CIRME

11th International Scientific Meeting

MEASUREMENT UNCERTAINTY IN MEDICAL LABORATORIES: FRIEND OR FOE?

The value-assignment protocol for commercial calibrators:

How to Ensure Suitable Quality of Clinical Measurements

November 30th, 2017

Tony Orzechowski

Abbott Diagnostics

Director, R&D Quality Engineering, Statistics and Data Analytics

Presenter Biography

Tony Orzechowski (Orz - e - kow - ski)

Tony has over 30 years of experience in the development and application of **data analytics, statistics and quality improvement** methods in **manufacturing** and **product development**.

He received a mechanical engineering undergraduate and a manufacturing systems engineering master's degree from the University of Wisconsin - Madison. He is also a certified Lean Six Sigma Master Black Belt.

He is currently the Director of R&D Quality Engineering, Statistics and Data Analytics at Abbott Diagnostics where he has been responsible for managing the **reliability, predictive maintenance, specification development, statistical analysis, advanced data analytics and quality engineering** activities for the launch and support of new products and systems worldwide. He also currently serves as an adjunct professor at Northwestern University where he teaches the use of statistical quality improvement methods in new product development for the Master of Product Design and Development Management program.

The Essential Question …

"What amount of medical harm due to analytical error is it OK to let go undetected?"

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My personal translation
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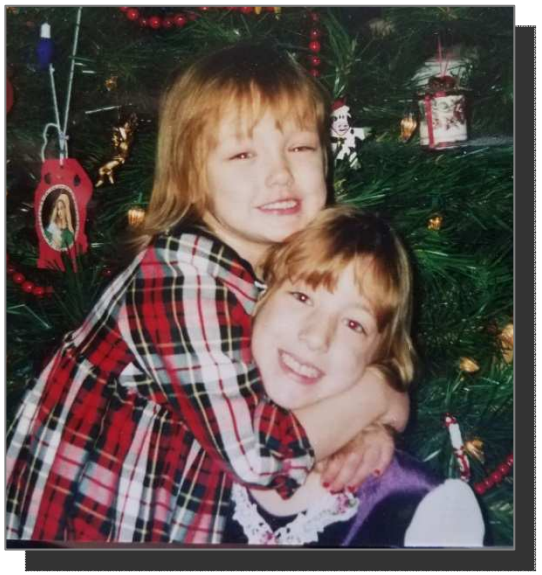
*"What amount of medical harm due to analytical error is acceptable **for me** to let go undetected when testing is done **on my girls**?"*



Agenda

Ensure Suitable Quality of Clinical Measurements

Guiding Principles

Relating Product Development Design Requirements to the Essential Question and Total Analytical Error

Control of Analytical Error

- **Design Requirements** – Allocation of Total Allowable Error
- **Design Control** – Control of Calibrator and Calibration Error by Design
- **Production Testing and Field Monitoring** – Delivering the Right Design over Time

Summary

Guiding Principles

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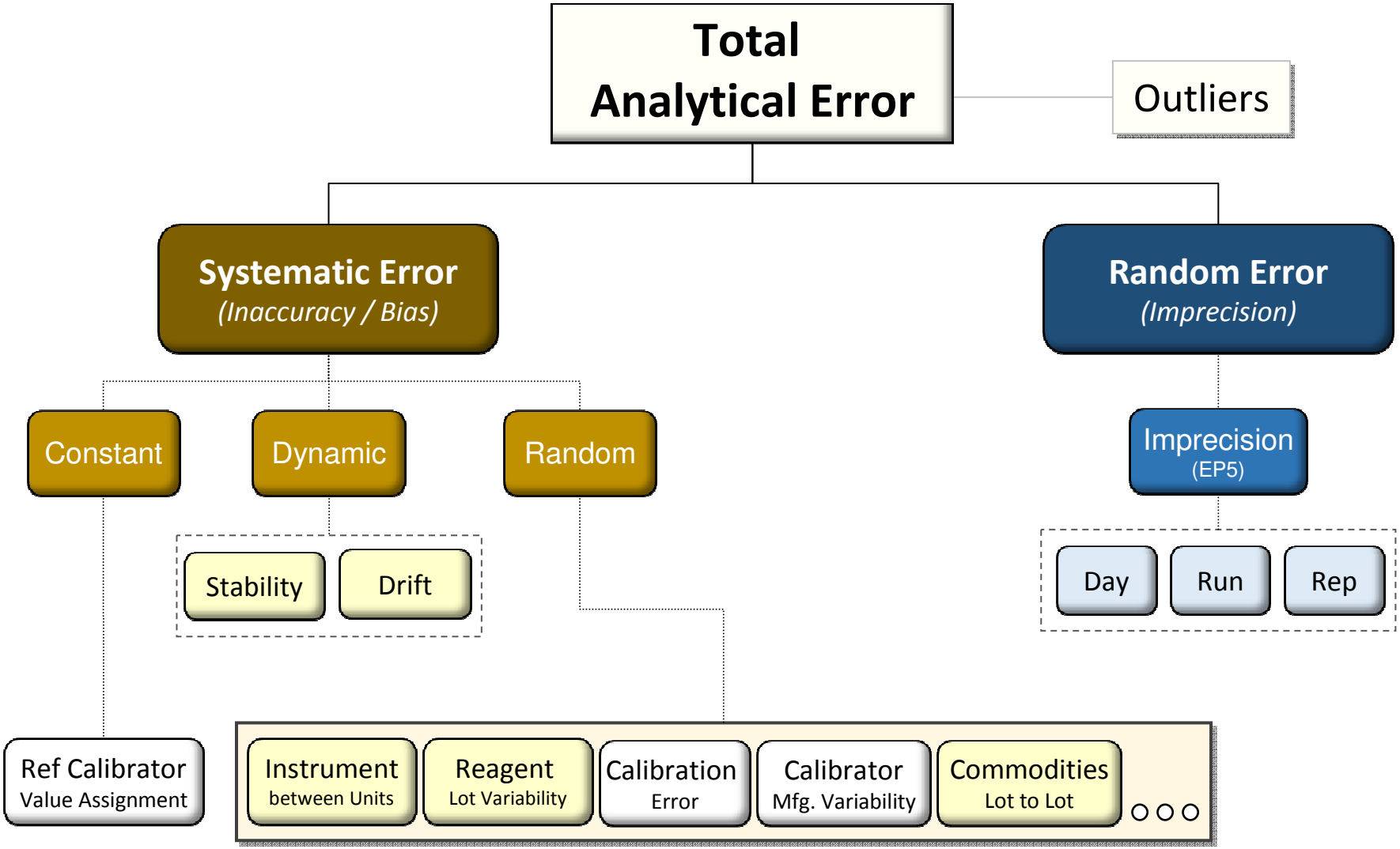
Sources of Analytical Error

All Key sources of Total Analytical Error Must be understood and addressed during System Design and Development

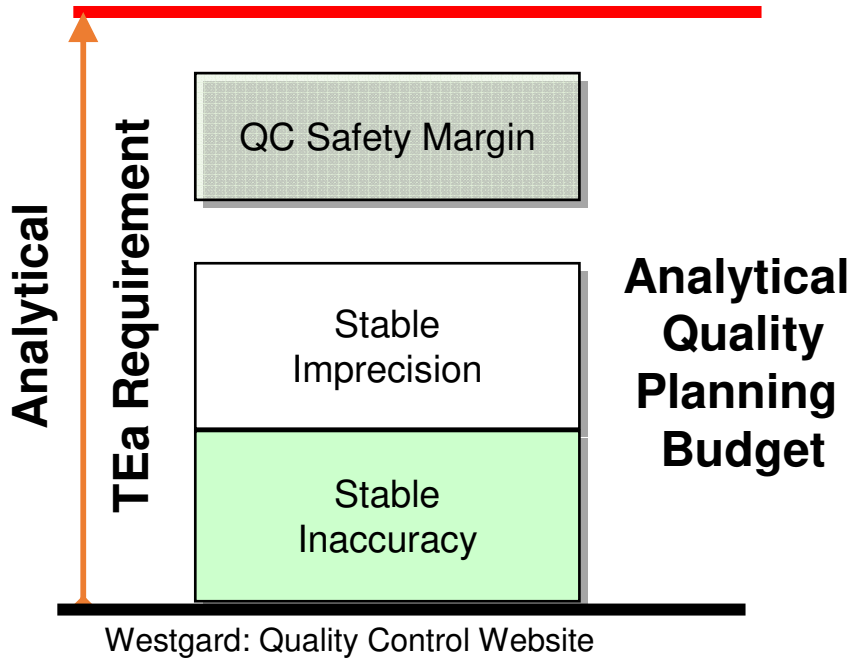


Translating TEa into Design Requirements

Error budgeting a Total Allowable Error (TEa) Design Input is a key foundation to building effective design specifications

Design Objectives:

- Will the design meet requirements?
- With what confidence?
- How robust is the product over time?



Westgard: Quality Control Website

Error Budgeting of TEa

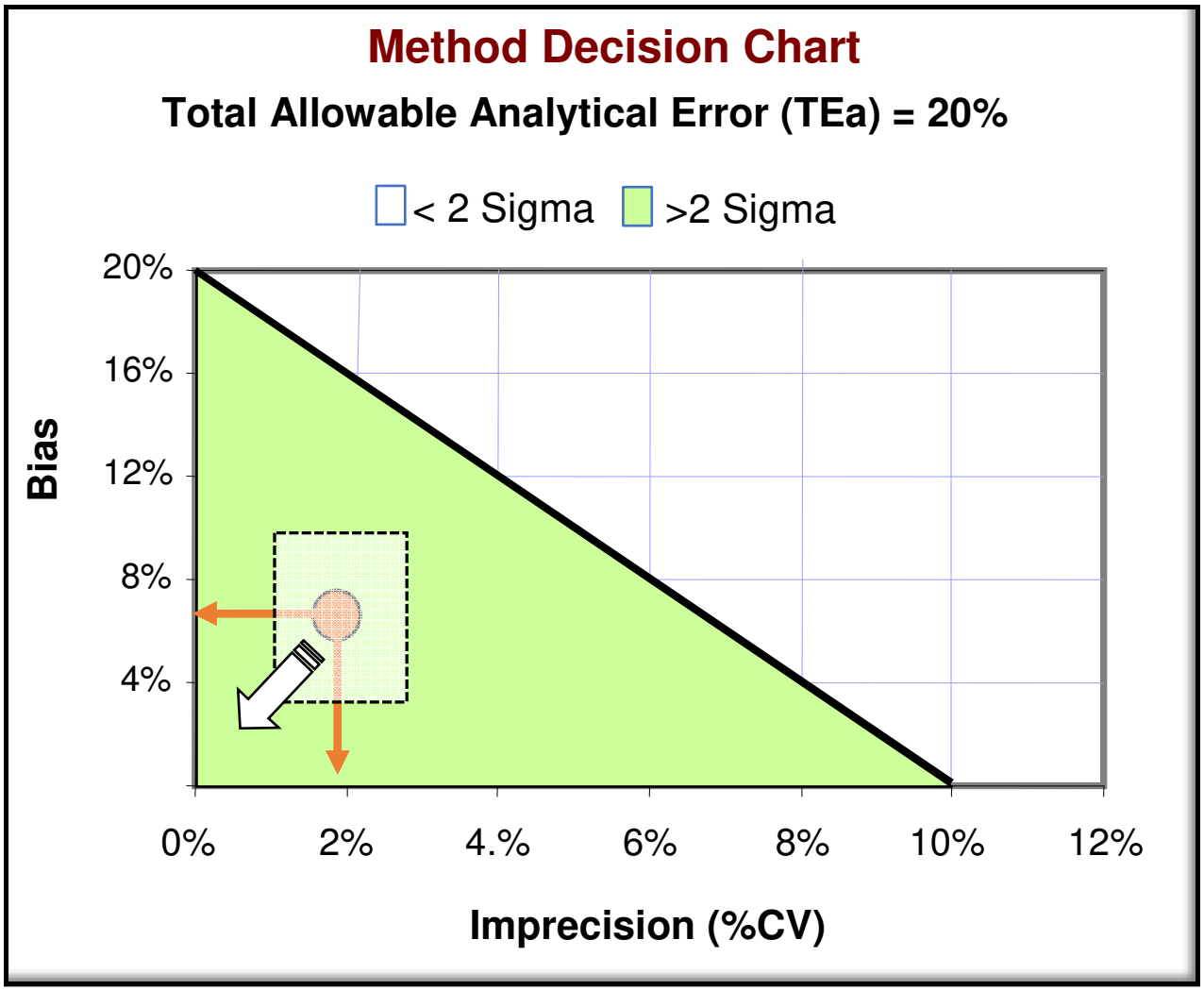
Translates the TEa requirements into lower level component specifications.

It realistically accounts for sources of error in the system design and the allocations that set the foundation of the product design specifications.

Instrument and Assay Design and Process specs are established to maintain this budget over time.

Method Decision Chart

Evaluating the Analytical System relative to Medical Utility Guides Our Development Efforts

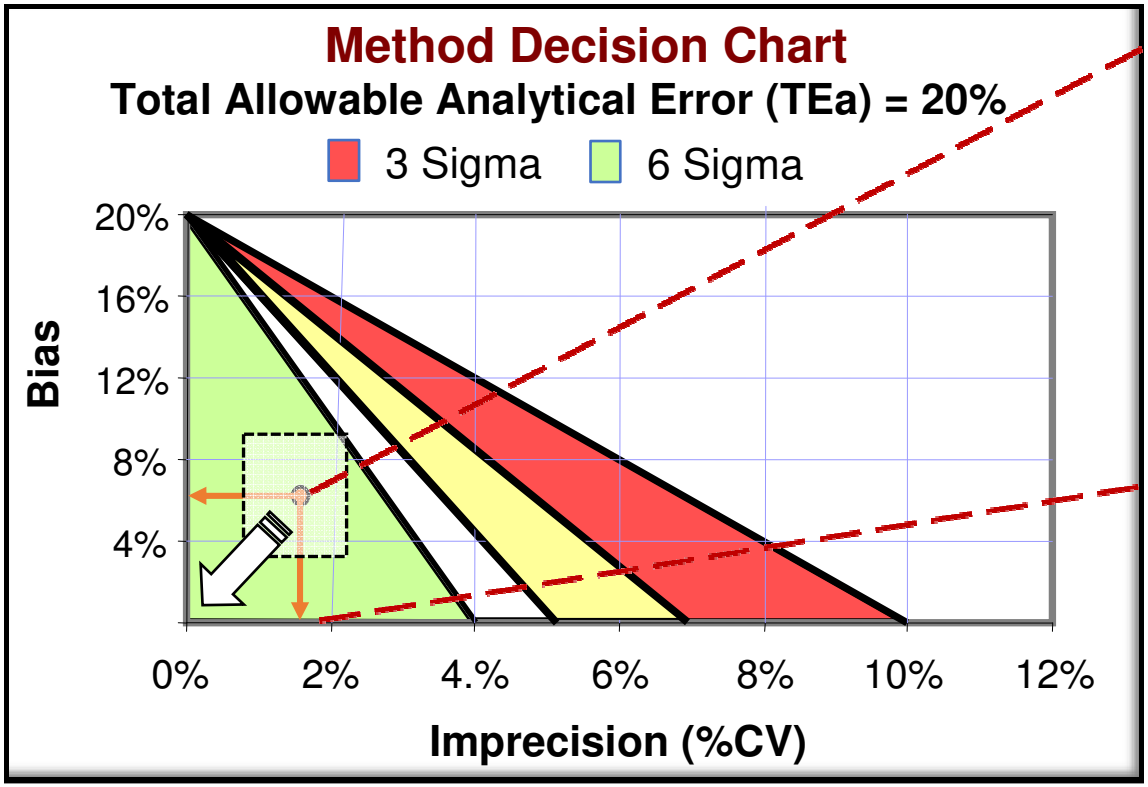


Westgard: Six Sigma and Quality Control

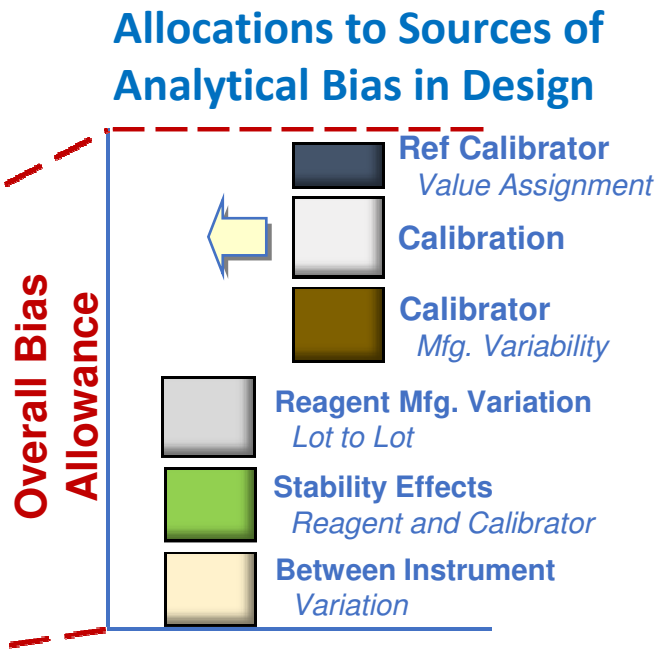
Method Decision Chart

Evaluating the Analytical System relative to Medical Utility Guides Our Development Efforts

$$\text{Sigma Value} = (TE_a - BIAS_a) / (\%CV_a)$$



Westgard: Quality Control

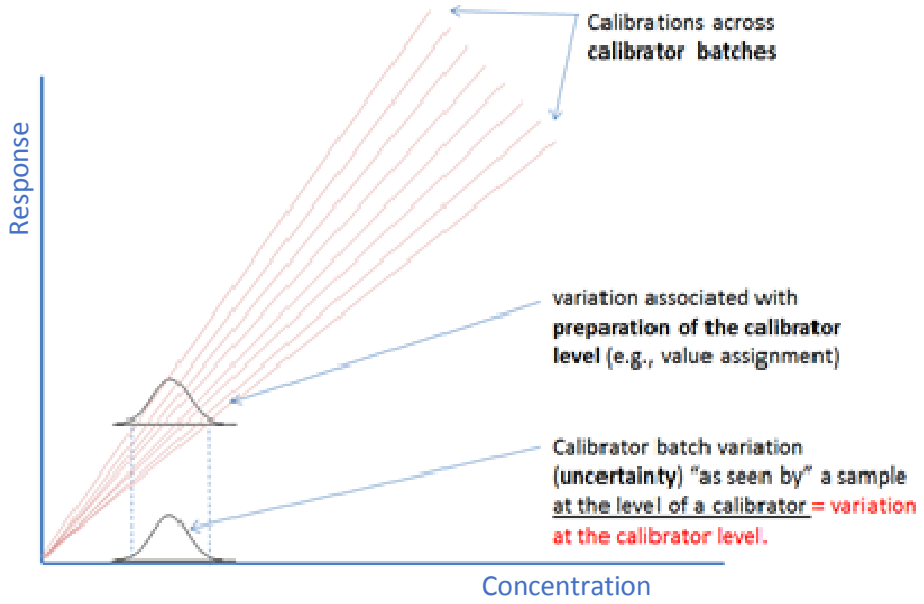


To target 6 Sigma Performance, we allocate maximum bias levels for each of the drivers of analytical bias

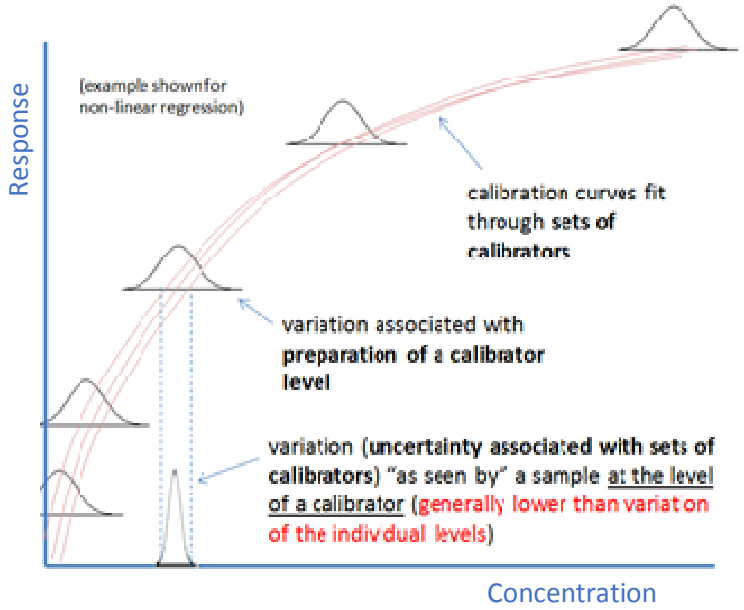
Calibrator's Role in Error Transmission

The calibrator set is the foundation for establishing the dose-response curve and allows us to report a consistent results for patient specimens under varying conditions

Single Point Calibration



Multi-Point Calibration



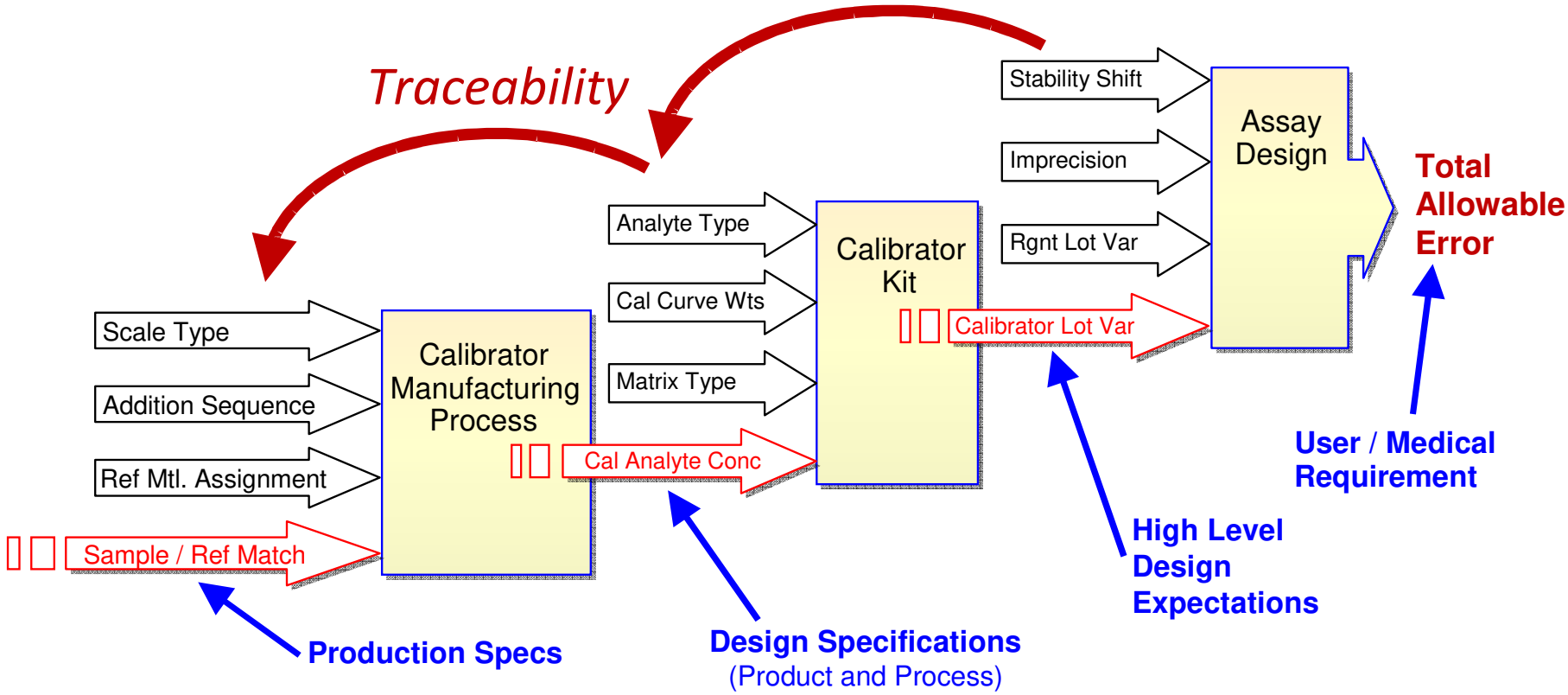
We rely upon calibration to tune out differences in the dose-response curve due to:

- **variation in reagent potency** due to the manufacturing process
- change in reagent potency over the **shelf life** of the reagent
- differences in **instruments** (optics, etc.)

Translating Requirements into Specs

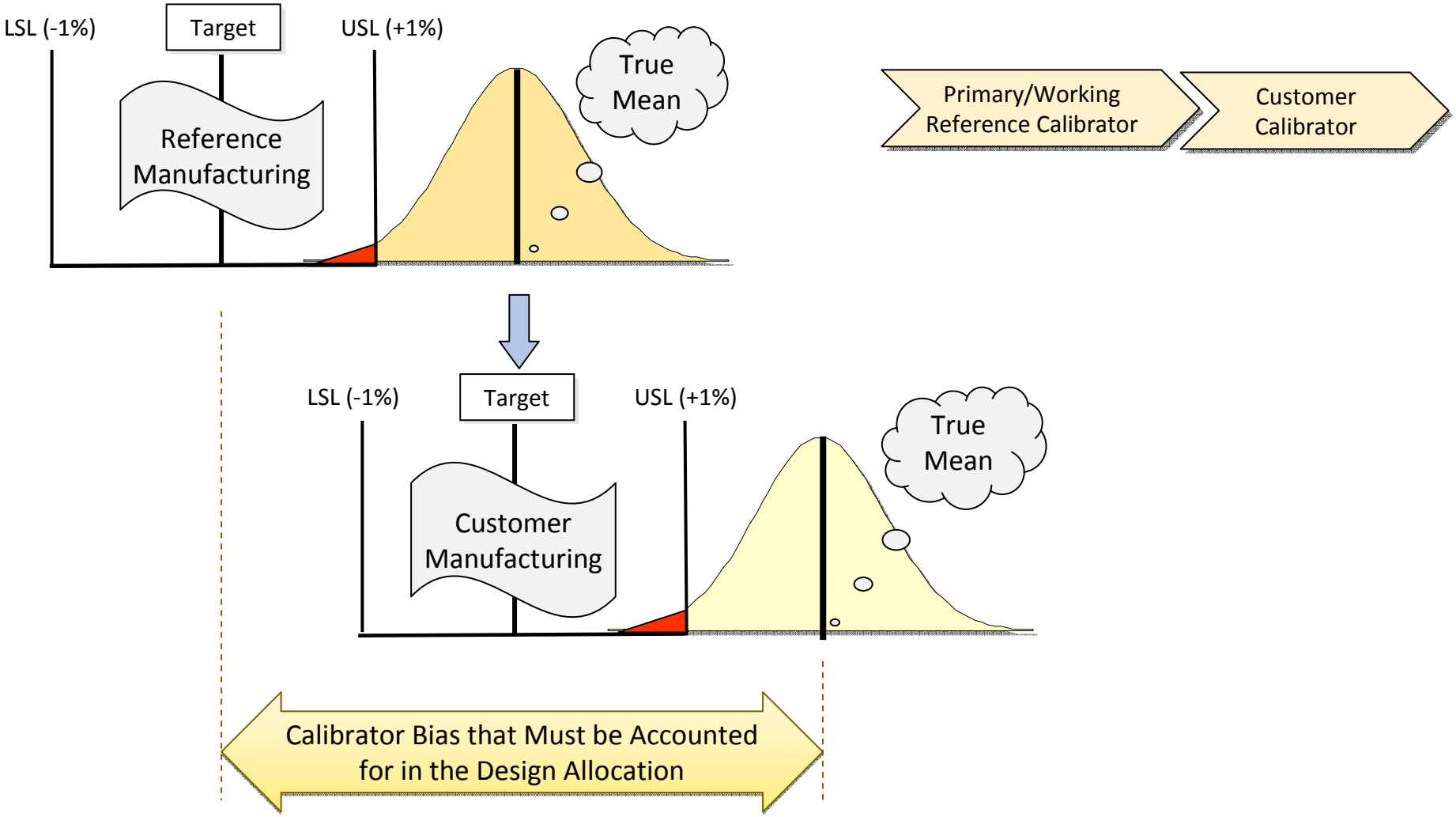
The role of R&D Scientists and Engineers is to identify the relationships in the translation process and design a robust product with this knowledge

Calibrator Design

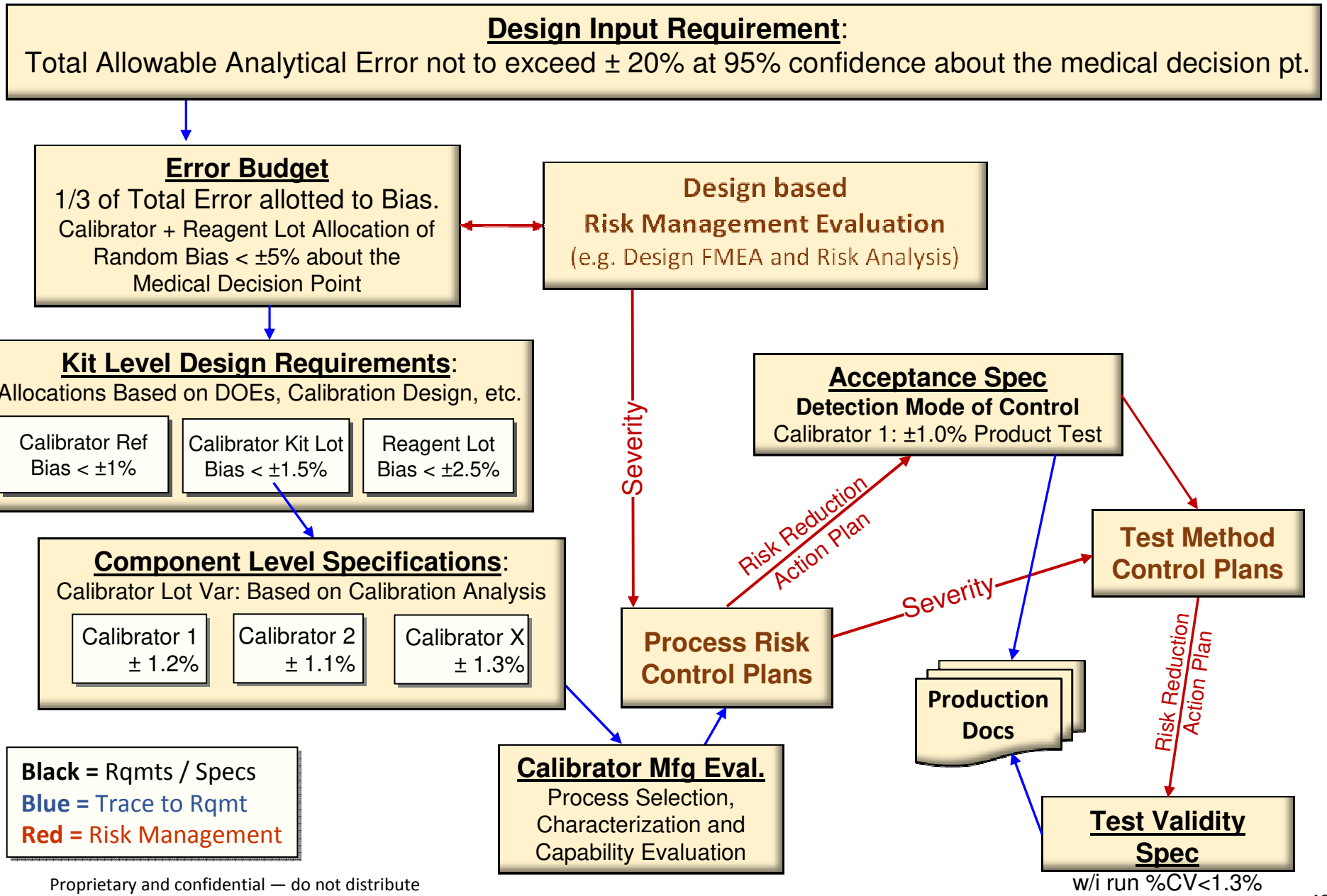


Calibrator Manufacturing

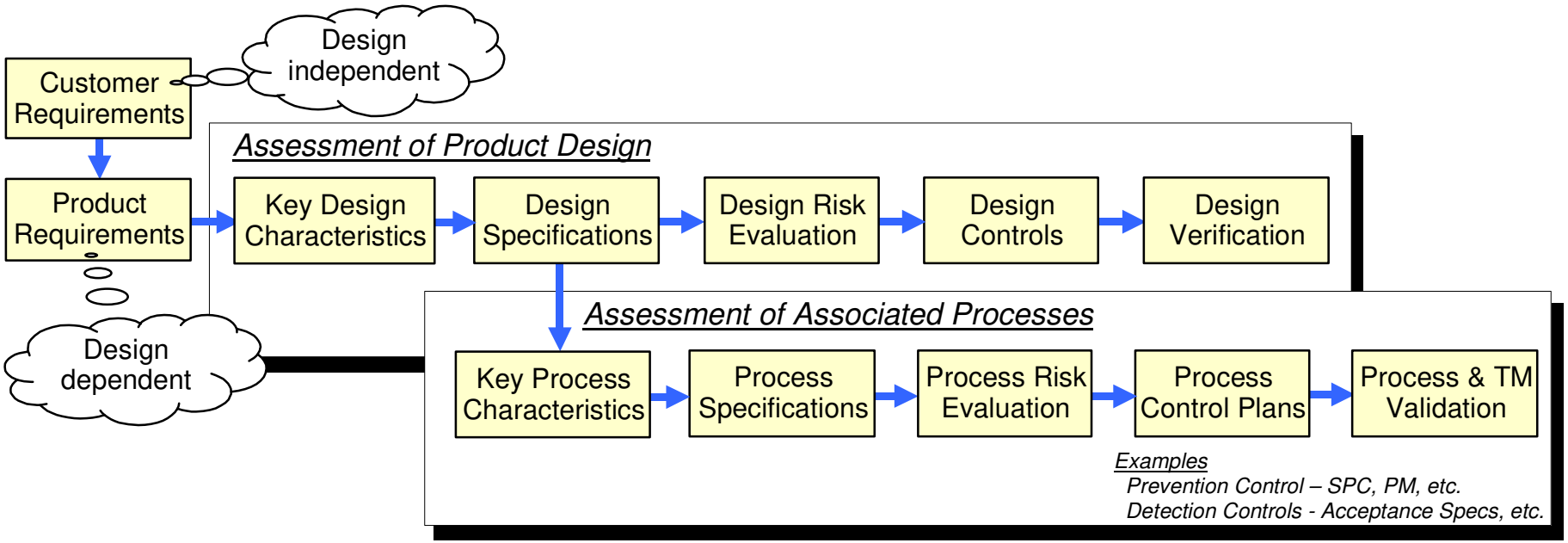
Uncertainty in the true value of a calibrator due to manufacturing or testing error in the Working Reference must be accounted for in impact to materials customer receive.



Translating Rqmts into Specs: IA Calibrator Example



Translation of Requirements into Production Specifications



Requirement: *Documented functions, conditions or capabilities that a medical device or process must meet to satisfy a user's needs, standards, or regulatory expectations*[1].

Specification: *Any requirement with which a product, process, service or other activity must conform.*[2]

FDA Guidance on Design Control

"Design controls are an interrelated set of practices and procedures that are incorporated into the design and development process, i.e., a system of checks and balances."

Calibration Robustness Study Overview

R&D Quality Engineering

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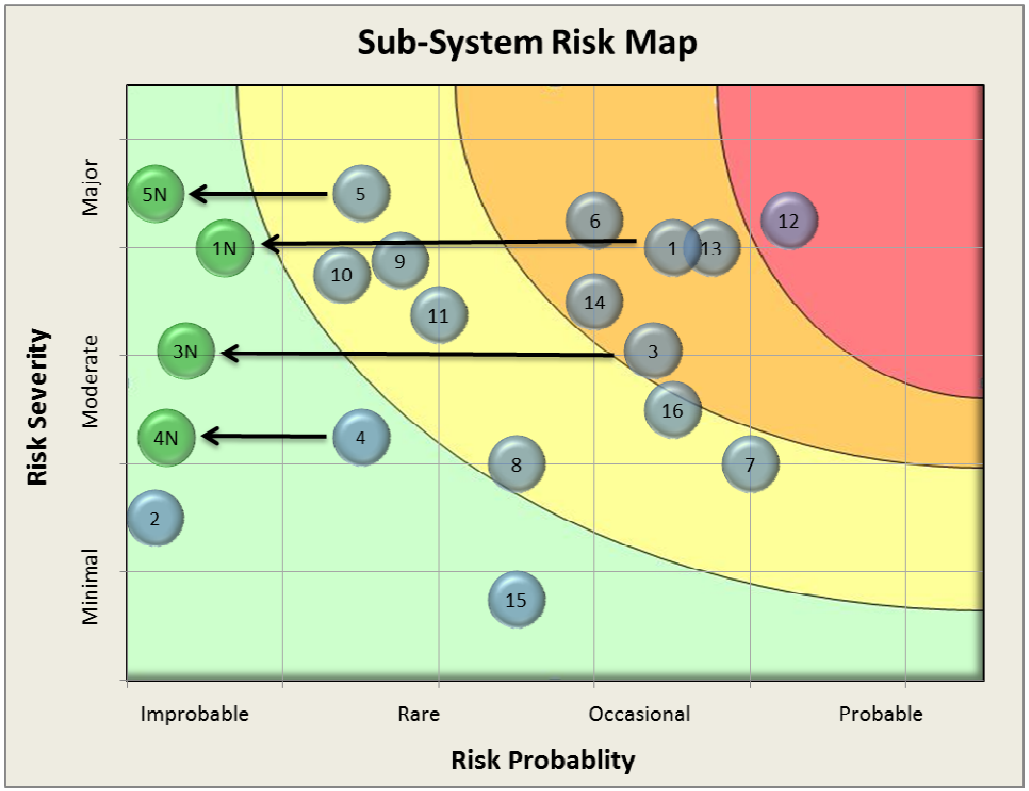
Technical Risk Map and Risk Reduction Process

Tracking and understanding technical risks critical to successful system development.
Rigorous technical risk management standard practice including risk reduction tracking.

Early Feasibility Phase
Risk Mapping and Control



Risk Identification

Tracking and understanding technical risks critical to successful system development.

Risk Monitoring and Control

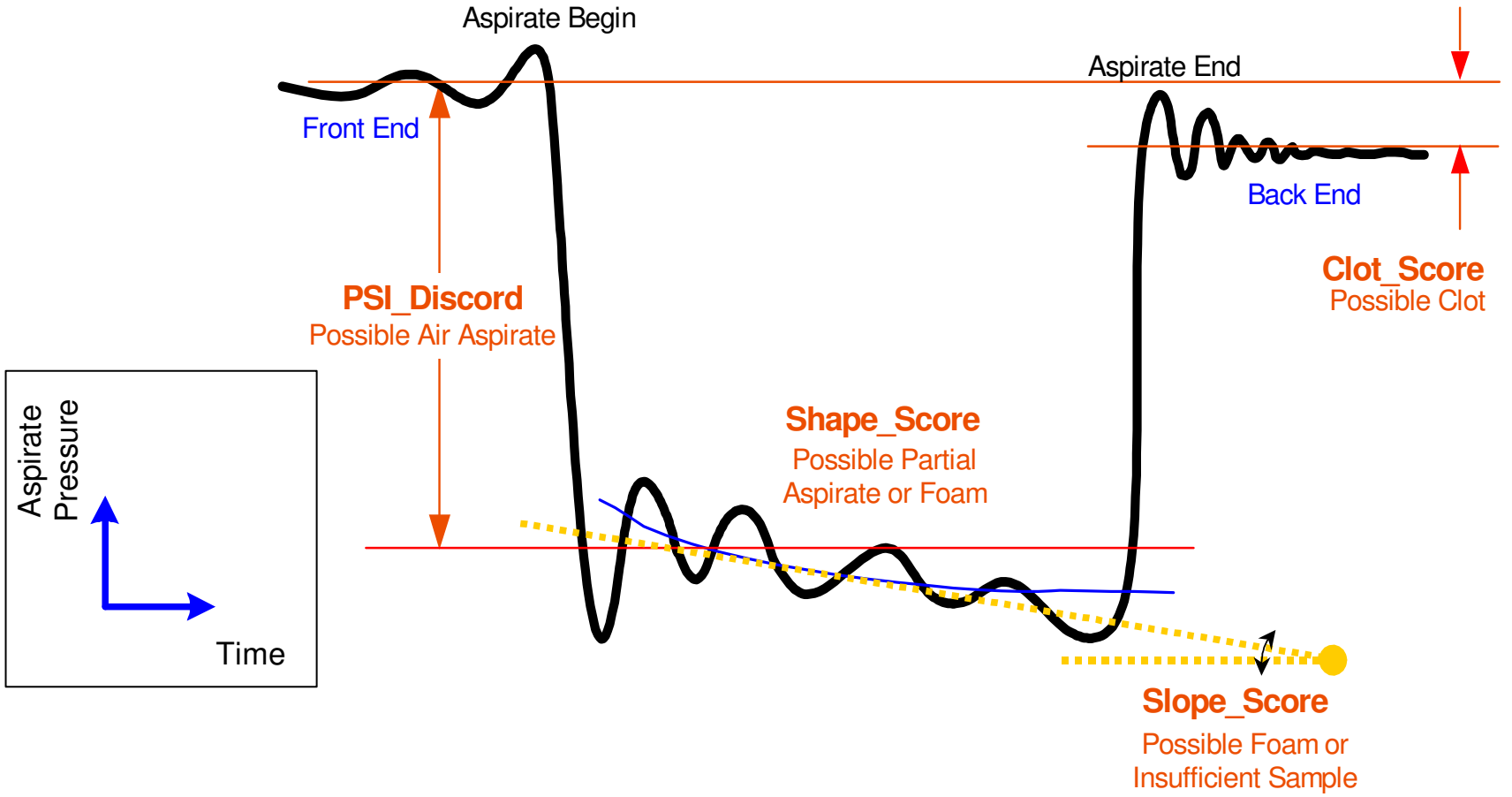
Rigorous technical risk management standard practice including risk reduction tracking.

A typical Risk Analysis may assess >1,000 potential risks and associated controls

Proactive Control of Quality – Example Pressure Monitoring

Detection of abnormal pressure profiles due to various induced failure modes

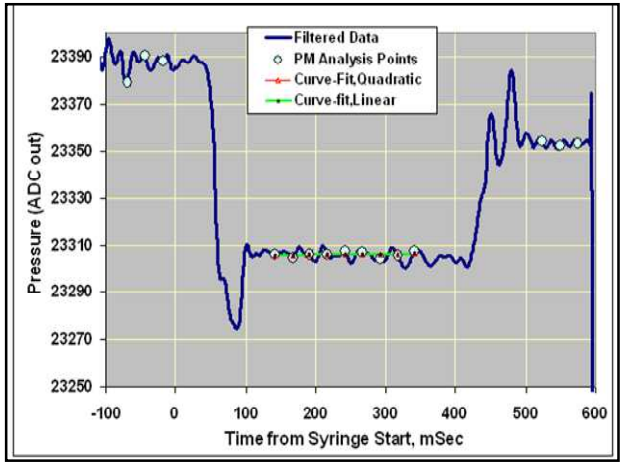
Evaluation of Aspirate Profile



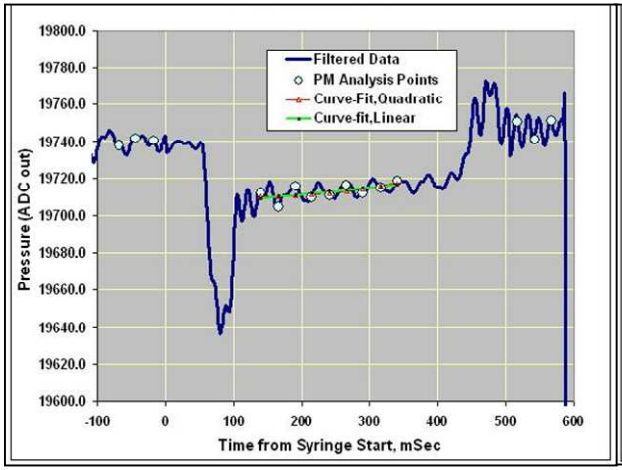
Proactive Control of Quality – Example Pressure Monitoring

Detection of abnormal pressure profiles due to various induced failure modes

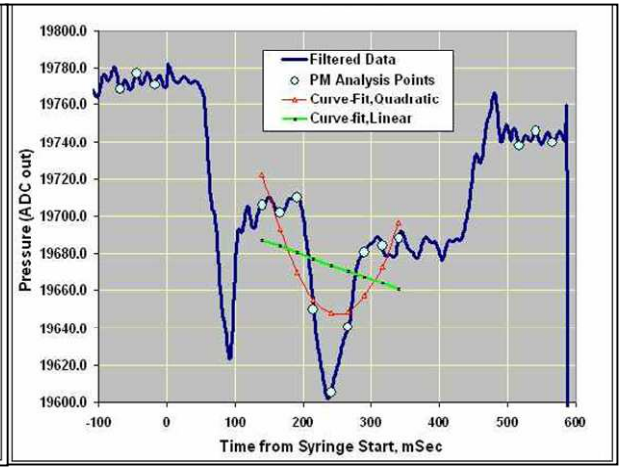
Aspiration Fault Types – Pressure Monitoring Profiles



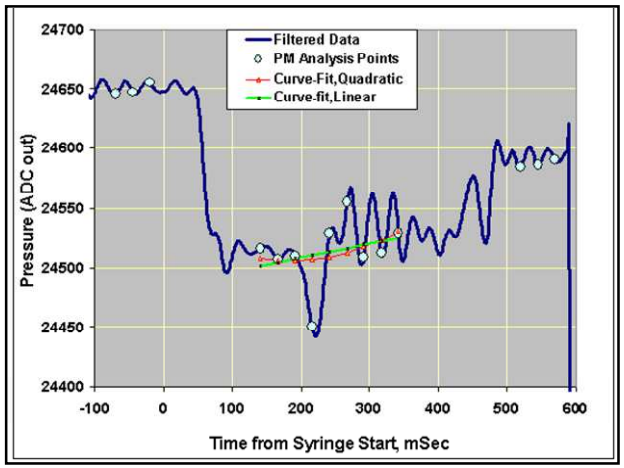
Normal



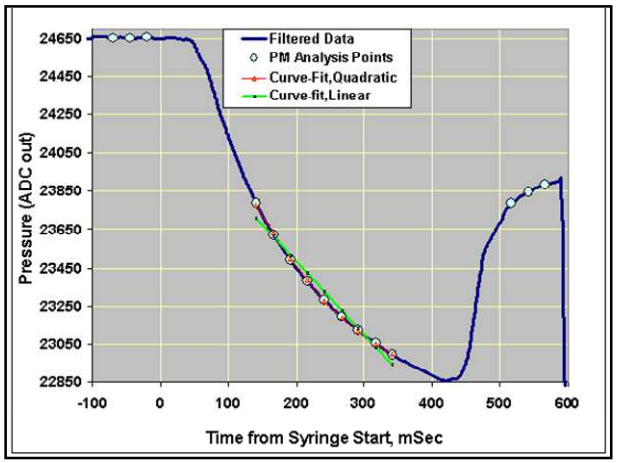
Air/Large Bubble



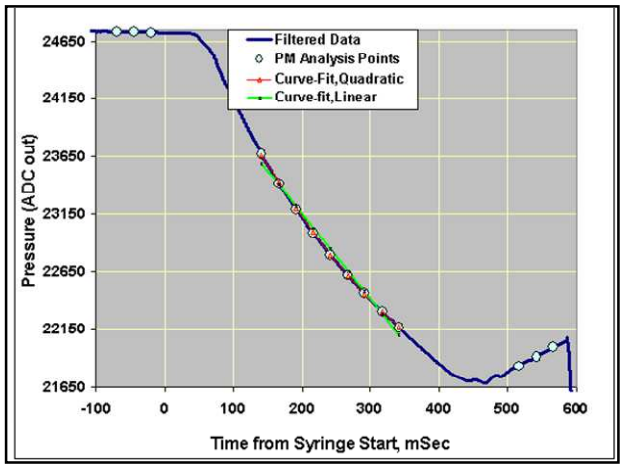
Foam



Insufficient Sample



Soft Clot



Clot/Viscous Sample

What this Means to Our Customers and to Patients

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More Accurate Results for Our Patients and Less issues with Calibration and QC for Our Laboratory Customers

Performance – Best In Class Performance of Products through Design

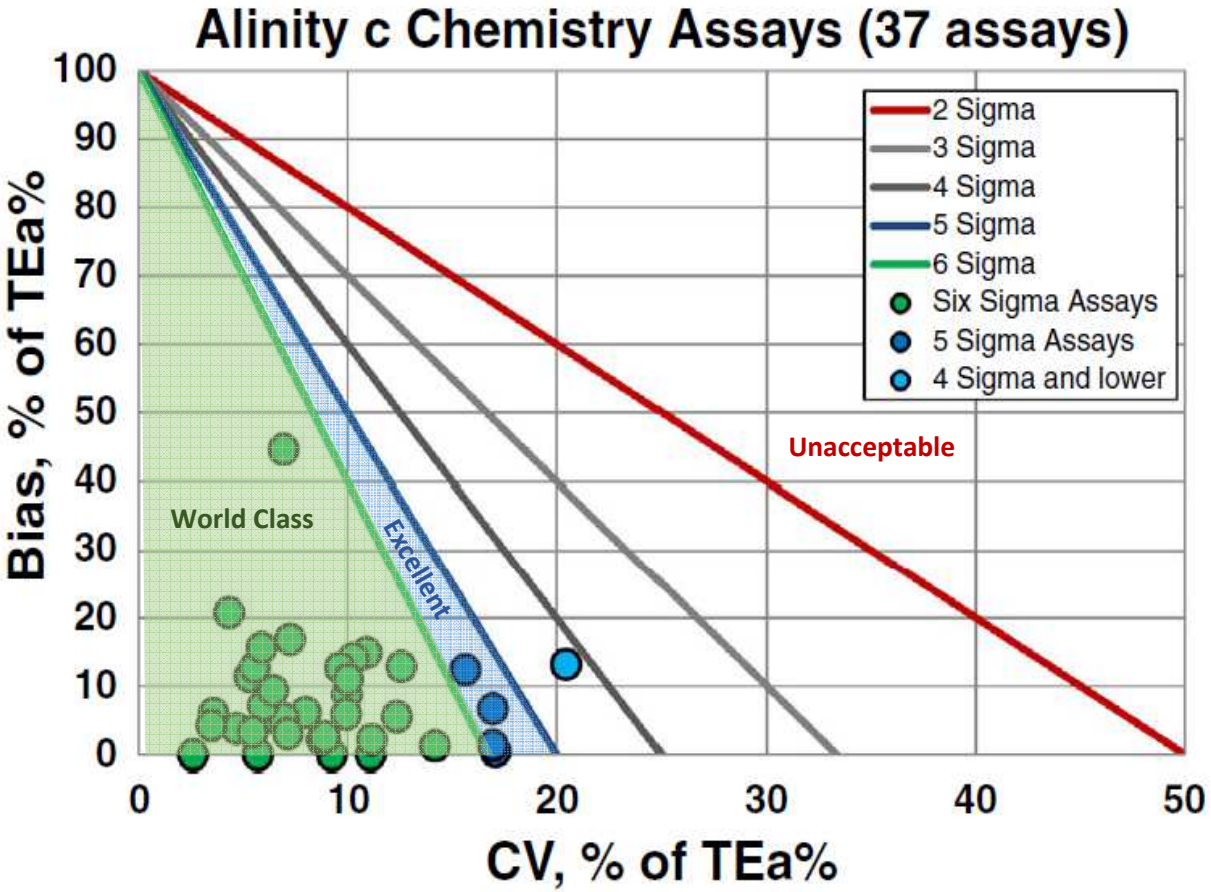


Fig. 1. Normalized Method Decision Chart for Alinity c Clinical Chemistry Assays.

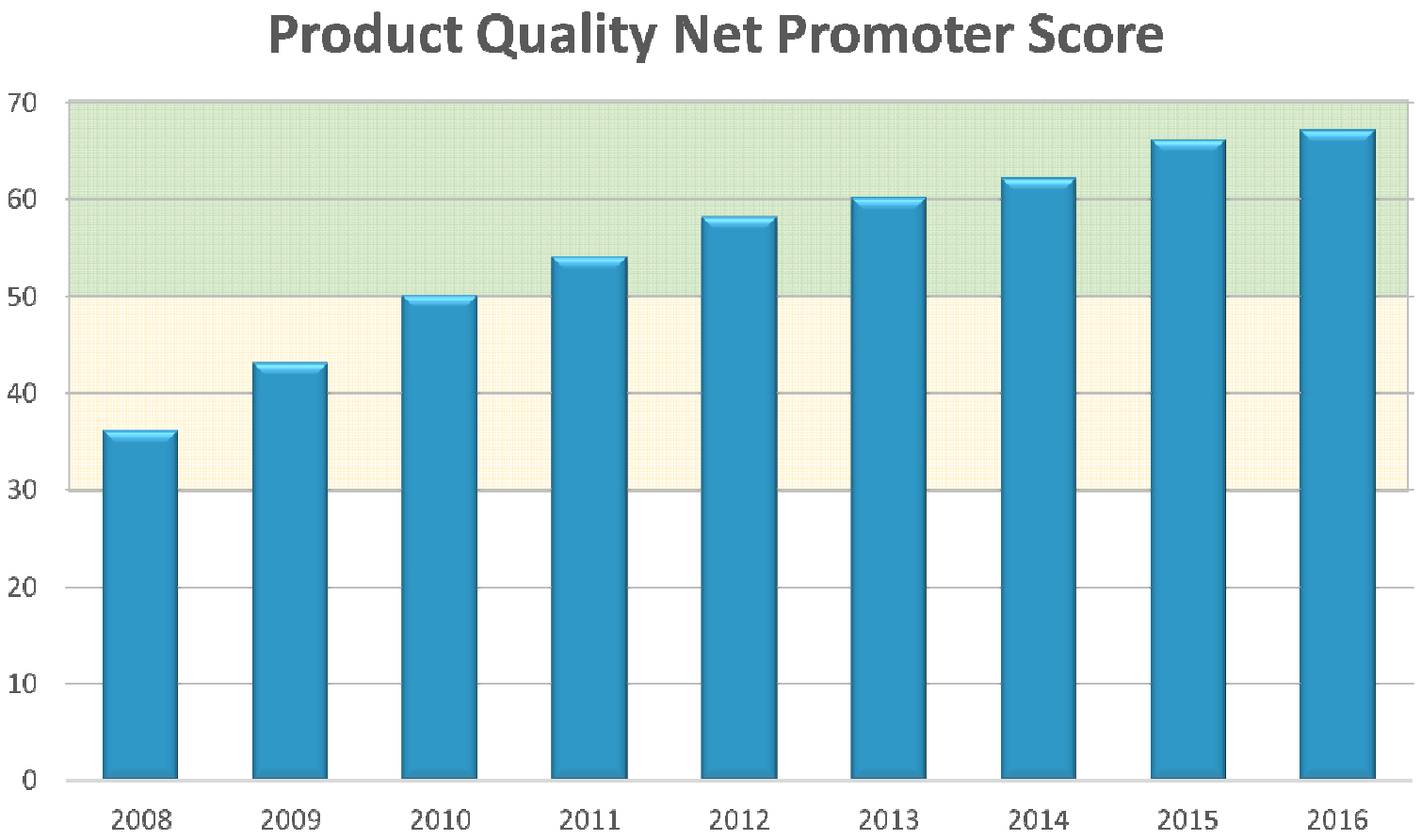
Sigma Metric Performance of Alinity System vs. ARCHITECT

- >90% of the IA and CC products were 5 sigma or greater.
- No assays were <3 Sigma.

published reference: Westgard, S., Clinical Biochemistry (2017), http://dx.doi.org/10.1016/j.clinbiochem.2017.09.005

Our Customers' View – Growing Customer Satisfaction

Our customers are noticing our improvement and would recommend us.



NPS above +50 is considered "Excellent," and above 70 is considered "World-class."
https://www.questionpro.com/blog/nps-considered-good-net-promoter-score/

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Thank You!!!

Grazie
Dhanyawaad
Arigato
Xie Xie
Danke
Shukran
Spasibo
Obrigado
Dziekuje
Gracias
Merci

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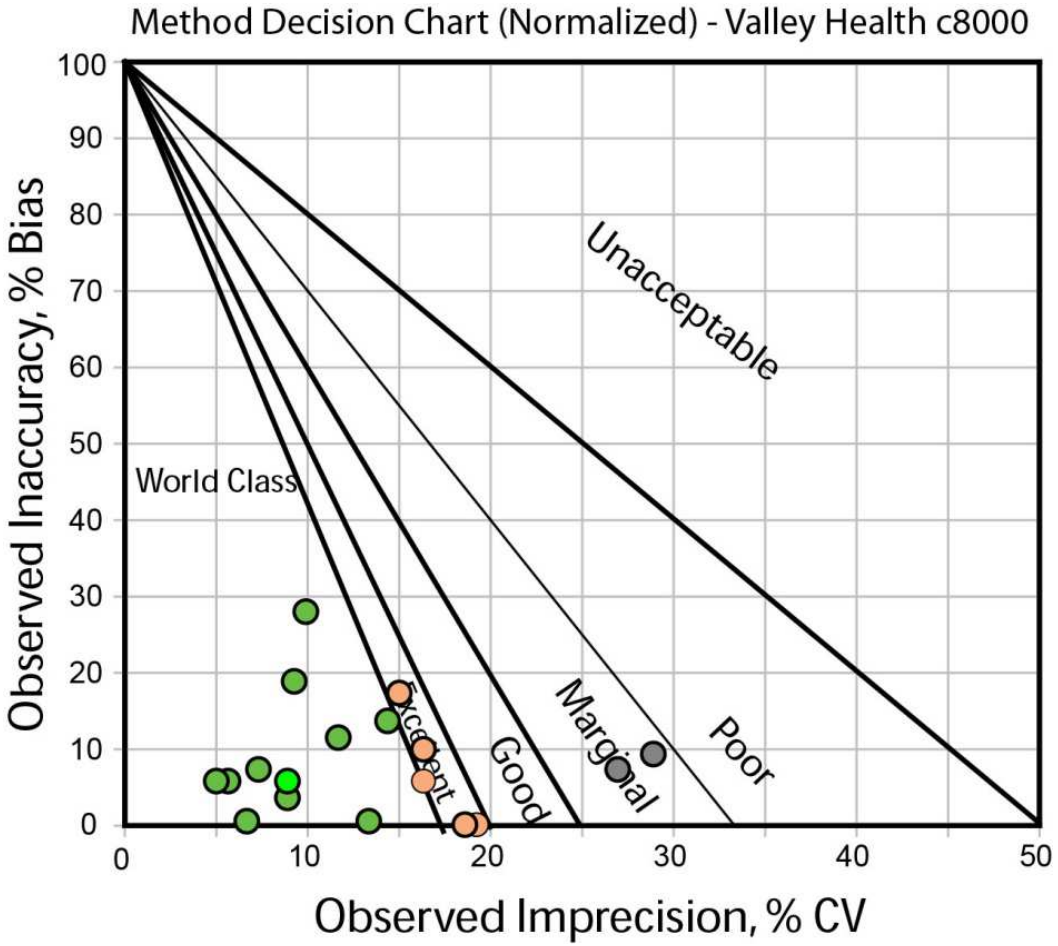
Back-up Materials

More Accurate Results for Our Patients and Less issues with Calibration and QC

Performance – Best In Class Performance of Products



Sigma Metrics
for 30 Abbott Diagnostics
ARCHITECT
Clinical Chemistry Tests