of respondents detecting the key acylcarnitine and/or suggesting the definitive diagnosis as part of their differential diagnosis, is given in the table below.

Sample	Enzyme/transporter defect	Diagnostic Acylcarnitine	Respondents
2017.A	Methylmalonyl CoA mutase deficiency (MMA: OMIM 251000)	C3, C3 based ratios, C4DC, Low free carnitine	41/41 ^C3 or C3 ratio, 12/41 ^C4DC 41/41 MMA
2017.B	Medium chain acyl CoA dehydrogenase deficiency (MCADD: OMIM 201450)	C8, C10:1, C6, C8/C10, C8/C2 ratio Low C0	41/41 ^C8, 26/41 ^ratio, 17/41 ^C10:1 20/41 low C0 41/41 MCADD
2017.C	Long-chain 3-hydroxyacyl CoA dehydrogenase deficiency (LCHAD: OMIM 609015)	^C14OH-C18OH ^C14:1OH-C18:1OH hydroxyacylcarnitines	35/41 ^LCOH, 35/41 LCHAD
2017.D	Very long chain acyl CoA dehydrogenase deficiency (VLCADD, OMIM 201475)	^C14:1 ^C14:1 based ratios low C0	37/40 ^C14:1 15/40 ^ ratio 37/40 VLCADD
2017.E	Beta ketothiolase deficiency (BKT, OMIM 203750),	^C5:1 ^C5OH	39/40 ^C5:1 39/40 ^C5:1 38/40 BKT
2017.F	Medium chain acyl CoA dehydrogenase deficiency (MCADD: OMIM 201450)	C8, C10:1, C6, C8/C10, C8/C2 ratio	40/40 ^ C8, 26/40 ^ratio, 13/40 ^C10:1 39/40 MCADD

The profiles from patients with medium chain acyl CoA dehydrogenase deficiency (2017.B & 2017.F), were characteristic of the disorders, 2017.B being carnitine deplete and 2017.F carnitine replete. The raised C8 was correctly identified by all laboratories who submitted results, and all suggested the correct diagnosis except for one lab who omitted any suggested diagnosis or follow up suggestions on 2017.F. All laboratories also correctly identified the sample from the patient with methylmalonic acidaemia, and most the sample from the patient with BKT. The sample from the patient with LCHAD (2017.C) caused some problems of detection of the long chain hydroxyacyl carnitines. One respondent had clearly made a pre- or post analytical error and duplicated the results from sample 2017.A, but 4 did not recognise the elevation in the diagnostic metabolites, which while subtle, (the patient was well at the time of sampling) were detected by most laboratories. This is worrying as acylcarnitine analysis is a preferred first line test for the detection of this disorder. The sample from the patient with VLCADD was correctly identified by most participants although the low free carnitine and increase in the (C16+C18:1)/C2 ratio, led 3 respondents to specify CPT2 or CACT to the exclusion of the correct diagnosis of VLCADD.

Proficiency per sample

Sample	No of returns	A (%)	I (%)	Total (%)
2017.A	41	100.0%	100.0%	100.0%
2017.B	41	100.0%	98.8%	99.4%
2017.C	41	87.8	85.4%	86.6%
2017.D	40	96.3%	93.8%	95.0%
2017.E	40	97.5%	96.3%	96.9%
2017.F	40	100.0%	98.8%	99.4%

Cumulative Scores

The maximum score achievable was 24 points.

Total Score	No of labs (who submitted results for both rounds)
24	31
23	1
22	2
21	2
20	2
14	1

7. Donation of samples

Once again, we are extremely grateful to the centres that can provide informative material for circulation. If any participants can provide samples in the future it would enormously facilitate this scheme, providing, as it does, genuine clinically derived samples for assay and interpretation. 3-4ml of lithium heparin anticoagulated whole blood or 50-60 30-50µl blood spots on Whatman (Schleicher & Schuell) 903 or Perkin Elmer 226 paper would provide sufficient material for one circulation. Samples for use in the scheme should be accompanied by a short clinical history and confirmation that informed consent/local ethical approval (as required in the referring centre) for use of the sample has been obtained.

Charles Turner
Clinical Scientist

Neil Dalton
Professor of Paediatric Biochemistry