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**Please read this bit first**

This CPD/ CEU exercise is designed to take approximately two hours as a small group exercise within your laboratory. The Thistle QA CPD No is: **MT-010**

Please keep a register of those taking part in the exercise. When the exercise is completed, please ask using the above email address, and we will send you a sheet showing the correct responses to each question.

Each attendee should claim one CPD points for completing the questions correctly, by retaining a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

# QC COURSE

**A course compiled by Dr. Jim McCulloch**

## MODULE 1 – INTRODUCTION

### The Purpose of QC

There is only one reason to perform Quality Control (QC) in the clinical laboratory. It is NOT performed solely because you have been told to do it; or because you want to fill in crosses on a wall chart; or because it is part of your accreditation protocols.

QC is done for the simple reason that patients deserve good quality results from path labs. A good and effective QC system is one that works to the benefit of patients. In fact, let's turn that phrase around. If your QC system does not maintain or improve the quality of your patient results – stop doing QC altogether. Or, just a thought, perhaps you should stop doing patient samples?

You will know that you work in a CLINICAL laboratory. Remember that well. You do not work in a STATISTICAL laboratory. What you offer your wards or referring doctors is very much a clinical service, albeit it one that uses statistics as a piece of information on which you have to make decisions. But stats are simply there to guide or alert us to potential problems. How many times have you been asked by a doctor if you are sure of your result? All to often the response is to say, well, my QC is within +/- 2 Standard Deviations (SDs). We then expect this clinical person to accept that piece of statistical nonsense. He or she does not understand or care about stats. Besides which, how good are your SDs anyway? Where did you get them? Are they wide and too generous, or tight and meaningful? The term SD means nothing without a deeper understanding of how to calculate effective SDs and use them efficiently.

This five-module course will attempt to help you understand, perform and use QC information effectively, to maintain or improve the quality of results you send back to your ultimate customer – the patient.

Effective QC

A definition of what constitutes an effective QC system will inevitably be personal and could generate plenty of discussion, perhaps even an argument. This is healthy, for QC is as much a set of opinions as a set of concrete facts. If anyone reads these pages and disagrees, great! The opinions presented are just that, opinions. So, let's get the definitions going.

- An effective QC system, as well as working for you and your patients, will be able to identify and reject ALL bad results, and recognize and accept ALL good results. Subsequent modules will explain why this is not possible, but for the moment let's accept it as an ideal state.

In real lab life, what that means is that your QC charts, for example the ubiquitous Levey-Jennings (L-J) charts, will NOT look perfect, with all results nicely tucked inside 1 SD. This is important – all subsequent understanding will depend on this being accepted and appreciated. Your L-Js MUST show out of control results, the inevitable 5% of results appearing outside 2SDs. If that figure of 5% confuses you, a later module on constructing L-J charts will help you understand what is a basic and important concept.

Once we accept that we have a real situation as regards controls and their limits, what we now need is a working set of protocols to help with decisions about what to do with those apparent out-of-control results, the inevitable and essential 5% outside YOUR OWN +/- 2 SD range. So, let's expand the definition of an effective QC system.

- An effective QC system, as well as working for you and your patients, will be able to identify ALL bad results, and accept ALL good results. But as this is not possible, it also requires some degree of training (that's why you are doing this course, right?) in interpreting and handling the 5% of results that MUST be outside the 2 SD limit.

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To reinforce this, please be very clear on the fact that if your L-J charts show consistently perfect QC, with all values dotted neatly within 1 SD, half above the mean line and half beneath it, then you have a problem! In fact you have a bad QC system.
Let me explain: if a lab takes the package insert values and uses them as the outer 2 SD control limits, the chances are that the ranges are 3 times as wide as they should be. Most package inserts actually tell you this, by saying that the ranges printed are for guidance only and that each lab MUST work out its own control limits. If you use the package insert values you are more or less using about +/- 6 SDs as your control limits. It is not surprising then that you will have "good" QC! The fact is it would take a systematic change of approximately ten times the standard deviation before the QC procedure would tell you have a problem. In other words, you would practically need to run out of reagent before you would notice you had a problem. Not a good idea.

Why are the package insert ranges too wide? To begin with they have been produced under foreign conditions, as every company supplying such material will have imported it from either Europe or the USA. Secondly, think on the system used by commercial companies to produce those ranges. They will have been established by the control material being sent to a number of labs for testing. The range thus has errors associated with between-lab variation, rather than simply in-lab variation, which is what you need for internal QC ranges.

The issue is that you MUST use your own SD ranges to operate your own QC system. You MUST know when your QC results are outside your own SD range, to decide on what action you need to take. If you still worry about this, wait until you get to a later module. It will be explained in greater detail in Module 4.

Please repeat my patient samples

An anxious doctor phones to ask you to repeat his patient sample tests. The first set of results was as follows:

| **TEST** | **FIRST RESULT** | **REPEAT** |
|---|---|---|
| Sodium | 140 | |
| Creatinine | 140 | |
| Cross-match | AB negative | |
| HIV | Positive | |
| Haemoglobin | 14.5 | |
| Sputum | TB scanty | |

Now, in the column headed REPEAT write in the results which you would be happy with as being "the same" i.e. statistically not significantly different from the first result. The results you write in can be either above or below the first set of results. That does not matter. What does is that they are your opinion of what constitutes the same result – and please do not necessarily write in exactly the same value, unless you strongly feel that no other result would be acceptable clinically. In an ideal world labs would always get the same answer, but we live in a very real path lab world. So get realistic and write in what would make you happy with the first set of results. And do that now, BEFORE continuing with this module, before reading the next paragraph.

Right, assuming you have filled in the last column, let's discuss what you wrote. Chances are that you would accept a repeat sodium result from about 137-143 as being "the same" as the first result. With creatinine a range from about 132-148 would be OK as repeats, while Hb would probably be acceptable from 14.0-15.0. The scanty TB result would need to be scanty or 1+ to substantiate the first result, with a negative repeat result not acceptable i.e. giving a different clinical interpretation. Let me repeat that – a different result is one that gives a different clinical interpretation. The final two tests to be repeated, the cross-match and the HIV are more clear-cut. No other result except an IDENTICAL result would be acceptable.

## CPD Questions: NB – select the single choice you consider MOST correct

1. Although the sodium and the creatinine were identical numerically in the first set of results, you would be willing to accept a wider variation in creatinine on repeat. Why?

   A) Labs make more mistakes when measuring creatinine than when measuring sodium.
   B) Patient results vary more for creatinine than for sodium, i.e. the Biological Variation (BV) is greater for creatinine.

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2. The Hb range is also quite wide. Select the most likely reason for this:
   A) Hb is badly performed in the lab.
   B) The BV is high for Haemoglobin.

3. Why would a negative for the TB slide be unacceptable?
   A) We would need to repeat for a third time and we are too short staffed.
   B) The clinical interpretation between negative and scanty is different.

4. Consider the requirement that we need to get the exact same set of results for the two qualitative tests - in effect there is zero tolerance for mistakes with tests such as cross-matching and HIV. Select the statement that you agree with most:
   A) The clinical prediction of the tests cannot be different.
   B) These tests are so well done by every laboratory that errors cannot occur.

5. Consider briefly why there are some tests where we are "allowed" a fairly large error, e.g. creatinine, some where we have little allowable error, e.g. sodium, and some where no error whatsoever is permitted.
   A) All tests have different performance standards, and some have designed with zero errors.
   B) The clinical requirement is different for serial changes in creatinine, compared to sodium.

Hands up those who grumbled that they thought this was meant to be a QC course, so what are patient results doing here? Congratulations to those who kept their hands down! The reason is obvious, when you think about it. QC is about patients, as stated already.

So, what do you take from the above illustration concerning acceptable repeat test results from this patient? Several things, I believe:

- Acceptable ranges for patients vary from test to test, based on something called Biological Variation. This will be discussed in MUCH detail in a later module, but can basically be defined here as the natural variation in concentration seen in each analyte tested in the lab. This can be different for each analyte of course, but also will vary depending on the analyte concentration and the individual under study. In other words, it varies a lot!
- If errors or variations in test result are accepted for patient samples, then they must be accepted for QC samples too. Variation is in fact inevitable and healthy; the job of a QC system is to identify unacceptable i.e. too much, variation.
- YOUR job is to decide what to do when variation seems too much. And if for variation, you assume dispersion of results, or Standard Deviations then you have got the picture.
- Finally, it should be clearer that we run CLINICAL labs, not STATS labs.

Learning the language of QC

Definitions are boring and most of us don't read dull and boring lists, so here there will only be what we need to get started – the rest will follow.

**QC procedure**

This is a specific protocol for analyzing a specific number of control materials and interpreting the outcome. In our type of labs, this usually means collecting test results on stable control materials, then plotting those control observations on a control chart with specific limits.

**Control chart**

This is a graphical method for displaying control results and helping to evaluate whether a particular test method is in or out of control. Today these charts are generally called L-J Charts, after the two authors of a paper published in 1950 – even though their recommendations are never followed and their suggestions seem very old fashioned today. History has been kind to Levey and Jennings.

**Control limits**

These are lines drawn on the Control Chart to illustrate the limits of acceptable results on control material. Traditionally, the outer limits of control are set at +/- 2 Standard Deviations (SDs) – this will be much discussed and considered in a later module. The concept is that when a control result is inside the control limits, that particular assay run is deemed to be 'in control' and patient results can be reported with a degree of confidence. Conversely, when the control result is outside the control limits, the run is considered to be 'out of control' and thus patient results cannot be reported. This hard and fast situation represents that mythical ideal state yet again, but is adequate to allow us to move on, for the moment.

*Westgard Rules*

Dr. James Westgard has published widely in the QC field for decades and has rightly come to be regarded as the guru of pathology QC. His rules, the Westgard Rules, were established as an attempt to introduce even more statistical rules into a clinical service. They can he helpful and will be discussed in a later module, but they are still simply a good attempt to interpret stats information.

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Who defines what is considered 'good enough' quality?

At a seminar many years ago I asked that question, concentrating on the 'who' part. The general reaction was that 'experts' must decide. Okay so far, but now let's define what is meant by 'expert'. This is not as easy as it looks.

When the original Accreditation Committee sat in South Africa, in roughly 1994, I recall some debate about how the length of time that samples and pathology records should be retained. About twenty 'experts' sat around the table, deliberating and talking endlessly about factors that affect the storage and retention of, say, histology sections, or blood samples, or even QC records. This continued until it became obvious that the 'experts' had no idea how long such items be retained. Everyone spoke about what happened 'in my lab' but none of us knew what was correct, or appropriate or even legally required.

This story illustrates several things, including the well-known fact that experts will often disagree, as well as the reluctance of such experts to confess they do not know the answer!

The same situation applies to deciding what is and what is not acceptable quality. The patient illustration earlier is important here, as it shows that we each carry around somewhere in our experience, an idea of what is good enough for each test. Generally this is a combination of knowledge about the performance of this test in our own lab experience; plus a feeling for what variations patients will have – a feeling that is based to some extent on the reference ranges we use, the wider the range, the more patient variation there will be, roughly speaking.

Three sets of acceptable performance standards will be discussed, namely CLIA'88, Biological Variation, and the Acceptable Standards used by Thistle QA in South Africa.

**CLIA'88**

The USA law entitled the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88) was one of the first ever to attempt to define minimum standards for all laboratory tests. There have been many subsequent changes and alterations to this law, and these changes are well discussed by James Westgard (www.westgard.com).

Four categories exist in CLIA'88 regulations, from waived to high complexity, but only three are relevant to us here, as follows.

Waived tests have the lowest quality requirement. Such tests include Faecal Occult Blood (FOB), urine pregnancy tests and various dipstick or tablet urine tests.

Moderate complexity tests comprise about 75% of all tests performed in labs today. CLIA'88 includes much more than traditional stats QC procedures, namely, calibration, procedure manuals, corrective actions and record retention. The general requirement is that the lab analyse two levels of QC materials on each day of testing, although this recommendation is subject to many 'ifs and buts' and is far from a hard and fast rule.

High complexity tests are either difficult to perform or are those that the lab has modified from the manufacturer's instructions. For statistical QC, the labs must demonstrate compliance with certain stringent requirements including evaluation of the instrument and reagent stability, and the establishment of the labs own acceptability criteria to assess QC performance.

CLIA'88 has remained at the forefront of all subsequent attempts to define acceptable standards of performance. However, the question needs to be asked: where did the CLIA'88 standards come from? As far as can be ascertained, the answer is that 'experts' decided on the standards. The standards listed in CLIA'88 are thus opinions, not facts.

*Biological Variation (BV)*

The concentration of many analytes can vary over an individual's lifetime, simply because of the biological factors involved in the ageing process. In addition, certain analytes have predictable biological rhythms or cycles, be they daily, monthly or seasonal. Most analytes, however, do not have such cyclical rhythms, but rather fluctuate randomly around a homeostatic setting point. These variations are collectively called Biological Variations. For example compare the wide BVs found in serum creatinine (related to exercise, diet, muscle mass etc) to the smaller variation found in serum calcium (under tight homeostatic control).

Knowledge of such BVs can be applied to the setting of quality specifications, for example, total allowable error, standards in EQAs, as well as precision and bias.

Dr. Callum Fraser, one of the leading proponents of BV as a basis for setting quality standards, said that "the quality of tests performed in laboratory medicine must allow our clinicians to practice good medicine."

BV is a valid setting point from which to begin the quest for acceptable standards of performance. It has the advantage that it is related to biology, and thus is appropriate as a means to control biological variation in pathology test results. In addition BV standards are verifiable by actual laboratory measurement and have not been 'invented' by a panel of 'experts'.

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## Thistle QA Acceptable Standards

The acceptable standards developed and applied by Thistle QA – and shown on Page 2 of each report - were initially based on both CLIA'88 and BV. Dr. Callum Fraser took those concepts and designed the Thistle QA acceptable standards. Subsequent changes have taken place, including a blending of CLIA'88 and BV to create a single desirable and acceptable standard, as well as modifications suggested by a local panel of experts, based on achievable technical standards, as well as clinical needs.

These standards have thus been designed by an overseas expert and modified to fit our local circumstances by local pathologists and other experts. They can truly be regarded as the first local attempt to define appropriate and achievable standards of performance.

## Let's define levels of 'quality' responsibility

Each and every one of us has duties and responsibilities with regard to quality standards in our laboratory. In fact, ask yourself: which of my daily activities does NOT affect the quality of my patient results? The answer is that everything you do has an impact: from ordering quality instruments or reagents to training staff, from deciding how often to run QC samples to discussing patient results with wards or clinicians, and from writing protocols to drawing up leave rosters. Everything has a quality impact.

Your patient deserves good quality: it is your duty to assist in providing it.

## CPD questions

6. QC is performed to satisfy accreditation requirements.
   A) True
   B) False

7. Why must 5% of control results be outside the +/- 2 SD ranges you have established yourself?
   A) Because 95% of results must be inside the +/- 2 SD ranges
   B) The 2 SD ranges have been created using the Probability Theory, which states that if a result is inside +/- 2 SD, then it is unlikely you have an analytical problem; and if too many result are outside the +/- 2 SD ranges, you have a problem.

8. Explain why it is not "good laboratory practice" to use package insert ranges to control your laboratory analytical performance.
   A) They are guides only, and the package insert should tell you this.
   B) Because you will not know when you have a problem until it is serious.

9. Why is the control requirement wider for creatinine than for sodium?
   A) Because BV is wider for creatinine than for sodium.
   B) Because sodium is easier to measure

10. Is Biological Variation a suitable starting point towards establishing acceptable laboratory standards of analytical performance?
    A) Yes
    B) Yes (this is not a typing error!)