

## **ERNDIM DPT Center Prague**

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and

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## **Proficiency Testing Centre Prague Annual Report 2009**

## 1. Introduction

In 2009 proficiency testing in our centre was running as a regular ERNDIM scheme.

#### 2. Geographical distribution of participants

Eighteen laboratories from 15 countries have participated in our Diagnostic Proficiency Testing scheme in 2009, for details see the below table:

Country	Number				
Country	of participants				
Austria	1				
Croatia	1				
Cyprus	1				
Czech Republic	1				
Denmark	1				
Finland	1				
France	1				
Germany	4				
Greece	1				
Kingdom of Saudi Arabia	1				
Latvia	1				
Malaysia	1				
Poland	1				
Slovakia	2				
Switzerland	1				
in total	19				

## 3. Logistics of the scheme

✓ Two surveys: 2009/1 – samples A, B and C 2009/2 – samples D, E and F

Origin of samples: Five urines obtained from patients with known diagnoses (samples were provided by organizers) + a common sample from DPT Basel (distributed in all five DPT schemes).

The samples with the exception of the common sample C have been reanalyzed in our lab after heat-treatment. The diagnostically relevant metabolites were detected in all five samples after 3-day incubation at RT.

- ✓ Six heat-treated urines together with results protocols were distributed to the participants at ambient temperature using the courier FedEx. Based on the report of the courier 16 parcels were delivered within 3 days; we consider this transportation time acceptable.
- ✓ The following protocol for heat inactivation is being used: Thiomersal 100 mg/l of urine is added and urine is heated at 56°C for one hour in water bath (this temperature is checked in urinary sample and not only in the water bath). The urinary samples have been frozen until shipment.
- ✓ Tests required in 2009: amino acids, organic acids, mucopolysaccharides, oligosaccharides and purines/pyrimidines

#### 4. Schedule of the scheme in 2009

Sample distribution	March 23, Monday
Start of analysis of Survey 2009/1	April 6, Monday
Survey 2009/1 – results submission	April 24, Friday
Survey 2009/1 – report	May 22, Friday
Start of analysis of Survey 2009/2	June 8, Monday
Survey 2009/2 – results submission	June 26, Friday
Survey 2009/2 – report	October 8, Thursday
Annual meeting of participants	October 23, Friday
Annual report 2009	November 30, Monday

## 5. The receipt of samples and results

Date of receipt of samples (samples sent on March 23, 2009)

date of receipt (reported by participants)	number of participants	date of receipt (reported by courier service)	number of participants
1 day	7	1 days	14
2 days	3	2 days	3
4 days	2	3 days	2
7 days	1	-	-
not indicated	6	-	-

#### **Deadlines of the results submission**

	2009/1	2009/2
in time	14	16
1 day delay	1	-
3 days delay	1	1
4 days delay	1	-
6 days delay	1	ı
no answer	2	2

## 6. Samples

#### Sample A

**Patient:** The sample was obtained from a 36-years old man with thymidine phosphorylase deficiency (MNGIE syndrome). The diagnosis was established by demonstrating enzyme deficiency in lymphocytes and completed by molecular analysis. The sample was obtained from our repository.

Analytical performance: The presence of thymidine and/or 2'-deoxyuridine, and of thymine and/or uracil was considered a correct analytical result. The presence of thymine and/or uracil only was considered a partially correct analytical result. The analytical performance was slightly suboptimal (71%).

*Interpretative proficiency:* Thymidine phosphorylase deficiency was considered correct diagnosis. The interpretative proficiency score for this sample in laboratories that detected thymidine and/or 2'-deoxyuridine was good, overall proficiency was slightly suboptimal (76%).

**Recommendations:** Confirmation of diagnosis by enzymatic assay and/or mutation analysis was considered helpful. Recommendation to carry out analysis of purines and pyrimidines for those participants that did not perform P/P analysis was considered also helpful.

**Overall impression:** Moderately difficult DPT sample with an average proficiency score. It is important to note that several participants observed thymine and uracil in organic acid analysis but did not perform the analysis of purines and pyrimidines; they concluded that the patient suffered from dihydropyrimidine dehydrogenase deficiency.

#### Sample B

**Patient:** A 6 year old boy with alkaptonuria due to deficiency of homogentisate dioxygenase. The diagnosis is solely based on demonstrating the urinary excretion of homogentisic acids. The sample was obtained from our repository.

Analytical performance: All participants analyzed organic acids and demonstrated massive excretion of homogentisic acid, which was considered good analytical performance. Results of many pre-investigations exhibited unusual variation, which most likely results from the interference of homogentisate with these tests. The largest variation was observed for creatinine, acetone and protein determination.

*Interpretative proficiency:* The diagnosis of alkaptonuria was considered correct. The proficiency score for this sample was excellent (100%).

**Recommendations:** A plethora of recommendations was reported, all of the following were considered correct: massive excretion of homogentisate is sufficient for diagnosis, enzymatic confirmation is not required, mutation analysis is available.

Overall impression: An easy sample with excellent total proficiency score (100%).

#### **Sample C** (common sample)

**Patient:** The common sample provided by the DPTC Basel. This sample was obtained from a 6-years old girl with Salla disease, diagnosis was confirmed by molecular genetic analysis.

Analytical performance: Increased excretion of free sialic acid was considered a correct analytical result regardless of the employed technique (TLC or HPLC or photometric). The analytical performance was poor (47%).

*Interpretative proficiency:* Salla disease was considered correct diagnosis. The interpretative proficiency score for this sample in laboratories that detected increased excretion of free sialic acid was good, overall proficiency was poor (47%).

**Recommendations:** Confirmation of diagnosis by measuring of free sialic acid in urine/cultured skin fibroblasts and/or mutation analysis was considered helpful.

*Overall impression:* A sample with poor total proficiency score (47 %).

#### Sample D

**Patient:** A 8 year old girl with Hyper-IgD syndrome due to mevalonate kinase deficiency. The diagnosis was confirmed by molecular genetic analysis. The sample was obtained from our repository.

**Analytical performance:** All 17 participants analyzed organic acids, 16 participants reported elevated excretion of mevalonolactone and/or mevalonic acid, such analytical finding was considered correct. The analytical performance for this sample was good (94%).

*Interpretative proficiency:* The diagnosis of Hyper-IgD syndrome due mevalonate kinase deficiency was considered correct. The proficiency score for this sample was good (94%).

**Recommendations:** Confirmation of diagnosis by enzyme assay of mevalonate kinase activity in fibroblasts or lymphocytes and/or mutation analysis was considered helpful.

**Overall impression:** An easy sample with a good total proficiency score (88%).

#### Sample E

**Patient:** An 8 year old girl with propionic acidemia due to the deficiency of propionyl-CoA carboxylase. The diagnosis was confirmed by molecular genetic analysis. The sample was obtained from our repository.

**Analytical performance:** All participants analyzed organic acids and demonstrated increased excretion of 3-hydroxy-propionate and methylcitrate, presence of these metabolites was considered a good analytical performance.

*Interpretative proficiency:* The diagnosis of propionic acidemia was considered correct. The proficiency score for this sample was excellent (100%).

**Recommendations:** Confirmation of diagnosis by enzyme assay of propionyl-CoA carboxylase activity in fibroblasts or leucocytes and/or mutation analysis was considered helpful.

*Overall impression:* An easy sample with an excellent total proficiency score (100%).

#### Sample F

**Patient:** The sample was obtained from a 15-years old male with mucopolysaccharidosis type I due to deficiency of  $\alpha$ -L-iduronidase. The diagnosis was confirmed by enzyme and molecular genetic analyses. The sample was obtained from our repository.

Analytical performance: A report on elevated concentration of glycosaminoglycans together with an increased proportion of dermatan s ulphate and/or heparan sulphate was considered a correct analytical result. The analytical performance for this sample was good (94%).

*Interpretative proficiency:* The diagnosis of mucopolysaccharidosis type I (either alone or with other MPS types) was considered good while suspicion for MPS (other types of MPS or non-specified MPS) was considered helpful but incomplete. The interpretative proficiency score for this sample was 88%.

**Recommendations:** For participants who evaluated GAG fractions the measurement of appropriate enzymes (N-acetylgalactosamine-4-sulphatase, α-L-iduronidase, iduronate-2-sulphatase) in leucocytes or cultured fibroblasts was considered helpful. For one participant who did not perform any GAG analysis the recommendation to do GAG analysis was considered helpful.

Overall impression: Typical DPT sample with an average proficiency score.

## 7. Scoring of results

Three criteria have being evaluated: analytical performance, interpretative proficiency and recommendations for further investigations. Due to the large variability in reporting results in various countries recommendations to treatment are not evaluated in proficiency testing, however, they are still reported and summarized by the scheme organizers.

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

The total score was calculated as a sum of these three criteria. The maximum that can be achieved is 5 points per sample, i.e. 15 points per survey and 30 points per year.

# 8. Score of participants for individual samples Survey 2009/1

Lab no	phosp		ple A nidine se defic	ciency	Sample B Alkaptonuria			Sample C Salla disease				
	A	I	R	T	A	I	R	T	A	I	R	T
1	0	0	0	0	0	0	0	0	0	0	0	0
2	2	2	1	5	2	2	1	5	0	0	0	0
3	1	2	1	4	2	2	1	5	0	0	0	0
4	1	0	1	2	2	2	1	5	2	2	1	5
5	2	2	1	5	2	2	1	5	0	0	0	0
6	2	2	1	5	2	2	1	5	0	0	0	0
7	0	0	0	0	2	2	1	5	0	0	0	0
8	1	0	1	2	2	2	1	5	2	2	1	5
9	2	2	1	5	2	2	1	5	2	2	1	5
10	2	2	1	5	2	2	1	5	0	0	0	0
11	2	2	1	5	2	2	1	5	0	0	0	0
12	2	2	1	5	2	2	1	5	2	2	1	5
13	2	2	1	5	2	2	1	5	0	0	0	0
14	1	2	1	4	2	2	1	5	2	2	1	5
15	0	0	1	1	2	2	1	5	2	2	1	5
16	2	2	1	5	2	2	1	5	0	0	0	0
17	0	2	1	3	2	2	1	5	2	2	1	5
18	2	2	1	5	2	2	1	5	2	2	1	5
19	0	0	0	0	0	0	0	0	0	0	0	0

**Survey 2009/2** 

Lab		Sam	ple D				ple E				ple F	
	Hy	per-IgI	) syndr	ome	Pı	ropioni	c acide	mia		MPS	type I	
no	A	I	R	T	A	I	R	T	A	I	R	T
1	0	0	0	0	0	0	0	0	0	0	0	0
2	2	2	1	5	2	2	1	5	2	2	1	5
3	2	2	1	5	2	2	1	5	2	2	1	5
4	2	2	1	5	2	2	1	5	2	2	1	5
5	0	0	0	0	2	2	1	5	0	0	1	1
6	2	2	1	5	2	2	1	5	2	2	1	5
7	2	2	1	5	2	2	1	5	2	2	1	5
8	2	2	1	5	2	2	1	5	2	2	1	5
9	2	2	1	5	2	2	1	5	2	2	1	5
10	2	2	1	5	2	2	1	5	2	2	1	5
11	2	2	1	5	2	2	1	5	2	2	1	5
12	2	2	1	5	2	2	1	5	2	2	1	5
13	2	2	1	5	2	2	1	5	2	2	1	5
14	2	2	1	5	2	2	1	5	2	2	1	5
15	2	2	1	5	2	2	1	5	2	1	1	4
16	2	2	1	5	2	2	1	5	2	1	0	3
17	2	2	0	4	2	2	1	5	2	2	1	5
18	2	2	1	5	2	2	1	5	2	2	1	5
19	0	0	0	0	0	0	0	0	0	0	0	0

A – Analytical score, I – Interpretative score, R – Recommendations, T – Total score

## 9. Total score of participants for individual surveys and their performance in 2009

Lab	Survey 2009/1	Survey 2009/2	Total point
no	[points]	[points]	2009
1	0	0	0
2	10	15	25
3	9	15	24
4	12	15	27
5	10	6	16
6	10	15	25
7	5	15	20
8	12	15	27
9	15	15	30
10	10	15	25
11	10	15	25
12	15	15	30
13	10	15	25
14	14	15	29
15	11	14	25
16	10	13	23
17	13	14	27
18	15	15	30
19	0	0	0

#### 10. Score summary in 2009

Sample	Diagnosis	Analytical [%]	Interpretative [%]	Recommendations [%]	Total [%]
A	Thymidine phosphorylase deficiency	79	76	82	80
В	Alkaptonuria	100	100	100	100
C	Salla disease	47	47	47	47
D	Hyper-IgD syndrome	94	94	88	92
E	Propionic acidemia	100	100	100	100
F	MPS type I	94	88	94	92

<sup>&</sup>quot;Easy" and "difficult" samples were included in the surveys. The analytical and interpretative performance was good to very good for most diagnoses.

## 11. Satisfactory performance

The participants who obtained 18 or more points in the year 2009 are considered as satisfactory performers, two participants did not return any results and one participant did not reach the threshold of satisfactory performance.

## 12. Annual meeting of the participants

The annual meeting of participants of the Proficiency Testing Centre Prague took place during the ERNDIM Meeting 2009 in Basel on 23<sup>rd</sup> October 2009, seven laboratories were represented. The following items were discussed during the annual meeting of our DPT centre:

#### 1. Information

- training course, meeting ERNDIM
- ERNDIM is aiming at accrediting Schemes
- Possible changes in DPT (sample recruitment and distribution, web based system at CSCQ)
- 20% discount upon submission of suitable samples for distribution
- 2. Tests required for to 2010
  - amino acids, organic acids, mucopolysaccharides, oligosaccharides and purines/pyrimidines
- 3. Submission of results
  - the participants approved the acceptance of 2009 results submitted past the deadline
- 4. Discussion of results of samples A-F
  - scoring of 2009 results proposed by organizer has been accepted

## 13. Changes planned in 2010

✓ Submission and evaluation of results and reporting via web: the system is now being developed by B. Fowler, X. Albe and V. Kozich; testing of this system is now in a pilot phase.

#### 14. Tentative schedule of DPT scheme and fee in 2010

Sample distribution	March 8, Monday
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Start of analysis of Survey 2010/1	March 22, Monday
Survey 2010/1 – results submission	April 9, Friday
Survey 2010/1 – report	May 7, Friday
Start of analysis of Survey 2010/2	May 24, Monday
Survey 2010/2 – results submission	June 11, Friday
Survey 2010/2 – report	August 13, Friday
Annual meeting of the participants	to be determined
Annual report 2010	November 29, Monday

Next annual meeting of participants will take place on August  $31^{th}$  during the  $45^{th}$  Annual Symposium of SSIEM in Istanbul.

The Executive Board and Board of Trustees of ERNDIM determined the DPT fee for 2010 in the amount of 320 €.

## 15. Certificate of participation in Proficiency Testing for 2009

The certificate of participation will be provided by the ERNDIM to all participants, who returned the results of both surveys.

Prague, December 5, 2009

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