ERNDIM
Diagnostic Proficiency Testing Centre Central Europe
Nijmegen / Amsterdam

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1. Introduction

The Quality Assurance Program (QAP) for Diagnostic Proficiency Testing (DPT) of Inherited Metabolic Diseases is organised by ERNDIM. The DPT centre of Central Europe is one of the four DPT centres of ERNDIM and is located in Nijmegen (NL). The other DPT centres are located in Sheffield (UK) for the region of Northern Europe, in Lyon (F) for the region of Southern Europe, and, in Prague (CZ) for the region of Eastern Europe. Each DPT centre has approx. 20 participants.

The SKML (previously called SKZL) is a Dutch QAP-organisation collecting samples of urine from patients with metabolic diseases (participants are obliged to deliver these samples). Twice a year SKML distributes these samples to the participants of the DPT scheme, evaluates all results, prepares a report and make the reports available to the participants. Once a year a meeting of the participants is organised to discuss the results, to bring faulty results into focus and to discuss recommendations for improvement.

2. Participants

In 2004 the DPT centre Central Europe had 20 participants from Germany, The Netherlands, Belgium and the United Kingdom.

Country	Number of participants
Germany	7
The Netherlands	10
Belgium	2
UK	1

3. Logistics of the scheme

In the DPT scheme 2004 six samples were distributed:

2004.1: patient L, M an P
2004.2: patient N, O and R

Sample L was the common sample which has been distributed by all four DPT centres.

In 2004 thiomersal had been added to the samples.
After heat inactivation the samples had been shipped by room temperature.
The result form was distributed by e-mail. Participants returned the result form by e-mail as well.

4. Timetable of the scheme

DPT survey 2004.1:	
Shipment of samples:	January 12, 2004
Deadline for returning results:	January 30, 2004
Report of survey	May 5, 2004
DPT survey 2004.2:	
Shipment of samples:	June 14, 2004
Deadline for returning results:	July 2, 2004
Report of survey:	August, 20, 2004
Meeting of participants:	September 2, 2004 (SSIEM, Amsterdam, NL)

5. Receipt of samples and results

Survey 2004.1 : Samples had been sent to 20 participants and 19 (samples L and M) and 18 participants (sample P) returned their results.

Survey 2004.2 : Samples had been sent to 20 participants ; 18 of these returned their results.

6. Scoring of results

The merits of a the scoring system of a DPT scheme were discussed at the September meeting of the Scientific Advisory Board of ERNDIM in 2002. At the end of the year 2002 a final scoring system has been agreed upon. In 2003 the scoring system is introduced as a pilot and in 2004 the scoring system was used.

For each individual sample a score can be achieved for:

Analytical performance:	Correct results of the appropriate tests	score: 2
	Partially correct or non-standard methods	score: 1
	Unsatisfactory or misleading	score: 0
Interpretative performance:	Good (diagnosis was established)	score: 2
	Helpful but incomplete	score: 1
	Misleading / wrong diagnosis	score: 0
Recommendations:	Helpful	score: 1
(for further investigations)	Unsatisfactory or misleading	score: 0
		=======
	Total:	score: 5

7. Scores of participants for individual samples

Lab	Total 2003	Samples in 2004 (maximum score is 30)						
		L	M	N	O	P	R	Total 2004
1	28	5	5	5	5	5	5	30
2	25	5	5	5	5	5	5	30
3	30	5	5	5	5	4	5	29
4	24	5	4	5	5	4	4	27
5	19	5	5	5	5	5	5	30
6	24	5	4	5	5	5	3	27
7	25	5	5	5	5	5	0	25
8	27	5	5	5	5	1	5	26
9	20	5	5	0	0	5	0	15
10	25	5	5	5	5	5	5	30
11	21	5	5	2	5	0	2	19
12	21	5	5	5	5	5	4	29
13	26	5	1	2	5	5	1	19
14	24	5	0	5	4	3	3	20
15	24	0	0	1	5	0	3	9
16	23	5	5	1	5	5	2	23
17	24	5	5	2	5	5	2	24
18	14	5	5	0	0	5	0	15
19	15	-	-	-	-	-	-	-
20	20	1	1	5	1	5	2	15
21	4	5	5	4	5	5	4	28

8. Distribution of total scores for individual laboratories

See table in item 7. In the DPT – centre Central Europe the following was observed.
A score of more than 75% correct diagnoses which means 23 points or more is achieved by 13 / 20 labs. A score below 75% (less than 23 points) was found in 7 / 20 labs.
And a score below 50% (less than 15 points) was found in 1 lab.

9. Summary of scores

Sample	Diagnosis	Correct diagnosis
L	Mevalonic aciduria	17 / 19
M	Alfa-mannosidosis	16 / 19
P	No abnormalities indicating a metabolic disorder	18 / 18
N	Sarcosinuria/emia	13 / 18
O	Mucopolysaccharidosis type III (M. Sanfilippo)	16 / 18
R	No indication for metabolic disorder	11 / 18

10. Meeting of participants, in Amsterdam (August 31, 2004)

Present: Abeling, van den Berg, van den Bergh, Dorland, Duran, Eyskens, van Gennip (chairman), Gerlo, Haas, Huijmans, Kluijtmans, van Landeghem, Onkenhout, Poorthuis, Reijngoud, Ruijter, Ruitenbeek, de Sain, Sass, Spaapen, Verhoeven, Vincent, Wamelink and Holtrop (secretary).

1. Welcome.
The chairman welcomes the participants.

2. Minutes of the meeting held at October 3, 2003 Maastricht.
No comments. The minutes are finalised with thanks to Holtrop for preparing.

Advice: To check whether your results have been received at the SKML office ask for "confirmation of reading" when you have sent your results. For instructions see your e-mail programme.

3. Information
None.

4. Annual contribution of DPT samples
Participants have the obligation to provide DPT-samples (one sample each year). This is necessary, otherwise we cannot continue this QA-scheme. Please send your sample to the SKML office. How to send samples ?
The samples have to be heat-inactivated (see Annual report 2003, item 3a) AND the data form for samples in stock has to be completed. The sample and the data form have to be sent to the SKML office (prof. dr. Willems at Nijmegen). **Action: all**

The new data form for samples in stock will be sent to all participants. **Action: Holtrop**

Urine samples from patients treated with medication a.o. antibiotics can be used but the medication (e.g. depakine) must be specified on the in stock data form. The medication should not be so interfering that diagnosis is obscured.

5. Discussion of the results of the survey 2004-1 (samples L, M and P) and 2004-2 (samples N, O and R).
Sample L in survey 2004.1 was the common sample which will be discussed at the ERNDIM joint meeting.
The result reports had been evaluated by prof. dr. Willems and by the scientific advisor for the DPT-scheme, dr. van Gennip.

For a correct analytical interpretation 2 points can be scored; for a correct diagnosis another 2 points can be gained and a correct advice for further investigations will give another 1 point. In total a maximum of 5 points per sample can be scored. For 6 samples the total score can be 30.

<u>Sample M (2004.1): Alfa-mannosidosis</u>
The diagnosis was found by nearly all participants. A low uric acid, high oxalate, slightly elevated GAG in methylene blue test was found. One participant reported a positive Brand reaction. (how possible ?).

<u>Sample P (2004.1): No abnormalities indicating a metabolic error of metabolism</u>
There was a large range of results of uric acid: 0.48 – 2.3 ; this might be due to a dimension problem. Two participants reported elevated levels of amino acids Asp and Lys but did not comment on that in their diagnosis. From one lab the results are not included in the report although they had been sent to the SKML office.

In this sample with these results, further investigations on lysosomal enzymes which was suggested by one participant will not help you any further.

Sample N (2004.2): Sarcosinuria / emia
Some participants had difficulties with this sample. Advice: when there are difficulties with a sample you can always ask for a new sample.

Sarcosine was found in a large range: 780 – 2000. Suggestion: maybe this metabolite should be included in the ERNDIM quantitative scheme of amino acids as well.

When using the Brand test check the sensitivity, linearity and detection limits of this test. The test has to be validated with different amounts of analyte. When the test is used for diagnostics then the lab has to check the reliability of the test.
The Brand test can be used in practice to detect patients with cystinuria.

Sample O (2004.2): Mucopolysaccharidosis type III (M. Sanfilippo)
The diagnosis "mucopolysaccharidosis" without further details is okay – the score will be 2 points.
The diagnosis SLY might be due to technical problems in the 1-dimensional electrophoresis – it is better to use 2-dimensional electrophoresis.

Sample R (2004.2): No indication for metabolic disorder
One participant uses capillary electrophoresis for the detection of purines and pyrimidines and found two peaks with the same migration. This might be due to a technical problem.
One participant found an elevated thiosulphate which is very unusual. Which method was used ?

Is anything known about the medication which was given to this patient, e.g. Ca-suppletion or anti-convulsiva ? Maybe this could clarify some reported results. Medication, when known, should be mentioned in the clinical description of "normal" patients as well. Prof. Willems will be asked to see to this. **Action: van Gennip / Willems**

6. Overview of the DPT-scores in 2003 (pilot) and 2004.

In the Scientific Advisory Board of ERNDIM (SAB) it was decided that a true "poor performer" in the DPT-scheme is a participant who scores less than 15 (out of 30) points. A score of 15 or more is still acceptable. In the DPT-centre Central Europe we previously discussed a score of less than 75% (which is less than 23 out of 30 points). According to the definition of the SAB, in 2004 in our DPT-centre we only had 1 participant who is a true "poor performer" (score: 9 points).
This participant will be requested to contact the scientific advisor of the DPT-scheme to make further arrangements with respect to support.

In future (will probably start in 2004 ?) an indication will be mentioned on the ERNDIM certificate and a warning letter will be sent to the true poor performers.

In 2003 participants still receive a certificate for participation in the ERNDIM QAP schemes.

7. Any other business

The number of mistakes in the result reports have been reduced since last year. It has been improved but still not correct. To the opinion of the participants reports should be correct.

8. Date of the next DPT meeting

The next meeting will be organised on September 6, 2005 in Paris at the SSIEM venue.

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Amsterdam, June 2005
S. Holtrop