Quality assurance and Quality Control in haematology

Dr. Shabnam Roohi

What is quality?

Quality is doing the right things

and doing those things right.

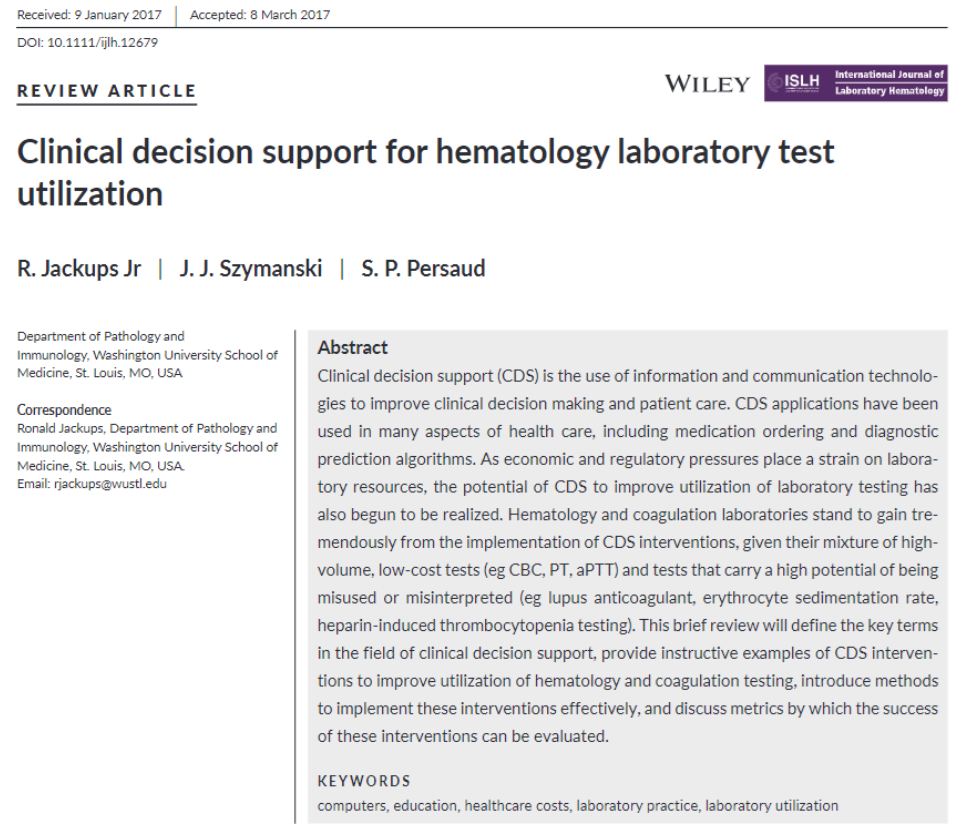
Philip Crosby

Doing the Right Things

= **Appropriateness**

Knowledge of those who order laboratory tests

- Order the right test
- For the right reason
- On the right patient
- At the correct time



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REVIEW ARTICLE

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Clinical decision support for hematology laboratory test utilization

R. Jackups Jr | J. J. Szymanski | S. P. Persaud

Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, USA

Correspondence
Ronald Jackups, Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, USA.
Email: rjackups@wustl.edu

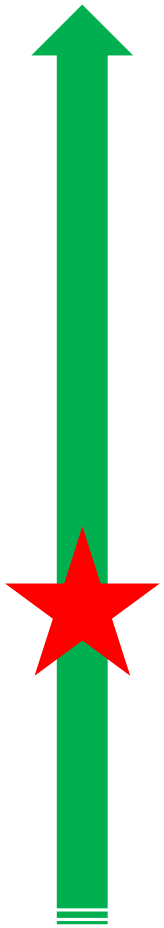
Abstract

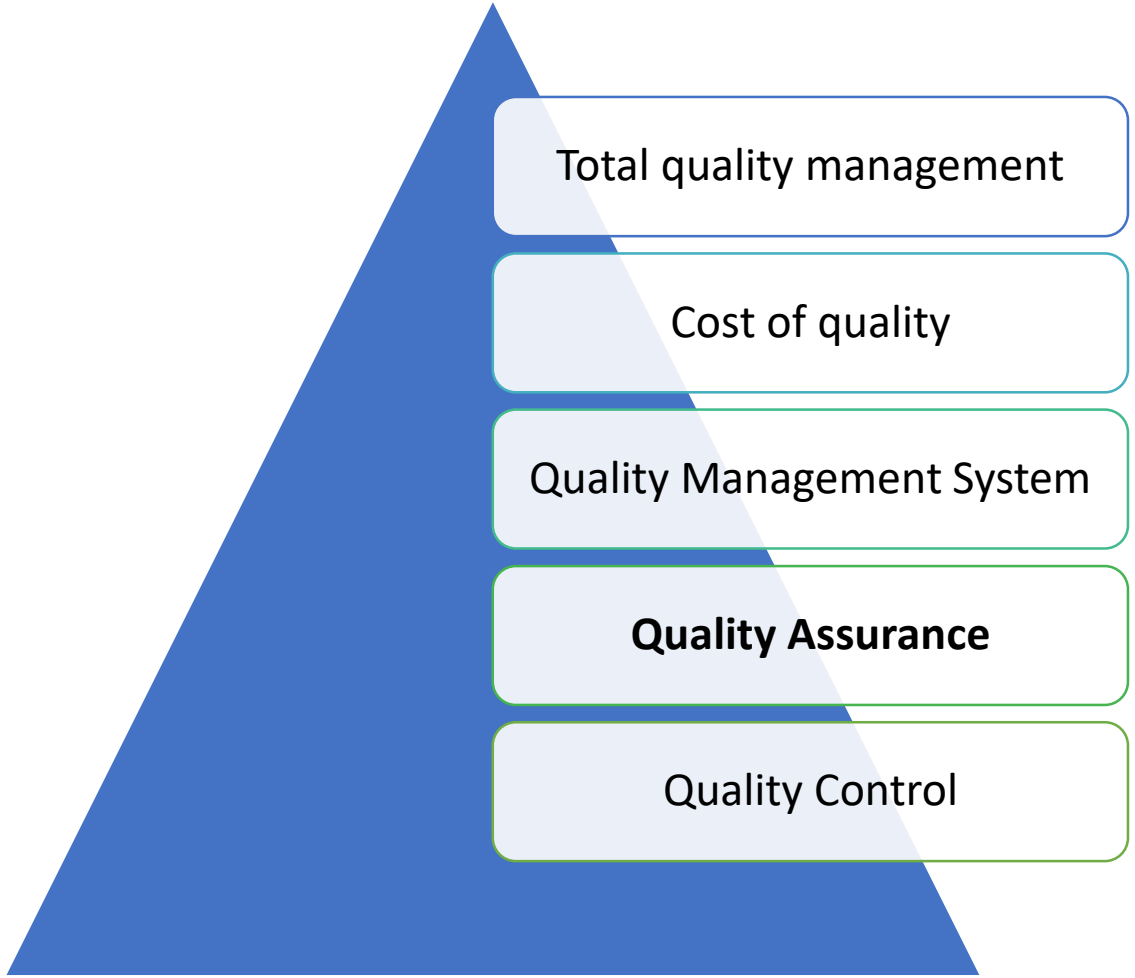
Clinical decision support (CDS) is the use of information and communication technologies to improve clinical decision making and patient care. CDS applications have been used in many aspects of health care, including medication ordering and diagnostic prediction algorithms. As economic and regulatory pressures place a strain on laboratory resources, the potential of CDS to improve utilization of laboratory testing has also begun to be realized. Hematology and coagulation laboratories stand to gain tremendously from the implementation of CDS interventions, given their mixture of high-volume, low-cost tests (eg CBC, PT, aPTT) and tests that carry a high potential of being misused or misinterpreted (eg lupus anticoagulant, erythrocyte sedimentation rate, heparin-induced thrombocytopenia testing). This brief review will define the key terms in the field of clinical decision support, provide instructive examples of CDS interventions to improve utilization of hematology and coagulation testing, introduce methods to implement these interventions effectively, and discuss metrics by which the success of these interventions can be evaluated.

KEYWORDS

computers, education, healthcare costs, laboratory practice, laboratory utilization

Doing Things Right





"Totally satisfied employee serving totally satisfied customers"

Costs that support good quality and costs that result from poor quality

Interrelated Technical and Management processes

Process measurement only

Method control only

How Quality Control, Quality Assurance, and QMS Differ

- QC, QA, and QMS and their related terms are not the same.
- They are different and have specific definitions for the medical laboratory.
- Use these terms correctly and ensure that others in your laboratory understand the differences as well.

Quality Control

- It monitors the performance of examination methods to give assurance that the value(s) obtained on the specimen is/are likely to be accurate.
- QC, however, does not detect
  - Incorrect specimen identification
  - A specimen collected at an inappropriate time.

QC is only clause 7.3.7.2

QC
• Method control • Method accuracy • Batch-related and time-limited • Does not prevent preexamination or postexamination errors!

Quality Assurance

- Quality assurance (QA) is a set of process measurements, not specimen measurements.
- QA includes measures of,
  - The numbers and locations of patients who do not have proper identification
  - The numbers and types of unacceptable specimens and their sources
  - The numbers and types of reporting errors
  - Result turnaround times.
- Your laboratory needs to track key quality indicators in preexamination, examination, and postexamination processes.

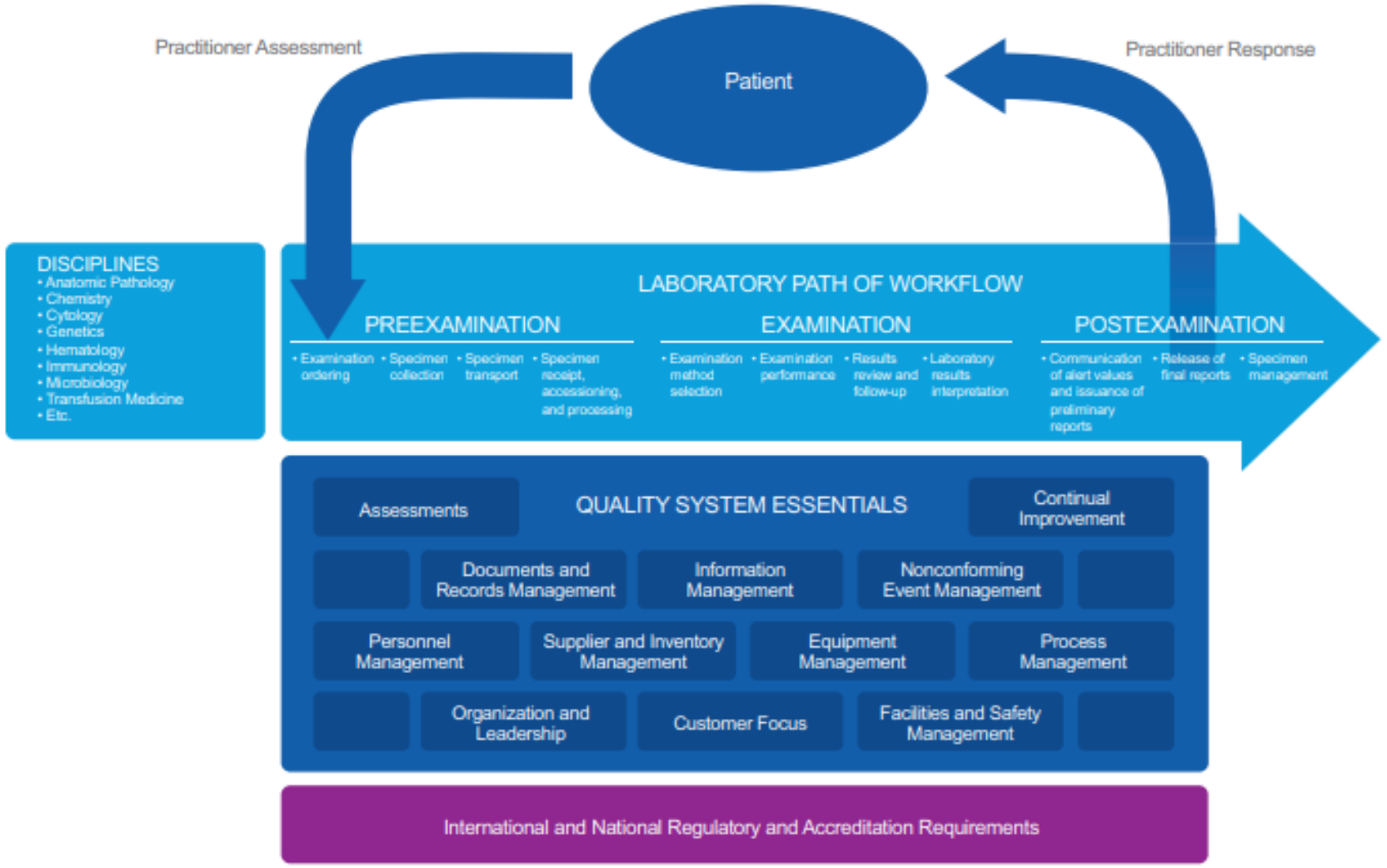
QA is only clauses

- 7.3.7.3 External quality assessment
- 8.8 Evaluations

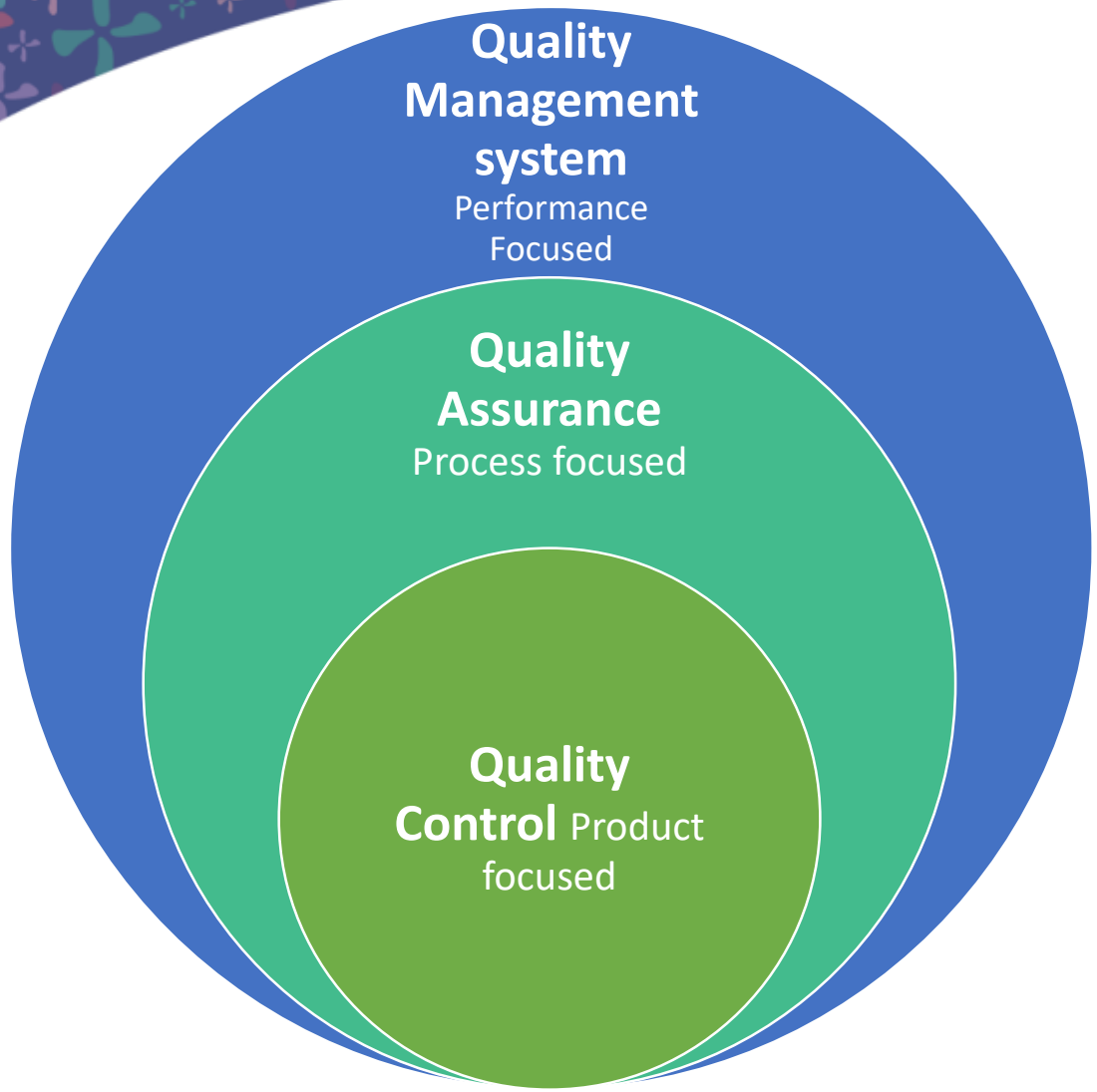
Quality Assurance

- QA ≠ QC !
- Process measurement and monitoring
- Preexamination processes
- Examination processes
- Postexamination processes

QMS model



The quality management system (QMS) organizes required management and path of workflow processes and is much broader than QC or QA alone.



Quality Management System

- ISO 15189:2022
- Integrated processes
- **QC** is only clause 7.3.7.2
- **QA** is only clauses
  - 7.3.7.3 External quality assessment
  - 8.8 Evaluations

In the present environment of limited resources, quality cannot be taken for granted, so the historical perspective of **quality control** and **quality assurance** needs to be superseded by a comprehensive view of the internationally accepted quality practices applied to a laboratory's entire scope of work.

QA in the preanalytical phase

The steps of the preanalytical phase

Preparation prior to sampling

Patient variables (Drug history)
Patient identification

Sampling/handling

Venipuncture procedure
Quality of specimen (clots, anticoagulant type & ratio)

Storage/transport

Sample temperature
Stability

Preparation prior to analysis

Equipment
Reagent

Understanding functionality of your equipment & reagents

Equipment

- Principles of operation
- Verification (IQ/ OQ/ PQ)
- Startup or daily checks
- Shutdown procedure
- Normal sights and sounds of the instrument
- Familiarize staff to troubleshooting manual

Reagents

- Acceptance criteria
- Lot verification
- Recall

Monitor

- **% of inappropriate samples**
  - Under filled/ overfilled/ clotted samples
  - Type of anticoagulant
  - Timed samples
- **Number of samples exceeding the time limit for transportation**
  - Time of collection and time of processing sample should be tracked.
- **Adequacy of request forms**
  - Purpose of the test for coagulation testing
- **Equipment down time**

QA in the analytical phase

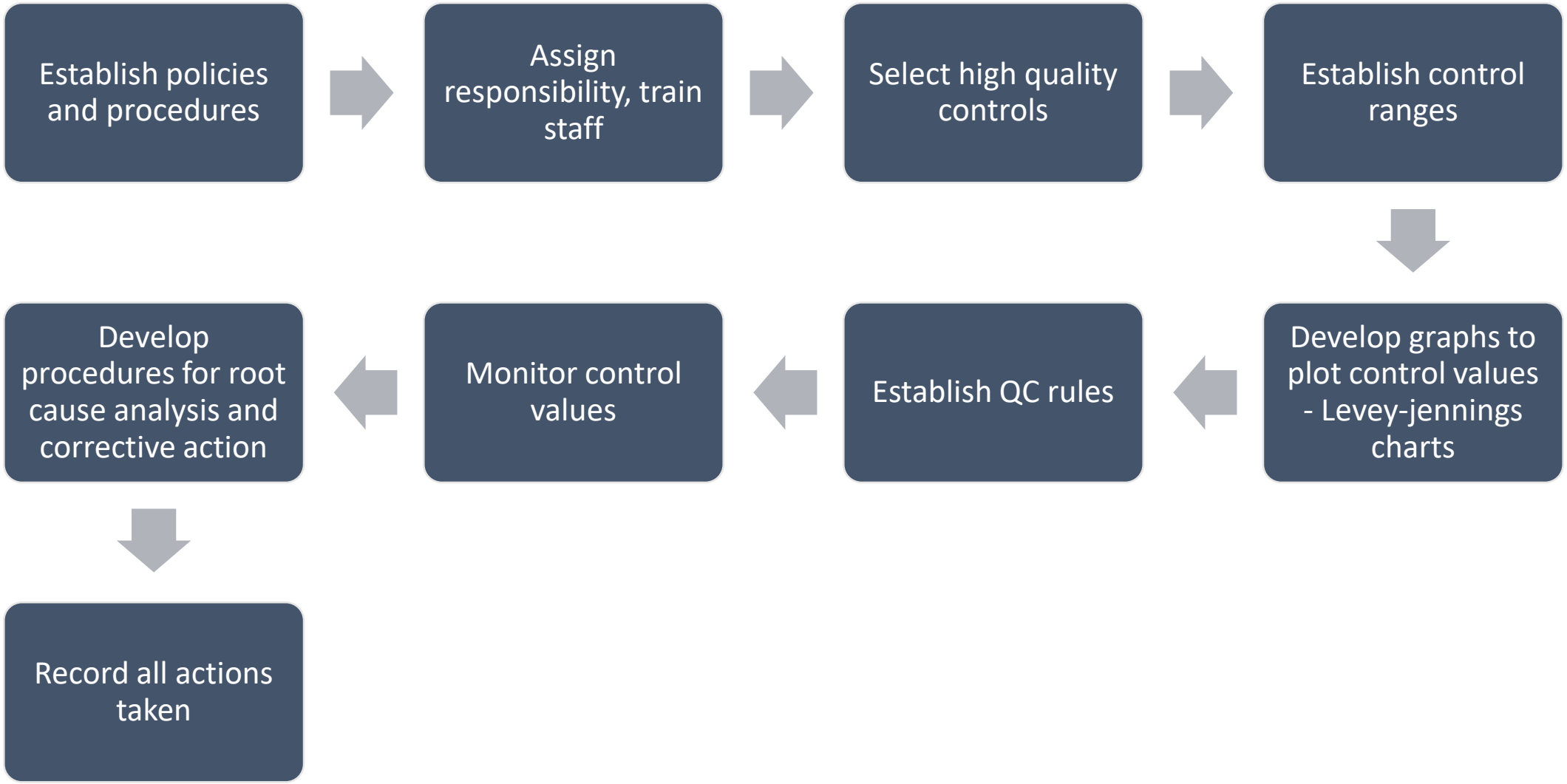
Components

- Internal Quality Control
  - Commercial controls (2 or 3 level)
  - Patient samples as control (retained patient sample)
  - Moving average
- External Quality Assurance
- Harmonization of equipment results

Quality Control Program Contents

- QC Plan *for each analyte*
  - Types of controls
  - Prepared or purchased?
  - Instrument / method internal or external?
  - Levels (low, normal, high)
  - Value of 3rd party controls
- Number to test and frequency
  - Mfg. recommendations
  - Regulatory or accreditation requirements
- Expected ranges
- Action to take in response to out-of-control situations
- Records to maintain
  - QC material lot # and expiry
  - Date QC performed
  - ID of person performing QC
  - Expected QC range
  - Results obtained
  - Statistical analysis of quantitative results
  - Actions taken
- Laboratory director reviews

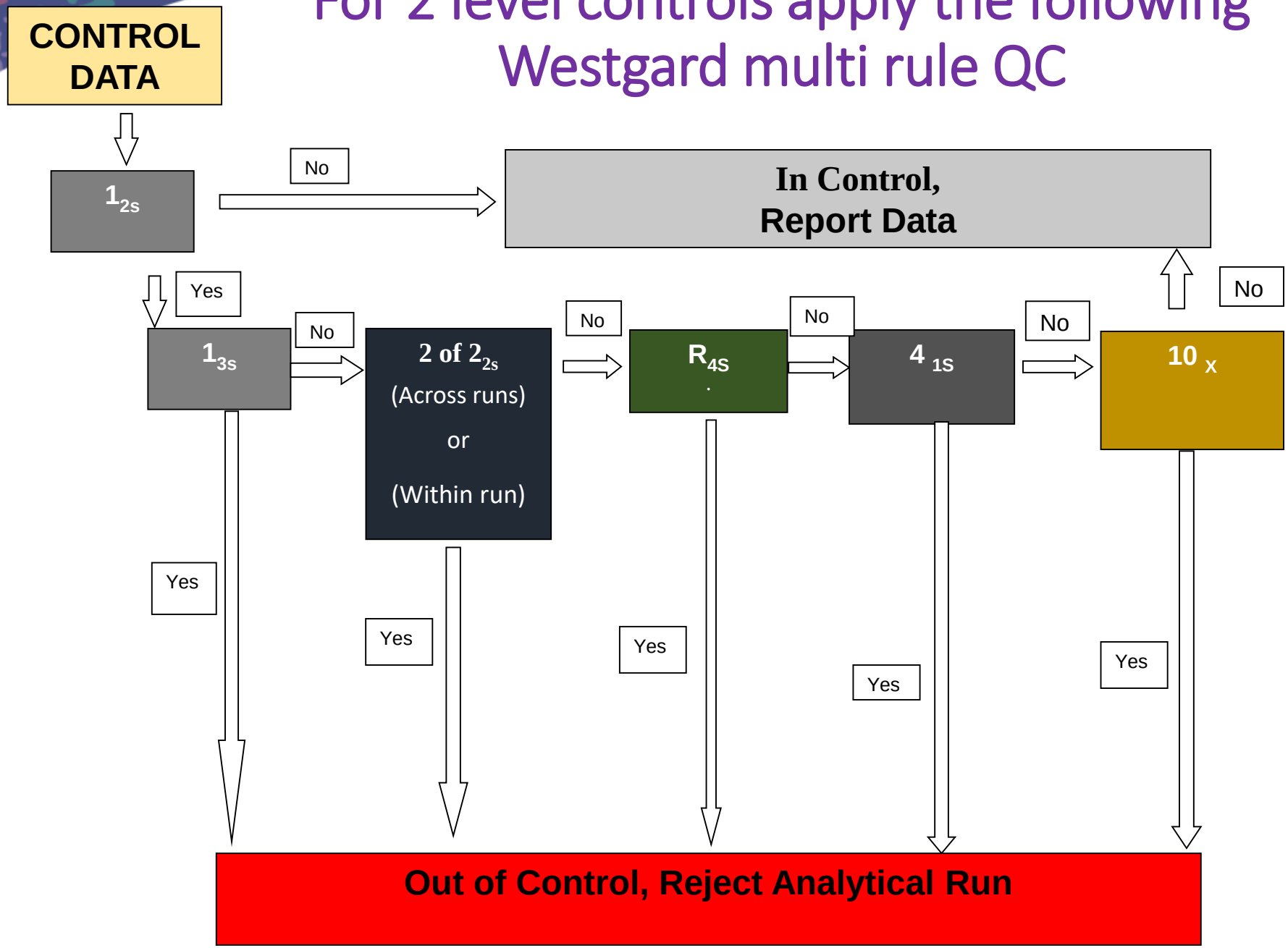
Implementation steps



Establish policy and procedure

- Frequency to assay QC materials
- The frequency to assay QC specimens is a function of several parameters:
  - The analytical stability of the method
  - How much error can be tolerated without impact on patient care (TEa)
  - Number of patient samples measured over a period of time
  - The need to verify and document the reliability of clinical results at the time they are reported.

For 2 level controls apply the following Westgard multi rule QC



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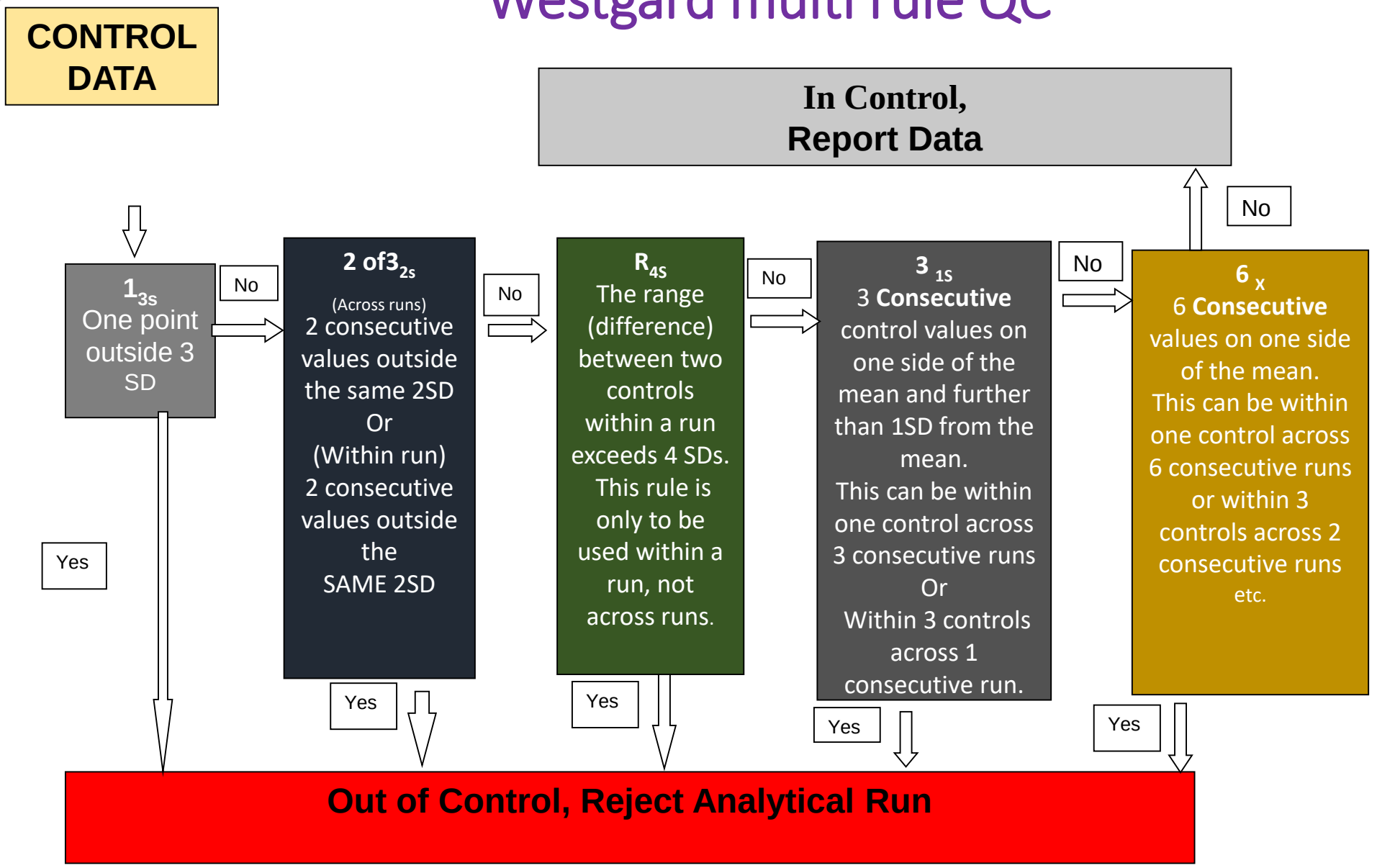


Trouble shooting

IQC out due to equipment, reagent or calibration error

Should patient results reported between the last acceptable run and the rejected run be repeated?

Base decision on the nature and size of the error.

Retest patient samples If analytical errors have clinical significance

Sigma metrics

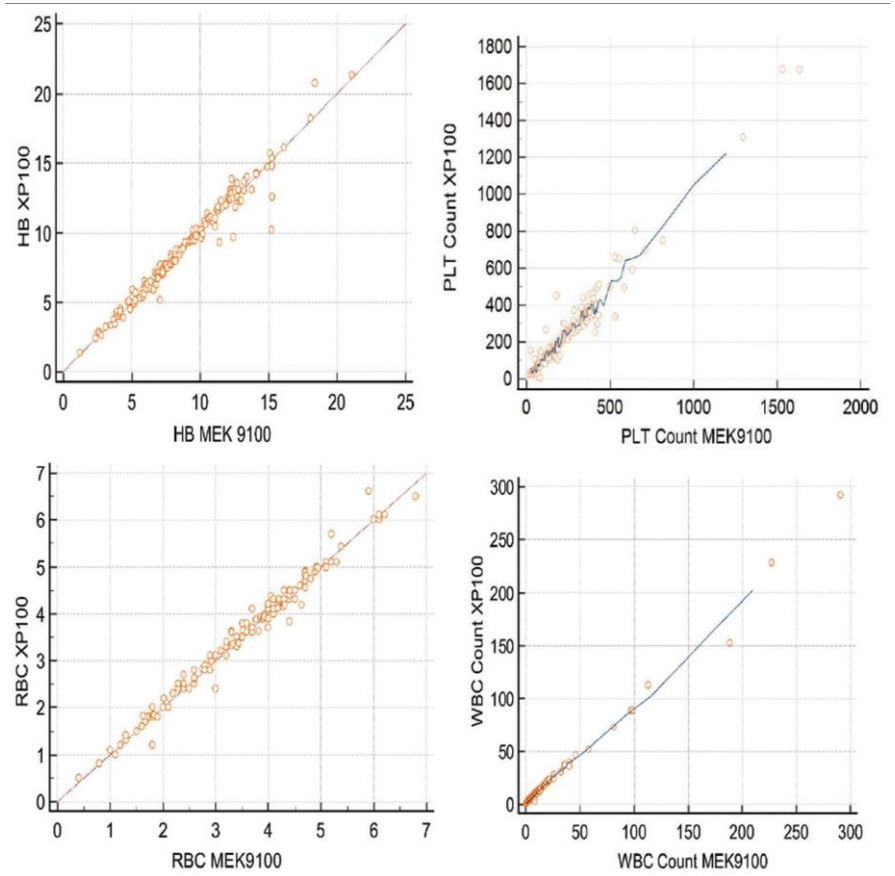
- Sigma Metric Analysis provides an objective assessment of analytical methods and provides the critical design information needed for operational implementation.

Method

- Define total allowable error (TEa) specification (Various databases available for reference)
- Evaluate analytic performance of method
  - Imprecision (from replication experiment or from routine IQC data)
  - Bias (comparison of methods, PT survey, Peer Comparison)
  - Calculate sigma metric using formula S=(TEa – Bias)/CV
- Sigma metric of **>3** is considered to be acceptable performance

Retained sample testing/ patient repeats

- These are done for inter instrument and intra instrument comparison.
- This is in addition to IQC
- Can help when control material is not available
- In resource poor settings



Scatter plot for comparability (correlation) of results for hemoglobin, platelet count, red blood cell count, and white blood cell count in 150 samples.

Retained Patient Control

- Two-three patient samples with specific parameters.
- SD of differences between results on 10 duplicate samples is determined and +2SD limits specified.
- Subsequent duplicate values should be within these defined limits.
- Can be used over a 24 hour period.
- Cost efficient.
- Can be used to detect systematic error.
- Transferable between instruments and modes.

WBC (x 10^9/L)				
Specimen	**1st count**	**2nd count**	**d**	**d^2**
1	5.4	5.8	0.4	0.16
2	8.3	10.5	2.2	4.84
3	17.2	18.0	0.8	0.64
4	5.4	5.4	0	0
5	12.2	11.8	0.4	0.16
6	14.3	13.8	0.5	0.25
7	6.2	6.4	0.2	0.04
8	8.2	8.6	0.4	0.16
9	7.3	7.5	0.2	0.04
10	5.4	5.9	0.5	0.25

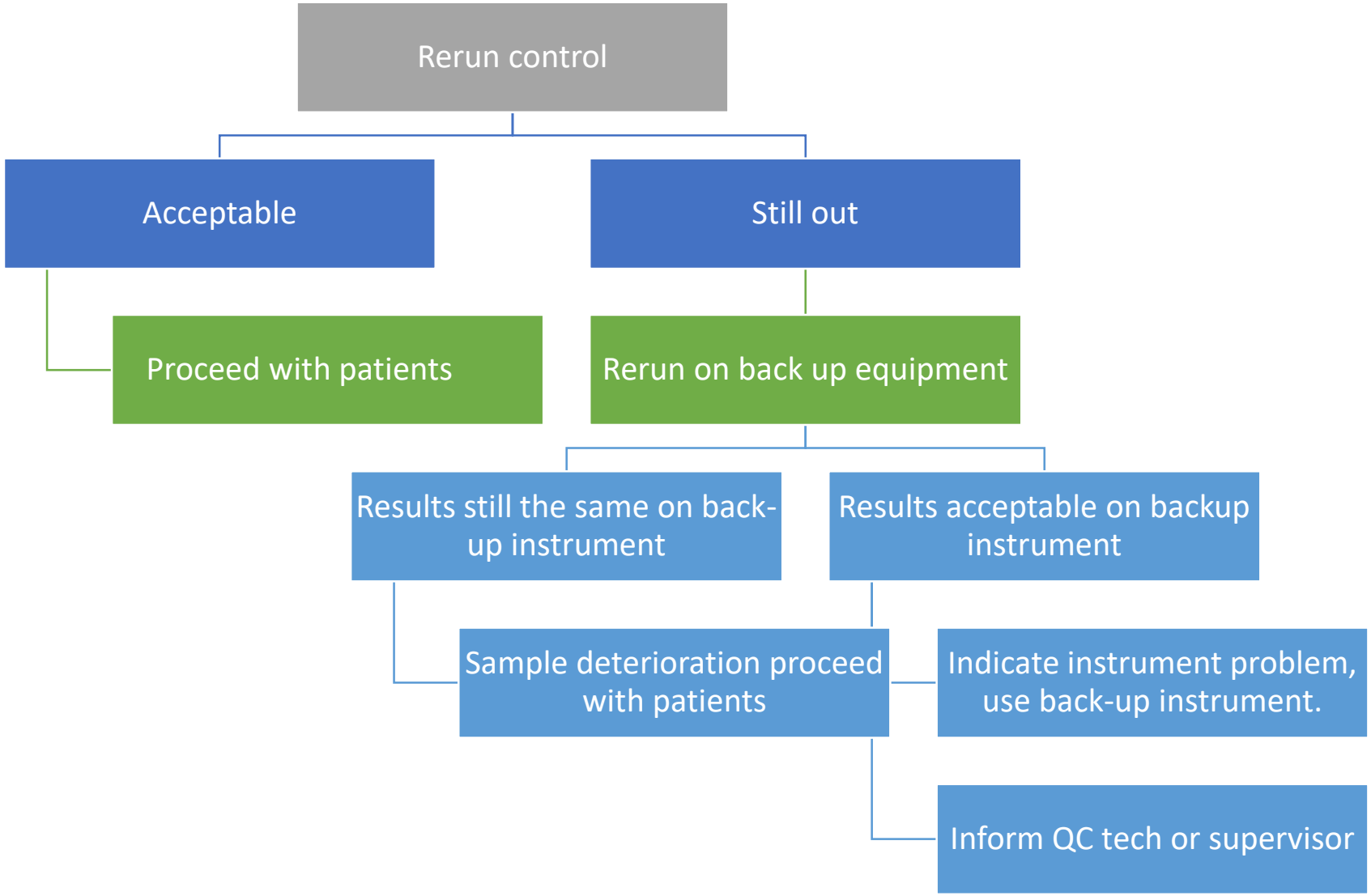
Retained Patient Control Allowable standard deviation

Sample Type	WBC	HGB
Control 1	5.0-10.0 x $10^3/mm^3$	12.0-15.0 mg/dL
Control 2	10.0-15.0 x10^3 /mm^3	7.0-10.0 mg/dL

• Parameter	Control 1	Control 2
WBC	± 0.6	± 1.4
RBC	± 0.14	± 0.14
HGB	± 0.3	± 0.3
HCT	± 2.0	± 2.0
MCV	± 2.0	± 2.0
PLT	± 40.0	± 40.0

Just like commercial controls, have policy for “Outliers” and corrective action.

Control Decisions

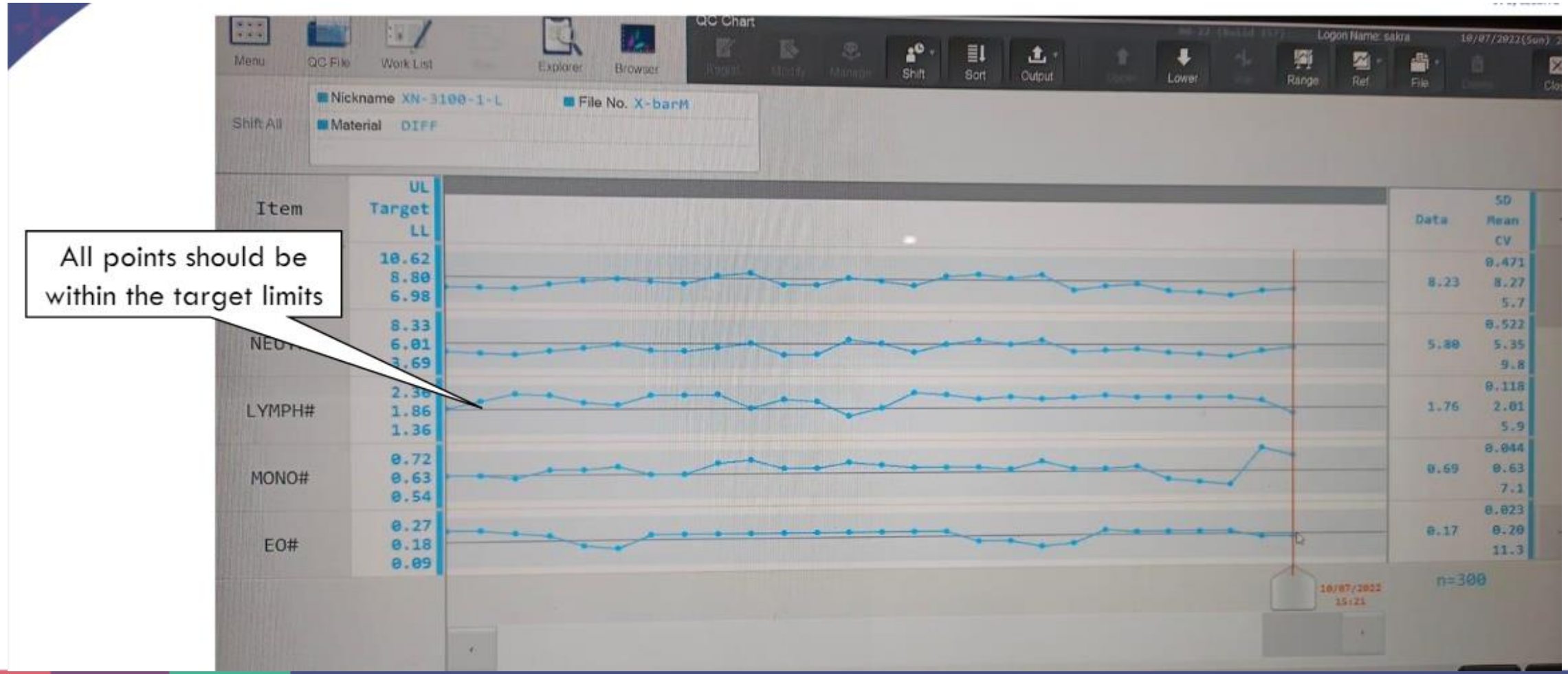


Moving Average
XB Analysis & XM Analysis

- XB Analysis is a cost effective quality control method that allows for continuous monitoring of system performance using patient samples along with commercial controls.
  - X = Mean
  - B = Bull (for Brian S. Bull, M.D.)
- XB evaluates RBC indices which are typically stable for an individual patient, from day to day, and stable for patient population over time.
- XM Analysis is a quality-control method that uses an Exponentially Weighted Moving Average (EWMA) of CBC, Diff, NRBC and Reticulocyte parameters and compares them with known target values, to monitor instrument performance.
- The lab's assayed commercial control is the final indicator to determine if the analyzer is in or out of control.

Moving Average
XB Analysis & XM Analysis

Run 1000 samples, calculate mean, standard deviation and target limits.



Moving Average
XB Analysis & XM Analysis

If the XB/ XM value is out of range, check:

- Which parameters are most affected
- If the change is sudden or ongoing
- Batch contained samples from particular population (renal, oncology)
- Process assayed commercial IQC.
  - If IQC is within acceptable limits, then evaluate and reset the target values.
  - If IQC is out of acceptable limits then follow the guidelines for IQC outliers.
  - Refer to equipment: Using XB/ XM for Troubleshooting Specific Cases.

PT-EQA Program

Verifies the ability of testing and examination methods to achieve accurate results

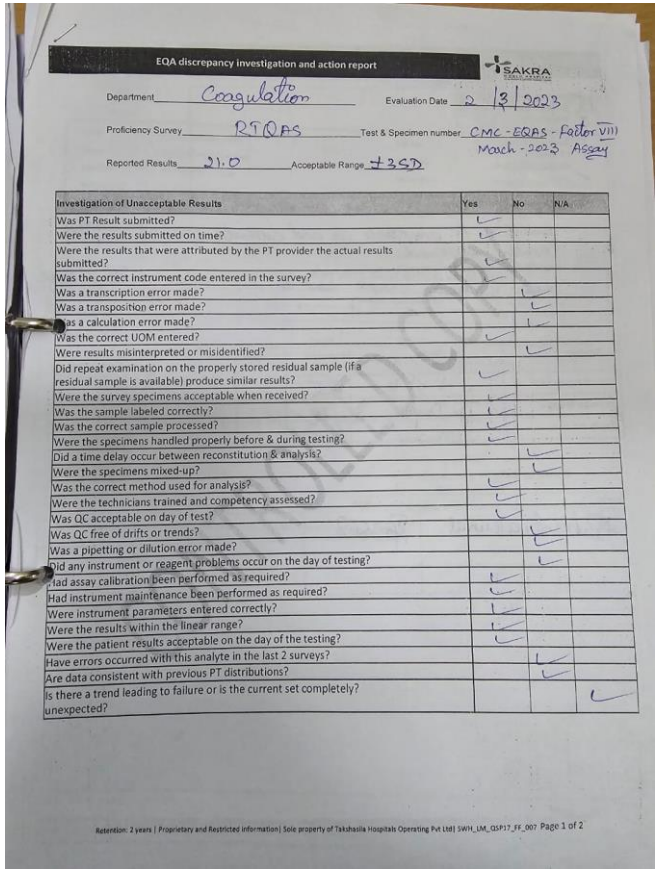
PT testing schemes available

- AIIMS (CBC, peripheral smear, Reticulocyte count)
- CMC Vellore (Coagulation parameters)
- Tata memorial Hospital (flow cytometry)
- Biorad (Haematology)
- Randox (Haematology, coagulation urine routine)
- RML (Haematology, electrophoresis urine etc.)

PT-EQA Program

PT Records

- ID of persons handling, preparing, processing, and examining each sample
- Results submitted
- Performance report received
- Lab director review
- Follow-up action taken



EQA discrepancy investigation and action report

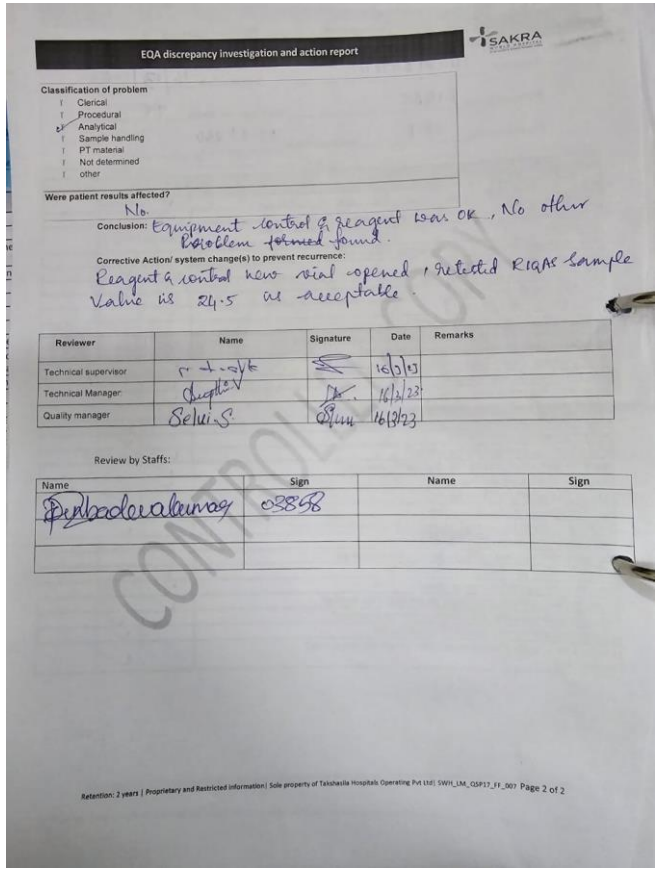
Department: Coagulation Evaluation Date: 2/3/2023

Proficiency Survey: RTQAS Test & Specimen number: CMC-EQAS-Factor VIII March-2023 Assay

Reported Results: 21.0 Acceptable Range: ±3SD

Investigation of Unacceptable Results	Yes	No	N/A
Was PT Result submitted?	✓		
Were the results submitted on time?	✓		
Were the results that were attributed by the PT provider the actual results submitted?	✓		
Was the correct instrument code entered in the survey?	✓		
Was a transcription error made?		✓	
Was a transposition error made?		✓	
Was a calculation error made?		✓	
Was the correct UOM entered?	✓		
Were results misinterpreted or misidentified?		✓	
Did repeat examination on the properly stored residual sample (if a residual sample is available) produce similar results?	✓		
Were the survey specimens acceptable when received?	✓		
Was the sample labeled correctly?	✓		
Was the correct sample processed?	✓		
Were the specimens handled properly before & during testing?	✓		
Did a time delay occur between reconstitution & analysis?		✓	
Were the specimens mixed-up?		✓	
Was the correct method used for analysis?	✓		
Were the technicians trained and competency assessed?	✓		
Was QC acceptable on day of test?	✓		
Was QC free of drifts or trends?		✓	
Was a pipetting or dilution error made?		✓	
Did any instrument or reagent problems occur on the day of testing?		✓	
Had assay calibration been performed as required?	✓		
Had instrument maintenance been performed as required?	✓		
Were instrument parameters entered correctly?	✓		
Were the results within the linear range?	✓		
Were the patient results acceptable on the day of the testing?	✓		
Have errors occurred with this analyte in the last 2 surveys?		✓	
Are data consistent with previous PT distributions?		✓	
Is there a trend leading to failure or is the current set completely? unexpected?			✓

Retention: 2 years | Proprietary and Restricted information| Sole property of Takshasila Hospitals Operating Pvt Ltd| SWH_LM_QSP17_FF_007 Page 1 of 2



EQA discrepancy investigation and action report

Classification of problem
- [ ] Clerical
- [ ] Procedural
- [x] Analytical
- [ ] Sample handling
- [ ] PT material
- [ ] Not determined
- [ ] other

Were patient results affected?
No.

Conclusion: Equipment control & reagent lot are OK, No other problem ~~formed~~ found.

Corrective Action/ system change(s) to prevent recurrence:
Reagent & control new vial opened, retested RIQAS sample value is 24.5 as acceptable.

Reviewer	Name	Signature	Date	Remarks
Technical supervisor	[illegible]		16/3/23	
Technical Manager	[illegible]		16/3/23	
Quality manager	Selvi S		16/3/23	

Review by Staffs:

Name	Sign	Name	Sign
[illegible]	03858		

Retention: 2 years | Proprietary and Restricted information| Sole property of Takshasila Hospitals Operating Pvt Ltd| SWH_LM_QSP17_FF_007 Page 2 of 2

Verify consistency between more than one instrument or method

- It is required that test results performed using different methods or performed at multiple sites be evaluated at least once in 6 months.

- Native patient sample aliquots are measured using two or more methods (or instruments) to confirm agreement or to adjust the calibration of different methods to achieve agreement in results for patient samples.

Verify consistency between more than one instrument or method

- One method/ instrument is chosen to represent the primary method to which others will be adjusted to achieve equivalent results.

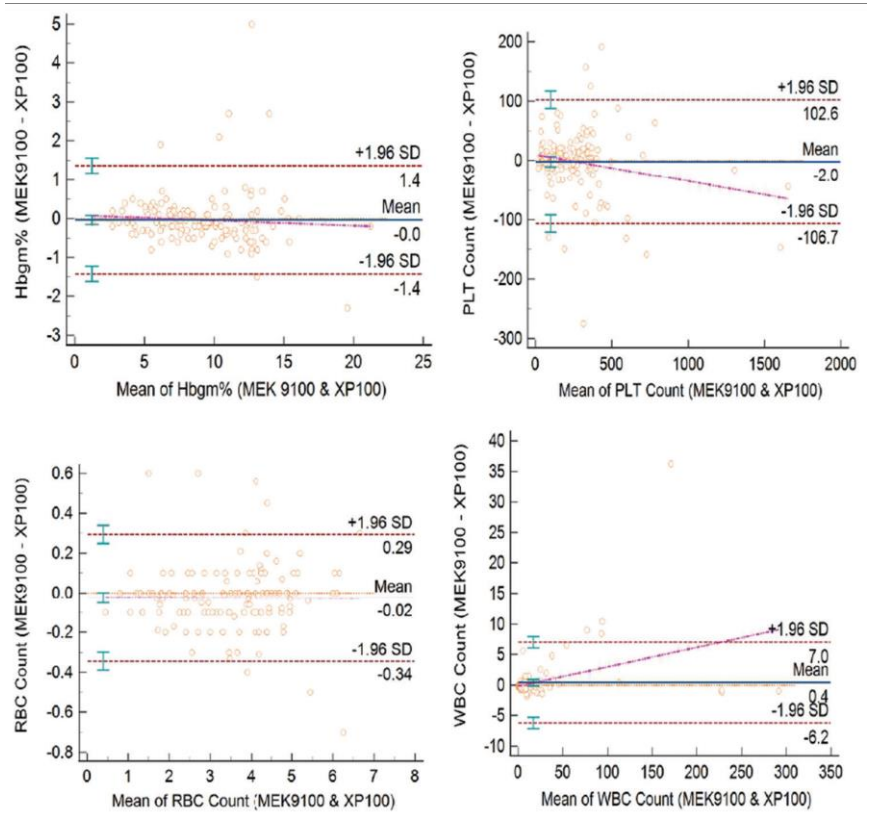
- The primary method is chosen based on quality and reliability of results

METHOD COMPARISON LOG

Department:				Name of Equipment.1						Name of Equipment. 2					
S.NO	Analysis date	Analysis Time	UHID	PARAMETER		PARAMETER		PARAMETER		PARAMETER		PARAMETER		PARAMETER	
				Equip. 1	Equip. 2	Equip. 1	Equip. 2	Equip. 1	Equip. 1	Equip. 2	Equip. 2	Equip. 1	Equip. 2	Equip. 1	Equip. 2
Average bias % (Σ(x-y)/Σx*100)															
Regression analysis															
Remarks															

Verify consistency between more than one instrument or method

- Splitting of one or more individual patient samples, or a small pool from several samples are analysed
  - On a weekly basis for high volume methods,
  - A monthly or quarterly basis for lower volume or very stable methods,
  - The regulatory minimum of every 6 months.
- A larger number of samples (minimum of 40) are recommended if the monitoring is performed less frequently.
- A correlation coefficient r of 0.8- 0.9 is considered acceptable.



Bland–Altman plot of hemoglobin, platelet, red blood cell count, and white blood cell count in 150 samples used for comparability.

Leishman stain quality check

- PH of the buffer checked every day, using a PH meter and two standard PH solutions
- One control slide is prepared every day staining quality is checked as per the table.

Nuclei	Purple
Cytoplasm	
Erythrocytes	Deep pink
Reticulocytes	Grey-blue
Neutrophils	Orange-pink
Lymphocytes	Blue; some small lymphocytes deep blue
Monocytes	Grey-blue
Basophils	Blue
Granules	
Neutrophils	Fine purple
Eosinophils	Red-orange
Basophils	Purple-black
Monocytes	Fine reddish (azurophil)
Platelets	Purple

Internal QC for manual differential

Frequency

daily

A peripheral smear is prepared from randomly selected specimen.

RBC morphology is reported as per the classification

100 cell manual differential count is done by all authorized personnel on this control slide.

Platelet count is done as per the procedure

A set of reference slides with established parameters are established to assess the competence of an individual to perform differential and morphological identification of leukocytes.

Questionable or abnormal smears should be referred to a supervisor or pathologist for verification.

pH Calibration and QC check

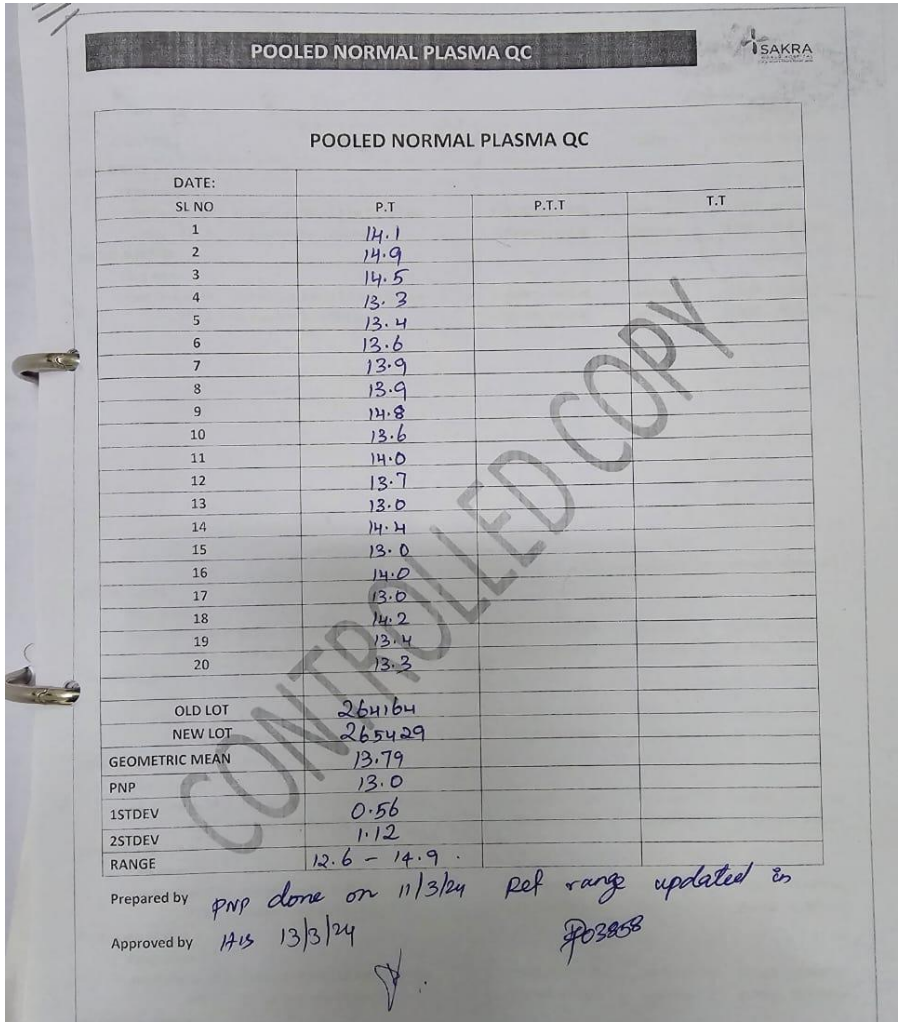
Check the calibration with the 3 standards at Ph 4, 7, and 10 every day.

Check PH of Leishman stain buffer.

Note the PH of calibrators and Leishman stain in the maintenance log of PH meter

Prothrombin Time

- Ensure report contains
  - Time taken by the test specimen to clot,
  - Mean, Normal Prothrombin Time (MNPT)
  - International Normalized Ratio (INR).
- MNPT (geometric mean of prothrombin time of 20 apparently normal healthy individuals) should be determined for every new lot of reagents, type of reagent and the instrument used and INR calculated accordingly.
- Determine Biological Reference Intervals (BRI) with each lot of reagents, type of reagent, technique and the instrument used



POOLED NORMAL PLASMA QC

SAKRA

POOLED NORMAL PLASMA QC

DATE:

Sl NO	P.T	P.T.T	T.T
1	14.1		
2	14.9		
3	14.5		
4	13.3		
5	13.4		
6	13.6		
7	13.9		
8	13.9		
9	14.8		
10	13.6		
11	14.0		
12	13.7		
13	13.0		
14	14.4		
15	13.0		
16	14.0		
17	13.0		
18	14.2		
19	13.4		
20	13.3		
OLD LOT	264164		
NEW LOT	265429		
GEOMETRIC MEAN	13.79		
PNP	13.0		
1STDEV	0.56		
2STDEV	1.12		
RANGE	12.6 - 14.9		

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Prepared by PNP done on 11/3/24 Ref range updated in

Approved by AHS 13/3/24 P03858

Automated reticulocyte counts

- Automated reticulocyte counts shall be performed using only appropriate controls.
- Manual verification should be performed on at least one sample once in a week keeping in mind the bias that automated reticulocyte count is higher than manual reticulocyte count.

Monitor

- % IQC outliers/ Sigma metric
- % PT rejections
- % Repeat tests

QA in the Post-Analytical phase

Rule of three

Rule of three

Correlation checks between the Hgb and Hct are a significant part of quality assurance for the CBC and are known as the "rule of three." The formulas for correlation checks/rule of three are as follows:

$$Hgb \times 3 = Hct \pm 3, \text{ and } RBC \times 3 = Hgb.$$

Example: 14.8 (***Hgb***) × 3 = 44 (patients actual hematocrit result is 45 L/L)
11.0 (***Hgb***) × 3 = 33 (patients actual hematocrit result is 32 L/L)

The exception to this rule is in patients with hypochromic red cells. These patients will have hematocrits that are more than three times the hemoglobin

Delta check

What is Delta check

Delta checks involve comparison of lab test results of current sample with that of previous sample from the same patient based on specified criteria.

What is the use of Delta check

- Used as a patient-based quality assessment tool to detect errors and provide a safety net for identifying testing errors that might otherwise go unnoticed.
- Contamination of blood by intravenous fluids might be detected only by a delta check alert.
- Delta check not only acts as a quality control tool in the laboratory but also may allow automated release of results of haematology analysers that pass the delta check

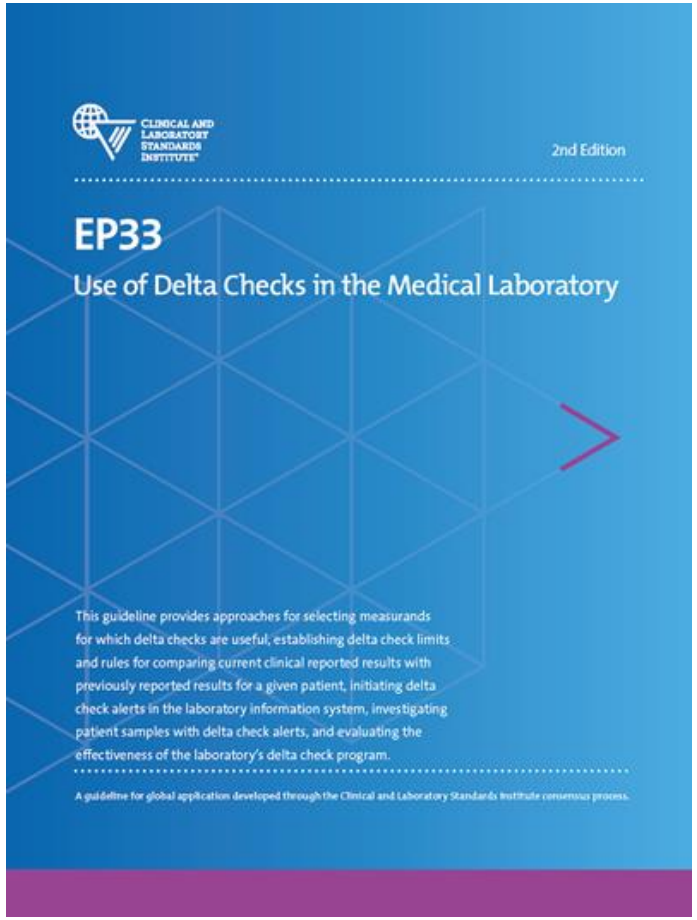
Delta check methods

- Commonly used delta check methods include
- Delta difference= Current Result - Previous Result
- Delta percent change= $\frac{Current\ Result - Previous\ Result}{Previous\ Result}$ X 100
- Rate difference = $\frac{Current\ Result - Previous\ Result}{Current\ test\ time - Previous\ test\ time}$
- Rate percent change=[$\frac{Current\ Result - Previous\ Result}{Previous\ Result}$ X 100]/$Current\ test\ time - Previous\ test\ time$

For which parameters is delta check done?

Delta check is done for

- Haemoglobin
- Haematocrit
- MCV
- Platelet count



What to do if delta check fails

- If a delta value exceeds the established limit, the test result is held for manual review.
- Check for the following
- Specimen mix-up
- The quality control data
- Specimen quality, volume, and integrity
- Clinical history of patient to rule out IV fluid, transfusion, surgery, bleeding etc.

Validation of Automated Complete Blood Count

- Set up slide review criteria based on guidelines.
- Verify the criteria at your lab before implementation.
- Review the slides as per the criteria.

Review > Lab Hematol. 2005;11(2):83-90. doi: 10.1532/LH96.05019.

The international consensus group for hematology review: suggested criteria for action following automated CBC and WBC differential analysis

P W Barnes [1], S L McFadden, S J Machin, E Simson; international consensus group for hematology

Affiliations + expand

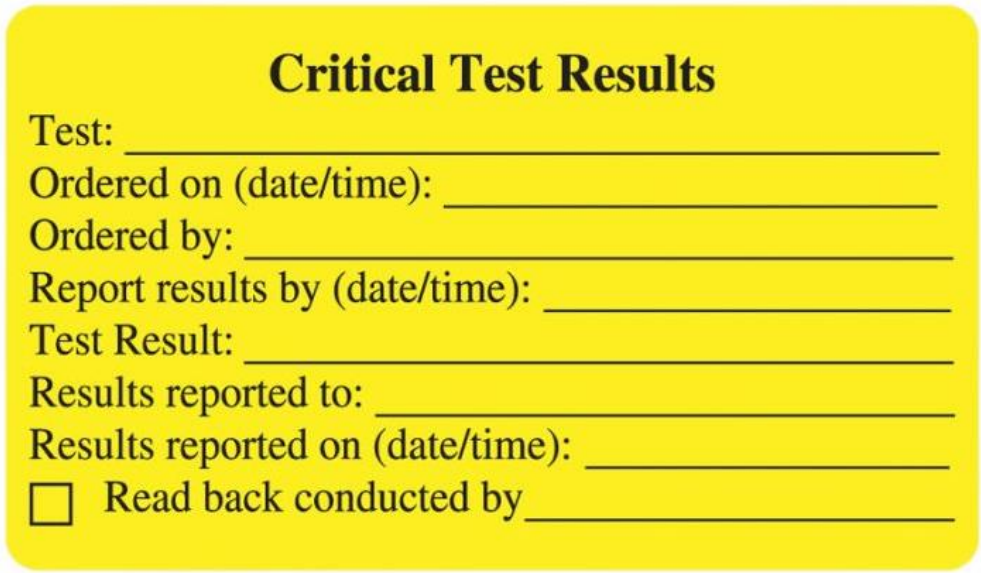
PMID: 16024331 DOI: 10.1532/LH96.05019

Validation of Automated Complete Blood Count

- Compare morphology with CBC. The following procedures give a rough comparison:
- Size of the RBC is roughly equal to the nucleus of a small lymphocyte, use this the verify MCV
- Total leukocyte count(cells/ µl) $= \frac{Total\ number\ of\ leukocytes\ in\ ten\ 10X\ microscopic\ fields}{10}$ X 200
- Platelet count(cells/ µl)= $= \frac{Total\ number\ of\ Platelets\ in\ ten\ 100X\ microscopic\ fields}{10}$ X 15000 (20000 for finger prick smear)
- These estimates should approximate (± 20 %) that obtained by the cell analyzer.
- If the estimate does not match the automated cell count
- Obtain the original blood specimen,
- Confirm patient identity,
- Repeat the automated analysis,
- Prepare a new smear.

Monitor

- TAT
- Delta check failures
- Information of critical alerts
- Reporting errors



Critical Test Results

Test: _____

Ordered on (date/time): _____

Ordered by: _____

Report results by (date/time): _____

Test Result: _____

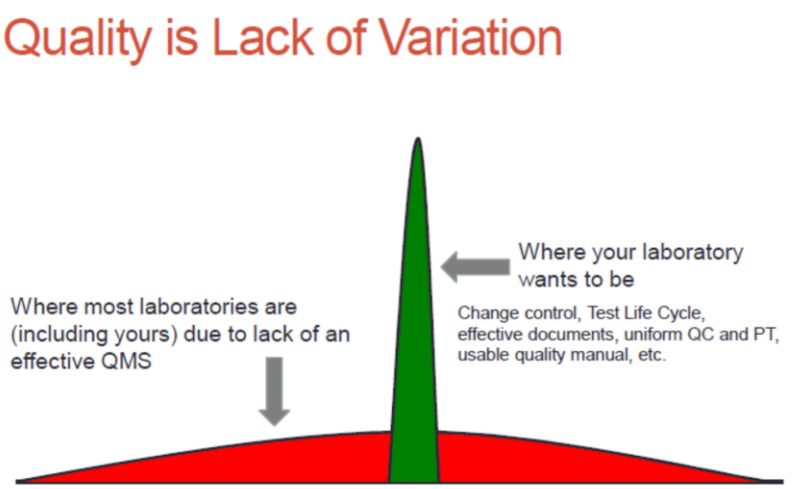
Results reported to: _____

Results reported on (date/time): _____

☐ Read back conducted by_____

Take home message

In the present environment of limited resources, quality cannot be taken for granted, so the historical perspective of **quality control** and **quality assurance** needs to be superseded by a comprehensive view of the internationally accepted quality practices applied to a laboratory's entire scope of work.



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Thank You