

Reference Value Assignment of a Commutable EQA



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Introduction

One of the primary functions of an EQA provider is to guide on accuracy, however, the 'true' value of an EQA sample may be compromised due to manufacturing processes. The RCPAQAP provides a Liquid Serum Chemistry Program using commutable samples sourced from consenting male and female haemochromatosis patients. We sought to determine the accuracy of routine Chemical Pathology methods in this program.

Method

The RCPAQAP contracted Reference Laboratories in Germany, Wales, and Australia to analyse the November 2023 Liquid Serum Chemistry samples (23-03 and 23-04) for measurands where metrologically traceable reference methods are currently available. ALT, ALP, Amylase, AST, CK, GGT and LDH values were assigned using the IFCC (37°C) reference method. Cholesterol, Creatinine, Glucose, Triglycerides and Urate values were derived using the Isotope Dilution Gas Chromatography Mass Spectrometry reference method. Cortisol and Testosterone values were obtained by Isotope Dilution Liquid Chromatography-Tandem Mass Spectrometry. Sodium, Potassium, Calcium and Magnesium employed a Standard Addition ICP-MS method. The assigned reference values were then compared to the all-result medians returned by 255 participating laboratories in Australia and New Zealand.

Results

Returned all result medians for 10 of the measurands in this study were within the reference value expanded uncertainties (at a 95% confidence level) for both samples indicating overall excellent accuracy, noting, however, that some uncertainties were wider than anticipated for a reference method. For both samples, 24-03 and 24-04, AST, GGT, LDH, Urate, Cortisol and Testosterone the all-result medians were outside the reference value expanded uncertainties. The ALT all result median for sample 23-03 and Cholesterol all result median for sample 23-04 were also outside the reference value expanded uncertainties (Table 1). Apart from Cortisol and Testosterone, the other measurands in Table 1 were within the RCPAQAP Analytical Performance Specification and not enough to be clinically significant.

Discussion

The unexpected wider uncertainties for the reference values may stem from reference laboratories accounting for multiple variables when assigning secondary values to unknown samples¹. Variability in less stable measurands, such as LDH, AST, and ALT, could be influenced by transport conditions or variations in the number of freeze/thaw cycles prior to analysis. While the Abbott and Beckman Coulter groups dominated the median, other chemistry analysers listed in Table 2 did not exhibit method-related biases. Notably, the Siemens Atellica analysers showed a high bias for cortisol and a low bias for testosterone.

References

1. Gates K, Chang N, Dilek, et al. The Uncertainty of Reference Standards – A Guide to Understanding Factors Impacting Uncertainty, Uncertainty Calculations, and Vendor Certifications. Journal of analytical Toxicology, 2009; 33: 532-539.

Table 1 Summary of All Result Medians, Reference Values and their Expanded Uncertainties. Highlighted medians are outside the Expanded Uncertainties of the associated Reference Value.

Measurand	Unit	Sample 23-03 Median	Reference Value	Expanded Uncertainty (95%)	Sample 23-04 Median	Reference Value	Expanded Uncertainty (95%)
ALT	U/L	26	28.44	0.7	30	31.1	1.3
ALP	U/L	76	76.1	2.1	78	78.3	2.2
Amylase	U/L	60	60.3	1.8	54	53.8	1.6
AST	U/L	43	46.6	1.0	33	36.0	1.1
Creatine Kinase	U/L	95	96.5	2.6	114	116.1	3.0
GGT	U/L	45	48.8	1.2	48	51.3	1.6
LDH	U/L	164	171.1	4.7	121	126.3	2.8
Calcium	mmol/L	2.40	2.33	0.18	2.36	2.29	0.18
Cholesterol	mmol/L	4.6	4.47	0.1	4.85	4.67	0.10
Creatinine	umol/L	69	68.66	1.19	88	87.57	1.52
Glucose	mmol/L	5.9	5.77	0.12	6.8	6.65	0.14
Magnesium	mmol/L	1.74	1.726	0.049	1.72	1.715	0.073
Potassium	mmol/L	4.2	4.17	0.19	4.2	4.21	0.22
Sodium	mmol/L	140	138.7	5.5	140	139.6	5.6
Triglycerides	mmol/L	1.64	1.61	0.03	2.52	2.46	0.05
Urate	mmol/L	335	343.1	5.90	432	440.9	7.58
Cortisol	nmol/L	249	241	3.2	287	276	4.5
Testosterone	nmol/L	2.9	2.5	0.16	12.2	9.4	0.61

Table 2 Summary of the Chemistry analysers enrolled in the Liquid Serum Chemistry Program.

Measurement System	n
Abbott ARCHITECT - c16000	10
Abbott ARCHITECT - c4000	16
Abbott ARCHITECT - c8000	6
Abbott Alinity c	39
Beckman Coulter AU480	29
Beckman Coulter AU5800	12
Beckman Coulter AU680	25
Beckman Coulter AU700	6
Ortho-Clinical Diagnostics VITROS 4600	23
Ortho-Clinical Diagnostics VITROS 5600(c)	7
Ortho-Clinical Diagnostics VITROS XT 7600(c)	13
Roche Diagnostics cobas c 303	2
Roche Diagnostics cobas c 501	14
Roche Diagnostics cobas c 702	21
Siemens ADVIA 1800	1
Siemens Atellica CH	24
Siemens Dimension EXL	7
Total	255

Conclusion

Reference value assignment for the Liquid Serum Chemistry program has the potential to provide valuable information on continued accuracy across different manufacturer methods to the pathology profession. Further, it guides on any potential shifts that may impact the use of harmonised reference intervals.