Best Practices in Designing Your Lab's QC Program to Match Your Lab's Quality Goals

An Introduction

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Acknowledgements

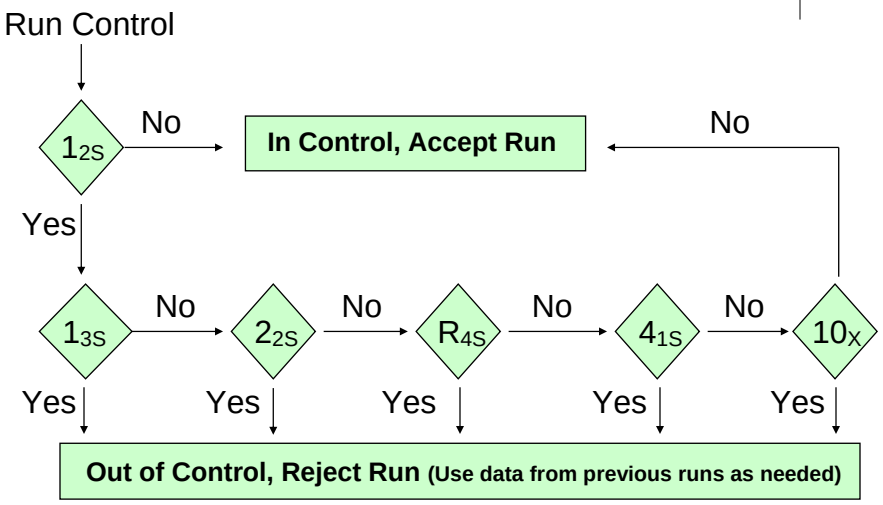
This presentation presents a summary of the work of others.

The most prominent have been:

- Dr. James Westgard
- Dr. George Cembrowski
- Dr. Carmen Ricos
- Dr. Callum Fraser
- Dr. Curtis Parvin

Quality control in clinical diagnostics would be much less advanced without their contributions

Statistical Process Control (before QC design)



Common QC Management Mistakes

- Absence of QC design
  - Control statistical error rather than clinically relevant error
  - Same QC rules applied for all tests
  - Universal application of 1-2s rule
  - Effects cost and quality of patient test results
- Absence of quality specifications
  - Many labs don't know how good their test performance needs to be
- Misuse of package insert values for fixed mean and SDs

A Definition

Quality Control Design in the clinical diagnostic setting refers to the process of identifying what quality is required for each test offered and the statistical process controls needed to alert the user if the quality goal is not being met.

How to Design a Quality Control System

1. Identify what quality specifications are suitable for each test in the laboratory menu.
2. Evaluate the performance of each test in the laboratory.
3. Select statistical process controls that will identify when the test performance does not meet the quality specification.
4. Reassess for performance changes.

Adapted from CLSI C24: A3 Guideline

The Need for Quality Specifications

- Quality specifications dictate the performance characteristics that must be realized in our test systems for them to satisfy their purpose.
- In the absence of quality specifications, there is no way to determine whether the control procedures being utilized are appropriate.

The Quality Specification Hierarchy

- How do non-experts know what to select?
- 1999 Stockholm Conference organized by IFCC, WHO and IUPAC
- Consensus statement on Quality Specification hierarchy:
  1. Goals based on clinical outcome
  2. Goals based on clinical decision making
     a. Clinician survey
     b. Biological variation
  3. Goals based on expert opinion
     a. National and international expert bodies
     b. Expert local groups or individuals
  4. Goals set by regulatory providers
  5. Goals based on state of the art
     a. Data found in peer programs

Selecting a Quality Specification

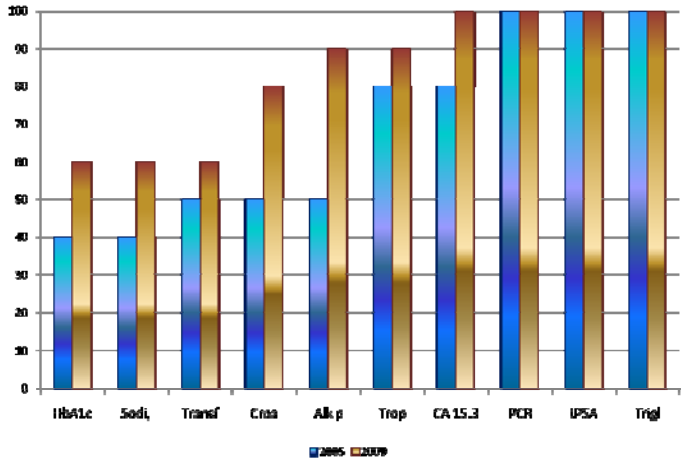
- Goals based upon clinical outcome and clinician survey are rare, so many experts believe biological variation (BV) is the best option

- Limitations for labs using BV:
  - For a few analytes there are questionable estimates of bias and/or imprecision due to a small number of papers published or conflicts between published papers
  - Data is available only for a limited number of analytes (300+)
  - Total allowable error derived from BV seems to be too restrictive in some cases compared to technological capacities (chloride, HbA1C, sodium, etc.)

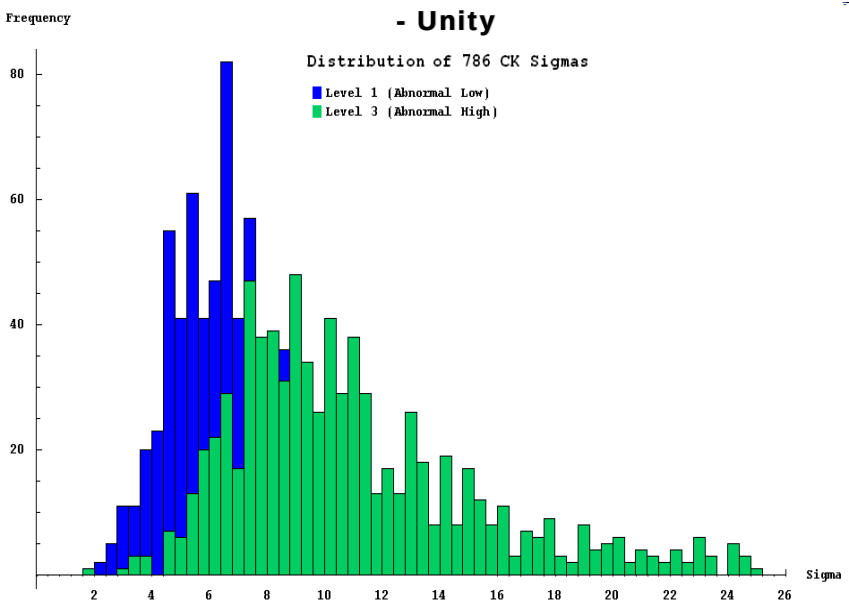
Biological Variation

- SEQC (Dr. Ricos)

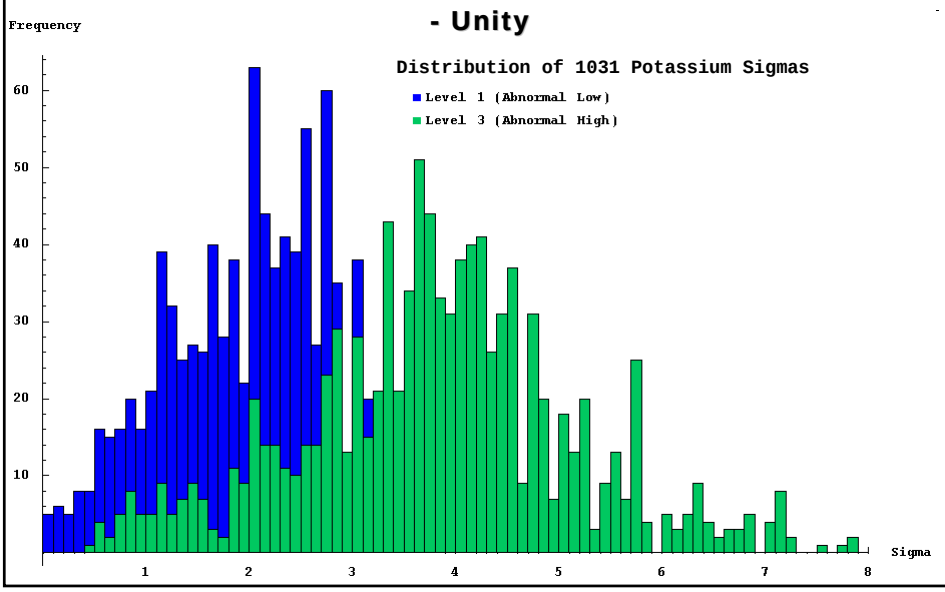
% of results reaching specifications based on BV



Biological Variation



Biological Variation



Evaluating Laboratory Performance

Two factors need to be considered to assess laboratory performance for quality control design:

- Bias – the % distance between laboratory mean and target
- Imprecision – normally the coefficient of variation (CV%).

Determining Bias

- Bias is expressed as a percentage (%).
- Bias is usually calculated with respect to some group or a reference target.
- Bias is calculated as $100 \times \frac{\text{Your } \bar{x} - \text{Group } \bar{x}}{\text{Your } \bar{x}}$
- The group may be the peer group from an interlaboratory program scheme, or it may be a group of laboratories which share patients.

Determining Imprecision

- Imprecision is usually expressed as a percentage (%).
- Normally, the coefficient of variation is indicated in the literature as s_{meas}.
- For quality control design, using the monthly – or short term CV will give an optimistic result.
- The long term (>3 months) CV will give a more realistic result.

Designing the Quality Control System

- Once the quality specifications have been decided on and the laboratory performance has been evaluated, appropriate statistical process controls can be determined.
- The primary criteria for selecting a statistical process control is to choose one that has sufficient error detection to meet the quality specification selected, but has the lowest possible probability of false rejection.

Error Detection Required

Current Total Error = bias + zs_{meas}

Where z is 1.65 for 95% probability.

We need to detect when an error occurs such that it and our Current Total Error exceed our Total Allowable Error.

This is called the Critical Error or S_{crit}

Calculating S_{crit}

$TE_a = bias + zs_{meas} + s_{crit}s_{meas}$

Which means that

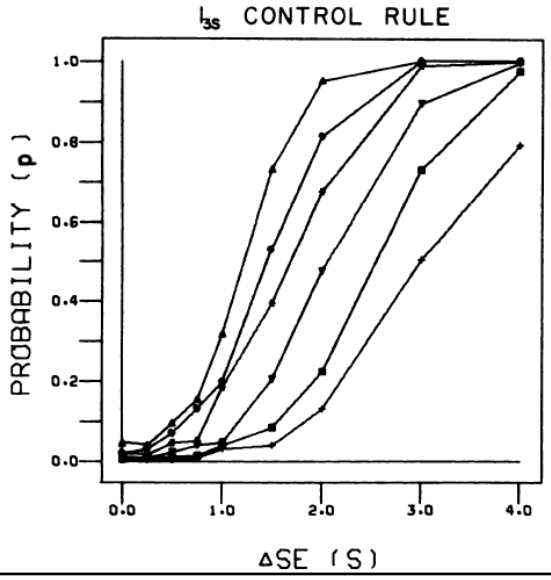
$S_{crit} = (TE_a\text{-}bias)/s_{meas} - z$

So, given bias, $s_{meas,}$ and TE_a, we can calculate how large an error we need to detect to stay within our TE_a.

Choosing QC Rules

- Each QC rule has a certain amount of error detection power and a certain chance of false rejection.
- We need to choose QC rules with sufficient error detection to detect s_{crit} but with the lowest false rejection probability.
- The error detection power and probability of false rejection have been well studied for most QC rules.

Determining the Error Detection of a Rule



Selecting the appropriate rules

- After computing S_{crit} for the test in question, select the QC rules that have an error detection power sufficient for the S_{crit} computed.
- From the selected QC rules, determine which have the lowest false detection rate – use this one.
- Manually, this process is computationally intensive and requires quite a bit of time.

Westgard Advisor

Using statistical theory and computer simulation, Dr. Westgard has analyzed the performance characteristics of some 68 combinations of QC rules and embedded the probabilities of error detection and false rejection into an algorithm.

Westgard Advisor

Given an input of TEa, bias, s_{meas}, his algorithm calculates s_{crit} and selects the QC rule combination that has sufficient error detection with the lowest false rejection probability.

This approach significantly reduces the burden of QC design and effectively automates it.

Real World Example

- Westgard published a paper in 1990 where this analysis was first done in a lab.
- For 14 out of 18 tests, a $1_{3.5s}$ rule was selected for sodium, potassium, glucose, urea nitrogen, creatinine, phosphorus, uric acid, cholesterol, total protein, total bilirubin, GGT, ALP, AST, and LD

Real World Example

- A single $1_{2.5s}$ rule was selected for albumin.
- A multirule QC procedure was found for Cl and CO_2
- A special QC strategy was implemented for calcium by averaging the results of duplicate measurements.

Real World Impact

- Changes in QC procedures resulted in a cost savings of $1,450 per month, or $17,400 per year.
- Total savings of $87,000 over the expected 5 year lifetime of the instrument.

Thank you for your kind attention!