

What do laboratories need from an External Quality Assessment (EQA) Programme – is it time to redefine the aims of EQA?

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Introduction

EQA is defined as a system designed to objectively assess the quality of results by an external agency. The aims were defined by the IFCC in 1983¹ in that they should:

- provide a measure of the quality of a test
- supplement IQC procedures
- provide a measure of the “state of the art” of a test
- obtain consensus values when true values are unknown
- investigate factors in performance.

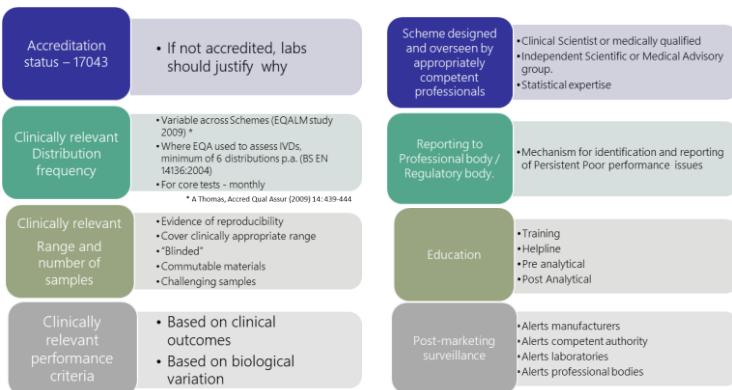
¹Buttner J, Borth R, Boutwell JH, Broughton PMG, Bowyer RC. International Federation of Clinical Chemistry, Scientific Committee Expert Panel on Nomenclature and principles of Quality Control in Clinical Chemistry. Approved recommendation (1983) on quality control in clinical chemistry. Part 3. External quality control. J Clin Chem Clin Biochem. 1983 Dec; 21(12): 885-92.

By using dedicated designs and samples, EQA can be used to provide a wealth of additional information such as assessment of trueness, inter and intra-laboratory variation, robustness of methods; sensitivity and specificities, linearity, post market vigilance, act as an educational stimulus, assess pre- and postanalytical factors as well as provide evidence for harmonisation strategies.

Expectations of EQA Provider

In most countries, outside North America, the choice of EQA provider lies with the laboratory, where a range of factors should be considered in undertaking that choice².

Figure 1 Factors influencing choice of EQA²



²External quality assessment: best practice. James D, Ames D, Lopez B, et al. J Clin Pathol 2014; 67 : 651–655

EQA Programme Design

In the design a number of factors need to be considered such as: number, frequency and type of samples, target value, statistical analysis and the analytical performance specification (APS). The use of material as close as possible to the patient sample minimizes any matrix effect and allows the assessment of accuracy. Other factors to consider include: stability, homogeneity, clinically relevant concentrations at clinical decision limits, Figure2, and use of challenging samples.

Clinically relevant samples

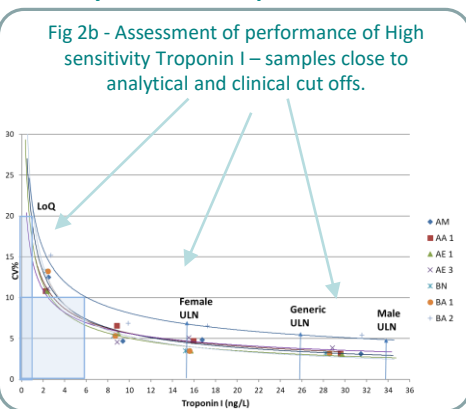
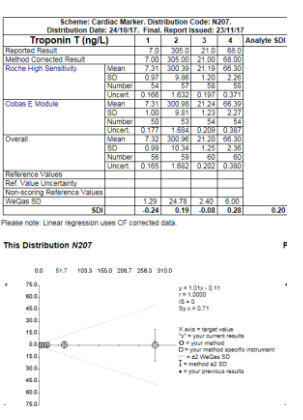
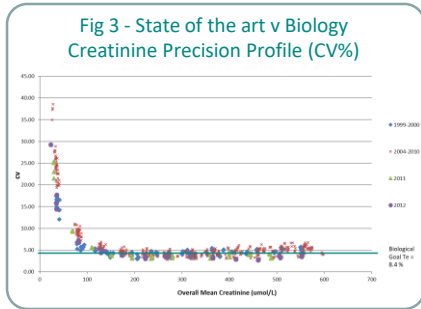
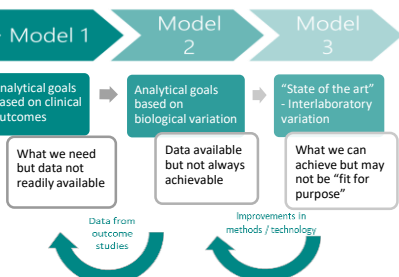


Fig 2b – Clinically relevant ranges



Clinically relevant APS

Laboratories should ensure that the quality is appropriate for the needs of the clinical service. It is therefore essential that EQA evaluation criteria should also reflect clinical need. A hierarchical strategy for APS proposed by the EFLM is suggested³.



³Sandberg S, Fraser CG, Horvath AR, Jansen R, Jones GRD, Oosterhuis W, et al. Defining analytical performance specifications: consensus statement from the 1st strategic conference of the European federation of clinical chemistry and laboratory medicine. Clin Chem Lab Med 2015;53:833–5.

Statistical design

The target value varies greatly and is often dependant on the matrix and availability of higher order reference methods. The advantages of the latter is that it provides a true assessment of accuracy, establishes metrological traceability, a requirement of ISO 15189, an independent assessment of manufacturer traceability claim, is not influenced by the number of devices, and is useful in the post market vigilance.

Fig 4 –Weqas reports - Use of higher order reference method target values.

Glucose (mmol/l)	1	2	3	4	Analyte SDI
Reported Result	11.4	8.1	20.7	1.8	
Method Corrected Result	11.40	8.10	20.70	1.80	
Hexokinase	Mean	11.42	8.21	21.11	1.85
	SD	0.20	0.19	0.41	0.05
	Number	170	170	168	95
	Uncert	0.016	0.012	0.032	0.004
Cobas C Module	Mean	11.43	8.20	21.13	1.80
	SD	0.17	0.13	0.31	0.04
	Number	91	95	92	91
	Uncert	0.016	0.013	0.033	0.004
Overall	Mean	11.39	8.21	21.05	1.88
	SD	0.20	0.19	0.40	0.05
	Number	191	168	168	96
	Uncert	0.016	0.012	0.032	0.004
Reference Values	ID-GCMS	11.40	8.15	20.95	1.78
	Inc. Uncertainty	0.100	0.070	0.190	0.008
Non-scoring Reference Values	Wetlab SD	0.34	0.25	0.65	0.12
	SDI	0.00	-0.20	-0.38	0.23
	Sigma Metrics				
	Critical Level 1.7 mmol/l				7.4
	Minimum Acceptable score	1.42			
	MAPS Allowable TE	6.9%			
	MAPS Allowable bias %	2.20%	Lab (bias) %		0.2%
	MAPS Allowable CV %	2.90%	Lab CV %		0.9%

Assessment of:

Traceability - Full traceability chain to ID-GCMS Reference method.

Accuracy – Comparison to peer group and reference method. From the linear regression analysis equation, $y=mx+c$, the trueness (bias) is calculated at the critical level (x), which for glucose is 7.0 mmol/L.

when $x=7.0$ then $y = 0.99*(7.0)+0.09 = 7.02$ mmol/L
Bias = $(y-x)/x*100 = (7.02-7.0)/7.0*100 = 0.2\%$

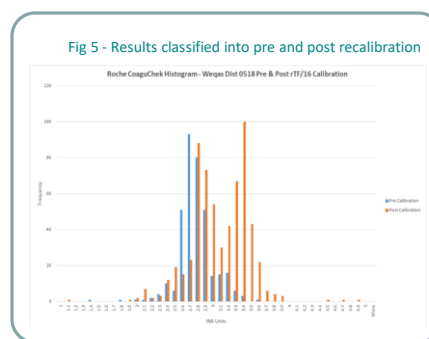
Imprecision (CV%) = $S_y/x = 0.064/7.0*100 = 0.9\%$

APS – from Biological variation, TE = 6.9%

Linearity – Range of concentration span clinically relevant range.

Uncertainty – provided at end of 12 month review calculated as a between batch CV% from replicate measurements.

Post market vigilance- e.g INR thromboplastin recalibration

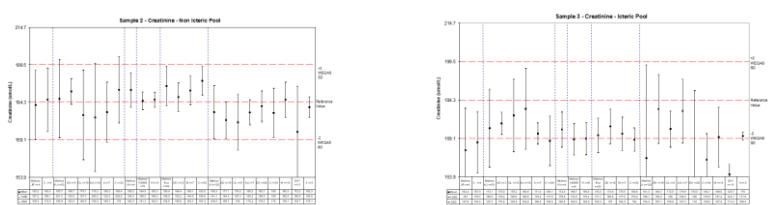


Wide variation of results was observed. The results were classified into pre and post calibrated strip lots and analysed. The pre calibration strips compared well with the results from a previous distribution of the same material, (Median 2.8) however much higher results and a wider distribution of results was observed for the post calibration strips. Weqas immediately contacted the manufacturer and sent them the data.

Education

EQA Programmes play an important role in the continuous education of laboratory staff and should include educational elements relating to: Pre-analytical effects, performance of methods, susceptibility of methods to interference, and the interpretation of the results.

Fig 6a,6b - Typical example of Weqas Interference Reports – effect of icterus on creatinine



The reference value (ID-GCMS) was 184.3 µmol/L for sample 2 and 184.4 µmol/L for sample 3

Fig 7a-d, Assessment of analytical sensitivity of Pregnancy testing kits.

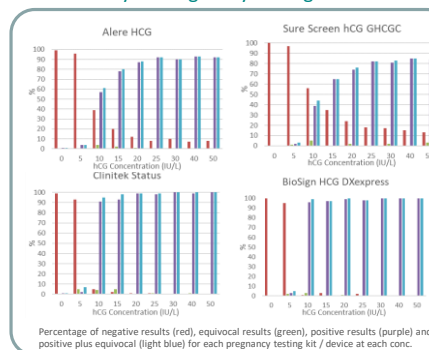


Table 1 - Assessment of analytical specificity of total Bile Acid methods

Four pools of human serum were prepared, and spiked with approximately 100µmol/L of each of the major bile acids and target value assigned using an ID-GCMS method.

	CHOLIC ACID ID-GCMS Target 103.2 µmol/L				DEOXYCHOLIC ID-GCMS Target 108.8 µmol/L			
Returned results	mean	SD	n	% recovery	mean	SD	n	% recovery
overall	101.18	7.54	111	98.06	137.80	15.87	110	126.68
Enz-Thio-NADH	99.89	6.59	95	96.81	141.27	15.64	94	129.87
Enz-Formazan	89.5	1.50	5	86.74	137.00	15.00	2	125.94
Enz-Formazan (Sentinel)	112.41	4.90	15	108.95	119.42	5.08	15	109.78

	URSODEOXYCHOLIC Gammatic target 100 µmol/L				CHENOXYCHOLIC ID-GCMS Target 77.1 µmol/L			
Returned results	mean	SD	n	% recovery	mean	SD	n	% recovery
overall	57.81	8.44	107	57.81	56.05	7.30	107	72.66
Enz-Thio-NADH	56.00	4.44	98	56.00	54.25	4.61	95	70.32
Enz-Formazan	51.50	0.5	2	51.50	51.00	2.00	2	66.11
Enz-Formazan (Sentinel)	90.47	3.33	15	90.47	77.05	2.88	12	99.88

The study highlights the importance of using reference methods to assign target values rather than consensus mean and presents strong evidence on the variability in specificities of the methods for the different bile acids.

Conclusion

The primary intention of an EQA provider is to monitor the performance of laboratories and to support quality improvements for the benefit of patients. It is therefore proposed that the definition should be broadened to include education, troubleshooting support, the assessment of the pre and post analytical phase, post market vigilance, and the monitoring of harmonisation strategies.