RANDOX

EDUCATIONAL GUIDE

Understanding Multi-rule QC

QUALITY CONTROL

Introduction

Multi-rule QC is a comprehensive approach to quality control in laboratory settings, employing a set of statistical rules to detect errors and ensure accurate and reliable results. By incorporating these rules into your quality control practices, you can effectively monitor and evaluate the performance of laboratory testing processes. In this guide, we'll explore the reasons for errors in the laboratory and each of the multi-rules. The accepted process for applying these rules can be seen in figure 1 below, but generally, laboratories should **apply more multi-rules to poor-performing and high-risk tests.** With stable, well-performing tests, you can use fewer multi-rules.

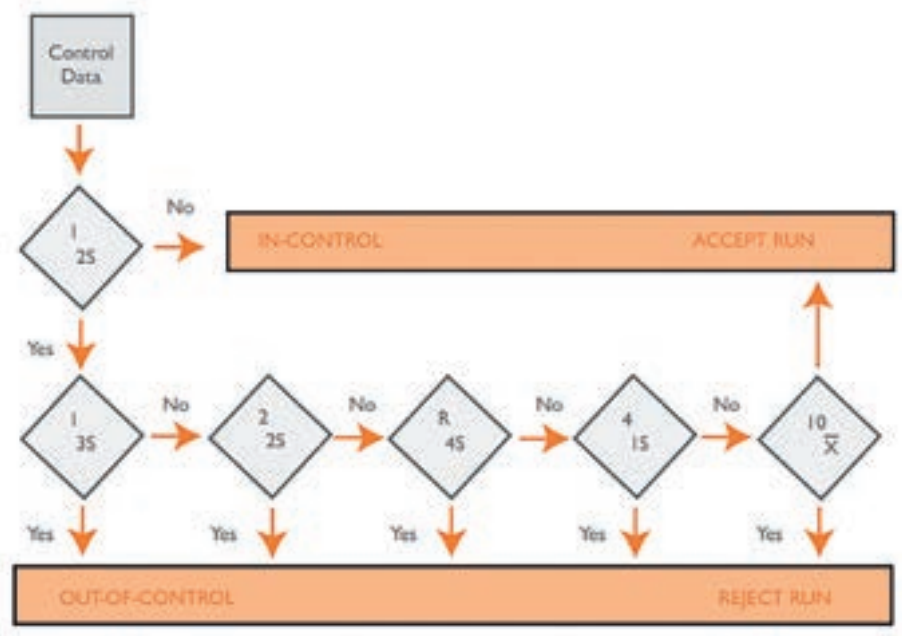


Figure 1. Flow diagram showing the recommended procedure for applying Multi-rule QC

Understanding the Causes of Deviation

It is important to consider the various causes that can lead to deviations. By understanding these causes, laboratories can make informed decisions in interpreting and responding to QC results within the multi-rule framework. There are 2 main types of analytical error which can occur: random errors and systematic errors, which are described in table 1.

Table 1

TYPE OF ERROR	DESCRIPTION
Random Error	Random error refers to the inherent variability or fluctuations in measurement results that occur due to **uncontrollable factors.** Random errors introduce unpredictable variations in individual measurements, resulting in slightly different values each time the measurement is taken. While random errors cannot be eliminated completely, quality control measures aim to minimize their impact to ensure the overall accuracy and precision of test results.
Systematic Error	Systematic error, also known as bias, represents **consistent** and **predictable deviations from the true value in measurement results.** Unlike random errors, systematic errors do not cancel each other out over multiple measurements but instead, introduce a consistent offset or shift in the measurements. Systematic errors can arise from factors such as calibration issues, equipment malfunctions, or procedural flaws. Quality control measures are designed to detect and minimize systematic errors through regular calibration, proper maintenance, and adherence to standardized protocols.

Some of the common reasons for these types of errors are detailed below:

Natural Biological Variation:

Biological samples inherently exhibit variability due to individual physiological differences. The unique characteristics of each patient, such as age, genetics, and health conditions, can influence the test results. It is essential to consider the expected range of biological variation when interpreting QC data. Deviations beyond the established multi-rule thresholds may occur due to legitimate biological variation, and laboratories should exercise caution before considering them as errors.

Analytical Variability:

Instrumentation, reagents, and assay methods introduce variability in test results. Some degree of imprecision and bias is implicit in any measurement process. This analytical variability can contribute to deviations that trigger the multi-rule QC flags. Laboratories should regularly monitor and evaluate the performance characteristics of their assays to differentiate between true shifts and random variations caused by analytical variability.

Stability Issues:

The stability of control materials, reagents, and samples is crucial for accurate and reliable testing. Changes in temperature, storage conditions, or sample degradation can impact the test results. Deviations beyond the multi-rule thresholds may occur if stability is compromised. Proper handling, storage protocols, and regular assessment of control material stability are essential to minimize the impact of stability-related variations.

Matrix Effects:

Different sample matrices, such as blood, urine, or cerebrospinal fluid, have varying compositions that can influence the measurement process. Interfering substances present in patient samples, such as medications or endogenous compounds, can also affect test outcomes. Matrix effects can contribute to deviations beyond the multi-rule thresholds and laboratories should consider the potential matrix effects and employ appropriate dilution or sample pre-treatment techniques to mitigate their impact.

Method-specific Characteristics:

Each assay method has its unique characteristics and limitations. Some methods may inherently have a wider variation or be susceptible to specific interferences. Understanding the performance characteristics of the assay methods used and considering their limitations is crucial when interpreting QC data within the multi-rule framework. Method-specific factors should be taken into account to differentiate valid deviations from potential issues.

By considering these causes of deviation, along with others, laboratories can adopt a pragmatic approach to interpreting multi-rule QC results. It is important to avoid overreacting to deviations that may have valid explanations. Laboratories should investigate and assess the underlying causes of deviations before making decisions on result rejection or corrective actions. A thorough understanding of the various factors contributing to deviations ensures a robust and effective implementation of multi-rule QC in maintaining the quality and accuracy of laboratory testing processes.

Multi-rule QC

The multi-rules are denoted using subscript abbreviations in this document. These abbreviations combine numbers and letters to represent each rule's key characteristics. The numbers indicate the number of data points involved, such as 1, 2, 3, or 4, while the letters represent the type of analysis performed on the data points, such as "$_S$" for sequential or "$_T$" for trend analysis. For example, "2_S" signifies the analysis of two consecutive data points for sequential shifts, and "4_{1S}" represents the analysis of four consecutive data points for sequential shifts. Other formats for denoting these rules include numeric representation (e.g., 1:2s) or descriptive representation (e.g., Sequential Shift Rule).

Using a combination of multi-rules is the most effective way of recognising out-of-control events. The application of multi-rules will help achieve a high rate of error detection, whilst reducing false rejections. This will result in fewer redundant repeats and less time spent carrying out futile troubleshooting and ultimately, less unnecessary expense.

1_{2S} Rule

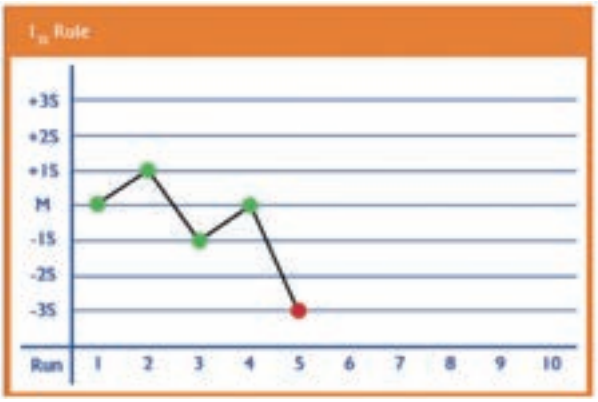
Any data point that exceeds two standard deviations from the mean of the control sample set is considered significant and requires further investigation. Firstly, this rule serves as an early warning system, enabling laboratories to detect errors and deviations in real time. Timely investigation and resolution of identified issues reduce the risk of inaccurate results, thereby enhancing patient safety.

While this rule is valuable for identifying potential issues, it is important to note that it should not be used as a sole criterion for rejecting results. 1 in every 20 results will fall outside 2 standard deviations, therefore It is important to consider that there can be legitimate reasons for such deviations and rejection solely based on the 1_{2S} rule may lead to unnecessary retesting, increased costs, and potential delays in reporting results.

1_{2S} rule is violated when a single QC result is more than ±2 standard deviations from the mean.

1_{3S} Rule

This rule expands on the 1_{2S} rule, by identifying **data points that exceed three standard deviations from the mean** of a control sample set. This rule serves as an additional criterion for flagging potential outliers and deviations. However, it is important to note that the 1_{3S} rule, like the 1_{2S} rule, should not be used as the sole criterion for result rejection. While deviations exceeding three standard deviations indicate significant differences, there can be valid reasons for such variations in certain cases. Rejection based solely on the 1_{3S} rule may lead to unnecessary retesting and potential delays in reporting results. It is essential to consider additional factors such as clinical relevance, patient history, and method performance when deciding whether to reject a result.



1_{3S} rule is violated when a single QC result is more than ±3 standard deviations from the mean.

2_{2S} Rule

The 2_{2S} rule is a crucial component of multi-rule QC that plays a significant role in quality control within laboratory settings. This rule is designed to detect shifts in the measurement process by analysing the relationship between consecutive control measurements. It identifies situations where **two consecutive data points fall on the same side of the mean but differ by more than two standard deviations.**

The application of the 2_{2S} rule allows laboratories to detect subtle yet significant shifts in the testing system. While other rules focus on individual data points, the 2_{2S} rule examines the consecutive relationship between them. This aspect provides additional sensitivity in identifying shifts that may go undetected by other rules.

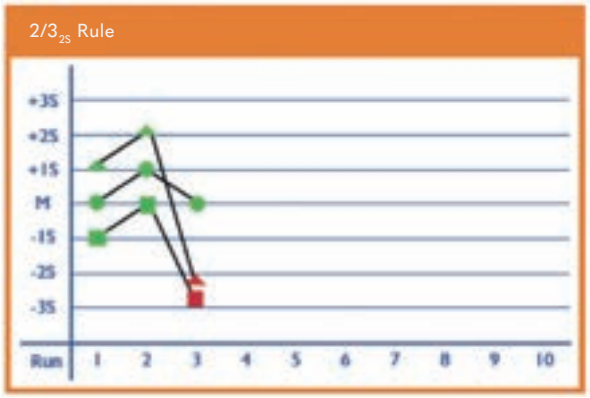
The significance of the 2_{2S} rule lies in its ability to capture changes in the measurement process that may not be detected by single datum point analysis. It serves as a complementary tool to other rules by identifying shifts that may occur gradually over time. By detecting such shifts early on, laboratories can take prompt action to investigate and rectify the underlying issues.

2_{2S} rule is violated when 2 consecutive QC results are greater than $\pm$2 standard deviations and on the same side of the mean.

$2/3_{2S}$ Rule

This rule is a fundamental component of multi-rule QC that focuses on consecutive control measurements to identify shifts in the measurement process. It examines situations where **two out of three consecutive data points fall on the same side of the mean and differ by more than two standard deviations.** By analysing the consecutive relationship between data points, this rule enhances sensitivity in detecting shifts that may go unnoticed by other rules.

Furthermore, the $2/3_{2S}$ rule serves as a foundation for other multi-rules. It complements the individual datum point analysis performed by rules such as the 1_{2S} and 1_{3S}, providing an additional layer of sensitivity in detecting shifts. Together, these rules create a comprehensive framework for identifying deviations and ensuring the overall quality of laboratory testing processes.

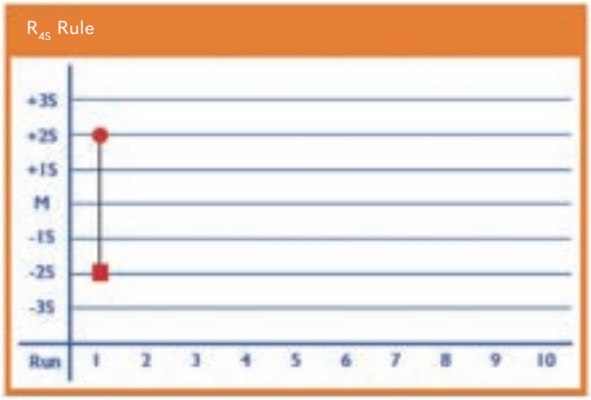


$2/3_{2S}$ rule is violated when any 2 levels of control in a run exceed 2 standard deviations on the same side of the mean.

R_{4S} Rule

The R_{4S} rule is designed to identify significant deviations in control values within a single run by examining the difference in standard deviations. This rule is violated when **the difference between control values exceeds a threshold of 4 standard deviations.** Its purpose is to detect random errors that may affect the accuracy and reliability of test results. By comparing the standard deviations of the control values, laboratories can identify situations where there is a substantial difference.

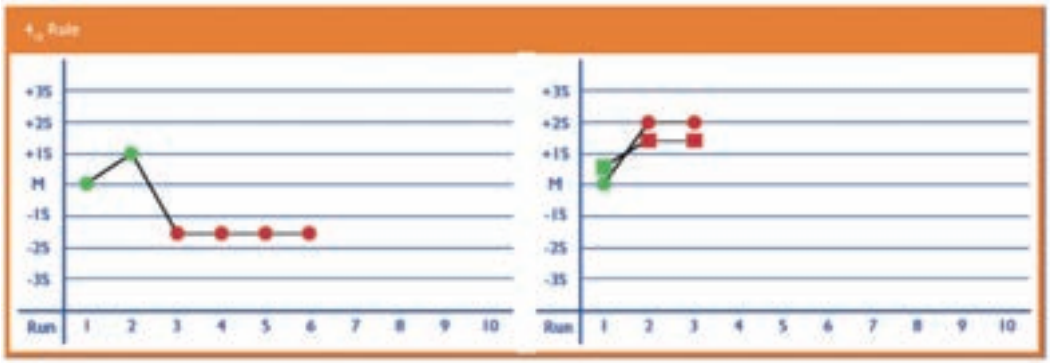
It's important to note that the R_{4S} rule focuses specifically on random errors and does not address systematic shifts or trends in the data. Other rules within the multi-rule QC framework, such as the 1_{2S}, 2_{2S}, and 1_{3S} rules, target different types of deviations and provide a comprehensive approach to quality control.



R_{4S} rule is violated when at least a difference of 4 standard deviations between control values within a single run.

4_{1S} Rule

The 4_{1S} rule is designed to identify situations where **four consecutive data points fall on the same side of the mean and exhibit a significant trend.** It is particularly useful in detecting subtle but consistent shifts in the measurement process. By analysing the consecutive relationship between control measurements, the 4_{1S} rule provides insights into the ongoing performance of the testing system. It serves as an additional layer of scrutiny to ensure the stability and accuracy of test results. By examining the consecutive relationship between control measurements, the 4_{1S} rule enhances the sensitivity in identifying persistent deviations. It serves as a valuable criterion for identifying significant trends and shifts that may impact the accuracy and reliability of test results.

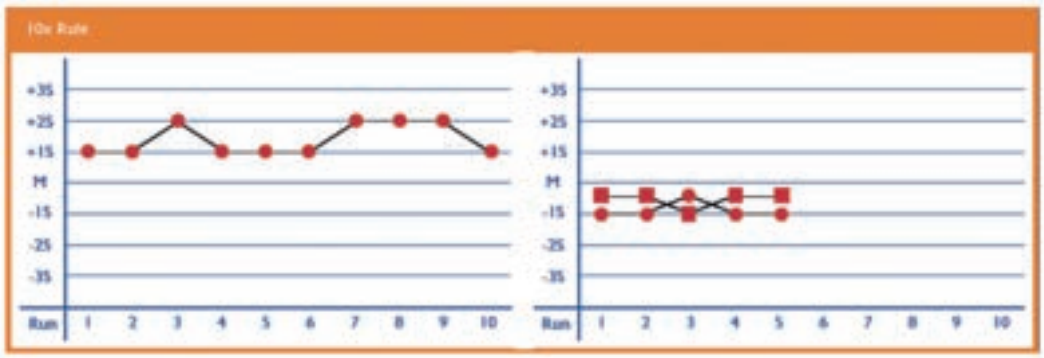


4_{1S} rule is violated when 4 consecutive control results within a run, for the same control, exceed +1SD

10_X Rule

The 10_X rule is a powerful tool for detecting systematic errors in laboratory testing processes. It is violated when **10 consecutive control results, regardless of their level, fall on the same side of the mean.** This rule aims to identify persistent biases that may arise within or across runs. While violation of the 10_X rule does not necessarily require the rejection of the entire run, it serves as an indication that instrument maintenance or calibration is needed.

The 10_X rule can be modified to consider different numbers of consecutive results on the same side of the mean, such as 7, 8, 9, or 12. Each variation provides differing levels of sensitivity to systematic bias. Laboratories may choose to adapt the rule based on their specific requirements and desired level of detection.

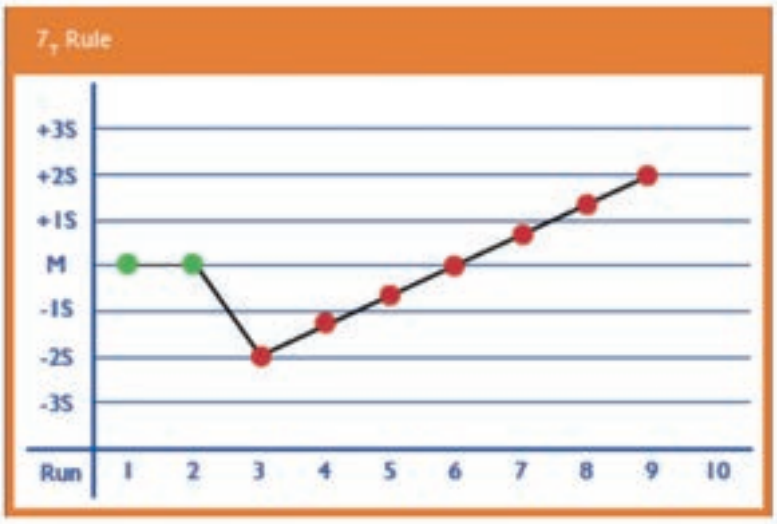


10_X is violated when 10 consecutive control results regardless of the level, fall on the same side of the mean.

7_T Rule

In addition to these multi-rules, some laboratories include the 7_T rule. This focuses on identifying situations where **a trend of seven consecutive data points is increasing or decreasing.** This rule serves as a powerful tool for detecting sustained shifts or trends in the measurement process. By considering the direction of seven consecutive data points, laboratories can detect gradual shifts in the measurement process that may impact the accuracy and reliability of test results.

The 7_T rule enhances the overall sensitivity of multi-rule QC by providing a specific focus on sustained trends while complementing other rules by capturing gradual shifts in the testing system, enabling laboratories to take proactive measures to investigate and rectify underlying issues.



7_T is violated when 7 consecutive control results for a single level, show a trend in the same direction, either increasing OR decreasing

Troubleshooting out of Control Events

The exact procedure for troubleshooting will vary depending on the discipline of the laboratory, however, the root cause of an error can be placed into 1 of 5 categories:

1. Materials – a problem with the test materials, for example, the assay reagents or sample.
2. Methods – problems can arise when procedures are not followed to the letter.
3. Equipment – faulty or uncalibrated equipment accounts for many errors common in the laboratory.
4. Human error – errors in recording results, pipetting technique etc.
5. Environmental – incorrect storage or transportation of samples or assay materials.

Once the cause of the issue has been identified, corrective actions should be taken as detailed below:

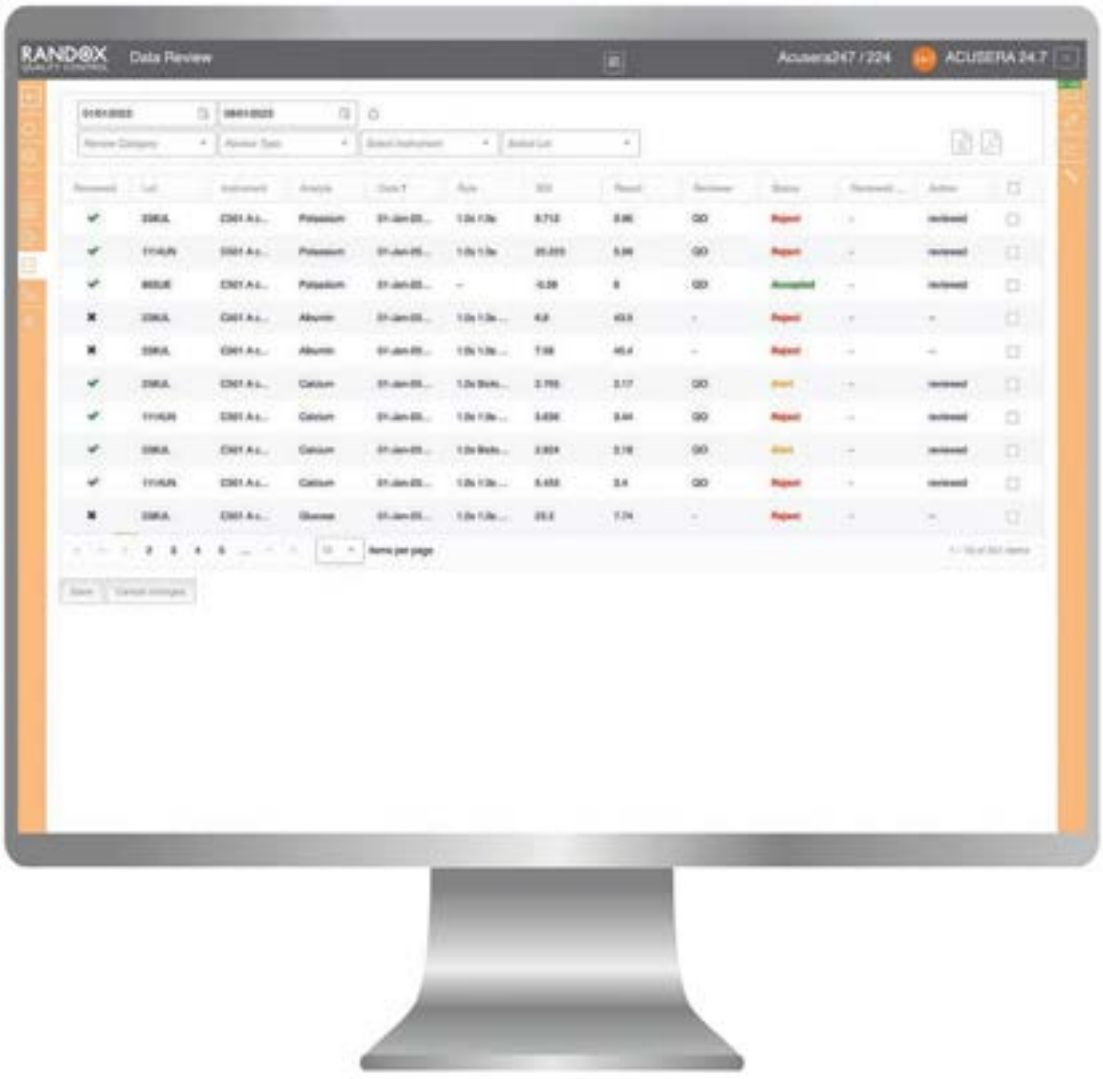
- Make one change at a time – this will allow you to determine if this was, in fact, the cause of the error.
- Monitor the improvement of the change on your QC and, more importantly, patient samples.
- Document the solution – this will help in future troubleshooting by you or other members of the laboratory staff.
- Implement procedures which will prevent this error from recurring.

Acusera 24•7

Designed for use with the Acusera range of third-party controls, the Acusera 24•7 software will help you monitor and interpret your QC data. Access to an impressive range of features, including interactive charts, the automatic calculation of Measurement Uncertainty & Sigma Metrics and live peer group data generated from our extensive database of laboratory participants, ensures Acusera 24•7 is the most comprehensive package available.

Our user-friendly software package includes the ability to automatically check your QC data against the multi-rules discussed in this guide and flag nonconformities to reduce the need for laborious manual statistical analysis and aid in improving the accuracy and precision of all laboratory results.

The image below shows the Acusera 24•7 data review section, which can be setup to accept and reject results based on predefined multi-rules or provide an alerts when thresholds are approached.



Conclusions

By identifying causes of deviation, including random and systematic errors, instrument malfunctions, environmental factors, and operator errors, laboratories can proactively address potential sources of variation, ensuring the accuracy and reliability of test results.

The multi-rules discussed in this guide serve as valuable tools for detecting outliers, shifts, and trends in quality control data. Each rule has its own significance and application, contributing to the overall assessment of the testing system's performance. Adhering to these rules allows laboratories to identify potential issues promptly, initiate investigations, and take corrective actions to maintain the integrity of test results.

Finally, by following a systematic approach, laboratories can identify the root causes of deviations, evaluate the impact on patient results, and implement corrective measures. This may involve instrument recalibration, reagent replacement, retraining of operators, or other appropriate actions to bring the testing system back into control. Regular monitoring of quality control data, adherence to multi-rules, and timely troubleshooting contribute to enhanced patient safety, accurate diagnoses, and improved overall laboratory performance.

References

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