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QAP for qualitative urinary organic acid analysis

Annual Report 2013 (Sheffield)

Scheme Design

The scheme has been designed and planned by Mrs C Scott and Prof R J Pollitt as Scientific Advisor/Scheme Organiser and deputy Scientific Advisor/Scheme Organiser, respectively, both appointed by and according to procedures laid down by the ERNDIM Board.

Samples and shipment

All EQA materials are 2 ml of heat-treated urine. All samples are obtained following local ethical and consent guidelines. Three sets of three samples (numbered 205-213) were dispatched together in April 2013. Submission deadlines were 21st June (samples 205-207), 20th September (samples 208-210) and 22nd November (samples 211-213).

Participation

Active participants (reporting on at least one set of samples in the year) are shown in Table 1 (page 2). The numbers of participants remain steady. New applicants are distributed between the Sheffield and Heidelberg qualitative urinary organic acid schemes which are run separately. The two organising laboratories each participate in the other's scheme.

Results

Laboratories were asked to analyse the sample sets at intervals during the year as if they were separate circulations. Eighty-eight laboratories returned results for all three sets; two returned only two, one laboratories made only a single return, and three made no return.
All submitted results are treated as confidential information and are only shared with ERNDIM approved persons for the purposes of evaluation and reporting.

Table 1: Geographical distribution of registered participants

	2013	***2012***	***2011***	***2010***	***2009***	***2008***	***2007***
Argentina	2	2	2	2	2	1	2
Australia	6	6	6	6	6	6	6
Belgium	6	5	5	6	7	5	5
Brazil	2	2	2	-	1	1	1
Canada	1	1	1	1	1	1	1
Columbia	1	1	1	1	1	-	-
Czech Republic	-	-	1	-	-	-	-
Democratic Republic of China	1	1	2	2	1	1	1
Finland	2	1	1	1	1	1	1
France	15	15	15	13	13	14	13
Germany†	1	1	1	1	1	1	1
Israel	3	3	3	4	3	2	2
Japan	1	1	1	1	1	1	1
Lebanon	1	1	1	1	1	1	1
Malaysia	3	3	3	4	3	3	2
New Zealand	1	1	1	1	1	1	2
People's Republic of China	9	8	10	7	7	6	6
Portugal	2	2	2	2	2	2	2
Republic of Korea	1	1	1	1	1	1	1
Republic of Ireland	1	1	1	1	1	1	1
Republic of Singapore	1	1	1	1	1	1	-
South Africa	2	2	2	2	1	1	-
Spain	6	6	6	6	6	5	5
Turkey	3	3	3	3	2	2	-
United Kingdom	18	18	18	19	20	20	20
USA	5	3	3	3	4	4	4
Venezuela	-	1	1	1	1	1	1
Vietnam	1	1	1	-	-	-	-
TOTAL	**94**	**91**	**95**	**90**	**89**	**83**	**79**

† Heidelberg laboratory

Scoring of results

To enable data reduction the results were scored as shown below:

Satisfactory	4	Helpful but incomplete	3
Not helpful	2	Slightly misleading	1
Misleading	0		

One point was deducted for each transposed sample number.

For the 2014 scheme onwards another criterion 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.

Table 2: Distribution of scores for individual samples (laboratories making returns)

Sample	Scores				
	0	**1**	**2**	**3**	**4**
Sample 205 6 year old boy with global developmental delay No abnormality was detected.	1	-	-	-	86
Sample 206 15 year old girl investigated for renal stones Massive amounts of 3-hydroxyisovalerate and 3-methylcrotonylglycine with no detectable increase in 3-hydroxypropionate or methylcitrate. Results diagnostic of isolated 3-Methylcrotonyl-CoA carboxylase deficiency.	1	-	3	-	83
Sample 207 5 year old male with vomiting and unusual odour A large peak of isovalerylglycine and a modest increase in 3-hydroxy-isovalerate. In the absence of any other specific abnormality this pattern is diagnostic of Isovaleryl-CoA dehydrogenase deficiency (Isovaleric acidaemia).	-	-	-	-	87
Sample 208 2 year old girl with a first febrile seizure No abnormality was detected	2	-	1	2	86
Sample 209 6 week old boy, vomiting, acidotic Significantly increased excretion of methylmalonic acid and methlycitrate with increased 3-hydroxypropionic acid. Results consistent with a diagnosis of Methylmalonic Aciduria.	-	-	-	-	91
Sample 210 28 year old women with encephalopathy. Orotic acid was detected in potentially significant amounts. Recommend orotic acid quantitation along with urgent plasma ammonia analysis, and urine and plasma amino acids to exclude a urea cycle defect	15	-	2	1	72
Sample 211 3 year old female with mild developmental delay Marked increased excretion of malonic acid and moderately increased excretion of methylmalonic acid. Results consistent with malonic acidaemia.	-	-	1	1	87
Sample 212 15 year old male with increased creatinine kinase and autism Marked excretion of 3-hydroxybutyrate accompanied by a strong dicarboxylic aciduria and modest excretion of 3-hydroxdicarboxylic acids. Glutarate excretion was particularly marked and with ethylmalonate also increased and a small peak or 2-hydroxyglutarate. No acylglycines were detected. Despite this, the overall pattern, particularly the increased excretion of glutarate, is suggestive of a mild multiple acyl-CoA dehydrogenation defect of the ethylmalonic-adipic aciduria type.	-	1	6	9	73
Sample 213 3 year old male with macrocephaly Nothing specifically diagnostic.	-	-	1	-	88

Table 3: Cumulative scores for 2011 - 2013 (current Sheffield participants only)

The maximum annual scores for 2012 & 2011 were 18. The maximum scores for 2013 were 36. An average score per case has not been provided in this annual report due to the new scoring system. An average score as a percentage of the maximum score achievable over the past 3 years has been provided when there have been 3 returns for 3 consecutive years.

Lab Number	No of returns 2013	Total score 2013 (out of 36 for 3 returns)	Number of returns 2012	Total score 2012 (out of 18 for 3 returns)	Number of returns 2011	Total score 2011 (out of 18 for 3 returns)	**Average score as a percentage over 3 years*.**
2	3	32					
3	3	34	3	18	3	18	**98**
4	3	36	3	18	2	12	
5	3	36	3	18	3	18	**100**
7	3	36					
10	3	34	3	14	3	15	**85**
11	3	36	3	18	3	16	**96**
12	3	36	3	18	3	18	**100**
13	3	36	3	18	3	18	**100**
14	3	35	3	18	3	14	**93**
15	3	35	3	13	3	18	**90**
17	3	36	3	18			
18	3	36	3	18	3	18	**100**
19	3	36	3	18	3	18	**100**
21	3	36	3	18	3	18	**100**
24	3	36	1	4	3	15	
25	3	36	3	16	3	18	**96**
26	3	35	3	18	3	18	**99**
27	3	36	3	18	3	18	**100**
29	3	34	3	18	3	13	**89**
31	3	36	3	18	3	16	**96**
32	3	36	3	16	3	17	**94**
35	3	36	3	18	3	18	**100**
38	3	36	3	16	3	13	**87**
48	3	32	3	16	3	13	**83**
49	3	34	3	18	3	13	**89**
51	3	36	3	18	3	15	**94**
52	3	35	3	18	2	12	
65	3	34	3	18	3	18	**98**
66	3	36	3	18	3	17	**98**
83	3	28	3	18	3	17	**90**
85	3	34	3	18	3	18	**98**
86	3	36	3	18	3	18	**100**
88	3	36	3	16	3	15	**91**
90	3	36	3	18	3	14	**93**
92	3	36	3	17	3	17	**96**
93	3	36	3	18	3	18	**100**
94	3	36	3	18	3	18	**100**
96	3	36	3	18	3	18	**100**
98	3	36	3	18	3	18	**100**

Lab Number	No of returns 2013	Total score 2013 (out of 36 for 3 returns)	Number of returns 2012	Total score 2012 (out of 18 for 3 returns)	Number of returns 2011	Total score 2011 (out of 18 for 3 returns)	**Average score as a percentage over 3 years*.**
101	3	35	3	18	3	18	**99**
102	3	36	3	18	3	18	**100**
104	3	28	3	16	3	7	**68**
106	3	36	3	18	3	18	**100**
108	3	35	3	18	3	18	**99**
111	3	36	3	18	3	18	**100**
113	3	30	3	10	3	10	**64**
114	3	32	3	14	2	3	
119	3	36	3	18	3	14	**93**
120	3	36	3	18	3	18	**100**
121	3	36	3	18	2	12	
126	3	36	3	18	3	18	**100**
128	3	36	3	18	3	14	**93**
130	3	36	3	18	3	18	**100**
132	3	34	3	18	3	6	**76**
133	3	36	3	18	3	18	**100**
134	1	8	0	n/a	1	6	
135	3	36	3	18	3	18	**100**
137	3	36	3	18	3	18	**100**
138	3	32	3	18	3	18	**96**
139	3	36	3	16	3	18	**96**
141	3	32	3	18	3	14	**89**
142	3	36	3	13	2	9	
143	3	36	3	18	3	16	**96**
144	3	35	3	18	3	17	**97**
146	3	36	3	18	3	18	**100**
147	3	36					
148	3	36	3	18	3	16	**96**
149	2	24	3	18	2	12	
151	n/a	n/a	2	3	1	6	
152	2	22	3	13	3	7	
153	3	36	3	18	3	16	**96**
154	n/a	n/a	n/a	n/a	n/a	n/a	
155	3	36	3	18	3	14	**93**
156	3	32	3	18	3	18	**96**
157	3	35	3	18	3	14	**91**
158	3	33					
159	3	36	3	18	3	13	**91**
160	3	28	3	16	3	18	**89**
163	3	36	3	18	3	18	**100**
164	3	36	2	12	2	8	
165	3	36	3	18	3	16	
166	3	30	3	11	3	10	**67**
167	3	36					
168	3	34	3	14	3	18	**91**
170	3	30	3	16	3	14	**83**
172	3	35	3	18	3	18	**99**

Lab Number	No of returns 2013	Total score 2013 (out of 36 for 3 returns)	Number of returns 2012	Total score 2012 (out of 18 for 3 returns)	Number of returns 2011	Total score 2011 (out of 18 for 3 returns)	**Average score as a percentage over 3 years*.**
174	3	36	2	12	3	12	
175	2	20					
176	3	32					
178	3	36	2	12	3	16	
179	3	31	3	14	3	15	
180	3	32	3	18	3	8	**78**
181	n/a	n/a	3	16	3	14	

* Average score only available of 3years of full returns.

Your Laboratory Number in the above Table is

Commentary

Overall this year's samples were more challenging that those in 2012 with only 59% of participants achieving maximum scores compared to 89% in 2012. Samples 210 and 212 provided the most problems. Sample 210 was from a patient with a moderate amount of orotic acid in the urine. Only seventy-four of the ninety-one laboratories correctly identified orotic acid. Identifying orotic acid on the organic acid profile is a well established technical problem for a number of reasons including chromatographic systems (column polarity, gas flow rate and temperature profile) as well as peak recognition and co-elution problems. Orotic acid detection is important in many conditions as this may be the only abnormal diagnostic test and subsequently failing to identify it may result in a missed opportunity for diagnosis. Fictitious details were provided with this sample to mimic an OTC female carrier. Fictitious details are only used in situations where a suitable sample from a real case is difficult to source or when there has been a specific request from a donor.

Sample 212 also proved problematic for many laboratories. This sample was from a patient with a genetically confirmed diagnosis of multiple-acyl-CoA dehydrogenase deficiency. Interpretation was difficult in this case due to the significant ketosis and the failure to appreciate the significance of the increased glutarate and ethylmalonic acid. In this case it is unlikely that a diagnosis would be made on the urine organic acids alone and checking the plasma acylcarntine profile may have reduced the number of laboratories failing to suggest the correct diagnosis.

The other samples in the 2013 distribution all scored well with the majority of laboratories achieving maximum points.

It is appreciated that in all the cases the urine organic acid profile is only part of the diagnostic profile and where the organic acid profile does not give a clear diagnosis the further investigations box is key when it comes to scoring. The 'Further investigations' box should indicate any additional investigations you consider necessary to interpret or confirm conclusions based on the analytical results. The 'Additional comments' box may also be used for caveats or to suggest other lines of investigation based on the clinical presentation rather than the analytical findings. Suggestions should follow a logical hierarchy with simple group investigations such as amino acid chromatography or blood-spot acylcarnitine profiling (if indicated) taking precedence over much more specific investigations such as gene sequencing.

Certificates of Participation and Performance

We are required to define "Participation" and "Satisfactory Performance" for the purpose of the ERNDIM Annual Certificate which covers all ERNDIM schemes. For this urinary organic acid scheme we have defined "Participation" as requiring at least two returns during the year. Defining "Satisfactory Performance" is more problematical as in some years there are more difficult samples than in others.

The criteria for satisfactory performance remain the same as in 2012:for three returns a score of 11/18 (61%), which equates to a score of 22/36 under the new scoring system, and for two returns a score of 15 or more. On this basis all participating laboratories were deemed satisfactory with the exception of one laboratory in which only one return was submitted and three laboratories in which no returns were made. Satisfactory Performance" criteria are always somewhat arbitrary and in practice even a single missed or wrong diagnosis can be highly damaging. Thus the reason(s) for failure to correctly report on any of the samples in the scheme should be investigated locally and appropriate remedial action taken.

We thank Lynne Darwin for administering our participant database and dealing with the returns, and Jennifer Watkinson for preparing and dispatching the samples. We hope that you continue to find this scheme useful.

Yours sincerely

Mrs C Scott	Professor J R Bonham	Professor R J Pollitt
Scientific Advisor		Deputy Scientific Advisor

Scheme organisers