INTERNATIONAL INSTITUTE FOR PATHOLOGY AND FORENSIC SCIENCE RESEARCH

COLLEGE of AMERICAN PATHOLOGISTS FOUNDATION

DAVID UMAHI FEDERAL UNIVERSITY OF HEALTH SCIENCES UBURU, EBONYI STATE.

# Strategies for Quantitative and Qualitative Quality Control.

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Week 3

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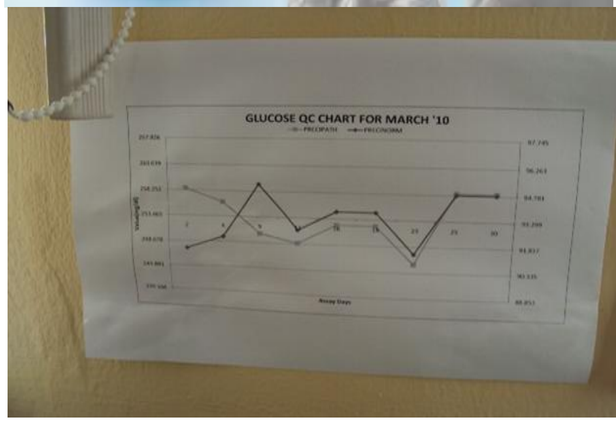
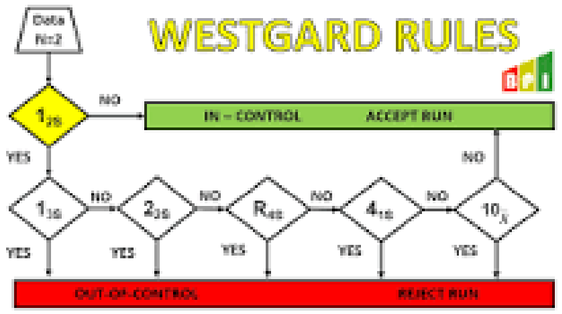
*Advancing Laboratory Quality Management Systems for Better Patient Outcomes*

# Outline

- Preamble / Introduction
- Basic Quality Control Theories and Practices
- Monitoring of QC data – the use of Westgard rules
- Updates on External Quality Assessment (EQA) - Proficiency Testing (PT)
- AI-driven quality control and automation in modern laboratory workflows.



# Introduction

**Why Quality ?**

# The patient across the globe defines quality in 3 ways…

**In this order…**

- “Don’t Harm Me”
- “Heal Me”
- “Be nice to me”

***Quality care in a nutshell - Greg Manning***

# Obligated to do No Harm

- In medical school, the first concept expressed to students is a Latin phrase, *primum non nocere*, meaning “first, do no harm.”
- This phrase is well known among health workers and dates back to Hipocrates. However, in reality, the situation is slightly different.
- According to the report of the Institute of Medicine, each year in the USA, approximately 98,000 people die from medical errors (Kohn et al., 2000). Unfortunately, more people have died each year during mid-1990s from medical errors than from AIDS or breast cancer (Kohn et al., 2000).

**The first part of MLSCN induction pledge / oath :**

- Put the interest and wellbeing of the patient above my personal interest and convenience

MLSCN Rule of professional conduct

# Harm / Benefit to patient ?

Any Laboratory test conducted without a valid QC program is considered a harm to the patient.

# Consider this real life story:


A couple that had been married for 50 years were healthy except he required blood thinner medication for a treatable heart condition. However, incorrect prothrombin test results led to several increases in his medication. He died shortly after of a brain hemorrhage from over-medication.

# Wrong Patient Results Can:

- Endanger patient lives.
- Prolong suffering.
- Add significant cost (money and time) to patient treatment.

The right QC approach will detect and prevent errors.

# Introduction

The **goal** of QC is to detect errors and correct them before patients' results are reported

# Basic Quality Control Theories and Practices

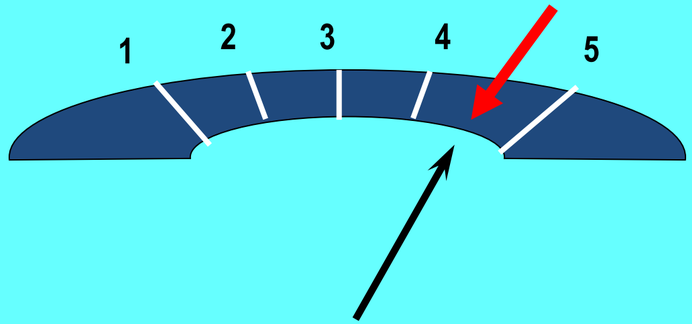
# What is Control ?

- material that contains the substance being analyzed
  - include with patient samples when performing a test
- used to validate reliability of the test system
  - run after calibrating the instrument
  - run periodically during testing

**Controls**

**A substance similar to patients' samples that has an established concentration.**

**Controls are used to ensure the procedure is working properly.**

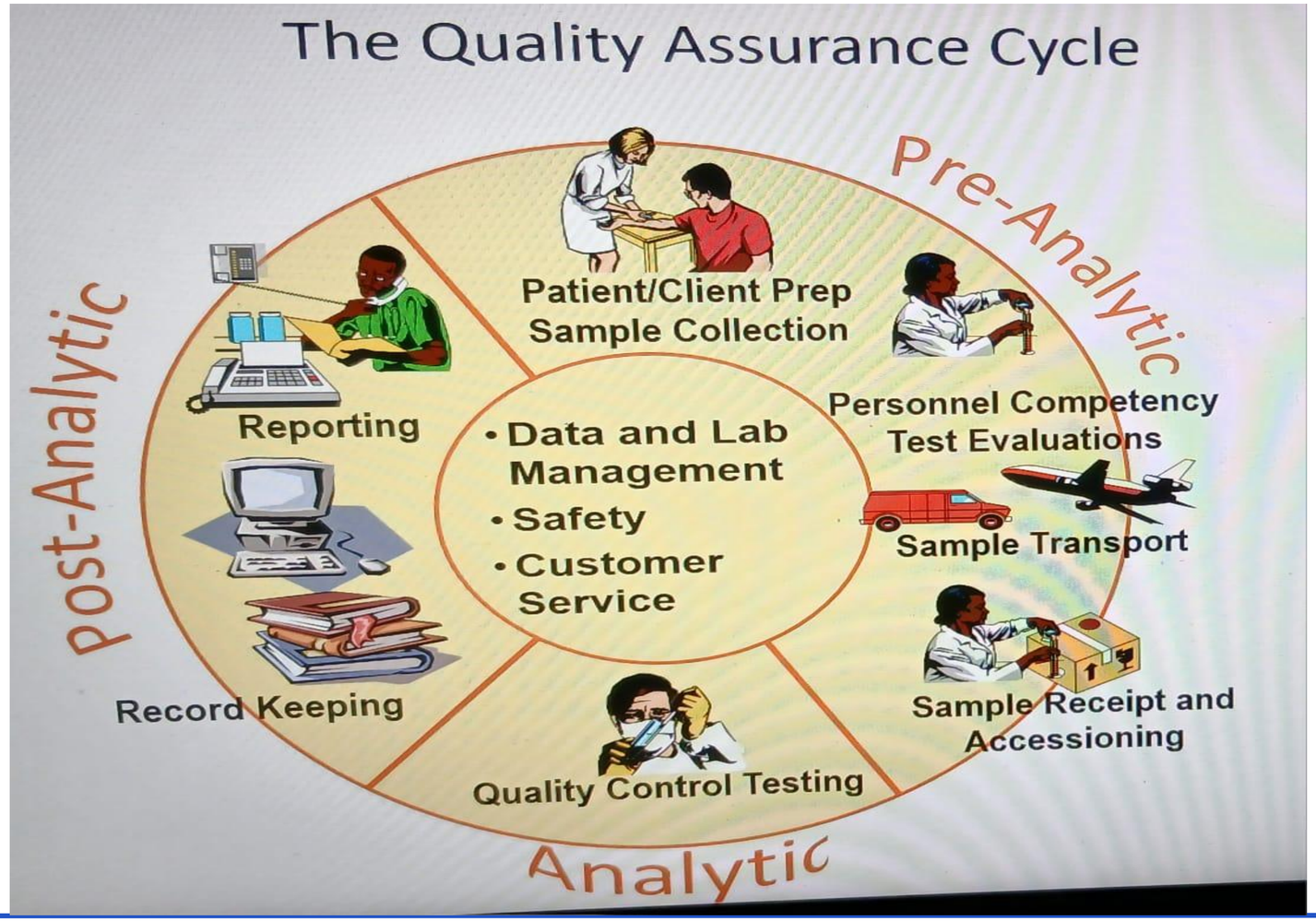


# Quality Control is not an orphan

**Defining quality terms**


- The quality management system (QMS) is the overall system that oversees and ensures the quality of the end product. This system includes quality control and quality assurance, and other steps like risk management and CAPA.
- Quality assurance (QA) is the proactive part of the system. QA ensures the correct procedures are in place to ensure a high quality and compliant product or service.
- Quality control (QC) is the inspection part of the system where the product or service is assessed to pick up any defects or quality issues.

# Quality Control is not an orphan




- **Quality Assurance** in a clinical or Medical laboratory is a system that encompasses pre-analytical, analytical, and post-analytical factors.
- **Quality control is part of a quality assurance system.**

# Definition

**Quality Control (QC)** is part of quality management focused on fulfilling quality requirements ISO 9000:2015

QC is examining “control” materials of known substances along with patient samples to monitor the accuracy and precision of the complete examination (analytic) process.

# Quality Control is a requirement of ISO 15189

ISO 15189:2022

Medical laboratories — Requirements for quality and competence

Published (Edition 4, 2022)

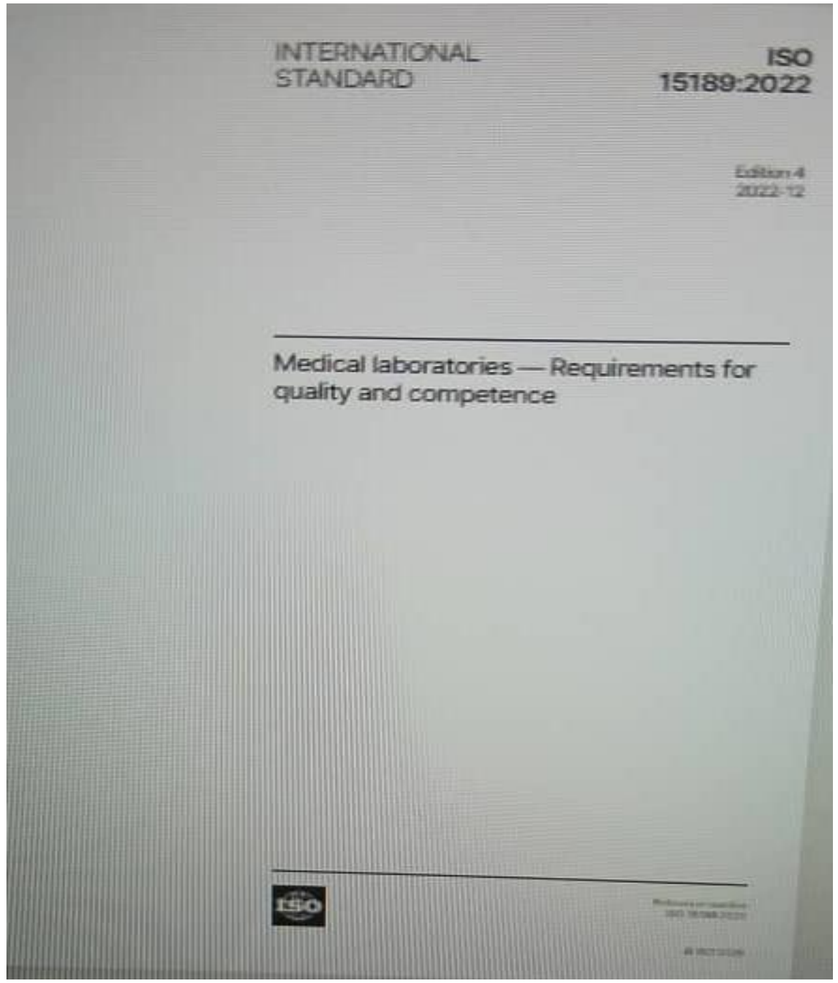
Clause 1-3 : Scope, Normative references, Terms and Definitions.

- Clause 4 (4.1 - 4.3) General requirements
- Clause 5 (5.1 - 5.6) Structural and governance requirements
- Clause 6 (6.1 - 6.8) Resource requirements
- Clause 7 (7.1 - 7.8) Process requirements
- Clause 8 (8.1 - 8.9) Management Systems requirements

**7.3.7 Ensuring the validity of examination results**

- **7.3.7.1 General**
- **7.3.7.2 Internal Quality control (IQC)**
- **7.3.7.3 External quality assessment (EQA)**
- **7.3.7.4 Comparability of examination results**

# Quality Control is a requirement of ISO 15189




## Internal quality control (IQC)

The laboratory shall select IQC material that is fit for its intended purpose. When selecting IQC material, factors to be considered shall include:

1) stability with regard to the properties of interest;
2) the matrix is as close as possible to that of patient samples;
3) the IQC material reacts to the examination method in a manner as close as possible to patient samples;
4) the IQC material provides a clinically relevant challenge to the examination method, has concentration levels at or near clinical decision limits and when possible, covers the measurement range of the examination method.

# Characteristics of Control Materials

- appropriate for the diagnostic sample
- values cover medical decision points
- similar to test sample (matrix)
- available in large quantity; ideally enough for one year
- can store in small aliquots

# Types of Control Materials

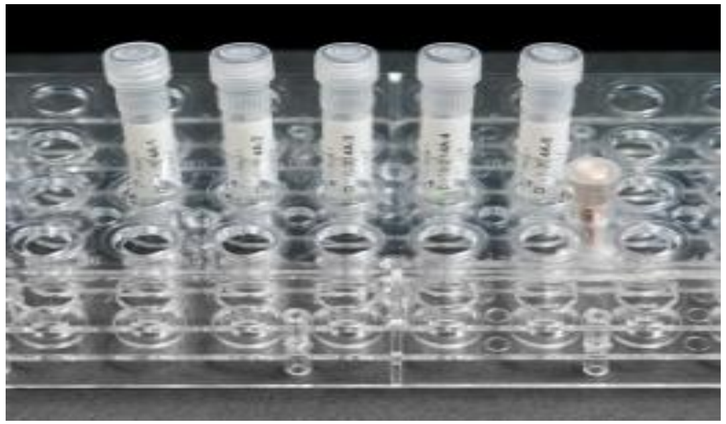
- Dried Plasma in form of Dried Tube specimen
- may be frozen, freeze-dried, or chemically preserved.
- requires very accurate reconstitution if this step is necessary.

**Other forms of QC**

- built-in controls
- reference organisms

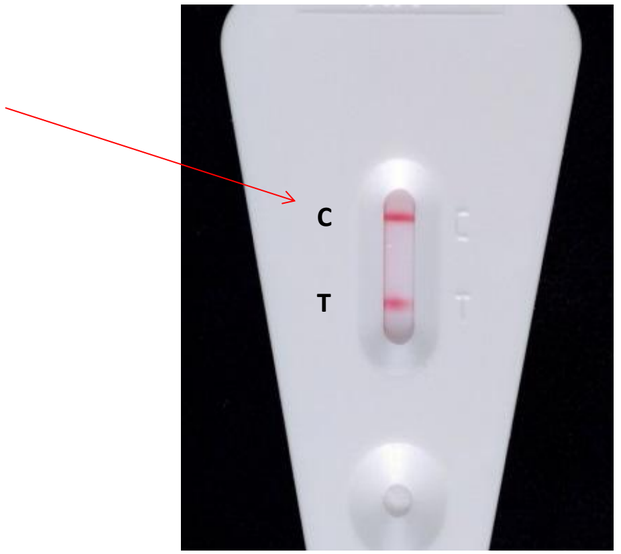
# Sources of Control Materials

- **commercially prepared**
- made “in house” e.g Dried Tube specimen (DTS)
- obtained from another laboratory, usually central or reference laboratory



# Built – in Control Materials

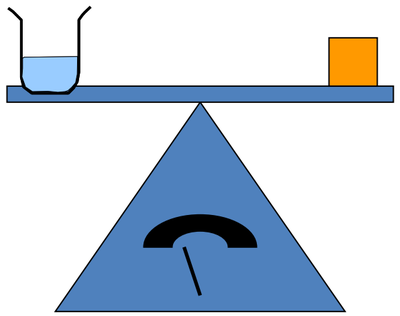
- integrated into the design of a test kit device
- automatically run with each test performed
- assess certain aspects of kit performance
- may not assess entire testing process

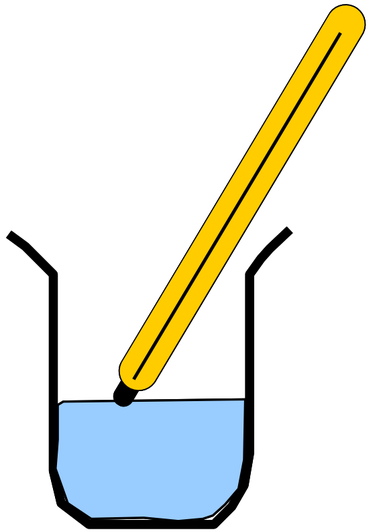


# Quantitative Examinations

**Measure** the quantity of a particular substance in a sample

Measurements should be both accurate and precise





- measure the quantity of a particular substance in a sample
- quality control for quantitative tests is designed to assure that patient results are:
  - accurate
  - reliable

# Qualitative Examination Methods

Examinations that do not have numerical results:

- growth or no growth
- positive or negative
- reactive or non-reactive

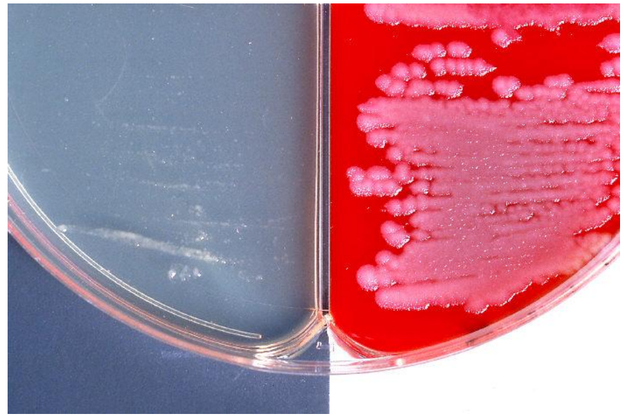

# Semi - Qualitative Examination Methods

Results are expressed as an estimate of the measured substance:

- “trace amount”, “moderate amount,” or “1+, 2+, or 3+”
- number of cells per microscopic field
- titers and dilutions in serologic tests

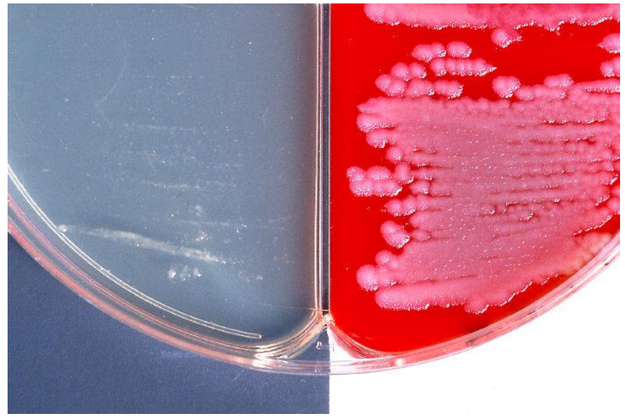
# Stock Cultures for QC

- reference strains
- in-house developed strains
- predictable reactions in stains and media
- ensure media, reagents and supplies work as intended
- **Sterility + Viability checks**



# Sources for Obtaining Reference Strains

- **ATCC**-American Type Culture Collection
- **NTCC**-National Type Culture Collection (UK)
- **CIP**- Pasteur Institute Collection (France)
- TB Supranational Reference Laboratories **(SRLs)** Milan, Italy



# Stain Management

Continued Attention

No Attention

- use established procedure for preparation or reconstitution
- label: content, concentration, date prepared and placed in service, expiration, initials
- store appropriately

# Quality Control for Stains

## As appropriate for particular stain:

- check with known organisms or cells
- examine for crystal shards or for precipitation
- examine for contaminants such as bacteria and fungi

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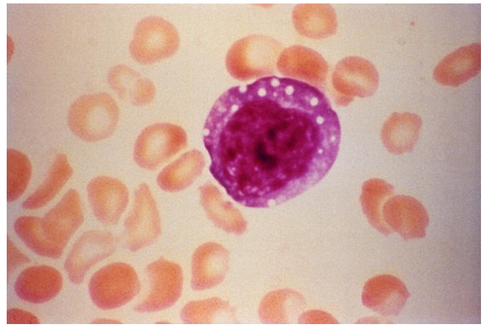
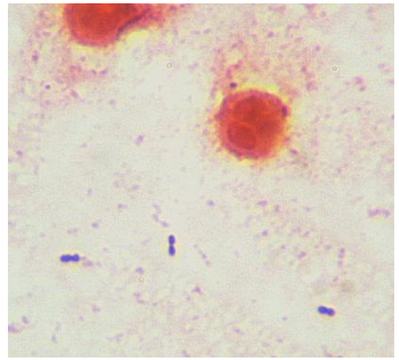
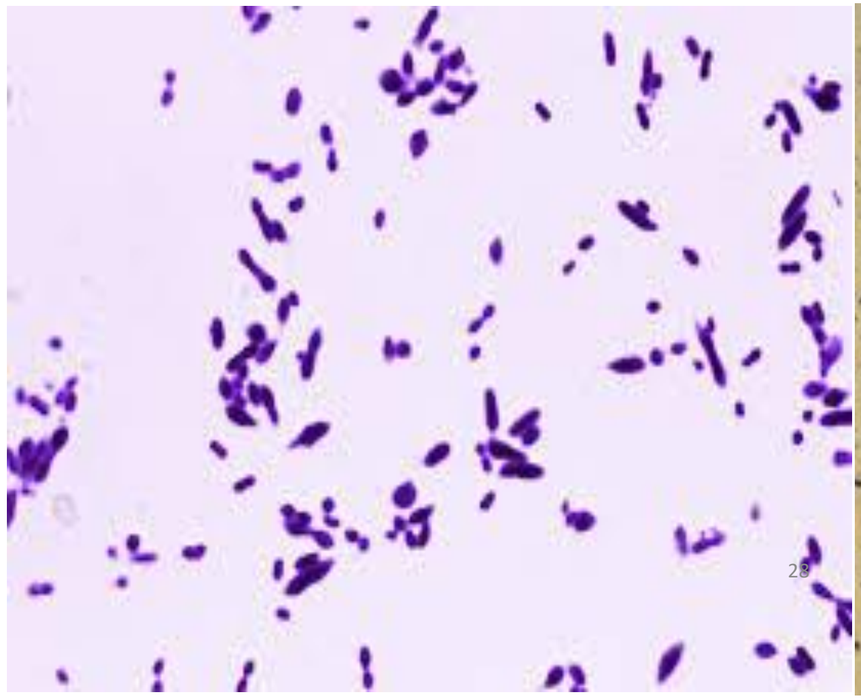


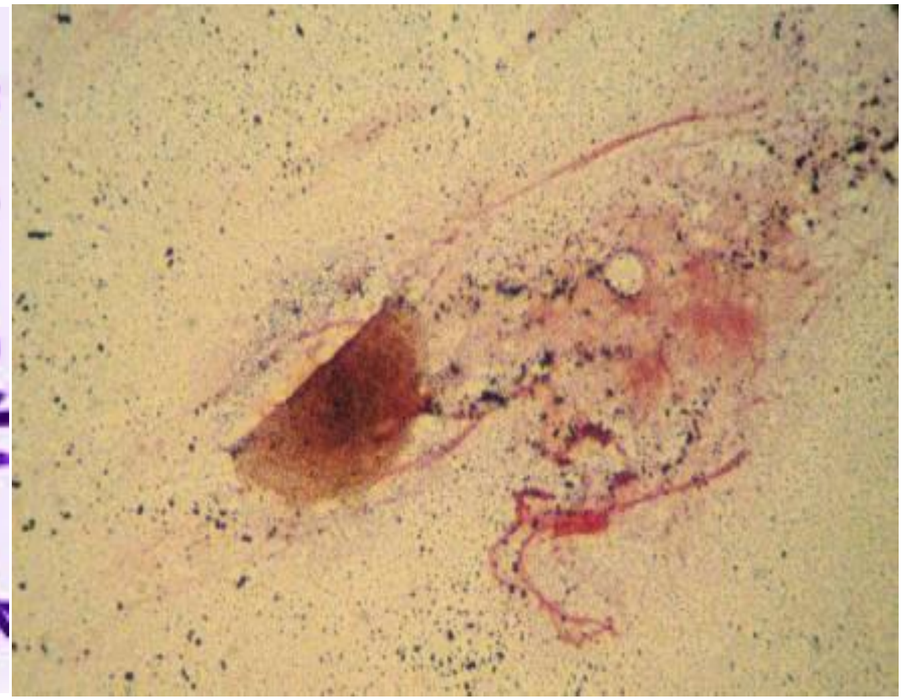
Left:
Wright stain

Right:
Gram stain



# Gram Stain picture





Good Quality

Poor Quality

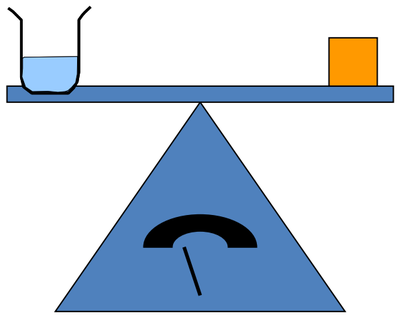
# Quality Control of Growth Media

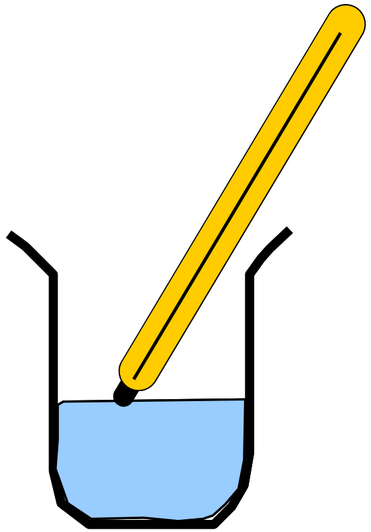
- keep records for media prepared in-house
- record outcomes in a dedicated media logbook for:
  - pH, sterility, ability to support growth using stock cultures, biochemical response of stock cultures
- frequency
  - test each new batch or lot number

# Quantitative Examinations

**Measure** the quantity of a particular substance in a sample

Measurements should be both accurate and precise



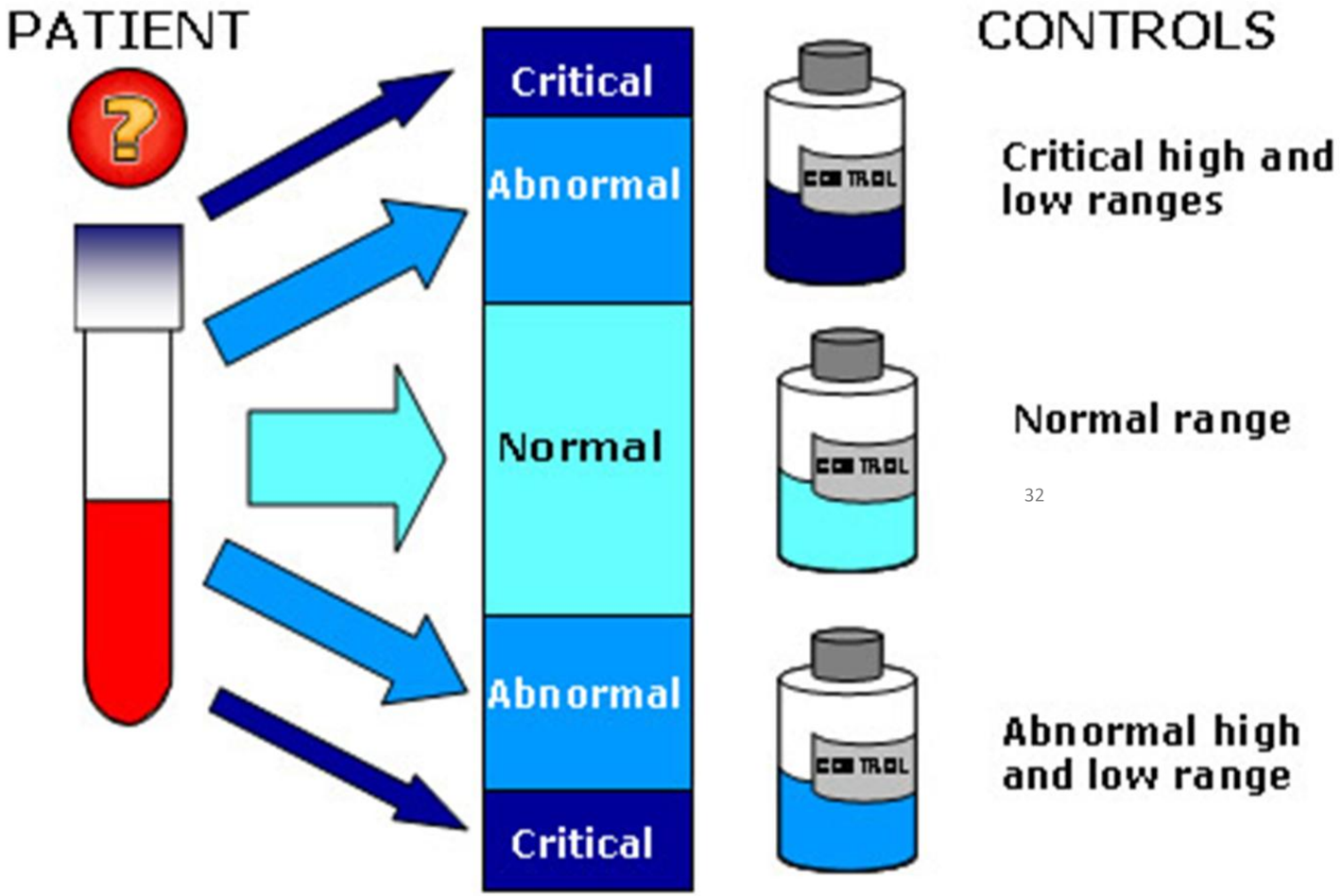


- measure the quantity of a particular substance in a sample
- quality control for quantitative tests is designed to assure that patient results are:
  - accurate
  - reliable

# Quantitative Control Materials

| | |
|---|---|
| **ASSAYED** | Target value predetermined<br>Verify and use |
| | |
| **UNASSAYED** | Target value not predetermined<br>Full assay required before using |
| | |
| **"IN-HOUSE"** | In-house pooled sera<br>Full assay, validation |

# Choosing Control Materials

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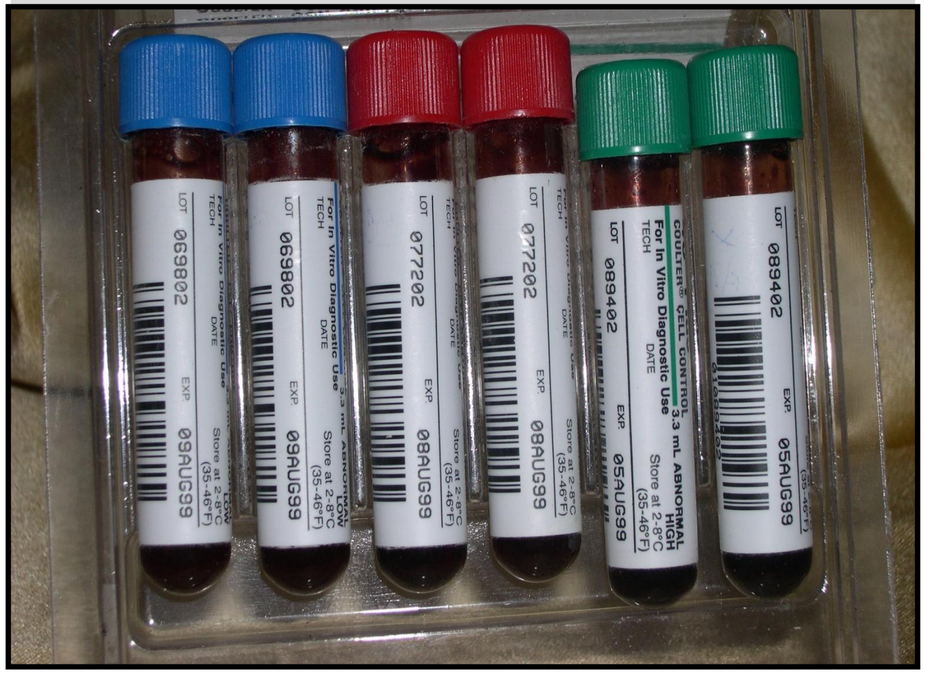
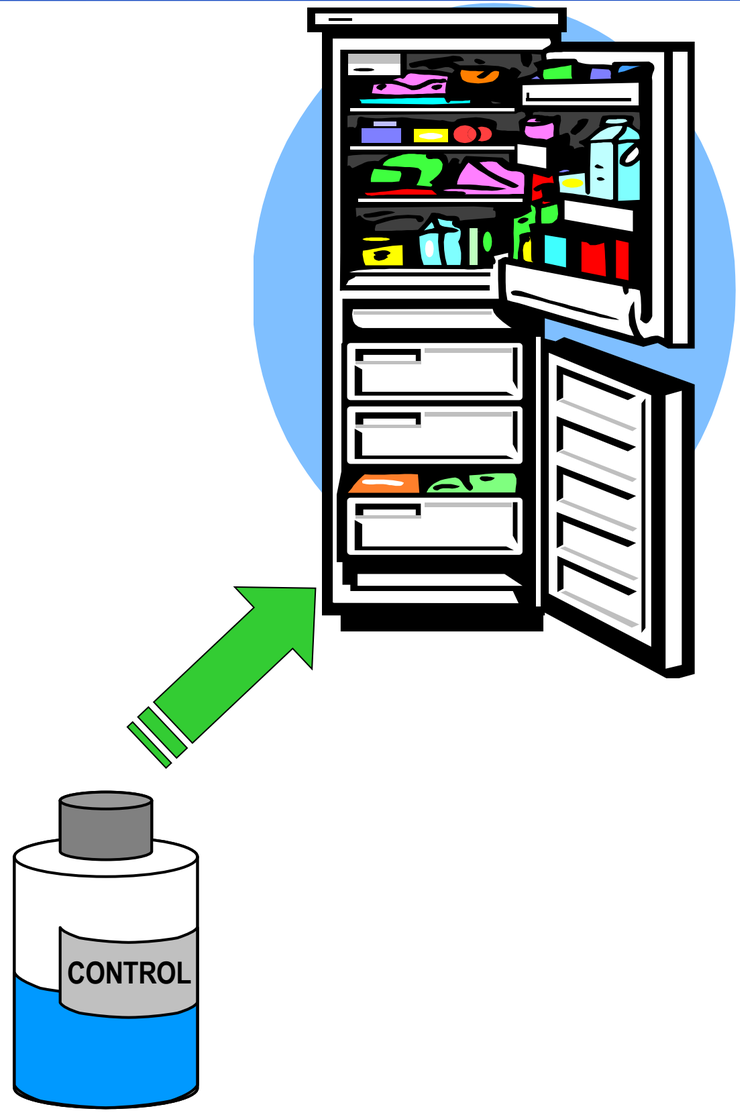
- values cover medical decision points
- Similar to the test sample
- controls are usually available in high, normal, and low ranges



# Preparation and Storage of Control Material

- adhere to manufacturer's instructions
- keep adequate amount of same lot number
- store correctly



# Desirable number of controls

- **Good**: If one control:
  - accept results if control is within ± 2SD unless shift or trend
- **Better**: If 2 levels of controls
  - apply Westgard multirule system

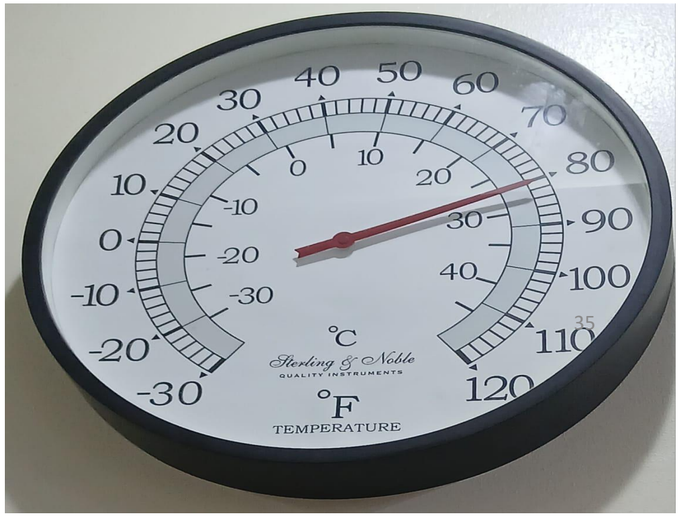


# Measurement of Variability

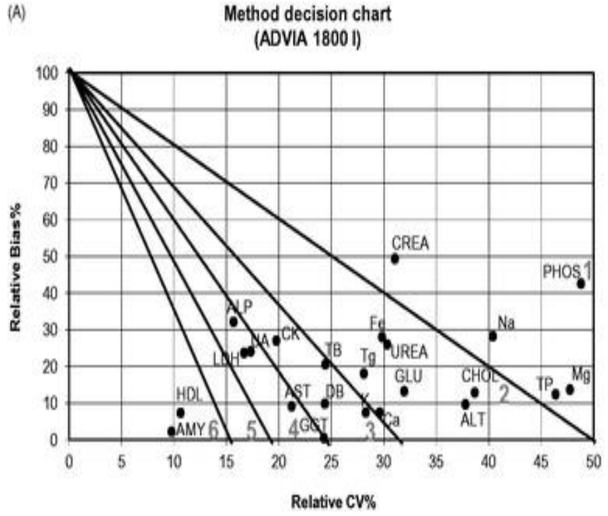
**Variability is a normal occurrence when a control is tested repeatedly**

Affected by:

Operator technique




Environmental conditions

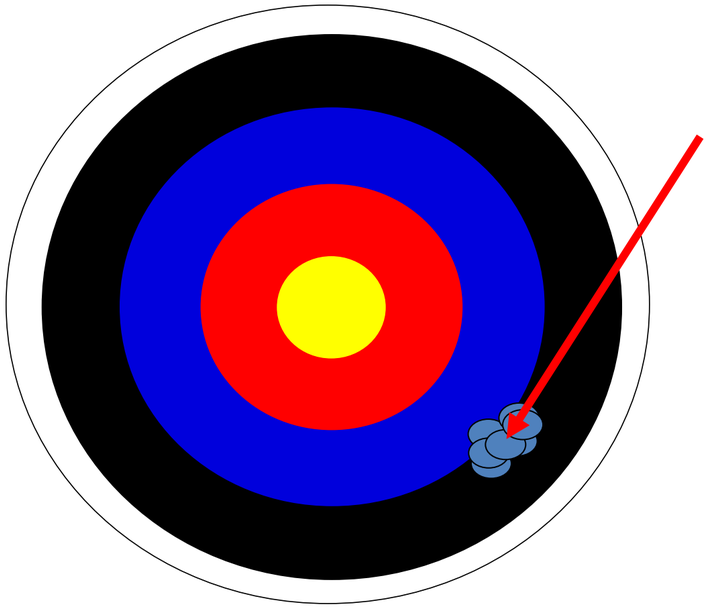



Performance characteristics of the measurement

The goal is to differentiate between variability due to chance from that due to error

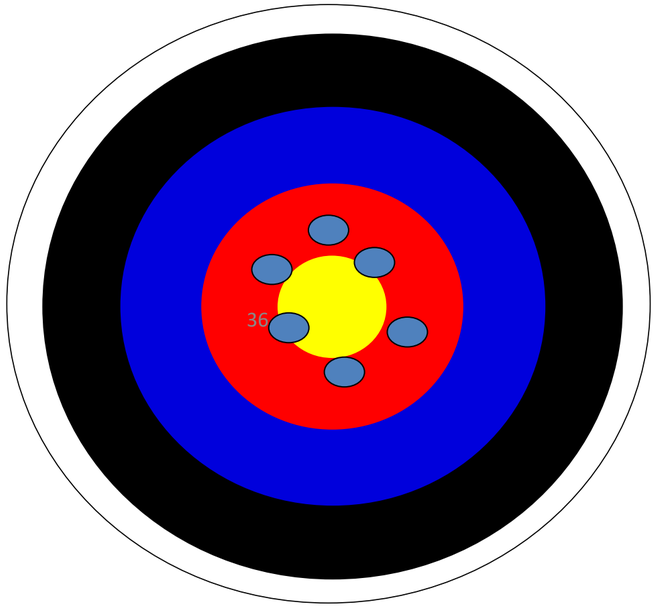
# Definitions

Reproducibility or closeness of results to each other



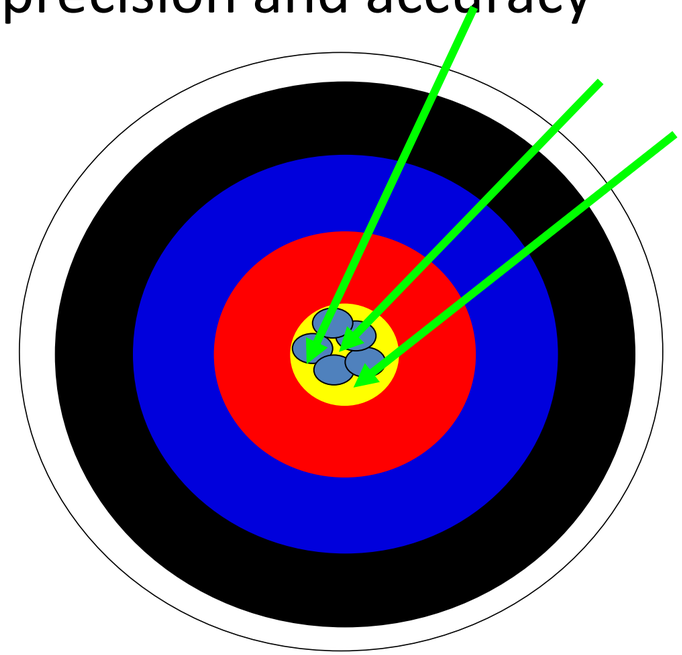
**Precision**

The closeness of the measured result to the true value



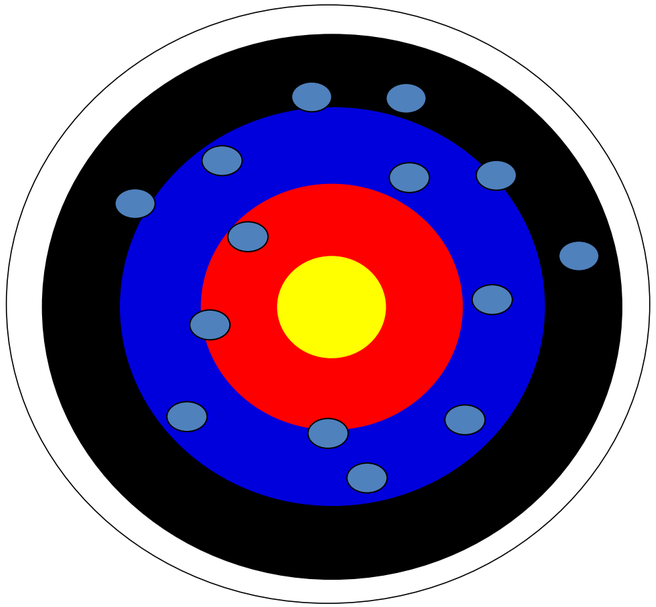
**Accuracy**

The ability to maintain both precision and accuracy



**Reliability**

# Probable causes of Inaccuracy / Imprecision



- Erratic (fluctuation) temperature
- Plugged pipette/tips
- Problems with photometer (bulb)
- dirty cuvette
- poor mixing
- evaporation of controls
- evaporation of standards
- reagent deterioration (improper storage)
- poor pipetting

# QC Implementation steps

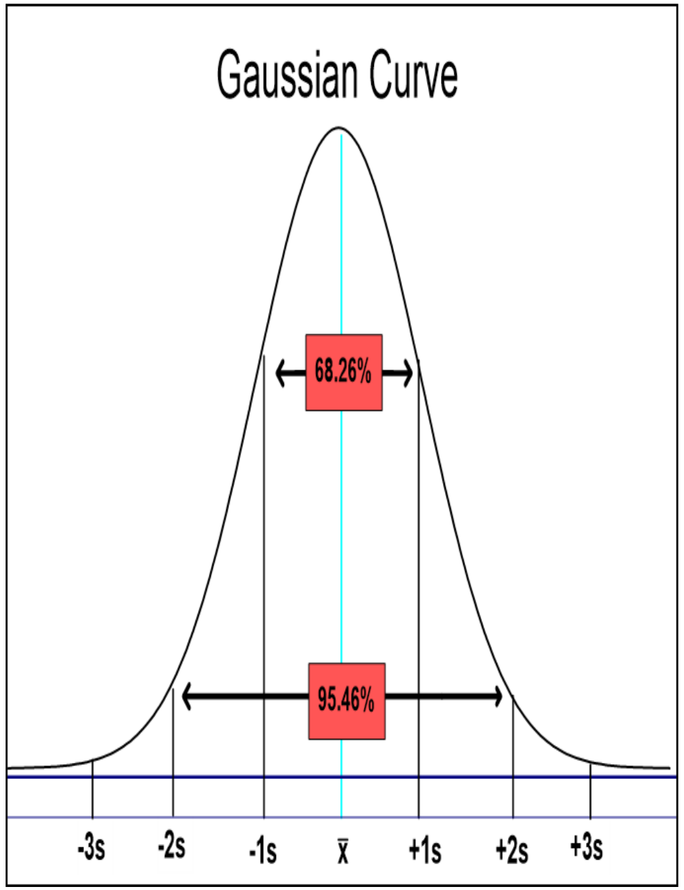
- establish policies and procedures
- assign responsibility, train staff
- select high quality controls
- **establish control ranges**
- **develop graphs to plot control values - Levey-Jennings charts**
- **monitor control values**
- develop procedures for corrective action
- record all actions taken

# QC Implementation steps

- Calculate the mean and SD of the control material for a single data population.
- Use the calculated mean and SD on the QC chart.
- Use the right QC rules for your method
- Plot the control values versus time on a control chart.
- If a significant change occurs in accuracy or precision, then the QC rule failures alert you to the change.
- Investigate, resolve, and document the rule failure before patient results are reported.

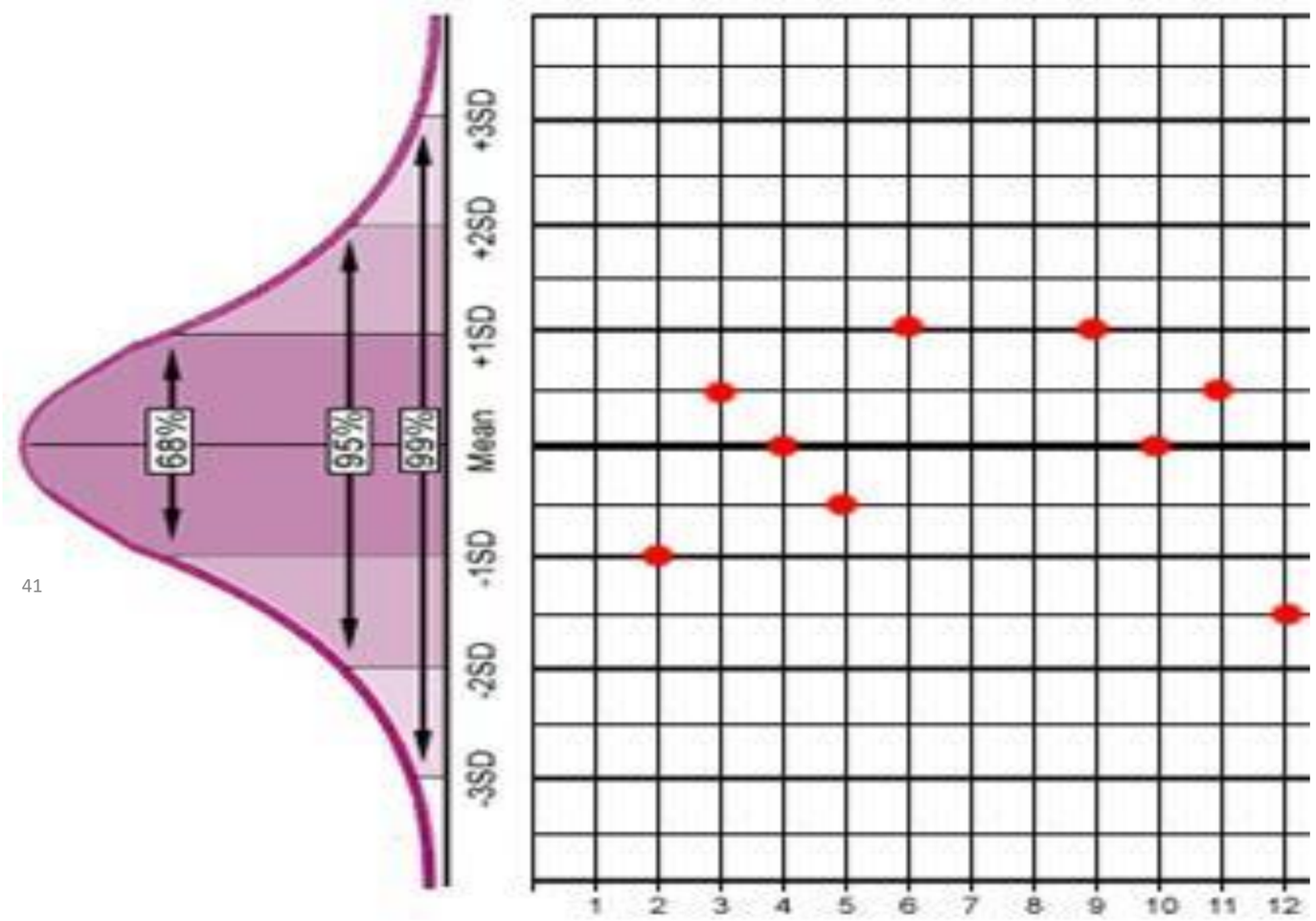
# SQC operates on the principle of Gaussian (Normal) distribution

- showing that data near the mean are more frequent in occurrence than data far from the mean.
- Many naturally-occurring phenomena appear to be normally-distributed.
- For example, the distribution of the heights of human beings.
- The average height is found to be roughly 175 cm (5' 9"), counting both males and females.
- most people conform to that average.
- Meanwhile, taller and shorter people exist, but with decreasing frequency in the population.
- According to the empirical rule, 99.7% of all people will fall with +/- three standard deviations of the mean, or between 154 cm (5' 0") and 196 cm (6' 5").
- Those taller and shorter than this would be quite rare (just 0.15% of the population each).



# Levey-Jennings Chart

QC analysis relies on the ability to predict that any stable system will produce
the same distribution of data
on both the Gaussian curve
and the QC chart.

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# Statistical QC (SQC)

- Mean ( $\overline{x}$ )
  - –The average of a set of values
  - –Used in the calculation to determine bias

    measure of systematic error (error in a given direction)

- Standard deviation (SD)
  - Used to measure distribution/scattering of a group of values around a mean
  - Primary indicator of precision
  - Measure of random error (error in any direction)

$$\text{Mean } \overline{X} = \frac{\sum x_i}{N}$$

$X_i$ = individual value
N = number of individual values

Standard Deviation

$$SD = \sqrt{\frac{\sum (x_i - x)^2}{N-1}}$$

$\Sigma$ = sum (of the differences)
$X_i$ = individual value
X = mean of individual values
N = number of individual values

# Establishing QC ranges

- Run new control to obtain 20-30 data pts over a 30 day period
- Run in parallel with current control material
- All new controls must be within the manufacturer's product package insert range
- Calculate mean and SD
- Develop Levey-Jennings charts, plot results

**QC Data for Glucose Control Level 1 (mmol/L)**
**Lot No : 56789**

| JAN. 2025 | | JAN. 2025 | | JAN. 2025 | | JAN. 2025 | |
|---|---|---|---|---|---|---|---|
| Day | Result | Day | Result | Day | Result | Day | Result |
| 1 | 5.7 | 9 | 5.3 | 17 | 5.8 | 25 | 5.3 |
| 2 | 5.7 | 10 | 5.5 | 18 | 5.7 | 26 | 5.4 |
| 3 | 5.6 | 11 | 5.5 | 19 | 5.8 | 27 | 5.5 |
| 4 | 5.5 | 12 | 5.6 | 20 | 5.7 | 28 | 5.8 |
| 5 | 5.8 | 13 | 5.7 | 21 | 5.8 | 29 | 5.3 |
| 6 | 5.7 | 14 | 5.7 | 22 | 5.9 | 30 | 5.8 |
| 7 | 5.8 | 15 | 5.5 | 23 | 5.9 | 31 | 5.4 |
| 8 | 5.6 | 16 | 5.7 | 24 | 5.5 | | |

Mean = 5.6 mmol/L, SD = 0.1 mmol/L

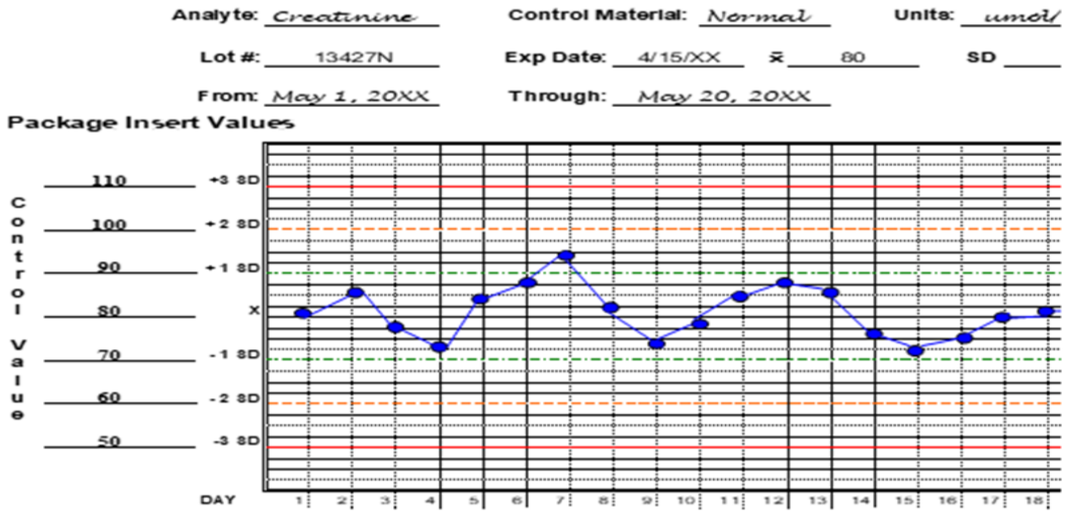
The QC range is: 5.4 – 5.8 mmol/L

# Levey-Jennings Control Chart

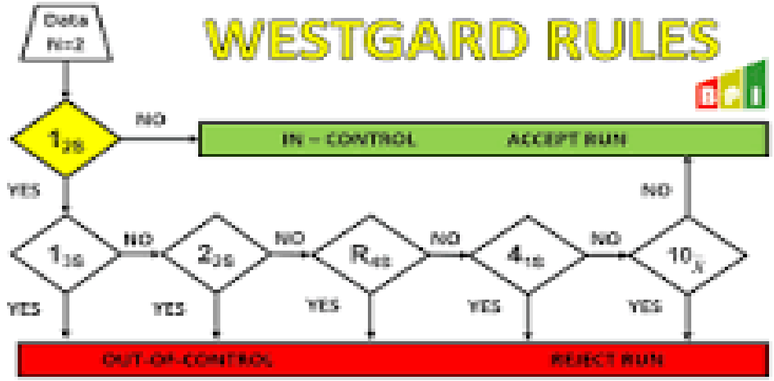
Walter A. Shewhart is an American physicist, engineer and statistician, sometimes known as the *father of statistical quality control*

Levey-Jennings Control Chart is named after Stanley Levey and E. R. Jennings who suggested in 1950 that Shewhart's individuals control chart could be used in the clinical laboratory.





# Monitoring of QC data – the use of Westgard rules



# Westgard Multirule System

- A “multi-rule” system developed by Dr. James O. Westgard based on statistical concepts
- A combination of decision criteria or rules to assess if a system is in control
- Used when at least 2 levels of control are run with the examination run
- Cannot use with only one control


https://westgard.com/lessons/westgard-rules/westgard-rules/westgard-sigma-rules.html

# Westgard Multi rule System Titles

- $1_{2S}$ rule
- $1_{3S}$ rule
- $2_{2S}$ rule
- $R_{4S}$ rule
- $4_{1S}$ rule
- $10_{X}$ rule

**Used when 2 levels of control material are analyzed per run.**

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**RULES**

| $7\bar{x}$ | $8\bar{x}$ | $9\bar{x}$ | $10\bar{x}$ | $12\bar{x}$ |
|---|---|---|---|---|

# Control Rule Nomenclature

$A_L$ or $A:L$

**A** = number of control measurements involved

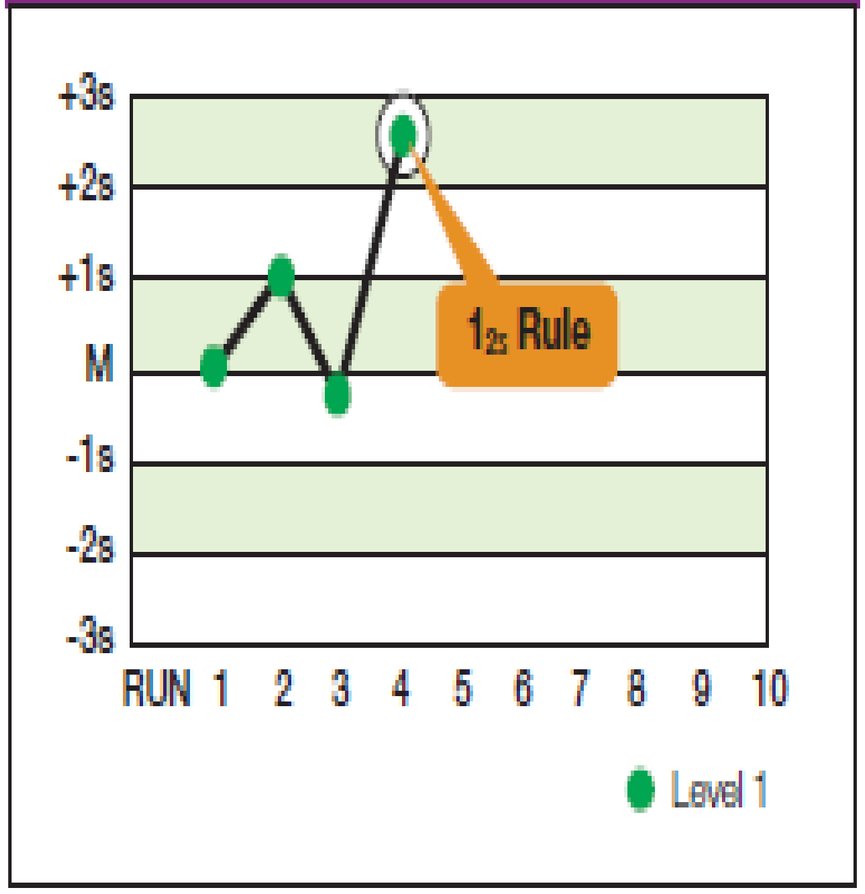
**L** = control limits often expressed as **the mean <u>assigned</u> to the L-J chart ± a multiple of the SD**

# Westgard Multirule System

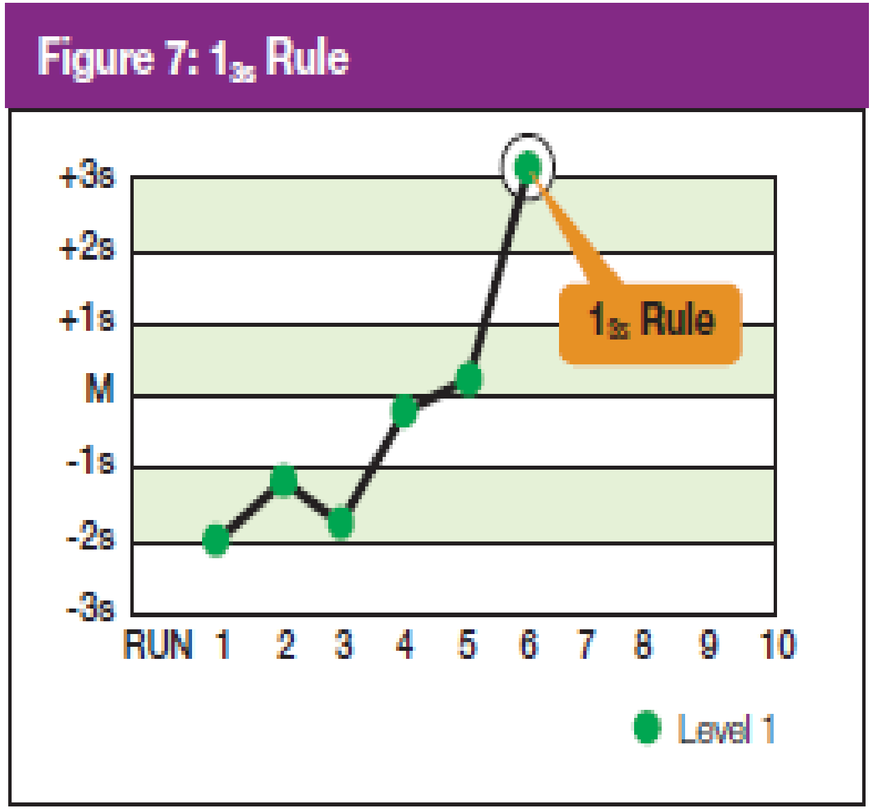
**RULE** $1_{2s}$

This is a warning rule that is violated when a single control observation is outside the ±2s limits. Remember that in the absence of added analytical error, about 4.5% of all quality control results will fall between the 2s and 3s limits. This rule merely warns that random error or systematic error may be present in the test system. The relationship between this value and other control results within the current and previous analytical runs must be examined. If no relationship can be found and no source of error can be identified, it must be assumed that a single control value outside the ±2s limits is an acceptable random error. Patient results can be reported.

Figure 6: $1_{2s}$ Rule



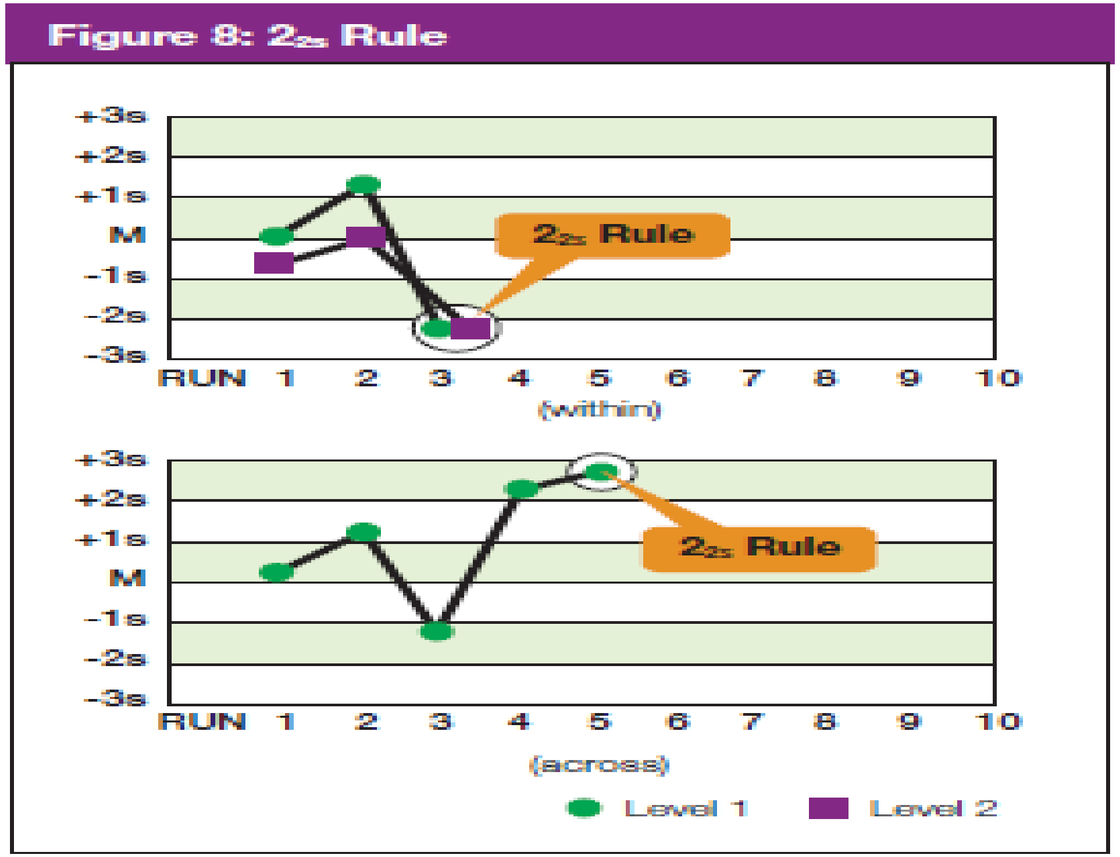
# Westgard Multirule System - $1_{3S\ rule}$




- If either of the two control results falls outside of ±3SD, rule is violated
- Run must be **rejected**
- If $1_{3S}$ not violated, check $2_{2S}$

# Westgard Multirule System - $2_{2S\ rule}$

- 2 consecutive control values for the same level fall outside of ±2SD in the same direction, or
- Both controls in the same run exceed ±2SD
- **Patient results cannot be reported**
- Requires corrective action



# The Westgard Sigma Rules™

- Multirule QC uses a combination of decision criteria, or control rules, to decide whether an analytical run is in-control or out-of-control.
- The well-known Westgard multirule QC procedure uses 5 different control rules to judge the acceptability of an analytical run.
- Over time, Westgard have developed a variety of QC design and planning tools to support laboratory efforts to select SQC procedures that are right for their specific intended clinical use and the method performance observed in their laboratory.
- A new tool called “Westgard Sigma RulesTM” was developed to achieve this purpose and as well distinguish this approach from the original Westgard Rules.

# Six Sigma Defined

- A quality discipline that focuses on product and service excellence to create a culture that demands perfection (on target, every time!)
- ***But, it is much more!***


- Six Sigma methodology was developed by Motorola, Inc. to reduce the cost of products, eliminate defects, and decrease variability in processing.
- It consists of five steps: define, measure, analyze, improve, and control (DMAIC)
- These steps are universal and could be applied to all sectors of industry, business, and healthcare.
- The sigma value indicates how often errors are likely to occur; the higher the sigma value, the less likely it is that the laboratory reports defects or false test results.
(Westgard, 2006)

# Sigma Metrics

$$\text{Sigma} = [(TE_A - |\text{Bias}_{obs}|)/SD_{obs}]$$

## Bias

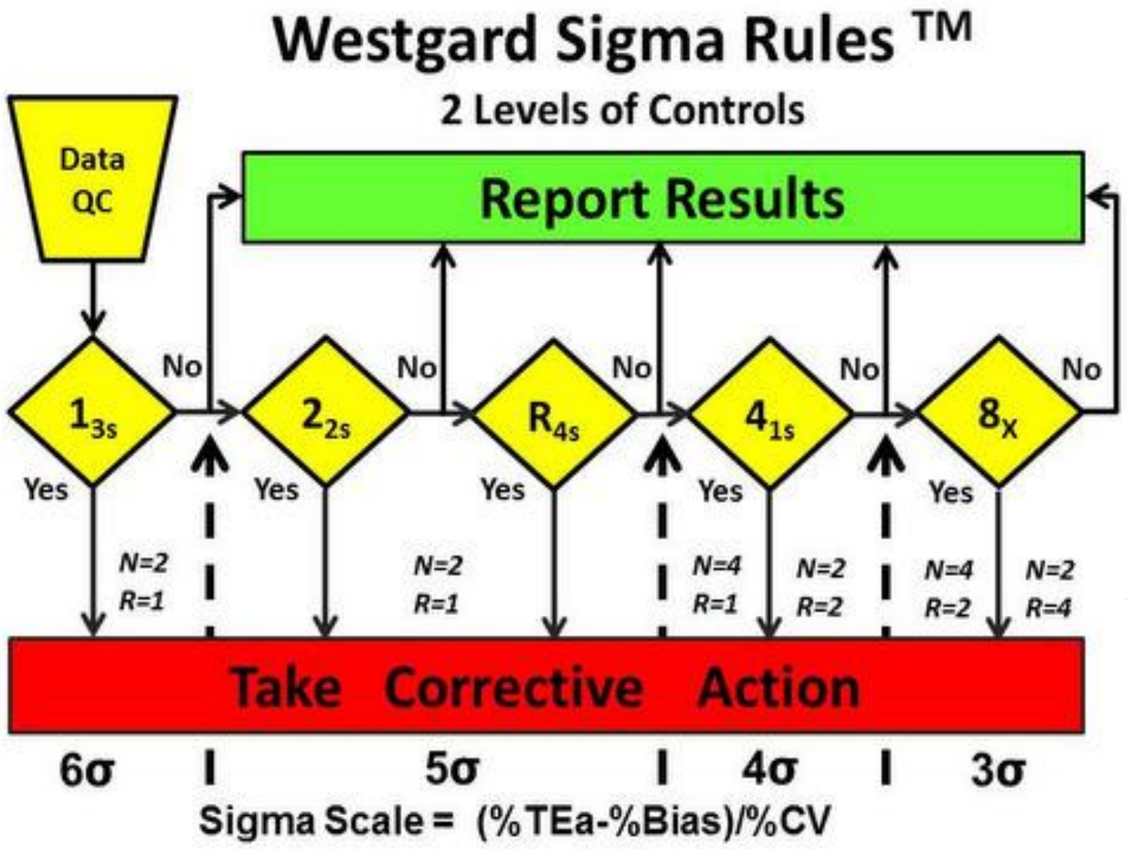
- Bias is the **systematic** difference between the results obtained by the laboratory's test method (the mean) and the results that would be obtained from an accepted reference (Target value).
- The reference may be another test method, a standard, or a consensus reference like a proficiency program or an inter-laboratory peer-comparison program.
- SD is the total analytical standard deviation of the test method.
- **Bias = Mean (X) – True Value (TV)**

# The Westgard Sigma Rules™

- Right selection of QC rules impact the QC program significantly by maximizing error detection capability and reducing false rejection
- Over time, Westgard have developed a variety of QC design and planning tools to support laboratory efforts to select SQC procedures that are right for their specific intended clinical use and the method performance observed in their laboratory.
- Westgard introduced a new tool that is quicker and easier to and this tool is called “Westgard Sigma RulesTM” to distinguish this approach from the original Westgard Rules.

**James O. Westgard, Sten A. Westgard**
**September 2014**

# Westgard Sigma rules for 2 levels of control materials




- Looks just like the Westgard Rules diagram except there is no 2 SD warning rule.
- The most important change is the Sigma-scale at the bottom of the diagram. That scale provides guidance for which rules should be applied based on the sigma quality determined in your laboratory.
- Here's how it works. The dashed vertical lines that come up from the Sigma Scale show which rules should be applied based on the sigma quality determined in your laboratory.
- For example: 6-sigma quality requires only a single control rule, $1_{3s}$, with 2 control measurements in each run one on each level of control).
- The notation N=2 R=1 indicates that 2 control measurements are needed in a single run.

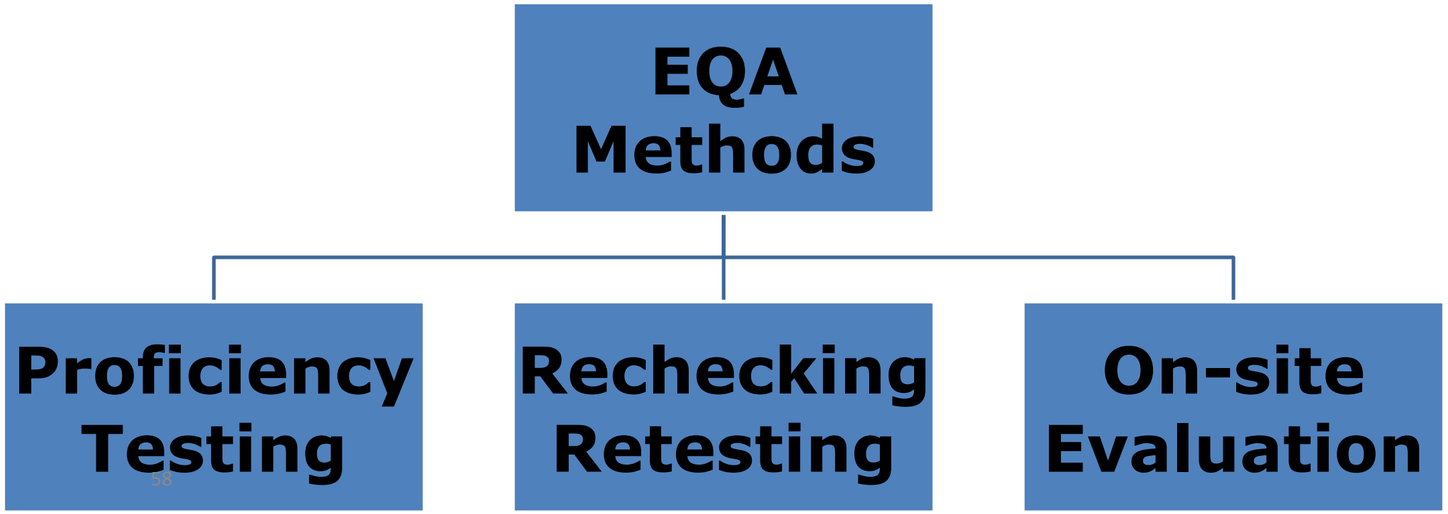
**James O. Westgard, Sten A. Westgard**
**September 2014**

# Updates on External Quality Assessment (EQA) - Proficiency Testing (PT)

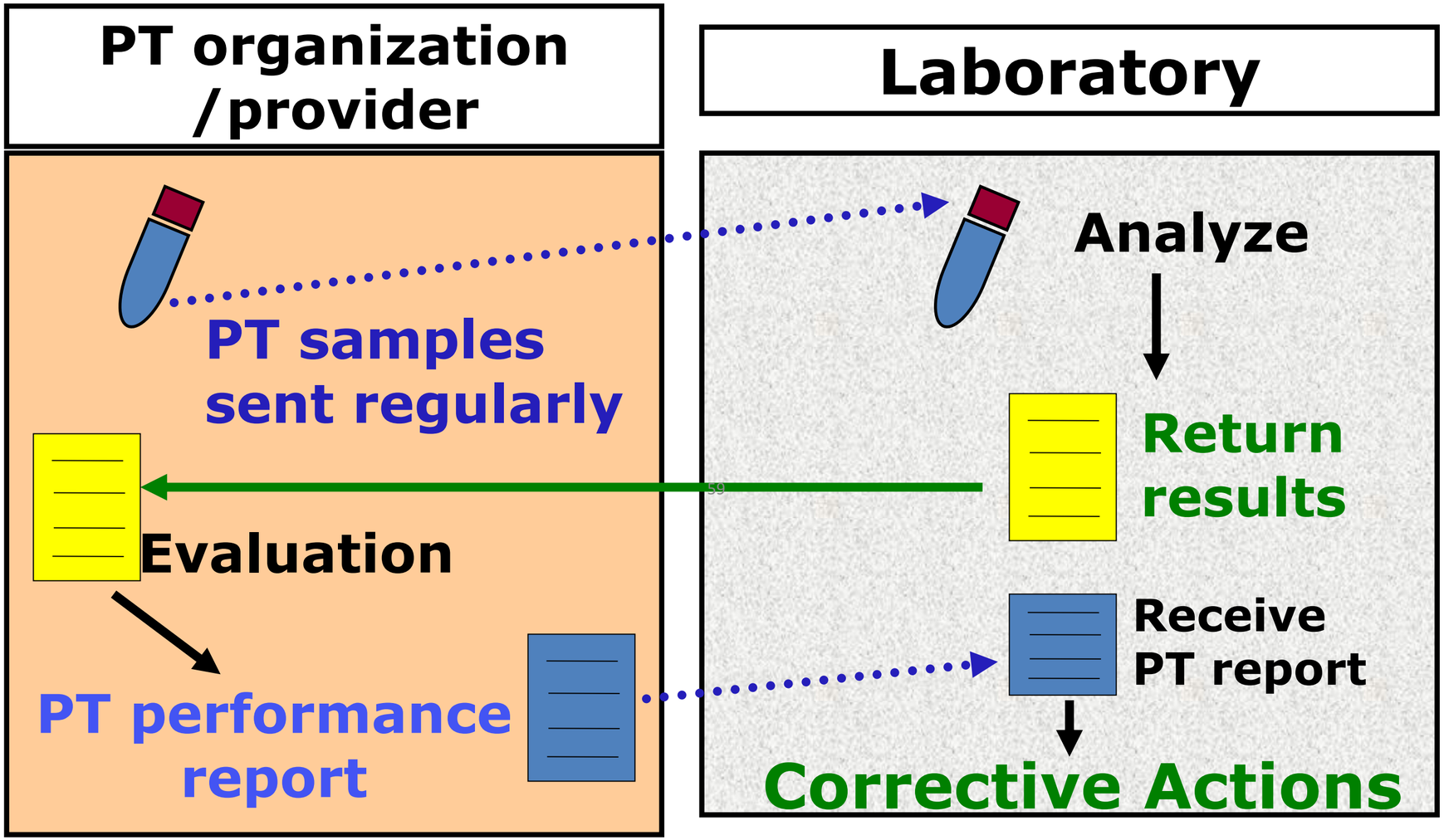
# External Quality Assessment (EQA)

## External Quality Assessment

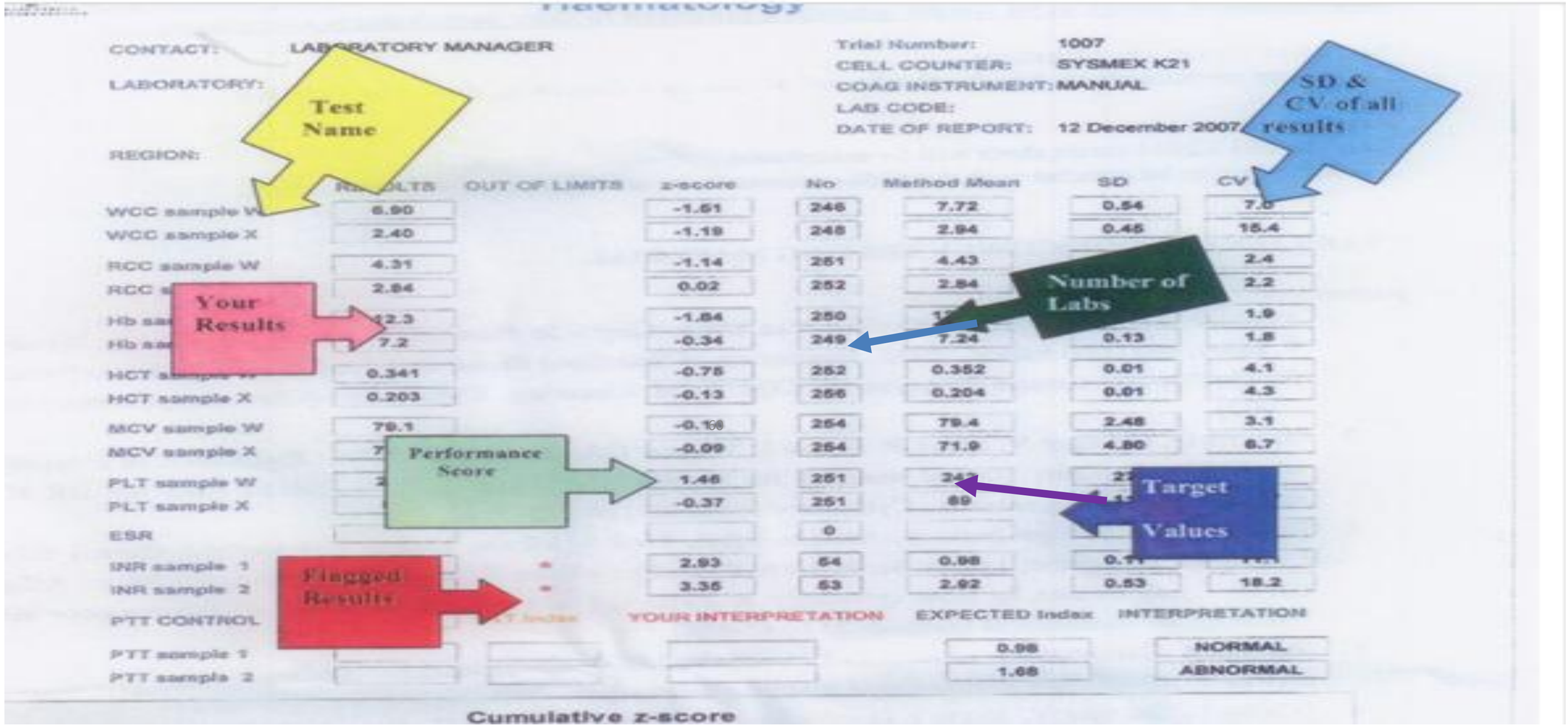
A system for objectively checking the laboratory's performance using an external agency or facility



# Proficiency Testing Process



# Interpretation of PT Data



# PT program scorecard in Nigeria

## PT providers

1. National EQA Laboratory (NEQAL) operated by MLSCN, Nigeria.
2. College of American Pathologist (CAP), USA.
3. National Health Laboratory Services (NHLS), South Africa
4. IRESSEF, Senegal
5. National HIV Program, Nigeria
6. CDC International Laboratory Branch Atlanta
7. NTBLCP, Nigeria
8. Supral National Lab –Milan, Italy

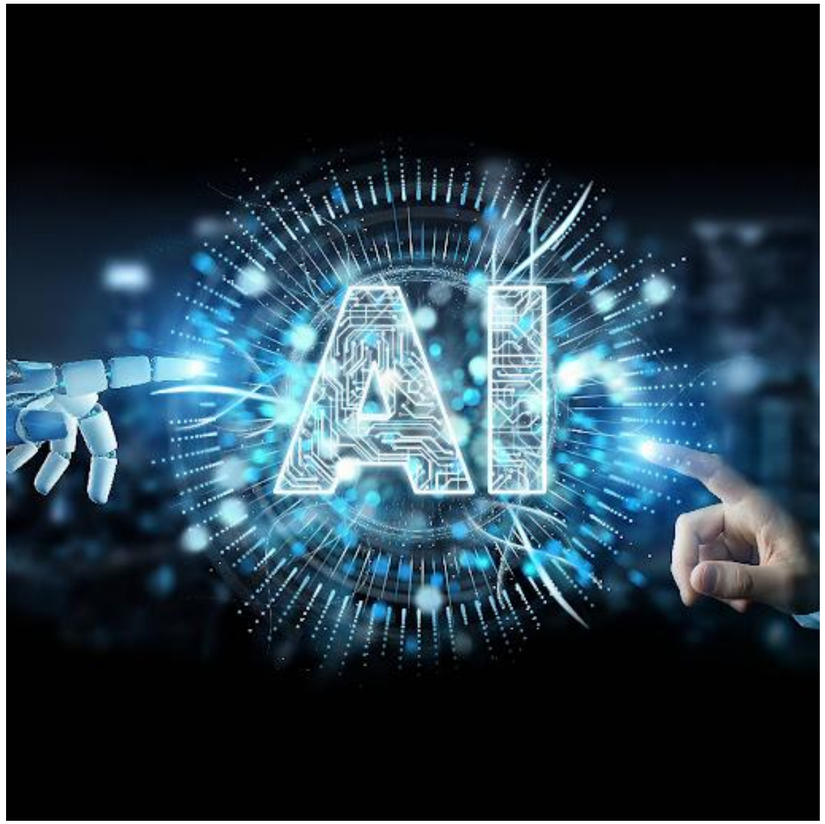
## Other Details

1. NEQAL currently provide PT panels to over 600 Laboratories across all the states in Nigeria.
2. Other PT Providers provide panels to selected few Laboratories as supported by PEPFAR program in Nigeria

# AI-driven quality control and automation in modern laboratory workflows

# Artificial Intelligence use in Clinical Laboratory

- Use of machines and computers to mimic Human intelligence through learning and programing
- AI has been in existence for close to 70 years and has been used subtly in most of the automated systems including Laboratory automation.
- The use of AI in Clinical Lab has been demonstrated in **few Labs** based on available information.



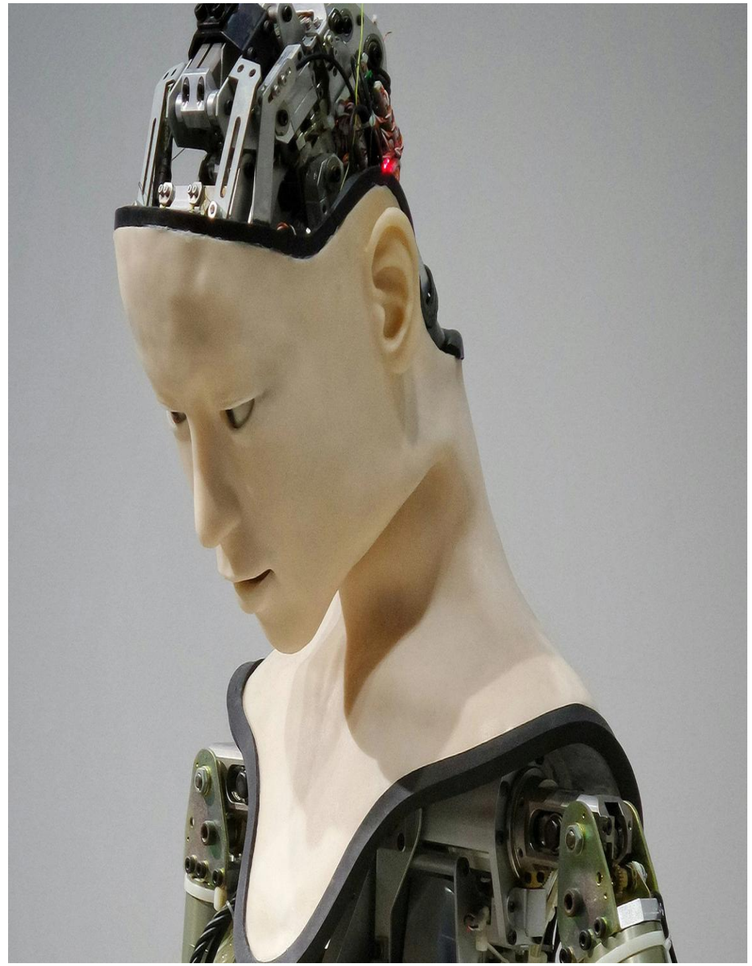
# Artificial Intelligence Algorithm use in QA / QC

- Identify QC patterns and trends resulting in automated flagging
- Clinical interpretation of Lab results e.g FBC comments
- The predictive capability of AI can be leveraged in Equipment maintenance to indicate possible breakdown
- AI powered LIMS can be used in Delta check
- Automated review / approval processes and predictive inventory use to alert reordering

https://www.autoscribeinformatics.com/resources/blog/artificial-intelligence-ai-within-lims-and-the-laboratory

# Is the Lab ready ?

- For AI to be beneficial and improve Lab system : setting up the algorithm properly is key.
- Pre- service and in-service training curriculum of MLS needs to be updated to address relevant skills required to adapt to changes introduced by automation and AI
- Setting up AI models for Lab use requires collaborative effort : Medical Laboratory professionals, IT experts and other stakeholders

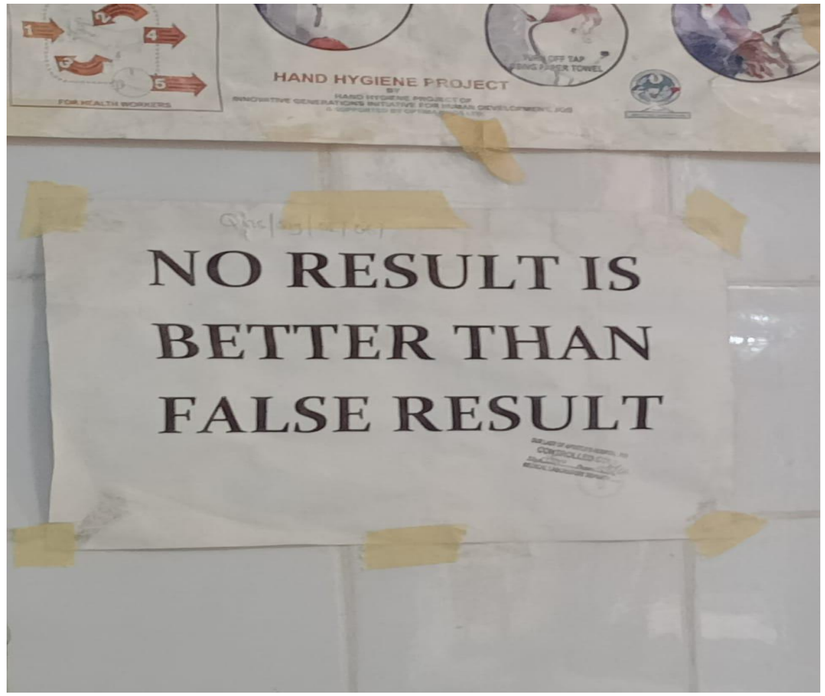


# Key messages

- A QC program allows the laboratory to differentiate between normal variation and error.
- EQA is a system for objectively checking the laboratory's performance using an external agency or facility
- For AI to be beneficial and improve Lab system : setting up the algorithm properly is key.

# Conclusion

**Any Laboratory test conducted without a valid QC program is considered a harm to the patient.**



# Acknowledgement


- WHO/CLSI Laboratory Quality Management System Training Toolkit
- National QMS ToT curriculum
- ISO 15189 : 2022
- David Burnett – a practical guide to ISO 15189 in Laboratory medicine
- SLMTA Training Toolkit.
- Beracah Consulting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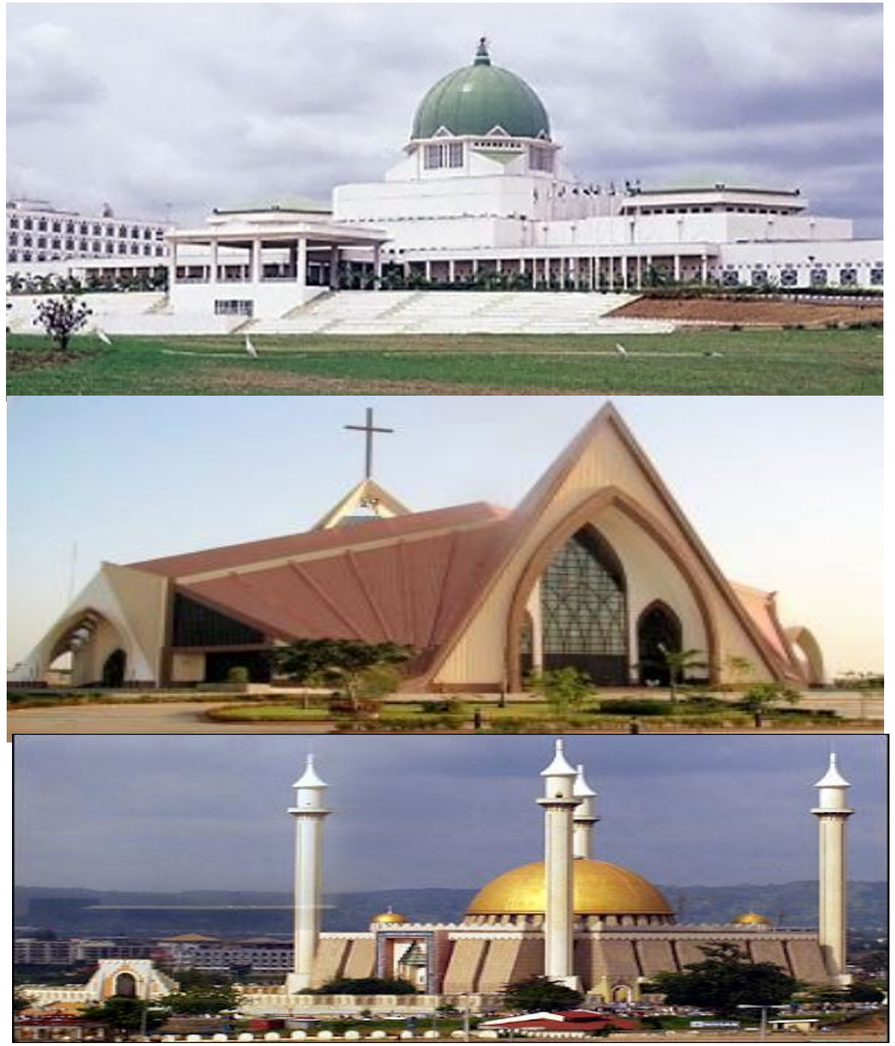
# Greetings from Abuja



# Thank You

**NEXT WEEK:**

Ensuring Compliance Through Laboratory Assessments & Audits

- Conducting internal audits for quality improvement and accreditation readiness
- Key elements of ISO 15189 compliance and regulatory expectations
- Digital audit tools for enhancing accuracy and efficiency in assessments

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