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16th April 2013

ERNDIM QAP for qualitative urinary organic acid analysis

Annual Report 2012 (Sheffield)

Participation

Active participants (reporting on at least one set of samples in the year) are shown in Table 1. 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.

Table 1: Geographical distribution of registered participants

	2012	*2011*	*2010*	*2009*	*2008*	*2007*	*2006*
Argentina	2	2	2	2	1	2	1
Australia	6	6	6	6	6	6	6
Belgium	5	5	6	7	5	5	4
Brazil	2	2	-	1	1	1	1
Canada	1	1	1	1	1	1	1
Columbia	1	1	1	1	-	-	-
Czech Republic	-	1	-	-	-	-	-
Democratic Republic of China	1	2	2	1	1	1	1
Finland	1	1	1	1	1	1	1
France	15	15	13	13	14	13	11
Germany†	1	1	1	1	1	1	1
Israel	3	3	4	3	2	2	2
Japan	1	1	1	1	1	1	1
Lebanon	1	1	1	1	1	1	1
Malaysia	3	3	4	3	3	2	2
New Zealand	1	1	1	1	1	2	2
People's Republic of China	8	10	7	7	6	6	4
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	-	-
South Africa	2	2	2	1	1	-	-
Spain	6	6	6	6	5	5	5
Turkey	3	3	3	2	2	-	-
United Kingdom	18	18	19	20	20	20	21
USA	3	3	3	4	4	4	2
Venezuela	1	1	1	1	1	1	1
Vietnam	1	1	-	-	-	-	-
TOTAL	**91**	**95**	**90**	**89**	**83**	**79**	**72**

† Heidelberg laboratory

Samples and results

Three sets of three samples (numbered 196-204) were dispatched together in April 2012. Laboratories were asked to analyse the sets at intervals during the year as if they were separate circulations. Eighty-three laboratories returned results for all three sets, four returned only two, four laboratories made only a single return, and two made no return.

Scoring of results

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

Satisfactory	2	Helpful but incomplete	1
Not helpful	0	Slightly misleading	-1
Misleading	-2	Failing to return a result	0

One point was deducted for each transposed sample number.

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

Sample	Scores				
	-2	**-1**	**0**	**1**	**2**
Sample 196 3 year old girl presenting with a hypoglycaemic encephalopathy. No relevant medical history. Sample taken after recovery. No abnormality was detected.	-	-	-	2	87
Sample 197 14 month old boy with severe ketosis following a mild illness Increased excretion of tiglylglycine with two peaks of 2-methyl-3-hydoxybutryic acid and a small peak of 2-methylacetoacetate. Diagnosis Beta-ketothiolase deficiency.	1	-	5	4	79
Sample 198 2 year old girl with severe autism and developmental delay Large peak of 2-hydroxyglutarate with its lactone present. Diagnosis consistent with 2-hydroxyglutaric aciduria – suggest check chirality to determine if D or L form. Diagnosis D-2 hydroxyglutaric aciduria.	3	1	1	2	82
Sample 199 6-month-old boy with cardiomyopathy and neutropenia Increased excretion of 3-methylglutaconic acid and 3-methylglutaric acid. Results indicative of 3 methylglutaconic aciduria. Given the clinical details, cardiomyopathy & neutropenia, Barth Syndrome – 3-methylglutaconic aciduria type II - would be most likely. Diagnosis Barth Syndrome	1	-	-	-	86

Sample 200 3-year-old boy with mild developmental delay No abnormality was detected.	-	-	-	-	87
Sample 201 10-day-old baby in keto-acidotic crisis Increased excretion of 3-hydroxypropionic acid along with significantly increased propionylglycine, tiglylglycine and methylcitrate. This is consistent with propionyl-CoA carboxylase deficiency (Propionic Acidaemia). The hippurate peak is unusually prominent suggesting the administration of benzoate. Diagnosis Propionic Acidaemia.	-	-	1	1	85
Sample 202 4-year old boy with unsteady gait No abnormality was detected.	-	-	-	-	84
Sample 203 12-month old boy with large head and abnormal movements Significantly increased excretion of glutarate and 3-hydroxyglutarate. Diagnosis of Glutaric Aciduria type 1 (GA1) (glutaryl-CoA dehydrogenase deficiency).	-	-	1	1	82
Sample 204 5- year old female with seizures, white matter changes, history of aggression and autism. Moderate excretion of 4-hydroxybutyric acid along with detectable 4,5-dihydroxyhexanoate lactones. Results indicative of succinic semialdehyde dehydrogenase deficiency (SSADH). Mild to moderate increased pyroglutamic acid (5-oxoproline), which is most likely secondary to drug administration. Valproate metabolites detected. Diagnosis SSADH deficiency.	9	-	1	-	74

Table 3: Cumulative scores for 2010 - 2012 (current Sheffield participants only)

The average score is **per sample reported**. The maximum annual scores were 18.

	2012		2011		2010		2010-2012
Lab No	No of Returns	Total Score	No of Returns	Total Score	No of Returns	Total Score	Average Score
3	3	16	3	17	3	18	1.89
4	3	18	3	16	3	18	1.93
5	3	18	3	18	3	10	1.70
6	3	18	3	18	3	18	2.00
7	3	16	3	18	3	18	1.93
10	3	18	3	13	3	18	1.81
11	3	18	3	18	3	16	1.93
12	3	18	2	12	3	14	1.83
13	3	18	3	18	3	15	1.89
14	3	18	3	17	3	18	1.96
15	3	13	3	18	3	18	1.81
17	3	18	3	14	3	18	1.85
18	3	18	3	18	3	18	2.00
19	3	18	3	15	3	18	1.89
21	3	18	3	18	3	18	2.00
24	3	16	3	18	3	18	1.93
25	3	18	3	18	3	18	2.00
26	3	18	3	17	3	18	1.96
27	3	16	3	16	3	14	1.70
29	3	18	3	13	3	18	1.81
31	3	18	3	18	3	18	2.00
32	3	18	3	18	3	18	2.00
35	3	18	3	18	3	17	1.96
38	3	18	3	18	3	18	2.00
48	3	18	3	18	3	13	1.81
49	3	18	2	12	3	10	1.67
51	3	18	3	18	3	18	2.00
52	3	18	2	12	2	10	1.90
65	3	18	3	18	3	18	2.00
66	3	18	3	15	3	18	1.89
83	3	16	3	15	3	18	1.81
85	3	18	3	18	3	18	2.00
86	3	18	3	18	3	18	2.00
88	3	18	3	14	2	12	1.83
90	1	6	2	13			
92	3	18	3	18	3	18	2.00
93	3	17	3	17	3	18	1.93
94	3	18	3	18	3	16	1.93
96	3	18	3	18	3	18	2.00
98	3	18	3	18	3	18	2.00
101	3	18	3	18	3	18	2.00
102	3	18	3	18	3	18	2.00
104	3	16	3	7	3	15	1.41

	2012		2011		2010		2010-2012
Lab no	No of Returns	Total Score	No of Returns	Total Score	No of Returns	Total Score	Average Score
106	3	18	3	18	3	15	1.89
108	3	18	3	18	3	18	2.00
111	3	18	3	18	3	18	2.00
113	3	10	3	10	3	13	1.22
119	3	18	3	18	3	18	2.00
120	3	18	3	18	3	18	2.00
126	3	14	3	15	3	14	1.59
128	3	11	3	10	3	14	1.30
130	3	18	3	18	3	18	2.00
132	3	18	3	18	3	18	2.00
134	3	18	3	18	3	18	2.00
135	3	18	3	18	3	18	2.00
137	3	16	3	18	3	18	1.93
138	3	13	3	8	3	17	1.41
139	3	18	3	18	3	18	2.00
141	1	6	1	6	3	7	
142	3	13	2	9	2	12	1.62
143	3	18	3	16	3	18	1.93
144	3	18	3	15	3	18	1.89
146	3	16	3	13	3	16	1.67
147	3	18	3	14	2	18	2.08
148	3	18	3	16	3	18	1.93
149	3	16	3	14	3	18	1.78
151	3	18	2	12	3	18	2.00
152	2	3	1	6	3	12	1.17
153	3	13	3	7	3	13	1.22
154	3	16	3	13	3	14	1.59
155	3	18	3	14	3	18	1.85
156	3	18	3	16	3	18	1.93
157	3	18	3	18	3	9	1.67
158	3	18	3	14	3	18	1.85
159	1	6	3	16	3	10	-
160	3	18	3	17	3	14	1.81
163	3	18	3	13	3	6	1.37
164	3	14	3	18	3	12	1.63
165	3	18	3	8	3	7	1.22
166	2	12	3	12	3	13	1.54
167	3	18	3	6	3	12	1.33
168	3	18	3	18	3	13	1.81
170	3	16	3	14	3	18	1.78
172	1	6	3	15	3	18	-
175	2	12	3	15	-	-	-
176	3	14	-	-	-	--	-

	2012		2011		2010		2010-2012
Lab No	No of Returns	Total Score	No of Returns	Total Score	No of Returns	Total Score	Average Score
178	3	10	3	6	-	-	-
179	3	18	3	16	-	-	-
180	2	12	2	8	-	-	-

Commentary

Overall this year's samples were less challenging that those in 2011 with 89% of participants achieving maximum scores compared to 85% in 2011. Sample 204 from a patient with succinic semialdehyde dehydrogenase deficiency (SSADH) proved to be the most problematic with 11% of participants failing identify or appreciate the significance of 4-hydroxybutyric acid. There was an added complication to this sample in the fact that the patient also had an increased pyroglutamic acid excretion. Sample 198 (2-hydroxyglutaric aciduria) was also problematic for a number of laboratories. Again this was mainly due to the failing to appreciate the significance of the key metabolite – 2-hydroxyglutaric acid. Sample 197 also resulted in 11% of participant scoring less then the maximum marks. This was mainly due to the inability of many laboratories to distinguish between two disorders with similar patterns of metabolites. When sending samples out to participants we always attempt to use real clinical details and these should also help guide the participant.

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 be used for caveats or to suggest other lines of investigation based on the clinical presentation rather than the analytical findings." Ideally, in both cases, 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.

We have retained the same criteria for "Satisfactory Performance" in 2012 as in 2011. Thus a score of 11 or more based on three returns (maximum possible score 18), or of 7 or more where only two returns have been received (maximum possible score 12) has been classed as satisfactory. On this basis three of the eighty six qualifying participants have been deemed unsatisfactory. We will be sending individual letters, drawing attention to areas that appear particularly problematical, to laboratories failing these formal "Satisfactory Performance" criteria. However, such 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.

A Change In Scoring for 2013

It has been agreed that for 2013 we will change to the scoring system to bring harmonisation of performance assessment within ERNDIM. The new scoring system will be on a 0 to +4 point scale. In addition there will be a critical error score which can be assigned when a sample report contains seriously misleading findings or conclusions with serious clinical consequences. Absence of critical errors will be required for satisfactory performance.

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

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Scheme organisers