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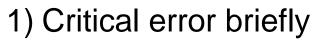
QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

Introduction of 'Critical Error' in evaluation of interpretative schemes

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

Outline

FRNI



- 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

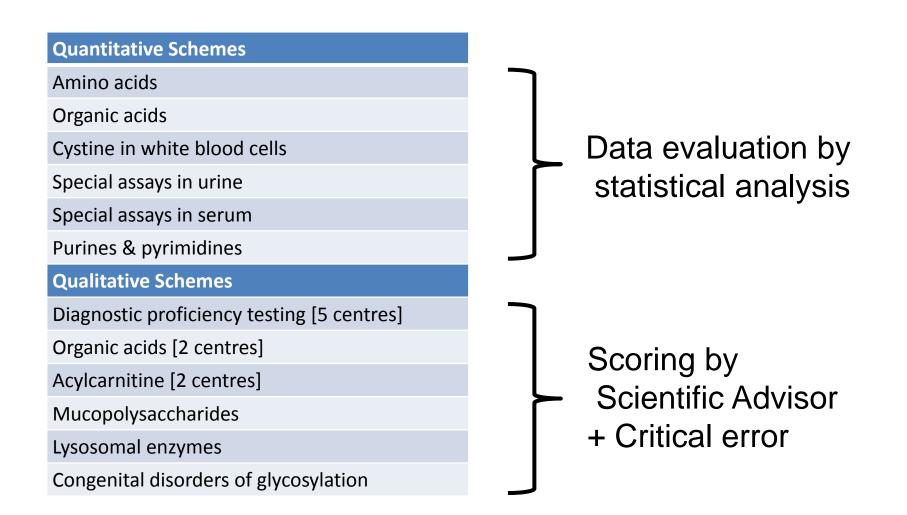


Critical error briefly

- 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





Scoring of interpretative schemes

Harmonised scoring for all interpretative schemes

- 1. Analytical performance
 - correct test results
 - partially correct
 - unsatifactory or misleading

2. Interpretation + advice

- correct diagnosis and appropriate further tests recommended
- helpful but incomplete
- misleading/wrong diagnosis

Maximum 4 points per sample

2 points 1 point 0 points

2 points

1 point 0 points

Scores required for satisfactory performance



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 \rightarrow performance support letter



Introduction of critical error



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



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



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



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

Sample: Mucopolysaccharidosis type I

Number of returns: 19

Proficiency:Analytical82%Interpretation 82%Overall82%

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



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:Analytical68%Interpretation 66%Overall67%

Critical error: sample not eligible



Scheme: DPT Netherlands 2014

Sample: Hypophosphatasia (ALPL defect)

Number of returns: 19

Proficiency:Analytical89%Interpretation 89%Overall89%

Critical error: sample not eligible



Scheme: DPT 2014 (common sample)

Sample: Hyperornithinemia-hyperammonemiahomocitrullinuria (HHH) syndrome

Number of returns: 98

Proficiency: Analytical 67% Interpretation 72% Overall 70%

Example 6

Scoring common sample DPT 2014

Analytical

Elevated homocitrulline1 pointElevated orotic acid1 point

Interpretation/diagnosis

HHH syndrome2 pointsAny urea cycle disorder1 point

Critical error: Failure to report elevated orotic acid N=3

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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:Analytical93%Interpretation 86%Overall89%

Critical error: Diagnosis 'normal', i.e. failure to report MPS N=2



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



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



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

- 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