17.5: Quality control and quality assurance

QC is an inherent component of any good study and a good laboratory. It is a process of routine checks designed to detect any deficiencies that could compromise the results of laboratory analysis and suggest how these might be corrected. An example would be checks that the laboratory always gets the same result for a split specimen. QC checks should be specified in the laboratory work plan and in SOPs. A useful resource that discusses general laboratory QC issues is Ratliff (2003).

QA is a set of activities aimed at evaluating the accuracy of laboratory analysis and to guide improvements if inaccuracies are detected. QA provided by a resource external to the field laboratory is complementary to QC and should be established to monitor and improve the quality of laboratory procedures and validate the effectiveness of a QC programme. For example, a reference laboratory may supply specimens that are analysed ‘blind’ with the results compared to those of the reference laboratory and all the other laboratories participating in the same QA scheme.

5.1 Reproducibility of test results

The reliability of laboratory results should be tested by regular checks on their reproducibility. The level of acceptable variation will depend both on the test and study. This information is normally predefined in SOPs, test manuals, and the study protocol. Many test systems have inbuilt controls for this purpose, using standardized reagents of known concentration or quantity. The use of such standard controls is important, but not necessarily sufficient, to monitor the quality of test procedures. Depending on the procedure, samples should be tested in duplicate or re-read by a second technician. The frequency with which such repeats are performed depends upon how well the laboratory is running and how long it has been doing the test. Typically, when a test is first introduced or a new staff member is conducting the test, a high frequency of such checking is appropriate, with a decreased frequency as the procedures become more familiar, assuming the re-tests are showing negligible differences to the original results. In many circumstances, it will be appropriate to ensure that duplicate analyses are done on between 5% and 10% of samples on a routine basis. It is
sometimes possible and advisable to seed known positive or known negative samples into test runs, which are labelled in such a way that the laboratory staff running the test cannot spot them. This is particularly important if it is expected that the great majority of samples will either test negative or test positive (for example, seeding a positive result if a long run of negatives is expected). Needless to say, a system will need to be in place to remove these QC test results from the data on the study samples. Where POC diagnostic tests are administered by field staff, it may be essential for a supervisor to review or repeat tests in the field, as results may become less reliable over time.

Reproducibility should be checked within batches, between batches, and from day to day or week to week by the use of appropriate controls. Intra-observer variation can be determined by having duplicate samples processed by the same observer at different times, and inter-observer variation measured by having the same samples processed independently by two different staff members. Inter-product variation is tested by comparing new vs old batches of staining solutions, media, reagents, and so on, on a group of the same samples.

It is essential that immediate remedial action is taken if QC checks reveal a problem.

5.2 Internal quality control

Two types of QC can be distinguished—‘internal’ and ‘external’. Internal QC comprises procedures that are introduced within the field laboratory. External QC involves external monitoring such as the duplicate testing of samples in another reference laboratory to serve as a ‘gold standard’ or ‘blind’ measurement in the field laboratory of a set of samples provided by an external reference laboratory.

The essence of internal QC lies in a tight circle of checks, reporting, evaluation, and action. It is essential to have detailed manuals of every procedure, with a checklist to be consulted each time the procedure is run. Well-kept records, with regular review of these by the supervisors, are key elements in QC. Laboratory QC procedures must be an integral part of the work plan for the study.

5.3 External quality assurance

A major reason for external QA programmes is to check the accuracy of test results. Reproducibility can be assessed adequately by internal QC procedures, but checks on accuracy are best done, for many tests, in collaboration with other laboratories. The results from a laboratory may be highly reproducible within that laboratory but might be consistently incorrect. There are a range of external QA programmes which offer both testing of site-generated samples and/or the provision of a panel of samples with known characteristics that are specific for each assay (for example, biochemistry and haematology analysers). If specimens are selected for QA checks after they have been analysed locally and in such a way that the laboratory staff will not know which specimen will be selected, the use of site-generated QA systems are to be preferred to QA that depends on specimens provided by the external laboratory, since the laboratory staff will know which these QA panel specimens are and may take particular care with them.

SOPs need to be developed for the shipping and reception of samples for QA. An investigation request form should accompany samples that are sent, and every effort should be made to ensure that transport conditions are appropriate and the same for all samples (for example, route, packing conditions, and type of container). Attainment of levels of proficiency by the laboratory and its staff may be a prerequisite prior to involvement in some studies; but, after that,
external QA activities would be most frequent during training phases and at the beginning of a field study but should continue throughout. If a problem is detected, it is essential that the reason for this is investigated immediately and that this leads to effective remedial action.

The WHO has produced a list of pre-qualified QC laboratories (<http://apps.who.int/prequal/lists/pg_qclabslist.pdf>), and a link to the United Kingdom National External Quality Assessment Service is <www.ukneqas.org.uk/content/Pageserver.asp>.