Weqas | GLOBAL PROVIDER OF QUALITY IN DIAGNOSTIC MEDICINE

UKAS PROFICIENCY TESTING 4301 | UKAS CALIBRATION 4301

Tel: +44 (0) 2920 314750
E-mail: contact@weqas.com
Web: www.weqas.com

Weqas
Unit 6, Parc Tŷ Glas
Llanishen, Cardiff, UK
CF14 5DU

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

Author Names: M.A. Thomas, S. Jones, G. Davies
Weqas, Cardiff and Vale University Health Board, Cardiff, UK

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 1983[1] 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.

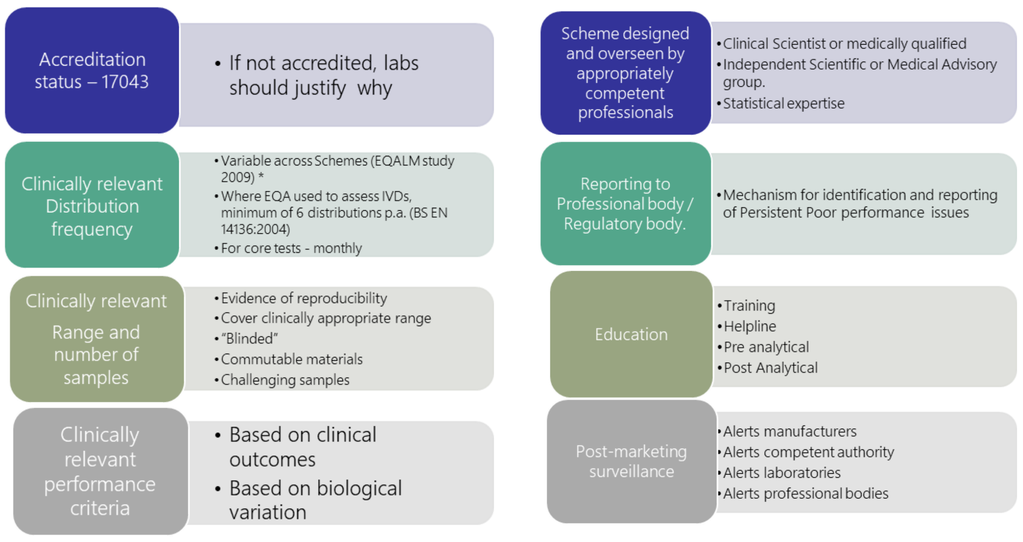
[1]Buttner J, Borth R, Boutwell JH, Broughton PMG, Bowyer RC. International Federation of Clinical Chemistry, Scientific Committee Expert Panel on Nomenclature and principles of Quality Control in Clinical Chemistry. Approved recommendation (1983) on quality control in clinical chemistry. Part 3. External 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 choice[2] .

Figure 1 Factors influencing choice of EQA[2]



[2]External 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 - Assessment of performance of High sensitivity Troponin I – samples close to analytical and clinical cut offs.

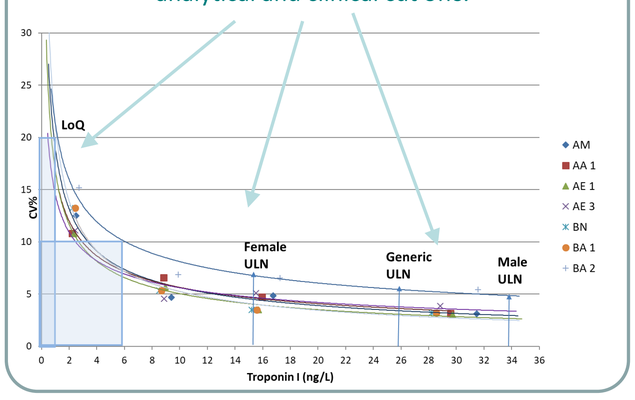


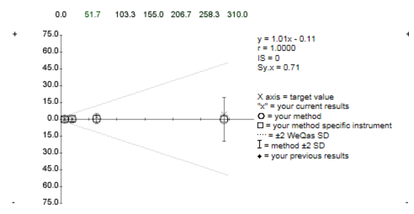
Fig 2b – Clinically relevant ranges

Scheme: Cardiac Marker. Distribution Code: N207.
Distribution Date: 24/10/17. Final. Report Issued: 23/11/17

Troponin T (ng/L)		1	2	3	4	Analyte SDI
Reported Result		7.0	305.0	21.0	68.0	
Method Corrected Result		7.00	305.00	21.00	68.00	
Roche High Sensitivity	Mean	7.31	300.39	21.19	66.30	
	SD	0.97	9.86	1.20	2.26	
	Number	54	57	58	58	
	Uncert.	0.166	1.632	0.197	0.371	
Cobas E Module	Mean	7.31	300.98	21.24	66.39	
	SD	1.00	9.81	1.23	2.27	
	Number	50	53	54	54	
	Uncert.	0.177	1.684	0.209	0.387	
Overall	Mean	7.32	300.96	21.20	66.30	
	SD	0.99	10.34	1.25	2.36	
	Number	56	59	60	60	
	Uncert.	0.165	1.682	0.202	0.380	
Reference Values						
Ref. Value Uncertainty						
Non-scoring Reference Values						
WeQas SD		1.29	24.78	2.40	6.00	
SDI		-0.24	0.19	-0.08	0.28	0.20

Please note: Linear regression uses CF corrected data.

This Distribution *N207*



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 suggested[3].

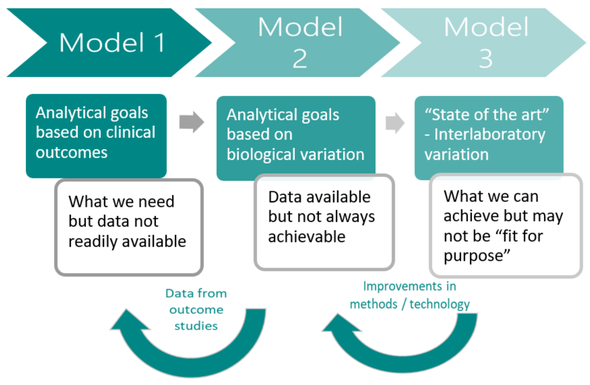
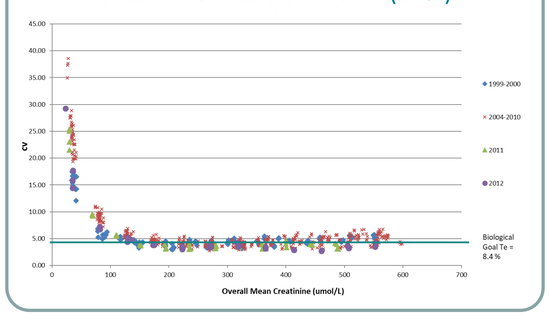


Fig 3 - State of the art v Biology Creatinine Precision Profile (CV%)



[3]Sandberg 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.

Scheme: Serum Chemistry. Distribution Code: RH.
Distribution Date: 2/01/18. Final. Report Issued: 24/01/18

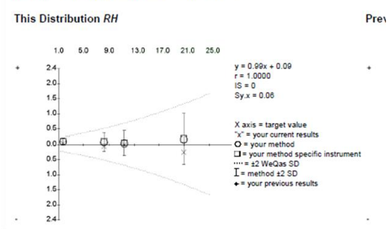
Glucose (mmol/l)		1	2	3	4	Analyte SDI
Reported Result		11.4	8.1	20.7	1.8	
Method Corrected Result		11.40	8.10	20.70	1.80	
Hexokinase	Mean	11.42	8.21	21.11	1.85	
	SD	0.20	0.15	0.41	0.05	
	Number	170	172	169	168	
	Uncert.	0.015	0.012	0.032	0.004	
Cobas C Module	Mean	11.45	8.26	21.13	1.88	
	SD	0.17	0.13	0.31	0.04	
	Number	91	95	92	91	
	Uncert.	0.018	0.013	0.033	0.004	
Overall	Mean	11.39	8.21	21.05	1.86	
	SD	0.22	0.15	0.46	0.06	
	Number	191	188	188	186	
	Uncert.	0.016	0.011	0.033	0.004	
Reference Values ID-GCMS		11.40	8.15	20.95	1.76	
Ref. Value Uncertainty		0.100	0.070	0.190	0.020	
Non-scoring Reference Values						
WeQas SD		0.34	0.25	0.65	0.12	
SDI		0.00	-0.20	-0.38	0.34	0.23

Sigma Metrics
Critical Level 1: 7 mmol/l

Minimum Acceptable score MAPS Allowable TE 6.9%	1.62	Critical Level 1 Sigma score	7.4
MAPS Allowable bias %	2.20%	Lab [bias] %	0.2%
MAPS Allowable CV %	2.90%	Lab CV %	0.9%

Please note: Linear regression uses CF corrected data.

This Distribution *RH*



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%) = Sy.x/ x = 0.064/7.0*100 = 0.9%

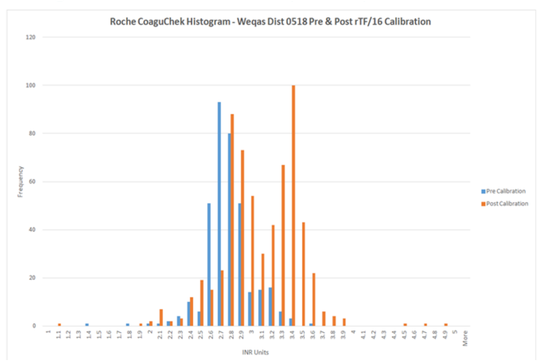
APS – from Biological variation, TE = 6.9%

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

Fig 5 - Results classified into pre and post recalibration

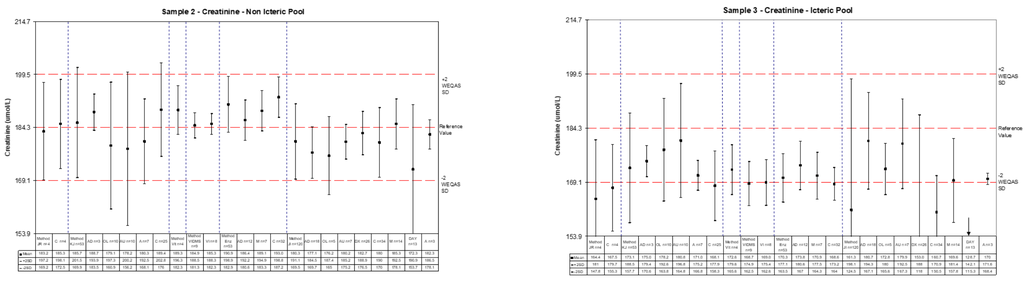


Wide variation of results was observed. The results were classified into pre and post calibrated strip lots and analysed. The pre calibration strips compared well with the results from a previous distribution of the same material, (Median 2.8) however much higher results and a wider distribution of results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

Education

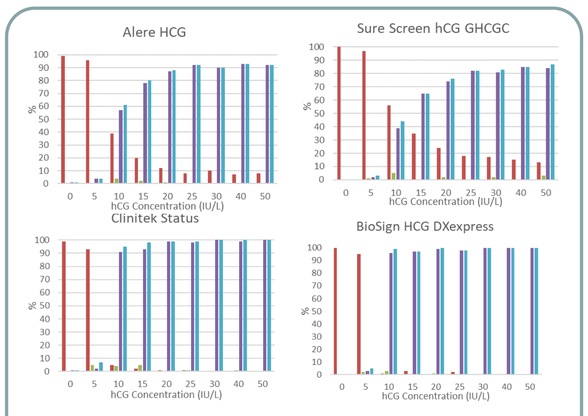
EQA Programmes play an important role in the continuous education of laboratory staff and should include educational elements relating to: Pre-analytical effects, performance of methods, susceptibility of methods to interference, and the interpretation of the results.

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.



Percentage of negative results (red), equivocal results (green), positive results (purple) and positive plus equivocal (light blue) for each pregnancy testing kit / device at each conc.

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				DEOXYCHOLIC ID-GCMS Target			
	103.2 µmol/L				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
POOL ID	URSODEOXYCHOLIC Gavimetric target				CHENODEOXYCHOLIC ID-GCMS Target			
	100 µmol/L				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.