

1.0 Quality Control - Materials And Methods

1.1 Introduction

'Quality control' and 'quality assurance' are terms whose meanings are often confused. Quality assurance relates to the overall measures taken by the laboratory to ensure and regulate quality, whereas quality control describes the individual measures which relate to the monitoring and control of analytical results.

We have seen that method validation quantifies a method's performance capabilities and limitations. In routine use, specific controls need to be applied to the method to verify that it remains in control and is performing in the way expected. During the validation stage, the method was largely applied to samples of known content. Once the method is in routine use it is used for samples of unknown content. Suitable control can be applied by continuing to measure samples of known content, which may be secondary or working standard solutions, thus allowing the analyst to decide whether unexpected and unwanted changes are occurring in the method performance. In practice these known samples should be measured with every batch of samples as part of the quality control process.

The sort of checks made will depend on the nature, criticality and frequency of the analysis, batch size, degree of automation, and test difficulty and also on the lessons learnt during development and validation processes. Quality control can take a variety of forms, both inside the laboratory (internal) and between the laboratory and other laboratories (external).

1.2 Internal QC

This include the use of: blanks; chemical calibrants; spiked samples; blind samples; replicate analyses and QC samples. The use of control charts is recommended, particularly for monitoring results from QC control samples.

The types of QC used must be sufficient to ensure the quality of the results. Different sorts of quality control may be used to monitor different types of variation within the process. QC samples, analysed at intervals will indicate drift in the system; use of various types of blanks will indicate what are the contributions to the instrument signal besides those from the analyte; duplicate or triplicate analyses give a check of repeatability.

QC samples are known samples, in sufficient quantities as to be available for repetitive analysis which over a given period of time are sufficiently stable and homogeneous to give the same result (subject to random variation in the performance of the analytical method). Over this period the random variation in performance of the analytical method can be monitored by monitoring the analysed value of the QC sample, for example by plotting it on a control chart.

The use of blanks enable the analyst correct and remove any contributions to the response which are not attributable to the analyte.

Replicate analysis provides a means of checking for changes in precision in an analytical process, which could adversely affect the result.

Blind analysis is effectively a form of replicate analysis and provides a means of checking objectivity as well as precision. It consists of replicated test portions placed in the analytical batch, possibly by the laboratory supervisor, and is so-called because the analyst is not normally aware of the identity of the test portions or that they are replicates. Thus, the analyst has no preconceived ideas that the particular results should be related.

Standards and chemical calibrants placed at intervals in an analytical batch enable checks to be made that the response of the analytical process to the analyte is stable.

It is the responsibility of the laboratory management to set and justify an appropriate level of quality control, based on risk assessment, taking into account the reliability of the method, the criticality of the work, and the feasibility of repeating the analysis if it doesn't work correctly first time. It is widely accepted that for routine analysis, a level of internal QC of 5% has been identified as reasonable, i.e., 1 in every 20 samples analysed should be a QC sample. However, for robust, routine methods with high sample throughput, a lower level of QC may be reasonable. For more complex procedures, a level of 20% is not unusual and on occasions even 50% may be required. This may typically involve the use of a reference material containing a certified or known concentration of analyte, followed by replicate analyses of the sample and spiked sample (a sample to which a known amount of the analyte has been deliberately added). Those analyses undertaken more frequently should be subject to systematic QC procedures incorporating the use of control charts and check samples.

1.3 Using Control Charts

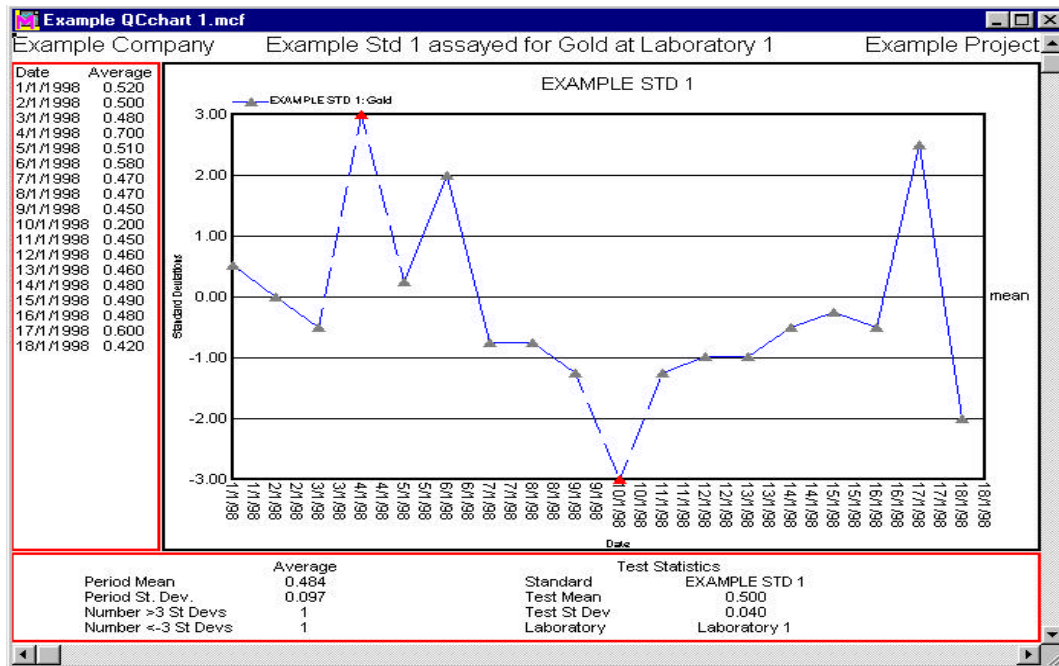
Statistical quality control (QC) charts are a simple but powerful tool for monitoring the stability of an analytical procedure. Conceptually they are very simple: a standard material is measured regularly and the analytical responses are plotted in time order on a chart; if the chart displays other than random variation around the expected result it suggests that something has gone wrong with the measurement process. To help decide if this has happened control limits are plotted on the chart: the responses are expected to remain inside these limits. Rules are decided upon which will define non-random behaviour.

The most commonly used charts are called Shewhart charts. Shewart, who worked for Bell laboratories, described random measurement errors as being due to 'chance causes' and distinguished the latter from 'assignable causes', which would be anything that could change the level of a measurement (i.e., cause bias) or change the precision. If a measurement system is stable such that it exhibits random variation around a given reference value and the size of that variation (as measured by the standard deviation) remains constant, he would say it is 'in statistical control' or simply 'in control'. The objective in using control charts is to achieve and maintain this state of statistical control.

Using control charts, once they are properly set up, is simply a matter of plotting the points and applying whatever set of rules has been decided on. There are, however, a few practical points worth considering.

Limits are set for the values on the chart (an example is given in figure 1). Conventionally, 'warning limits' are set at ± 2 standard deviations about the mean value, and 'action limits' are set at ± 3 standard deviations about the mean value. Provided the plotted QC values conform to rules defining when bias, swings and out of control results and trends pertaining to the set limits, the QC is deemed to be satisfactory. Providing the QC sample value is acceptable it is likely that results from samples in the same

batch as the QC sample can be taken as reliable. It is important that the acceptability of the value obtained with the QC sample be verified as early as practicable in the analytical process so that in the event of a problem as little effort as possible has been wasted on unreliable analysis of the samples themselves.



In order to set realistic limits on the control chart, the initial calculations of mean and standard deviation must reflect the way the method is actually intended to be used on a day-to-day basis. Thus readings should mimic all possible variations in operating conditions: different analysts; variations in laboratory temperature etc.. If this is not done, then the standard deviation will be unrealistically small, resulting in limits being set on the chart, too small to be complied with in normal use.

Apart from acting as a working tool to monitor measurement stability, a control chart is a very useful historical record of the measurement process. As such, the more information it contains the better. The analyst will rarely have time to reflect on problems encountered in a particular assay; however, if the problems are noted on the chart, recurring problems will eventually be identified and action to rectify them should follow.

Where the control chart contains extra information, such as a code for the instrument used and for the analyst who performed the assay, it is worthwhile examining these records periodically: even if instruments or analysts give acceptably close results when the charts are first set up, it does not mean that they will continue to do so forever afterwards. If the control chart data are maintained as a computer record, as well as on the paper chart in the laboratory, it makes such retrospective investigations much easier.

In planning experimental studies of any kind, the standard deviation is an essential parameter in determining the appropriate sample size. Control charts contain all the information required for determining the standard deviation and are, therefore, a kind of laboratory database.

If a measurement system has poor precision a control chart does not, in itself, improve this state of affairs. The poor precision will be reflected in a large standard deviation that will result in wide control limits. Provided that the system is in statistical control the routine measurements will stay within these limits and no action will be signalled. Control charts are, however, as useful starting point for any quality improvement programme that attempts to improve the precision of an assay, i.e., reduce measurement error.

If we have two (or more) replicate measurements for our control samples, then from each pair we can obtain an estimate of the standard deviation being achieved by a single analyst on a single instrument at any one time and can combine all these estimates into a single pooled estimate. This estimate is what we would use in determining the repeatability of the method. As such it estimates the very best precision that is achievable under current conditions. Accordingly, it provides a benchmark against which to judge current performance. If current performance (including between-analyst and between-instrument variation) is very much worse than this, it may be possible to improve precision substantially by assigning a single analyst and/or a single instrument to this assay. Alternatively, it may be possible by careful study of the measurement process to reduce the variation between analysts and between instruments. If, on the other hand, the current standard deviation is close to that based on within-run variation, it is unlikely that the assay can be substantially improved by such studies: if better precision is required, a very detailed study of the sources of error present even a single analyst using one set of equipment must be carried out and ways of eliminating or reducing such errors identified

1.4 External QC

For example proficiency testing (also known as external quality assessment). Proficiency tests enable laboratories to compare their performance in terms of accuracy and precision with those of their peers by analysing the same samples using their routine analytical methods, which are prepared and circulated by the scheme organisers. The results obtained by all the laboratories are analysed and compared with a reference value for the determinands by the scheme organisers and the laboratory performance is reported back to the participants. Proficiency testing is a key component of the quality control activity of analytical laboratories. Proficiency testing helps to highlight reproducibility performance between laboratories and systematic errors, i.e. bias. It can also be used to determine repeatability but this can also be checked more cost effectively using internal controls. Proficiency testing and other types of intercomparison are accepted as being an important means of monitoring traceability at national and international levels. Accreditation bodies recognise the benefit of these schemes and strongly encourage laboratories to participate in proficiency testing as an integral part of their quality assurance protocols. It is important to monitor proficiency testing results as a means of checking quality assurance and take action as necessary. In certain instances, accreditation bodies may specify participation in a particular proficiency testing scheme as a requirement of accreditation. The value of proficiency testing is of course only as good as the schemes themselves. Very often, there may not be scheme available which is relevant to the types of analysis that the laboratory wishes to check, especially if it is working in isolation.

An example of a proficiency testing scheme is 'Aquacheck', a service for laboratories involved in analysis of waters, wastes and environmental samples for chemical and microbiological contaminants. Aquacheck operates internationally and currently serves approximately 400 laboratories in 40 countries. It offers distributions of samples of different kinds 40 times a year and covers over 560 determinands in clean waters, waste waters, saline waters, soils, biota and sludges.

The following conclusions/comments are applicable to participation in proficiency testing schemes:

1. Participation is frequently required by legislation;
2. Participation is frequently required by accreditation agencies;
3. Proficiency testing schemes are frequently required to conform to the Internal Protocol;
4. The International Protocol is simple, easily understood and produces results which are very transparent;
5. Participation gives the laboratory and its customers confidence in the analytical result;
6. Proficiency testing schemes may give information on methodology used by participants;
7. Proficiency testing schemes may be used to validate methodology is sufficient participants use the same method;
8. Excess test material may be used as Internal Quality Control material, having been characterised by the results of the proficiency testing schemes; but
9. Proficiency testing normally reflects the best a laboratory can do. Blind proficiency tests are not that common at present.