Quality Control **Troubleshooting**

A Step-by-Step Guide to Identification and Resolution of Error in Clinical Test Systems

Start Here

Are any control values in this run at or greater than 2s?

NO → Test system is in control.

YES → 1_{2s} Screening Rule Violation

? Is at least one control value in this run greater than 3s?

YES → 1_{3s} Rule Violation

? Other than the control value that is greater than 3s, are any other control values in this run greater than 2s?

YES → 1_{2s}, 1_{3s} Rule Violations

? Are the outlying control values on the same side or opposite side of the mean?

Same Side ◗◖

Statistically significant systematic error is present. A shift has probably occurred. Investigate components of the test system that can cause a shift in performance. Identify and correct source(s) of the error and repeat all patient samples in this run.

Opp Side ◖◗

R_{4s} Rule Violation

Statistically significant random error is present. Investigate possible sources of random error. Identify and correct source(s) of the error and repeat all patient samples in this run.

NO

? Does it appear that most of the recent values for this level of control are on the same side of the mean?

YES

? Was the control range established recently?

YES

Review the process and assumptions used to establish the limits for this level of control. Ensure these limits incorporate more than one calibration, maintenance cycle, operator or lot of reagent. Recalculate the control limits. Determine the need to repeat the test after verifying the control limits and comparing to peer group data.

NO

A trend may be present. Investigate adherence to maintenance schedule, reagent integrity, and temperature for temperature sensitive tests. Repeat patient samples affected by the 3s error.

NO

? Is there a difference of at least four standard deviations between this control value and any other control value in this run?

YES

R_{4s} Rule Violation

Statistically significant random error is present. Investigate possible sources of random error. Identify and correct source(s) of the error and repeat all patient samples in this run.

NO

May indicate random or early systematic error. Investigate possible sources of random error and components of the test system that can affect an isolated portion of the method curve. Identify and correct source(s) of the error. Repeat patient samples affected by the 3s error.

NO → ? How many levels of control were tested in this run? Two or three?

The following decision boxes are used to detect smaller systematic error.

Two Control Levels

? Are the last 4 control values for a single level of control greater than 1s on the same side of the mean?

YES

4_{1s} Rule Violation Application: Within Control Material

GO TO

NO

? Are the last 4 control values for all levels of control greater than 1s on the same side of the mean?

YES

4_{1s} Rule Violation Application: Across Control Material

GO TO

NO

? Are the last 8, 10 or 12 control values for a single level of control on the same side of the mean?

YES

8x, 10x, 12x Rule Violation Application: Within Control Material

GO TO

NO

? Are the last 8, 10 or 12 control values for all levels of control on the same side of the mean?

YES

8x, 10x, 12x Rule Violation Application: Across Control Material

NO

No bias is present for this analytical run. Random error may be present and may be acceptable (expected). There may also be the initial phase of systematic error or deterioration of reproducibility (precision). Continue to monitor the test.

Three Control Levels

? Are the last 3 control values for a single level of control greater than 1s on the same side of the mean?

YES

3_{1s} Rule Violation Application: Within Control Material

GO TO

NO

? Are the last 3 control values for all levels of control greater than 1s on the same side of the mean?

YES

3_{1s} Rule Violation Application: Across Control Material

GO TO

NO

? Are the last 9 or 12 control values for a single level of control on the same side of the mean?

YES

9x or 12x Rule Violation Application: Within Control Material

GO TO

NO

? Are the last 9 or 12 control values for all levels of control on the same side of the mean?

YES

9x or 12x Rule Violation Application: Across Control Material

NO

No bias is present for this analytical run. Random error may be present and may be acceptable (expected). There may also be the initial phase of systematic error or deterioration of reproducibility (precision). Continue to monitor the test.

★ A small systematic error may be present that affects the method curve. Review the magnitude of the bias to determine whether or not the bias is medically relevant (clinically significant). Eliminate the bias by performing instrument maintenance or calibrating the method. You may report patient results, if the bias is not medically relevant. (NOTE: Some tests like potassium and pH are very precise. Do not use this rule for tests which have very small standard deviations.)

If the error persists and cannot be corrected, it may be an artifact of an incorrect mean/range. Re-evaluate the test mean and range. They may have been based on limited data or did not sufficiently account for test system variables, such as calibration, reagent lot changes or maintenance.

YES → ? Is only one control value in this run between 2s and 3s?

NO

? Are the control values on the same side or opposite side of the mean?

Opposite Side ◖◗

R_{4s} Rule Violation

Statistically significant random error is present. Investigate possible sources of random error. Identify and correct source(s) of the error and repeat all patient samples in this run.

Same Side ◗◖

2_{2s} Rule Violation Application: Within Run

Statistically significant systematic error is present. Investigate components of the test system that can affect the entire method curve. Identify and correct source(s) of the error and repeat all patient samples in this run.

YES

? Is this the first or second time within the last 5 runs that this level of control has been between 2s and 3s?

1st Time

2nd Time

? Was the value for this level of control greater than 2s on the last analytical run or on an earlier run?

Last Run

? Are the outlying control values on the same side or opposite side of the mean?

Opposite Side ◖◗

R_{4s} Rule Violation

Some random error may be present. There is no statistical process rule that identifies random error across runs. However, randomized sample size or reagent volumes and electrical power fluctuations can cause such an effect. Determine the need to repeat patient samples based on the medical relevance of the error and criticality of the test.

Same Side ◗◖

2_{2s} Rule Violation Application: Across Runs

Statistically significant systematic error is present. Investigate components of the test system that can affect a single or isolated portion of the method curve. Identify and correct source(s) of the error and repeat patient samples in this area of the method curve.

Earlier Run

? Are the outlying control values on the same side or opposite side of the mean?

Same Side ◗◖

Systematic error may be present. However, 5% of the values (or 1 in 20) should be between 2s and 3s. Look for a possible shift or trend. Calculate an SDI using the last 20 runs and your cumulative mean and standard deviation.

Opposite Side ◖◗

Possible problem with precision. Investigate source(s) of random error. Divide the standard deviation calculated from the last 20 or more values by the lab cumulative standard deviation. The calculated result should be equal to or less than 1.0. Other sources for comparison include historical QC data from a previous control lot number or the manufacturer's claims for the method's between-run precision.

? Is the SDI greater than or equal to 1.5?

NO → Continue to monitor the test or re-establish the mean and range.

YES

There may be a shift or trend. Recalibrate instrument/kit or perform instrument maintenance. Rerun control.

Document corrective action. Determine the need to repeat patient samples based on the medical relevance of the bias and criticality of the test. No further action is required.

NO

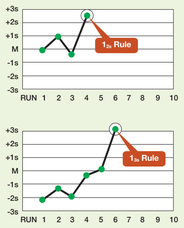
? Was the bias corrected?

YES

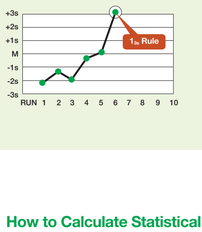
NO

Determine the need to repeat patient samples based on the medical relevance of the bias and criticality of the test. Evaluate those variables that could cause subtle shifts or trends. Investigate source(s) of systematic error. It may be necessary to evaluate the test mean and range. They may have been based on limited data or did not sufficiently account for system variables; e.g., they were obtained from a single lot of reagent or calibration cycle.

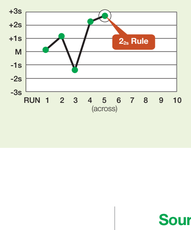
Developed by Greg Cooper, CLS, MHA
Manager, Laboratory Quality Systems & Education
Bio-Rad Laboratories



Rule: 1_{2s}
This is the "warning rule". If one control measurement exceeds the mean ±2s, then the technologist must consider other controls in the run ("within-run") and in previous runs ("across-run") before accepting the run and reporting the results. This rule should not be used as a run rejection rule, except in the case where a test is considered problematic (unstable), and tight control is required.

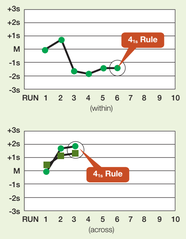


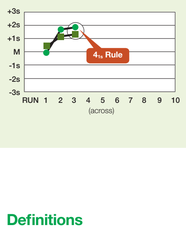
Rule: 1_{3s}
This rule detects random error. It may also point to systematic error. The run is considered out of control when one control value exceeds the mean ±3s. This rule is applied within the run only.



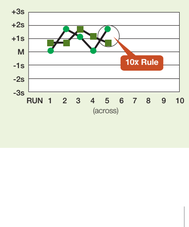
Rule: 2_{2s}
This rule detects systematic error. It should be applied within and across runs. This rule is violated within the run when two consecutive control values (or 2 of 3 control values when 3 levels are being run) exceed the "same" (mean +2s) or (mean –2s) limit. The rule is violated across runs when the previous value for a particular control level exceeds the "same" (mean +2s) or (mean –2s) limit.

Rule: R_{4s}
This is a "range" rule and it detects random error. This rule is applied within the run only. This rule is violated when the difference in standard deviation between two consecutive control values (or 2 of 3 control values when 3 levels are being run) exceeds 4s.





Rule: 4_{1s}
This rule detects non-critical systematic error and is applied both within and across control materials. This rule is violated within the control material when the last four values of the same control level exceed the "same" (mean +1s) or (mean –1s) limit. The rule is violated across control materials when the last four consecutive values for different control levels exceed the "same" (mean +1s) limit or (mean –1s) limit. This rule does not require rejection of the run. Rather, it can be an indicator to perform instrument maintenance or instrument/kit calibration.



Rule: 10_x
This rule detects systematic error and is applied both within and across control materials. The rule is violated across control materials when the last 10 consecutive values, regardless of control level, are on the same side of the mean. The rule is violated within the control material when the last 10 values for the same control level are all on the same side of the mean. This rule may be modified to 9 replicates when running three control levels, or 8 replicates when running 4 control levels. This rule may not require rejection of the run. Rather, it can be an indicator to perform instrument maintenance or instrument/kit calibration.

How to Calculate Statistical Parameters for a Levey-Jennings Chart

Step One
Collect a minimum of 20 data points for each level of control. Data points must be obtained from 20 separate analytical runs that reflect variables such as calibration frequency, change of reagent or reagent lot, operator technique, temperature/humidity of testing location, daily/weekly maintenance, etc. All new control products should be compared to previously validated controls (parallel testing).

Note: 90 data points are recommended before finalizing mean and standard deviation.

Step Two
Calculate the mean and standard deviation from the data points collected. Use a statistical test for outliers before eliminating any questionable data points. Calculate the statistical control limits from $\bar{x} \pm 2s$ and $\bar{x} \pm 3s$.

Note: Use control package insert ranges only as guidelines. Ranges are based on reagent lots and materials available at the time of value assignment. During the life of the control lot, manufacturers may reformulate tests or begin using a new source of raw materials for kit/reagent production. Published ranges cannot account for variables, such as calibration or reagent lot changes. Laboratories should use peer group statistics when such data are available, because these data are more timely and relevant.

Sources of Random Error

1. Power supply
2. Double pipetting of control sample
3. Misplacement of control sample within the run
4. Air bubbles in water supply
5. Random air bubbles in reagent or sample pipette system
6. Incorrect reconstitution of the control product
7. Inappropriate storage of control in frost-free freezers
8. Use of non-reagent grade water in the test system
9. Operator technique

Sources of Systematic Error (Shifts & Trends)

1. Improper alignment of sample or reagent pipettes
2. Drift or shift in incubator chamber temperature
3. Inappropriate temperature/humidity levels in the testing area
4. Change of reagent or calibrator lot
5. Deterioration of reagent while in use, storage or shipment
6. Deterioration of calibrator while in use, storage or shipment
7. Deterioration of control product while in use, storage or shipment
8. Incorrect handling of control product (e.g., freezing when not recommended)
9. Inappropriate storage of control products in frost-free freezers
10. Failing light source
11. Use of non-reagent grade water in the test system
12. Recent calibration
13. Change in test operator
14. Specimen carry-over
15. Obstruction of tubing

Definitions

Medically Relevant Error
A degree of analytical error that can adversely affect or change the patient diagnosis, prognosis, or treatment plan.

Random Error
Any random deviation from the laboratory mean. There is "expected" or "acceptable" random error, which generally lies anywhere between ±3s of the mean. It follows that any deviation greater than ±3s is considered "unacceptable" random error. Because of its random nature, this type of error is unpredictable and difficult to detect.

Systematic Error
A trend or shift away from the laboratory's established mean. Small amounts of systematic error are tolerable. Systematic error will remain until corrective action is taken.

Trend
A gradual, often subtle, increase or decrease in control values and possibly patient values.

Shift
A sudden and eventually stable change in control values and possibly patient values.

Technical Service

Get help with Quality Control products, QC Program or EQAS Technical Service

Within the United States
1-800-854-6737

Outside the United States
Contact your local Bio-Rad office

Bio-Rad Product Information
1-800-2-BIORAD
www.bio-rad.com/qualitycontrol

Laboratory QC Portal
www.QCNet.com