Multisite study of AST analytical performance reveals disparities in global performance specifications

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♦ Abstract

Evaluating the performance of 19 laboratories and 30 instruments from around the world reveals that CLIA and Rilibak performance specifications are probably too lenient, and that “Ricos goals” are a more appropriate performance specification.

♦ Introduction

Analytical Performance specifications (also known as allowable total error goals, TEa) for AST are not harmonized throughout the world. Allowable total error specifications range from 12% to 21% depending on the country or EQA/PT program. Since the clinical use and interpretation of the AST test is standardized, the goals to judge method acceptability would also benefit from standardization. However, standardizing on an analytical performance specification that no current methods on the market can achieve would be counter-productive; it would require all methods to drastically increase their use of control materials, rules, and QC frequency without necessarily providing any tangible benefit to patient care.

It would be beneficial to compare analytical performance specifications with current analytical performance of AST methods. If current methods cannot achieve today’s TEa goals with high reliability, that may indicate that some performance specifications aren’t realistic or practical for today’s laboratories.

♦ Methods

Methods: 30 instruments (Abbott ARCHITECT instruments, ranging from the c16000, c8000, to the c4000 model) from 19 laboratories in 8 countries participated in a Sigma Verification program (see table 1), where they routinely report their analytical performance data. Imprecision was estimated from routine controls (typically Bio-Rad), with 1 to 3 months of data. Bias or inaccuracy was estimated from EQA/PT programs, peer group comparisons, or comparisons of the observed mean vs. the assayed/target means of the controls.

♦ Results

Using the data from these laboratories, their ability to achieve the allowable total errors from CLIA proficiency testing criteria, German Rilibak, the biological variation-based "Ricos Goals", the 2017 revised “Ricos Goal”, and the Australian RCPA goals were assessed. These specifications range from 12% to 21% TEa.

The method of evaluation the appropriateness of performance specifications was assessed by the calculation of analytical Sigma-metrics. Performance was evaluated using analytical Sigma-metrics. The standard Sigma-metric equation was used:

Sigma-metric = (TEa - bias) / CV

The percentage of laboratories able to achieve 5 Sigma (excellent) performance or better based on these goals was determined. A target of achieving 80% or better was considered success.

Laboratory	Instrument	Bias source	CV source	% Bias	% CV
Bumrungrad International Hospital, Bangkok	c16000	CAP PT	Bio-Rad controls	2.2	1.1
Bangkok R.I.A. laboratory, Bangkok	c16000	RIQAS	Bio-Rad controls	0.1	1.9
Guizhou Provincial People's Hospital, Guiyang	c8000	Bio-Rad peer group	Bio-Rad controls	2.6	2.5
QHMS, Hong Kong	c8000	Bio-Rad peer group	Bio-Rad controls	0.18	1.52
	c8000			0.10	0.87
PPUKM, Kuala Lumpur	c8000	Bio-Rad peer group	Bio-Rad controls	3.4	3.63
Praram 9 Hospital, Bangkok	c4000	Bio-Rad peer group	Bio-Rad controls	2.5	2.02
	c8000			2.5	1.99
Innovative Diagnostics, Singapore	c8000	Bio-Rad peer group	Bio-Rad controls	4.74	2.16
	c8000			3.17	2.03
	c16000			1.06	1.97
	c16000			2.3	1.88
Loh Guan Lye & Sons, Penang	c8000	RCPA EQA	Bio-Rad controls	1.2	2.3
	c8000			0.8	2.5
Penang Pantai Premier Pathology, Penang	c8000	Bio-Rad peer group	Bio-Rad controls	4.5	3.3
Prodia Laboratories, Bandung, Bekasi, Semarang	c4000	Bio-Rad peer group	Bio-Rad controls	2.1	3.9
	c4000			1.8	3.1
	c4000			2.5	3.1
Ramathibodi Hospital, Lean and SDMC laboratories, Bangkok	c16000	RIQAS	Technopath controls	0.5	1.45
	c16000			0.5	1.9
	c16000			0.5	3.0
Serdang Hospital, Kajang	c8000	Bio-Rad peer group	Bio-Rad controls	0.5	2.3
	c8000			7.05	3.23
	c8000			2.3	2.06
Sunway Medical Centre, Selangor	c8000	Bio-Rad peer group	Bio-Rad controls	1.8	2.0
	c4000			0.9	2.0
INVITRO laboratories, Moscow	c8000	Bio-Rad peer group	Bio-Rad controls	1.3	2.37
Winchester Medical Center, Winchester, Virginia	c8000	Bio-Rad peer group	Bio-Rad controls	1.0	1.85
	c8000			0.5	2.31
	c8000			3.7	2.18

Table 1: Laboratories, instruments, sources of bias and CV data and performance

♦ Results continued.

% of Instruments able to meet AST Sigma Performance goals at decision level of 40 mg/dL				
TEa Goal	**>6 Sigma**	**>5 Sigma**	**>4 Sigma**	**<4 Sigma**
RCPA (12%)	20.0	36.67	66.67	33.33
2017 Ricos (13.4%)	30.0	66.67	80.00	20.00
Ricos (16.69%)	66.67	80.00	86.67	13.33
CLIA (20%)	80.00	86.67	100.0	0
Rilibak (21%)	83.33	90.00	100.0	0

While performance was available for multiple levels throughout the working range, the study focused on Sigma-metrics at the critical decision level of 40 mg/dL.

100% of labs and instruments can achieve CLIA and Rilibak performance specifications, indicating that these TEa goals may be too lenient. These quality requirements may function more like a rubber stamp than a performance standard.

In contrast, only one of three instruments are able to achieve an good level of quality or better using the RCPA goal, and according to that standard, nearly 1 in 3 labs would be considered marginal or unacceptable. This is a high level of failure and would represent a crisis in the laboratory diagnostics market, if the goal was enforced. However, the fact that we do not see frequent clinical problems with the test results, may be further evidence that this goal doesn’t match the clinical use of the test.

For the older “Ricos goal”, over 80% of the methods achieve 4 Sigma or higher at the critical decision level, with less than 4% receiving unacceptable grades. The 2017 revised “Ricos goal” just meets our acceptability rate of 80%, but there are 1 in 4 labs that are marginal or unacceptable (3 Sigma or worse). Again, this is unlikely to be acceptable in today’s marketplace.

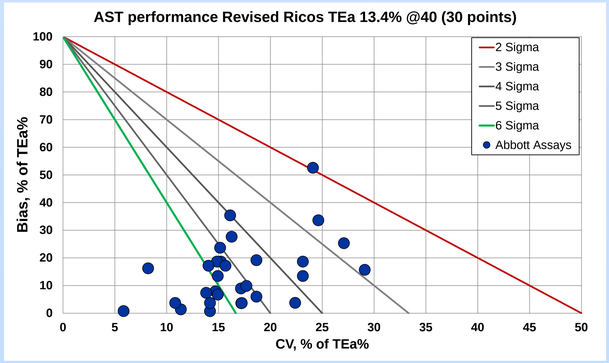

Figure 1. Normalized Method Decision Chart (MEDx) displays Sigma performance of 29 instruments benchmarked to a “Ricos goal” of 13.4% allowable total error.

♦ Limitations

Only one instrument system is represented in this study, so the findings may not reflect the capability of other diagnostic manufacturers to achieve AST performance targets. Other studies should be done to evaluate the other manufacturers.
The heterogeneous nature of data collection (i.e. different controls, different ways to determine bias) may have injected too much variation in the study results. It also would be preferable to assess bias against a reference method or material. Typically, however, laboratories cannot perform this type of bias assessment due to the impractical expense of such methods and materials. While the laboratories included in this study may not practice ideal bias assessments, they nevertheless represent a global sample of analytical performance, provide a true “real world” snapshot of routine operation. Thus the findings of this study are more realistic for future implementation.

♦ Conclusion

Given today’s AST methods, adopting a tighter analytical performance specification is possible and desirable. Using either the 2014 “Ricos goal” or the 2017 revised “Ricos goal” still provides a high rate of success for laboratories to achieve acceptable performance on the Sigma-metric scale. The RCPA goal, however, appears too difficult for a high percentage of laboratories to achieve at good or better performance.

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