Rethinking Traditional Lab QA/QC:

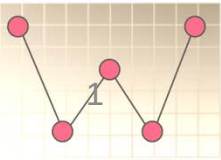
Understanding Weaknesses in Existing Requirements and Mastering Useful Methods and Metrics to Raise Your Lab's Analytical Accuracy

October 1st , 2013

Laboratory Quality ConFab

James O. Westgard, PhD Sten Westgard, MS
Westgard QC, Inc.

Westgard QC



Goals of this presentation

- **The Ugly** What's the typical QC in labs?
- **The Bad** Are our assays fit for purpose?
- **The Good**

  How do we redesign our testing to do the Right QC Right - AND save time, effort and money?

- Tools for Assessment, Assurance and Optimization
  - Sigma-metric Equation
  - Method Decision Chart
  - OPSpecs Chart

Westgard QC

Disclosure: Know your Westgards

“a” Westgard

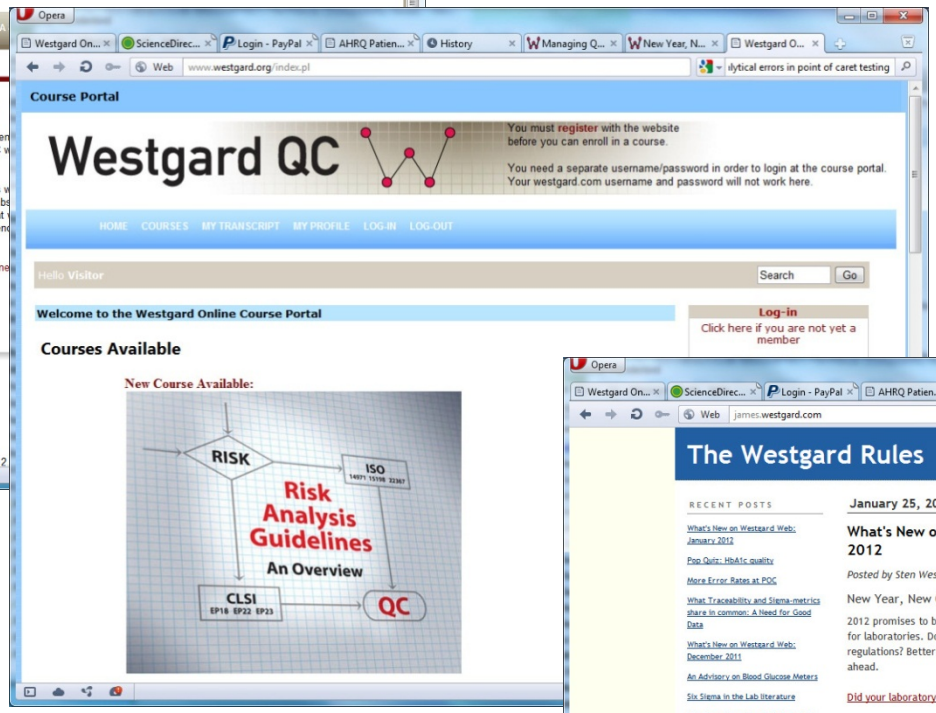
- 20+ years at Westgard QC
- Publishing
- Web
- Blog
- course portal

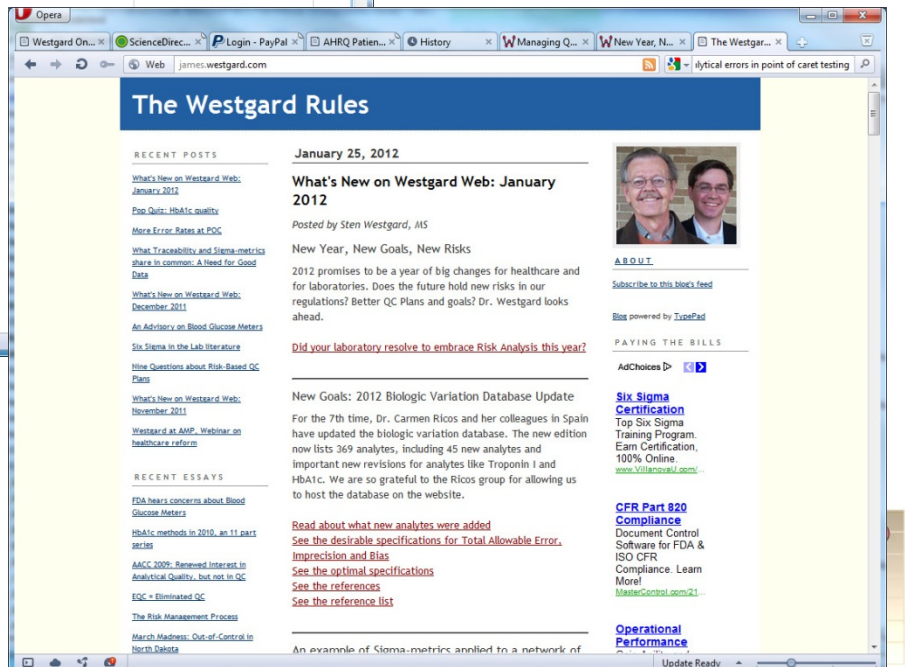
“The” Westgard

- 40+ years at the University of Wisconsin
- “Westgard Rules”
- Method Validation
- Critical-Error graphs
- OPSpecs

Westgard QC

Brief Overview of Westgard Web





Website:
>34,000 members
>3 million views
>450+ essays,
guest essays,
lessons,
QC applications,
reference resources

Course Portal:
Training in QC, Method Validation, Risk Analysis, Quality Management

Blog:
>250 Short articles
Q&A

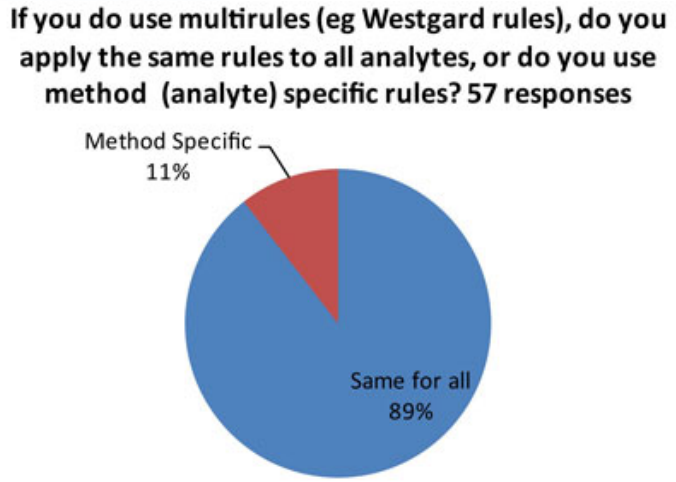
How do labs really perform QC?

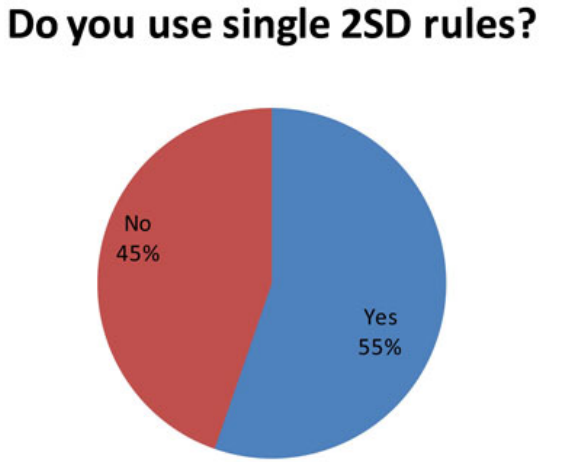
- A 2011 survey of IQC of 86 labs in the UK
- Multiple answers allowed, since different tests will have different practices in the same lab
- Special thanks to David Housley

What rules do labs use?

- 89.5% use the *same* QC procedure for *all* analytes

- 55.3% use single 2 SD rules

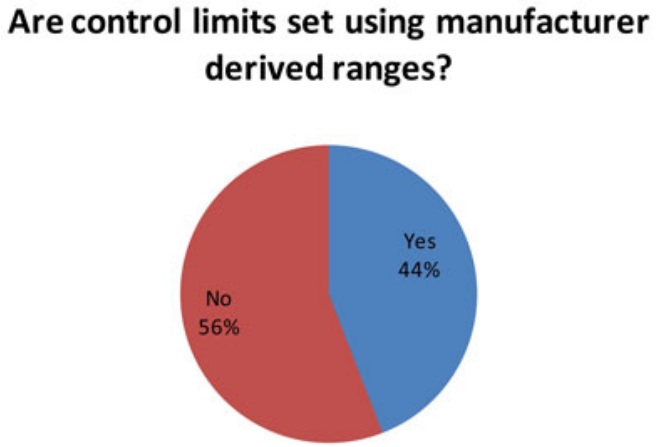




What control limits do labs use?

- 56% use manufacturer derived ranges to set control limits

- 81.3% use peer group or EQA data to set control limits



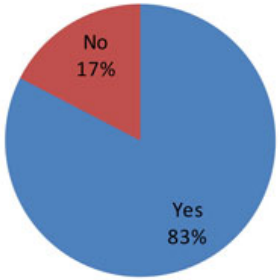
How do labs trouble-shoot?

- 82.6% **repeat the control** on failed QC flag

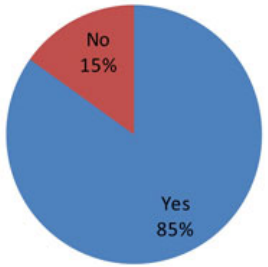
- 84.9% **run a new control**

- 93.7% re-calibrate, then re-run the control

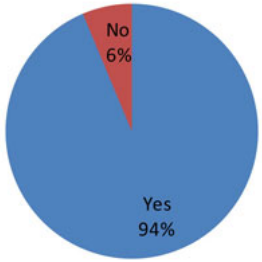
Out-of-control QC: Do you respond by repeating the control?



Out-of-control QC: Do you respond by re-running with new control?



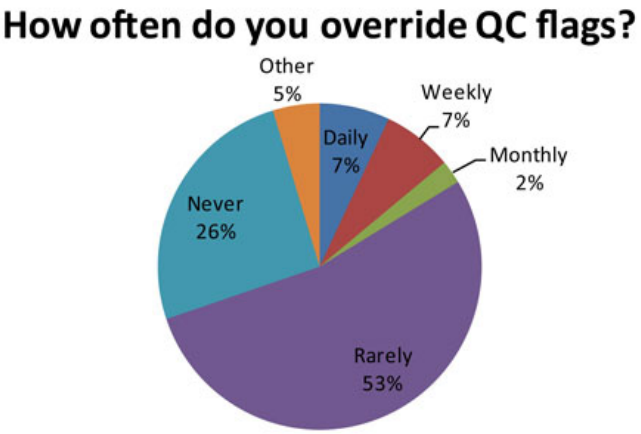
Out-of-control QC: Do you re-calibrate, then re-run control?



QC

How often are labs letting errors out the door?

- How often is out of control (non-ideal) IQC accepted (eg in order to ensure work is completed) ? 84 labs



Daily	6
Weekly	6
Monthly	2
Rarely	46
Never	22
Other	4

1 in 6 labs regularly *ignore* QC outliers

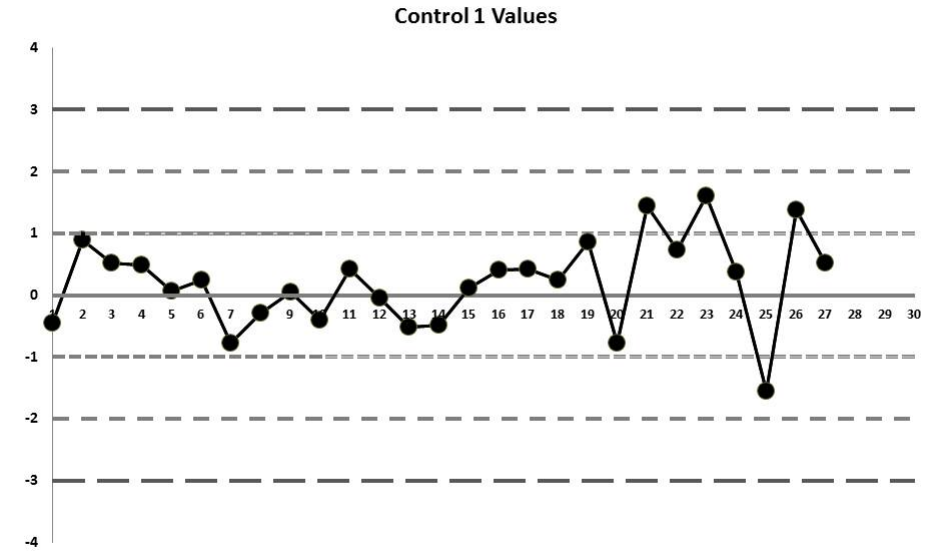
Is “Quality Compliance” the problem, rather than the cure?

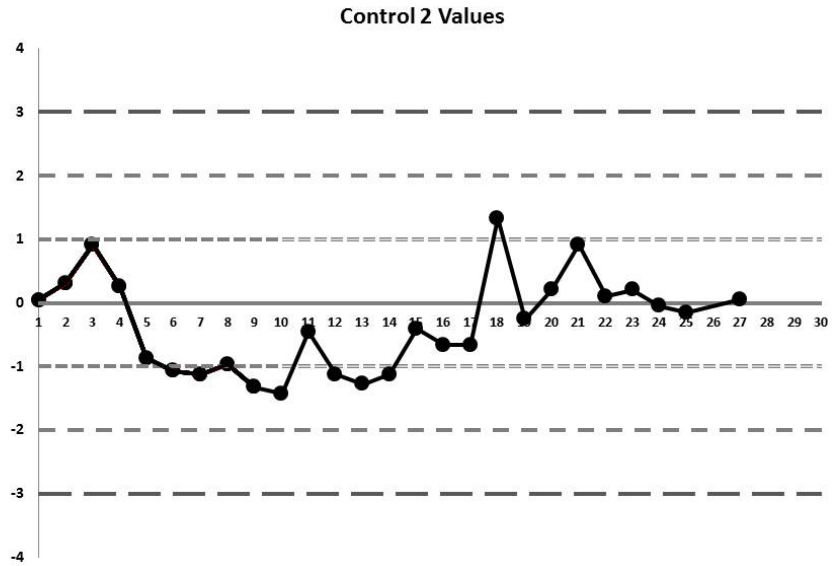
- We’re doing the right thing wrong
  - Corrupting our QC system
  - Corroding our trust in QC
  - Compromising test results
  - Trapping Cash

Westgard QC

When you use the manufacturer recommended SD, problems aren't as obvious

- All data within 2 SD. Too good to be true?





When our QC isn't working, what happens?

Clinical consequences of erroneous laboratory results that went unnoticed for 10 days

Tse Ping Loh, Lennie Chua Lee, Sunil Kumar Sethi et al. *J Clin Pathol* March 2013, Vol 166, No.3 260-261

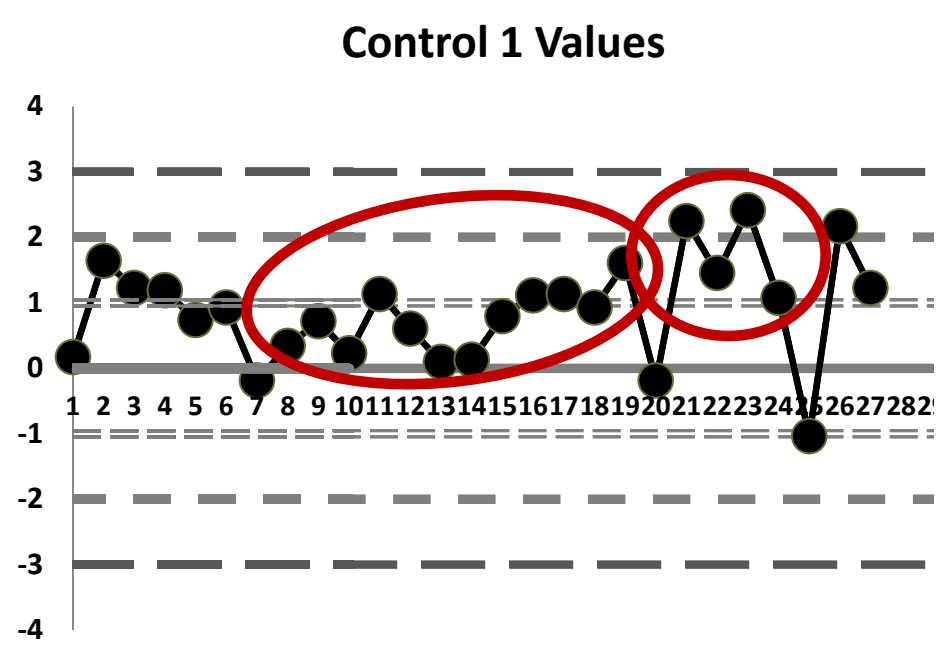
- 1 test error
- 5 tests in error
- 63 results in error

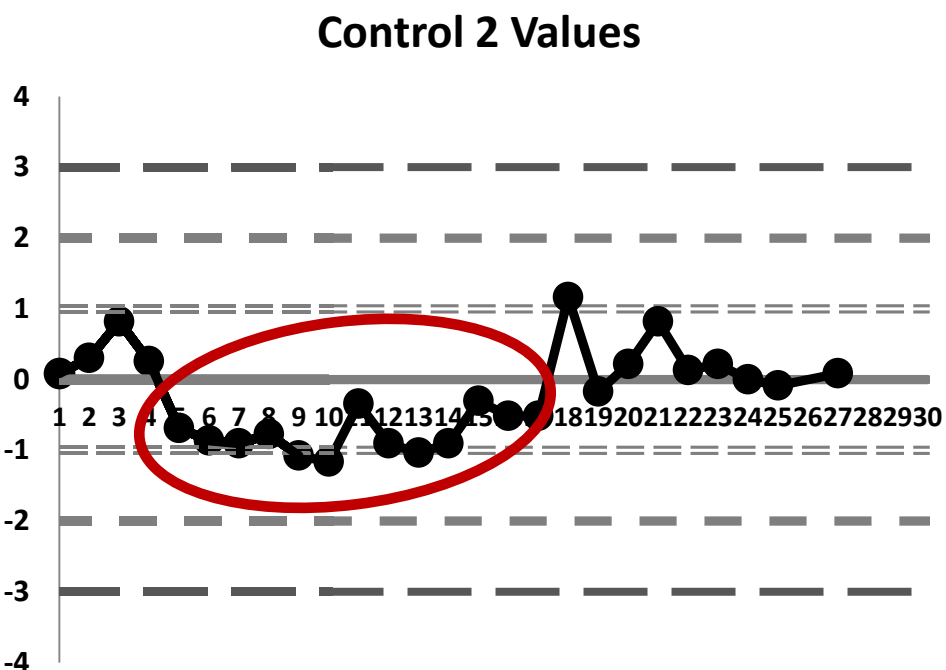
Case	Primary diagnosis	Purpose of testing	Laboratory test	Units	Erroneous results	Corrected results	Potential clinical consequence	Actual clinical consequence
1	Autoimmune thyroid disease on carbimazole	Diagnostic work-up	ATG ATPO	IU/l IU/l	>3000 >1000	404 876	Repeat testing TSH: <0.02 mIU/l Free T4: 16.6 pmol/l	None
2	Syncope	Diagnostic work-up	ATG ATPO	IU/l IU/l	69 691	<20 150	None TSH: 6.90 mIU/l Free T4: 16.6 pmol/l	None
3	Partial empty sella	Disease monitoring	IGF-1	ng/ml	1509	55	Repeat testing	Repeat testing
4	Pituitary microadenoma	Disease monitoring	GH IGF-1	µg/l ng/ml	38.5 614	2.09 130	MRI imaging for suspected GH secreting adenoma	Repeat testing
5	Automimmune thyroid disease	Disease monitoring	ATG ATPO	IU/l IU/l	96 277	<20 13	Erroneous results not seen by physician	None
6	Vitreous haemorrhage	Diagnostic work-up	ATG ATPO	IU/l IU/l	92 37	<20 <10	None TSH: 0.86 mIU/l Free T4: 16.8 pmol/l	None
7	Hypoadrenalism	Diagnostic	ACTH	pmol/l	41.1	2.1	Misdiagnosis as primary hypoadrenalism	Adrenal CT-scan ordered
8	Congenital adrenal hyperplasia	Disease monitoring	ACTH	pmol/l	102	36.6	Misdiagnosis of poor compliance to glucocorticoids	None
9	Hypothyroidism on L-thyroxine replacement	Diagnostic work-up	ATG ATPO	IU/l IU/l	126 366	23 <10	Misdiagnosis of Hashimoto's disease and need for repeat testing TSH 0.05 mIU/l Free T4: 18.4 pmol/l	None
10	Grave's disease	Diagnostic work-up	ATG ATPO	IU/l IU/l	300 >1000	<20 49	None TSH: <0.02 mIU/l Free T4: 12.7 pmol/L	None
11	Automimmune thyroid disease	Disease monitoring	ATPO	IU/l	>1000	191	None	None
12	Hypoglycaemia for investigation	Diagnostic	GH IGF-1 Repeat testing GH IGF-1	µg/l ng/ml µg/l ng/ml	39.5 765 6.82 783	2.16 178 0.97 180	Misdiagnosis of acromegaly	None
13	Metastatic thyroid cancer	Disease monitoring	ATG	IU/l	97	<20	None	None
14	Thyroid cancer, post-surgical removal	Disease monitoring	ATG	IU/l	>3000	28	Misdiagnosis of cancer recurrence, need for further laboratory and imaging studies	None
15	Thyroid cancer, post-surgical removal	Disease monitoring	ATG	IU/l	140	<20	Misdiagnosis of cancer recurrence, need for further laboratory and imaging studies	None

The free thyroxine and thyrotropin concentrations measured together with the thyroid auto-antibody tests are provided.
ACTH, adrenocorticotrophic hormone (reference interval: 0.0–10.2 pmol/l), ATG, anti-thyroglobulin antibodies (negative if <40 IU/l), ATPO, anti-thyroid peroxidase antibodies (negative if <50 IU/l), GH, growth hormone (male <3.00 µg/l; female <8.00 µg/l), IGF-1, insulin-like growth factor-1 (87–238 ng/ml), free T4, free thyroxine (10.0–23.0 pmol/l), TSH, thyrotropin, (0.45–4.50 mIU/l).

Would the right QC have caught the error?

- 49 patients affected (IGF, ATG, ATPO, GH, ACTH)
  - 4 procedures ordered erroneously (including a CT Scan)
  - 7 patients ordered for retesting
  - 6 misdiagnoses



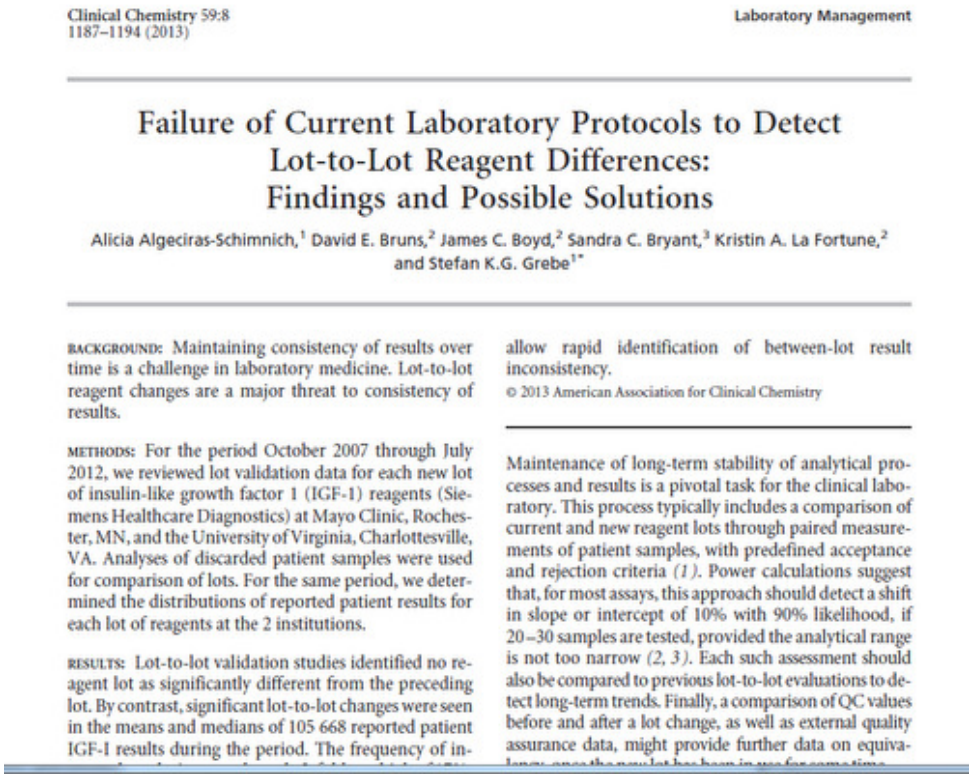


Turns out, bad QC in one lab wasn't the only problem…

For 2 YEARS, Mayo Clinic: **about 5% of all IGF-1 tests were false positives.**

"If the Mayo Clinic observations are generalized, a laboratory performing 1000 IGF-1 tests/month would be expected to generate around **50 false-positive results each month**. Some of these can be expected to lead to **follow-up appointments or further testing and, ultimately, increased financial burden and anxiety for patients**."

UVA: 8-month period in 2011, "20 abnormally high IGF-1 results in 17 patients that did not agree with clinical findings. In 17 of the 20 samples, the IGF-1 concentrations measured by a mass spectrometric method were within reference intervals. In 7 of the patients, expensive growth hormone suppression tests were done; the results were within reference intervals in 6, with the result in the seventh nondiagnostic."



Clinical Chemistry 59:8
1187–1194 (2013)

Laboratory Management

Failure of Current Laboratory Protocols to Detect Lot-to-Lot Reagent Differences: Findings and Possible Solutions

Alicia Algeciras-Schimnich,[1] David E. Bruns,[2] James C. Boyd,[2] Sandra C. Bryant,[3] Kristin A. La Fortune,[2] and Stefan K.G. Grebe[1*]

BACKGROUND: Maintaining consistency of results over time is a challenge in laboratory medicine. Lot-to-lot reagent changes are a major threat to consistency of results.

METHODS: For the period October 2007 through July 2012, we reviewed lot validation data for each new lot of insulin-like growth factor 1 (IGF-1) reagents (Siemens Healthcare Diagnostics) at Mayo Clinic, Rochester, MN, and the University of Virginia, Charlottesville, VA. Analyses of discarded patient samples were used for comparison of lots. For the same period, we determined the distributions of reported patient results for each lot of reagents at the 2 institutions.

RESULTS: Lot-to-lot validation studies identified no reagent lot as significantly different from the preceding lot. By contrast, significant lot-to-lot changes were seen in the means and medians of 105 668 reported patient IGF-1 results during the period. The frequency of in-

allow rapid identification of between-lot result inconsistency.

Maintenance of long-term stability of analytical processes and results is a pivotal task for the clinical laboratory. This process typically includes a comparison of current and new reagent lots through paired measurements of patient samples, with predefined acceptance and rejection criteria *(1)*. Power calculations suggest that, for most assays, this approach should detect a shift in slope or intercept of 10% with 90% likelihood, if 20–30 samples are tested, provided the analytical range is not too narrow *(2, 3)*. Each such assessment should also be compared to previous lot-to-lot evaluations to detect long-term trends. Finally, a comparison of QC values before and after a lot change, as well as external quality assurance data, might provide further data on equiva-

Goals of this presentation

- **The Ugly:** Are we doing the right QC?
- **The Bad: Are our assays fit for purpose?**
- **The Good**

  Can we redesign our testing to do the Right QC Right - AND save time, effort and money?

- Tools for Assessment, Assurance and Optimization
  - Sigma-metric Equation
  - Method Decision Chart
  - OPSpecs Chart

Westgard QC

What about our HbA1c methods?

"A manufacturer NGSP certification does not guarantee accuracy of a result produced in the field. We often observed significant differences between lots of reagents in this study."

Clinical Chemistry 56:1
44–52 (2010)

Six of Eight Hemoglobin A_{1c} Point-of-Care Instruments Do Not Meet the General Accepted Analytical Performance Criteria

Erna Lenters-Westra[1,2*] and Robbert J. Slingerland[1,2]

BACKGROUND: Hemoglobin A_{1c} (Hb A_{1c}) point-of-care (POC) instruments are widely used to provide rapid-turnaround results in diabetic care centers. We investigated the conformance of various Hb A_{1c} POC instruments (In2it from Bio-Rad, DCA Vantage from Siemens, Afinion and Nycocard from Axis-Shield, Clover from Infopia, InnovaStar from DiaSys, A1CNow from Bayer, and Quo-Test from Quotient Diagnostics) with generally accepted performance criteria for Hb A_{1c}.

METHODS: The CLSI protocols EP-10, EP-5, and EP-9 were applied to investigate imprecision, accuracy, and bias. We assessed bias using 3 certified secondary reference measurement procedures and the mean of the 3 reference methods. Assay conformance with the National Glycohemoglobin Standardization Program (NGSP) certification criteria, as calculated from analyses with 2 different reagent lot numbers for each Hb A_{1c} method, was also evaluated.

RESULTS: Because of disappointing EP-10 results, 2 of the 8 manufacturers decided not to continue the tween different reagent lot numbers for all Hb A_{1c} POC instruments.

Diabetes is one of the most challenging health problems of the 21st century. The International Diabetes Federation estimates that more than 250 million people around the world have diabetes *(1)*. Currently diagnosis and follow-up are usually done in special diabetes care centers. Many patients have their blood drawn a week before they visit the physician to ensure that laboratory results are available for appropriate clinical action. By providing results rapidly following blood collection, point-of-care (POC)[3] instruments could minimize patient inconvenience and possibly avoid an extra visit to the clinic. Studies have confirmed that immediate feedback of hemoglobin A_{1c} (Hb A_{1c}) results improves glycemic control in type 1 and insulin-treated type 2 diabetic patients *(2–4)*.

Limited information is available regarding the analytical performance of POC instruments that

See also the 12-part series
http://www.westgard.com/hba1c-methods.htm

Westgard QC

"A rose is a rose is a rose"

In the Real World! HbA1c – A case study

- Hemoglobin A1c example
  - E Lenters-Westra, RJ Slingerland. Six of Eight Hemoglobin A1c Point-of-Care Instruments Do Not Meet the General Accepted Analytical Performance Criteria. Clin Chem 2010;56:44-52.
  - DE Bruns, JC Boyd. Few Point-of-Care Hemoglobin A1c Assay Methods Meet Clinical Needs. Clin Chem 2010;56:4-6.

“A Teaching Moment!”

- Real World Learning
  - Series of 10 web lessons related to POC HbA1c
    - Abstract, analysis
    - Quality requirements (Bruns and Boyd)
    - Validation experiments (Lenters)
    - Statistical data analysis
    - Method Decision Chart
    - Performance on PT surveys
  - http://westgard.com/hba1c-methods-part11/print.htm

How good is good enough?

- Diagnostic criterion is 6.5 %Hb
  - 5.7-6.4 gray zone, pre-diabetic
- Treatment criteria of Δ0.5 %Hb (@7%Hb)
- CAP 2011 PT criterion = 7% (8% 2010)
- NGSP criterion for agreement ± 0.75 %Hb
- Maximum CV of 3%, desirable CV of 2%
- Maximum bias to prevent misclassification
  - 0.1 %Hb at 6.5 %Hb is 1.5% bias
  - 0.2 %Hb at 6.5 %Hb is 3.0% bias

Bruns & Boyd
Effect of Bias on Classification

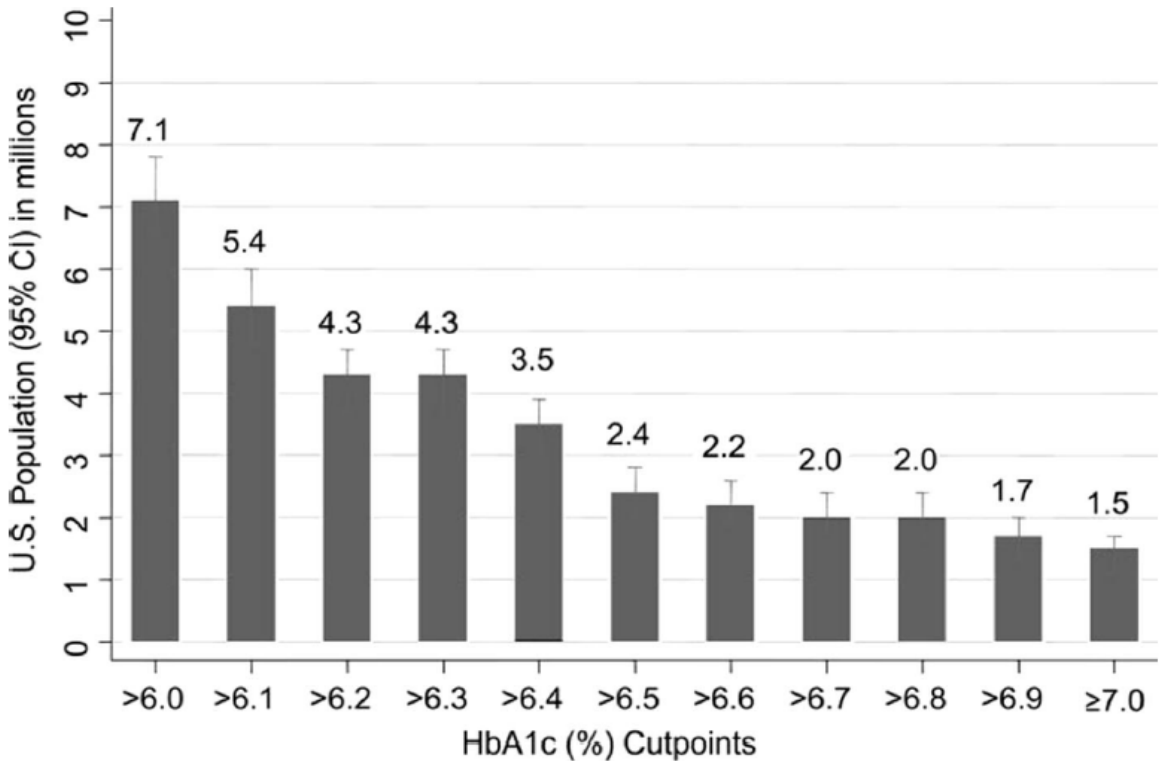


Fig. 1. Distribution of estimated numbers of persons without a history of diabetes in the US 2000 Census population (age ≥20 years) at different Hb A_{1c} cutpoints.

Reprinted with permission from *Diabetes Care* [Selvin et al. *(13)*].

Precision results from Lenters Study

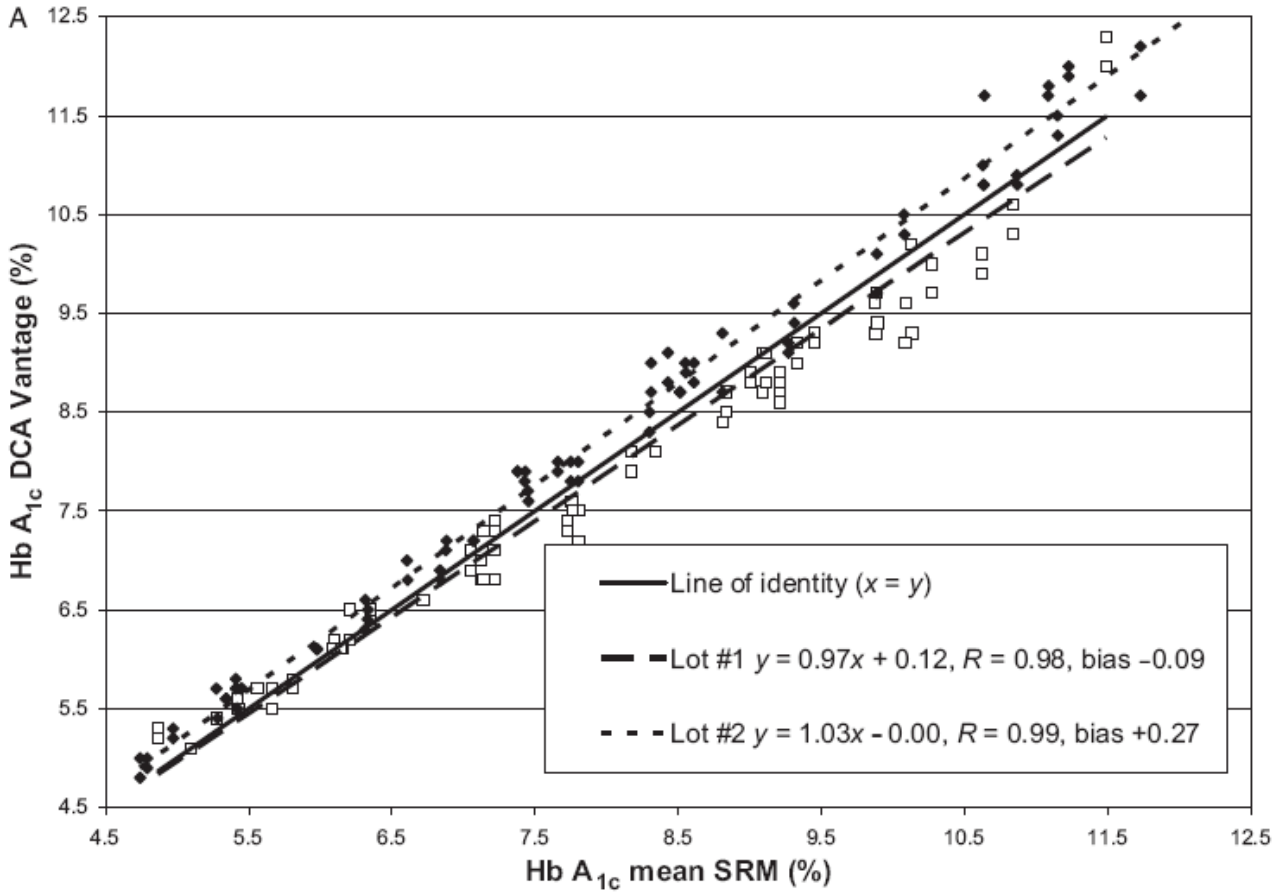
Table 1. EP-5 total CV imprecision results from the different POC instruments.

	In2it	DCA Vantage	Clover	InnovaStar	Nycocard	Afinion
Patient sample 1	4.9% (5.1%)[a]	1.8% (5.1%)	4.0% (5.0%)	3.2% (5.2%)	4.8% (4.8%)	2.4% (4.7%)
Patient sample 2	3.3% (11.2%)	3.7% (11.2%)	3.5% (11.9%)	3.9% (11.5%)		
Nycocard normal control					5.3% (6.1%)	
Nycocard abnormal control					5.2% (11.6%)	
Afinion control CI						1.4% (6.3%)
Afinion control CII						1.8% (8.2%)

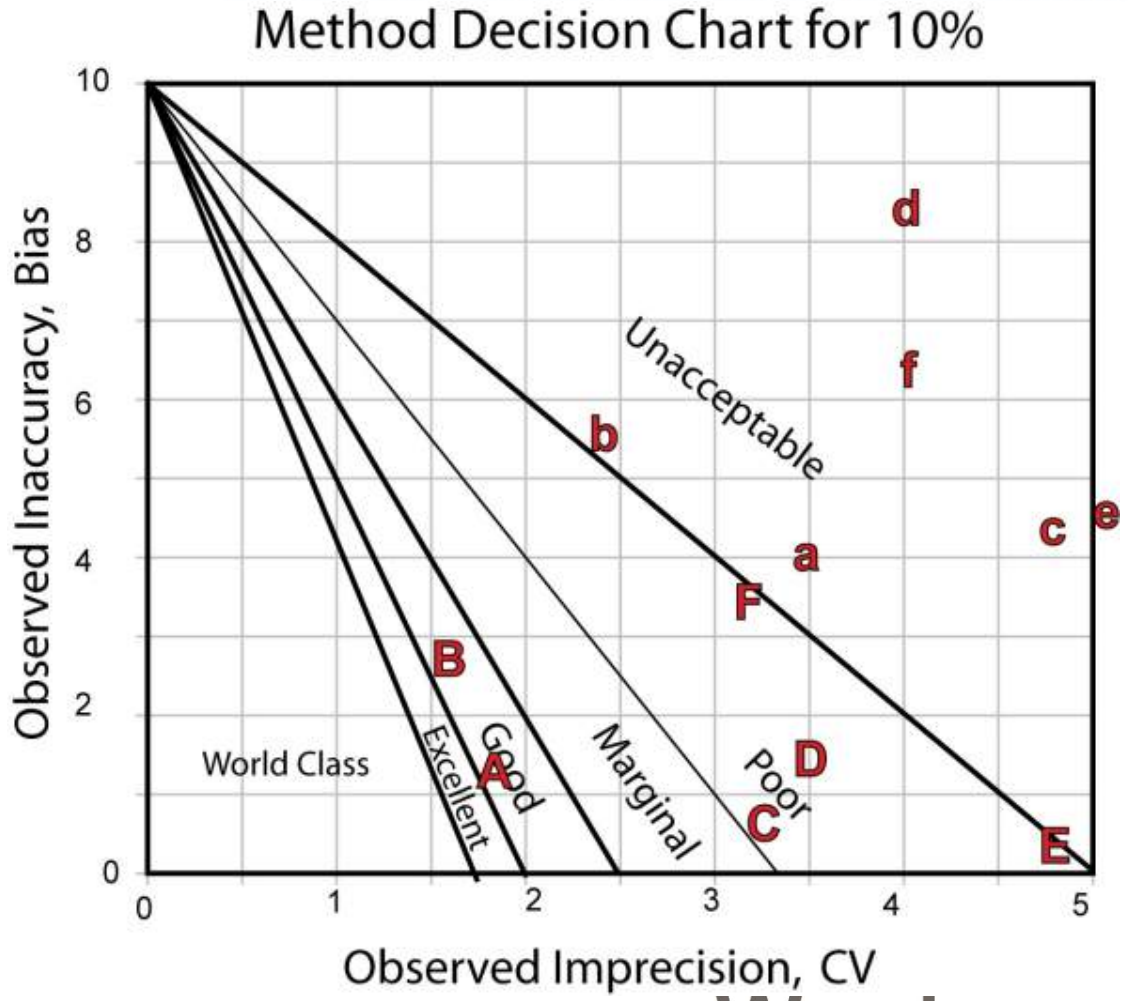
[a] Hb A_{1c} value of the sample/control are in parentheses.

Lenters-Westra E, Slingerland RJ. Six of Eight Hemoglobin A1c Point-of-Care Instruments Do Not Meet the General Accepted Analytical Performance Criteria. Clin Chem 2010;56:44-52.

Accuracy results - Comparison with avg of 3 reference methods



2010: 6 out of 8 HbA1c Devices



Unfortunately, we are great at Reporting Results

(but not so good at assuring their quality or efficiency)

"21.8% of the laboratories using different HbA1c methods are not able to distinguish an HbA1c result of [7.5%] from a previous HbA1c result of [7.0%]."

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 13, Number 4, 2011

DOI: 10.1089/dia.2010.0148

One in Five Laboratories Using Various Hemoglobin A_{1c} Methods Do Not Meet the Criteria for Optimal Diabetes Care Management

Ema Lenters-Westra, B.Sc.,[1,2] Cas Weykamp, Ph.D.,[3] Roger K. Schindhelm, M.D., Ph.D., MEPI,[1] Carla Siebelder, B.Sc.,[3] Henk J. Bilo, M.D., Ph.D.,[4,5] and Robbert J. Slingerland, Ph.D., EURCLINCHEM[1,2]

Abstract

Background: We assessed the reference change value (RCV) of currently available hemoglobin A_{1c} (HbA_{1c}) laboratory assays, which is defined as the critical difference between two consecutive HbA_{1c} measurements representing a significant change in health status.

Methods: We examined the individual laboratory coefficients of variation (CVs) in the Dutch/Belgian quality scheme based on 24 lyophilized samples and calculated the RCV per laboratory ($n = 220$) and per assay method. In addition, two pooled whole blood samples were sent to the participating laboratories. The individual laboratory results were compared to the assigned value ± an allowable total error (TE_a) of 6%.

Results: At HbA_{1c} values of 41.0 mmol/mol (5.9%-Diabetes Control and Complications Trial [DCCT]) and 61.8 mmol/mol (7.8%-DCCT), 99% and 98%, respectively, of the laboratories reported a value within a TE_a limit of 6%. The analytical CV of the HbA_{1c} method used in 78% of the laboratories is <2.4%. The mean RCV at an HbA_{1c} value of 53 mmol/mol (7.0%-DCCT) for methods of Bio-Rad is 5.9 mmol/mol (0.59%-DCCT); for Arkray/Menarini, 4.3 mmol/mol (0.43%-DCCT); for Roche, 6.5 mmol/mol (0.65%-DCCT); for Tosoh, 3.3 mmol/mol (0.33%-DCCT); and for other methods, 6.3 mmol/mol (0.63%-DCCT).

Why can't we assume every lab test is good?

- Isn't every method on the market a "quality method"?

  "Conclusion 7-1. The 510(k) clearance process is not intended to evaluate the safety and effectiveness of medical devices with some exceptions. The 510(k) process cannot be transformed into a premarket evaluation of safety and effectiveness as long as the standard for clearance is substantial equivalence to any previously cleared device."

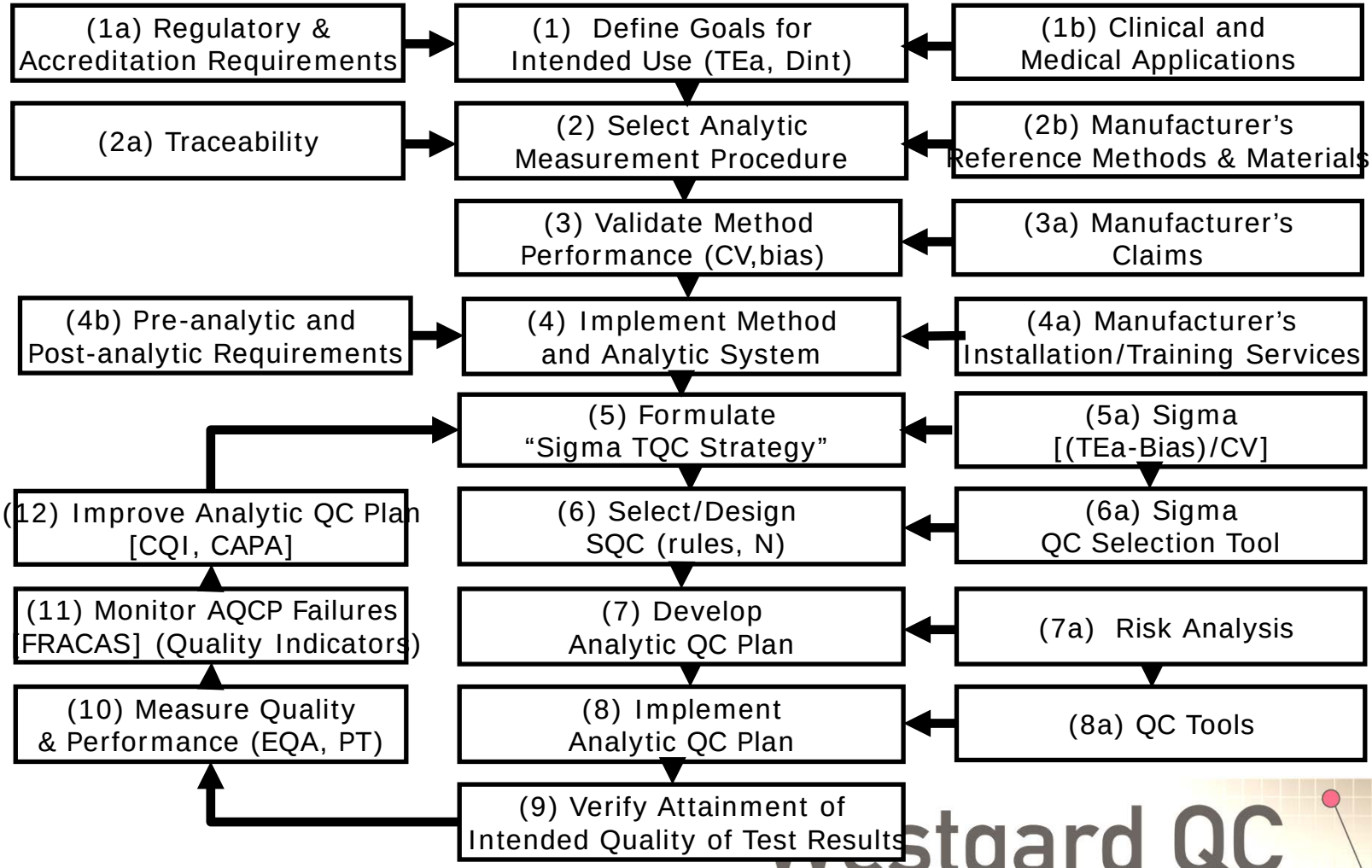
  Reference. Institute of Medicine 2011: Medical Devices and the Public's health: the FDA 510(k) Clearance Process at 35 years, prepublication copy

Moving beyond Bad and Ugly

If we do the *right* QC
with the *right* method,
we can reduce or eliminate
all of those wasteful QC practices

How/Where do we start?

Where do we go? How do we get there? Six Sigma Quality System

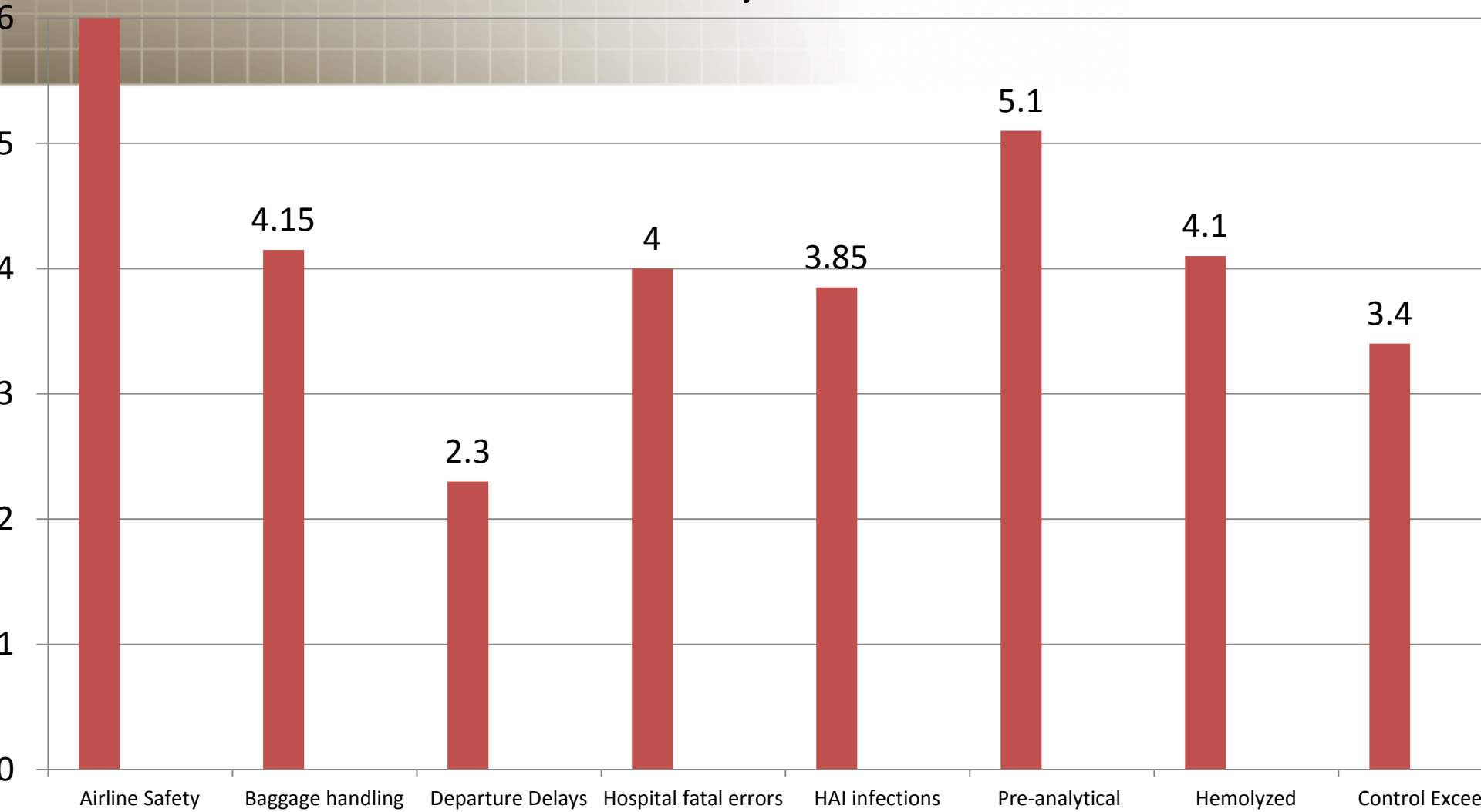


Six Sigma – Our use here
Defines the *Shape* of the target

- Defects Per Million (DPM)
- Scale of 0 to 6 (Sigma short-term scale)
- 6 is world class (3.4 dpm)
- 3 is minimum for any business or manufacturing process (66,807 dpm)

Westgard QC

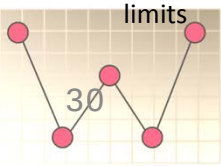
Sigma Metrics of Common Processes, Healthcare and Laboratory Processes



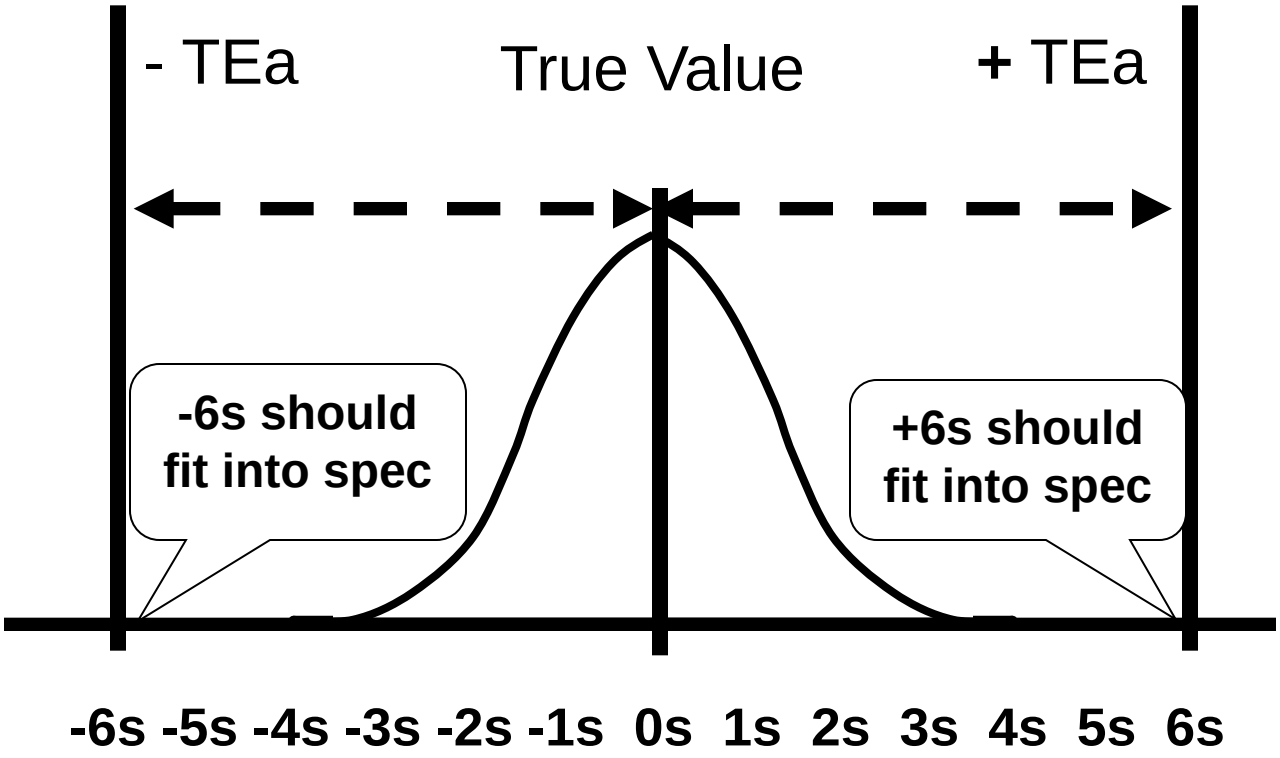
Sources: Landrigan et al, Temporal Trends in Rates of Patient Harm Resulting from Medical Care. NEJM 2010;363:2124-34.

M Antonia Llopis et al, Quality indicators and specifications for key analytical-extranalytical processess in the clinical laboratory. CCLM 2011;49(3):463-470.

Westgard QC



Six Sigma:
A slightly more technical view



Six Sigma
Outcome of reaching the goal

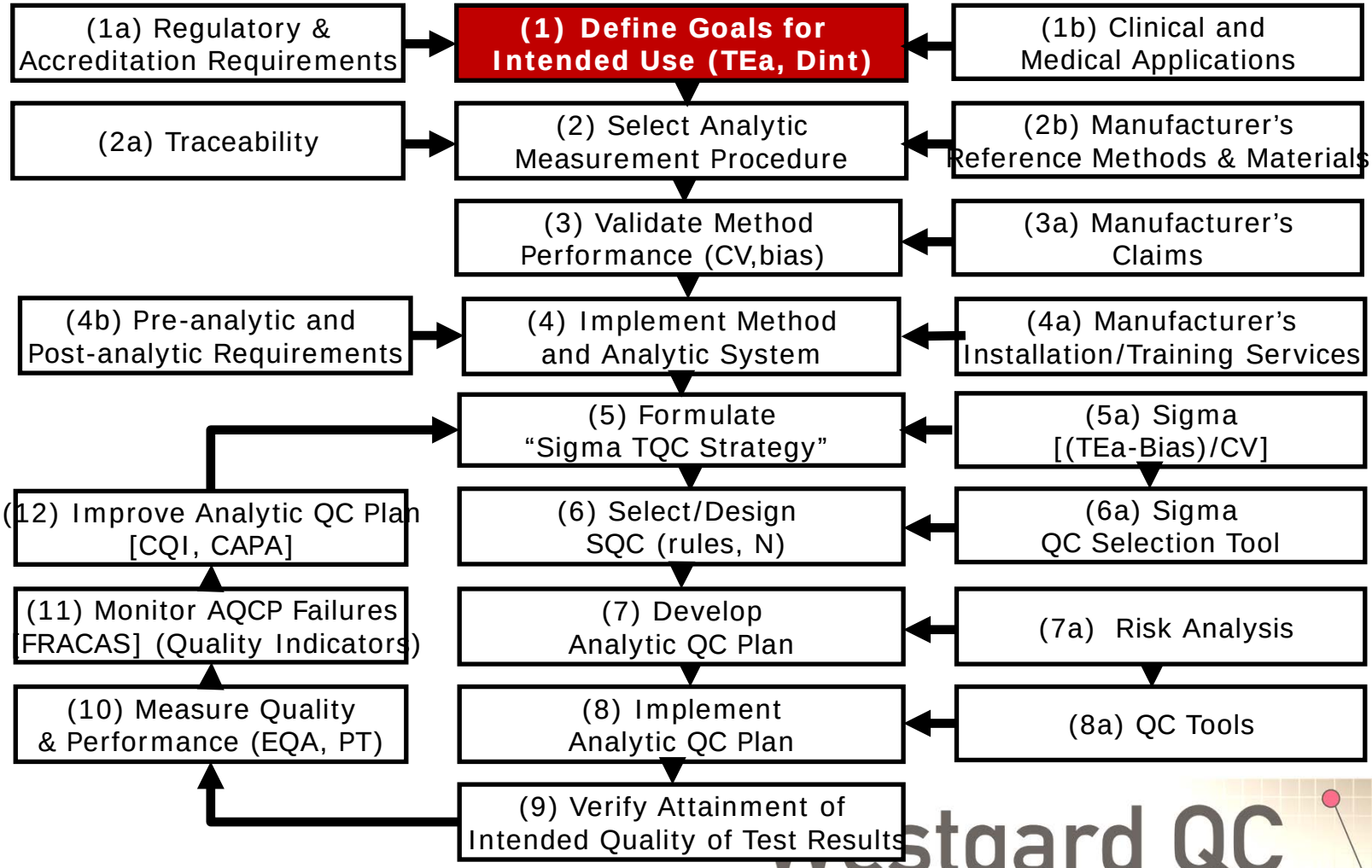
- Very few defects
- Much less rework, work-arounds, and wasted effort and resources

- Reduced costs
- Improved performance and profitability: **Efficiency and Effectiveness**

Six Sigma:
Defines the
Shape
of the Target

(now, how big is the target
and how do we know if we hit it?)

Where do we start? Select a Goal



Quality Requirements: Where to find them

Total Allowable Errors (TEa)

- PT/EQA groups
- CLIA
- RCPA
- Rilibak
- Biologic Variation Database "Ricos Goals"
- Your Clinical Decision Intervals (BEST)
  - Evidence-based Guidelines
  - Clinical Pathways

	Analyte	Biological Variation		Desirable specification		
		CVw	CVg	I(%)	B(%)	TE(%)
S-	11-Desoxycortisol	21.3	31.5	10.7	9.5	27.1
S-	17-Hydroxyprogesterone	19.6	50.4	9.8	13.5	29.7
U-	4-hydroxy-3-methoxiimandelate (VMA)	22.2	47.0	11.1	13.0	31.3
S-	5' Nucleotidase	23.2	19.9	11.6	7.6	26.8
U-	5'-Hydroxyindolacetate, concentration	20.3	33.2	10.2	9.7	26.5
S-	α1-Acid Glycoprotein	11.3	24.9	5.7	6.8	16.2
S-	α1-Antichymotrypsin	13.5	18.3	6.8	5.7	16.8
S-	α1-Antitrypsin	5.9	16.3	3.0	4.3	9.2
S-	α1-Globulins	11.4	22.6	5.7	6.3	15.7
U-	α1-Microglobulin, concentration, first morning	33.0	58.0	16.5	16.7	43.9
P-	α2-Antiplasmin	6.2	---	3.1	---	---
S-	α2-Globulins	10.3	12.7	5.2	4.1	12.6
S-	α2-Macroglobulin	3.4	18.7	1.7	4.8	7.6
U-	α2-Microglobulin output, first morning	29.0	32.0	14.5	10.8	34.7
P-	α-aminobutryic acid	24.7	32.3	12.4	10.2	30.5
S-	α-Amylase	8.7	28.3	4.4	7.4	14.6
S-	α-Amylase (pancreatic)	11.7	29.9	5.9	8.0	17.7
U-	α-Amylase (pancreatic)	39.0	78.4	19.5	21.9	54.1
U-	α-Amylase concentration, random	94.0	46.0	47.0	26.2	103.7
P-	α-Carotene	24.0	65.0	12.0	17.3	37.1
S-	α-Carotene	48.0	65.0	24.0	20.2	59.8
S-	α-Fetoprotein(non hepatic carcinoma)	12.2	45.6	6.1	11.8	21.9
S-	α-Tocopherol	13.8	15.0	6.9	5.1	16.5

Quality Requirements

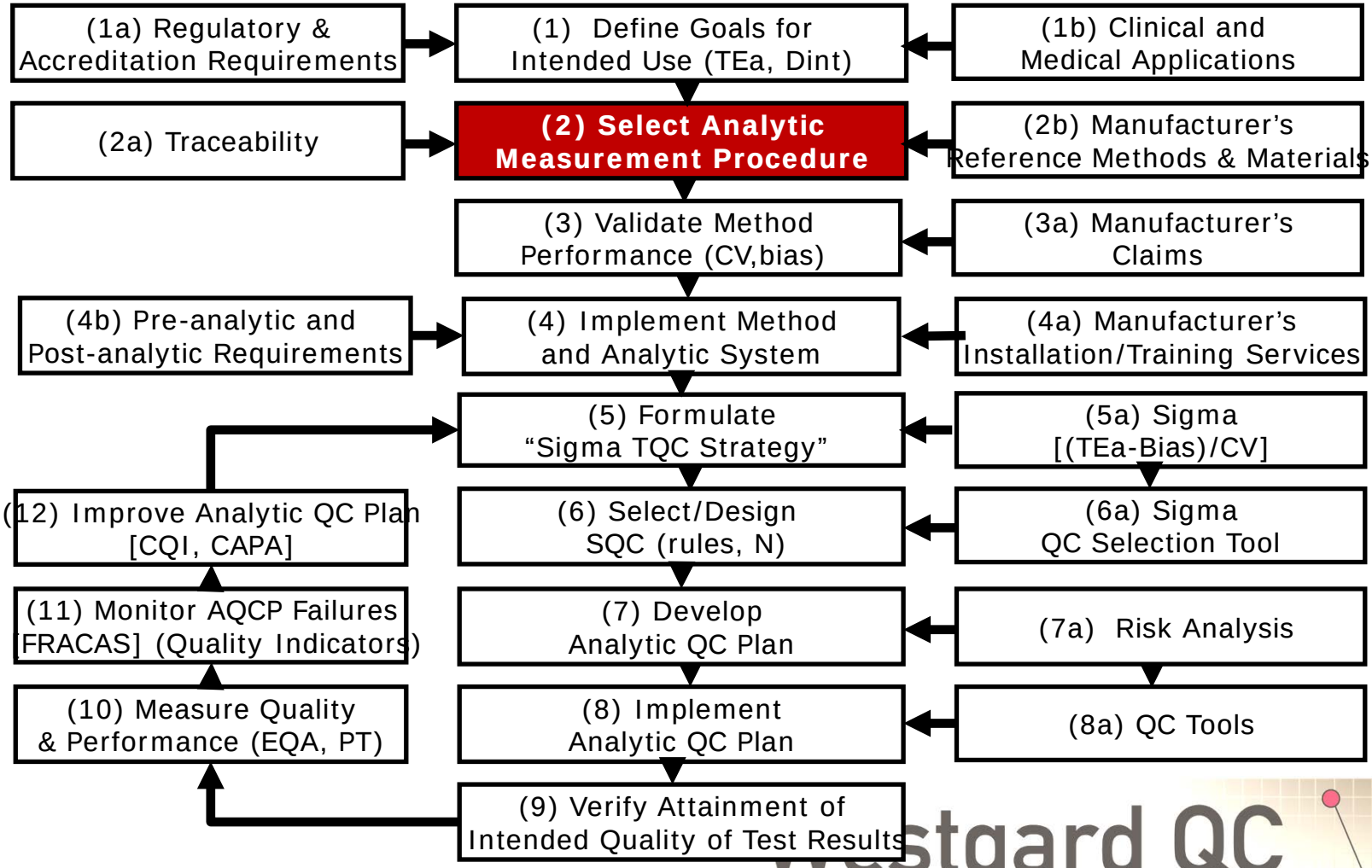
- Minimum analytical quality requirements
- Minimum Specifications from Biological Variation database
- Optimal Biological Variation database specifications
- Rilibak - German Guidelines for Quality
- Biological Variation in Patients with Disease
- CLIA Requirements for Analytical Quality
- Clinical Quality Requirements
- European Biologic Goals
- Biological Variation Database references
- Biological Variation Database reference list
- RCPA (Australasian) Quality Requirements
- Quality Requirements for Dogs, Cats, and Horses?
- 1999 Stockholm Consensus Statement

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

How good does HbA1c have to be?

• CLIA:	None given
• Rilibak (Germany)	18%
• NGSP 2013	7%
• CAP PT 2013	6%
• “Ricos Goal”	4.3%
• UK MAPS	6.3-7.0%

What's next? Select a Method



What method to select?

Clin. Lab. 2012;58:1171-1177

ORIGINAL ARTICLE

Evaluation of Three Turbidimetric Assays for Automated Determination of Hemoglobin A1c

AMANDINE BARROT [1], ANNE MARIE DUPUY [1], STÉPHANIE BADIOU [1], ANNE SOPHIE BARGNOUX [1], JEAN PAUL CRISTOL [1]

[1] Department of Biochemistry, Lapeyronie Hospital, Montpellier, France

SUMMARY

Background: To compare the results of HbA1c determination obtained through immunoassays versus the HPLC method currently used routinely in our laboratory.
Methods: We evaluated immunoturbidimetric assays for the HbA1c measure on three analyzers, specifically the Roche Cobas Integra 400+® (Roche Diagnostics, Indianapolis, IN, USA), Ortho Clinical Diagnostics Vitros 5.1 FS® (Ortho Clinical Diagnostics, NY, USA), and Siemens Dimension RxL® (Siemens Healthcare Diagnostics, NY, USA), in comparison with the HPLC Menarini HA 8140® (Menarini Diagnostics, Rungis, France) currently used in our laboratory.
Results: Analytical performances including precision, analytical range, recovery, carryover, erythrosedimentation and comparison studies were acceptable leading to results with a level of exactitude in accordance with the recommendations of the National Glycohemoglobin Standardization Program (NGSP).
Conclusions: The three immunoassays tested can be used interchangeably and will be satisfactory for laboratories who cannot invest in a HPLC analyzer.
(Clin. Lab. 2012;58:1171-1177. DOI: 10.7754/Clin.Lab.2012.111222)

KEY WORDS

Hemoglogin A1c, immunoassay, chromatography, turbidimetry

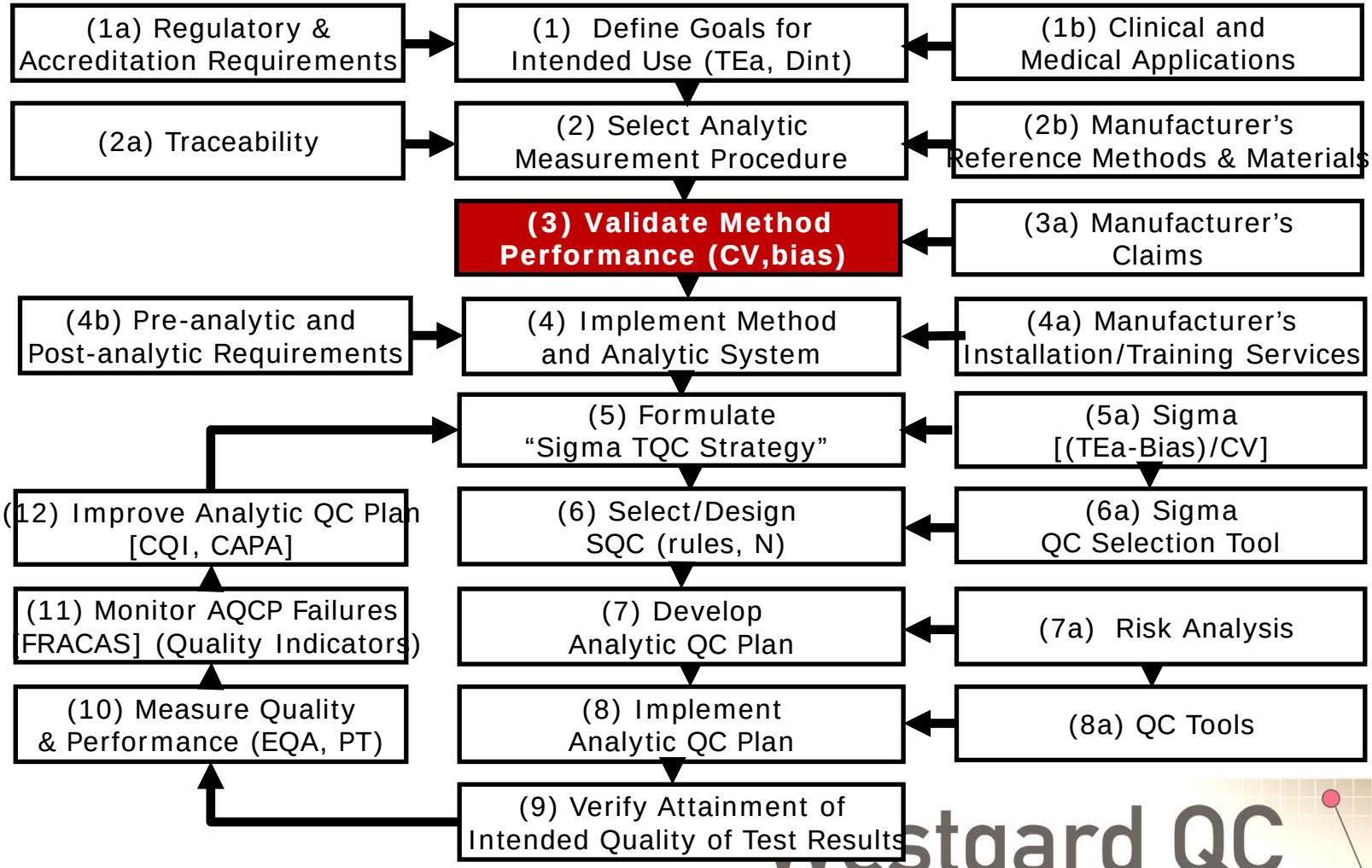
INTRODUCTION

(HPLC) system used in the DCCT Central Laboratory as a reference method, was set up. Finally, in 2001 the IFCC (International Federation of Clinical Chemists) standard appeared, based on the HPLC/mass spectrophotometry or the HPLC/capillary electrophoresis. In these methods, an endoprotease enzymatically cleaves the N-terminal hexapeptides from the HbA beta chains,

Clin Lab 2012;58:1171-1177

Westgard QC

Where do we go? How do we get there? Six Sigma Quality System



Three keys to Assess Quality

Sigma-metrics *(shape of target)*

Quality Requirements *(size of target)*

- Method Performance Data

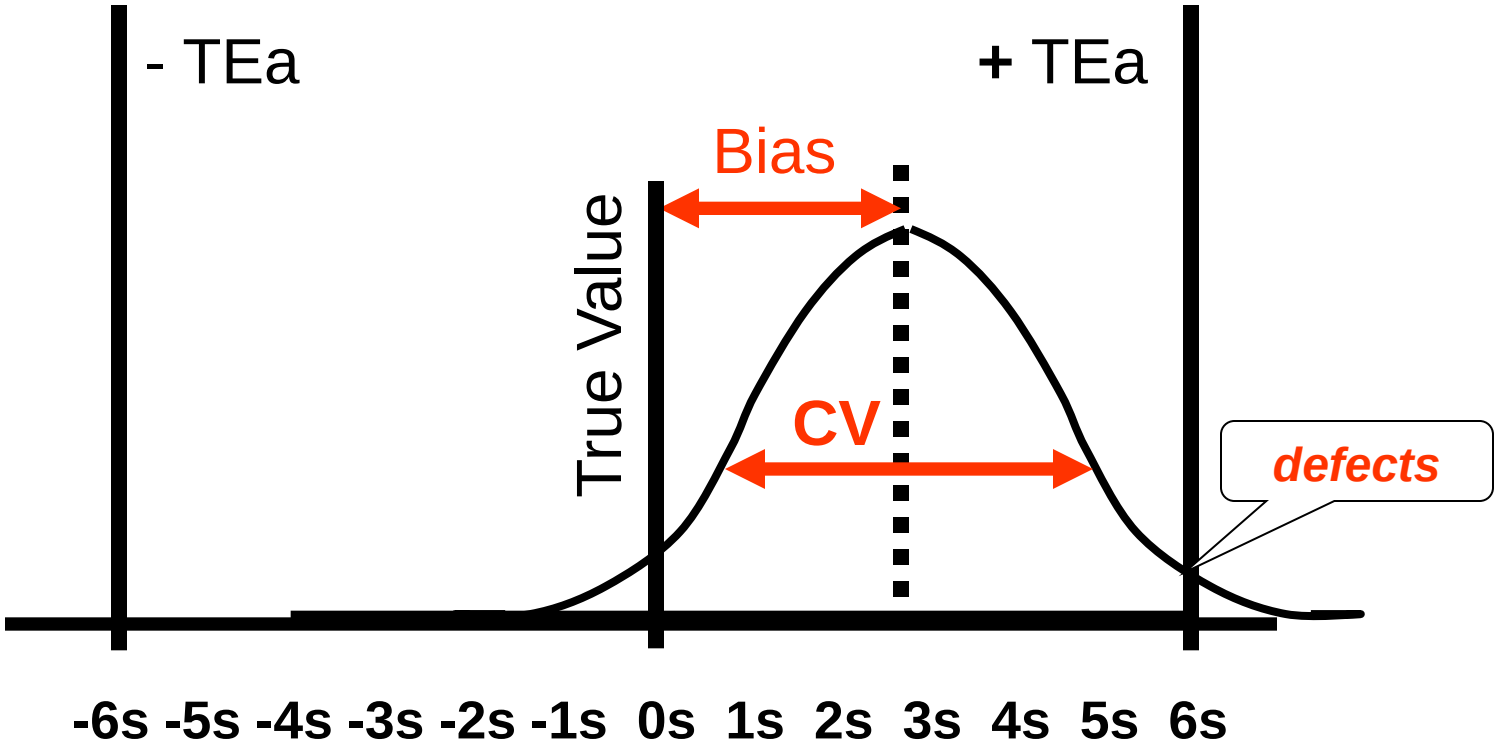
How do we measure (Six) Sigma performance (the arrow)?

Measure Variation

- Can we measure imprecision (CV)?
- Can we measure inaccuracy (bias)?

Sigma metric equation for analytical process performance

Sigma-metric = (TE_a – Bias)/CV



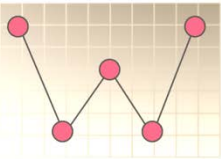
Example Sigma-metric Calculation

- 2 HbA1c POC devices,
  data from 2011 CCLM study
  - CAP PT criterion for acceptability = 7%
  - Total Precision (CV): 2.66%
  - Bias at 5.17 mmol/L: 2.7%

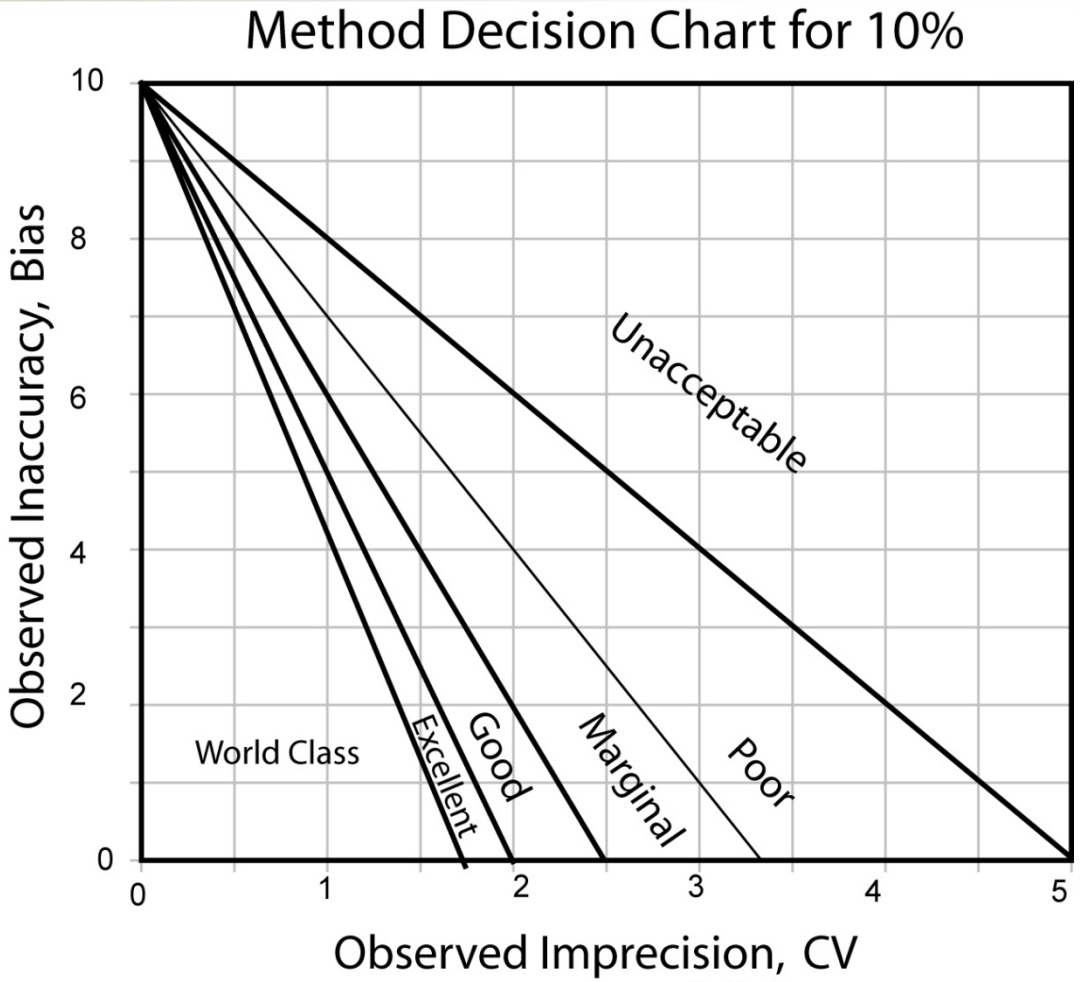
- Sigma = (7 – 2.7) / 2.66
  = 4.34 / 2.66
  = 1.6

http://www.westgard.com/2012-3-poc-hba1c.htm

Westgard QC

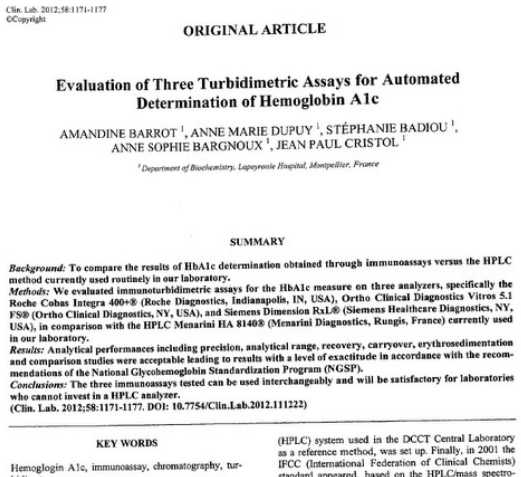


Display of Sigma-metrics:



Where can we find imprecision data?

Method	Between-run CV at 5.7 % HbA1c	Between-run CV at 7.1% HbA1c	Estimated CV at 6.5% HbA1c
A	1.5	0.6	1.05
B	2.18	1.25	1.715
C	1.21	1.01	1.11



Clin. Lab. 2012;58:1171-1177
©Copyright

ORIGINAL ARTICLE

Evaluation of Three Turbidimetric Assays for Automated Determination of Hemoglobin A1c

AMANDINE BARROT [1], ANNE MARIE DUPUY [1], STÉPHANIE BADIOU [1], ANNE SOPHIE BARGNOUX [1], JEAN PAUL CRISTOL [1]

[1] Department of Biochemistry, Lapeyronie Hospital, Montpellier, France

SUMMARY

Background: To compare the results of HbA1c determination obtained through immunoassays versus the HPLC method currently used routinely in our laboratory.
Methods: We evaluated immunoturbidimetric assays for the HbA1c measure on three analyzers, specifically the Roche Cobas Integra 400+® (Roche Diagnostics, Indianapolis, IN, USA), Ortho Clinical Diagnostics Vitros 5.1 FS® (Ortho Clinical Diagnostics, NY, USA), and Siemens Dimension RxL® (Siemens Healthcare Diagnostics, NY, USA), in comparison with the HPLC Menarini HA 8140® (Menarini Diagnostics, Rungis, France) currently used in our laboratory.
Results: Analytical performances including precision, analytical range, recovery, carryover, erythrosedimentation and comparison studies were acceptable leading to results with a level of exactitude in accordance with the recommendations of the National Glycohemoglobin Standardization Program (NGSP).
Conclusions: The three immunoassays tested can be used interchangeably and will be satisfactory for laboratories who cannot invest in a HPLC analyzer.
(Clin. Lab. 2012;58:1171-1177. DOI: 10.7754/Clin.Lab.2012.111222)

KEY WORDS

Hemoglogin A1c, immunoassay, chromatography, tur-

(HPLC) system used in the DCCT Central Laboratory as a reference method, was set up. Finally, in 2001 the IFCC (International Federation of Clinical Chemists)

Westgard QC

Where can we find bias data?

College of American Pathologists (CAP) GH2 Survey Data:

(updated 5/13)

The American Diabetes Association (ADA) recommends that laboratories use only HbA1c assay methods that have been NGSP certified and report results as "%HbA1c". The ADA also recommends that all laboratories performing HbA1c testing participate in the College of American Pathologists (CAP) fresh sample proficiency testing survey (see ADA Recommendations section on this website for more details). CAP GH2 data for the **first** survey of 2013 are summarized below. The NGSP target or reference values are based on replicate analyses using seven NGSP certified secondary reference methods.

2013 GH2-A (fresh pooled samples)

		GH2-01			GH2-02			GH2-03		
[1] NGSP %HbA1c Reference Value (95% CI)		7.11 (7.05-7.17)			9.32 (9.26-9.38)			6.07 (6.-01-6.13)		
	no. labs	Mean %HbA1c	Mean bias	% CV	Mean %HbA1c	Mean bias	% CV	Mean %HbA1c	Mean bias	% CV
* Abbott Architect c System	78	7.21	0.10	4.0	9.53	0.21	3.5	6.10	0.03	3.2
* Axis-Shield Afinion	24	7.14	0.03	3.3	9.02	-0.30	3.0	6.11	0.04	3.1
* Bayer A1cNOW®	16	6.37	-0.74	5.3	8.27	-1.05	4.1	5.40	-0.67	7.3
* Beckman AU systems	37	6.92	-0.19	5.5	9.16	-0.16	4.6	5.89	-0.18	5.0
* Beckman Synchron LX Systems	10	6.91	-0.20	3.5	9.41	0.09	2.2	6.29	0.22	8.2
* Beckman UniCel DxC Synchron	233	7.01	-0.10	3.5	9.45	0.13	3.6	6.06	-0.01	4.2
* Beckman UniCel DxC Synchron (orig)	143	7.01	-0.10	3.6	9.46	0.14	3.8	6.05	-0.02	4.2
* Bio-Rad D-10	210	7.16	0.05	2.7	9.41	0.09	2.6	6.14	0.07	2.6
* Bio-Rad Variant II	97	7.04	-0.07	2.1	9.37	0.05	2.2	5.97	-0.10	2.2
* Bio-Rad Variant II Turbo	152	7.16	0.05	2.6	9.43	0.11	2.0	6.05	-0.02	2.6
* Bio-Rad Variant II Turbo 2.0	51	7.12	0.01	2.2	9.35	0.03	2.3	6.11	0.04	2.6

Where can we find bias data?

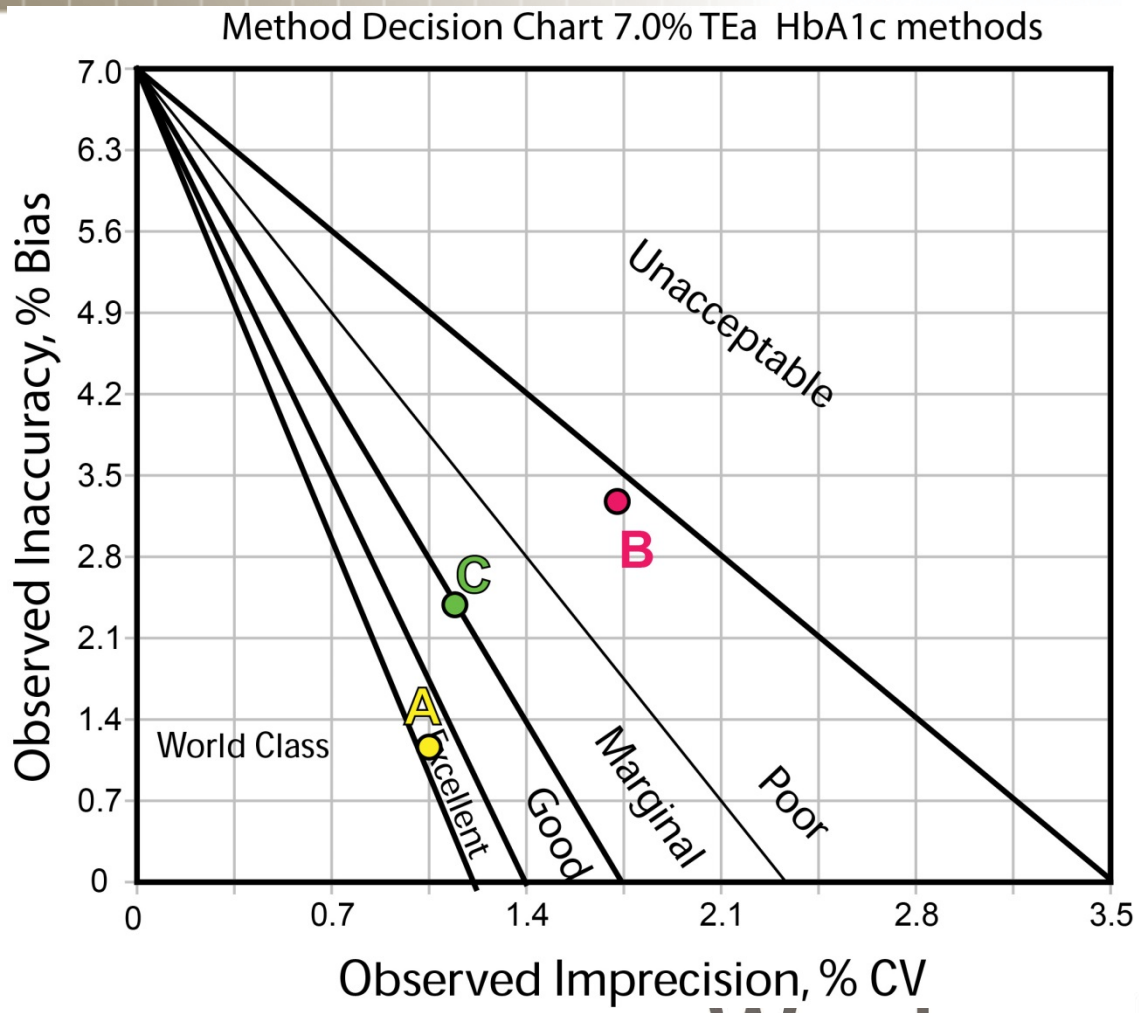
Method	Bias at 6.07 % HbA1c	Bias at 7.1% HbA1c	Bias at 6.5% HbA1c
A	0.98	1.32	1.15
B	-2.67	-3.95	-3.31
C	0.84	4.28	2.56

What are the Sigma-metrics at 6.5?

Method	Imprecision CV	Bias	Sigma-metric
A	1.05	1.15	5.57
B	1.715	3.31	2.15
C	1.11	2.56	4.0

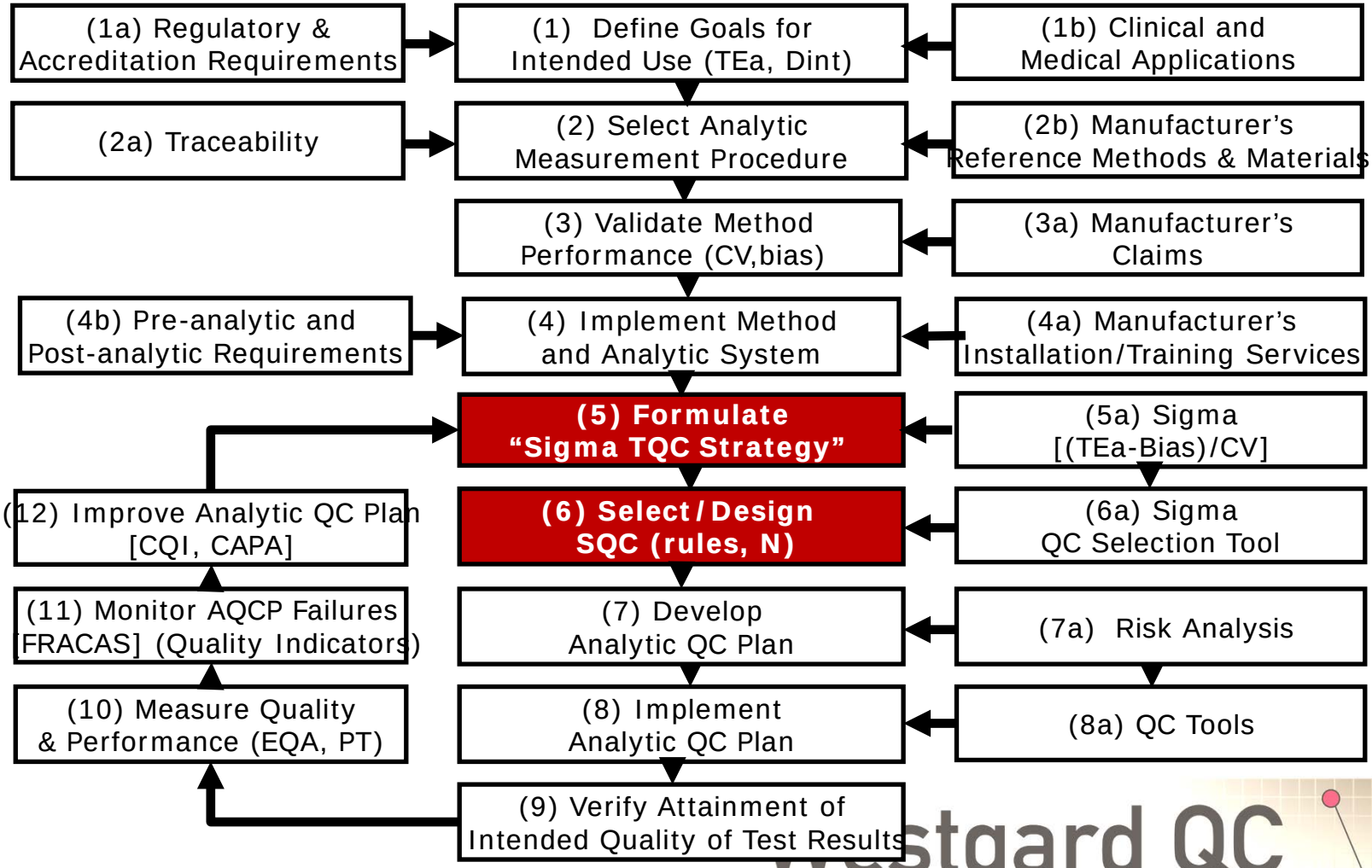
- Sigma = (7 – 3.31) / 1.715
  = 3.69 / 1.715
  = 2.15

2012: 3 Automated HbA1c Methods



Westgard QC

Where do we go? How do we get there? Six Sigma Quality System



Three keys to Assess Quality

Sigma-metrics *(shape of target)*

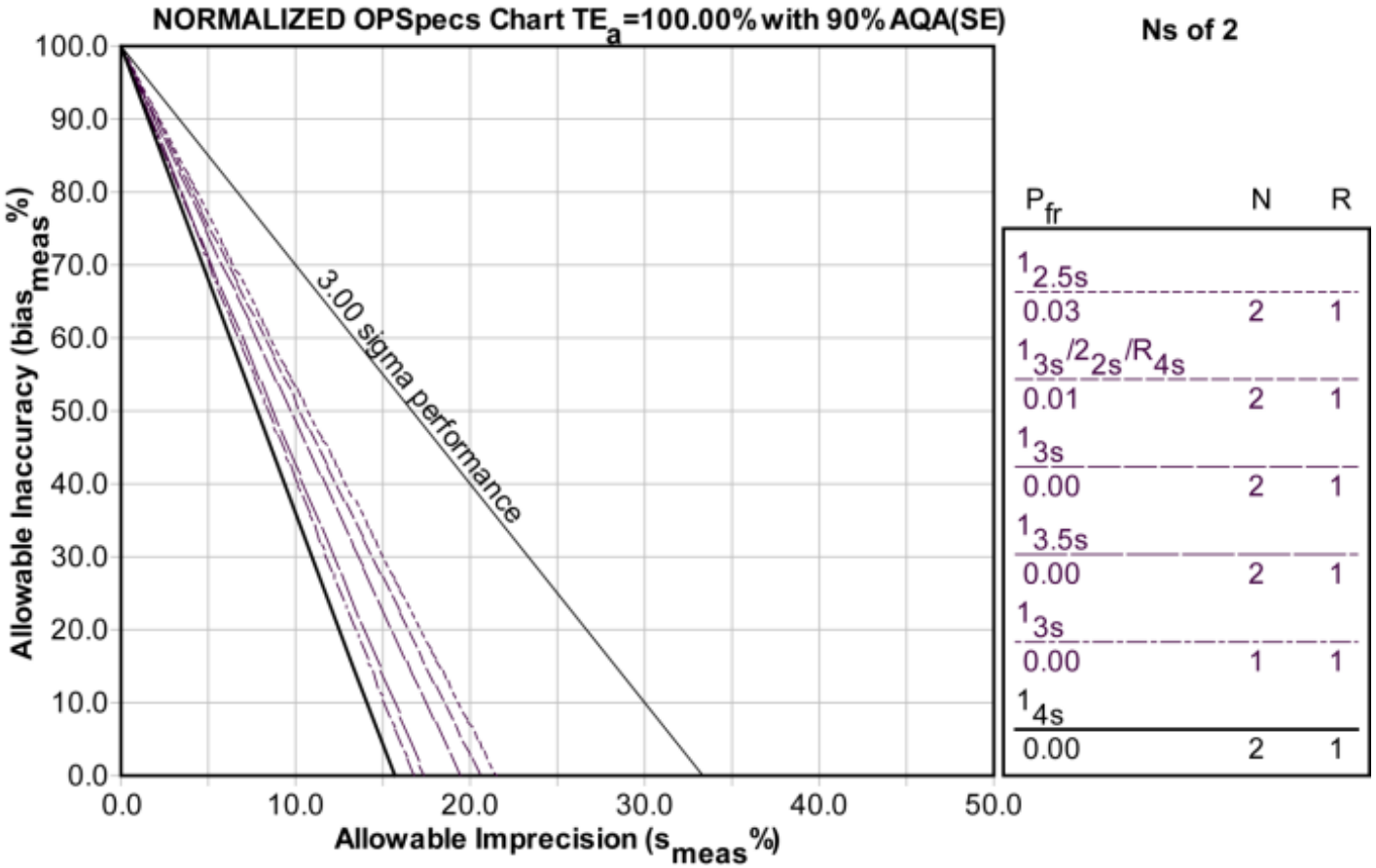
Quality Requirements *(size of target)*

Method Performance Data *(arrow)*

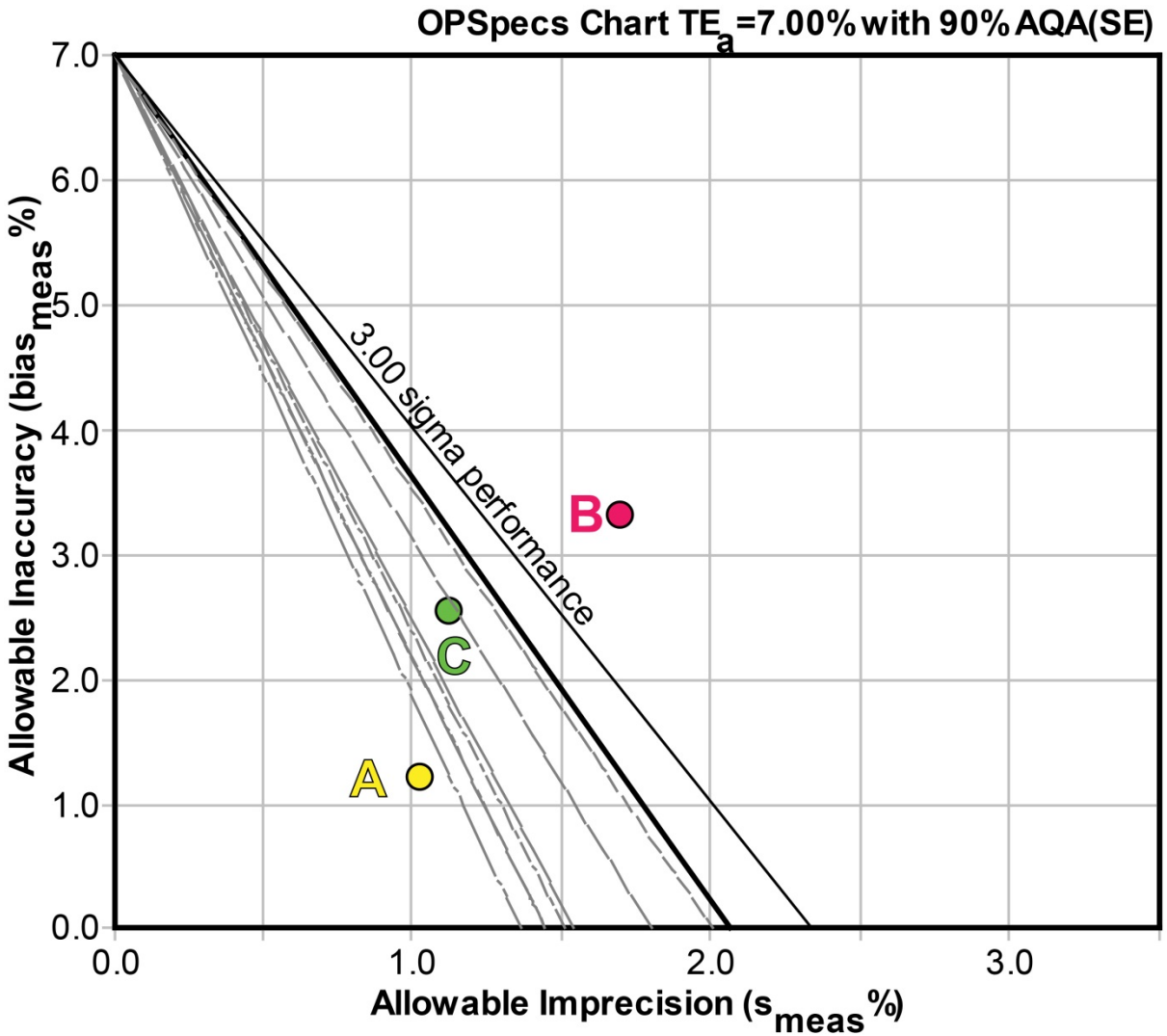
Now what do we do? ***The Right QC***

Operating Specifications (OPSpecs) chart:

Optimizing QC Design



OPSpecs HbA1c methods



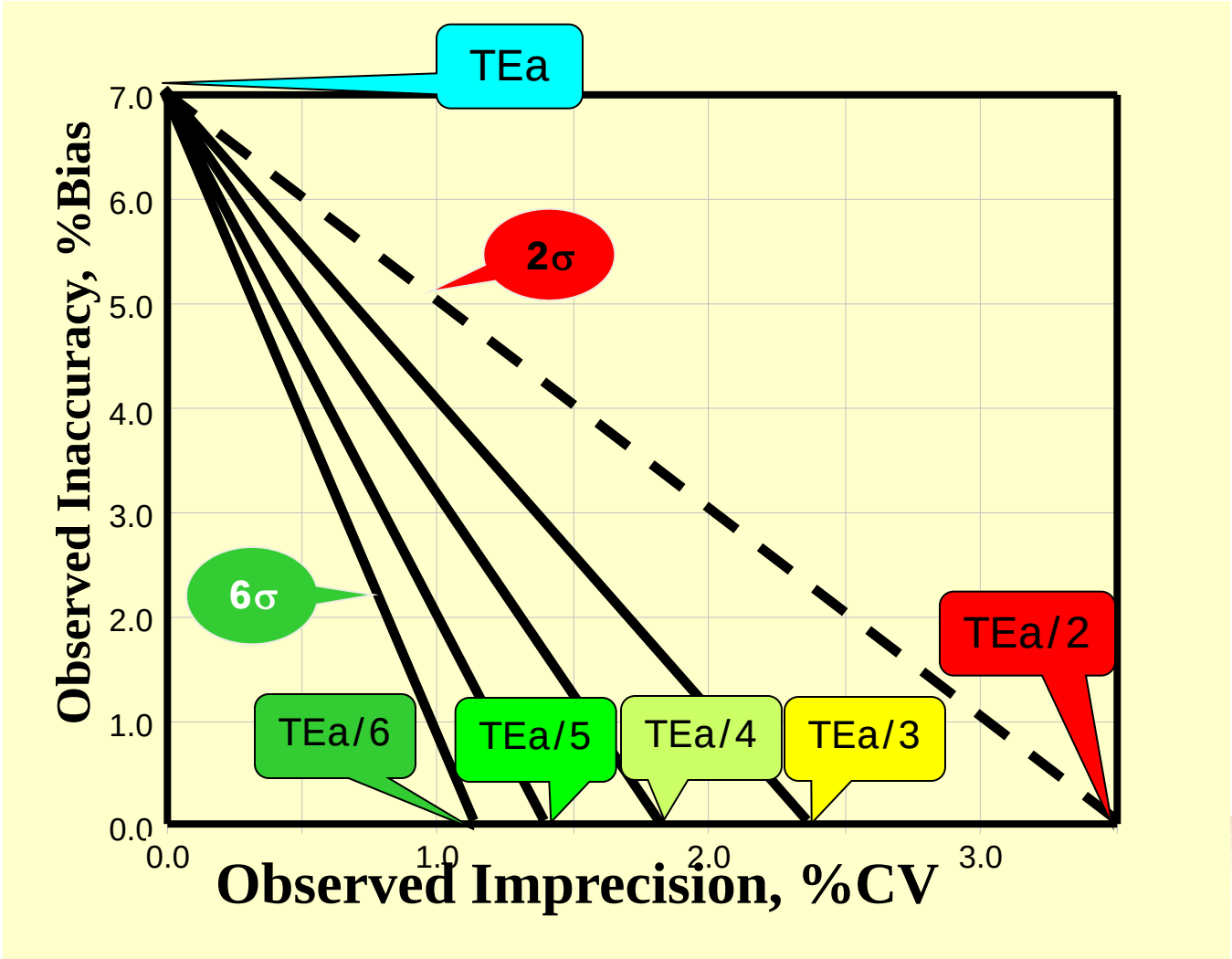
P_{fr}	N	R
$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$		
0.08	8	1
$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$		
0.03	4	2
$1_{3s}/2_{2s}/R_{4s}/4_{1s}$		
0.03	4	1
1_{3s}		
0.01	4	1
$1_{2.5s}$		
0.03	2	1
$1_{3s}/2_{2s}$		
0.01	2	1
$1_{3s}/2_{2s}/R_{4s}$		
0.01	2	1
1_{3s}		
0.00	2	1

Review of essential Six Sigma tools! How prepare Method Decision Chart?

- Define Allowable Total Error
  - HbA1c = 7.0% (2012 CAP TEa criterion)
- Scale graph
  - Y-axis from 0 to TEa
  - X-axis from 0 to TEa/2
- Draw lines for TE criteria
  - TE = Bias + M*SD

  If SD=0, then y-intercept = TE; If Bias=0, then x-intercept = TE/M

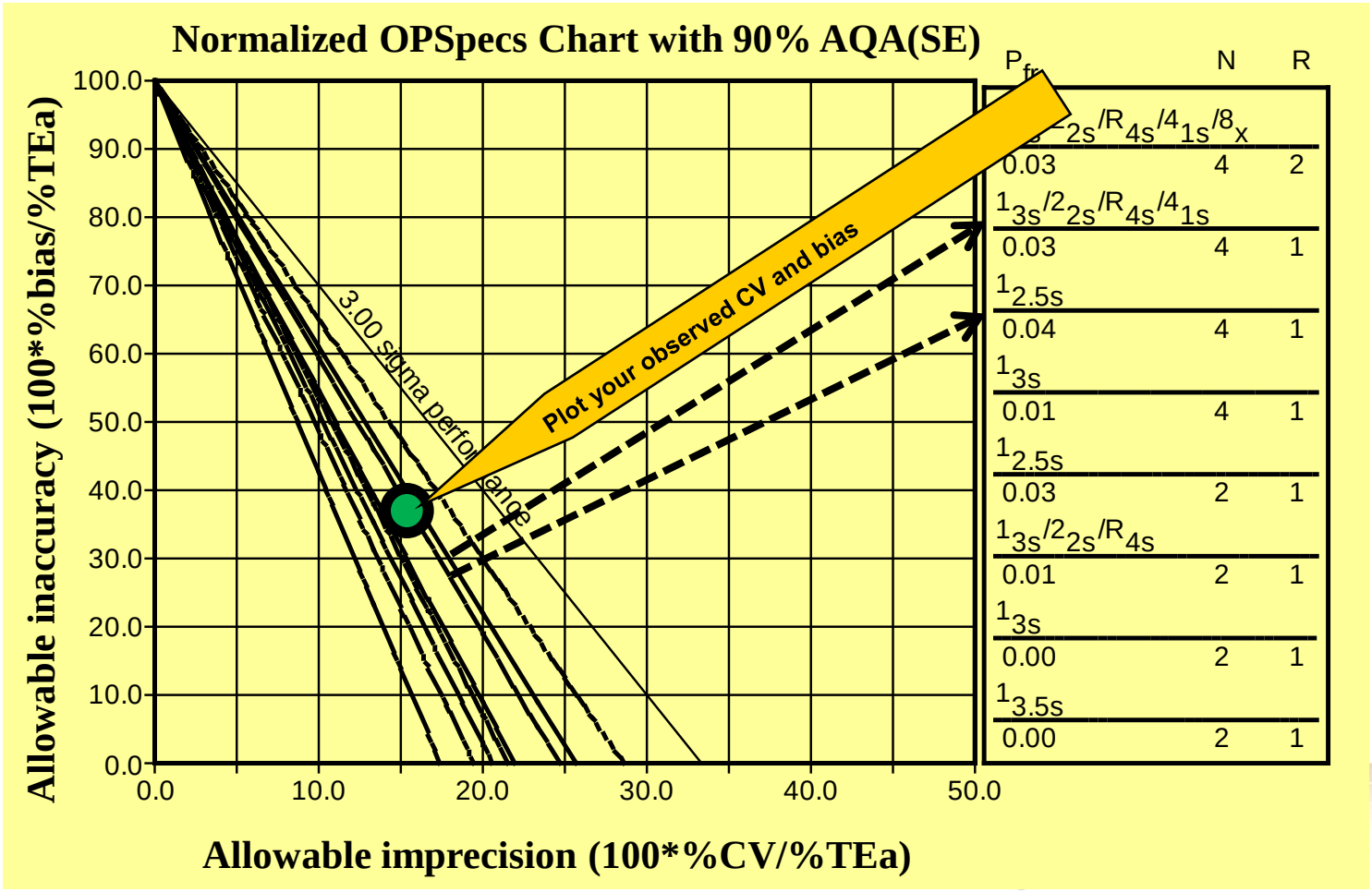
How prepare Method Decision Chart?
HbA1c: CAP TEa=7.0%



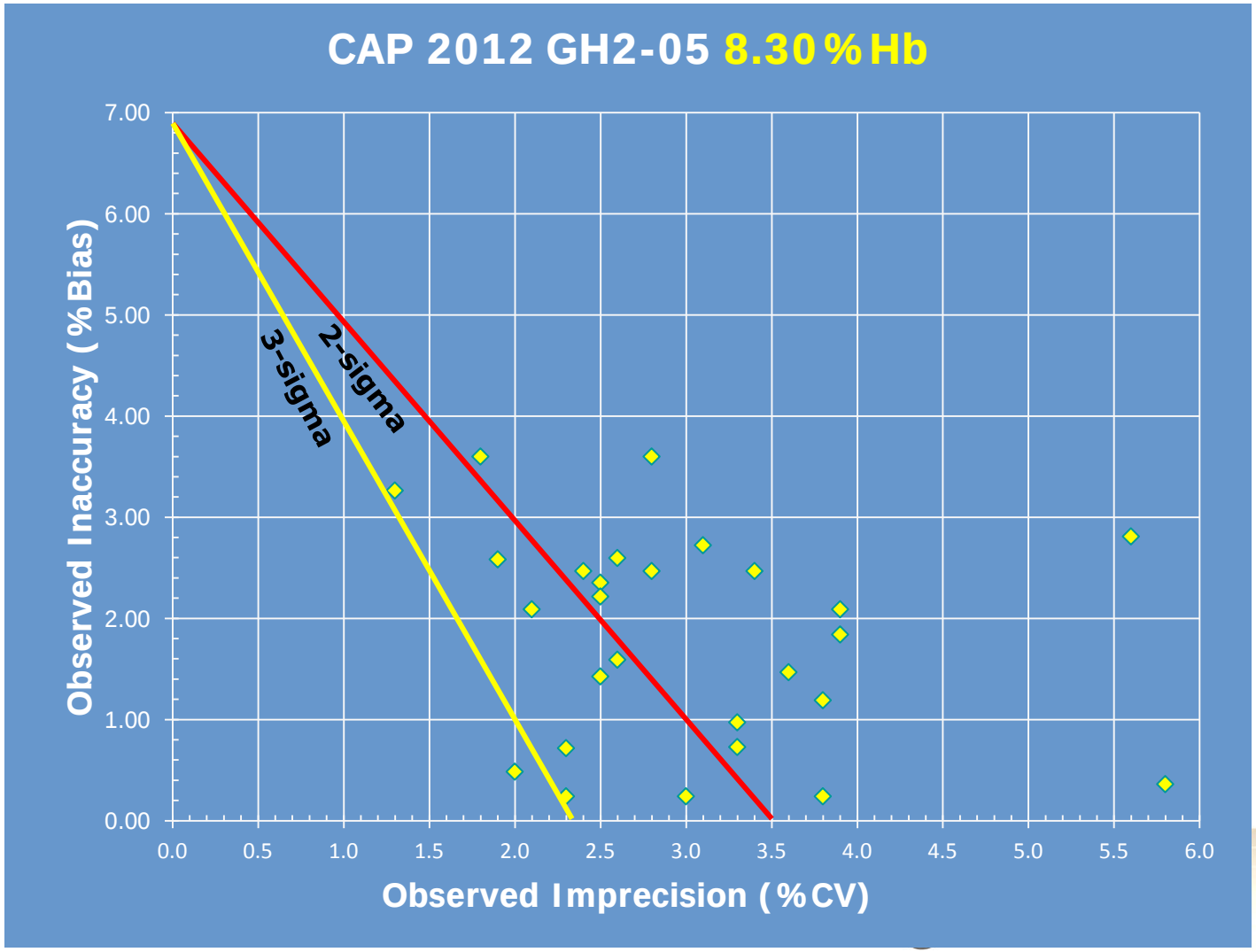
Normalized Method Decision and Operating Specifications Charts

- Scale y-axis 0 to 100%
  - Calculate y-coordinate as Bias/TE
- Scale x-axis 0 to 50%
  - Calculate x-coordinate as CV/TEa
- HbA1c example
  - Bias=2.56%, CV=1.11%
  - Y-coordinate would be 2.56/7.0 or 37%
  - X-coordinate would be 1.11/7.0 or 16%

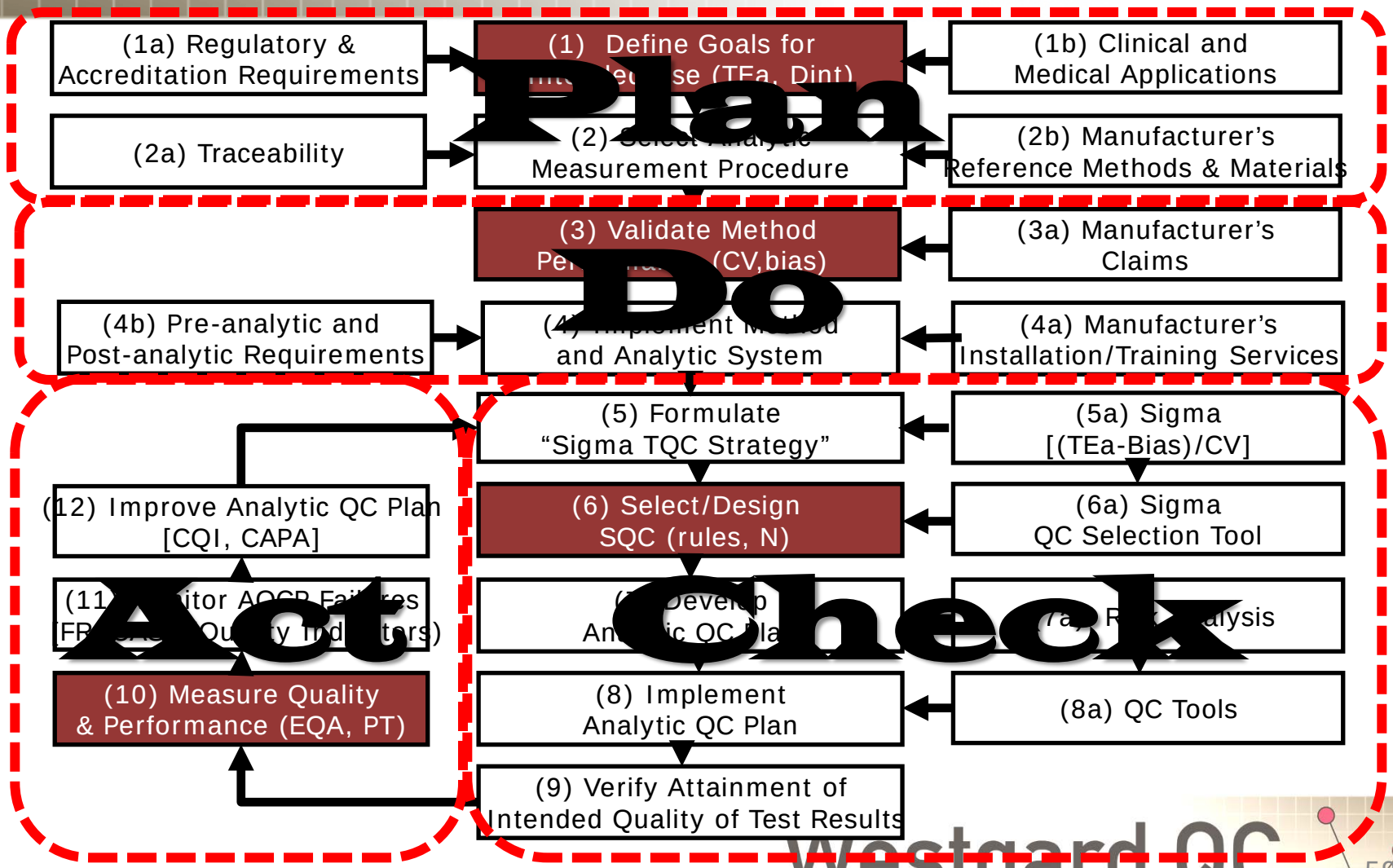
Normalized Chart of Operating Specifications (OPSpecs)



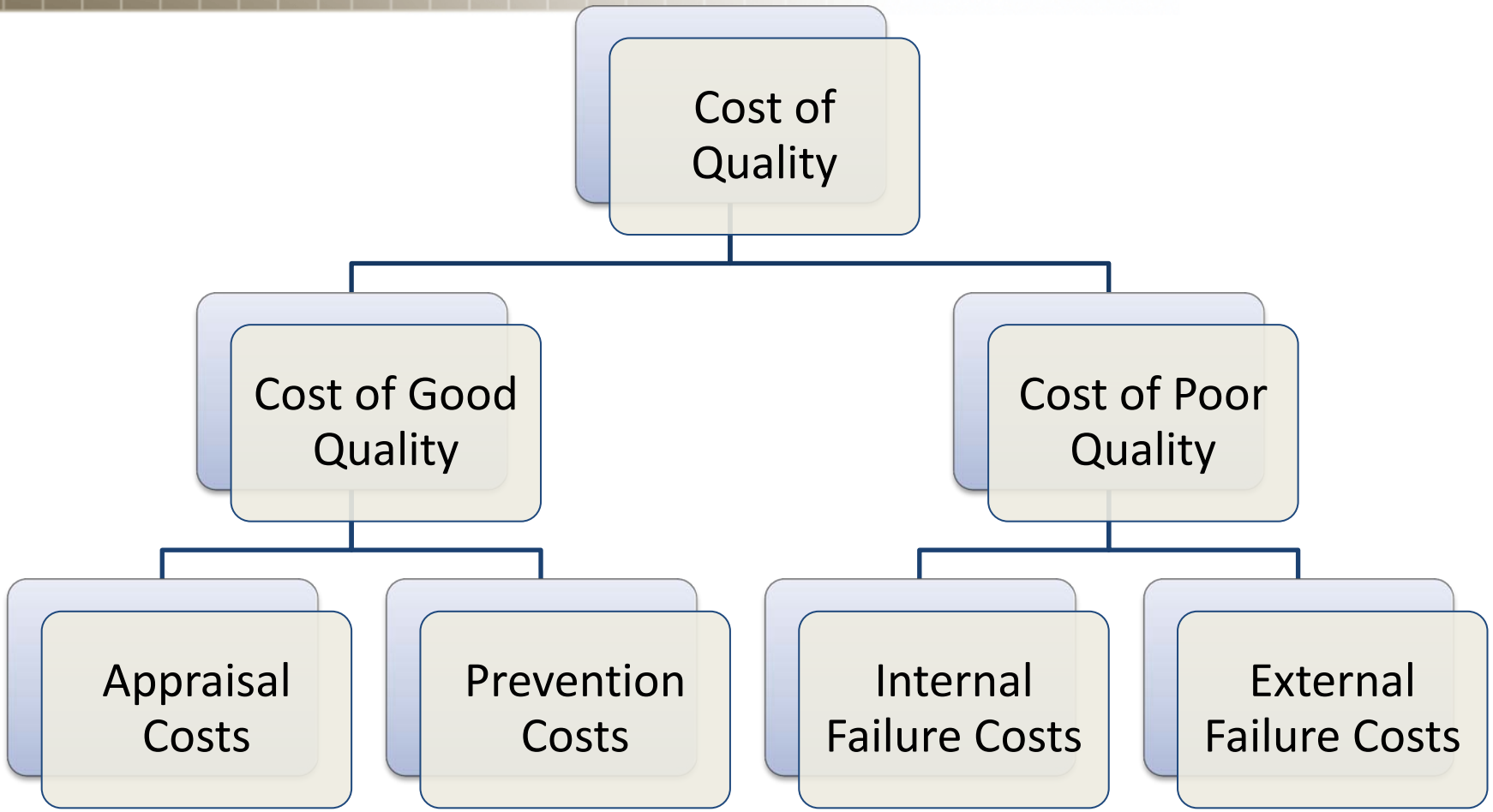
Sigma Proficiency Assessment



Six Sigma Quality System Getting Started!



What would be the benefits? Better efficiency, lower cost



Implications of Sigma-metric analysis: Quality Control

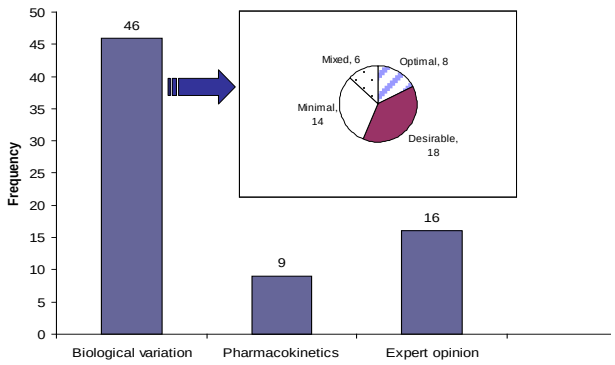
- Dramatic impact of **world class** performance
  - ***Less* QC Effort Needed?**
  - Fewer, maybe NO, repeated controls
  - Fewer Service Visits or Tech Support Calls
  - Fewer recalibrations, trouble-shooting episodes
  - Better compliance for PT, EQA, etc.

How do the savings manifest themselves?

2011 Leeds Health system
- 9 chemistry analyzers
- 7 immunoassay analyzers
- 71 analytes

50% reduction in recals

70% of analytes 4-6 Sigma



Original Article

The implementation of a system for managing analytical quality in networked laboratories

Nuthar Jassam[1], Chris Lindsay[2], Kevin Harrison[1], Douglas Thompson[1], Mike P Bosomworth[1] and Julian H Barth[1]

[1]Department of Clinical Biochemistry, Leeds General Infirmary, Leeds LS1 3EX; [2]Siemens Healthcare Diagnostics, Sir William Siemens Square, Surrey, UK
Corresponding author: Mrs Nuthar Jassam. Email: nuthar.jassam@hdtf.nhs.uk

Abstract

Background: In a network of laboratories analytical variability between instruments, even of the same type, may exist for reasons beyond the control of laboratory staff. Controlling variability is a prerequisite for the application of shared reference ranges and for ensuring the transferability of patient test results. Controlling variability requires a robust, non-conventional quality system to detect poor performance of analysers that are geographically distant. Essential to this quality system is a set of well-defined quality specifications.

Methods: The approach used in our study started with (1) selection of a model for quality specifications based on biological variation; the 'three-level model' (TLM) was selected on the basis of its flexibility to accommodate various levels of analytical performance; (2) determination of the performance characteristics of the 71 analytes measured in core biochemistry in terms of imprecision and bias; (3) defining quality requirements in the form of imprecision, bias and total error for 71 analytes measured routinely in core biochemistry; and (4) developing software to assist a consistent wide application of the quality specifications and to monitor analytical indices to the common quality specifications.

Results: In this paper we describe how we have implemented this model across our network. Forty-six of the 71 analytes in our core laboratory repertoire were allocated to the TLM. We were able to demonstrate equivalence of results on all analysers, for 42 out of 46 analytes allocated to this model.

Conclusions: We propose that other networked laboratories should investigate the suitability of this quality system for use in their network.

Ann Clin Biochem 2011; 48: 136–146. DOI: 10.1258/acb.2010.010005

How do the savings manifest themselves?

2 hospitals in Netherlands:
Implementing 2006 onward

5 tests simulated effect:
2 SD = 270 rejections
Redesign = 9 rejections

Reduction of 261 “repeats”

Reduction in control mtls

Est. €21,183.04 savings

	Level 1				Level 2			
	QC applied				QC applied			
Analyte	2SD	6S	Total QC's	difference	2SD	6S	Total QC's	difference
ALAT	42	1	400	41	93	5	404	88
GGT	6	0	395	6	6	1	408	5
Triglycerids	21	1	408	20	20	0	407	20
Urea	1	0	411	1	11	0	413	11
Total bilirubin	0	0	417	0	70	1	418	69
Total				68				193

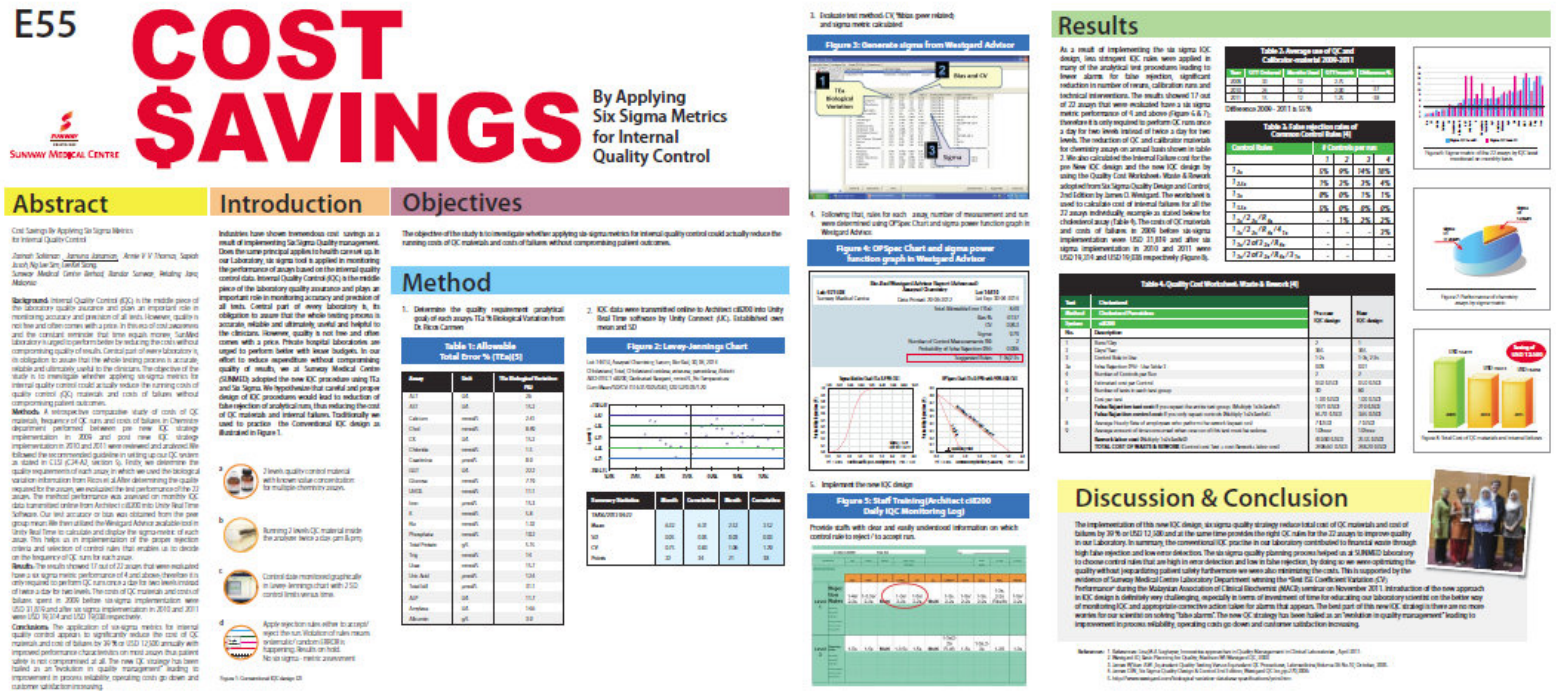
Counted for one analyser

Unnecessary reruns		261		
Average minutes/rerun		10		
Total time (minutes)		2610		
		44 hours		
Costs				
Salary/hour	€	19,96		
Salary costs			€	868,26
Average price/test	€	2,50		
Reagent costs			€	652,50
Total costs			€	1520,76
For 4 analysers				€ 6083,04
Savings on qc-material				€ 15100,00
Total savings				€ 21183,04

As the savings are calculated over only 5 analytes the real savings will be even higher.

http://www.westgard.com/saving-with-six-sigma.htm

How do the savings manifest themselves?


E55

COST $AVINGS

By Applying Six Sigma Metrics for Internal Quality Control

SUNWAY MEDICAL CENTRE

Abstract

Introduction

Objectives

Method

Results

Discussion & Conclusion

- 2012 AACC poster, Sunway Medical Centre, Thailand
- Reduced use of QC and calibrator material by 38% (2011)
- Savings of over $19,000 USD in 2010 and 2011 (failure costs reduced)

Sigma-metric Quality System

Dr. Joseph Litten,
Industry Workshop
Applications of Sigma-metrics

Estimated Sigma-metrics of prospective vendors using vendor data and CAP surveys

Calculated actual Sigma-metrics of analytes
(30 shown)

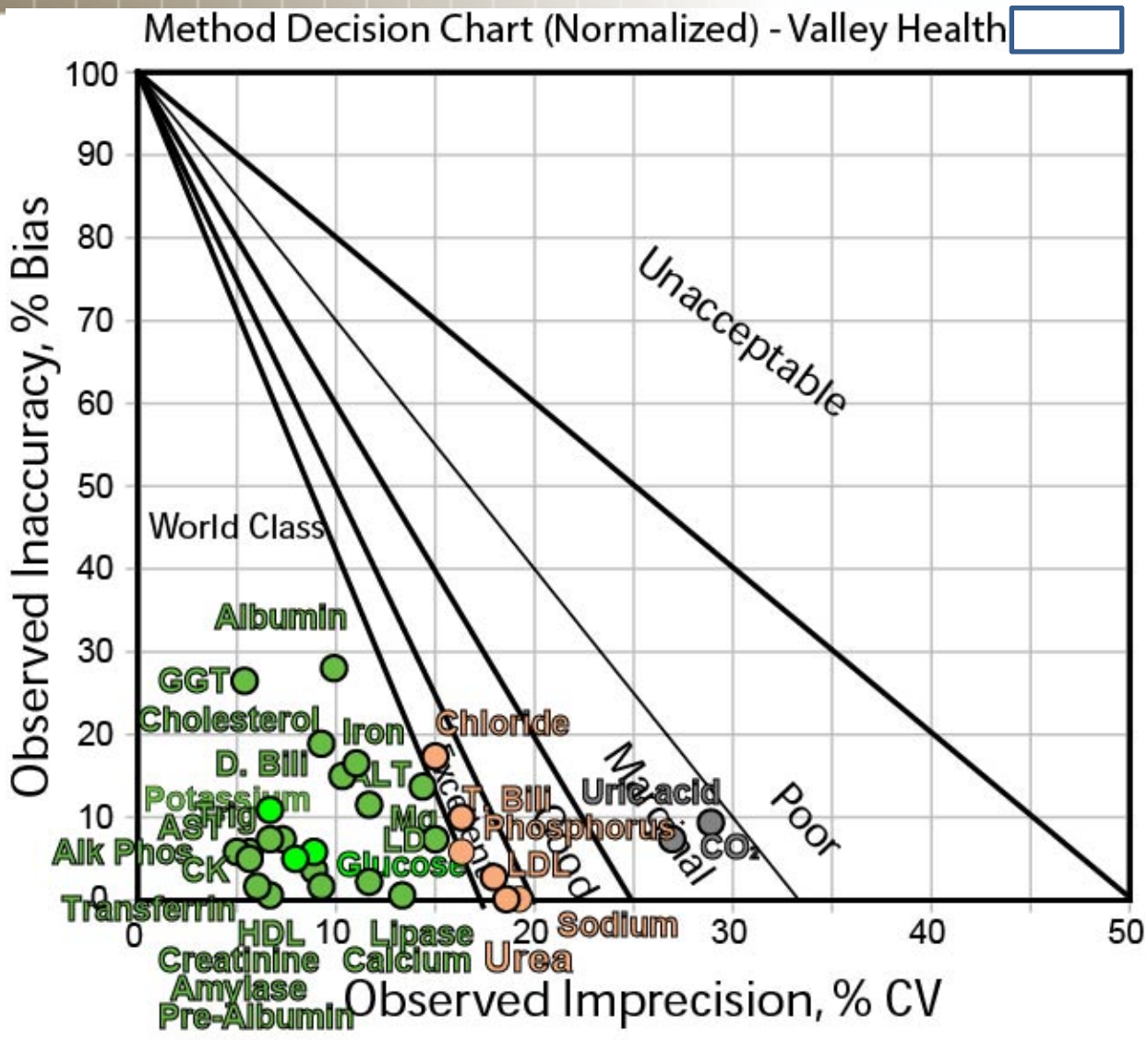
ValleyHealth
Winchester Medical Center

Summary of Sigma Metric Estimations – 30 Chemistry Tests using CLIA goals

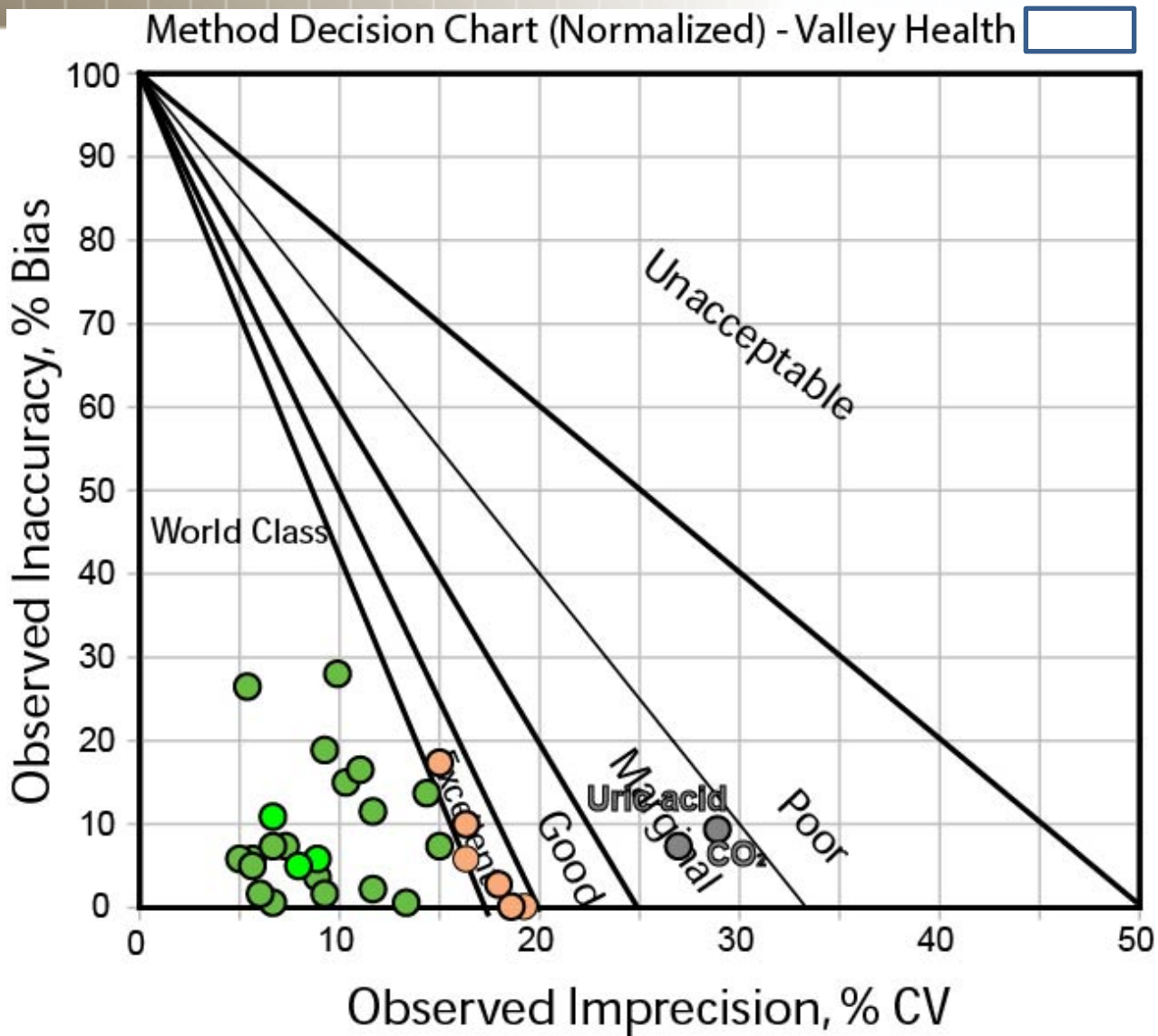
	Sigma Metric				
Vendor	***>6.0***	***5.0***	***4.0***	***3.0***	***<3.0***
Vendor 1	**53%**	20%	13%	13%	**0%**
Vendor 2	45%	14%	17%	10%	14%
Vendor 3	23%	30%	17%	27%	3%
Vendor 4	30%	13%	13%	30%	13%
Vendor 5	50%	0%	17%	20%	13%
Vendor 6	30%	13%	20%	20%	17%

Westgard QC

Valley Health MEDx



Valley Health MEDx

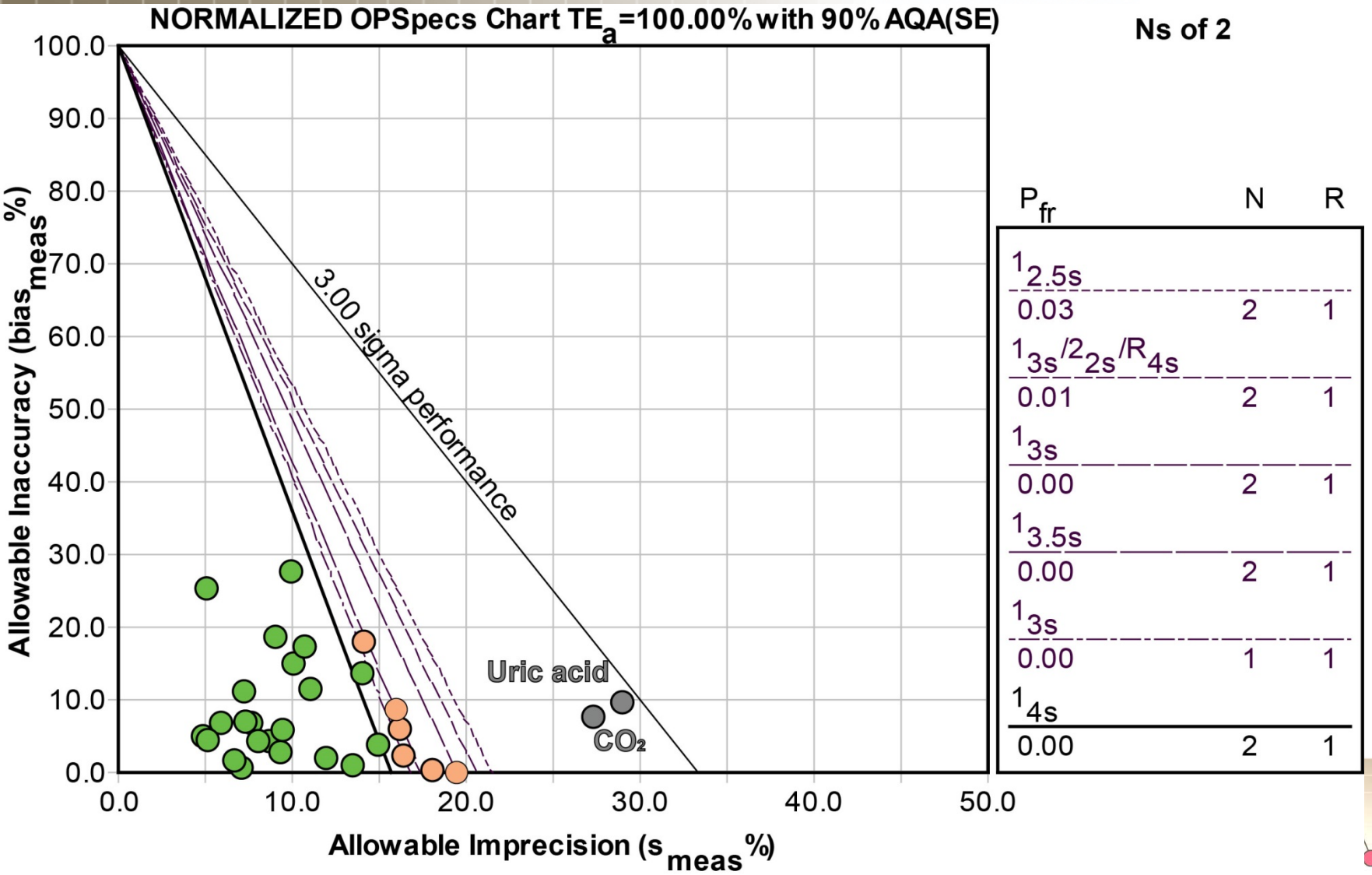


Dr. Litten:

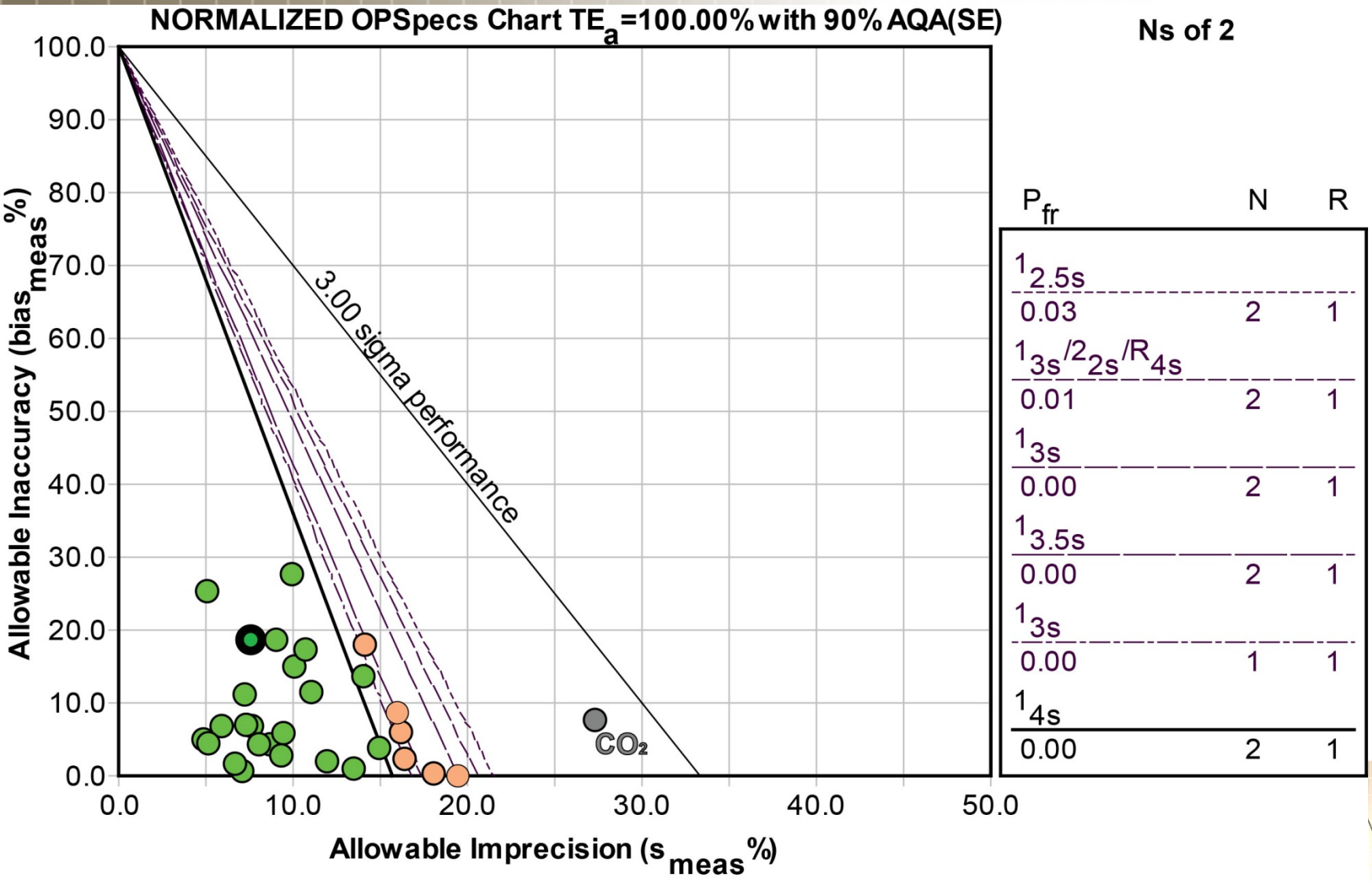
93% of analytes were above 5 Sigma

None were below 3 Sigma

OPSpecs: Valley Health



OPSpecs: Valley Health



P_{fr}	N	R
$1_{2.5s}$		
0.03	2	1
$1_{3s}/2_{2s}/R_{4s}$		
0.01	2	1
1_{3s}		
0.00	2	1
$1_{3.5s}$		
0.00	2	1
1_{3s}		
0.00	1	1
1_{4s}		
0.00	2	1

Savings from Changes in Quality Control Program

- Reagent and Supplies
  - Approximately 45% savings in reagents and supplies for running controls
    - Chemistry: $8,000 savings
    - Cardiac Markers: $55,000 savings
- Control Material Savings
  - Approximately 45% savings in control material
    - Approximately $10,000 annual savings

Savings from Changes in Quality Control Program

- Labor Savings
  - Savings from running QC q12 hour versus q8 hour
    - ~$11,000 per year (1 hour per day) 0.175 FTE
  - Less investigation of QC failures
    - Over 40% fewer QC failures to investigate

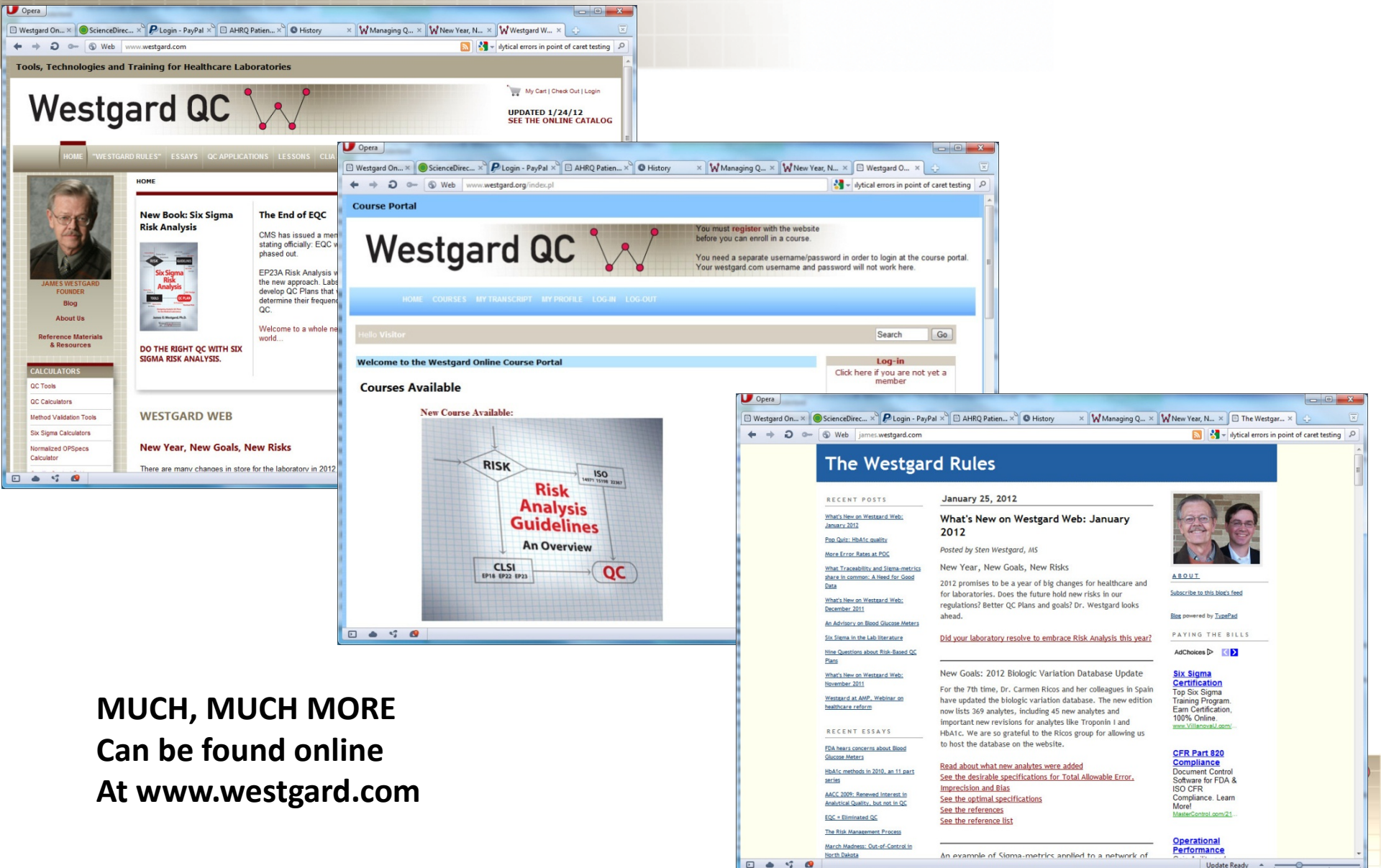
Conclusion:

- High Quality is a Triple Win!
  - Easier for the lab
  - Cheaper for the health system
  - Better for the patients

- *Assess* and *Assure* with Sigma metrics, MEDx charts **so you have the right method/instrument**

- Optimize QC and performance with OPSpecs charts **so you have the right QC**

Merci! (Questions?)



MUCH, MUCH MORE
Can be found online
At www.westgard.com