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**
PD Dr. Ralph Fingerhut
University Children´s Hospital
Newborn Screening Laboratory
Steinwiesstr. 75
CH-8032 Zurich
Switzerland
**Tel:** +41 44 266 7732
**Fax:** +41 44 266 8110
**Email:** ralph fingerhut²kispi.uzh.ch

**Deputy Scientific Advisor/Scheme Organiser**
Prof. Dr. Johannes Häberle
University Children´s Hospital
Departement of Metabolism
Steinwiesstr. 75
CH-8032 Zurich
Switzerland

# Annual Report Zurich 2017

**Date of issue: 19th April 2018**

***Amended report issued: 1st May 2018[1]***

## 1. Scheme Design

The scheme has been designed and planned by Dr. Ralph Fingerhut as Scientific Advisor/Scheme Organiser, appointed by and according to procedures laid down by the ERNDIM Board.

## 2. Samples

All EQA materials are 30-50 µl of lithium heparin or EDTA 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 (2017.01.A-C and 2017.02.A-C) were sent out to the 40 laboratories from 23 countries worldwide assigned to the Zurich centre of the ERNDIM dried blood spot acylcarnitine scheme. One laboratory was an Educational Participant. The first circulation was sent out on 28th July 2017, with a return date of 28th August 2017 and the second on 17th October 2017 November with a return date of 20th November 2017.

## 4. Receipt of results

Returns for circulation 2017.01.A-C were received from 36 (90%); 29 of these arrived by the initial due date. For circulation 2017.02.A-C valid returns were received from 36 (90%); 31 of these arrived before the due date. Due to problems with the email account of the scheme advisor, it is possible that results were sent in time, but were not received. For this reason it was decided, that as no results had been published, results submitted after the submission deadlines would be accepted so that no laboratory would be disadvantaged.

The Educational Participant is not included in the statistics; the laboratory did not report results.

There were 3 laboratories, excluding the Educational Participant, who failed to make a return on either circulation. All other laboratories (36) reported on both sample circulations.

## 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

| Version Number (& Date) | Amendments |
|---|---|
| [1] version 2 (01 May 2018) | • Page 3, Tables 2 & 3: updated to reflect changes to scores in Appendix 1 (see below).<br>• Page 5, Appendix 1: interpretation scores for samples 2017.01.A-C have been updated for labs 26 and 37. |

samples is twelve and twenty-four for the whole sample set of six samples per year. To obtain satisfactory performance a score 66.7% (16/24 points) or more should be achieved on two returns. For the 2017 scheme, sample 2017.02.C was classed as an Educational sample (see section 6) so the level necessary for satisfactory performance was adjusted to 13/20 points.

Laboratories that participate only in one circulation are treated as non-submitters.

For 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. For the 2017 scheme no critical errors were identified.

## 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.

All 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.

**Table 1**: Diagnoses of 2017 samples

| Sample | Clinical Information | Enzyme/ transporter defect | Diagnostic Acylcarnitines | Respondents |
|---|---|---|---|---|
| **2017.01.A** | 6 month old boy, normal psychomotor development, under treatment | Cobalamin B | C3, C4DC | C3, C4DC |
| **2017.01.B** | Diagnosed in NBS, normal development, under treatment | MCAD | C6, C8, C10, C10:1 | C6, C8, C10, C10:1 |
| **2017.01.C** | Diagnosed in NBS, under treatment | 3-HMG-CoA lyase deficiency | C5-OH, C6DC | C5-OH, C6DC |
| **2017.02.A** | 4 year old boy, metabolic acidosis, under treatment | Isovaleric acidaemia | C5 | C5 |
| **2017.02.B** | Diagnosed in NBS, normal development, under treatment | MCAD | C6, C8, C10, C10:1 | C6, C8, C10, C10:1 |
| **2017.02.C** | Nine month old boy, fever, vomiting, diarrhea and mild dehydration | Glutaric acidaemia (low excretor) | C5DC | C5DC |

The profiles from patients with medium-chain acyl-CoA dehydrogenase deficiency (2017.01.A & 2017.02.B), and Isoveric acidaemia (2017.02.A) were characteristic of the disorders and were correctly assigned by all laboratories who submitted results. Reduced total proficiency is most likely due to a mix-up of samples 2017.01B & C in one laboratory. In sample 2017.01.A (Cobalamin B disorder) all laboratories correctly identified elevated propionylcarnitine (C3), only 2 laboratories reported additional measurement of methionine, however the low/decreased methionine was not considered for interpretation, which could have been a hint to Cobalamin disorders primarily, rather than PA or MMA. 3-HMG-CoA lyase deficiency (2017.01.C) was only correctly identified by 17 laboratories, and Glutaryl-CoA dehydrogenase deficiency (2017.02.C) only by 10 laboratories. 4 laboratories measured borderline or slightly elevated glutarylcarnitine, but did not consider GA-I. Since the patient with GA-I is a low excretor, the correct interpretation was a real challenge. However, together with the sample of the patient with 3-HMG-CoA lyase deficiency it becomes quite clear that the overall detection of dicarboxylic acids is a challenge.

**Table 2:** Proficiency per sample

| Sample | No of returns | A (%) | I (%) | Total (%) |
|---|---|---|---|---|
| **2017.01.A** | 36 | 98.6 | 80.6 | 89.6 |
| **2017.01.B** | 36 | 95.8 | 91.3 | 94.4 |
| **2017.01.C** | 36 | 72.2 | 84.7 | 78.5 |
| **2017.02.A** | 36 | 100 | 97.2 | 98.6 |
| **2017.02.B** | 36 | 100 | 97.2 | 98.6 |
| **2017.02.C** | 36 | 33.3 | 29.2 | 31.3 |

Due to the low overall proficiency, sample 2017.02.C has been classed as an Educational sample and is not included in the total scores in Appendix 1.

## 7. Cumulative Scores

The maximum score achievable was 20 points, due to the classification of sample 2017.02.C as an Educational sample.

**Table 3:** Cumulative scores

| Total Score | No of labs (who submitted results for both rounds) |
|---|---|
| 20 | 11 |
| 19 | 11 |
| 18 | 9 |
| 17 | 2 |
| 16 | 1 |
| 15 | 0 |
| 14 | 0 |
| 13 | 0 |
| 12 | 0 |
| 11 | 1 |
| 10 | 1 |
| **Total Labs:** | **36** |

## 8. Overall proficiency

The full scores for all laboratories registered for the 2017 scheme are in Appendix 1 (page 4). Two laboratories scored less than 13/20 points and will be sent performance support letters.

## 9. Donation of samples

Once again, we are extremely grateful to the centres that have provided 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. 3-4 ml of lithium heparin anticoagulated whole blood or 70-80 30-50 µl 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.

## 10. Changes for the 2018 scheme

### a) Change to score required for satisfactory performance

As agreed by the Scientific Advisory Board, the score required for satisfactory performance in the 2018 scheme will change from 66.7% to 70%.

**b) Change in Scientific Advisor**

For the 2018 scheme the organising centre for this scheme will be Rome. ERNDIM would like to thank Dr Fingerhut for all his hard work organising this scheme and evaluating the results during 2017 and welcome Dr Cristiano Rizzo as the new Scientific Advisor for this scheme.

**Dr Ralph Fingerhut**
**Clinical Scientist**

**Note:** This annual report is intended for the participants of the Acylcarnitines in DBS Zurich scheme. The contents of this report or data derived from the use or analysis of ERNDIM EQA materials must not be used in written publications or oral presentations unless the explicit prior consent of ERNDIM has been granted.

**Appendix 1** Full scores for all laboratories registered for the 2017 scheme (* A = analytical; I = Interpretation; ** sample 2017.02.C was classed as an Educational sample and the scores for this sample were not included in the total scores)

| Anonymised lab no. | No. of returns (0/1/2) | Total Score (1st +2nd round) | % of Max Score | 1st round | | | | | | | 2nd round | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 2017.01.A | | 2017.01.B | | 2017.01.C | | 1st round score | 2017.02.A | | 2017.02.B | | 2017.02.C** | | 2nd round score |
| | | | | A* | I* | A* | I* | A* | I* | | A* | I* | A* | I* | A* | I* | |
| **1** | 2 | 19 | 95% | 2 | 2 | 2 | 2 | 1 | 2 | 11 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **2** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **3** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **4** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **5** | 2 | 18 | 90% | 2 | 2 | 2 | 2 | 1 | 1 | 10 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **6** | 2 | 19 | 95% | 2 | 1 | 2 | 2 | 2 | 2 | 11 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **7** | 2 | 19 | 95% | 2 | 2 | 2 | 2 | 1 | 2 | 11 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **8** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **9** | 2 | 17 | 85% | 2 | 2 | 1 | 1 | 1 | 2 | 9 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **10** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **11** | 2 | 19 | 95% | 2 | 1 | 2 | 2 | 2 | 2 | 11 | 2 | 2 | 2 | 2 | 1 | 0 | 8 |
| **12** | 2 | 19 | 95% | 2 | 2 | 2 | 2 | 1 | 2 | 11 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **13** | 2 | 18 | 90% | 2 | 2 | 2 | 2 | 1 | 1 | 10 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **14** | 2 | 10 | 50% | 2 | 0 | 2 | 0 | 2 | 0 | 6 | 2 | 0 | 2 | 0 | 0 | 0 | 4 |
| **15** | 2 | 18 | 90% | 2 | 2 | 2 | 2 | 1 | 1 | 10 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **16** | 2 | 19 | 95% | 2 | 1 | 2 | 2 | 2 | 2 | 11 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **17** | 0 | | | | | | | | | | | | | | | | |
| **18** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 1 | 0 | 8 |
| **19** | 2 | 19 | 95% | 2 | 2 | 2 | 2 | 1 | 2 | 11 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **20** | 2 | 11 | 55% | 2 | 1 | 0 | 0 | 0 | 0 | 3 | 2 | 2 | 2 | 2 | 1 | 1 | 8 |
| **21** | 2 | 18 | 90% | 2 | 1 | 2 | 2 | 1 | 2 | 10 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **22** | 0 | | | | | | | | | | | | | | | | |
| **23** | 2 | 18 | 90% | 2 | 2 | 2 | 2 | 1 | 1 | 10 | 2 | 2 | 2 | 2 | 1 | 0 | 8 |
| **24** | 2 | 18 | 90% | 2 | 1 | 2 | 2 | 1 | 2 | 10 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **25** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **26** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **27** | 2 | 16 | 80% | 2 | 1 | 2 | 2 | 1 | 0 | 8 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **28** | 0 | | | | | | | | | | | | | | | | |
| **29** | 2 | 19 | 95% | 2 | 2 | 2 | 2 | 1 | 2 | 11 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **30** | 2 | 18 | 90% | 2 | 1 | 2 | 2 | 1 | 2 | 10 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **31** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **32** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **33** | 2 | 17 | 85% | 2 | 1 | 2 | 2 | 1 | 1 | 9 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **34** | 0 | | | | | | | | | | | | | | | | |
| **35** | 2 | 19 | 95% | 2 | 2 | 2 | 2 | 1 | 2 | 11 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **36** | 2 | 20 | 100% | 2 | 2 | 2 | 2 | 2 | 2 | 12 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **37** | 2 | 18 | 90% | 1 | 1 | 2 | 2 | 2 | 2 | 10 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **38** | 2 | 18 | 90% | 2 | 1 | 2 | 2 | 1 | 2 | 10 | 2 | 2 | 2 | 2 | 2 | 2 | 8 |
| **39** | 2 | 19 | 95% | 2 | 1 | 2 | 2 | 2 | 2 | 11 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |
| **40** | 2 | 19 | 95% | 2 | 2 | 2 | 2 | 1 | 2 | 11 | 2 | 2 | 2 | 2 | 0 | 0 | 8 |