CORE DIAGNOSTICS

Sigma Metrics for Next Generation Clinical Chemistry Assays

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1. BACKGROUND

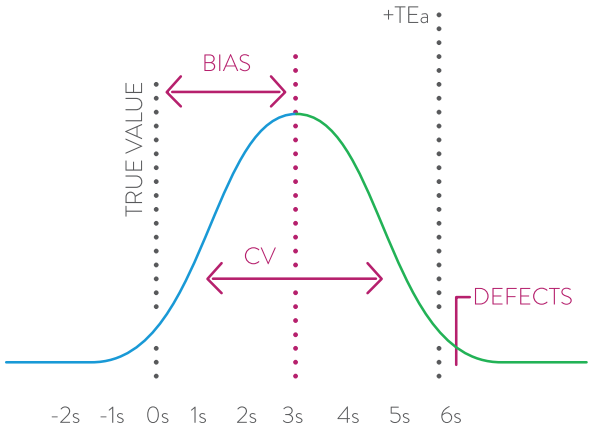
Six Sigma is a well-established tool that can objectively assess the performance of a process with the goal of increasing quality output and minimizing error. Although these metrics began in the manufacturing sector, Six Sigma has been applied across numerous industries, including healthcare. For laboratorians, Six Sigma (or Sigma) metrics are useful for assessing the performance of instruments and assays. An optimal process will have a Sigma value of 6 (6-Sigma) or greater, which indicates a defect rate of 3.4 errors per million opportunities. Healthcare processes in general, and laboratory test performance specifically, can fall short of this metric. The Sigma values for laboratory processes are typically in the 3 to 4 range and sometimes even lower[1]. For comparison, a Sigma value of 3 (3-Sigma) indicates a defect rate of 66,800 errors per million, which is considered marginal performance and not ideal from a clinical perspective.

Sigma metrics are also valuable for benchmarking and comparing different laboratory assays or comparator systems; this is an especially helpful tool when a side by side comparison would be expensive due to the large number of products offered per system. A Sigma metric compares the precision and bias performance of the assay to the laboratory total allowable error (TEa) goal. Achieving a Sigma value of 6 is a mark of world-class assay performance. Unfortunately, most clinical chemistry and immunoassays on the market do not meet this standard[2].

Assays with high Sigma values benefit the laboratory by reducing errors and providing clinicians with consistent and accurate results. This 'right first-time' paradigm improves turn-around-time (TAT), curtailing the need for repeat testing[3]. Turn-around-time is an essential benchmark for labs to leverage patient and clinician satisfaction, and it also influences patient care[4]. Hospital performance indicators, such as Emergency Department (ED) length of stay, are influenced by lab TAT[5]. Thus, high-performing assays (high Sigma) can add value to patient care and provide better customer satisfaction than average-performing assays.

These benefits allow a lab to remain competitive, reduce headcount needs, and decrease quality control testing to remain financially solvent in today's evolving healthcare marketplace.

Figure 1: Sigma Metric Variables



2. METHODS

This study evaluated the Sigma performance of 16 ARCHITECT and 15 Alinity c system clinical chemistry assays across several therapeutic areas. A Sigma metric was calculated for each assay per the following equation:

SIGMA METRIC = (TEa – |BIAS|)/PRECISION

THE SIGMA METRIC VARIABLES ARE:

TEa:
The assay-specific total allowable error (TEa) was obtained from recognized organizations such as Clinical Laboratory Improvement Amendments (CLIA) and German Medical Association on Quality Assurance in Medical Laboratory Examinations – Rili-BAEK.

Bias:
Bias is the difference between the measured value and the true value of a sample. For calculating bias, the use of an internationally recognized standard or method is preferred to allow comparison across different manufacturer systems. A recognized standard or reference method (e.g., NIST) at a medically relevant concentration was tested. The % difference from the target was calculated as the bias.

Precision:
The precision of an assay describes the variability of the measurement of a sample and is often reported as a coefficient of variation (CV). In this study, the within-laboratory CV was used from a sample with a concentration near to that of the reference sample used to determine the bias.

After calculating Sigma metrics for each assay, a precision profile chart was created to compare the precision performance of the assays tested on the ARCHITECT and Alinity c systems.

3. SIGMA DATA

Low imprecision and bias were observed across the measuring intervals for all of the next generation ARCHITECT and Alinity c system clinical chemistry assays tested (Table 1a and 1b). Additionally, 6-Sigma metrics were achieved for 12 of the ARCHITECT clinical chemistry assays tested and all of the Alinity c clinical chemistry assays tested (Figure 2a and 2b). Furthermore, the data highlight the accuracy of these assays when measured against recognized standards, even when tested at a low medically relevant concentration for each analyte across both platforms.

Figure 2a: Sigma Metrics for Next Generation ARCHITECT Clinical Chemistry Assays[6]

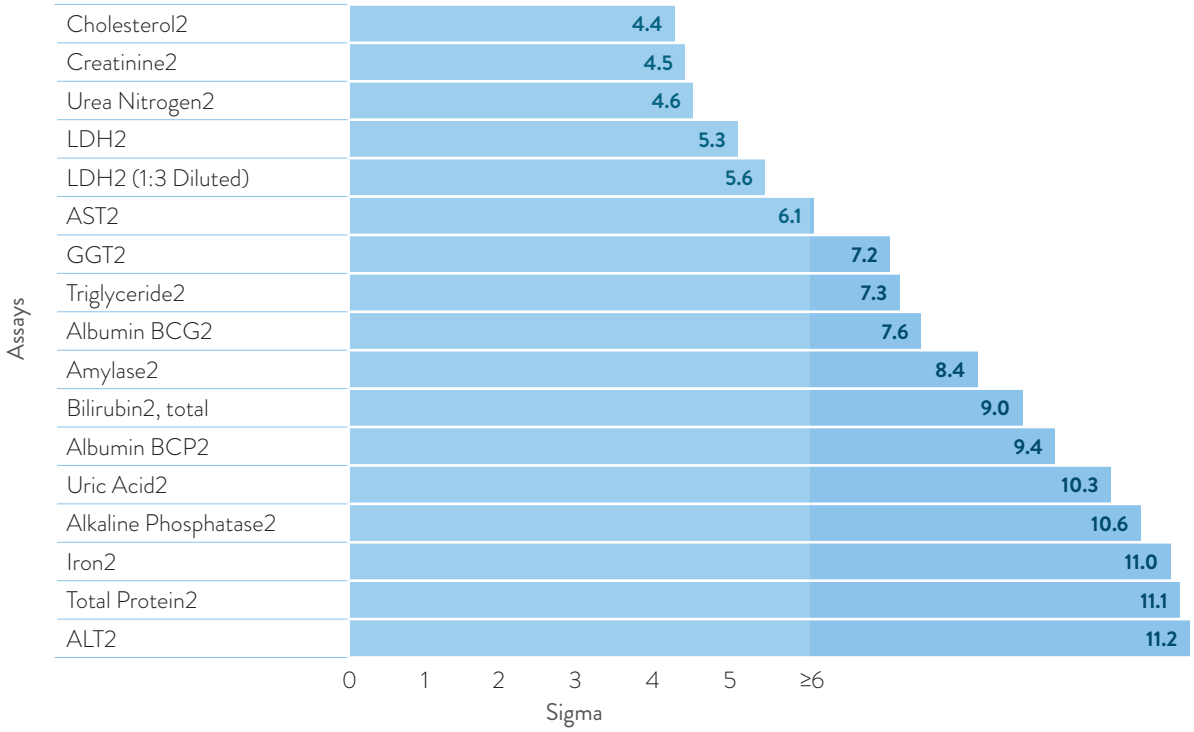


Figure 2b: Sigma Metrics for Next Generation Alinity c Clinical Chemistry Assays[6]

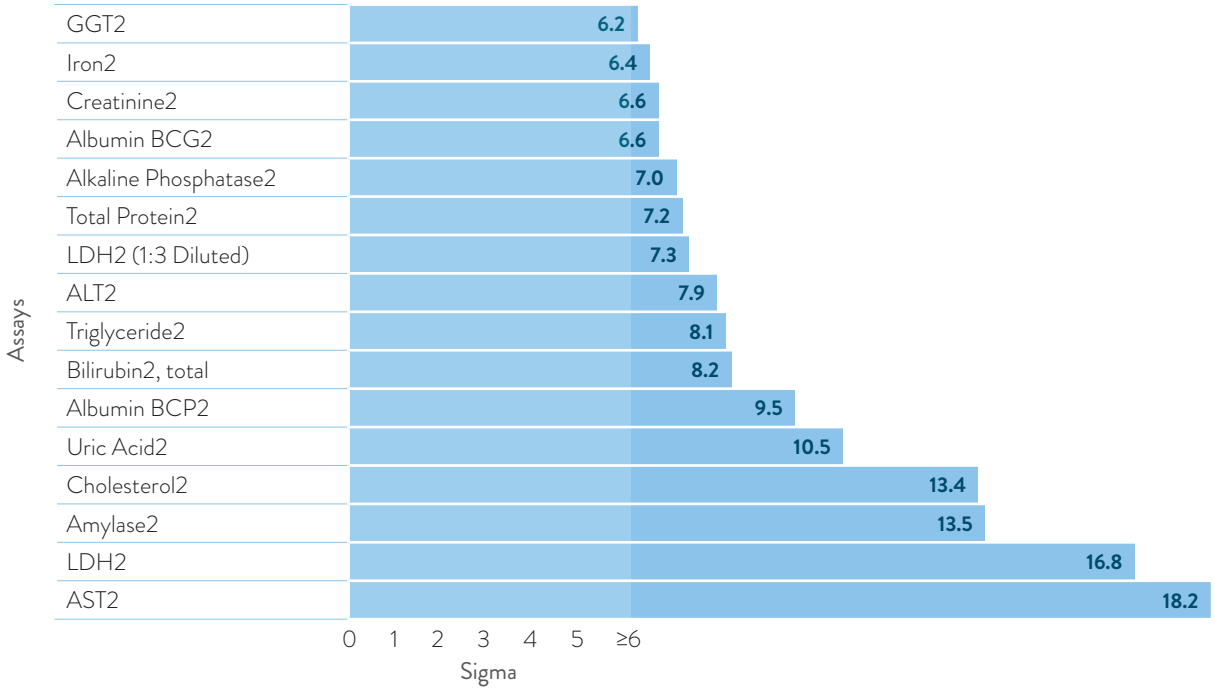


Table 1a: Sigma Metrics for Next Generation ARCHITECT Clinical Chemistry Assays[6]

ARCHITECT Assays	Standard	Target	%CV	% Bias	TEa	Sigma
Cholesterol2	Human Cholesterol Abell-Kendall	236 mg/dL	2.0	1.1	10[a]	**4.4**
Creatinine2	NIST SRM 967	0.85 mg/dL	3.5	-4.1	20[g]	**4.5**
Urea Nitrogen2	NIST SRM 912	20 mg/dL	2.7	3.3	15.5[b]	**4.6**
LDH2	IFCC Traceable Material	360.4 U/L	3.0	1.9	18[f]	**5.3**
LDH2 (1:3 Diluted)	IFCC Traceable Material	360.4 U/L	3.0	-1.2	18[f]	**5.6**
AST2	ERM-AD457/IFCC	105.2 U/L	1.9	3.2	15[b]	**6.1**
GGT2	ERM-AD452/IFCC	114.1 U/L	2.8	1.6	22[h]	**7.2**
Triglyceride2	ACS Grade Glycerol	180 mg/dL	2.1	1.0	16[e]	**7.3**
Albumin BCG2	ERM-DA470/IFCC	3.7 g/dL	1.6	2.1	14[c]	**7.6**
Amylase2	IRMM/IFCC-456	309 U/L	1.6	2.0	15.7[b]	**8.4**
Bilirubin2, total	Human Neonatal Bilirubin	2.85 mg/dL	2.2	1.9	22[f]	**9.0**
Albumin BCP2	ERM-DA470/IFCC	3.8 g/dL	1.4	-0.9	14[c]	**9.4**
Uric Acid2	NIST SRM 913	10 mg/dL	1.2	1.0	13[d]	**10.3**
Alkaline Phosphatase2	IFCC Traceable Material	336.6 U/L	1.6	-0.9	18[e]	**10.6**
Iron2	NIST SRM 3126	50 ug/dL	0.9	-5.3	15.3[i]	**11.0**
Total Protein2	NIST SRM 927	7.0 g/dL	0.8	-0.7	10[d]	**11.1**
ALT2	ERM-AD454k/IFCC	103.8 U/L	1.4	4.5	22[a]	**11.2**

Table 1b: Sigma Metrics for Next Generation Alinity c Clinical Chemistry Assays[6]

Alinity c Assays	Standard	Target	%CV	% Bias	TEa	Sigma
GGT2	ERM-AD452/IFCC	114.1 U/L	3.1	-2.5	22[h]	**6.2**
Iron2	NIST SRM 3126	50 ug/dL	1.8	-3.7	15.3[i]	**6.4**
Creatinine2	NIST SRM 967	0.85 mg/dL	2.9	-0.6	20[g]	**6.6**
Albumin BCG2	ERM-DA470/IFCC	3.7 g/dL	1.4	4.8	14[c]	**6.6**
Alkaline Phosphatase2	IFCC Traceable Material	336.6 U/L	2.4	1.0	18[e]	**7.0**
Total Protein2	NIST SRM 927	7.0 g/dL	1.2	-1.6	10[d]	**7.2**
LDH2 (1:3 Diluted)	IFCC Traceable Material	360.4 U/L	2.0	3.8	18[f]	**7.3**
ALT2	ERM-AD454k/IFCC	103.8 U/L	1.9	5.4	20[a]	**7.9**
Triglyceride2	ACS Grade Glycerol	180 mg/dL	2.0	0	16[e]	**8.1**
Bilirubin2, total	Human Neonatal Bilirubin	2.85 mg/dL	2.6	-0.4	22[f]	**8.2**
Albumin BCP2	ERM-DA470/IFCC	3.7 g/dL	1.3	-1.9	14[c]	**9.5**
Uric Acid2	NIST SRM 913	6.8 mg/dL	1.0	2.5	13[d]	**10.5**
Cholesterol2	Human Cholesterol Abell-Kendall	212 mg/dL	0.7	0.6	10[a]	**13.4**
Amylase2	IRMM/IFCC-456	309 U/L	1.0	1.7	15.7[b]	**13.5**
LDH2	IFCC Traceable Material	360.4 U/L	1.0	2.0	18[f]	**16.8**
AST2	ERM-AD457/IFCC	103.9 U/L	0.7	3.1	15[b]	**18.2**

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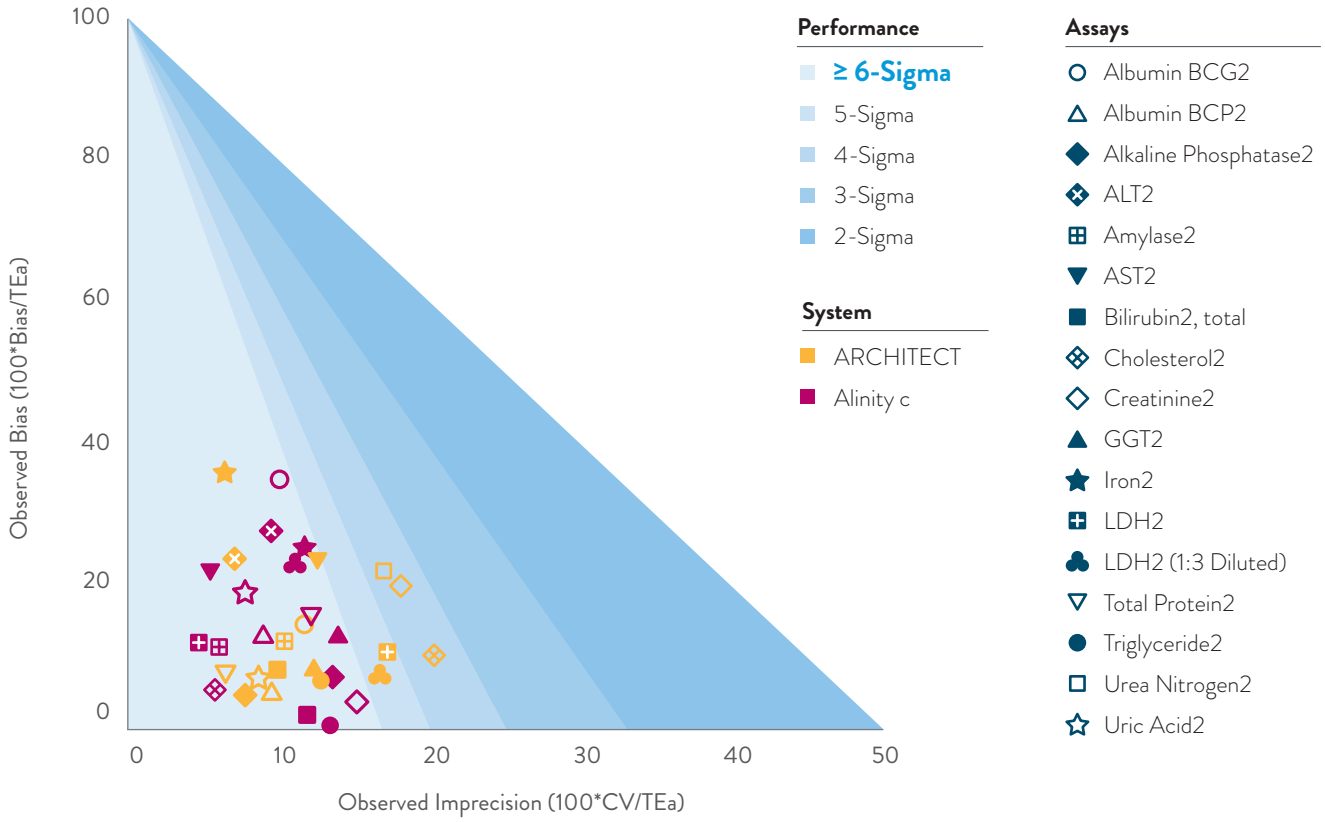
The Sigma profile chart in Figure 3 shows the consistency in assay quality results across the ARCHITECT and Alinity c platforms. With most assays performing in the 6-Sigma range, laboratory personnel can have confidence in the results reported for these clinical chemistry assays on the ARCHITECT and Alinity c platforms.

Figure 3: Normalized Method Decision Chart[6]



4. CONCLUSION

In today's healthcare environment, a laboratory's measure of success and profitability is increasingly driven by the satisfaction of its customers: physicians, nurses, patients, and laboratory personnel. Selecting assays that offer higher efficacy and reliability can give a lab confidence in their results and provide a competitive advantage. Sigma metrics are a powerful tool for selecting the most sensitive assays and allowing for comparison of assay performance across platforms and vendors. Sigma metrics of 6 or higher signify world-class assay performance, a key objective for Abbott during the assay design process. The exceptional performance of the ARCHITECT and Alinity c next generation clinical chemistry assays tested in this study reflect this commitment to world-class assay design and performance.

Transitioning to assays that achieve a high Sigma metric can aid laboratorians in meeting that 'right first-time' performance target, which leads to improved turnaround time (TAT). When both accuracy and TAT excel, lab personnel can be confident in the performance of their assays, offering tremendous value to the healthcare system and positively influencing patient care.

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