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# ERNDIM QAP
# for qualitative urinary organic acid analysis

## Annual Report 2004 (Sheffield)

## Participation

Active participants (reporting on at least one sample in the year) are shown in Table 1. Laboratories in the Netherlands, originally in the Sheffield scheme, were transferred to Heidelberg for 2004. The two schemes are run separately, usually circulating different samples, but try to keep the same general philosophy and format. To assist this, the two organising laboratories each participate in the other's scheme.

**Table 1: Geographical distribution of participants**

| | ***2004*** | ***2003*** | ***2002*** | ***2001*** | ***2000*** | ***1999*** |
|---|---|---|---|---|---|---|
| United Kingdom | 21 | 21 | 22 | 21 | 21 | 21 |
| France | 13 | 13 | 11 | 11 | 11 | 10 |
| Italy | 0 | 0 | 0 | 1 | 9 | 9 |
| The Netherlands | 0 | 10 | 9 | 8 | 8 | 8 |
| Belgium | 6 | 6 | 6 | 6 | 7 | 7 |
| Germany | 1† | 1† | 1† | 1† | 9 | 9 |
| Australia | 6 | 6 | 6 | 6 | 6 | 6 |
| Spain | 5 | 5 | 5 | 5 | 5 | 5 |
| USA | 0 | 0 | 0 | 5 | 5 | 5 |
| Austria | 0 | 0 | 0 | 0 | 3 | 3 |
| Canada | 0 | 0 | 0 | 3 | 3 | 3 |
| Czech Republic | 0 | 0 | 0 | 0 | 2 | 2 |
| Denmark | 0 | 0 | 0 | 2 | 2 | 2 |
| Republic of China | 4 | 4 | 3 | 3 | 2 | 2 |
| Israel | 2 | 2 | 1 | 1 | 1 | 1 |
| Portugal | 2 | 2 | 1 | 1 | 1 | 1 |
| Sweden | 0 | 0 | 0 | 2 | 2 | 2 |
| Switzerland | 0 | 0 | 0 | 0 | 2 | 2 |
| Other countries | 7* | 7 | 6 | 11 | 14 | 14 |
| **TOTAL** | **67** | **77** | **71** | **87** | **113** | **112** |

† Heidelberg laboratory; * One participant each from Argentina, Brazil, Finland, Republic of Ireland, Lebanon, Malaysia and Taiwan

## Samples and results

Three sets of three samples (total 9; sample numbers 124-132) were distributed in 2004. Sixty-one laboratories returned results for all three circulations.

**Table 2: Receipt of results into the executive centre within the specified time period (approximately 6 weeks from dispatch) :**

| *Number of returns in 2004* | *Number of participants* | | | | |
|---|---|---|---|---|---|
| | *0 Late* | *1 Late* | *2 Late* | *3 Late* | *Total* |
| 1 | - | - | - | - | 0 |
| 2 | 4 | 1 | 2 | - | 7 |
| 3 | 43 | 11 | 4 | 2 | 60 |

## Instrumentation

Six of the active participants used predominantly GC, the remainder GC-MS. We plan to update our information on instrumentation and workload in 2005.

## Scoring of results

Summary results for the individual returns were dispatched earlier. To enable data reduction and analysis of long-term performance the results were scored as shown below:

| | |
|---|---|
| 2 | satisfactory |
| 1 | helpful but incomplete |
| 0 | unhelpful |
| -1 | slightly misleading |
| -2 | misleading. |

A score of zero was given for failing to return an individual result.

Where samples were interchanged or misnumbered participants were penalised 2 points but otherwise given the best possible score that could be obtained by reassigning the results.

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

| **Sample** | **Scores** | | | | |
|---|---|---|---|---|---|
| | **-2** | **-1** | **0** | **1** | **2** |
| #124 Normal pattern | 1 | - | - | - | 63 |
| #125 DOPA metabolites | 11 | 3 | 4 | 10 | 36 |
| #126 3-Methylcrotonyl-CoA carboxylase deficiency | - | - | 1 | 1 | 62 |
| #127 Normal pattern | 1 | - | 4 | - | 59 |
| #128 Glutaryl-CoA dehydrogenase deficiency | 1 | - | 2 | 0 | 61 |
| #129 Normal pattern | - | 2 | 1 | 1 | 60 |
| #130 Hyperoxaluria type 1 | 6 | 1 | 1 | - | 55 |
| #131 Normal pattern | - | 1 | 1 | 1 | 60 |
| #132 D-Glyceric aciduria | - | 1 | - | 23 | 39 |

**Table 4: Cumulative scores for 2004 and the five preceding years (current Sheffield participants only)**

| Year | 2004 | | | 2003 | 2002 | 2001 | 2000 | 1999 |
|---|---|---|---|---|---|---|---|---|
| Lab ID no | Number of returns | Late returns | Total score | Total score | Total score | Total score | Total score | Total score |
| 3 | 3 | 0 | 17 | 16 | 12 | 13 | 10 | 10 |
| 4 | 2 | 0 | 12 | 14 | 17 | 12 | 15 | 18 |
| 5 | 3 | 0 | 15 | 12 | 15 | 17 | 18 | 18 |
| 6 | 3 | 0 | 18 | 13 | 18 | 17 | 14 | 18 |
| 7 | 3 | 0 | 14 | 16 | 18 | 18 | 14 | 18 |
| 9 | 3 | 0 | 18 | 9 | 18 | 18 | 18 | 18 |
| 10 | 3 | 1 | 17 | 16 | 14 | 15 | 15 | 10 |
| 11 | 3 | 0 | 18 | 12 | 18 | 18 | 18 | 14 |
| 12 | 2 | 0 | 12 | 16 | 14 | 18 | 18 | 18 |
| 13 | 3 | 0 | 17 | 12 | 12 | 17 | 18 | 18 |
| 14 | 2 | 1 | 12 | 10 | 13 | 17 | 8 | 16 |
| 15 | 3 | 1 | 16 | 16 | 11 | 17 | 17 | 18 |
| 17 | 3 | 0 | 13 | 13 | 14 | 11 | 12 | 18 |
| 18 | 3 | 0 | 11 | 16 | 18 | 17 | 14 | 17 |
| 19 | 3 | 0 | 18 | 16 | 18 | 15 | 13 | 18 |
| 21 | 3 | 0 | 14 | 16 | 12 | 12 | 16 | 18 |
| 24 | 3 | 0 | 18 | 12 | 18 | 17 | 18 | 18 |
| 25 | 3 | 0 | 17 | 14 | 16 | 17 | 18 | 18 |
| 26 | 3 | 0 | 18 | 16 | 18 | 17 | 18 | 18 |
| 27 | 3 | 1 | 9 | 1 | 4 | -1 | 11 | 7 |
| 28 | 3 | 0 | 7 | 4 | 14 | 15 | 14 | 18 |
| 29 | 3 | 0 | 17 | 16 | 14 | 15 | 18 | 17 |
| 31 | 3 | 0 | 18 | 16 | 18 | 17 | 17 | 17 |
| 32 | 3 | 1 | 11 | 16 | 18 | 12 | 18 | 18 |
| 35 | 3 | 0 | 17 | 16 | 18 | 17 | 18 | 18 |
| 38 | 3 | 0 | 18 | 16 | 18 | 18 | 18 | 15 |
| 42 | 3 | 0 | 14 | 16 | 18 | 18 | 18 | 18 |
| 43 | 3 | 2 | 16 | 11 | 17 | 18 | 16 | 14 |
| 44 | 3 | 0 | 17 | 15 | 18 | 15 | 14 | 18 |
| 48 | 2 | 0 | 11 | 8 | 16 | 10 | 14 | 18 |
| 49 | 3 | 1 | 12 | 11 | 15 | 18 | 14 | 18 |
| 51 | 3 | 0 | 17 | 12 | 18 | 18 | 17 | 14 |
| 52 | 3 | 0 | 16 | 13 | 10 | 18 | 18 | 18 |
| 65 | 3 | 1 | 18 | 16 | 16 | 14 | 18 | 18 |
| 66 | 3 | 0 | 18 | 14 | 14 | 17 | 18 | 18 |
| 69 | 2 | 2 | 10 | 5 | 4 | 2 | 8 | 12 |
| 76 | 3 | 0 | 13 | 13 | 18 | 16 | 18 | 6 |
| 79 | 3 | 2 | 13 | 14 | 17 | 11 | 13 | 18 |
| 83 | 3 | 1 | 18 | 16 | 15 | 17 | 18 | 18 |
| 85 | 3 | 3 | 14 | 12 | 16 | 17 | 18 | 14 |
| 86 | 3 | 0 | 16 | 12 | 11 | 17 | 14 | 15 |
| 88 | 3 | 1 | 14 | 5 | 8 | 10 | 18 | 11 |
| 90 | 3 | 0 | 17 | 15 | 11 | 11 | 17 | 12 |
| 92 | 3 | 0 | 17 | 16 | 17 | 17 | 12 | 12 |
| 93 | 3 | 1 | 18 | 16 | 18 | 17 | 14 | 18 |
| 94 | 3 | 0 | 17 | 6 | 14 | 13 | 11 | 16 |
| 96 | 3 | 0 | 15 | 10 | 12 | 17 | 6 | 18 |

| Year | 2004 | | | 2003 | 2002 | 2001 | 2000 | 1999 |
|---|---|---|---|---|---|---|---|---|
| Lab ID no | Number of returns | Late returns | Total score | Total score | Total score | Total score | Total score | Total score |
| 98 | 3 | 2 | 16 | 16 | 17 | 18 | 16 | 18 |
| 101 | 3 | 1 | 17 | 16 | 16 | 18 | 18 | 18 |
| 102 | 3 | 0 | 17 | 13 | 17 | 16 | 18 | 18 |
| 104 | 3 | 0 | 14 | 12 | 16 | 17 | 14 | 11 |
| 106 | 3 | 0 | 18 | 10 | | | | |
| 108 | 3 | 1 | 14 | 12 | 16 | 8 | 10 | 14 |
| 111 | 3 | 0 | 18 | 9 | 18 | 17 | 18 | 18 |
| 113 | 3 | 0 | 9 | 0 | 10 | 12 | 7 | 6 |
| 114 | 3 | 0 | 13 | 7 | 6 | 17 | 14 | 13 |
| 119 | 0 | 0 | 17 | 12 | 18 | 17 | 6 | |
| 120 | 3 | 0 | 12 | 8 | 16 | 10 | | |
| 121 | 3 | 0 | 16 | 12 | 11 | 12 | | |
| 126 | 3 | 0 | 11 | 15 | | | | |
| 127 | 2 | 2 | 7 | | | | | |
| 128 | 2 | 0 | 12 | 4 | | | | |
| 130 | 3 | 2 | 18 | 16 | | | | |
| 131 | 3 | 0 | 13 | 9 | | | | |
| 132 | 3 | 0 | 8 | 8 | | | | |
| 133 | 3 | 0 | 15 | 5 | | | | |
| 134 | 3 | 3 | 17 | 9 | | | | |
| Maximum score | 3 | 3 | 18 | 16 | 18 | 18 | 18 | 18 |

**Table 5: Ranking of scores for 2004** (Fifteen laboratories scored 18, fifteen scored 17 and were ranked 16th equal; six scored sixteen and were ranked 31st equal, etc)

| **Score** | 18 | 17 | 16 | 15 | 14 | 13 | 12 | 11 | 10 | 9 | 8 | 7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Rank** | 1 | 16 | 31 | 37 | 40 | 47 | 52 | 58 | 62 | 63 | 65 | 66 |

## Commentary

Last year (2003), following the suggestion of the ERNDIM Scientific Advisory Board, we started providing a structured response form for each sample distributed. The idea was to encourage succinct reports that would address the three main and two subsidiary questions:

- what are the major analytical findings?
- what is the most likely diagnosis?
    - how certain is it?
    - what, if any, are the possible alternatives?
- what further investigations are required to confirm or clarify the diagnosis?

All but two of the 64 returning participants in circulation #1 of 2004 used the form provided or adapted their reports to follow the same format. This was of considerable help to us in assessing the returns and we felt that it had also focussed attention more clearly on the requirements of the referring physician.

An interesting finding from this year's circulations is the degree to which the given clinical details influenced interpretation. Three samples (#129, #130 and #132) were allegedly from children with renal stones. Suspected renal stone is a fairly common reason for requesting metabolic investigations though only a small minority of such patients turn out to have a disorder of intermediary metabolism.

***Sample #129*** was from a healthy child but three respondents diagnosed a metabolic disease (two hyperoxaluria type 1, one a defect in purine metabolism). This "false positive" rate is comparable to that obtained in July 2000 when 3 of the 104 participants diagnosed hyperoxaluria type 1 from a comparable sample (#90). We commented at the time that interpretation tends to be influenced by estimates of prior odds based on the given clinical information but that these details are seldom complete and are sometimes misleading. Interestingly, in the following circulation a normal sample (#92) described as from "Male, 7 year old, learning difficulties, urinary sediment" failed to elicit any false positive diagnoses.

***Sample #130*** was indeed from a genuine case of hyperoxaluria type 1 and was identified as such by the majority of participants.

***Sample #132*** was from a patient with D-glyceric aciduria but again was ascribed to a patient with renal stones. All but one of the returning participants correctly identified the glyceric acid peak. Despite the lack of an excess of oxalate most (87%) diagnosed hyperoxaluria type 2. This was a reasonable suggestion given the clinical presentation and knowing that oxalate is easily lost from urine unless special precautions are taken. It did, however, require appropriate confirmatory investigations (initially chirality or urine collection for quantitative oxalate): omitted completely by three respondents and limited to enzyme assay (requiring liver biopsy) or mutation analysis of the D-glycerate dehydrogenase gene by nine others.

This sample had been circulated twice before (as samples # 24 and # 44), in both cases with speech delay and microcephaly as the presenting features. The results are tabulated below.

| Sample | # 24 | # 44 | # 132 |
|---|---|---|---|
| Number of returns | 55 | 78 | 63 |
| Number identifying glyceric acid (%) | 48 (87) | 71 (91) | 62 (98) |
| Number giving hyperoxaluria type 2 as preferred diagnosis | 2 | 0 | 55 |

We hope that you continue to find the scheme useful.

Yours sincerely

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**Scheme organisers**