

TECHNOPATH CLINICAL DIAGNOSTICS

What is Six Sigma and how does it apply to control materials?

THE QUALITY CONTROL COMPANY



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Introduction

What challenge are we addressing in this report?

For decades, laboratories have been challenged with implementing standardised QC processes and naturally have looked to some of the solutions that were seen as synonymous with best practices for QC. However, given the latest generation of engineering, higher precision methods, more automated instruments and the proliferation of new instruments, new methods and new tests, many of the legacy solutions have quickly become outdated. Now more than ever, there is a greater need for more advanced, more efficient QC procedures.

What solutions do we propose?

Technopath and Westgard have combined forces, in a strategic partnership, to deliver the most advanced QC solutions and educational services on the market. Combining Technopath's class-leading products with expert opinion and educational services from Westgard will allow laboratories around the world to get access to the most up-to-date information on advancements in quality control testing and analysis.

Technopath Clinical Diagnostics work in partnership with Westgard Inc. to provide quality control training and education services to customers around the world. Find our contact details at the end of this report.





What is Six Sigma and how does it apply to control materials?

Six Sigma is a well-known quality management approach that uses multiple tools to achieve the goal of reducing errors and defects in any process. Six Sigma began in companies like General Electric and Motorola, but has spread to service sectors and even to healthcare institutions and the clinical laboratory.

The central focus of Six Sigma is to measure the number of defects-per-million opportunities (DPM, or DPMO) in any process. This DPM rate is then converted into a simple scale of 0 to 6, which is called the Sigma-metric of the process. Achieving Six Sigma on the short term scale means that only 3.4 defects are expected per million outcomes of the process. To put it in laboratory terms, a Six Sigma test on that scale would only be expected to produce about 4 defective results per million tests run. At the quality level of Six Sigma, processes become highly efficient and effective, reducing the effort required to maintain them and maximizing the reliability and profitability of that process.

On the other hand, a three Sigma process is expected to produce more than 67,000 defects per million outcomes. Outside of healthcare, a process that is below three Sigma is often considered too costly and defect-prone to operate efficiently. In business and manufacturing, a process below three Sigma would be identified as a target for radical improvement, redesign or replacement. For analytical processes, the Sigma-metric is calculated using data obtained from control materials. Imprecision from routine control performance and Bias (Trueness) can be obtained by comparing the control mean of the laboratory with the control mean of the peer group. Then a third variable is used, a quality requirement in the form of an allowable Total Error (TEa), which represents the goal for performance.

These three variables are arranged in the following equation to calculate the Sigma-metric:

Sigma-metric = (TEa – Bias) / CV [all parameters expressed as %]

More detailed discussion of the Sigma-metric equation can be found in the literature and reference manuals ⁽¹⁾.



Using IAMQC[™] Peer to analyse your Sigma Metrics

IAMQC[™] Peer now offers end-users the opportunity to automatically calculate and review their sigma metric performance. The system will automatically calculate imprecision and bias and once the end-user has defined their acceptability criteria (i.e Total Allowable Error), the software will automatically calculate a sigma score for every assay that is tested in the laboratory using the following calculation:

Sigma-metric = (TEa – Bias) / CV [all parameters expressed as %]

Upon login the end-user selects SETUP>TOTAL ALLOWABLE ERROR:

номе	BASE TABLES	PEER STATS	DATA MINING	SETUP	REPORTS	SAF	SUPPORT LOG OUT
Nelcome, Ger Kenne	edy ENGLISH 🗹			Laboratory Demographics		Lab Search (ID)	Laboratory: ADMIN PORTAL V
				Instrument			IRL qcsoftware@technopathcd.com
strument - Click to E	dit Setup		La	¹⁵ Setup Users		View Peer Data	Data
ARCHITECT i1000SR	l - c4000		N/	A Un-Archive Instruments		PEER	ENTER DATA
ARCHITECT i2000SR	l - ISR55079		N//	A and the local		PEER	ENTER DATA
ARCHITECT i2000SR	l - SR06217		N//	A C Upioad		PEER	ENTER DATA
				IAMQC Transfer			
There are un-mappe 1/02/2017 4:32:33 1/02/2017 4:32:33 1/02/2017 4:32:34 2401058, i1SR5291 1/02/2017 4:32:34	ad records! Use Web AM: Beginning data AM: Set Date/Time AM: Loading data f 9) - 52367_2017-02- AM: User TD LAC	or PC Communicator i upload for the file Irom file -01_1485912764389_Q QC	r to complete the m CRELEASED.CSV	_ Total Allowable Error	uu log:	R Torongon, JANNETS 1	



The system will display an entry table presenting the end-user with the opportunity to enter their Total Allowable Error (TEa) for each of the assays they test in their laboratory:

CHNOPATH Ical diagnostics	HOME BASE TABLES + PEER STATS I	DATA MINING SETUP + REPORTS +	· SAF + SUPPORT + LOGOL	л										
	MULTICHEM IA PLUS (05P76-10): Setup Total Al	llowed Errors:												
		Save Values												
	Analyte	Level 1	Level 2	Level 3										
	Alpha Fetoprotein (AFP) {3P36}	10.00	10.00	10.00										
	BNP (1-32) {8K28}	5.00	5.00	5.00										
	C-Peptide {3L53}	25.00	25.00	25.00										
	CA 125 {2K45}	30.00	30.00	30.00										

Click on each individual QC product to enter the TEa for the assays included in that product. The system facilitates a comment for each entry, if the end-user wants to cite the reference for the TEa that was entered (i.e CLIA or Ricos Desirable or RiliBak etc.). Click SAVE to post entries to the database.

Once the TEa limits have been entered, the end-user can go to the sigma metric report section by clicking on REPORTS>SIGMA METRICS in the main menu:

Server and a server and a server a serv				Techno	pathCD Website	TECHNICAL LIBRARY	
TECHNOPATH clinical diagnostics							
HOME BASE TABLES PEER STATS	DATA MINING	SETUP	REPORTS	SAF	SUPPORT	LOG OUT	
Welcome, Ger Kennedy ENGLISH ~			Peer Reports	arch (ID)	S Laborat	ory: ADMIN PORTAL ~	
			Sigma Metrics		qcsoftwa	IRL are@technopathcd.com	
Instrument - Click to Edit Setup	Last Data	Submission		View Peer Data		Data	
ARCHITECT i1000SR - c4000	N/A			PEER	EN	TER DATA	
ARCHITECT i2000SR - ISR55079	N/A			PEER	EN	TER DATA	
ARCHITECT i2000SR - SR06217	N/A			PEER	EN	TER DATA	
Information Panel							
There are un-mapped records! Use Web or PC Communicator 01/02/2017 4:32:33 AM: Beginning data upload 01/02/2017 4:32:33 AM: Set Date/Time for the file 01/02/2017 4:32:34 AM: Loading data from file (e401058, 118582319) - 52367 2017-02-01_1455912764389_00 01/02/2017 4:32:34 AM: User ID LAQC	c to complete the mapping	3. Most recen	t upload log:	toward and the s	* *		
Technopath Life S	ciences Park, Fort Henry, Ballina	a, Co. Tipperary	, Ireland qcsoftware@1	FechnopathCD.com			
	Copyright © 2017 Technopath	h Clinical Diagn	ostics All rights reserved				
	Privacy	Terms Discla	imer				



The system will display the Sigma Metric Report screen. Click on the product you would like to review, followed by the lot number of interest, then click on the instrument of interest or select ALL. Finally, click on the time period you wish to review:

HOM	BASE TABLES 👻 PEER ST	ATS DATA MINING	SETUP - REPORTS	+ SAF + S	UPPORT + LOGO	DUT	
Select Q	Product:						
MULTICH	M U (05P80-10) / MULTICHEM P	(05P81-10) / MULTICHEM	I IA PLUS (05P76-10) / MU	ILTICHEM S PLUS (ASSAYED)		
Select Ki	Name:						
3440515	34405152 34405153 / 345061	51 34506152 34506153	/ 34809151 34809152 3	4809153 / 35404	161 35404162 3540	4163	
Select In	trument:						
ALL /	RCHITECT ci8200 - ISR03821 / AF	RCHITECT i2000SR - ISR54	789 / ARCHITECT 12000S	R - ISR54788			
Select D	te Period:						
LIFETIM	•						
Apr 2017	/ Mar 2017 / Feb 2017 / Jan 2	2017*					

The system will automatically calculate and display the sigma metric report for the criteria selected:



May 2017 / Apr 2017 / Mar 2017 / Feb 2017 / Jan 2017*

Sigma Summary: Analyte TCD Level Sigma Score TCD Level Sigma Score TCD Level Sigma Score C-Peptide (3L53) ng/mL 6 6 Cortisol (8D15) nmol/L 6 6 Ferritin (7K59) (i) ng/mL 2 6 4						
Analyte	Units	TCD Level 1 Sigma Score	TCD Level 2 Sigma Score	TCD Level 3 Sigma Score		
C-Peptide {3L53}	ng/mL	6	6	6		
Cortisol {8D15}	nmol/L	6	6	6		
Ferritin {7K59} (i)	ng/mL	2	6	4		
High Sensitive Troponin I {3P25}	ng/L	4	4	6		
Human Chorionic Gonadotropin (BhCG) {7K78}	IU/L	2	3	6		
Thyroid Stimulating Hormone (TSH) {7K62}	mIU/L	6	6	6		
Triiodothyronine: Free (FT3) {7K63}	pmol/L	3	4	2		

This interactive report includes a normalised method decision chart (screen left) displaying all assays for the criteria selected previously, a Sigma Metric summary table (screen right) outlining the calculated sigma score for each assay and a detailed summary table displaying further information on the statistics used for the calculation (NOTE: the end-user must scroll down to review the detailed summary table – see the following screen shot). The end-user can click on an individual point on the normalised method decision chart to view the information associated with that point.



The end-user can scroll down to review the following detailed summary table:

CHNOPATH NICAL DIAGNOSTICS	HOME	BASI	e tables 👻	PEE	R STAT	s D	ATA MI	NING	SE	TUP -	REP	orts -	SAF		SUPPOF	п -	LOG	OUT				J					
	Sigma Detailed.						Level 1								Level 2							Level 3					
	Analyte	Units	Instrument	Mean	SD	% CV	Peer Mean	% Bias	% TEa	Sigma Calc	Sigma Score	Mean	SD	% CV	Peer Mean	% Bias	% TEa	Sigma Calc	Sigma Score	Mean	SD	% CV	Peer Mean	% Bias	% TEa	Sigma Calc	Sigma Score
	C-Peptide {3L53}	ng/mL	ISR54789	342.00	11.11	3.25	330.22	3.57	25.00	6.60	6	1372.65	29.77	2.17	1356.77	1.17	25.00	10.99	6	2614.64	63.13	2.41	2606.88	0.30	25.00	10.23	e
	Cortisol (8D15)	nmol/L	ISR54789	101.49	2.95	2.91	98.31	3.23	25.00	7.49	6	403.61	10.86	2.69	400.67	0.73	25.00	9.02	6	911.26	17.93	1.97	932.68	2.30	25.00	11.54	6
	Ferritin {7K59} (i)	ng/mL	ISR54789	21.22	0.95	4.49	20.08	5.70	17.00	2.52	2	172.24	4.41	2.56	171.71	0.31	17.00	6.52	6	370.94	12.45	3.36	359.02	3.32	17.00	4.08	4
	High Sensitive Troponin I {3P25}	ng/L	ISR54789	21.54	0.84	3.91	20.65	4.33	20.00	4.01	4	57.91	2.41	4.16	56.58	2.35	20.00	4.25	4	3920.80	83.70	2.13	3702.30	5.90	20.00	6.60	
	Human Chorionic Gonadotropin (BhCG) {7K78}	IU/L	ISR54789	4.09	0.47	11.57	4.38	6.64	30.00	2.02	2	23.09	1.62	7.00	24.63	6.26	30.00	3.39	3	454.60	17.45	3.84	457.57	0.65	30.00	7.65	1
	Thyroid Stimulating Hormone (TSH) {7K62}	mIU/L	ISR54789	0.04	0.00	2.85	0.04	5.75	23.70	6.29	6	5.99	0.12	1.96	5.60	6.87	23.70	8.59	6	20.13	0.50	2.49	19.56	2.89	23.70	8.35	
	Triiodothyronine: Free (FT3) {7K63}	pmol/L	ISR54789	4.24	0.14	3.28	4.20	0.88	11.00	3.09	3	7.88	0.18	2.30	7.91	0.37	11.00	4.62	4	15.57	0.48	3.11	16.18	3.78	11.00	2.32	

This table includes details on the individual instrument statistics for each assay, each level, including; Mean, SD, CV, Peer Mean, % Bias from the peer mean, % TEa, Sigma Calculated score, Given sigma score based on the calculation.

Summary

The Sigma Metric report in IAMQC Peer allows end-users to review an automatic calculation of their sigma performance at any given time. This feature enables end-users to address poor assay performance, adjust their QC protocol according to the sigma value (see next section for more details) and continue to monitor their sigma performance on a regular basis. End-users can work toward improvement of performance using sigma metric trending.



Reviewing Laboratory Quality Control frequency using Sigma Metrics.

In 2011 a collective opinion paper on findings of formal assembly of opinion leaders on laboratory quality policies and procedures was published in Clinical Chemistry Laboratory Medicine ⁽²⁾.

The outcome of the discussions were that once an assay was assigned a Sigma score, and based on this analysis and risk assessment, that a recommendation could be made to outline recommended intervals for QC based on risk analysis. Assays could now be divided into different performance categories with different QC requirements:

Six Sigma group performance indicators

- >6 σ (excellent reliable assays) evaluate with one QC per day (alternating levels between days) and a 1:3.5 s rule
- $4\sigma-6\sigma$ (suited for purpose assays) evaluate with two levels of QC per day and the 1:2.5 s rule.
- $3\sigma-4\sigma$ (poor performer assays) use a combination of rules with two levels of QC twice per day.
- $<3\sigma$ (problematic assays) maximum QC, three levels, three times a day. Consider testing specimens in duplicate



Next Steps

Technopath is happy to offer practical options to introduce more efficient and robust QC procedures into the laboratory. Consolidated multi-analyte quality control materials, such as the Multichem[®] range available from Technopath Clinical Diagnostics (Technopath), enable clinical laboratories to significantly reduce handling requirements, reclaim storage space and minimise waste, leading to a more efficient quality control process. Now in addition multi-rules called 'Westgard Sigma Rules' are available to optimise the number of rules and control measurements to take into account the analytical Sigma-metric of the test method.

Whether you have questions about our products, services, or support, Technopath is here to help. Choose from the options below. A Technopath representative will contact you.

IAMQC Software support: iamqcsupport@technopathcd.com Sigma Verification Program services: info@technopathcd.com



References

- 1. JO Westgard, *Six Sigma Quality Design and Control*, 2nd Edition. Westgard QC, Madison WI 2006
- 2. 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



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