ERNDIM Diagnostic Proficiency Testing Challenge for the harmonization of results submission and reporting tools

Christine Vianey-Saban

Viktor Kozich, Brian Fowler, Mick Henderson

Xavier Albe

ERNDIM

- European Research Network for evaluation and improvement of screening, Diagnosis and treatment of Inborn errors of Metabolism
- www.erndim.org
- Established in 1994
- Operates 12 EQA schemes for biochemical genetic testing
- Quantitative and qualitative schemes
- European-wide scale, but more and more laboratories from all over the world
- 362 participants in 2013

Participation data for 2013

ERNDIM
QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

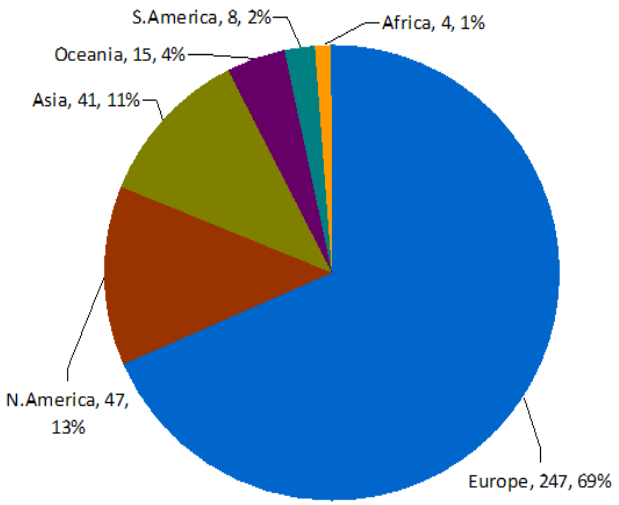
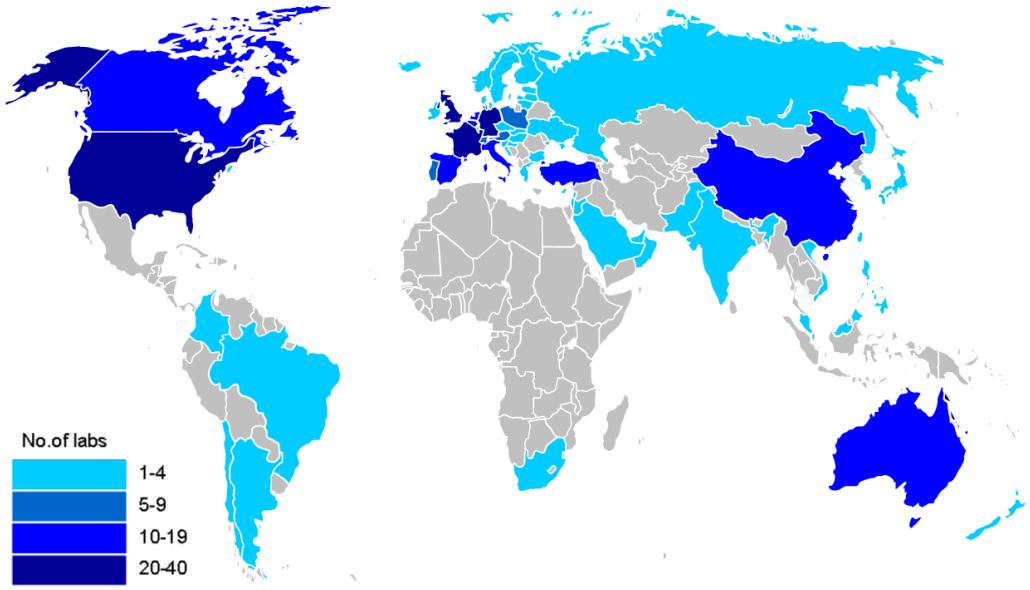


Fig 1. No. of EQA participants by continent

No. of labs = 362 (6% ↑ on 2012)

No. of participating countries = 58 (7% ↑ on 2012)

No. of EQA Scheme participations	2013	Difference to 2012
Quantitative Schemes		
Amino acids in urine	255	+12
Cystine in white blood cells	33	-1
Lysosomal enzymes in fibroblasts	72	+1
Organic acids in urine	112	+8
Purines & pyrimidines in urine	57	+2
Special assays in urine	172	+4
Special assays in serum	213	+6
Qualitative Schemes		
Acyl carnitines in dried blood spots [2 centres]	123	+6
Congenital disorders of glycosylation	61	0
Diagnostic proficiency testing in urine [5 centres]	104	+3
Organic acids in urine [2 centres]	190	+1
Urine Mucopolysaccharides (n.b. ran as pilot 2010-11)	104	0
Total	**1496**	**+42**



No. of EQA participants by country

Diagnostic Proficiency Testing

- 5 organising centres : Czech Republic, France, Switzerland, The Netherlands, United Kingdom
- Maximum 25 participants per centre
  - Difficulty of obtaining sufficient urine
  - Need to create an intimate forum in which results, including mistakes, can be discussed
- 103 participants in 2013

Diagnostic Proficiency Testing

- Six urine samples from patients with a specific inborn error of metabolism or from controls are distributed once a year by each of the centres, but analyzed in two surveys
- Participants are required to perform any relevant tests in order to reach a diagnosis, according to the provided clinical information
- Results are scored according to 2 criteria
  - Analytical performance : 2 points
  - Interpretative proficiency, including recommendations for further investigation to confirm the diagnosis : 2 points

DPT reporting before 2011

- Submission of results
  - Word format form, established by each scheme organiser
  - Sent by e-mail or by fax
- Analysis of results
  - Each scheme organiser copied manually and analysed results through a “in house” Excel or Word file developed by each of them
- Reporting : edited manually by each scheme organiser
  - 2 reports (one for each survey of 3 urine samples), sent to all participants
  - Annual report with scoring sent to all participants and available on the ERNDIM web-site

DPT reporting before 2011

- Cumbersome work for the scheme organisers
- High risk of errors : transcription and analysis of results
- No harmonization of the 5 DPT schemes
- Not acceptable for accreditation

→ Project developed in collaboration with CSCQ

Project in 3 steps

- Development of a common web submission application to allow participants to enter their results
- Development of a program for the scheme organiser allowing
  - Analysis of the data
  - Scoring
  - Edition of a personalized report
- Development of a program for editing the Annual Report

Challenge of the web submission

- Include all tests that can be performed on urine samples
- For each test, give the possibility to analyse many different metabolites

  For example : urinary organic acid analysis allows identifying more than 300 metabolites: impossible to include all of tem in a static list
- Both quantitative and qualitative data, even for a same test or for a same analyte
- Includes textual data : comments, diagnosis, recommendation

Web submission application

- Hosted par CSCQ web-site
- Same format for all participants but specific to each centre and to each survey
- Several steps : every participant
  1. Selects the tests he performed
  2. Enters the results for each test
  3. Gives interpretation
  4. Indicates recommendation for further investigation

Quality Control Center Switzerland

ERNDIM PROFICIENCY TESTING SCHEMES

European Research Network for evaluation and improvement of screening, Diagnosis and treatment of Inherited disorders of Metabolism

ERNDIM
QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

Logged in on 2013-09-26 18:45:39

Survey
→ 13-06-D3
13-05-D3

Options
Logout
Back

Results entry

Survey **13-06-D3** - Laboratory **36**

Selected sample: **E**

Select sample → D E F

Clinical picture	Male, 2nd child of non consanguineous parents, investigated at 2 years of age because of dorso-lumbar kyphosis, pectus carinatum, genu valgum and vertebral dysplasia. Urine was collected at 10 years of age: his weight is 24.4 kg and height 99.5 cm.		
Comment			
Treatment			
	Sex: M	**Age (diag):** 2 Year(s)	**Age (pres.):** 10 Year(s)

Samples received on (yyyy-mm-dd): Send to the CSCQ

Step 1 : Selection of used analytes/methods

Selection

Step 2 : Analytical results input

1. Pre-investigations (0/0)
2. Amino acids (0/0)
3. Organic acids analysis (0/0)
4. Purines and Pyrimidines (0/0)
5. Lysosomal storage diseases (0/0)
6. Special assays (0/0)

Step 3 : Interpretation input

Interpretation

Step 4 : Further lab investigations

Recommendations

Step 5: Proof reading

Proof reading

Specify analytes and methods used for the survey and sample

Preinvestigations

Analyte	Method	Selection
Creatinine	Enzymatic assay	☑
pH	Dip stick	☑
Blood	Dip stick	☑
Nitrites	Dip stick	☑
Glucose	Dip stick	☑
Protein	Dip stick	☑
Ketones	Dip stick	☑

Back to **Result entry**

Amino acid analysis

Analyte	Method	Selection
Amino acid quantitative	LC-MS/MS	☑

Back to **Result entry**

Organic acid analysis

Analyte	Method	Selection
Organic acids column chromatography	Method 1/TMS Oxymation ethyl acetate GC/MS no stable isotopes	☑
Organic acids column chromatography	Method 2/TMS Oxymation ethyl acetate GC/MS with stable isotopes	☐
Homogentisic acid	GC-MS	☐
Succinylacetone	GC-MS/stable isotope dilution	☐
Lactate	Enzymatic assay	☐

Step 1 : Selection of used analytes/methods

Selection

Step 2 : Analytical results input

1. Pre-investigations (0/0)
2. Amino acids (0/0)
3. Organic acids analysis (0/0)
4. Purines and Pyrimidines (0/0)
5. Lysosomal storage diseases (0/0)
6. Special assays (0/0)

Step 3 : Interpretation input

Interpretation

Step 4 : Further lab investigations

Recommendations

Step 5: Proof reading

Proof reading

Quality Control Center Switzerland

ERNDIM PROFICIENCY TESTING SCHEMES

European Research Network for evaluation and improvement of screening, Diagnosis and treatment of Inherited disorders of Metabolism

Logged in on 2013-10-0

Results entry : Organic acid analysis

Survey **13-06-D3**, sample **D** of the laboratory **36**

Select sample →

Remember	Data entered on this page are taken into account by the CSCQ only if you click on the *Send to the CSCQ* button (at the bottom of this form), before changing pages (other survey or sample)

Back to **Result entry**

Analyte	Method	Key Metabolite	Quant. result	Unit	Evaluation	Qual. result
Organic acids column chromatography	Method 1/TMS Oxymation ethyl acetate GC/MS no stable isotopes	2-methylacetoacetic acid	******	mmol/mol creat	Elevated	Specific metabolite of MAT deficiency
Organic acids column chromatography	Method 1/TMS Oxymation ethyl acetate GC/MS no stable isotopes	2-methyl-3-hydroxybutyric acid	******	mmol/mol creat	Grossly elevated	
Organic acids column chromatography	Method 1/TMS Oxymation ethyl acetate GC/MS no stable isotopes	Tiglylglycine	807	mmol/mol creat	Grossly elevated	

Step 1 : Selection of used analytes/methods

Selection

Step 2 : Analytical results input

1. Pre-investigations (0/0)
2. Amino acids (0/0)
3. Organic acids analysis (0/0)
4. Purines and Pyrimidines (0/0)
5. Lysosomal storage diseases (0/0)
6. Special assays (0/0)

Step 3 : Interpretation input

Interpretation

Step 4 : Further lab investigations

Recommendations

Step 5: Proof reading

Proof reading

Results entry : Interpretation

Survey **13-06-D3**, sample **D** of the laboratory **36**

Select sample → D E F

Remember	Data entered on this page are taken into account by the CSCQ only if you click on the *Send to the CSCQ* button (at the bottom of this form), before changing pages (other survey or sample)

Back to **Result entry**

Most Likely Diagnosis

Mitochondrial acetoacetyl-CoA thiolase (MAT) deficiency.

Other Possible Diagnosis

2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency.

Comments On Diagnosis

Although the excretion of 2-methylacetoacic acid, the specific metabolite to differentiate both disorders, is low, the clinical presentation of the patient is in agreement with MAT deficiency.

OMIM Diagnosis 203750 **Diagnosis Reliability** Certain

Step 1 : Selection of used analytes/methods

Selection

Step 2 : Analytical results input

1. Pre-investigations (0/0)
2. Amino acids (0/0)
3. Organic acids analysis (0/0)
4. Purines and Pyrimidines (0/0)
5. Lysosomal storage diseases (0/0)
6. Special assays (0/0)

Step 3 : Interpretation input

Interpretation

Step 4 : Further lab investigations

Recommendations

Step 5: Proof reading

Proof reading

Results entry : Recommendations

Survey **13-06-D3**, sample **D** of the laboratory **36**

Select sample → D E F

Remember	Data entered on this page are taken into account by the CSCQ only if you click on the *Send to the CSCQ* button (at the bottom of this form), before changing pages (other survey or sample)

Back to **Result entry**

Recommendations

Perform plasma acylcarnitine profile.
Confirm the diagnosis by measuring MAT activity in cultured skin fibroblasts and/or by performing mutation analysis of ACAT1 gene.

Initials (optional, max. 4 char.):

Send to the CSCQ | Cancel

Step 1 : Selection of used analytes/methods

Selection

Step 2 : Analytical results input

1. Pre-investigations (0/0)
2. Amino acids (0/0)
3. Organic acids analysis (0/0)
4. Purines and Pyrimidines (0/0)
5. Lysosomal storage diseases (0/0)
6. Special assays (0/0)

Step 3 : Interpretation input

Interpretation

Step 4 : Further lab investigations

Recommendations

Step 5: Proof reading

Proof reading

Diagnostic Proficiency Testing
Web submission report

Laboratoire N° : 36 (DPT France)

Name of head : Christine Saban

E-mail : christine.saban@chu-lyon.fr

Date of sample received : 16/05/2013

Date of reporting results : 26 September 2013 - 19:32:46

The results below have been sent and saved in the CSCQ database at the date and time indicated above.

13-06-D3 / Sample 2013-D **Lab 36**

Clinical picture

Patient sex : M Age at diagnosis : 1 Week(s) Age present : 12 Year(s)

First child of non consanguineous parents. He presented, during the first week of life, vomiting, tachypnea, metabolic acidosis with ketonuria, but no hypoglycemia, and no hyperammonemia. The urine sample has been collected at 12 years of age.

1. Analytical Results

Preinvestigations **Sample 2013-D Lab 36**

Analyte	Method	Key metabolite	Quant.	Unit	Evaluation
Creatinine	Enzymatic assay	--	6.5	mmol/l	
pH	Dip stick	--	6	-	
Blood	Dip stick	--			0
Nitrites	Dip stick	--			0
Glucose	Dip stick	--			0
Protein	Dip stick	--			0

Organic acid analysis					Sample 2013-D Lab 36
Analyte	Method	Key metabolite	Quant.	Unit	Evaluation
Organic acids column chromatography	Method 1	2-methylacetoacetic acid		mmol/mol creat	Elevated
Qualitative Results :	Specific metabolite of MAT deficiency				
Organic acids column chromatography	Method 1	2-methyl-3-hydroxybutyric acid		mmol/mol creat	Grossly elevated
Organic acids column chromatography	Method 1	Tiglylglycine	807	mmol/mol creat	Grossly elevated
Organic acids column chromatography	Method 2			mmol/mol creat	To be entered

Lysosomal storage diseases					Sample 2013-D Lab 36
Analyte	Method	Key metabolite	Quant.	Unit	Evaluation
Glycosaminoglycans fractionation	1-D electrophoresis				To be entered

2. INTERPRETATION

User Initials : USR1 — Lab 36

Most Likely Diagnosis

Mitochondrial acetoacetyl-CoA thiolase (MAT) deficiency.

Other Possible Diagnosis

2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency.

Comments On Diagnosis

Although the excretion of 2-methylacetoacic acid, the specific metabolite to differentiate both disorders, is low, the clinical presentation of the patient is in agreement with MAT deficiency.

Web submission application

- Available since 2011
- Mandatory for all participants since 2012

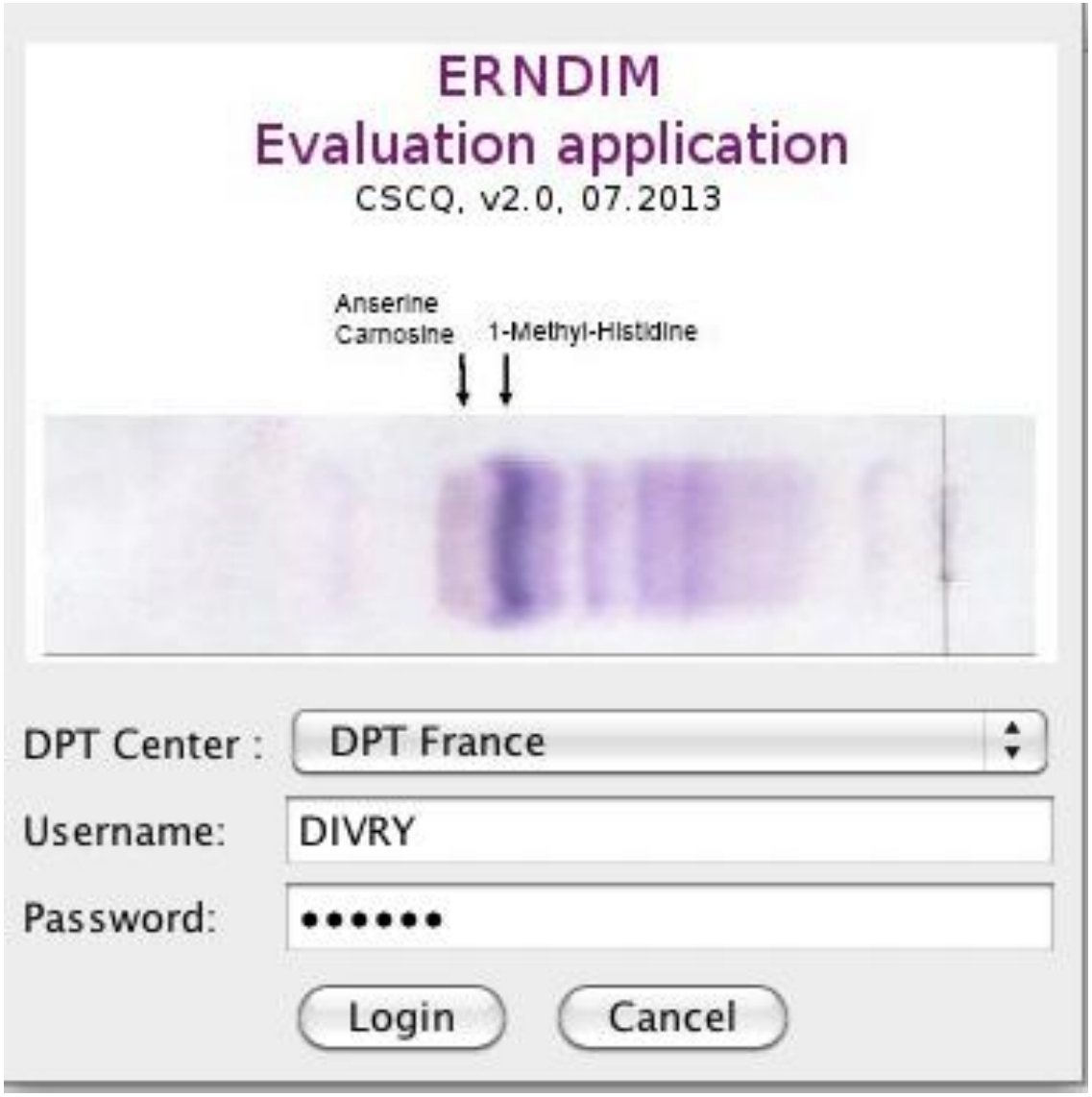
Challenge of the reporting program

- Processing of the user data
- Analysis of results
- Scoring
- Edition of a standardized and personalized report

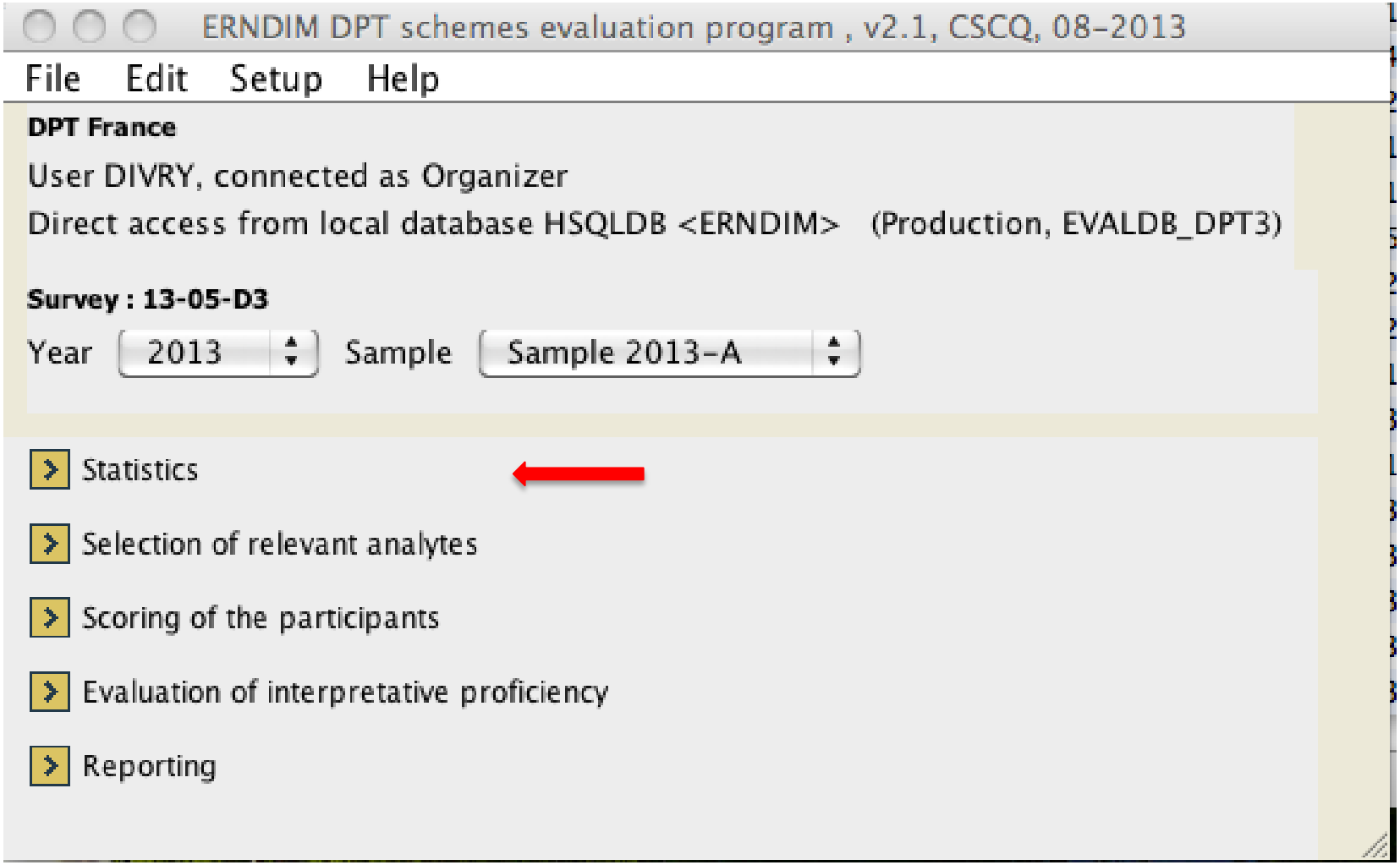
Reporting program

- The program which includes the data of the participants of each centre are sent by e-mail (password secured) to the scheme organizer
- The scheme organiser copies the program on his own computer
- The scheme organiser analyses results and edit personalized reports that he send to each participant by e-mail

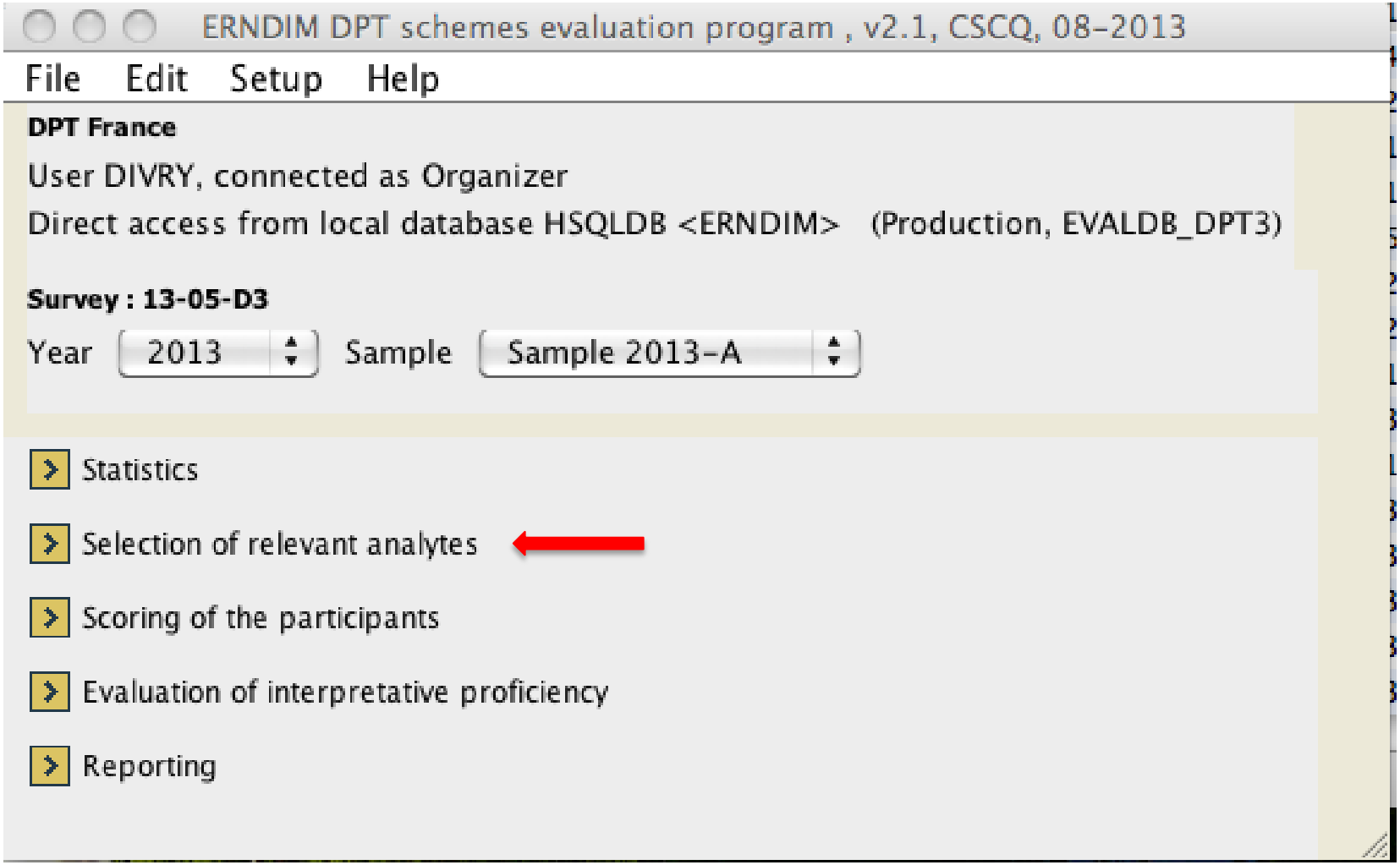
Reporting program



Reporting program



Reporting program



Analyt selection for survey 13-05-D3 - Sample 2013-A

Clinical information

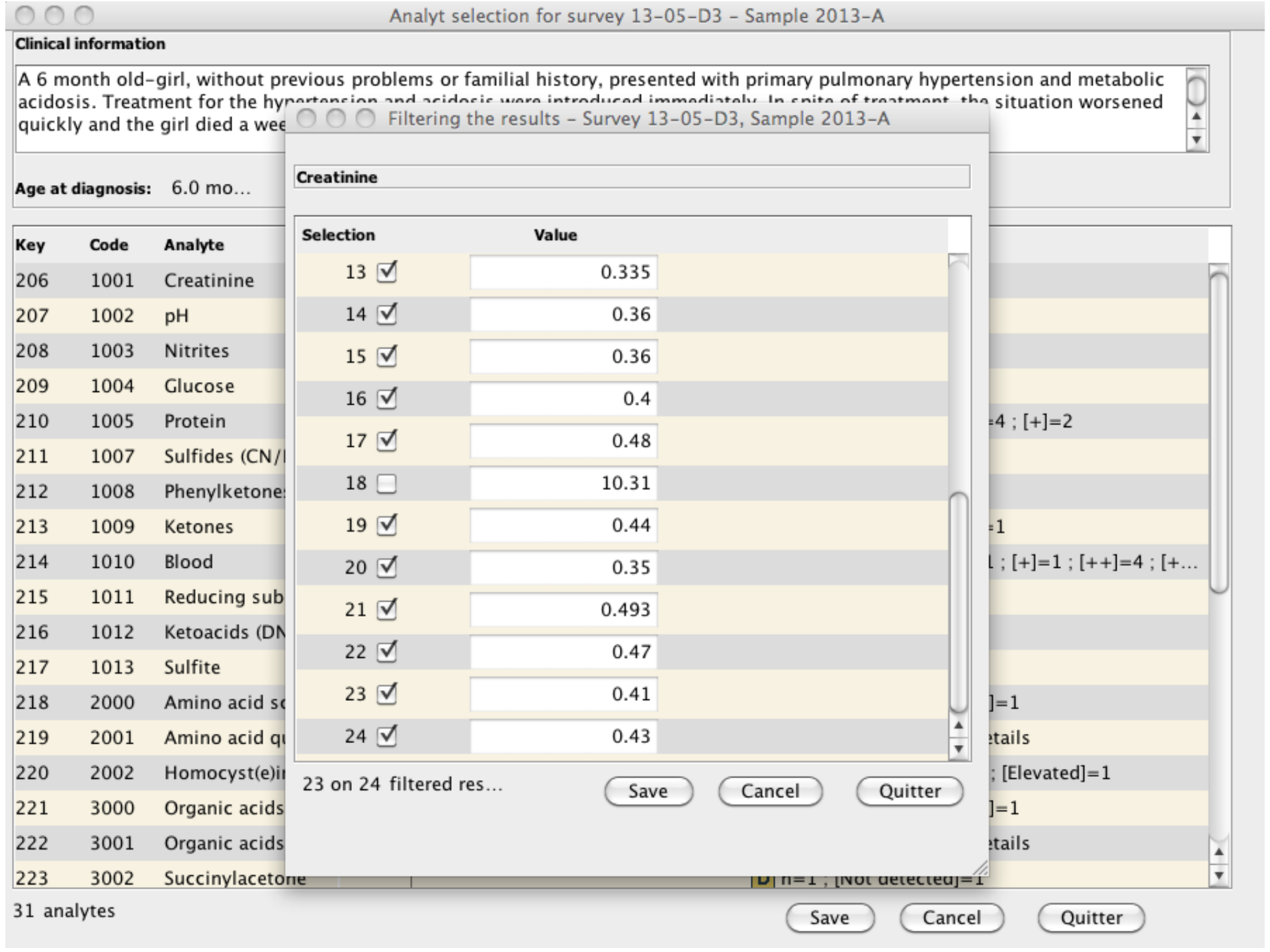
A 6 month old-girl, without previous problems or familial history, presented with primary pulmonary hypertension and metabolic acidosis. Treatment for the hypertension and acidosis were introduced immediately. In spite of treatment, the situation worsened quickly and the girl died a week later.

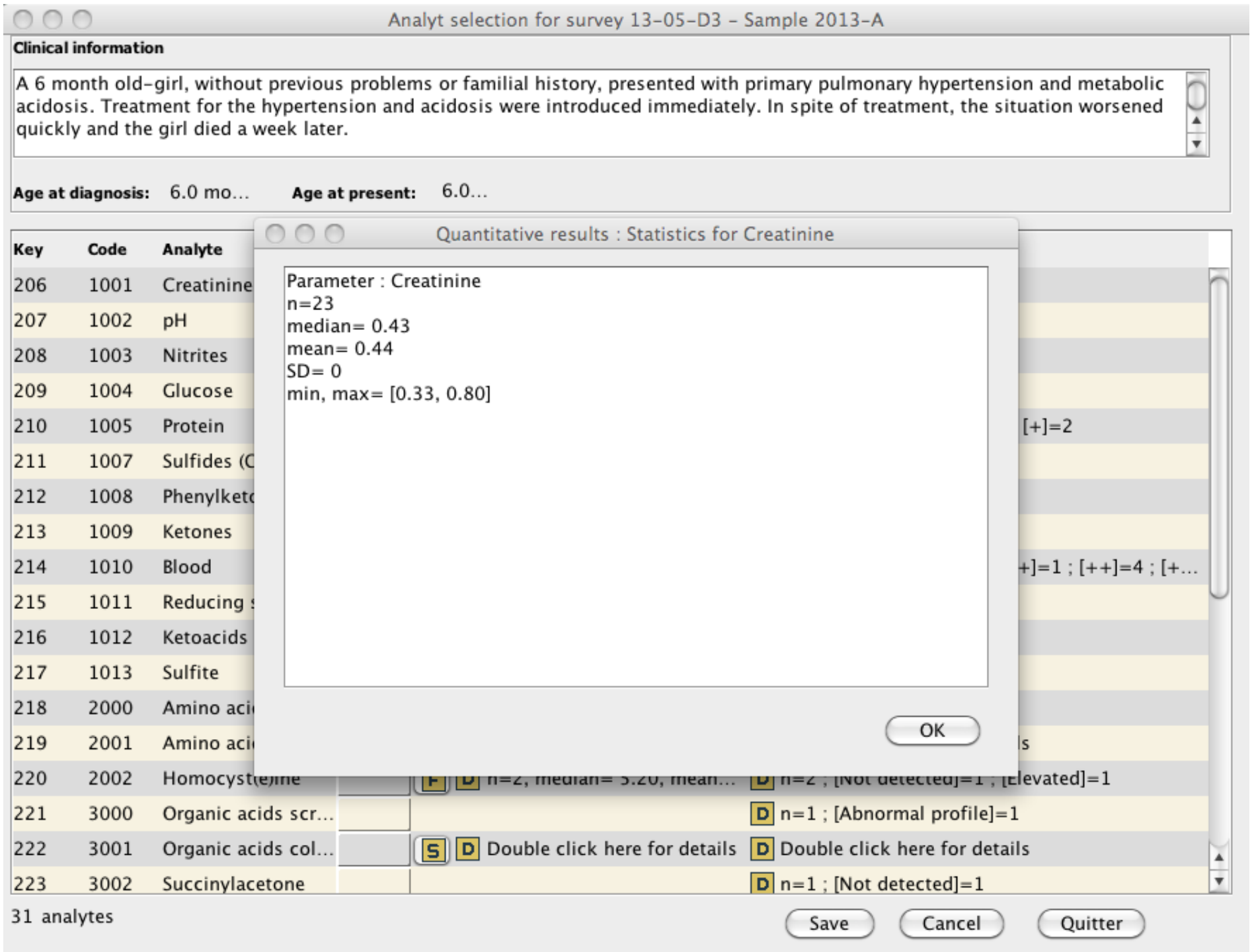
Age at diagnosis: 6.0 mo... **Age at present:** 6.0...

Key	Code	Analyte	Sel.	Quantitative results	Class results
206	1001	Creatinine	Selec...	F D n=23, median= 0.43, mea...	
207	1002	pH	Selec...	F D n=20, median= 5.00, mea...	
208	1003	Nitrites	Selec...		D n=17 ; [0]=16
209	1004	Glucose	Selec...		D n=19 ; [0]=19
210	1005	Protein	Selec...		D n=19 ; [0]=13 ; [Trace]=4 ; [+]=2
211	1007	Sulfides (CN/NP r...	Selec...		D n=1 ; [0]=1
212	1008	Phenylketones (F...	Selec...		D n=1 ; [0]=1
213	1009	Ketones	Selec...		D n=20 ; [0]=19 ; [Trace]=1
214	1010	Blood	Selec...		D n=19 ; [0]=2 ; [Trace]=1 ; [+]=1 ; [++]=4 ; [+...
215	1011	Reducing substa...	Selec...		D n=2 ; [0]=2
216	1012	Ketoacids (DNPH)	Selec...		D n=2 ; [Trace]=2
217	1013	Sulfite	Selec...		D n=8 ; [0]=7
218	2000	Amino acid scree...	Selec...		D n=1 ; [Abnormal profile]=1
219	2001	Amino acid quan...		S D Double click here for details	D Double click here for details
220	2002	Homocyst(e)ine		F D n=2, median= 5.20, mean...	D n=2 ; [Not detected]=1 ; [Elevated]=1
221	3000	Organic acids scr...			D n=1 ; [Abnormal profile]=1
222	3001	Organic acids col...		S D Double click here for details	D Double click here for details
223	3002	Succinylacetone			D n=1 ; [Not detected]=1

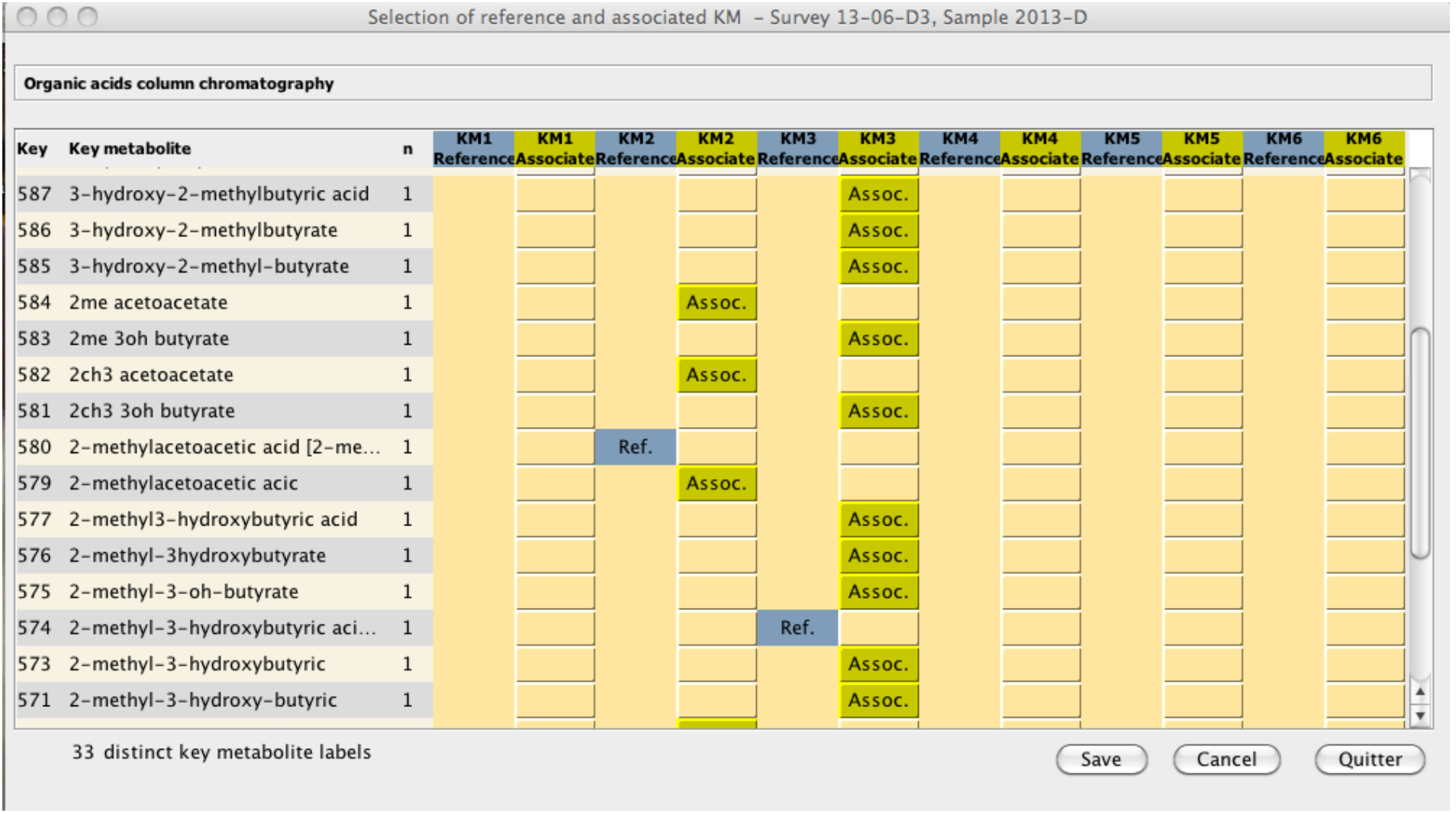
31 analytes

Save Cancel Quitter

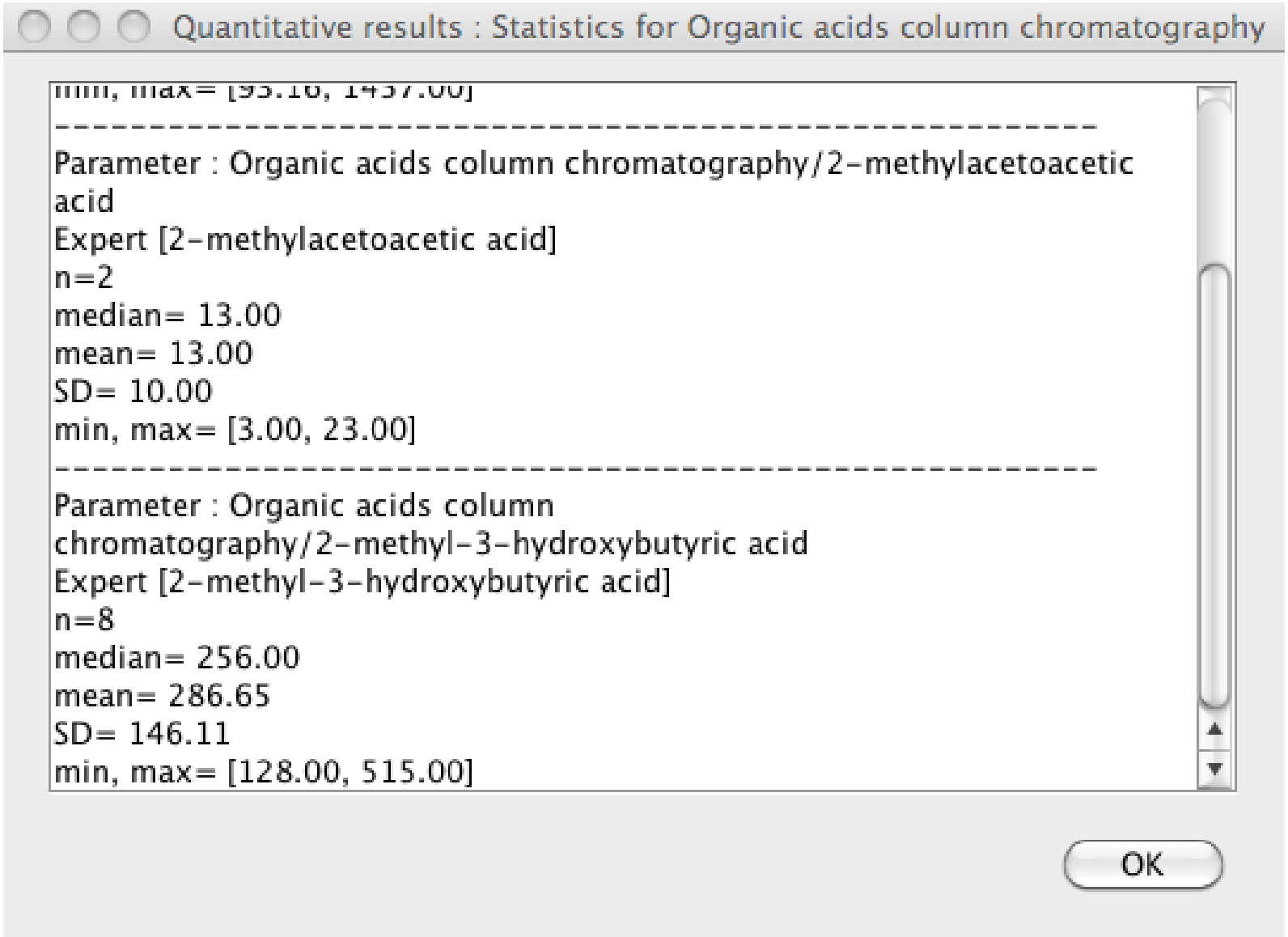

Analyt selection for survey 13-05-D3 - Sample 2013-A
Clinical information
A 6 month old-girl, without previous problems or familial history, presented with primary pulmonary hypertension and metabolic acidosis. Treatment for the hypertension and acidosis were introduced immediately. In spite of treatment, the situation worsened quickly and the girl died a wee
Age at diagnosis: 6.0 mo...
Key Code Analyte
206 1001 Creatinine
207 1002 pH
208 1003 Nitrites
209 1004 Glucose
210 1005 Protein
211 1007 Sulfides (CN/
212 1008 Phenylketone
213 1009 Ketones
214 1010 Blood
215 1011 Reducing sub
216 1012 Ketoacids (DN
217 1013 Sulfite
218 2000 Amino acid sc
219 2001 Amino acid qu
220 2002 Homocyst(e)in
221 3000 Organic acids
222 3001 Organic acids
223 3002 Succinylacetone
31 analytes
Save
Cancel
Quitter
Filtering the results - Survey 13-05-D3, Sample 2013-A
Creatinine
Selection Value
13 0.335
14 0.36
15 0.36
16 0.4
17 0.48
18 10.31
19 0.44
20 0.35
21 0.493
22 0.47
23 0.41
24 0.43
23 on 24 filtered res...
Save
Cancel
Quitter


Analyt selection for survey 13-05-D3 - Sample 2013-A
Clinical information
A 6 month old-girl, without previous problems or familial history, presented with primary pulmonary hypertension and metabolic acidosis. Treatment for the hypertension and acidosis were introduced immediately. In spite of treatment, the situation worsened quickly and the girl died a week later.
Age at diagnosis: 6.0 mo...
Age at present: 6.0...
Quantitative results : Statistics for Creatinine
Parameter : Creatinine
n=23
median= 0.43
mean= 0.44
SD= 0
min, max= [0.33, 0.80]
OK
Key Code Analyte
206 1001 Creatinine
207 1002 pH
208 1003 Nitrites
209 1004 Glucose
210 1005 Protein
211 1007 Sulfides (C
212 1008 Phenylketc
213 1009 Ketones
214 1010 Blood
215 1011 Reducing s
216 1012 Ketoacids
217 1013 Sulfite
218 2000 Amino aci
219 2001 Amino aci
220 2002 Homocyst(e)ine
221 3000 Organic acids scr...
222 3001 Organic acids col...
223 3002 Succinylacetone
[+]=2
+]=1 ; [++]=4 ; [+...
s
n=2, median= 5.20, mean...
n=2 ; [Not detected]=1 ; [Elevated]=1
n=1 ; [Abnormal profile]=1
Double click here for details
Double click here for details
n=1 ; [Not detected]=1
31 analytes
Save
Cancel
Quitter

Selection of reference and associate metabolites



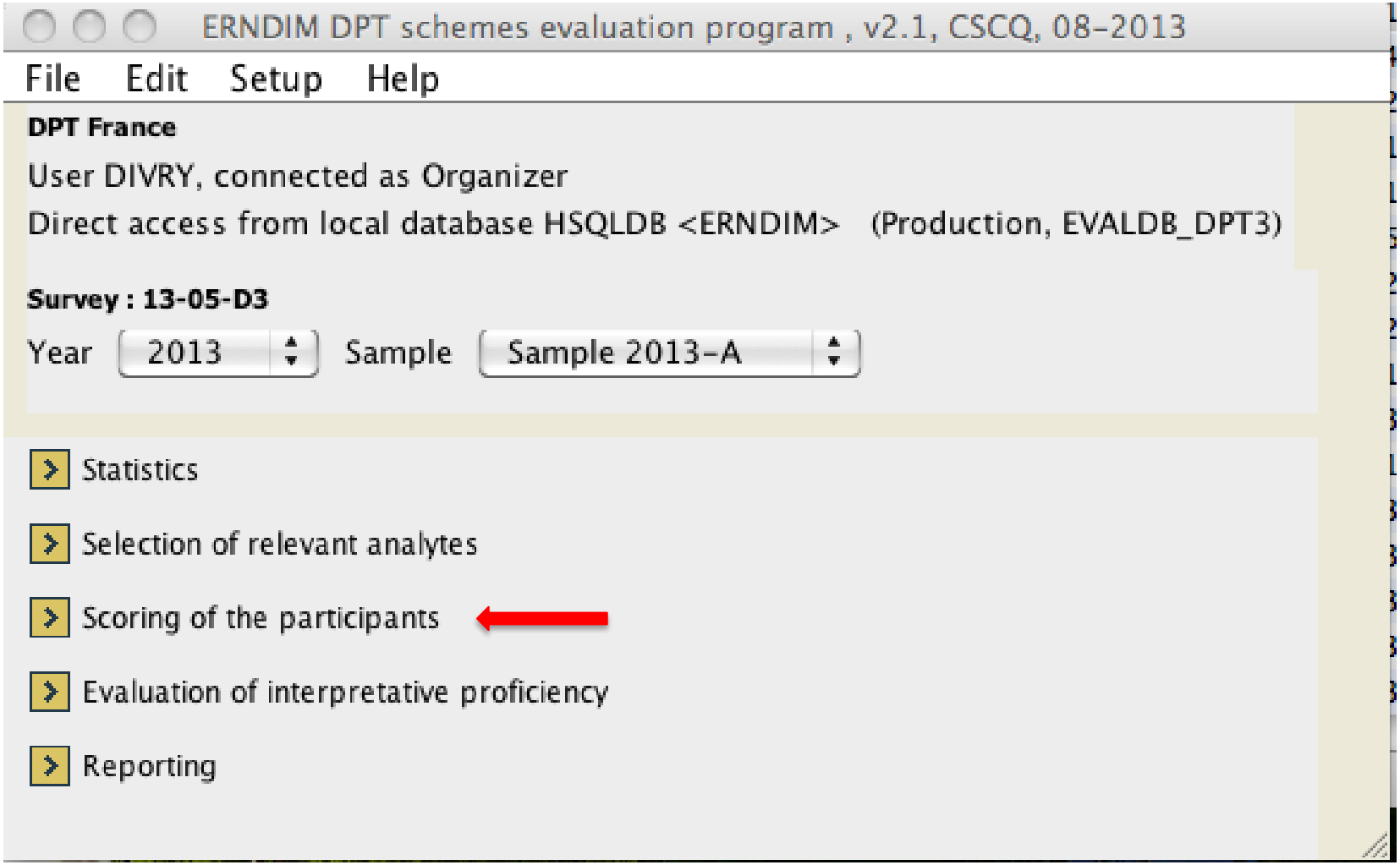
Statistics


Quantitative results : Statistics for Organic acids column chromatography
min, max= [93.10, 1437.00]

Parameter : Organic acids column chromatography/2-methylacetoacetic acid
Expert [2-methylacetoacetic acid]
n=2
median= 13.00
mean= 13.00
SD= 10.00
min, max= [3.00, 23.00]

Parameter : Organic acids column chromatography/2-methyl-3-hydroxybutyric acid
Expert [2-methyl-3-hydroxybutyric acid]
n=8
median= 256.00
mean= 286.65
SD= 146.11
min, max= [128.00, 515.00]
OK

Reporting program



Analytical performance for survey 13-06-D3 - Sample 2013-D

Clinical information

First child of non consanguineous parents. He presented, during the first week of life, vomiting, tachypnea, metabolic acidosis with ketonuria, but no hypoglycemia, and no hyperammonemia. The urine sample has been collected at 12 years of age.

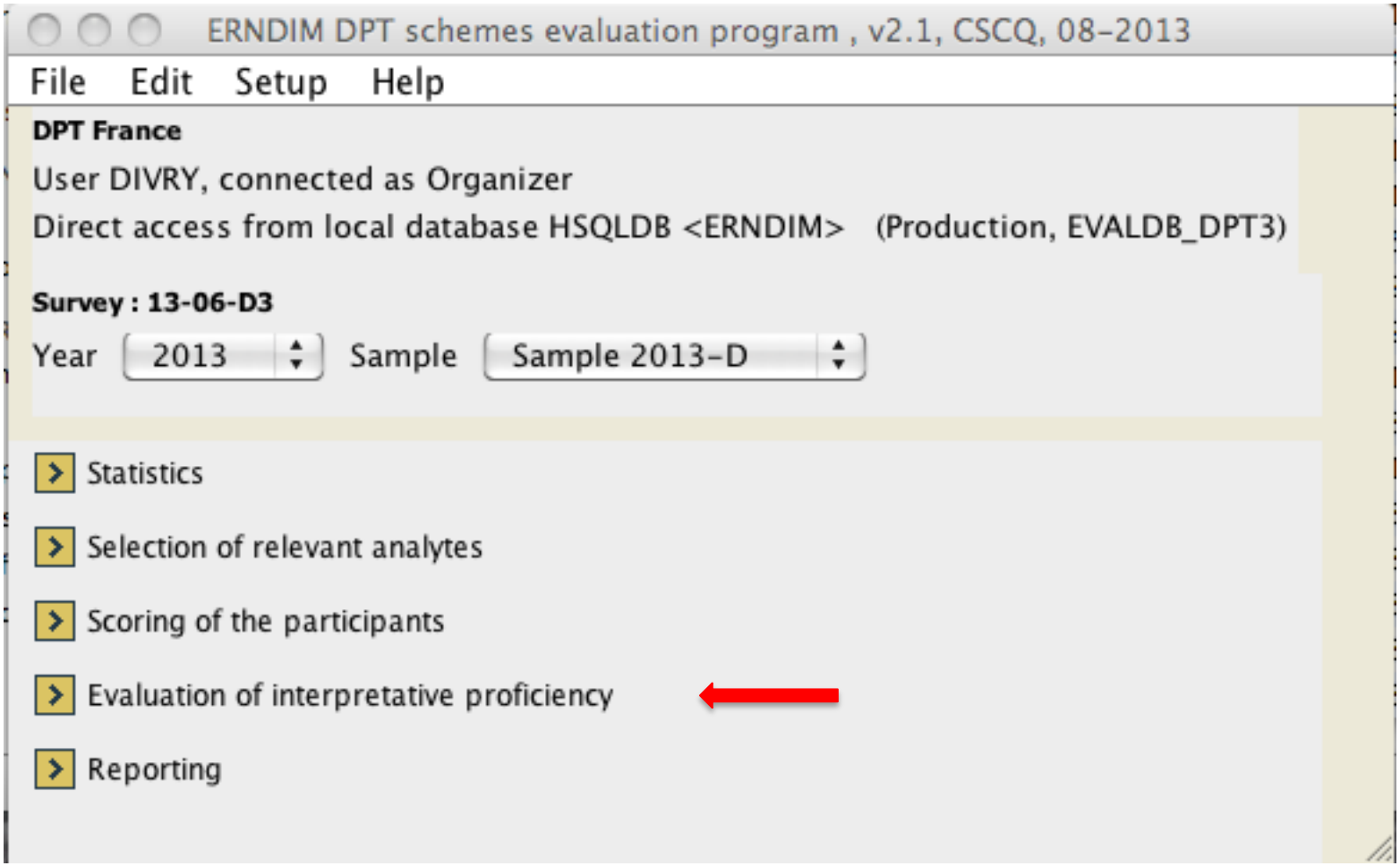
Age at diagnosis: 1.0 week **Age at present:** 1.0 y...

Key	Lab	AP Score	Total Score	Key metabolite	QT result	Class result	QL	Expert Comment
Organic acids column chromatography								
47127	1		3	KM 1:tiglylglycine [tiglylglyci...	289.0	Grossly eleva...		E --
47416	5		4	KM 2:2-methylacetoacetic aci...	23.0	Elevated		E --
46559	6		4	KM 3:2-methyl-3-hydroxybu...	--	Grossly eleva...		E --
46419	33		4	KM 1:tiglylglycine [tiglyl-glyc...	343.5	Grossly eleva...		E --
48978	34		4	KM 1:tiglylglycine [tiglylglyci...	1457.0	Grossly eleva...		E --
46949	38		4	KM 1:tiglylglycine [tiglyglicine]	--	Grossly eleva...		E --
45134	41		4	KM 1:tiglylglycine [tiglylglyci...	--	Grossly eleva...		E --
47107	55		4	KM 1:tiglylglycine [tiglylglyci...	--	Grossly eleva...		E --
48726	58		3	KM 1:tiglylglycine [tiglilglycine]	93.16	Elevated		E --
47960	62		4	KM 1:tiglylglycine [tiglylglyci...	--	Grossly eleva...		E --
46658	64		4	KM 1:tiglylglycine [tiglylglyci...	115.0	Elevated		E --
46120	70		4	KM 1:tiglylglycine [tiglylglyci...	556.0	Elevated		E --
48860	80		3	KM 1:tiglylglycine [tiglylglyci...	--	Grossly eleva...		E --
48062	88		3	KM 1:tiglylglycine [tiglylglyci...	363.0	Grossly eleva...		E --
47758	121		4	KM 1:tiglylglycine [tiglylglyci...	--	Grossly eleva...	D Huge...	E --
44559	126		4	KM 1:tiglylglycine [tiglylglyci...	--	Grossly eleva...		E --
48809	143		3	KM 1:tiglylglycine [tiglylglyci...	--	Grossly eleva...		E --

22 analytes

☑ Key metabolite only ☐ All

Save Cancel Quitter


ERNDIM DPT schemes evaluation program , v2.1, CSCQ, 08-2013
File Edit Setup Help
DPT France
User DIVRY, connected as Organizer
Direct access from local database HSQLDB <ERNDIM> (Production, EVALDB_DPT3)
Survey : 13-06-D3
Year 2013 Sample Sample 2013-D
Statistics
Selection of relevant analytes
Scoring of the participants
Evaluation of interpretative proficiency
Reporting

Clinical information

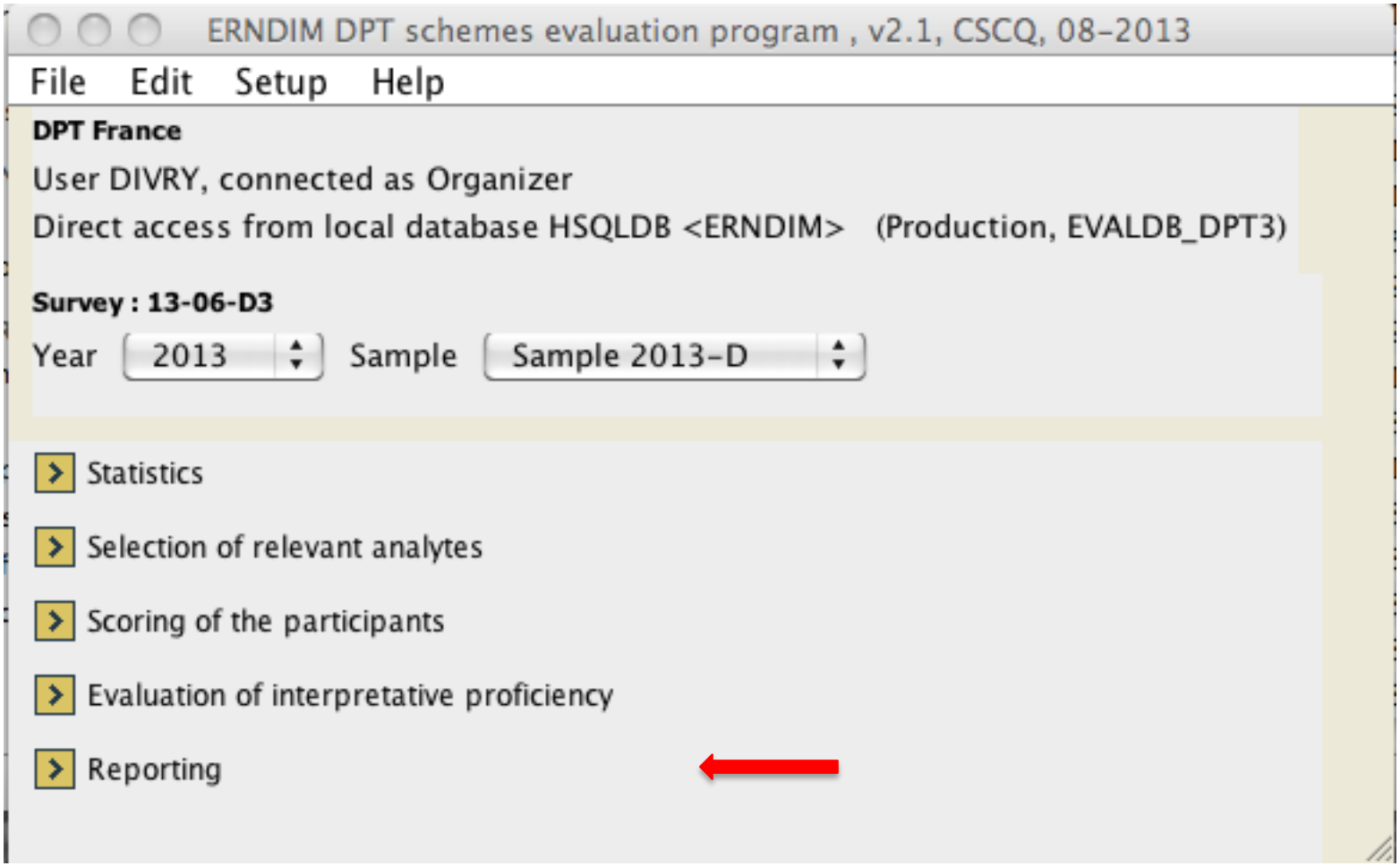
First child of non consanguineous parents. He presented, during the first week of life, vomiting, tachypnea, metabolic acidosis with ketonuria, but no hypoglycemia, and no hyperammonemia. The urine sample has been collected at 12 years of age.

Age at diagnosis: 1.0 week **Age at present:** 1.0 y...

Key	Lab	IP Score	Total Score	Diagnosis	Diagnosis Alt.	User comment & Recommendations	Expert Comm
1410	1		3	D 3-Oxothiolase deficiency	D 2-Methyl-3-Hydroxyb...	D C: Although the absenc..	E --
1415	5		4	D BETA-KETOTHIOLASE DEFI...	D 2-METHYL-3-HYDROX...	D R: - enzyme assay of B...	E --
1403	6		4	D ACETYL-CoA ACETYLTRA...	D	D R: Perform in vitro assa...	E --
1399	33		4	D Beta-ketothiolase deficien...	D	D C: Ketonuria is not pre...	E --
1442	34		4	D Beta-ketothiolase deficiency	D	D R: - Enzymatic activity...	E --
1406	38		4	D The organic acid profile in...	D	D C: The deficiency of be...	E --
1433	40		3	D 3-Ketothiolase deficiency...	D	D R: Enzyme activity in fi...	E --
1390	41		4	D Mitochondrial acetoacetyl...	D	D C: This diagnosis is to...	E --
1409	55		4	D 2-methyl-acetoacetyl-Co...	D	D R: Acylcarnitines; plas...	E --
1434	58		3	D 2-Methyl-3-hydroxybutyr...	D	D R: Enzymatic studies of..	E --
1422	62		4	D 3-oxothiolase deficiency	D	D C: The clinical presenta..	E --
1404	64		4	D Beta-ketothiolase (MAT) d...	D None.	D C: 2-methyl-3-hydrox...	E --
1396	70		4	D Ketothiolase deficiency (al...	D	D R: acylcarnitines in pla...	E --
1439	80		3	D Methylacetoacetyl-CoA th...	D	D C: 2-Methylacetoacetat..	E --
1426	88		3	D 2-methyl-3-OH-Butyryl-...	D 3-Ketothiolase deficency	D R: blood or plasma acyl..	E --
1419	121		4	D Mitochondrial Acetoacetyl...	D	D R: enzyme activity on c...	E --
1385	126		4	D Deficiency of mitochondri...	D	D R: Diagnostic confirma...	E --

22 participants

Save Cancel Quitter


ERNDIM DPT schemes evaluation program , v2.1, CSCQ, 08-2013
File
Edit
Setup
Help
DPT France
User DIVRY, connected as Organizer
Direct access from local database HSQLDB <ERNDIM> (Production, EVALDB_DPT3)
Survey : 13-06-D3
Year
2013
Sample
Sample 2013-D
Statistics
Selection of relevant analytes
Scoring of the participants
Evaluation of interpretative proficiency
Reporting

Report elements for survey 13-06-D3 - Sample 2013-D

Clinical information

First child of non consanguineous parents. He presented, during the first week of life, vomiting, tachypnea, metabolic acidosis with ketonuria, but no hypoglycemia, and no hyperammonemia. The urine sample has been collected at 12 years of age.

Age at diagnosis: 1.0 week **Age at present:** 1.0 y...

Report input

- Patient detailed information
- General comment on analytical performance (all participan...
- General comment on interpretative proficiency (all particip...
- General comment on recommendations (all participants)
- Overall impression on the survey
- Definitive diagnosis
- Definitive recommendations

Report display and PDF generation

Key	Lab	IP Score	Total Score	Proof reading	Report	
1410	1	2	3	Display	Display	PDF
1415	5	2	4	Display	Display	PDF
1403	6	2	4	Display	Display	PDF
1399	33	2	4	Display	Display	PDF
1442	34	2	4	Display	Display	PDF
1406	38	2	4	Display	Display	PDF
1433	40	2	3	Display	Display	PDF
1390	41	2	4	Display	Display	PDF
1409	55	2	4	Display	Display	PDF
1434	58	2	3	Display	Display	PDF
1422	62	2	4	Display	Display	PDF
1404	64	2	4	Display	Display	PDF

22 participants

Save Cancel Quitter

Personalized report

ERNDIM DPT France
Diagnostic Proficiency Testing

Southern Europe – Lyon Centre

Diagnostic Proficiency Testing

Survey report

13-06-D3

Report prepared by Dr C. VIANEY-SABAN and Dr C. ACQUAVIVA-BOURDAIN

Laboratory N°: 1 (ERNDIM DPT France)

Results of samples and evaluation of reporting

Sample 2013-D:	Mitochondrial acetoacetyl-CoA thiolase (MAT) deficiency also called beta-ketothiolase or 3-oxothiolase deficiency (OMIM 203750). ACAT1 gene

Participants details

First child of non cansanguineous parents. He presented during the fisrt week of life, vomiting, tachypnea, metabolic acidosis with ketonuria, but no hypoglycemia, and no hyperammonemia. The urine sample has been collected at 12 years of age. This patient has been treated from birth in our hospital and has a very good psychomotor development. MAT deficiency has been confirmed by enzymatic measurement in cultured skin fibroblasts (Centre de Biologie Est).

Analytical performance

Identification of increased 2-methyl-3-hydroxubutyrate, 2-methylacetoacetate and tiglylglycine was scored 2 points (16 labs), identification of only 2 metabolites was scored 1 point (6 labs).

Interpretative proficiency

The diagnosis of MAT, beta-ketothiolase or 3-oxothiolase deficiency was scored 2 points (all 22 labs).

Analytical details

Your score for analytical results: 1

Creatinine				
(n=22)	median=	6,56	[5.99-7.07]	□ Your result = 6.654
pH				
(n=19)	median=	6,00	[5.0-6.5]	□ Your result = 6.0
Nitrites				
0	(n=15)			□ Your result = 0
Glucose				
0	(n=17)			□ Your result = 0
Protein				
Trace	(n=2)			
0	(n=15)			□ Your result = 0
Sulfides (CN/NP reaction)				
0	(n=1)			
Phenylketones (FeCl3				
0	(n=1)			

Organic acids screening

Abnormal profile (n=1)

Investigations

Organic acids column	n (quant	n (qual)	Your results		
			Key metabolite	(quant)	(qual)
tiglylglycine	10	20	Tiglylglycine	289.0	Grossly elevated
2-methylacetoacetic acid	2	11	--	--	--
2-methyl-3-hydroxybutyric acid	8	18	--	--	--

Expert comment

Acylcarnitines	n (quant	n (qual)	Your results		
			Key metabolite	(quant)	(qual)
2-methyl-3-	1	2	--	--	--
tiglylcarnitine	1	2	--	--	--

Interpretation

Your 3-Oxothiolase deficiency

Your score for interpretation: 2 Your total score: 3

Recommendations for further tests

Your result- Plasmatic Acylcarnitines profile.
- Isoleucine challenge.
- Enzymatic assay in cultured fibroblasts.
- Molecular analysis of ACAT1 gene.
- Restricted protein and lipid intake

Reporting program

- Developed in 2012
- Successfully used by two scheme organizers in 2013
- Will be extended to all schemes in 2014

Edition of the Annual Report

- Under development
- Word file
  - Data taken from the reporting program
  - Possibility to introduce educational figures : metabolic pathways, mass spectrum, chromatographic profiles …

Conclusion

- Real challenge to develop these programs
- Possible thanks to the professional but friendly collaboration between ERNDIM and CSCQ
- These tools will permit harmonization and quality improvement of Diagnostic Proficiency Testing
- This approach will be extended to all ERNDIM qualitative schemes