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To

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Metabolic Laboratory

ERNDIM QA Scheme for Qualitative Blood Spot Acylcarnitine Analysis

Annual Report 2011

Participation

The geographical distributions of the active participants of the quality assurance scheme organized and distributed through the centre of Heidelberg in 2011 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	2
Austria	2
Belgium	5
Brazil	1
Bulgaria	1
China	3
Czech Republic	2
France	15
Germany	6
Greece	1
Lebanon	1
Luxembourg	1
Switzerland	3
The Netherlands	8
Turkey	3
United Kingdom	2
Total	56

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Samples and results

Two sets of three blood spot samples (total 6; sample number 17A, 17B, 17C, 18A, 18B, 18C) were distributed to 56 laboratories.

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

Table 2: Receipt of results

Circulation	In time returns	Late returns	Total
1. circulation	39	7	46
2. circulation	37	2	39

Shipment of the samples

Blood spot samples prepared on Whatman 903™ specimen collection paper were shipped on 09th September 2011 and on 04th April 2012.

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

		-2	-1	0	1	2
Sample 17A *)	Long-chain hydroxyacyl-CoA dehydrogenase deficiency (mild form)					
Sample 17B	Propionic acidaemia					46
Sample 17C *)	Medium-chain acyl-CoA dehydrogenase deficiency (mild form)					
Sample 18A	Cobalamin A deficiency			1		38
Sample 18B	Normal profile			5	11	23
Sample 18C	Medium-chain acyl-CoA dehydrogenase deficiency					39

*) Samples were excluded from scoring. For details see 'Comments on performance'

Comments on performance

The analytical and diagnostic performance in identifying **propionic acidaemia (#17B**) and a disorder of **cobalamin metabolism (#18A**) were nearly at 100%.

Sample **#18B** was collected from a healthy person. Only sixty-one percent regarded this acylcarnitine profil to be normal. Thirty-two percent diagnosed 3-methylcrotonyl-CoA carboxylase deficiency, HMG-CoA lyase deficiency, multiple carboxylase deficiency or HMG-CoA synthase deficiency based on the finding of increased C5OH. The reported concentrations for C5OH varied among the laboratories from 0.2 to 0.8 µmol/l and the upper normal levels from 0.14 to 0.66 µmol/l. A high upper normal level combined with the determination of a low concentration of C5OH and vice versa could explain the different outcome for sample #18B.

We regard the determination of organic acids in a urine sample as a helpful way to clarify the diagnosis. This approach was scored one point.

Sample **#17A** was taken from a patient with **long-chain hydroxyacyl-CoA dehydrogenase deficiency**. This was a difficult case because it was a mild type of LCHAD deficiency with only small increased concentrations of C16OH, C18OH and C18:1OH. Only fifty-two percent of the participants diagnosed LCHAD deficiency. Because it was a difficult analytical challenge to detect those small increases in metabolite concentrations sample #17A was excluded from the overall scoring.

Both sample **#17C** and **#18C** were cases of **medium-chain acyl-CoA dehydrogenase deficiency**.
Sample **#18C** clearly showed increased concentrations of C6, C8, C10:1 and C10 which where detected by all active laboratories.
Sample **#17C** was a mild type of MCAD deficiency which showed only borderline concentrations of the relevant metabolites. Sixty percent of the participants reported a normal profile. Thirty-seven percent of the laboratories found C8 increased, twenty-two percent C10:1 and fifteen percent increased C10. Table 4 shows the medians of the reported concentrations. The listed upper normal values ('norm') are the medians of the reported values for both samples.

Table 4: median of the reported concentrations [µmol/l]

	C6	**C8**	**C10:1**	**C10**
norm	0.2	0.2	0.16	0.25
#17C	0.1	0.235	0.1	0.14
#18C	0.4	1.3	0.47	0.71

Table 4 shows that in sample #17C only the C8 concentration is borderline increased. This explains the low performance for #17C. Like sample #17A this is a very difficult case. Therefore we decided to exclude sample #17C also from the overall scoring.

Scoring scheme

Individual returns for each sample were scored on the scale

2	Correct/satisfactory
1	Helpful but incomplete
0	Unhelpful / failing to return a result
-1	Slightly misleading
-2	Misleading

The ERNDIM organisation provides a single "Certificate" to cover participation and performance in all its schemes.
For the "Qualitative Acylcarnitine Scheme" we adopted the criteria to define "Participation" and "Satisfactory Performance" from the well-established system of the "Qualitative Organic Acid Scheme".
"Participation" will be defined as requiring all two returns during a year and "Satisfactory Performance" as obtaining a score of 7 or more out of maximum score 12.
We are aware that these criteria are rather arbitrary but we are convinced that they will represent the different contexts in which the participants are working.

For the exceptional situation in 2011 with two excluded samples a maximum of 8 points could be obtained. "Satisfactory Performance" was defined as obtaining a score of 4 or more.

The participants´ cumulative scores are shown in table 5. Cumulative scores are the scores for the whole year.

This year twenty participants (36%) got full marks!

Table 5: cumulative total scores 2011 (all registered laboratories that returned results for both circulations)

	Number of laboratories
Cumulative scores	**2011**
12	Not defined
11	Not defined
10	Not defined
9	Not defined
8	20
7	11
6	8
5	0
4	1
3	0
2	9
1	0
0	7

Your individual scores for #Sample 17A – 18C:

Sample #17A
Sample #17B
Sample #17C

Sample #18A
Sample #18B
Sample #18C

Your total score 2011

Your total score for 2011 was:

Your number of returns in 2011 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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