Beckman Coulter's DxC 500 AU Clinical Chemistry Analyzer, assessed by Six Sigma metrics, meets and exceeds the demands of CLIA 2024 performance specifications.

B-133

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BACKGROUND

The analytical Sigma-metric is a quality assessment tool, derived from the well-known Six Sigma management approach, and has been employed in Clinical Chemistry Assay performance assessments for over two decades. The analytical Sigma-metric, for an analyte or test in the clinical laboratory, is calculated using three variables that are routinely available; imprecision (CV), inaccuracy (bias) and total allowable error (TEa), all expressed as percentages or all in units. A range of assays were assessed for Sigma-metric performance including ISE chemistries for urine and serum, IgG serum and CSF, CRP serum and Glucose serum, urine and CSF, on the Beckman Coulter DxC 500 AU anlanyzer. The Beckman Coulter DxC 500 AU clinical chemistry analyzer* is the latest system from Beckman Coulter. It is a fully automated, random-access analyzer, designed for medium volume laboratories, with a throughput of 800 tests/hour including ISEs.

*Product In development. Pending clearance by the United States Food and Drug Administration and achievement of CE compliance. Not currently available for *in vitro* diagnostic use.

METHODS

To assess the 6-sigma performance of the assays on the DxC 500 AU system, the standard analytical equation was used; Sigma metric = (TEa-|Bias|)/CV. Precision data was generated following the CLSI EP05 guideline, utilizing the 20-day protocol with test samples at various levels tested twice a day with a minimum of two hours between runs. Relative bias was determined through a method comparison study tested, following the CLSI EP09-A3 guideline, between the DxC 500 AU and the DxC 700 AU analyzers, and evaluated a minimum of 100 samples completed over a minimum of three days. Bias was calculated at various levels across the dynamic range utilizing both the Passing-Bablok and Deming regression models. The 6-sigma performance was assessed against total error (TE) goals from various sources including the new CLIA 2024 performance criteria for serum, Royal College of Pathologists of Austral-Asia (RCPA) ALP for urine assays, and in one case, the Wisconsin State Lab of Hygiene (WSLH) goal for a CSF analyte.

RESULTS

Urine applications for ISEs and Glucose all demonstrated > 6-sigma performance. The glucose CSF demonstrated >5-sigma performance while the IgG CSF assay demonstrated > 3-sigma performance. For the serum applications, all assays demonstrated > 4-sigma performance, with CRP, glucose and chloride demonstrating > 6-sigma, IgG > 4-sigma and potassium and sodium > 5-sigma. Using Westgard Sigma Rules, this indicates that most assays do not require extensive multi-rule monitoring, but instead can rely on fewer rules with wider control limits. Summary data is summarised in the tables below.

Table 1: Summary of Sigma performance for Representative Clinical Chemistry assays on the DxC 500 AU analyzer.

Assay, Range and Units	Part Number	Sample	Concentration	TEa	Bias	CV	Sigma Performance
hs-CRP: 0.2 - 80 mg/L	OSR6199	Serum	1.1	30	3.2	1.3	> 6
			3.0	30	0.6	0.8	> 6
			9.1	30	0.9	1.0	> 6
			70.0	30	3.1	1.0	> 6
IgG: 75 - 3000 mg/dL	OSR6x172	Serum	504	20	0.6	1.2	> 6
			1798	20	3.5	2.4	> 6
			2576	20	3.8	3.7	4.4
IgG: 2 - 50 mg/dL	OSR6x172	CSF	4.1	20	2.6	5.6	3.1
			11.2	20	0.8	3.1	> 6
			36.3	20	0.1	2.6	> 6
Glucose: 10 - 800 mg/dL	OSR6x21	Serum	51	11.74	1.0	0.9	> 6
			121	8	1.2	0.9	> 6
			289	8	1.3	1.0	> 6
Glucose: 10 - 700 mg/dL	OSR6x21	Urine	56	10	1.0	0.7	> 6
			131	8	0.0	1.3	> 6
			343	8	0.4	0.9	> 6
Glucose: 10 - 800 mg/dL	OSR6x21	CSF	37	10	3.3	1.2	5.6
			123	10	1.6	0.8	> 6
			317	10	1.2	1.0	> 6

Table 2: Summary of Sigma performance for ISE Chemistry Reagents assays on the DxC 500 AU analyzer.

Assay, Range and Units	Part Number	Sample	Concentration	TEa	Bias	CV	Sigma Performance
Potassium: 1.0 - 10.0 mEq/L	AUH1011	Serum	2.5	11.86	-0.4	0.3	> 6
			4.5	6.73	0.4	0.3	> 6
			6.4	4.72	0.7	0.4	> 6
			8.5	3.53	0.9	0.5	5.2
Potassium: 2.0 - 200.0 mEq/L		Urine	9.9	10	2.0	0.5	> 6
			32.3	10	0.6	0.8	> 6
			100.4	10	0.2	1.0	> 6
			178.0	10	0.1	1.0	> 6
Chloride: 50 - 200 mEq/L		Serum	51.5	5	0.0	0.5	> 6
			76.0	5	0.2	0.4	> 6
			104.2	5	0.3	0.5	> 6
			150.1	5	0.4	0.5	> 6
Chloride: 15 - 400 mEq/L		Urine	25.7	15.58	0.9	1.1	> 6
			86.6	10	0.1	0.4	> 6
			151.8	10	0.0	0.5	> 6
			302.9	10	0.1	0.6	> 6
Sodium: 50 - 200 mEq/L		Serum	60.4	6.61	1.6	0.8	> 6
			110.1	3.63	0.1	0.5	> 6
			140.3	2.85	0.3	0.3	> 6
			172.3	2.32	0.6	0.3	5.8
Sodium: 10 - 400 mEq/L		Urine	21.4	18.7	0.1	1.7	> 6
			98.8	10	0.6	0.4	> 6
			250.9	10	0.7	0.5	> 6
			351.9	10	0.8	0.6	> 6

Once the Sigma metric is known, the simplest guide to QC optimization is the Westgard Sigma Rules. For a 6-sigma test, the Westgard Sigma Rules recommendation is just a 1:3s control rule with two control measurements. No other rules are necessary. For a 5-sigma just 3 of the Westgard Sigma Rules are needed: 1:3s/2:2s/R:4s. For a 3-sigma method, all the Westgard Sigma Rules are necessary. Implementing the 1:3s rule for a large number of 6-sigma assays can reduce the number of outliers, troubleshooting, repeated controls, recalibrations, etc.

RESULTS (CONTINUED)

Figures 1-3: Graphical representation of the sigma performance of Serum (figure 1), Urine (figure 2), and CSF (Figure 3) assays

Figure 1

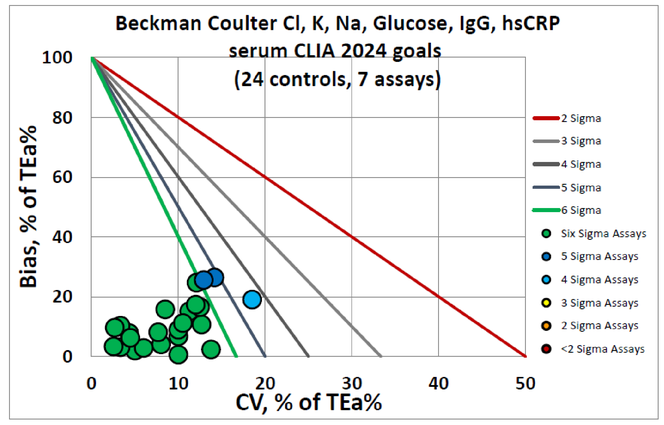


Figure 2

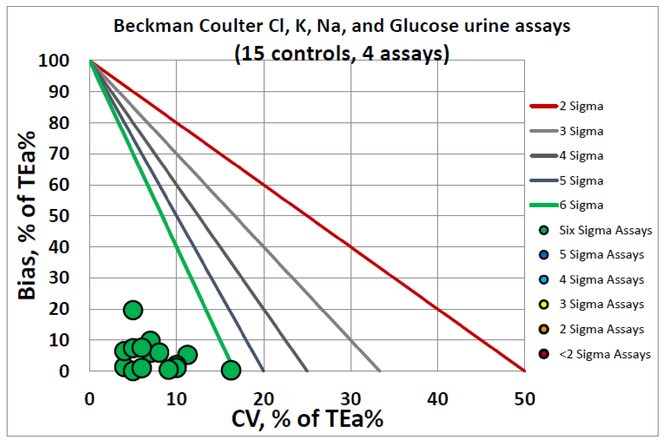
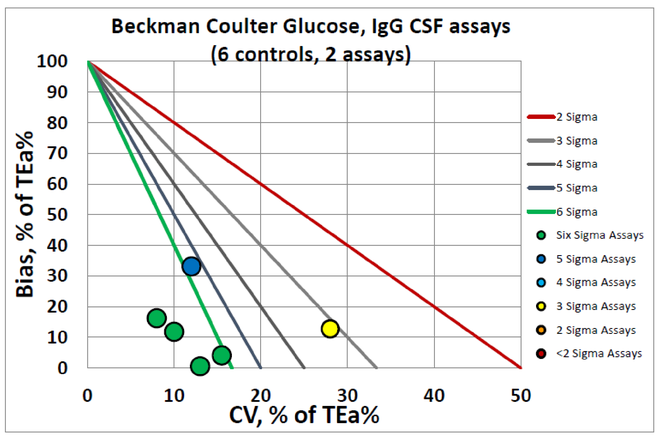


Figure 3



CONCLUSION

Excellent performance has been demonstrated for the assays evaluated, with all urine applications performing at >6-sigma and serum assay at > 4-sigma, and CSF assays performing at > 3-sigma. Sigma-metric analysis confirms the instrument will meet or exceed adherence to the coming, tighter CLIA 2024 performance specifications. Further, QC for these assays can be optimized to reduce the number of rules, levels, and runs implemented for routine monitoring. The resulting optimized process enables the laboratory to produce quality results efficiently with increased confidence for proper test interpretation.