www.erndim.org

Introduction of ‘Critical Error’ in evaluation of interpretative schemes

On behalf of ERNDIM Scientific Advisory Board
George Ruijter
Lyon 1-9-2015

Outline

1) Critical error briefly
2) Background on scoring of interpretative EQA schemes
3) Guiding priciples to identify critical error
4) Procedure to ratify critical error
5) Examples taken from 2014 schemes
6) Conclusion

Critical error briefly

- A critical error is an error that would be unacceptable to the majority of labs and would have a serious adverse effect on patient management

- A confirmed critical error will lead automatically to the classification ‘failure to achieve satisfactory performance’

ERNDIM schemes

Quantitative Schemes
Amino acids
Organic acids
Cystine in white blood cells
Special assays in urine
Special assays in serum
Purines & pyrimidines
Qualitative Schemes
Diagnostic proficiency testing [5 centres]
Organic acids [2 centres]
Acylcarnitine [2 centres]
Mucopolysaccharides
Lysosomal enzymes
Congenital disorders of glycosylation

Data evaluation by statistical analysis

Scoring by Scientific Advisor + Critical error

Scoring of interpretative schemes

Harmonised scoring for all interpretative schemes

1. Analytical performance

• correct test results	2 points
• partially correct	1 point
• unsatifactory or misleading	0 points

2. Interpretation + advice

• correct diagnosis and appropriate further tests recommended	2 points
• helpful but incomplete	1 point
• misleading/wrong diagnosis	0 points

Maximum 4 points per sample

Scores required for satisfactory performance

Generally around 60%

Scheme	Points satisfactory	max*
Diagnostic Proficiency Testing	15	24
Qualitative Organic Acids	22	36
Acylcarnitine (DBS)	16	24
CDG	15	24
Urine MPS	12	24
Lysosomal enzymes	25	42

* Depends on sample numbers, educational samples etc

Low score → performance support letter

Introduction of critical error

EuroGentest

HARMONIZING GENETIC TESTING ACROSS EUROPE

Eurogentest 2010: harmonization of EQA scoring systems across the disciplines

ERNDIM: introduction of critical error in 2014 schemes

Critical error

- A critical error is an error that would be unacceptable to the majority of labs and would have a serious adverse effect on patient management

  The EQA material provided (urine, dried blood spot) must be sufficient to establish diagnosis according to current standards of biochemical genetics diagnostic testing

- Absence of critical error is required to achieve satisfactory performance in a scheme

Guiding principles to identify critical error

- If clinical harm is to be expected as a result of wrong conclusions, the score critical error may be assigned
- Failure to perform a relevant test (DPT only)
- Failure to identify a relevant metabolite(s)
- Failure to establish a diagnosis when proficiency is high (e.g. >95%)

- Samples with no IEM known can NOT result in critical error

Procedure to establish critical error

- Scientific Advisors identify possible critical errors after completion of the survey based on the guiding principles

- Proposals are discussed within the Scientific Advisory Board during its spring meeting and based upon discussion either confirmed or rejected

Effect of critical error on performance assessment

- A confirmed critical error overrules score and results in ‘failure to achieve satisfactory performance’
- Scientific Advisor issues a performance support letter
- Appeals via ERNDIM administrative office

Example 1

Scheme: DPT Netherlands 2014 (SA: G. Ruijter)

Sample: Propionic acidemia

Number of returns: 19

Proficiency: 100%

Critical error: Failure to report OA abnormalities and/or propionic acidemia
N=0

Example 2

Scheme: DPT Switzerland 2014 (SA: B. Fowler)

Sample: Beta-ketothiolase deficiency

This female child was hospitalised at 2 years of age because of a complex viral infection associated with metabolic acidosis. Recovered well and subsequently remained healthy. Urine collected at 8 years of age whilst on specific treatment.

Number of returns: 19

Proficiency:	Analytical	97%
	Interpretation	82%
	Overall	90%

Critical error: Failure to report OA abnormalities

N=0

Example 3

Scheme: DPT Czech Republic 2014 (SA: V. Kozich)

Sample: Mucopolysaccharidosis type I

Number of returns: 19

Proficiency:	Analytical	82%
	Interpretation	82%
	Overall	82%

Critical error: Failure to perform and/or recommend mucopolysaccharides analysis
N=2

Example 4

Scheme: DPT Netherlands 2014

Sample: Mucopolysaccharidosis type III

An adult, retarded, woman with psychiatric problems, retinitis pigmentosa and brain atrophy. No dysmorphic features were noticed.

Number of returns: 19

Proficiency:	Analytical	68%
	Interpretation	66%
	Overall	67%

Critical error: sample not eligible

Example 5

Scheme: DPT Netherlands 2014

Sample: Hypophosphatasia (*ALPL* defect)

Number of returns: 19

Proficiency:	Analytical	89%
	Interpretation	89%
	Overall	89%

Critical error: sample not eligible

Example 6

Scheme: DPT 2014 (common sample)

Sample: Hyperornithinemia-hyperammonemia-homocitrullinuria (HHH) syndrome

Number of returns: 98

Proficiency:	Analytical	67%
	Interpretation	72%
	Overall	70%

Example 6

Scoring common sample DPT 2014

Analytical

Elevated homocitrulline	1 point
Elevated orotic acid	1 point

Interpretation/diagnosis

HHH syndrome	2 points
Any urea cycle disorder	1 point

Critical error: Failure to report elevated orotic acid

N=3

Example 7

Scheme: Urine Mucopolysaccharides (SA: G. Ruijter)

Sample: Mucopolysaccharidosis type III

7-year old female

Severe MPS III, DMB average 59 mg/mmol creat

Number of returns: 94

Proficiency:	Analytical	93%
	Interpretation	86%
	Overall	89%

Critical error: Diagnosis ‘normal’, i.e. failure to report MPS

N=2

Example 8

Scheme: Qualitative Acylcarnitines in DBS
(SA: C.D. Langhans)

Sample: Glutaric acidemia type I
6-month old girl with developmental retardation and macrocephaly

Number of returns: 47

Proficiency: 98%

Critical error: Failure to report elevated C5DC
N=1

Example 9

SCHEME: Qualitative organic acids in urine
(SA: C.D. Langhans)

Sample: Tyrosinemia type I

8-month-old boy after start of medication. At age 4 months rickets, nephromegaly and liver dysfunction

Elevated 4-hydroxyphenylacetic acid, 4-hydroxyphenyllactic acid, 4-hydroxyphenylpyruvic acid and succinylacetone

Number of returns: 86

Proficiency: 96%

Critical error: Failure to to identify any of the relevant metabolites

N=2

Example 10

SCHEME: Qualitative organic acids in urine
(SA: C.D. Langhans)

Sample: Isovaleric acidemia
13-year-old boy with acute acidosis

Number of returns: 87

Proficiency: 98%

Critical error: Failure to identify isovalerylglycine and to diagnose IVA
N=1/2

Conclusions

1) A critical error is an error that would be unacceptable to the majority of labs and would have a serious adverse effect on patient management

2) Critical errors must be ratified by the Scientific Advisory Board

3) Absence of critical error is required to achieve satisfactory performance in a scheme

Questions & suggestions: Scientific Advisors