Technical Note

Control Material Comparability Assessed by Sigma-metrics

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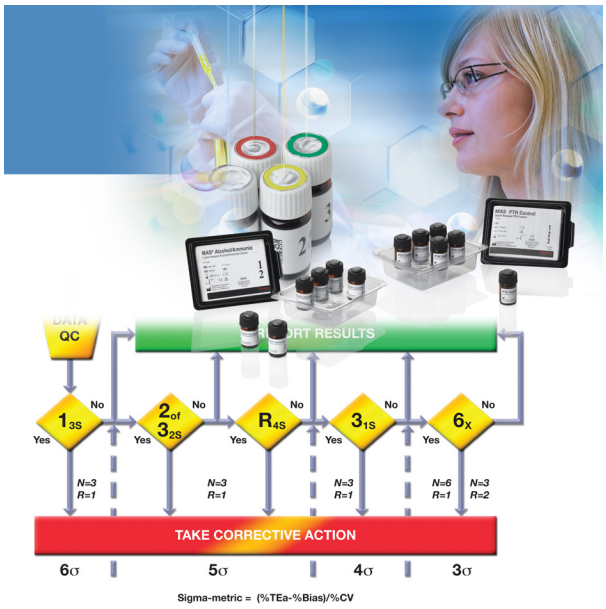
Abstract

The goal of this study was to determine the Sigma-metrics of two control materials on the same instrument. For twelve analytes (albumin, alanine aminotransferase, aspartate aminotransferase, creatinine kinase, glucose, creatinine, triglycerides, total protein, lactate dehydrogenase, digoxin, magnesium, and amylase) control materials from two different vendors were run to determine if they exhibited comparable performance. If both controls demonstrated the same Sigma-metrics, this indicates that controls are comparable and a switch can be made with no loss of quality control.



Introduction

Control materials are a critical analytical quality monitor for laboratories. Vendors of control material often market their products based on price and convenience of use. Too often the analytical quality of the control material is assumed and overlooked. Rarely is the actual analytical performance measured. Six Sigma metrics provide an objective comparative technique. For laboratories seeking consolidation or reduction in costs, the first step should be to confirm that no quality is compromised when switching between control vendors.

Six Sigma is a well-known benchmarking quality technique. It provides a simple intuitive scale from 0 to 6. If a process is performing at Six Sigma, on the short-term Sigma scale, only 3.4 defects are expected to occur per million opportunities. This is often expressed as DPM (defects per million). Six Sigma is considered world class performance. In industry and manufacturing, a process at Six Sigma is operating at peak efficiency, delivering maximum reliability and profitability.

If a process is performing at only Three Sigma, on the other hand, (again this is on the short-term Sigma scale), produces closer to 67,000 DPM. In industry and manufacturing, processes below Three Sigma are targeted for immediate improvement and/or redesign, or they are replaced, because those processes are causing excessive rework and instability.

In healthcare, when analytical processes are below Three Sigma, there is also a high rate of re-work, such as repeated controls, repeated recalibrations, re-testing the patient, etc.

The use of Six Sigma metrics to compare control performance is novel because the goal is not necessarily to achieve higher Sigma-metrics than the first control. Instead, the assumption is that the goal is to achieve comparable, similar performance. If an assay on an instrument is performing at Three Sigma, the laboratory wants controls to reveal that performance, not to make it look better or worse.

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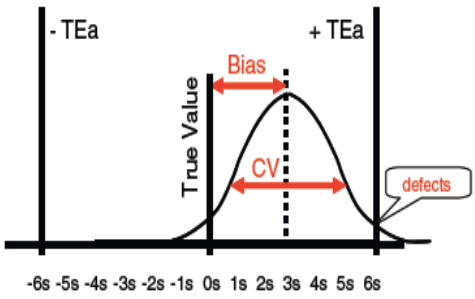
Methods

Controls from two vendors (Thermo Scientific™ MAS and Bio-Rad) were run on the same instrument (Dimension® RxL) at the ICM (Cardiac Institute of Montreal) from July to December, 2014.

- Imprecision was calculated from at least 20 control measurements.
- Bias was calculated as the difference between the observed mean and the control material target value.
- Quality requirements were selected mainly from CLIA proficiency testing criteria.

The Sigma-metric equation (see below for the graphic description) was used to calculate the Sigma-metric at each level, and an average Sigma-metric was then calculated for each analyte.



Test	Lot	Level	Mean	SD	%CV	% Bias	TaE	Sigma
ALB	1611 (MAS)	1	27.44	0.83	3.0	0.9	10.0%	3.0
		2	50.91	0.49	1.0	0.9	10.0%	9.4
		3	73.86	0.93	1.3	0.9	10.0%	7.3
	4648 (BioRad)	1	24.21	0.31	1.3	0.9	10.0%	7.1
		2						
		3						
ALT	1611 (MAS)	1	42.17	1.61	3.8	5.9	20.0%	3.7
		2	114.80	1.97	1.7	5.9	20.0%	8.2
		3	181.47	3.48	1.9	9.7	20.0%	5.4
	4648 (BioRad)	1	38.08	0.97	2.5	2.4	20.0%	6.9
		2						
		3						
AST2	1611 (MAS)	1	42.52	2.11	5.0	0.1	20.0%	4.0
		2	155.56	2.79	1.8	0.9	20.0%	10.6
		3	267.38	5.04	1.9	2.4	20.0%	9.3
	4648 (BioRad)	1	38.30	1.50	3.9	1.8	20.0%	4.6
		2	101.49	2.22	2.2	1.5	20.0%	8.5
		3	249.65	3.63	1.5	0.1	20.0%	13.6
CK1	1611 (MAS)	1	91.89	2.03	2.2	0.3	30.0%	13.4
		2	349.57	8.46	2.4	0.4	30.0%	12.2
		3	610.37	10.45	1.7	0.4	30.0%	17.3
	4648 (BioRad)	1	78.64	1.79	2.3	1.7	30.0%	12.4
		2	261.07	5.28	2.0	4.4	30.0%	12.6
		3	567.41	11.52	2.0	2.2	30.0%	13.7
GLU1	1611 (MAS)	1	3.70	0.11	3.1	5.2	10.0%	1.6
		2	11.47	0.20	1.7	3.3	10.0%	3.8
		3	19.31	0.30	1.6	3.3	10.0%	4.3
	4648 (BioRad)	1	3.50	0.08	2.3	6.1	10.0%	1.7
		2	6.88	0.13	1.9	2.7	10.0%	3.8
		3	20.66	0.37	1.8	3.3	10.0%	3.8
CREA1	1611 (MAS)	1	89.92	4.16	4.6	5.9	15.0%	2.0
		2	355.75	13.61	3.8	2.2	15.0%	3.3
		3	619.53	14.64	2.4	2.2	15.0%	5.4
	4648 (BioRad)	1	60.04	3.73	6.2	3.2	15.0%	1.9
		2	163.78	4.45	2.7	7.5	15.0%	2.8
		3	604.24	12.09	2.0	2.4	15.0%	6.3

Methods continued on next page

Methods

Test	Lot	Level	Mean	SD	%CV	% Bias	TaE	Sigma
TRIG	1611 (MAS)	1	1.10	0.07	6.0	4.1	25.0%	3.5
		2	1.83	0.09	4.7	3.9	25.0%	4.5
		3	2.52	0.11	4.2	3.8	25.0%	5.0
	4648 (BioRad)	1	0.99	0.06	6.3	10.5	25.0%	2.3
		2	1.47	0.09	5.8	4.8	25.0%	3.5
		3	2.43	0.11	4.4	5.8	25.0%	4.3
PROT3	1611 (MAS)	1	47.74	1.07	2.2	2.6	10.0%	3.3
		2	86.82	6.62	7.6	3.4	10.0%	0.9
		3	125.41	2.08	1.7	4.5	10.0%	3.3
	4648 (BioRad)	1	43.05	0.79	1.8	7.6	10.0%	1.3
		2	59.46	0.92	1.5	8.1	10.0%	1.2
		3	69.38	1.01	1.4	0.9	10.0%	6.3
LDI1	1611 (MAS)	1	110.92	5.22	4.7	7.6	20.0%	2.6
		2	229.32	5.24	2.3	7.2	20.0%	5.6
		3	351.51	7.44	2.1	5.0	20.0%	7.1
	4648 (BioRad)	1	108.13	4.62	4.3	8.1	20.0%	2.8
		2	174.97	6.51	3.7	16.6	20.0%	0.9
		3	434.26	12.68	2.9	24.1	20.0%	Negtive
DIG01	1611 (MAS)	1	1.20	0.10	8.2	4.5	20.0%	1.9
		2	2.32	0.13	5.7	0.0	20.0%	3.5
		3	3.39	0.18	5.2	0.4	20.0%	3.7
	4648 (BioRad)	1	0.62	0.10	15.9	3.7	20.0%	1.0
		2	2.08	0.17	8.3	9.4	20.0%	1.3
		3	3.39	0.18	5.2	10.9	20.0%	1.8
MG2	1611 (MAS)	1	0.44	0.02	4.4	0.0	25.0%	5.7
		2	1.15	0.03	2.4	0.5	25.0%	10.3
		3	1.85	0.05	2.5	1.3	25.0%	9.5
	4648 (BioRad)	1	0.42	0.02	3.9	5.9	25.0%	4.9
		2	1.07	0.03	2.6	7.4	25.0%	6.7
		3	1.66	0.03	2.1	3.9	25.0%	10.1
AMY2	1611 (MAS)	1	90.49	2.20	2.4	2.3	30.0%	11.4
		2	322.26	4.22	1.3	1.0	30.0%	22.1
		3	544.15	7.80	1.4	0.8	30.0%	20.4
	4648 (BioRad)	1	46.15	2.64	5.7	2.6	30.0%	4.8
		2	154.93	2.70	1.7	3.3	30.0%	15.3
		3	322.50	4.23	1.3	0.8	30.0%	22.3

Results

The results showed that the controls displayed comparable Sigma-metrics for a majority of the analytes (75% or 9 out of 12). However, for a several analytes (3 out of 12 or 25%), the MAS controls had higher Sigma-metrics than the Bio-Rad controls and would indicate different QC designs. This warrants further research to determine if one control material is experiencing a matrix effect with those method.

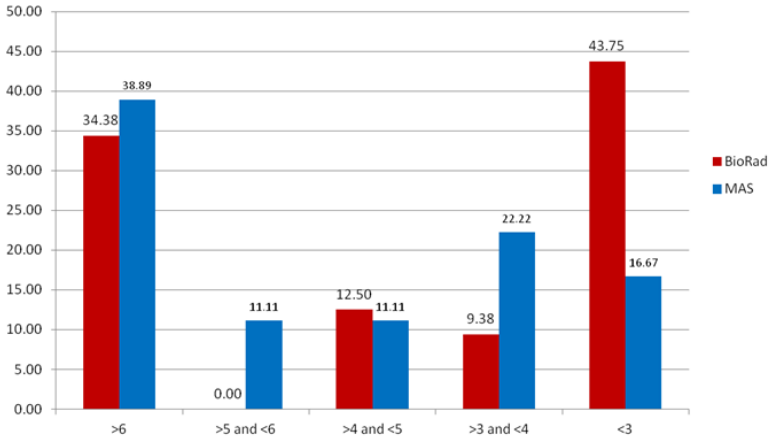
More important than the numerical comparability of the control material performance is the judgment that would be made about the Sigma-metric. In 2010, an international conference produced a consensus on QC design and frequency of QC:

> $>6\sigma$ (world class performance) – evaluate with one QC per day (alternating levels between days) and a 1:3.5 s rule.
>
> 4σ–6σ (good to excellent performance) – evaluate with two levels of QC per day and the 1:2.5 s rule.
>
> 3σ–4σ (marginal performance) – use a combination of rules with two levels ("Westgard Rules") of QC twice per day.
>
> $<3\sigma$ (poor performance) – maximum QC, three levels, three times a day. Consider testing specimens in duplicate.

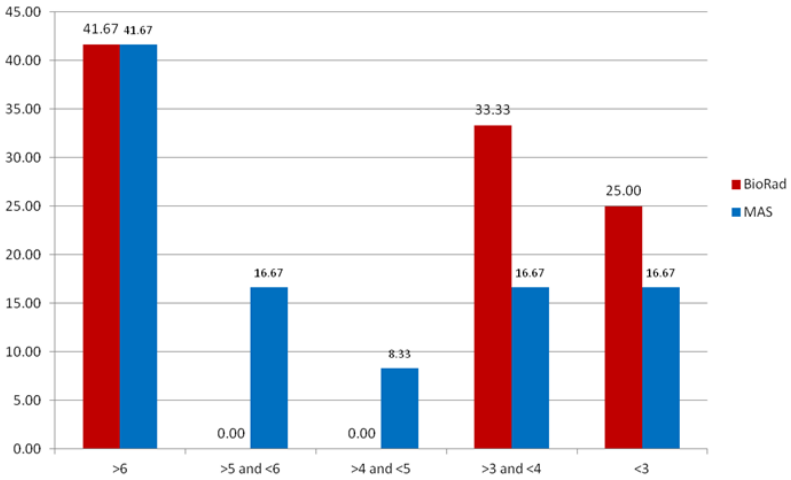
Cooper, et al. "Collective opinion paper on findings of the 2010 convocation of experts on laboratory quality", Clinical Chemistry Laboratory Medicine. 2011; 49(5):793-802.

Based on those criteria, nearly all of the methods are characterized in the same category (same QC rules, same QC frequency). Only in one case is there a significant difference (LD) in Sigma-metric that would result in different rules and different QC frequency. In three cases (ALT, Digoxin, Triglycerides) the Sigma performance of the assay is within one category of the expert consensus. That is, the QC rules and recommendations would be similar, but slightly different.

Sigma-metric Distribution of Control Materials of all levels measured on the Dimension RxL



Average Sigma-metric Distribution of Control Materials on Dimension RxL



Conclusion

Sigma-metrics provides a simple, practical tool to judge the comparability of control materials. Using Sigma-metrics on these 12 assays proved that in the vast majority of cases, the two control vendors provide comparable performance on this instrument. Thus, a laboratory can make a switch between control vendors without worrying about a loss in quality. Instead, other factors such as cost and convenience can be taken into account.

Performance was not identical and that does raise questions that could be answered by further research. For instance, if the MAS controls provide higher Sigma-metrics on the instrument assays than the Bio-Rad controls, does that indicate a matrix effect in one of the control materials? Also, is this difference in control material performance present only on this instrument or on other instruments as well?

References:

Westgard JO and Westgard SA, Six Sigma QC Design and Control, 2nd Edition, 2006, Westgard QC, Inc. Madison, WI.

Cooper, et al. "Collective opinion paper on findings of the 2010 convocation of experts on laboratory quality", Clinical Chemistry Laboratory Medicine. 2011; 49(5):793-802.

Control Material	> 6 Sigma	>5 but <6 Sigma	>4 but <5 Sigma	>3 but <4 Sigma	< 3 Sigma
MAS Control	Albumin, Amylase, AST, Creatinine Kinase, Magnesium,	LD, ALT	Triglycerides	Creatinine, Glucose, Digoxin	Total Protein
Bio-Rad Control	Albumin, ALT, Amylase, AST, Creatinine Kinase, Magnesium,			Creatinine, Glucose, Triglycerides	Total Protein, Digoxin, LD

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