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To

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Chairman
Center for Metabolic Diseases Heidelberg

Metabolic Laboratory

Heidelberg, 22nd April 2014

ERNDIM QA Scheme for qualitative urinary organic acid analysis

Annual Report 2013

Participation

The geographical distribution of the active participants of the quality assurance scheme organized and distributed through the centre of Heidelberg in 2013 is shown in Table 1. Sheffield and Heidelberg participate in each other's scheme and the two centers work closely together under the auspices of the ERNDIM Scientific Advisory Committee.

Table 1: Geographical distribution of participants

Country	Number of laboratories		Country	Number of laboratories
Austria	3		Lithuania	1
Belgium	1		Luxembourg	1
Bulgaria	1		New Zealand	1
Canada	7		Norway	1
Croatia	1		Philippines	1
Cyprus	1		Poland	2
Czech Republic	2		Slovakia	2
Denmark	1		Slovenia	1
Estonia	1		Spain	2
France	4		Sweden	2
Germany	13		Switzerland	3
Greece	1		The Netherlands	9
Hungary	1		Ukraine	1
India	2		United Arab Emirates	1
Italy	12		United Kingdom	1
Kingdom of Saudi Arabia	1		USA	11
Latvia	1			

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Samples and results

Three sets of three samples (total 9; sample numbers 205 - 213) were distributed to 94 laboratories.

Table 2 shows the number of returned results for each circulation and the number of late returns.

Table 2: Receipt of results

Circulation	In time returns	Late returns	Total
1. circulation	88	-	88
2. circulation	86	3	89
3. circulation	86	3	89

Eighty-nine percent of the participants returned results for all three circulations. Three laboratories (4%) did not respond to any of the circulations (see also table 3)

Table 3: returned results

Circulations	Number of laboratories	%
3	85	89
2	5	5
1	1	1
0	3	4

Shipment of the samples

As the years before we sent out the samples for all three circulations together. This is only for organizational reasons, especially to keep the costs for participating in this scheme as low as possible.

Please remember, the idea of the scheme is to measure the samples evenly spread over the year and to report the results near to the closing date!

Table 4: Distribution of scores for individual samples (laboratories making returns)

		4	3	2	1	0
Sample 205	Mevalonic aciduria	88				
Sample 206	Normal pattern	87		1		
Sample 207	Normal pattern	82		5		1
Sample 208	Propionic aciduria	89				
Sample 209	Normal pattern	89				
Sample 210	Alkaptonuria	89				
Sample 211	Normal pattern	88		1		
Sample 212	Isovaleric aciduria	89				
Sample 213	Methylmalonic aciduria	89				

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 and thirty-six for the whole sample set of nine samples per year.

To obtain satisfactory performance a score of 22 or more should be achieved on three returns and 14 or more when two returns have been submitted.

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.

Comments on performance

Sample 205:

Patient details: 21-month-old boy with facial dysmorphism, recurrent fever of unknown origin and skin rash

Known diagnosis: Mevalonic aciduria

Analytical details: The chromatogram showed intensive signals for mevalonolactone and its trimethylsilyl (TMS) derivative. A small but distinct peak for the trimethylsilyl derivative of mevalonic acid is detectable.
These metabolites were clearly identified by all participants

Overall Performance: 100%

Sample 206:

Patient details: 5-year-old girl with developmental delay

Known diagnosis: Normal pattern

Overall Performance: 99% regarded this organic acid profile to be normal.

Sample 207:

Patient details: newborn with neonatal seizures

Known diagnosis: Normal pattern

Overall Performance: 93% reported a normal profile.

Sample 208:

Patient details: 18-day-old infant presented with fever, vomiting and profound metabolic acidosis

Known diagnosis: Propionic aciduria

Analytical details: The chromatogram showed intensive peaks for the diTMS derivative of 3-hydroxypropionic acid, two signals for propionylglycine mono- and di-TMS and two peaks of the tetraTMS derivatives of methylcitric acid. Furthermore prominent peak for tiglylglycine diTMS was seen. The metabolites were identified by all participants.

Overall Performance: 100%

Sample 209:

Patient details: 3-year-old boy, mild mental retardation

Known diagnosis: Normal pattern

Overall Performance: 100%

Sample 210:

Patient details: 2-year-old boy with feeding difficulties and failure to thrive

Known diagnosis: alkaptonuria

Analytical details: The chromatogram is dominated by a large signal of the triTMS derivative of homogentisic acid and was identified by nearly all participants. One reported only malonic acid.

Overall Performance: 98 % reported alkaptonuria. One participant suspected a combined alkaptonuria / malonic aciduria.

Sample 211:

Patient details: 3-year-old boy with growth retardation

Known diagnosis: Normal pattern

Overall Performance: 99 % reported a normal organic acid profile

Sample 212:

Patient details: 4-year-old girl with several episodes of metabolic acidosis during infections

Known diagnosis: Isovaleric aciduria

Analytical details: The chromatogram showed two peaks for isovalerylglycine monoTMS (less intense) and diTMS. 3-hydroxyisovaleric acid is present. All participants reported increased isovalerylglycine.

Overall Performance: 100%

Sample 213:

Patient details: boy presented at age 16 months with ketoacidosis, hyperglycemia, and hyperammonemia

Known diagnosis: methylmalonic aciduria

Analytical details: Large peaks for the di- and triTMS derivative of methylmalonic acid and two peaks of the tetraTMS derivatives of methylcitric acid. All participants detected these metabolites.

Overall Performance: 100%

The participants´ cumulative scores are shown in table 6 and in figure 5.
Cumulative scores are the scores for the whole year. In 2013 seventy-seven participants (82%) got full marks!

Table 6: Cumulative total scores 2013
Number of all participants: all registered laboratories
Number of nonresponders: no results returned for any of the three circulations

	Percent of all participants
Cumulative scores	**2013**
36	82
35	-
34	7
33	-
32	1
31	-
30	-
29	-
28	-
27	-
26	-
25	-
24	5
23	-
22	-
21	-
20	-
19	-
18	-
17	-
16	-
15	-
14	-
13	-
12	1
11	-
10	-
9	-
8	-
7	-
6	-
5	-
4	-
3	-
2	-
1	-
0	3
Number of all participants	94
Number of Nonresponders	3

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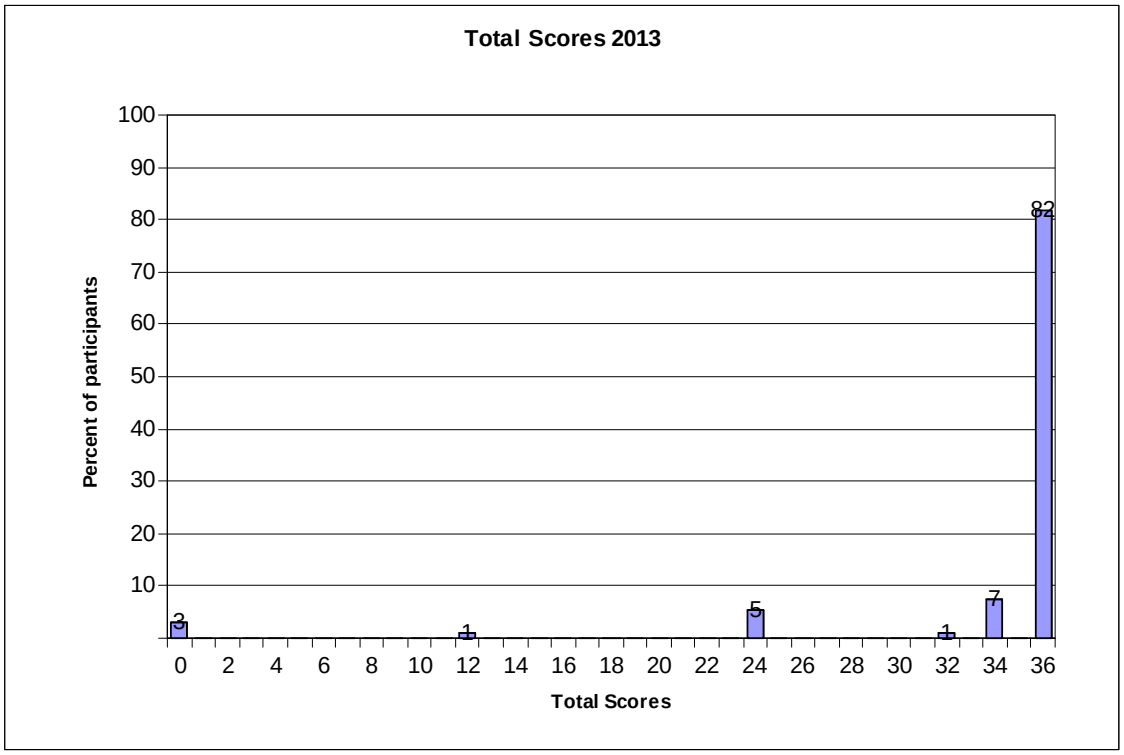


Fig. 6: Cumulative scores 2013

Your total score 2013

Your total score for 2013 was:

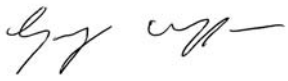
Your number of returns in 2013 was:

General comments

We would just 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 by more than one route (e.g. FAX and email, regular mail and FAX or email).

Special thank for the laboratories that supported us last year with samples. This is critical for the success of the program and will keep the scheme interesting. **It is most appreciated that you will continue to support us with urine from patients. Please send us at least 300 ml urine of any interesting patients you may have. We will cover the costs.**

Yours sincerely,



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