Common Myths and Delusions of QC

質控可以順其自然，無為而治嗎？

Richard Pang

PhD, FACB

ProQ@live.hk

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Myths of Lab Testing

Therapy & Diagnosis

Theranos 測試的一特點，是其所需的血量之少。只需要由指尖抽取數滴血液，Theranos 已足以測試多項疾病。但當中的秘密，Elizabeth Holmes 至今仍拒絕公開，這也令她飽受醫學界攻擊，包括是指其測試不準確。

http://www.scarcity.com.hk/elizabeth-holmes/

Delusions of QC

Fewer QCs

Smaller samples are just the beginning?

The technology and processes we've developed allow us to use dramatically smaller samples than are traditionally used. While charging dramatically less.

https://www.theranos.com/

Holmes 將會在今年8月 份在美國臨床化學協會（AACC）年會上公布 Theranos 的相關數據。那時可能就會知道 Theranos 手裡到底有哪些技術可以支撐自己的技術是可以被使用的。

https://www.aacc.org/meetings-and-events/2016-annual-meeting-and-expo

自順然其 [順其自然] [無為而治] 治而無為

- **[順其自然]**，就是在正確的時間，正確的地點，正確的方式做正確的事，其結果自然就正確。就是遵循因果報應，自然規律取捨。
- **[無為而治]** 被道家認為是「道」的重要特徵之一。它不是指不作為，而是指不經過深思熟慮，無目的地行為。無為而治者，道家認識到任何有目的的行為都可能使行為本身產生偏差。根據處理問題不同，「無為」的態度既可用於政治，也可以用於管理。道家各派在堅持「無為」本質的前提中，通常給予了「無為」更豐富的彈性和內涵。

佛 道

Myths and Delusions

A topic that frequently arises in discussions is related to the fundamentals of Quality Control (QC) because, despite the fact that everyone states to want QC, there is still little consensus on basic questions like what to do and how to do in order to achieve QC. Quality Control or just Quality Compliance, that's the question...

Disclaimers

In reality, I have already retired from the profession. The following PowerPoint presentation "Lacks *Power* and has No *Point*"

MLT Board CPD: 1 Point
Programme/Activity Code: 14160031

What is Quality Control?

英國公投脫歐後,
360萬人聯署再公投

Westgard QC

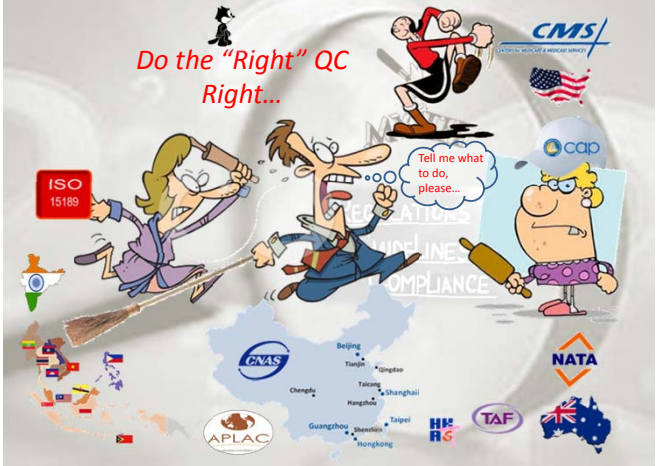
A Top 10 list of problems with QC and the "Westgard Rules"
And if you see a claim that they've "**modified**" the rules to make them better, be afraid....

http://www.westgard.com/lesson73.htm

Quality Control vs Quality Compliance

cap

Do the "Right" QC Right...



LABORATORY vs FACTORY

- FACTORY
  - Product is known
  - All products MUST be the same
- LABORATORY
  - Product is unknown
  - All products are different
    - One cannot predict what the results will be.

Diagnostics Industry

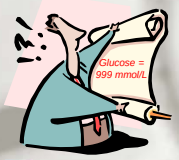
Focus on Quality

Both need QC

Variation is the Enemy
Laboratory Errors

分析前
Pre-analytical?
46%～68.2%

分析中**Analytical?**
<15%

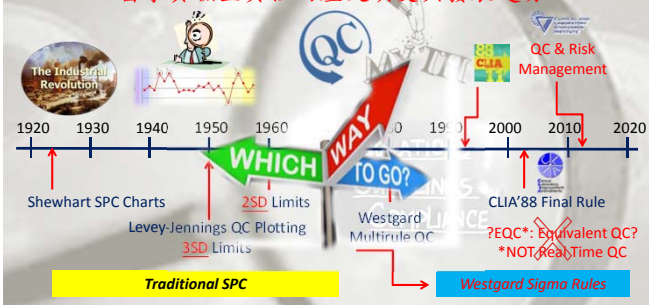


分析后
Post-analytical ?
18.5%～47%

What are those challenges?

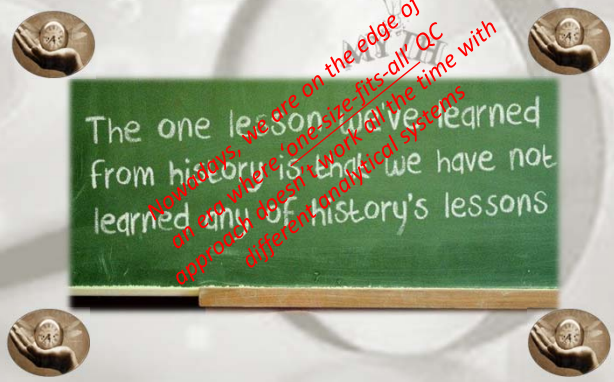
Clin Chem Lab Med. 2006;44(6):750-9.

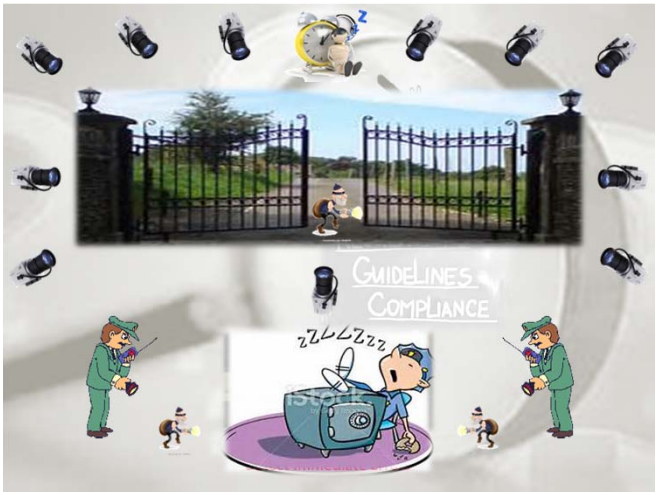
Traditional QC (SPC) and Sigma Metrics in Clinical Laboratories
醫學實驗室質控的歷史演變與發展趨勢



The Center for Medicare and Medicaid Services (CMS) has adopted a new Quality Control (QC) option under the Clinical Laboratory Improvement Amendments (CLIA) called the Individualized Quality Control Plan (IQCP) from January 2, 2016.

Time Flies…
Nearly half Century…The Way Forward…?





Do The Right QC Right
Detect Immediate Errors

- "Detect immediate errors that occur due to test system failure, adverse environmental conditions, and operator performance" (CLIA 493.1256)
  - Most importantly
- Perform corrective actions to "recover" before reporting of test results

CMS.gov
Centers for Medicare & Medicaid Services

http://www.clinchem.org/content/51/10/1911.full

Myths and Delusions of QC

Guidelines and SOPs

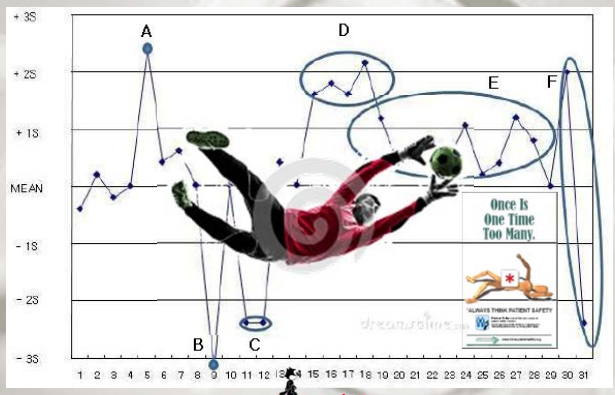
Just Read…
Don't Understand…
Didn't Follow…

Detect Immediate Errors

The power of the QC rule – **Detection**

EP23 says;
"Medical judgment is used to estimate the overall probability of harm due to receiving an incorrect result…"

Detect Immediate Errors



In and Out

Which Statement(s) are "True"?

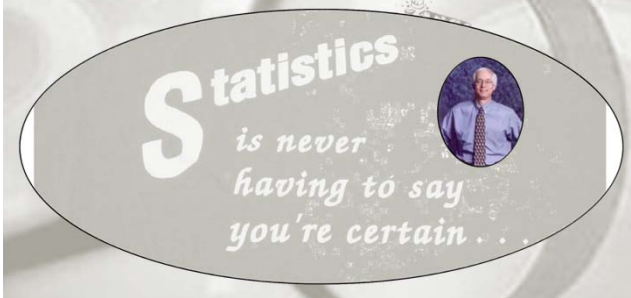
- QC is "in" so patient results are OK
- QC is "out" so patient results are wrong
- QC is "out" but patient results are OK
- QC is "in" but patient results are wrong

Principles and Assumptions of Statistical QC

Figure 2. Typical response curve for a detector. False alarms are shown by the y-intercept of the response curve; true alarms depend on the size of the "problem". Small problems are difficult to detect, therefore the detector should be designed to detect the size of the problems of interest, e.g., errors that would be medically important.

http://www.westgard.com/essay103.htm

American Statistical Association (ASA) T-Shirt



http://qcnetevents.com/content/IW_Parvin_AACC12.pdf/

P_{ed} vs P_{fr}

Sigma	Westgard rule	Levels	Measurements	p error detection	p false rejection
6.0	1 3.5s	2	1	0.98	0.01
5.8	1 3.5s	2	1	0.98	0.00
5.6	1 3s	2	1	0.97	0.00
5.4	1 3s	2	1	0.94	0.00
5.2	1 3s	2	1	0.91	0.00
5.0	1 2.5s	2	1	0.96	0.03
4.8	1 2.5s	2	1	0.93	0.03
4.6	1 3s	2	1	0.92	0.01
4.4	1 2.5s	2	1	0.96	0.04
4.2	1 2.5s	2	1	0.92	0.04
4.0	1 3x/2 2x/R 4x/4 1s	2	2	0.91	0.03
3.8	1 3x/2 2x/R 4x/4 1s	2	2	0.86	0.03
3.6	1 3x/2 2x/R 4x/4 1s	2	2	0.79	0.03
3.4	1 3x/2 2x/R 4x/4 1s	2	2	0.65	0.03
3.2	1 3x/2 2x/R 4x/4 1s	3	2	0.48	0.03
3.0	1 3x/2 2x/R 4x/4 1s	3	2	0.36	0.02

Reduce QC rules on six-sigma assays

Schoenmakers, Clin Chem Lab Med, 2011

"IQC To Detect Immediate Errors"

Myths or Facts?

- *This statement often leads laboratory personnel to incorrectly believe that QC will always catch errors, when in fact; it's the QC rule and frequency that determines if an out of control condition (OOC) will be caught.*
- *A poorly selected rule may not catch a smaller OOC condition until many many QC events have passed.*
- *The 2SD limits are generally not desirable because of the high Pfr, except occasionally they are necessary for low sigma analytes.*

The Quality Toolbox

Sigma Metrics

"Sigma"標準，的其定義 "DPM" 缺陷每百萬已經是一種風險的評估

- 1 % = One in a Hundred 3.9 Sigma
- 10,000 in 1 Million
- 1 PPM = Part Per Million Undefined >6 Sigma
- 1 in 1 Million
- DPM = Number of Defects Per Million
- 3.4 in 1 Million = 6 Sigma

西格瑪 (Sigma) 是一種表示品質的統計尺度。任何一個工作程式或工藝過程都可用幾個西格瑪表示。

TABLE 1.1 Sigma Table

Sigma	Defects per Million	Yield
6.0	3.4	99.9997%
5.0	233.0	99.977
4.0	6,210.0	99.379
3.0	66,807.0	93.32
2.5	158,655.0	84.1
2.0	308,538.0	69.1
1.5	500,000.0	50.0
1.4	539,828.0	46.0
1.3	579,260.0	42.1
1.2	617,911.0	38.2
1.1	655,422.0	34.5
1.0	691,462.0	30.9
0.5	841,345.0	15.9
0.0	933,193.0	6.7

Sigma Metrics

Examples for Practice

從理論到實踐

Anticipating Problems

- Lot–to-lot Changes
  - Evaluating new lots of reagents
    - When?
    - How?
    - What Criteria?

When?

- Ideally
  - Before the new lot is shipped
- Practically
  - When the new lot is received
- Suboptimally
  - When you are about to start the new lot

How?

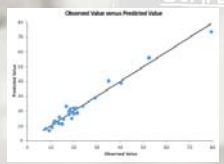
- Old lot vs New lot
- QC
- Patient sample correlation
  - N=20 or N=10 in duplicate
- Linear regression analysis
  - Slope and intercept

How?
Sigma-Metrics

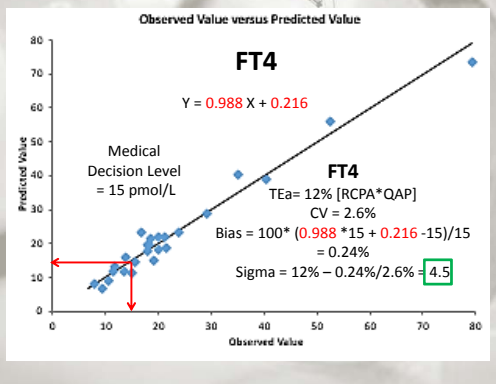
- Sigma statistics
  - Sigma = (TEa-Bias)/CV
  - Bias = TEa - (Sigma x CV)
    - CV = Variation of your current QC @Medical Decision Level
    - Bias = Difference between new lot and old lot

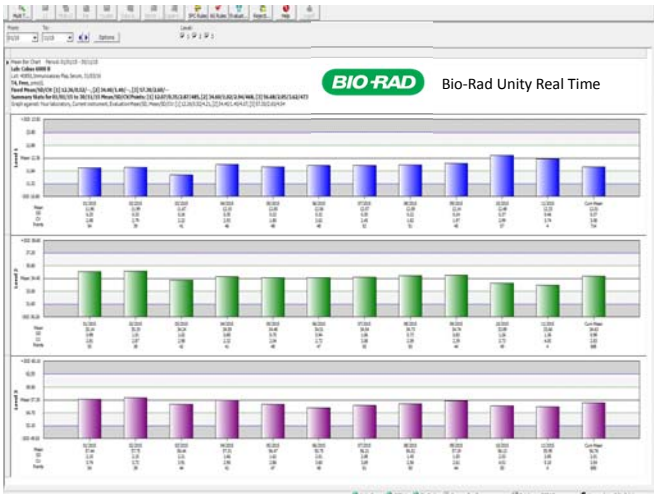
What Criteria?

- Bias between Lots
- Y = Slope * X + Intercept [y = ax + b]
- Bias = Y – X = Slope * X + Intercept – X
  - %Bias = 100 * (Y – X)/ X
  - %Bias = 100 * (Slope * X + Intercept – X)/ X



Scenario

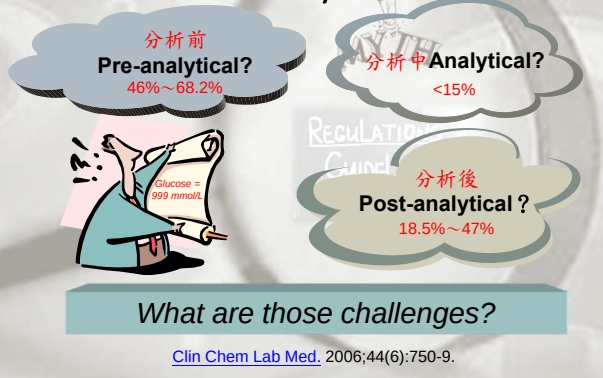




Interpretation

- Sigma >6 Excellent
- Sigma 4-6 Good
- Sigma 3-4 Marginal
- Sigma 2-3 Poor
- Sigma <2 Unacceptable

Variation is the Enemy Laboratory Errors



What are those challenges?

Clin Chem Lab Med. 2006;44(6):750-9.

Pre- and Post-analytical

- Specimen rejection rates
  - No. of specimens being rejected in the reception area per month/year
  - e.g., 3/1,000 = 3,000/1,000,000 = 4.3 Sigma
- Reporting errors
  - No. of erroneous/incorrect results being issued per month/year
  - e.g., 3/100,000 = 30/1,000,000 = 5.6 Sigma

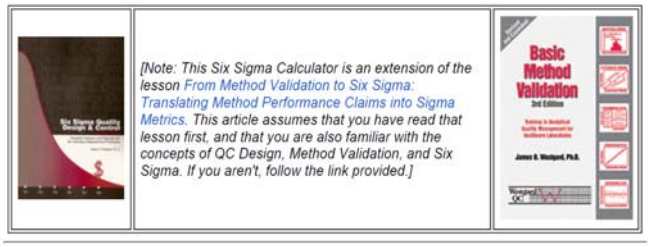
Sigma- Metric

DPM = Defects per Million

Westgard QC

The Six Sigma Calculators

NOTE: This page only works on browsers that support Javascript!



[Note: This Six Sigma Calculator is an extension of the lesson From Method Validation to Six Sigma: Translating Method Performance Claims into Sigma Metrics. This article assumes that you have read that lesson first, and that you are also familiar with the concepts of QC Design, Method Validation, and Six Sigma. If you aren't, follow the link provided.]

http://www.sigmavp.com/six-sigma-calculators.htm

Westgard QC

DPM (Defects Per Million) Calculator

Here you can calculate the Sigma-metric by counting the number of Defects in a sample.
Note that this calculator "rounds up" - to the nearest Sigma-Metric on the table on this website.

Enter the number of Defects Observed:	3
Enter the size of the sample: (how many total results were examined)	1000
Calculate Sigma Value	
Here are your Defects Per Million:	3000
Here is your Sigma-Metric:	4.3

Note also that if you know your Defect/Error rate as a percentage, you can enter it here with the sample size of 100 (i.e. a defect rate of 2% would be entered "2" in the defects observed, and "100" in the size of the sample).

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http://www.sigmavp.com/six-sigma-calculators.htm

QC Goalkeeper & Patient Safety

Test Turnaround Time (TAT)

Test Availability and Turnaround Time

The following tests are performed daily with results available the same day. Priority STAT turnaround times (receipt to result) are listed below.

Critical Test specimens should be delivered to the Clinical Laboratories immediately after collection. Turnaround (collect time to result time) for Critical Tests are:

Code Blue Whole Blood Gas Labs	30 minutes
Critical Care Whole Blood Gas Labs	30 minutes
Frozen Sections	30 minutes
Intra-Operative PTH	40 minutes

For all other tests consult the lab performing the test for test availability and turnaround times.

When the electronic interface between the lab system and the hospital clinical information system (IHIS) is down for an extended period of time, the labs will notify each nursing unit and will generate hard-copy interim reports as needed and will transport them to the units via the pneumatic tube system, or by messenger transport if necessary.

TEST	STAT	TEST	STAT
ABG	60 min.	Cortisol	60 min.
Acetaminophen (Datril®, Tempra®, Tylenol®, Liquiprin®, Tenlap®)	60 min.	CPK	60 min.
		Creatinine (Serum)	60 min.
Acetone	60 min.	CSF Glucose	60 min.
Alanine Amino-transferase (ALT/ SGPT)	60 min.	CSF Protein	60 min.
Albumin, Quantitative, Serum	60 min.	D-Dimer (High Sensitivity, Quantitative)	60 min.
Alcohol (Ethanol) Medical/Legal	60 min.	Digoxin (Lanoxin®)	60 min.

https://clinicallabs.osumc.edu/Documents/Test_Turnaround_Time.pdf

Westgard QC

TAT of Blood-gas Tests
≤30 min = OK
>30 min = Not Acceptable

DPM (Defects Per Million) Calculator

Here you can calculate the Sigma-metric by counting the number of Defects in a sample.
Note that this calculator "rounds up" - to the nearest Sigma-Metric on the table on this website.

Enter the number of Defects Observed:	3
Enter the size of the sample: (how many total results were examined)	8856
Calculate Sigma Value	
Here are your Defects Per Million:	339
Here is your Sigma-Metric:	4.9

Note also that if you know your Defect/Error rate as a percentage, you can enter it here with the sample size of 100 (i.e. a defect rate of 2% would be entered "2" in the defects observed, and "100" in the size of the sample).

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http://www.sigmavp.com/six-sigma-calculators.htm

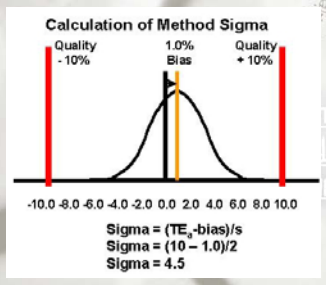
Quality Indicators

Outcome Measures

Quality Indicator	DPMO	Sigma
Pre-analytical		
Missing information on Pap requisitions	100,259	2.8
Correction of errors on ordered tests	3,123	4.3
Patients without ID bands	5,625	4.1
Specimen redraws	19,053	3.6
Therapeutic drug monitoring timing	207,140	2.4
Analytical		
Laboratory testing error	726	4.7
Laboratory proficiency testing	9,000	3.9
Post-analytical		
Laboratory reporting errors	533	4.8

Arch Pathol Lab Med 2000;124:516-9

Define the Analytical Quality (Sigma Metrics for Your Method)



For cholesterol, for example, the CLIA criterion is an allowable total error of 10%. If your method has a CV of 2.0% and a bias of 1.0%, then the Sigma metric for your method is 4.5 [(10-1)/2]

http://www.westgard.com/cliafinalrule9.htm

Westgard QC

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Process Design Calculator

Here you can calculate your Sigma-metric by analysis of variance measurements.

Enter the Quality Requirement or Tolerance Limit (in %): (If you don't know, look it up below)	8.0
Observed Bias (as a %): (If you don't know, start with 0)	0.2
Observed CV (as a %): (If you don't know, find out)	1.3
Calculate Sigma-Metric	6

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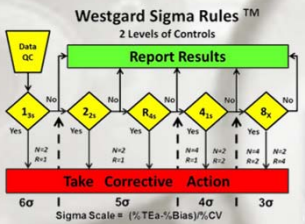
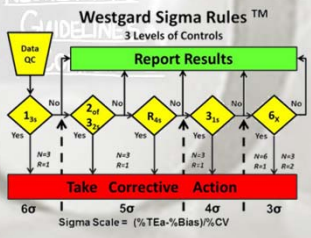
http://www.sigmavp.com/six-sigma-calculators.htm

Westgard Sigma Rules



To look for faster and simpler tools that will help laboratories select the right SQC for their own applications.



http://www.westgard.com/westgard-sigma-rules.htm

What's the Difference?

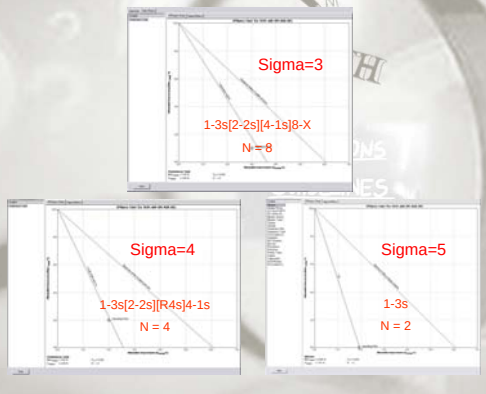
- Total Cholesterol
  - TEa = 10%,
  - Bias = 1.0%,
  - CV = 3.0%

  Sigma = 3
- Total Cholesterol
  - TEa = 10%,
  - Bias = 2.0%,
  - CV = 2.0%

  Sigma = 4
- Total Cholesterol
  - TEa = 10%,
  - Bias = 0.0%,
  - CV = 2.0%

  Sigma = 5

Sigma Metrics



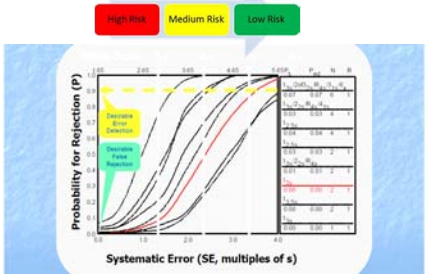
QC that is needed for Methods having Different Sigma Metrics

- *When your method Sigma is 6 or greater, you can do QC anyway you want, just be sure to keep the false rejections low by using wide control limits - at least 3s.*
- *When your method Sigma is 5 or so, use N=2 or 3 with 2.5s or 3.0s control limits.*
- *When your method Sigma is 4 or so, increase N=4 to 6 and use either the 12.5s single rule or a 13s/22s/R4s/41s multirule procedure.*
- *With method Sigmas below 4.0, run all the control you can afford. In addition, increase the frequency of instrument function checks, performance validation checks, and preventive maintenance.*
- *With method Sigmas below 3.0, look for a new and better method. You can't do enough QC to assure the quality of the test results from methods having less than 3.0 Sigma performance!*

Critical Systematic Error, SEc

$SE_c = [(TEa\text{-}bias)/s] - z$

σ - 1.65



http://www.westgard.com/sigma-metrics-lab2012.htm

Choosing OWN (Individualized) QC Rules Based on Error Rates

$SE_c = [(TEa\text{-}bias)/s] - z$

ΔSE_c	QC Rule		
	Low	Moderate	High
> 3	1-3.5s	1-3s	1-2.5s (D, I)
2-3	1-3s	1-2.5s	1-2s (D, I)
1-2	1-2.5s (D)	1-2s (D, +)	1-2s (D, +, I)
<1	1-2s (D, I)	1-2s (D, +, I)	1-2s (D, +, I)

D: examine QC chart Daily, **+**: Increase control frequency;
I: Initiate corrective action

Error Rate Categories
Low = method that experiences <3% QC flags/year
Moderate = method that experiences 3-10% QC flags/year
High = method that experiences >10% QC flags/year

By courtesy of
Alan Wu, PhD, FACB

Westgard QC

QC Design Calculator (Critical Systematic Error)

Here you can calculate the size of the error your QC must detect.

Enter the Quality Requirement or Tolerance Limit (in %): (If you don't know, look it up below)	8.0
Observed Bias (as a %): (If you don't know, start with 0)	0.2
Observed CV (as a %): (If you don't know, find out)	1.3
Calculate Critical-Error	4.35

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$SE_c = [(TEa\text{-}bias)/s] - z$

σ - 1.65

http://www.sigmavp.com/six-sigma-calculators.htm

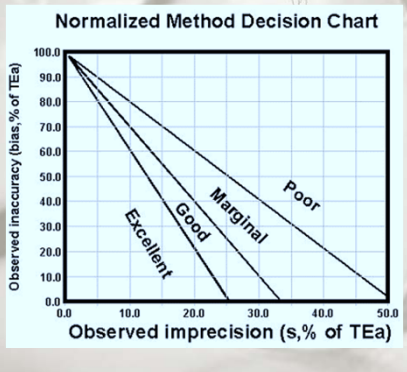
Sigma Metrics and QC Frequency

(Collective Opinion Paper)

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

Clin Chem Lab Med 2011; 49: 793-802.

Method Decision Chart

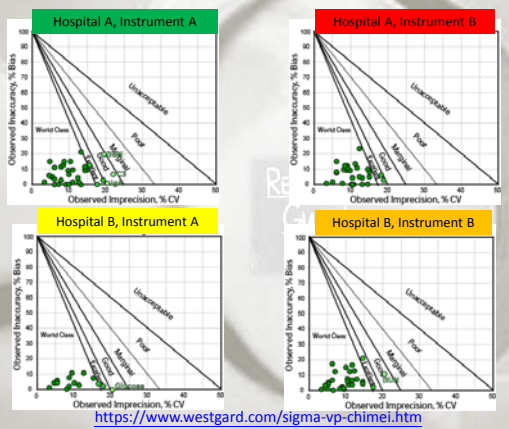


Westgard Sigma (Verification of Performance) VP Program

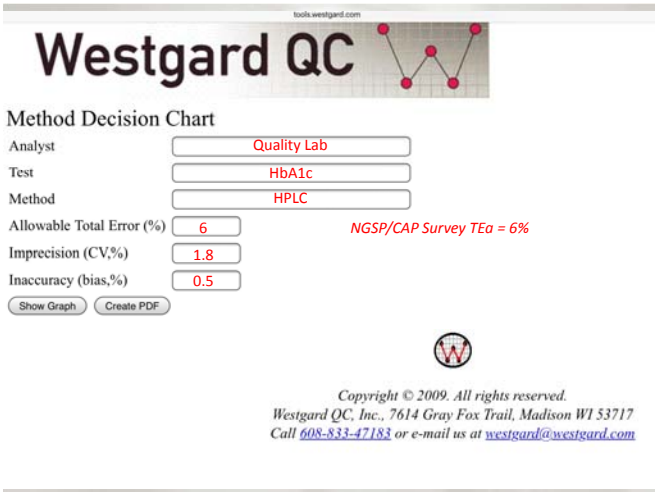
- Designate the necessary Quality Managers to learn and implement Six Sigma tools
- Adopt a standard set of Quality Goals, provided by Westgard QC
- Evaluate analytical performance
- Assess quality on the Sigma-scale
- Redesign QC based on the Sigma-metrics
- Apply and Request a review of laboratory data
- Implement and integrate Sigma-metric policies and procedures into the laboratory's Quality Manual
- Establish a continuous quality improvement plan to assess and update method Sigma-metrics

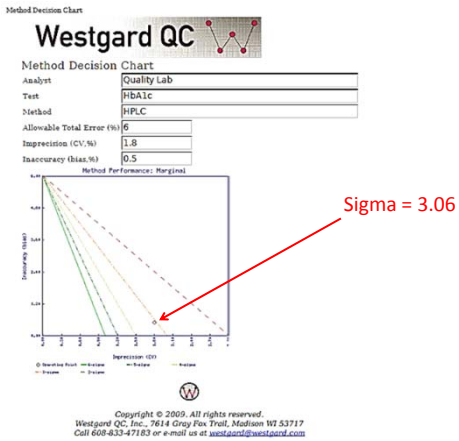
https://www.westgard.com/westgard-sigma-vp.htm

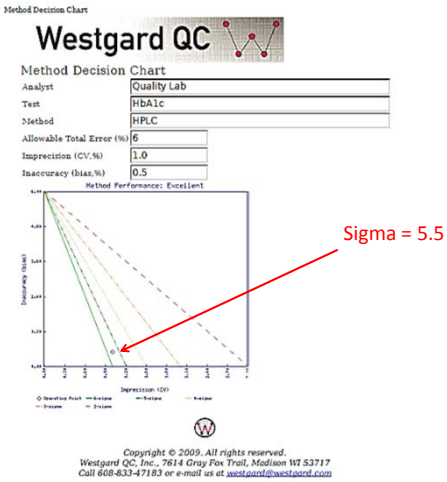
Performance Verification



https://www.westgard.com/sigma-vp-chimei.htm







Problems of using Sigma Metrics Desirability vs Practicality - I

- For pre- and post- analytical phases
- Sigma values = 5
  - 3/8,980
  - 8/24,000
  - 23/72,986
  - 103/310,980
  - 333/1,000,000

?Sample size (N)? Significant?

Problems of using Sigma Metrics Desirability vs Practicality - II

- For analytical phases
- Analyte Concentrations/activities
  - Cholesterol
  - Glucose
  - HbA1c
  - Calcium
  - ALT
  - Cortisol
  - Platelet Count

?Medical (Critical) Decision Levels? Significant?

Medical (Critical) Decision Levels

Test	Units	Reference Interval	Decision Levels				
HEMATOLOGY RELATED TESTS			1	2	3	4	5
Antithrombin-III	% of normal	80-120	50	75			
Bleeding Time	min	2.3-9.2	10	15			
Fibrinogen in plasma	mg/dL	200-400	30	100	500		
Folate in serum	ng/mL	2-15	1.5	4.0			
Hematocrit	L/L	0.43-0.51 M 0.38-0.46 F	0.14	0.33	0.56	0.70	
Hemoglobin	g/dL	14-17.8 M	4.5	10.5	17	23	
		12-15.6 F					
Mean corpuscular volume	fL (cu u)	84-96	80	100			
Partial thromboplastin time	sec	30	35	45	90		
Plasminogen	%	80-120	50	75	135		
Platelet count	K/uL	150-400	10	50	100	600	1000
Prothrombin time	sec	11.5	14	16	30		
Vitamin B12	pg/mL	200-900	170	250	1200		

4 Levels

5 Levels

http://www.westgard.com/decision.htm/

Problems of using Sigma Metrics Desirability vs Practicality - III

Quality Control Plan

High Risk | Medium Risk | Low Risk

QC Planning (Quality Goals)
品質目標的設定：從理論到實踐

MYTH

Plan "A"

Plan "B"

Plan "C"

REGULATIONS
GUIDELINES
COMPLIANCE

該怎麼做？

An American football player, coach, and executive.

Zero Defect?
零缺陷?

MYTH

Perfection

REGULATIONS
GUIDELINES
COMPLIANCE

"Perfection is not attainable, but if we chase perfection we can catch excellence."

Vince Lombardi

http://thinkexist.com/quotes/vince_lombardi/2.html

What is "ABC"

- A: Analytical
- B: Biological
- C: Clinical

MYTH

REGULATIONS
GUIDELINES
COMPLIANCE

D: Desirable

Analytical CV ≤ 1/2 ALE

CLIA Proficiency Limits

Analyte or Test	CLIA Criteria for Acceptable Performance
Alcohol, Blood	± 25%
Alanine Aminotransferase (ALT/SGPT)	± 20%
Albumin	± 10%
Alkaline Phosphatase	± 30%
Alpha-1 Antitrypsin	Target value ± 3 SD
Alpha-Fetoprotein (Tumor Marker) AFP	Target value ± 3 SD
Amylase	± 30%
Antinuclear Antibody	Target value ± 2 dilutions or positive/ negative
Antistreptolysin O	Target value ± 2 dilutions or positive/ negative
Anti-Human Immunodeficiency Virus	Reactive or nonreactive
Aspartate Aminotrasnferase (AST/SGOT)	± 30%
Bilirubin, Total	Target value ± 20% or ± 0.4 mg/dL (greater)
Calcium, Total	Target value ± 1.0 mg/dL
Carbamazepine	± 25%
Cell Identification	90% or greater consensus on identification
Chloride	± 5%
Cholesterol, High Density Lipoprotein	± 30%
Cholesterol, Total	± 10%
Complement C3	Target value ± 3 SD
Complement C3C	Target value ± 3 SD
Complement C4	Target value + 3 SD
Cortisol	± 25%
Creatine Kinase	± 30%
Creatine Kinase CK-MB	Target value ± 3 SD or presence/ absence

NOT Encouraged

http://www.qcnet.com/Portals/0/PDFs/CLIALimits(3-3-04).pdf

2014 Updates

Biological Variation Values

Desirable Analytical Quality Specifications for Imprecision, Bias and Total Error Upon Biological Variation

The following values are provided as a service to Bio-Rad Customers and are based upon desirable performance. The values are derived from Ricos C, Alvarez V, Cava F, Garcia-Lario JV, Hernandez A, Jimenez CV, Minichela J, Perich C, Simon M. "Current databases on biologic variation: pros, cons and progress" Scand J Clin Lab Invest 1999;59:491-500. These values are updated/ modified with the most recent specifications made available in **2014**. ***(denotes updated values)**

S = serum; U = urine; P = plasma; B = blood
CV_w = within-subject biological variation; CV_b = between-subject biological variation; Imp = imprecision; TE_a = total allowable error

		BIOLOGICAL VARIATION		DESIRABLE SPECIFICATIONS			
	ANALYTE	CV_w	CV_b	Imp (%)	Bias (%)	TE_a (%) p<0.05	TE_a (%) p<0.01
S	11-Deoxycortisol	21.3	31.5	10.7	9.5	27.1	34.3
S	17-Hydroxyprogesterone	19.6	50.4	9.8	13.5	29.7	36.4
U	5-HIAA concentration, 24 h	20.3	33.2	10.2	9.7	26.5	33.4
S	5'Nucleotidase	23.2	19.9	11.6	7.6	26.8	34.7
S	α1-Acid glycoprotein	11.3	24.9	5.7	6.8	16.2	20.0
S	α1-Antitrypsin	5.9	16.3	3.0	4.3	9.2	11.2
S	α1-Globulin	11.4	22.6	5.7	6.3	15.7	19.6

http://www.qcnet.com/Portals/0/PDFs/BVValues1Final.pdf

Minimum Specifications for Total Error, Imprecision, and Bias, Derived from intra- and inter-individual Biologic Variation

	Analyte	Biologic Variation		Minimum Specification		
		CV_I	CV_G	CV(%)	Bias (%)	TE_a
B-	Erythrocytes, count	3.2	6.1	2.4	2.6	5.5
P-	Factor V coagulation	3.6	---	2.7	---	---
P-	Factor VII coagulation	6.8	19.4	5.1	7.7	15.1
P-	Factor VIII coagulation	4.8	19.1	3.6	7.4	13.3
P-	Factor X coagulation	5.9	---	4.4	---	---
B-	Fructosamine	3.4	5.9	2.6	2.6	6.8
S-	Globulins, total	5.5	12.9	4.1	5.3	12.1
B-	Glutathione Peroxidase	7.2	21.7	5.4	8.6	17.5
S-	HDL Cholesterol	7.1	19.7	5.3	7.9	16.6
S-	HDL1 Cholesterol	5.5	27.2	4.1	10.4	17.2
S-	HDL3 Cholesterol	7.0	14.3	5.3	5.0	14.6
B-	Hematocrit	2.8	6.4	2.1	2.6	6.1
B-	Hemoglobin	2.8	6.6	2.1	2.7	6.2
B-	Hemoglobin A1C	1.9	5.7	1.4	2.3	4.6
P-	Homocysteine	9.0	40.3	6.8	15.5	26.6
S-	Immunoglobulin A	5.4	35.9	4.1	13.6	20.3
S-	Immunoglobulin G	4.5	16.5	3.4	6.4	12.0
S-	Immunoglobulin M	5.9	47.3	4.4	17.9	25.2
S-	Immunoglobulins, κ chain	4.8	15.3	3.6	6.0	12.0
S-	Immunoglobulins, l chain	4.8	18.0	3.6	7.0	12.9
S-	Lactate dehydrogenase, isoenzyme 1	2.3	9.3	1.7	3.2	6.1
S-	Lactate dehydrogenase, isoenzyme 2	3.3	2.4	2.5	1.5	5.6
S-	Lactate dehydrogenase, isoenzyme 3	2.8	3.6	2.1	1.8	5.2
S-	Lactate dehydrogenase, isoenzyme 4	5.9	5.3	4.4	3.0	10.3
S-	Lactate dehydrogenase, isoenzyme 5	6.0	9.6	6.0	4.7	14.6
B-	Lymphocytes, CD4	25.0	---	18.8	---	---

http://www.westgard.com/minimum-biodatabase1.htm

Optimal Specifications for Total Error, Imprecision, and Bias, Derived from intra- and inter-individual Biologic Variation

	Analyte	Biologic Variation		Optimal Specification		
		CV_I	CV_G	CV(%)	Bias (%)	TE_a
U-	α-Amylase	94.0	46.0	23.5	13.1	51.9
U-	α-Amylase pancreatic	39.0	78.4	9.8	10.9	27.0
S-	Alanine aminotransferase	18.0	42.0	4.5	5.7	13.1
U-	Albumin	36.0	55.0	9.0	8.2	23.1
U-	Albumin/creatinine	30.5	32.5	7.6	5.6	18.2
U-	Aldosterone	32.6	39.0	8.2	6.4	19.8
S-	Bilirubin	23.8	39.0	6.0	5.7	15.5
S-	Bilirubin, conjugated	36.8	43.2	9.2	7.1	22.3
U-	Calcium, concentration	27.5	36.6	6.9	5.7	17.1
U-	Calcium, output	26.2	27.0	6.6	4.7	15.5
S-	Creatine kinase	22.8	40.0	5.7	5.8	15.2
S-	γ-Glutamyltransferase	13.8	41.0	3.5	5.4	11.1
S-	Iron	26.5	23.2	6.6	4.4	15.3
U-	Magnesium, concentration	45.4	37.4	11.4	7.4	26.1
U-	Magnesium, output	38.3	37.6	9.6	6.7	22.5
U-	Phosphate, concentration	26.4	26.5	6.6	4.7	15.6
U-	Phosphate, output	18.0	22.6	4.5	3.6	11.0
U-	Potassium, concentration	27.1	23.2	6.8	4.5	15.6
U-	Potassium, output	24.4	22.2	6.1	4.1	14.2
U-	Protein, concentration	39.6	17.8	9.9	5.4	21.8
U-	Protein, output	35.5	23.7	8.9	5.3	20.0
U-	Sodium, concentration	24.0	26.8	6.0	4.5	14.4
U-	Sodium, output	28.7	16.7	7.2	4.2	16.0
S-	Triglyceride	20.9	37.2	5.2	5.3	14.0

< Prev Next >

http://www.westgard.com/optimal-biodatabase1htm.htm

Quality Specifications

- *Desirable*
  - $CV_A < 0.5 \times CV_I$
  - $B < 0.25 \times (CV_I^2 + CV_G^2)^{0.5}$
  - $TEa < 1.65 \times 0.5 \times CV_I + 0.25 \times (CV_I^2 + CV_G^2)^{0.5}$
- *Optimum*
  - $CV_A < 0.25 \times CV_I$
  - $B < 0.125 \times (CV_I^2 + CV_G^2)^{0.5}$
  - $TEa < 1.65 \times 0.5 \times CV_I + 0.125 \times (CV_I^2 + CV_G^2)^{0.5}$
- *Minimum*
  - $CV_A < 0.75 \times CV_I$
  - $B < 0.375 \times (CV_I^2 + CV_G^2)^{0.5}$
  - $TEa < 1.65 \times 0.5 \times CV_I + 0.375 \times (CV_I^2 + CV_G^2)^{0.5}$

http://www.westgard.com/biodatabase1.htm

The Stockholm Consensus (共識) Hierarchy

1. Evaluation of the effect of analytical performance on clinical outcomes in specific clinical situations
2. Evaluation of the effect of analytical performance on clinical decisions in general
   a. Data based on the components of biological variation
   b. Data based on analysis of clinicians' opinions
3. Published professional recommendations
   a. From national and international expert bodies
   b. From expert local groups or individuals
4. Performance goals set by
   a. Regulatory bodies
   b. Organisers of External Quality Assessment (EQA) schemes
5. Goals based on the current state of the art
   a. As demonstrated by data from EQA or Proficiency Testing Schemes
   b. As found in current publications on methodology.

Accred Qual Assur (2010) 15:323–330

What Types of Quality Goals do you use? (Recent Survey)

Westgard QC

- "We use different specifications for different analytes"
- "We use L-J chart with +/-3SD" "CLIA criteria"
- "Biological goals total error as Maximum Uncertainty Measurement for garanteed minimum clinical outcome"
- "All of the above. I have a basket of QS tailored the clinical utility of a test."
- "This is changing with the move towards ISO:15189 instead of CPA accreditation standards." "Standard Methods"
- "DPMO, percent achieved or percent error." "External proficiency program provides precision goals that we apply wherever they are provided. When we achive better precision we adjust, if poorer we try to maintain the target as otherwise you tend to flag on PT samples. For certain laboratories this causes problems as their precision may be acceptable but the manufacturer(s) has a method bias. When the reference range is different the bias can be acceptable, but in most instances the reference range is the same as all other laboratories using different manufacturer platforms."
- "Percentage of variance observed locally at specific levels (QC, calibrator & PT material), while keeping in mind CLIA'88 & CAP."

https://www.westgard.com/global-goal-comments.htm

2015-2016 Allowable Limits of Performance

Programs, Analytes and Allowable Limits of Performance

http://www.rcpaqap.com.au/

Quality Goals at the Crossroads: Growing, Going, or Gone? - Westgard https://www.westgard.com/gone-goals-gone.htm

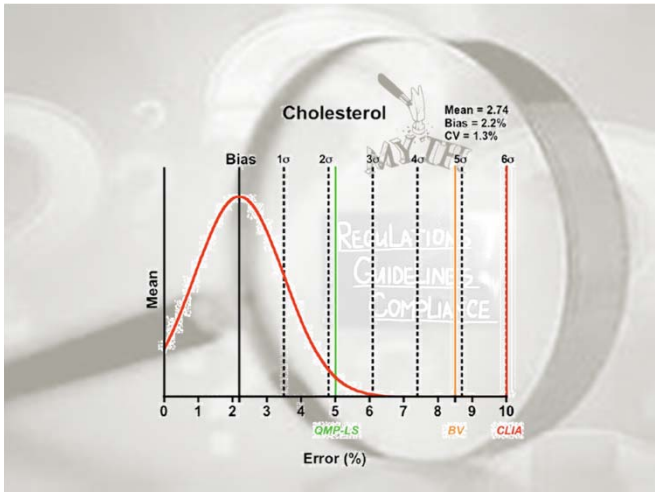
When we look at HbA1c, a heavily standardized and traceable measurand with certified equivalent methods, we can see that there are major differences between the recommendations:

EQA Programme	NGSP (US 2015)	SEKK Dmax (Czech)	Ricos Desirable TEa	RCPA (Austral-Asia)	Rilibak (German)	Spanish 2016 minimum consensus
HbA1c Performance Specification	6%	18%	3.0%	+/- 0.5 % / <10% 5% > 10%	18%	11%

Finally, let's look at cholesterol, one of the perennial favorite assays on this website:

EQA Programme	CLIA (US)	SEKK Dmax (Czech)	Ricos Desirable TEa	RCPA (Austral-Asia)	ProBioQual (France)	Rilibak (German)	Spanish 2016 minimum consensus	Belgian EQA
Cholesterol Performance Specification	10%	8.5%	9.01%	+/- 0.3 mmol/ <100 mmol 6% > 100 mmol	6%	13%	11%	9%

Here's yet another case where the CLIA goal is very close to the median recommendation of around 9%. SEKK, CLIA, the Spanish Consensus, and the Belgian EQA are all very close. Rilibak is only slightly higher, while RCPA and ProBioQual are again in an odd place: their specifications are smaller than the biologically desirable specification.



A Study of the Accuracy and Precision of Clinical Chemistry Determinations in 170 Canadian Laboratories

David B. Tonks

Tonks' Formula

Vol. 9, No. 2, 1963 CANADIAN LABORATORY SURVEY 219

The allowable limits of error were calculated by means of an empirical formula which the author has found to be useful. This formula is based upon the premise that errors should not exceed one-quarter of the normal range. This formula is as follows:

$$\text{Allowable limits of error (in \%)} = \pm \frac{(\frac{1}{4} \text{ of the normal range})}{(\text{mean of the normal range})} \times 100\%.$$

If the normal range for sodium is taken to be 135-145 mEq./L., then the allowable limits of error calculated by this formula are ± 1.8%. The maximum limits for any determination, however, were set at ± 10%, even though in some cases those calculated by the above formula exceeded this figure. For this study, then, the allowable limits of error have been established as follows: for sodium, ± 1.8%; for chloride, ± 2%; for total protein, ± 7%; for glucose, total reducing substances, phosphorus, urea nitrogen, NPN, and cholesterol, ± 10%. These limits are comparable with those used by other authors in similar studies (*1, 4, 8–11*).

Clin Chem 1963; 9: 217-233

Westgard QC

QUALITY REQUIREMENTS AND STANDARDS

I'm with Quality - Make Quality Great Again

Another slew of MU has hit the journals. The MU-TE debate continues in publications and online postings. But there are some reasons for hope...

Making Quality Great Again! I'm with Quality!

Some dismay, but less disagreement, on MU vs. TE

James O. Westgard, PhD, and Sten Westgard, MS
June 2016

http://www.westgardqc.com/make-quality-great-again.htm

Measurement Uncertainty (MU)

?The Role of QC Software

Monthly Summary Report

5.5.1.4 Measurement uncertainty of measured quantity values

- The laboratory *shall determine* measurement uncertainty for each measurement procedure in the examination phase used to report measured quantity values on patients' samples.
- The laboratory *shall define* the performance requirements for the measurement uncertainty of each measurement procedure and regularly review estimates of measurement uncertainty.

ISO 15189

MU: Measurement Uncertainty

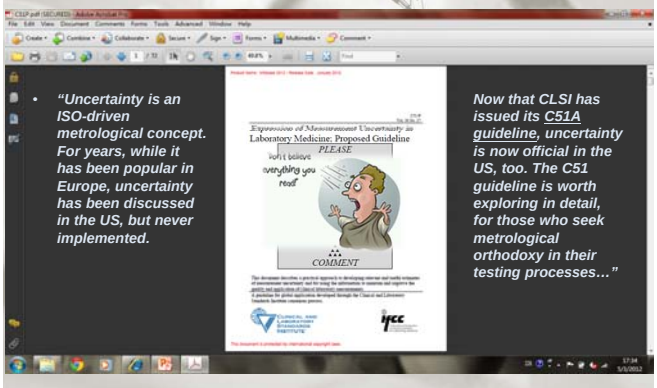
CATHAY PACIFIC

CX: Carrier eXpert

中華航空 CHINA AIRLINES

CI: Confidence Interval

Expression of Measurement Uncertainty in Laboratory Medicine: Proposed Guideline



- *"Uncertainty is an ISO-driven metrological concept. For years, while it has been popular in Europe, uncertainty has been discussed in the US, but never implemented.*

Now that CLSI has issued its C51A guideline, uncertainty is now official in the US, too. The C51 guideline is worth exploring in detail, for those who seek metrological orthodoxy in their testing processes..."

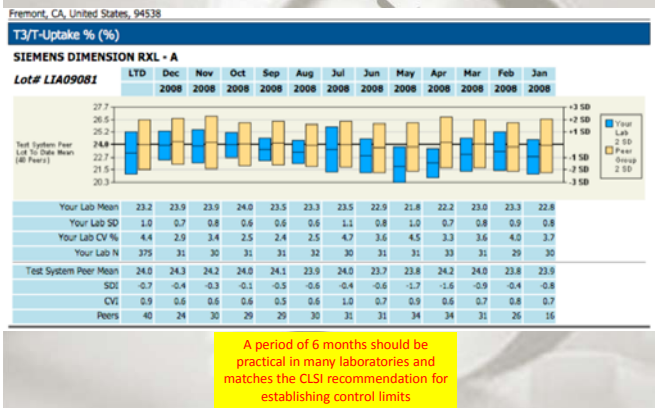
CLSI C51-A "Top-Down" Approach

- The guideline identifies a simple and practical methodology using SQC data obtained under "intermediate precision conditions, " i.e., a single laboratory and measurement principle, but with the changes in routine operating conditions (operations, reagent lots, calibrator lots, etc.). The laboratory should calculate a mid-term SD and utilize this estimate to express the standard uncertainty, then multiply by a coverage factor of 2 to express an expanded measurement uncertainty (95% confidence limit or interval).

What To Do…

- While there is no specific guidance for how many control measurements are needed, the estimate of the SD will be more reliable if at least 100 data points are included, which will often require that SQC data be collected over a period of several months. A period of 6 months should be practical in many laboratories and matches the CLSI recommendation for establishing control limits from a cumulative SD obtained from 6 successive months of routine SQC data.

Monthly Summary Report



A period of 6 months should be practical in many laboratories and matches the CLSI recommendation for establishing control limits

海灣戰爭期間，當時的美國國防部長拉姆斯菲爾德（Donald Rumsfeld）有一個著名的說法：

(The Unknown)

As we know
There are known knowns
There are things we know we know
We also know
There are known unknowns
That is to say
We know there are somethings we don't know
But there are unknown unknowns
The ones we don't know
We don't know

Donald Rumsfeld
Former United States Secretary of Defense
Department of Defense news briefing on February 12, 2002

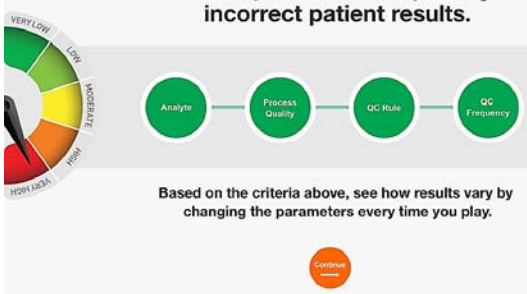
"世界上有我們知道我們知道的事情；有我們知道我們不知道的事情；還有我們不知道我們不知道的事情"

http://en.wikipedia.org/wiki/Unknown_unknown

Risk Assessment

http://52.10.201.150/riskcalculator/#welcome

There are four basic areas that can affect your Risk of reporting incorrect patient results.



Based on the criteria above, see how results vary by changing the parameters every time you play.

Continue

http://52.10.201.150/riskcalculator/#welcome

Your Risk Management Index:


Internal Quality Control (IQC) to Help Verify the Attainment of the Intended Quality of Results in Medical Laboratories: The Good, the Bad and the Risky

Quality Control – fitness for purpose

Can we report our analytical results and ensure that:

They are (the methods) fit for the intended purpose?

5.6.2.1 General
The laboratory shall design quality control procedures that verify the attainment of the intended quality of results.

"天作孽猶可恕自作孽不可活"
是什麼意思?

自然其順

[順其自然] 就是遵循因果報應，自然規律取捨

- 《尚書·太甲中》：『天作孽猶可違，自作孽不可逭』
- 《詩》云：「永言配命，自求多福。」

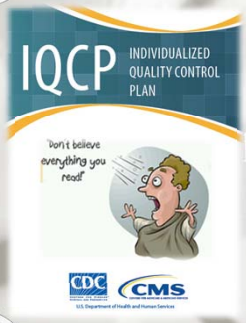
孽，災也。違逭相通，避也，逃也。言天災可避，自作災不可逃。

The lowest price is NOT always the best deal

儀器本身如果有先天的缺陷，哪多做質控也無補於事的！

選購儀器前一定要做足評估工作

道家認識到任何有目的的行為
都可能使行為本身產生偏差

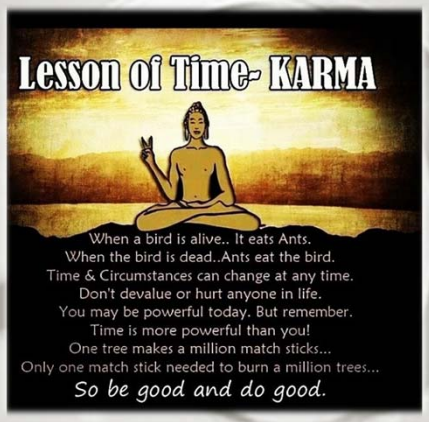


- *The Individualized Quality Control Plan (IQCP), based on the identified risk(s), is a comprehensive strategy that includes all control procedures to reduce residual risk and methods to immediately detect errors, using both prevention and monitoring strategies. The QCP is intended to proactively address potential risks before they occur and result in failures, compared to the practice of addressing failures after they occur.*

https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/IQCP-Workbook.pdf

Bring Home Messages

- *Traditional QC working together with Sigma-metric* is a powerful technique for managing the analytical quality of laboratory testing processes, but it must be implemented properly to provide the potential benefits.
- *Common myths and delusions that arise in discussions are related to the fundamentals of Quality Control (QC) because, despite the fact that everyone states to want QC, there is still little consensus on basic questions like what to do and how to do in order to achieve QC. Quality Control or just Quality Compliance, the question remains...*



Myths and Delusions of QC

Questions…