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To

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Changes: text added to page 7 on changes for the 2018 scheme on the level required for satisfactory performance.
Please discard the original report dated 01 February 2018

ERNDIM QA Scheme for Qualitative Blood Spot Acylcarnitine Analysis

Annual Report 2017

Participation

The geographical distributions of the active participants of the quality assurance scheme organized and distributed through the centre of Heidelberg in 2017 are shown in Table 1. London and Heidelberg participate in each other´s scheme and the two centers work closely together under the auspices of the ERNDIM Scientific Advisory Committee.

Country	Number of laboratories
Argentina	3
Austria	1
China	3
Croatia	1
France	15
Germany	9
Hong Kong	1
Luxembourg	1
Switzerland	1
The Netherlands	5
Total	40

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Samples and results

Two sets of three blood spot samples (total 6; sample number 2017.01, 2017.02, 2017.03, 2017.04, 2017.05 and 2017.06) were distributed to **40 laboratories**.

Thirty-seven laboratories (93%) returned results for both circulations. Two participants answered only to one, and one participant did not send results at all.

Table 2: Receipt of results

Circulation	In time returns	Late returns	Total
1. circulation	36	3	39
2. circulation	35	2	37

Shipment of the samples

Blood spot samples prepared on Whatman 903™ specimen collection paper were shipped on June 8th, 2017 and on October 4th, 2017.

Table 3: Distribution of scores for individual samples (laboratories making returns)

		4	3	2	1	0
Sample 2017.01	Propionic acidaemia	39	2			
Sample 2017.02	Long-chain hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency	28	1	7	1	2
Sample 2017.03	Isovaleric acidaemia	39				
Sample 2017.04	Cobalamin A deficiency	34	1		1	1
Sample 2017.05	Normal profile	36	1			
Sample 2017.06	3-hydroxy-3- methylglutaryl-CoA lyase deficiency	33	3	1		

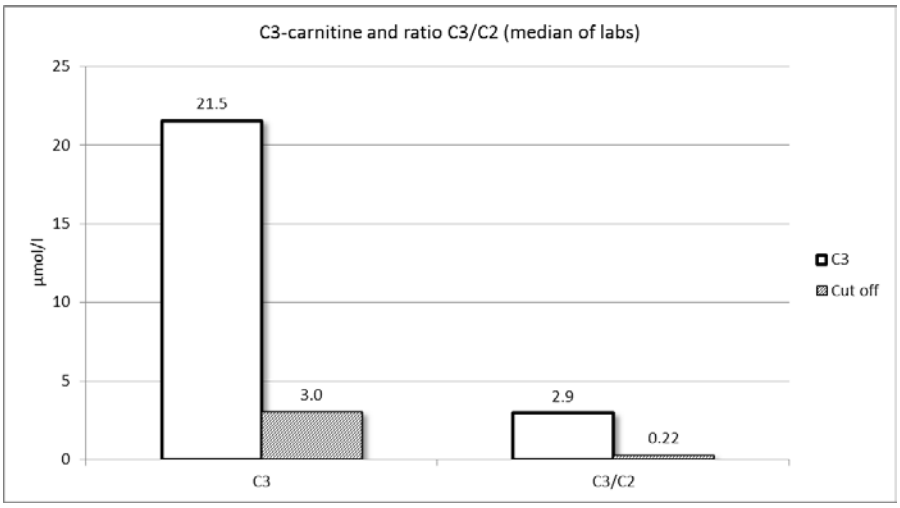
Comments on performance

Sample 2017.01:

Patient details: 7-year-old boy, presented with fever and metabolic acidosis

Known diagnosis: propionic acidaemia

Analytical details Elevated C3 and ratio C3/C2.



- Methylmalonic acid in DBS (Heidelberg): 0.98 µmol/l (< 2.14)

Analytical Performance: All labs clearly identified the relevant metabolite (100%)

Diagnostic Performance: All participants diagnosed either propionic acidaemia or methylmalonic acidaemia. The majority (90%) preferred PA over MMA as their first choice

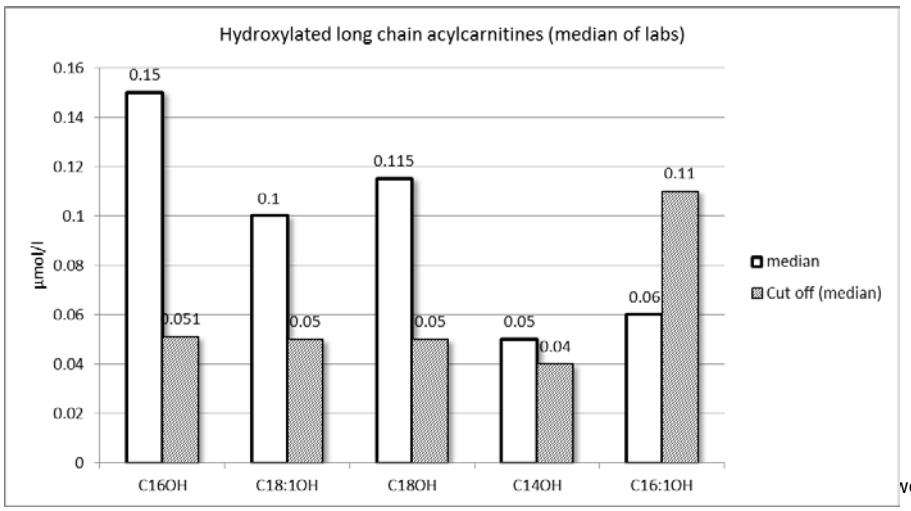
Overall impression: Very good analytical and diagnostic performance.

Sample 2017.02:

Patient details: 3-year old girl with recurring rhabdomyolysis

Known diagnosis: long-chain hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency

Analytical details Elevated C16-OH, C18:1-OH, C18-OH, C14-OH



Analytical Performance: overall 67 % reported elevated C16OH, C18:1OH and C18-OH. Only 18% found C14-OH elevated and 13% C16:1-OH.

Diagnostic Performance: 72% diagnosed LCHAD deficiency / mitochondrial trifunctional protein (MTFP) deficiency.

Overall impression: This was not an easy sample because the amounts of the relevant metabolites were only slightly elevated. Labs with somewhat higher upper cut-off levels were liable to miss the diagnosis.

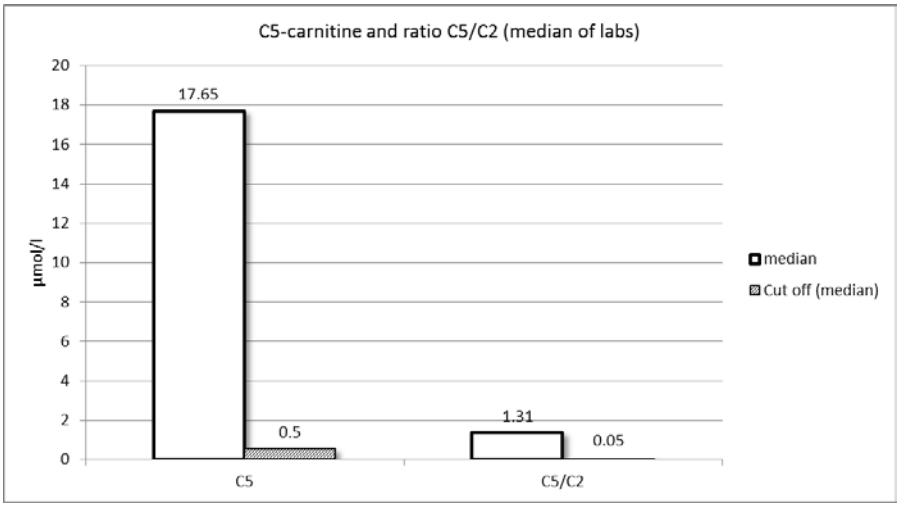
Critical error: Failure to diagnose LCHAD deficiency was deemed not to be a critical error by the ERNDIM Scientific Advisory Board due to the low overall performance.

Sample 2017.03:

Patient details: 4-year-old boy, poor feeder with frequent vomiting

Known diagnosis: isovaleric acidaemia

Analytical details Elevated C5 and ratio C5/C2.



Analytical Performance: 100%

Diagnostic Performance: 100%.

Overall impression: Very good analytical and diagnostic performance.

This was a straightforward sample.

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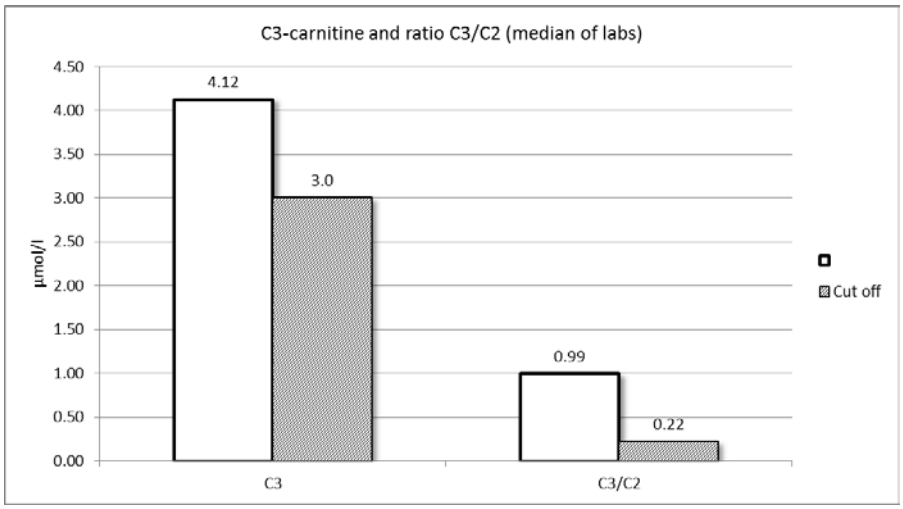
Sample 2017.04:

Patient details: 13-month-old girl, poor feeding with intermittent metabolic acidosis

Known diagnosis: cobalamin A deficiency

Analytical details Increased C3 and ratio C3/C2



- Methylmalonic acid in DBS (Heidelberg): 46.22 µmol/l (‹ 2.35)

Analytical Performance: 92% for C3-carnitine. Very conclusive could also be the ratio C3/C2, which was reported by only 49%.

Diagnostic Performance: 93% for methylmalonic acidaemia, propionic acidaemia or disorders of cobalamin metabolism.

Overall impression: Good analytical and diagnostic performance despite the relatively small elevation of C3-carnitine.

Critical error: A critical error was defined by the ERNDIM Scientific Advisory Board for failing to identify elevated C3-carnitine or any noticeable ratios and giving a normal diagnosis without recommending organic acid analysis in urine.

Sample 2017.05:

Patient details: 59-year old male presented with muscle pain

Known diagnosis: normal profile

Analytical details no abnormalities

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Analytical Performance: 68% of the labs found no abnormal acylcarnitines

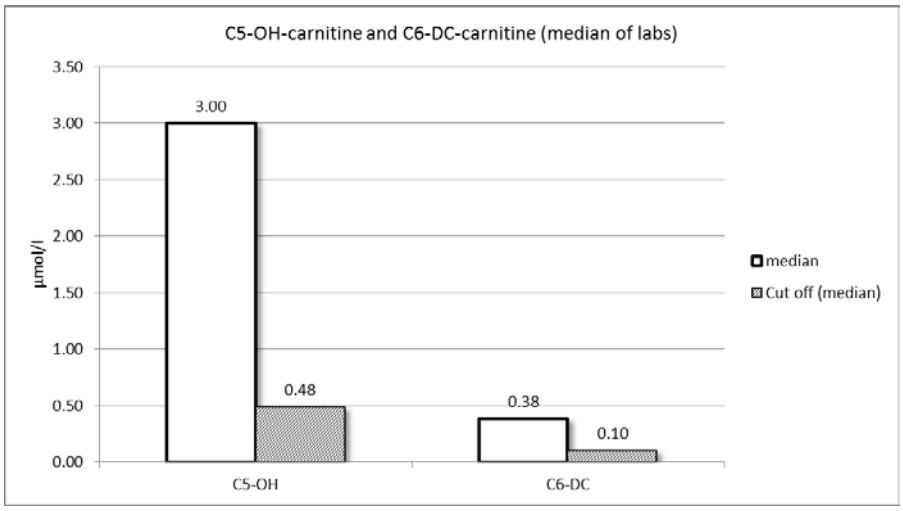
Diagnostic Performance: Normal control sample with acceptable performance (87%)

Sample 2017.06:

Patient details: 5-year-old boy with frequent episodes of vomiting

Known diagnosis: 3-hydroxy-3- methylglutaryl-CoA lyase deficiency

Analytical details Increased C5-OH and C6-DC



Analytical Performance: 76% reported elevated amounts of C5-OH and 57% C6-DC

Diagnostic Performance: The diagnosis of 3-hydroxy-3-methylglutaryl-CoA lyase deficiency or 3-hydroxy-3-methylglutaric aciduria was scored 2 points when given as main diagnosis or as an alternative diagnosis. This results in a diagnostic performance of 68% for 3-hydroxy-3-methylglutaryl-CoA lyase deficiency as primary choice and 89% when given as second choice.

Scoring of results

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.

4 Correct/satisfactory
3 Helpful but incomplete
2 Unhelpful
1 Slightly misleading
0 Misleading

The total score achievable for a single circulation of three samples is twelve. The maximal achievable score, full points for the year is twenty-four for the whole sample set of six samples in the year.

To obtain **satisfactory performance** a score of 16 or more should be achieved on two returns. Laboratories that participate only in one circulation are treated as non-submitters.

Another criteria for satisfactory performance will be 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.

The final scoring and all proposed critical errors will need to be ratified by the Scientific Advisory Board (SAB).

A **Performance Support Letter** will be sent to participants who have achieved a score less than 16 or if a confirmed critical error has been recognized.

Further information on the concept of 'critical error' can be found in the ERNDIM Newsletters 2015 at www.erndim.org.

News:

In **2017** a third center for Qualitative Acylcarnitines in dried blood spots started in Zurich with Dr Ralph Fingerhut as the Scientific Advisor.

In **2018** a trial will be possible for online submission of results for the Acylcarnitines.

The results can be electronically submitted on the website of the **Quality Control Center Switzerland CSCQ** in a way quite similar to the DPT schemes. Further information will be available soon.

So far the minimum requirement for satisfactory performance in the Qualitative Acylcarnitine scheme was 16 points on two returns.

In **2017** 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 (**17 points on two returns**).

This change was previously announced in the ERNDIM Newsletter 2017

Overall proficiency

The participants´ cumulative scores are shown in table 4. Cumulative scores are the scores for the whole year.

This year **twenty-three** participants got **full marks**. This is 62.2% of all participants that returned results for both circulations, and 57.5% of all registered participants.
One participant was identified by the ERNDIM Scientific Advisory Board who obtained a **critical error** (sample 2017.04)

Table 4: cumulative total scores 2017 (all registered laboratories that returned results for both circulations).

	Percent of participants				
Cumulative scores	**2017**	**2016**	**2015**	**2014**	**2013** (maximal achievable score was 20)
24	57.5	77.6	70.5	89.2	Not defined
23	5	12.1	9.8	-	Not defined
22	5	-	7.8	4.3	Not defined
21	10	-	2	4.3	Not defined
20	12.5	-	5.9	2.2	71.7
19	-	-	2	-	6.5
18	2.5	-	-	-	6.5
17	-	-	-	-	8.7
16	-	-	2	-	6.5
15	-	-	-	-	-
14	-	-	-	-	-
13	-	-	-	-	-
12	2.5	-	-	-	-
11	-	-	-	-	-
10	2.5	-	-	-	-
9	-	-	-	-	-
8	-	-	-	-	-
7	-	-	-	-	-
6	-	-	-	-	-
5	-	-	-	-	-
4	-	-	-	-	-
3	-	-	-	-	-
2	-	-	-	-	-
1	-	-	-	-	-
0	-	-	-	-	-
Number of all participants	40	58	58	62	60
Number of Nonresponders	1	6	3	16	14

Your individual scores for Sample 2017.01 – 2017.06:

Sample 2017.01

Sample 2017.02

Sample 2017.03

Sample 2017.04

Sample 2017.05

Sample 2017.06

Your total score 2017

Your total score for 2017 was:

Your number of returns in 2017 was:

General comments

We would like to point out here that we are not able to accept returns sent in after the report for the corresponding circulation has been mailed because this would not be compatible with the overall intention of the scheme. We are conscious of the fact that posted results could get lost on a variety of ways. Therefore it would be a good advice to send in results on more than one route (e.g. FAX and email, regular mail and FAX or email).

Appeal for contributing samples:

To keep the acylcarnitine scheme running we would like to encourage all participants to support us with samples. We need blood spots or whole blood. The shipping costs will be covered by us.

Please contact us under claus-dieter.langhans@med-uni-heidelberg.de for the details.

Yours sincerely,

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