ERNDIM Diagnostic Proficiency Testing Center, Prague

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Annual report 2001

1. Introduction

Since the three diagnostic proficiency testing centers (DPTCs) in Lyon, Nijmegen and Sheffield were already at/or above their capacity limit the Executive Board of ERNDIM decided to set up a fourth DPTC in Prague. In 2001 this DPTC has been running in a pilot phase without any cost to the participants. The pilot phase has been evaluated during the Executive and Trust Board meeting in Prague in September 2001 and the intention is to run the DPT scheme as a regular per-fee ERNDIM scheme starting in 2002.

2. Geographical distribution of the participants

Twenty-one laboratories from 12 countries of Eastern, Central and Southern Europe have participated in a pilot phase of the DPT scheme. Six of them were previous participants of Lyon DPTC and three labs participated in Nijmegen DPTC, the remaining labs were new.

Country	Number of participants
Austria	1
Bulgaria	1
Croatia	1
Cyprus	1
Czech Republic	3
Germany	3
Greece	2
Lithuania	1
Poland	1
Slovakia	3
Switzerland	3
Turkey	1
TOTAL	**21**

3. Logistic of the scheme

- 2 surveys: 2001/1 – patients A and B
  2002/2 – patients C, D and G
- Origin of samples – four patients diagnosed in the Institute of Inherited Metabolic Disorders in Prague (A, B, C and D). Their diagnoses were confirmed in Laboratory of Genetic Metabolic Diseases in Amsterdam.
- A common sample G from Nijmegen was included.
- Five heat-treated urines were shipped by express courier service at RT.
- Communication between the organizers and the participants occured by e-mail, fax and regular mail.

4. Timetable of the scheme

November 2000 – questionnaire sent to possible participants
February 2001 – evaluation of the questionnaire survey
April 30, 2001 – samples shipment
June 15, 2001 – deadline for results submission (Survey 1)
July 2, 2001 – report of Survey 1
August 4, 2001 – deadline for results submission (Survey 2)
August 26, 2001 – report of the Survey 2
September 4, 2001 – meeting of the participants
November 9, 2001 – annual report 2001

5. The receipt of samples and results

Receipt of samples

the same day	1
+48 hours	8
+72 hours	3
4 days	4
10 days	2
not indicated	3

Receipt of results

	Survey 1	Survey 2
till deadline	16	19
3 days later	3	-
> 3 days later	2	2

6. Scoring of results

Based on recommendation of participants a novel scoring system has been established. This system takes into consideration not only the establishment of diagnosis but also the analytical performance and the recommendations for the further actions (advices for further investigations and to the attending clinician).

Three criteria were evaluated:

A	Analytical performance	Correct results of the appropriate tests	2
		Partially correct or non-standard methods	1
		Unsatisfactory or misleading	0
I	Interpretative proficiency	Good (diagnosis was established)	2
		Helpful but incomplete	1
		Misleading/wrong diagnosis	0
R	Recommendations	Complete	2
		Helpful but incomplete	1
		Unsatisfactory or misleading	0

The **total score** is calculated as a sum of these three criteria. The maximum that can be achieved is 6 for one sample.
2 points for analytical performance were given if the crucial analyses were performed and typical results were found (e.g. TLC of oligosaccharides in α-mannosidosis), or if concentration of critical metabolite was abnormal according to local reference ranges (e.g. orotic acid in OTC deficiency or cystine in cystinuria).
2 points for recommendations were given if all therapeutic advices were reported (e.g. avoiding fasting, protein/leucin/fat restriction and carnitine supplementation in 3-hydroxy-3-methylglutaric aciduria or high fluid intake/urine alkalinization/medical treatment in cystinuria).

7. Scores of participants for individual samples

Survey 2001/1

Lab number	Sample A α-mann				Sample B HMGA			
	A	I	R	Total	A	I	R	Total
1	0	0	0	**0**	2	2	2	**6**
2	0	0	0	**0**	2	2	2	**6**
3	2	2	2	**6**	2	2	2	**6**
4	2	2	2	**6**	2	2	1	**5**
5	2	2	0	**4**	2	2	0	**4**
6	2	2	2	**6**	2	2	2	**6**
7	2	1	2	**5**	1	1	1	**3**
8	2	2	2	**6**	2	2	2	**6**
9	0	0	0	**0**	2	2	1	**5**
10	2	2	2	**6**	2	2	2	**6**
11	2	2	2	**6**	2	2	2	**6**
12	2	2	2	**6**	2	2	1	**5**
13	0	0	0	**0**	0	0	0	**0**
14	2	2	2	**6**	2	2	2	**6**
15	1	0	0	**1**	2	2	1	**5**
16	2	2	2	**6**	2	2	2	**6**
17	2	2	2	**6**	2	2	2	**6**
18	2	2	2	**6**	2	2	2	**6**
19	2	2	1	**5**	2	2	1	**5**
20	2	2	2	**6**	2	2	1	**5**
21	2	2	2	**6**	2	2	2	**6**

Survey 2001/2

Lab number	Sample C OTC het.				Sample D Cystinuria				Sample G MMA			
	A	I	R	Total	A	I	R	Total	A	I	R	Total
1	2	2	2	**6**	2	2	1	**5**	2	2	2	**6**
2	0	0	1	**1**	1	2	1	**4**	0	0	1	**1**
3	2	2	1	**5**	2	2	2	**6**	0	0	0	**0**
4	2	1	1	**4**	1	2	2	**5**	2	2	2	**6**
5	2	2	2	**6**	2	2	1	**5**	2	2	2	**6**
6	0	0	0	**0**	2	2	2	**6**	2	2	2	**6**
7	0	0	0	**0**	2	2	1	**5**	0	0	0	**0**
8	2	2	2	**6**	2	2	2	**6**	2	2	2	**6**
9	2	2	2	**6**	1	2	1	**4**	2	2	2	**6**
10	2	2	2	**6**	2	2	1	**5**	2	2	2	**6**
11	2	2	2	**6**	2	2	2	**6**	2	2	2	**6**
12	0	1	1	**2**	2	2	2	**6**	2	2	2	**6**
13	2	2	2	**6**	2	2	1	**5**	2	2	2	**6**
14	2	2	2	**6**	2	2	1	**5**	2	2	2	**6**
15	2	2	2	**6**	1	2	2	**5**	2	2	2	**6**
16	2	2	2	**6**	2	2	2	**6**	2	2	2	**6**

17	2	2	2	**6**	2	2	2	**6**	2	2	2	**6**
18	1	1	1	**3**	2	2	2	**6**	2	2	2	**6**
19	2	2	2	**6**	2	2	2	**6**	2	2	2	**6**
20	2	2	2	**6**	2	2	1	**5**	2	2	2	**6**
21	2	2	2	**6**	2	2	1	**5**	2	2	2	**6**

8. Distribution of total scores for individual laboratories

Lab number	Survey 2001/1	Survey 2001/2	Cumulative score	Cumulative score [%]
1	6/12	17/18	23/30	77
2	6/12	6/18	12/30	40
3	12/12	11/18	23/30	77
4	11/12	15/18	26/30	87
5	8/12	17/18	25/30	83
6	12/12	12/18	24/30	80
7	8/12	5/18	13/30	43
8	12/12	18/18	30/30	100
9	5/12	16/18	21/30	70
10	12/12	17/18	29/30	97
11	12/12	18/18	30/30	100
12	11/12	14/18	25/30	83
13	0/12	17/18	17/30	57
14	12/12	17/18	29/30	97
15	6/12	17/18	23/30	77
16	12/12	18/18	30/30	100
17	12/12	18/18	30/30	100
18	12/12	15/18	27/30	90
19	10/12	18/18	28/30	93
20	11/12	17/18	28/30	93
21	12/12	17/18	29/30	97

9. Summary of scores

Sample	Diagnosis	Analytical [%]	Interpretative [%]	Recommen-dations [%]	Total [%]
A	*α-Mannosidosis*	79	74	69	74
B	*3-Hydroxy-3-methylglutaric aciduria*	93	93	74	87
C	*OTC-heterozygote*	79	79	79	79
D	*Cystinuria*	90	100	76	89
G	*Methylmalonic aciduria*	86	86	88	87

10. Meeting of the participants

39th Annual Symposium of SSEIM, September 4, 2001, 9:30-11:30, Prague Congress Centre

Agenda

- Introduction
- Transfer of participants from other centres + geography
- Logistic of the scheme
- Survey 2001/1 samples A, B
- Survey 2001/2 samples C, D

- Common sample G
- Budget and fee for 2002
- Problems and evaluation of the trial period
- Varia
- Time of the next meeting

Participants present: Drs. Miljenka Naradin, Ksenija Fumic (Croatia), Anthi Drousiotou (Cyprus), Tomas Adam, Eliska Marklova, Viktor Kozich, Evzenie Pospisilova (Czech Republic), Gunter Rebentisch, Ina Knerr (Germany), Persephone Augoustides-Savvopoulou (Greece), Loreta Cimbalistiene (Lithuania), Ewa Pronicka, E. M. Maunowicz, Maciej Adamowicz (Poland), J. Skodova, Elena Gregova (Slovakia), Brian Fowler (Switzerland)
Apologies for absence: Drs. Nenad Blau, Bendicht Wermuth (Switzerland).

Results discussion
The results of all the samples were discussed.

- Missing orotic acid in the urine from OTC heterozygote in some labs – patricipants didn´t find any obvious reason for this misdiagnosis.
- Large discrepancies between concentrations of metabolites can be caused by variation in creatinine values. It was recommended that participants would submit the results both in mmol/mol creatinine and in mmol/l, and that creatinine would be included into the reports.
- Participants discussed large variation in cystine concentrations. Possible causes for these discrepancies include different preparation of sample that affects solubility of cystine (heating of urine at 37^{o}C, RT, sonication), variation in creatinine values and differencies in concentration reporting (cystine vs half-cystine).

Scoring system

- Two-point scoring system (correct/false diagnosis) was not considered satisfactory. The evaluation of the results should include analytical findings, their interpretation and the advice on further action.
- The participants proposed this new scoring system to become effective in 2002.
- Performance will be scored as a) cumulative b) as sliding windows encompassing 3 surveys, which will be updated after each survey. This window will include any additional samples.

“Poor performer”
The participants whose performance efficiency is less then 75% are considered to be a poor performer. Such a lab can request two additional samples per year for improving its proficiency. The participants are expected to improve within two years; if no improvement would be reached the lab will be asked to terminate participation in the scheme.

Recommendation for the next year

✓ **Shipment of the samples**

- Samples will be labelled as biological material and the participants will be notified prior the shipment; this notification will include the name of the express courier service.
- The participants accepted one distribution per year – most likely time of the next distribution will be March 2002.
- The shipment will contain six different samples (including the common sample).
- Normal urine will not be included.

✓ **Sample contribution**

- The participants are obliged to provide each year at least 250 –300 ml of the urine from a patient with an established inborn error of metabolism together with a short clinical information (the symptoms of the patient at the time when the disease was revealed; data of the time when urine was collected should be also included).

- Treatment of the samples – heat-treat the urine at 50^{o}C for 20 minutes. Make sure that this temperature is achieved in the entire urine sample, not only in the water bath.
- The greater volume of the sample about 1000 ml could be used as a common sample (in all four centres).
- Please, send the samples only after prior agreement with the scheme organizers.

Next meeting of the scheme participants
Next meeting will be held during the 40th Annual Symposium of SSIEM, September 2002, Dublin, Ireland.

Participation in 2002
The application forms for participation in QA Schemes were distributed from ERNDIM in September. If you did not receive it, please contact Dr. JR Bonham or Malcolm Heron (MalcolmHeron@msn.com).
The fee for 2002 will be 242 Euros and is payable to the Treasurer of ERNDIM.

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