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To

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ERNDIM QA Scheme for Qualitative Blood Spot Acylcarnitine Analysis

Annual Report 2015

Participation

The geographical distributions of the active participants of the quality assurance scheme organized and distributed through the centre of Heidelberg in 2015 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
Belgium	6
Brazil	1
Bulgaria	1
China	1
Czech Republic	2
France	17
Germany	7
Greece	1
Hong Kong S.A.R.	2
Lebanon	1
Luxembourg	1
Slovakia	1
Switzerland	3
The Netherlands	5
Turkey	3
United Kingdom	2
Total	58

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Samples and results

Two sets of three blood spot samples (total 6; sample number 2015.01, 2015.02, 2015.03, 2015.04, 2015.05 and 2015.06) were distributed to **58 laboratories**.

Three participants did not answer to any of the two circulations. Four laboratories returned results only for one circulation.

Table 2: Receipt of results

Circulation	In time returns	Late returns	Total
1. circulation	52	1	53
2. circulation	53	0	53

Shipment of the samples

Blood spot samples prepared on Whatman 903™ specimen collection paper were shipped on 17 September 2015 and on 18 December 2015.

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

		4	3	2	1	0
Sample 2015.01	Glutaric aciduria type I	52				1
Sample 2015.02	Propionic acidaemia	53	1			
Sample 2015.03	Normal profile	50	2	1		
Sample 2015.04	3-hydroxy-3-methylglutaryl-CoA lyase deficiency	47	3	2		1
Sample 2015.05	methylmalonic acidaemia	45	8			
Sample 2015.06	long-chain hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency	49			2	2

Comments on performance

Sample 2015.01:

Patient details: 2-year old girl presented with dystonia and movement disorders

Known diagnosis: glutaric aciduria type I

Analytical details C5DC was clearly elevated. The median of all reported values was 0.6 µmol/L with an upper reference limit of 0.15 µmol/l (median)
Increased ratios C5DC/C8, C5DC/C16 and Co/(C18+C16) were also detectable

Analytical Performance: 98%. Two points was given for the identification of elevated C5DC or (C5DC+C6OH)

Diagnostic Performance: 98%.

Overall impression: The majority of the participants clearly diagnosed glutaric aciduria type I

Critical error: A critical error was defined if detection of increased amounts of C5DC was missed and a normal diagnosis was given

Sample 2015.02:

Patient details: 5-year old boy with developmental delay and metabolic acidosis

Known diagnosis: propionic acidemia

Analytical details C3 and the ratio C3/C2 was clearly elevated. The median of all reported values was 22.2 µmol/L with an upper reference limit of 2.7 µmol/l (median)

Analytical Performance: 100%

Diagnostic Performance: 100%. Full points was given for the diagnosis of either propionic acidaemia or methylmalonic acidaemia

Overall impression: Very good analytical and diagnostic performance.

Sample 2015.03:

Patient details: 18-year old female with myopathy

Known diagnosis: normal profile

Analytical details free carnitine in the lower reference range, otherwise normal

Diagnostic Performance: 87%. Two points were deducted for the diagnosis of VLCAD with advice for costly further examinations

Sample 2015.04:

Patient details: 18-month-old boy presented with fever and acute hypoglycemia

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

Analytical details Clearly elevated amounts of C5OH and C6DC. The median of all reported values for C5OH was 3.2 µmol/L with an upper reference limit of 0.48 µmol/l (median)

For C6DC the corresponding medians were 0.3 µmol/l and 0.09 µmol/l

Analytical Performance: 85% for C5OH and 57% for C6DC. Two points was given for the identification of elevated C5DC or (C5DC+C6OH) and C6DC

Diagnostic Performance: 91%. Full marks were awarded if 3-hydroxy-3-methylglutaryl-CoA lyase deficiency was given either as most likely diagnosis or as a secondary choice

Critical error: A critical error was defined if the relevant metabolites were not detected resulting in a normal diagnosis

Sample 2015.05:

Patient details: 16-year-old female with history of metabolic crises in childhood. Acute admission with recurrent vomiting and increase of serum creatinine

Known diagnosis: methylmalonic acidaemia

Analytical details C3, C4DC and the ratio C3/C2 was clearly elevated

Analytical Performance: 100% for C3-carnitine but only 64% for C4DC

Diagnostic Performance: 81%

This sample was collected from a patient with methylmalonyl-CoA mutase deficiency (mut 0 type) who suffers from pre-terminal renal insufficiency. The patient is under carnitine supplementation. Beside increased propionyl-carnitine (C3), methylmalonyl-carnitine (C4DC) is clearly elevated in this sample. We determined in our laboratory 2.85 µmol/l (upper reference value 1.0 µmol/l) which is close to the median of all reported concentrations (2.26 µmol/l). This finding together with the age of the patient clearly points to methylmalonic aciduria rather than propionic aciduria. This was reflected by our scoring which was intended to award those who primarily diagnosed methylmalonic aciduria. One point was deducted for propionic aciduria as the most likely diagnosis.

Sample 2015.06:

Patient details: 21-year-old male with sensorimotor polyneuropathy and retinal abnormalities

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

Analytical details Hydroxylated long-chain acylcarnitines C16:1OH, C16OH, C18:1OH, C18-OH were elevated

Analytical Performance: 93%

Diagnostic Performance: 92%. LCHAD deficiency and/or mitochondrial tri-functional protein (MTFP) deficiency scored two points

Critical error: A critical error was defined if the relevant metabolites were not detected resulting in a normal diagnosis

Scoring scheme

In the process of ongoing accreditation of the ERNDIM organization 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. 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 participants´ cumulative scores are shown in table 4. Cumulative scores are the scores for the whole year.

This year thirty-six participants got full marks. This is 70.5% of all participants that returned results for both circulations, and 62.1% of all registered participants.

Table 4: cumulative total scores 2015 (all registered laboratories that returned results for both circulations)

	Percent of participants		
Cumulative scores	**2015**	**2014**	**2013** (maximal achievable score was 20)
24	70.5	89.2	Not defined
23	9.8	-	Not defined
22	7.8	4.3	Not defined
21	2.0	4.3	Not defined
20	5.9	2.2	71.7
19	2.0	-	6.5
18	-	-	6.5
17	-	-	8.7
16	2.0	-	6.5
15	-	-	-
14	-	-	-
13	-	-	-
12	-	-	-
11	-	-	-
10	-	-	-
9	-	-	-
8	-	-	-
7	-	-	-
6	-	-	-
5	-	-	-
4	-	-	-
3	-	-	-
2	-	-	-
1	-	-	-
0	-	-	-
Number of all participants	58	62	60
Number of Nonresponders	3	16	14

Your individual scores for Sample 2015.01 – 2015.06:

Sample 2015.01

Sample 2015.02

Sample 2015.03

Sample 2015.04

Sample 2015.05

Sample 2015.06

Your total score 2015

Your total score for 2015 was:

Your number of returns in 2015 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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