RANDOX

# EDUCATIONAL GUIDE

## Basic QC Statistics

QUALITY CONTROL

# Basic QC Statistics

*qual-ity con-trol* - noun

A system of maintaining standards in manufactured products by testing a sample of the output against the specification.

(Oxford Dictionary; Oxford Universities Press 2013)

When testing patient samples the outcome of the result will often be used to diagnose the patient, with an estimated 60 to 70% of all decisions regarding a patient's diagnosis and treatment based on laboratory test results. As a consequence, the quality of laboratory work is of the utmost importance in ensuring patients are correctly diagnosed and administered the appropriate treatment.

Laboratory Quality Control is therefore used as a process to monitor and evaluate the procedures and systems that produce patient results. This is designed to detect, reduce, and correct deficiencies in a laboratory's analytical process prior to the release of patient results. The Control results must be deemed satisfactory before the results of patient samples can be reported.

*To be confident that these results are completely accurate, a robust quality control system will need to be in place. Having good quality control will provide the clinician with a high degree of confidence in the clinical data generated by the lab.*

## EQA & IQC

Quality control will often come in two forms:

### External Quality Assessment (EQA)

EQA is a form of assessing a laboratory's analytical performance against other laboratories utilising the same methods and instruments. This involves the use of blind sampling, preventing the laboratory from knowing what the values should be and subsequently providing a better indication of accuracy. The laboratory will send their results to an independent scheme organiser to compare how their results compare with other laboratories. A report will be received comparing their individual performance against other participants in the programme.

### Internal Quality Control (IQC)

IQC will involve the day to day running of quality control within the laboratory. The QC results are often compared to predetermined target values which are either supplied by the QC manufacturer or calculated by the lab. If the QC results are within the pre-set limits then patient test results are released.

Running both together will help a laboratory ensure their systems and methods are all correct and make certain the results they are producing are accurate and reliable.

## Why Should We Run QC?

There are a number of potential consequences of not running QC or running infrequent or inadequate QC:

- Patient misdiagnosis
- Delays in patient treatment
- Inappropriate treatment
- Increased costs due to retests or unnecessary further investigations

All of the above problems can arise from not having a good quality control system in place. The consequence of these can be shown in the US where avoidable re-tests cost $200million USD per year.
*(For these reasons it is vital that laboratories have a robust quality control system in place.)*

## How Often Should We Run QC?

How often a laboratory should run QC will be very much dependant on the individual lab and their processes. Many factors will determine this, such as:

- The quantity of tests run per day
- Which tests are higher risk and have a higher impact if results are erroneous
- Experience and competency of laboratory staff
- The instrument, reagent and method in use
- Available time between QC evaluations
- Which assays are more stable compared to others

It is often recommended that QC is run at the beginning and end of each analytical run or when a batch of reagents is changed. ISO 15189 regulations however do not state a recommended QC frequency but they do recommend that:

**"Quality Control materials shall be periodically examined with a frequency that is based on the stability of the procedure and the risk of harm to the patient from an erroneous result."**

Laboratories must therefore consider all of the above factors and determine how often they should be running QC to ensure confidence in the results produced.

## Basic QC Statistics

There are a number of statistical terms commonly used when assessing laboratory performance; Mean ( $\bar{x}$ ), Standard Deviation (SD) and Coefficient of Variation (CV).

### Mean ( $\bar{x}$ )

The $\bar{x}$ is often used in clinical labs to identify the 'true value' of a set of data points. When a QC product is Assayed, predetermined targets values will have been established by the manufacturer and can therefore be taken as the true values. If a product however is unassayed, then a calculation of the $\bar{x}$ value is required to determine the target value and range for each specific lot of control. *The Clinical and Laboratory Standards Institute (CLSI) recommends that a minimum of 20 data points are used when establishing the mean for a set of control results.*

*In calculating the $\bar{x}$, the following equation is used:*

$$\sum x_n / n$$

$\sum$ = sum
$x_n$ = each value in the data set
n = the number of values in the data set

### Standard Deviation (SD)

The SD of a set of results is a measure of how disperse the values are about the $\bar{x}$ – i.e. it is a measure of precision. The SD is often used to establish limits or a range for the acceptability of results. Most laboratories will adopt a 2SD range meaning a result is deemed acceptable providing it falls within 2SD from the $\bar{x}$. *A low SD shows better precision, less variability and therefore more accurate results.*

*To Calculate SD, the following formula is used:*

$$SD = \sqrt{\left(\frac{\sum (x_n - \bar{x})^2}{n - 1}\right)}$$

SD = Standard Deviation
$\sum (x_n - \bar{x})^2$ = The sum of the square root of differences between individual QC values and the mean
$\bar{x}$ = Mean result
n = Number of values in the data set

By the laws of statistical probability, 68% of all results should fall within ± 1 SD of the mean, while 95% of all results should fall within ± 2 SD.

## Working Examples of Standard Deviation

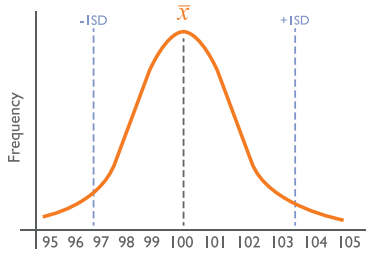
The individual results in example A and example B are significantly different and yet they have the same $\bar{x}$. SD can be used to distinguish between the sets of data by assessing the variability of the values around the $\bar{x}$. The SD for example B is much larger than that for example A as the values are more spread out about the $\bar{x}$. Example A illustrates a set of data with a close distribution around the $\bar{x}$ representing better precision or result reproducibility producing a lower standard deviation.

### Example A

$$SD = \sqrt{\frac{\sum (x_n - \bar{x})^2}{n - 1}}$$

$$SD = \sqrt{\frac{\sum (95-100)^2 + (96-100)^2 + (97-100)^2 \ldots}{10}}$$

SD= 3.32

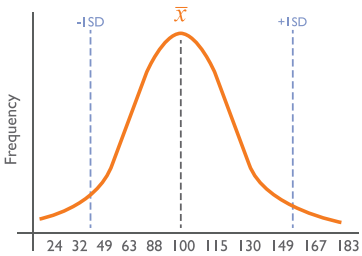



### Example B

$$SD = \sqrt{\frac{\sum (x_n - \bar{x})^2}{n - 1}}$$

$$SD = \sqrt{\frac{\sum (24-100)^2 + (32-100)^2 + (49-100)^2 \ldots}{10}}$$

SD= 54.29




## Ranges & Limits

Limits for data acceptability are defined using the $\bar{x}$ and standard deviation. These limits are used to define what is and more importantly what is not acceptable. The ranges for the limits are established at ± 1SD, 2SD and 3SD from the $\bar{x}$.

In Example A, 1SD was equal to 3.32, 2SD would therefore be equal to 6.64. A lab adopting a 2SD range would therefore accept any result that falls ± 6.64 from the mean.

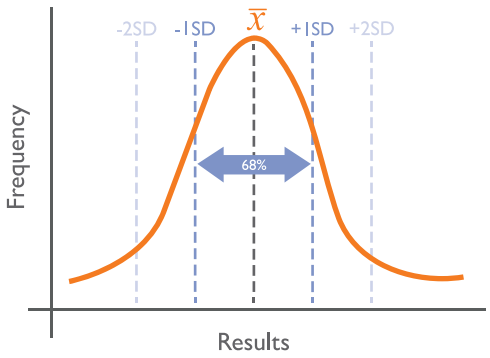
In a normal or Gaussian distribution if we were to create a range based on the $\bar{x}$ ± 1SD statistically 68% of all results should fall within this range.

If you were to widen the range to the $\bar{x}$ ± 2SD, then statistically 95% of all results should fall within this range. Statistically this means that it would be acceptable for 5% or 1 out of 20 results to fall outside 2SD.

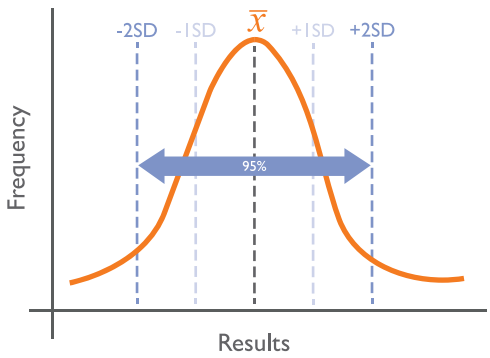
In a clinical laboratory these ranges and limits are used to determine the acceptability of a QC result. This includes both single data points from one sample or a group of data points from a run of samples. Overall acceptable data points will usually fall between 1SD and 2SD from the $\bar{x}$, data points that are outside the 3SD limit are generally considered out of control. A laboratory using an instrument or method with high standard deviations would have limited confidence in the accuracy of their data and therefore treatment decisions.

*High standard deviations equate to poor precision and greater variability between results.*

$\bar{x}$ +/- 1SD




$\bar{x}$ +/- 2SD



## Coefficient of Variation (CV)

A CV is a measure of variability and precision. This takes into consideration the magnitude of the overall result and expresses the SD as a percentage of the mean. This calculation will therefore allow comparison of precision at different concentrations of patient testing. *The lower the %CV the better the precision.*

*The following equation is used to measure CV:*

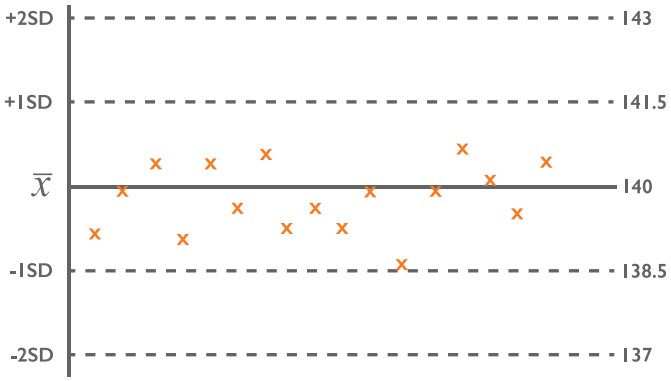
$$CV = \frac{SD}{\bar{x}} \times 100\%$$

CV = Coefficient of Variation
SD = Standard Deviation
$\bar{x}$ = Mean result

## Levey-Jennings Charts

Using the $\bar{x}$ and ±3s range a Levey-Jennings Chart can be created for each test. Levey-Jennings Charts will alert a laboratory to any identifiable trends, biases and precision problems with the daily QC or patient data. By doing this, laboratories can pinpoint and troubleshoot any problematic tests. The table below shows a Levey-Jennings Chart with good Quality Control results:

Levey-Jennings Charts



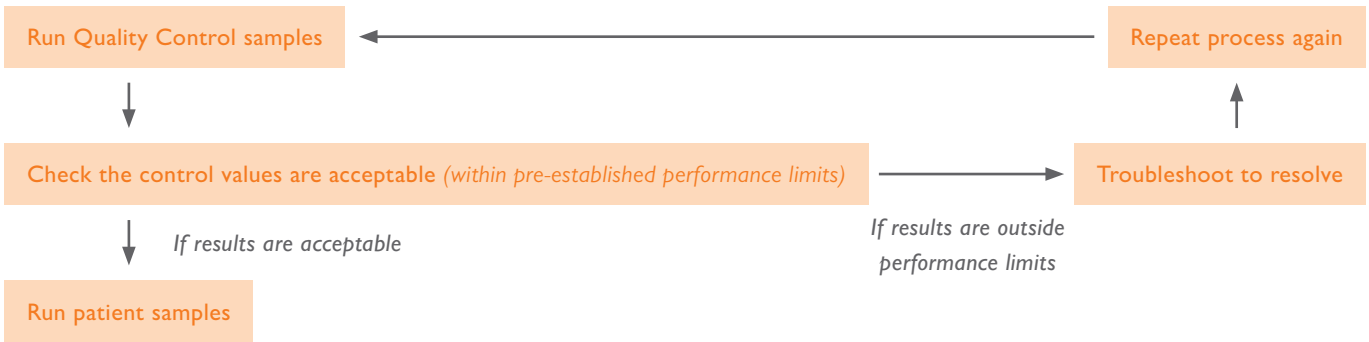

Good precision & accuracy

The Chart shows good precision and accuracy, with all results falling within 1SD.

As a rule, 68% of results should fall within 1SD of the $\bar{x}$ and 95% should fall within 2SD.

QC data greater than 2SD but within 3SD may not always indicate a false result i.e. 1 result in every 20 that falls outside 2SD limit is to be expected.

## The Complete Quality Control Process




## Summary

1. Establish $\bar{x}$ and set acceptable limits of performance
2. Run daily QC material
3. Create a Levey-Jennings Chart
4. Evaluate QC data before releasing patient test results

# ACUSERA True third party quality controls

As a world leading manufacturer of multi-analyte true third party controls, thousands of laboratories rely on Randox to accurately assess test system performance and ultimately empower them with the confidence required to release patient test results. With more than 390 analytes available, the number of individual controls required to cover your test menu is significantly reduced while simultaneously reducing costs, time and storage space. A choice of formats is available, including liquid or lyophilised, which ensures flexibility and suitability for laboratories of all sizes and budgets. Many features of the Acusera range can help you to meet ISO 15189:2012 requirements:

- Designed to react to the test system in the same manner as a patient sample, helping to reduce inconvenient shifts in QC results when reagent batch is changed and ultimately providing a true indication of laboratory performance.
- The presence of analytes at key decision levels ensures accurate instrument performance and eliminates the need for additional low/high controls at extra expense.
- Manufactured independently from any instrument, the Acusera range delivers unbiased performance assessment with any instrument or method, while eliminating the need for multiple instrument specific controls.

## Product Portfolio

Antioxidants | Blood Gas | Cardiac Markers | Routine Chemistry | Coagulation | Haematology | Diabetes Immunoassay | Immunology | Lipids | POCT | Therapeutic Drugs | Toxicology | Urine Chemistry

Uniquely combining more than 100 analytes conveniently in a single control, laboratories can significantly reduce costs and consolidate without compromising on quality. As true third party controls, unbiased performance assessment with any instrument or method is guaranteed.

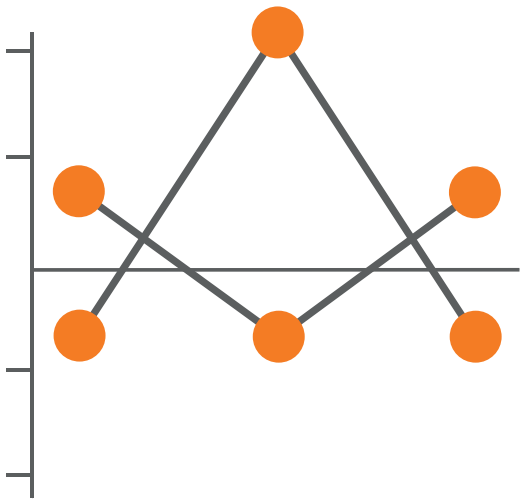
# ACUSERA 24•7 Interlaboratory Data Management

Designed for use with the Acusera range of third party controls, the Acusera 24•7 software helps laboratories monitor and interpret their 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.

- Advanced statistical analysis with automatic calculation of performance metrics including; Sigma, UM, TE & %Bias.
- Instantly discover how you compare to your peers with peer group statistics updated live in real-time reducing time and money spent troubleshooting.
- Interactive charts allowing you to add events and multiple data sets for quick and easy performance monitoring.
- Automated data import with bi-directional connection to LIMS (eliminating manual data entry).

## Software Features

Dashboard | Result History | Interactive Levey-Jennings Charts | Interactive Histogram Charts
Performance Summary Charts | Statistical Analysis Report | Statistical Metrics Report
Uncertainty of Measurement Report | Exception Report | Peer Group Statistics | Acusera Advisor
Audit Trail Report



'The laboratory shall have a procedure to prevent the release of patient results in the event of quality control failure. When the quality controls rules are violated and indicate that examination results are likely to contain significant errors the results shall be rejected… Quality Control data shall be reviewed at regular intervals to detect trends in examination performance'.

ISO 15189:2012

RANDOX
QUALITY CONTROL