UniversitätsKlinikum Heidelberg

Universitätsklinik für Kinder- und Jugendmedizin
Stoffwechselzentrum Heidelberg Stoffwechsellabor
Im Neuenheimer Feld 669 | 69120 Heidelberg

To

University Children's Hospital
Angelika-Lautenschläger-Klinik

Department of General Pediatrics
(General Pediatrics, Neurology, Metabolism, Gastroenterology, Nephrology)
Prof. Dr. med. G.F. Hoffmann
Chairman
Center for Metabolic Diseases Heidelberg

Metabolic Laboratory

Heidelberg, 05. May 2015

ERNDIM QA Scheme for qualitative urinary organic acid analysis

Annual Report 2014

Participation

The geographical distribution of the active participants of the quality assurance scheme organized and distributed through the centre of Heidelberg in 2014 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		Luxembourg	1
Belgium	1		New Zealand	1
Bulgaria	1		Norway	1
Canada	8		Philippines	1
Croatia	1		Poland	2
Cyprus	1		Slovakia	2
Czech Republic	2		Slovenia	1
Denmark	1		Spain	2
Estonia	1		Sweden	2
France	5		Switzerland	3
Germany	13		Serbia	1
Greece	1		South Africa	1
Hungary	1		The Netherlands	10
India	3		Ukraine	1
Italy	12		United Arab Emirates	2
Kingdom of Saudi Arabia	1		United Kingdom	1
Latvia	1		USA	12
Lithuania	1			

Im Neuenheimer Feld 669
69120 Heidelberg
Stoffwechsellabor:
Fon +49 (0)6221 56 8276
8423
Fax +49 (0)6221 56 5565

Neugeborenenscreening:
Fon +49 (0)6221 56 8278

stoffwechsellabor@uni-hd.de
www.stoffwechsel.uni-hd.de

Samples and results

Three sets of three samples (total 9; sample numbers 214 - 222) were distributed to **101 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	95	1	96
2. circulation	95	3	98
3. circulation	97	1	98

Ninety-three percent of the participants returned results for all three circulations. Two laboratories (2%) did not respond to any of the circulations (see also table 3)

Table 3: returned results

Circulations	Number of laboratories	%
3	94	93
2	5	5
1	0	0
0	2	2

Shipment of the samples

Date of sample dispatch: **02 April 2014**

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 (number of laboratories making returns)

		4	3	2	1	0
Sample 214	Normal pattern	82	10	4		
Sample 215	HMG-CoA lyase deficiency	93	2	1		
Sample 216	Methylmalonic aciduria *)	96				
Sample 217	Phenylketonuria	97		1		
Sample 218	Normal pattern	97	1			
Sample 219	Tyrosinaemia type I	86	9	3		
Sample 220	Normal pattern	88	4	6		
Sample 221	Normal pattern	91	3	4		
Sample 222	Hawkinsinuria	87	1			10

*) scores updated

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 15 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 214:

Patient details: 3-months-old girl with unspecified neonatal jaundice

Known diagnosis: Normal pattern

Details:	The chromatogram showed a prominent peak for glyceric acid. On the basis of this finding 14% diagnosed hyperoxaluria.
Overall Performance:	Full score 85%

Sample 215:

Patient details:	12-year old boy presented with vomiting and diarrhoea, hypoglycemia
Known diagnosis:	HMG-CoA lyase deficiency
Analytical details:	The chromatogram showed prominent peaks for 3-hydroxyisovaleric acid, 3-methylglutaric acid, three signals for 3-methylglutaconic acid (two peaks for the Z and E isomers of the di-TMS derivative and one peak for the tri-TMS derivative) and one signal for 3-hydroxy-3-methylglutaric acid. 3-methylglutaconic acid was reported by 99% of the participants and 3-hydroxy-3-methylglutaric acid by 97%. Other relevant metabolites were reported in different combinations. All four metabolites were detected by 77% of the laboratories.
Overall Performance:	All participants diagnosed either 3-hydroxy-3-methylglutaric aciduria (96%) or 3-methylglutaconic aciduria (4%)

Sample 216:

Patient details:	3-year-old boy with seizures and dystonic movement disorder
Known diagnosis:	methylmalonic aciduria
Analytical details:	100% of the laboratories detected methylmalonic acid whereas methylcitric acid was reported only by 88%.
Overall Performance:	Full score: 100%

Sample 217:

Patient details:	2-year-old boy with microcephaly and developmental delay
Known diagnosis:	phenylketonuria (PKU)

Analytical details: In this urine sample several metabolites diagnostic for PKU could be detected like phenylacetic acid, mandelic acid, 2-hydroxyphenylacetic acid, phenyllactic acid, 4-hydroxyphenyllactic acid, 4-hydroxyphenyllactic acid, phenylpyruvic acid and 4hydroxyphenylpyruvic acid. No laboratory reported all of those metabolites. 10% of the participants reported all metabolites except 4hydroxyphenylpyruvic acid.

Diagnostic Performance: Full score: 99%

Sample 218:

Patient details: 5-year-old girl showing autistic behaviour

Known diagnosis: Normal pattern

Overall Performance: Full score: 99%

Sample 219:

Patient details: 15-month-old girl with failure to thrive. Sample taken under therapy

Known diagnosis: tyrosinaemia type I

Analytical details: Metabolites to be detected were 4-hydroxyphenylacetic acid, 4-hydroxyphenyllactic acid, 4-hydroxyphenylpyruvic acid and succinylacetone.
20% of the laboratories reported all of these metabolites, 61% all metabolites except succinylacetone

Diagnostic Performance: Full score: 88%
88 % diagnosed a defect in tyrosine metabolism and 7% liver failure or hepatopathy

Sample 220:

Patient details: 5-year-old boy with choreoathetoid movements, acute encephalopathy

Known diagnosis: Normal pattern

Overall Performance: Full score:90%

Sample 221:

Patient details:	16-year-old boy with intestinal malabsorption
Known diagnosis:	Normal pattern
Overall Performance:	Full score: 93%

Sample 222:

Patient details:	4-year-old girl with psychomotoric retardation
Known diagnosis:	hawkinsinuria
Analytical details:	Two peaks for the diTMS derivative of 4-hydroxycyclohexylacetic acid. 88% of the participants detected this metabolites.
Overall Performance:	Full score: 89%
Comment:	**This sample is classified as an educational sample. Missing the diagnosis is not regarded to be a critical error**

The participants´ cumulative scores are shown in table 6 and in figure 5.
Cumulative scores are the scores for the whole year.

In 2014 fifty-five participants (54%) got full marks!

Table 6: Cumulative total scores 2013 - 2014
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	**2014**	**2013**
36	54	82
35	13	-
34	12	7
33	1	-
32	6	1
31	3	-
30	2	-
29	1	-
28	1	-
27	-	-
26	-	-
25	-	-
24	4	5
23	-	-
22	-	-
21	1	-
20	-	-
19	-	-
18	-	-
17	-	-
16	-	-
15	-	-
14	-	-
13	-	-
12	-	1
11	-	-
10	-	-
9	-	-
8	-	-
7	-	-
6	-	-
5	-	-
4	-	-
3	-	-
2	-	-
1	-	-
0	2	3
Number of all participants	101	94
Number of Nonresponders	2	3

stoffwechsellabor@uni-hd.de
www.stoffwechsel.uni-hd.de

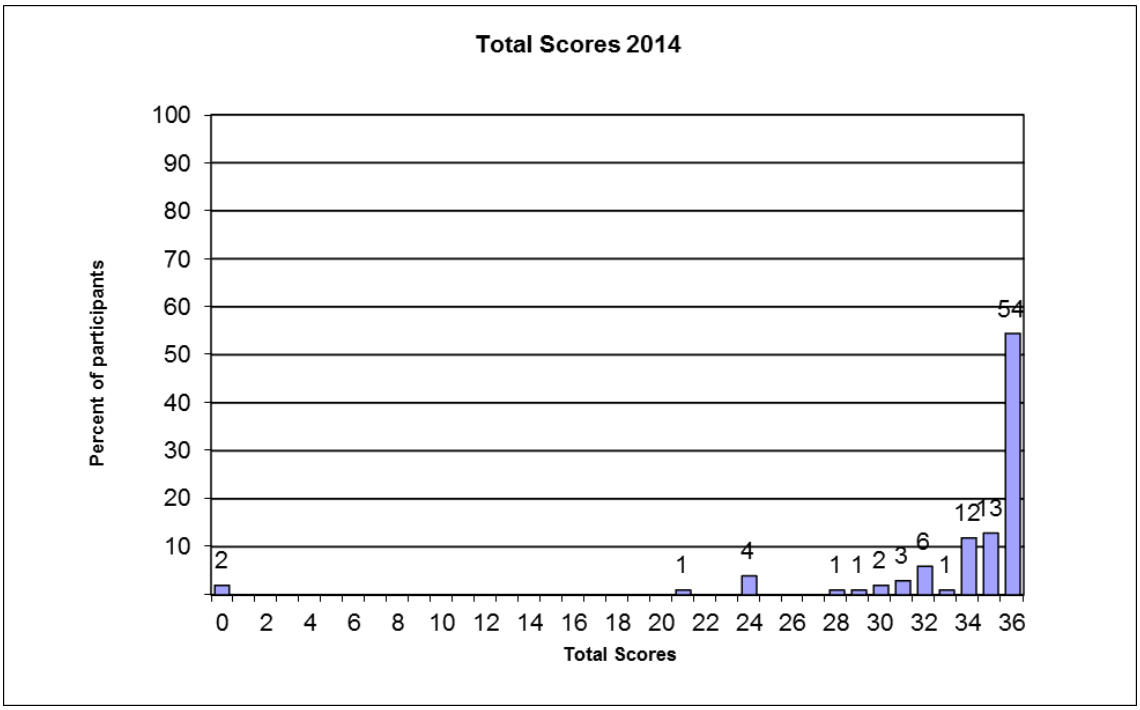


Fig. 6: Cumulative scores 2014

Your total score 2014

Your total score for 2014 was:

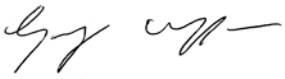
Your number of returns in 2014 was:

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,



Dr. C. D. Langhans

Laboratory of Metabolic Diseases

Dr. V. Peters

Laboratory of Metabolic Diseases

Prof. Dr. G. F. Hoffmann

Director
Department of General Paediatrics