Quality Control Issues in Point of Care Testing

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Summary

- Quality Control (QC) in Point of Care Testing (PoCT) is often thought of as a complex issue; however intelligent system analysis can simplify matters and greatly increase the chances of a well controlled system. What we want to achieve is a QC program which adequately controls the PoCT system, but does not excessively contribute to the operating costs or complexity of maintaining a PoCT instrument, or network of instruments.
- Don't neglect effective pre-analytical work: good documentation, operator training, monitoring, and analyser maintenance programs are essential, as for any analyser.
- Look closely at your analyser:
  Is it a "laboratory type" instrument or cartridge or strip based?
  Can it perform multiple test types or a single test only?
  How is it calibrated?
  Does it have built in self-check capabilities or an electronic check cartridge?
  Is the sample in contact with the instrument?
  What are the cartridge/strip/reagent storage requirements?
- Establish where the analysis is taking place and which system component is involved.
- Tailor your QC program to target this component, but still check the system as a whole.
- A common approach is to check cartridges/strips on delivery and run a QA sample at least monthly to check storage conditions and operator performance. If there is no independent electronic instrument check, daily QC checks are also recommended.
- Don't be afraid to stray beyond conventional QC models if necessary. Some PoCT systems are not adequately controlled by the application of conventional QC alone.

Introduction

Clinical Chemistry and Haematology have used established statistical QC and Quality Assurance (QA) processes for many years, with near universal adoption of Westgard type rules, and widespread use of moving mean XB (Bull's) type analysis, particularly in Haematology.[1,2]

PoCT is not a new phenomenon, ward glucose meters have been with us for decades, and remote blood gas analysers have been used for nearly as long. PoCT analysers however, still seem to present both laboratory and regulatory staff with ongoing quality control dilemmas.[3]

Part of the solution to QC issues lies in looking at a paradigm shift in the way manufacturers have viewed point of care technology in the last few years.

Many new generation devices are specifically designed for clinical staff, to fully replace the equivalent laboratory test, allowing it to be permanently performed at the point of care. We now find that many of these modern analysers do not fit with traditional laboratory QC systems – because they were not designed to be used in laboratories.[4]

Modern point of care analysers could more properly be regarded as a testing "system" with an "analyser" component, and the "cartridge/strip" component which used together, produce the result. This type of construction influences which parts of the system are actually tested when traditional QC specimens are run.

QC in PoCT Applications

Don't neglect pre-analytical quality; it's even more important

than in the laboratory. Confirm that the following are in place:

1. Thorough, documented, initial operator training sessions and records.
2. A program of regular training updates, or ongoing user monitoring to maintain skills at acceptable levels.
3. Sponsorship and education by professional laboratory staff.
4. Equipment which is treated with care and respect, and maintained according to the manufacturer's recommendations.

Instrument Types

Broadly, point of care instruments tend to fall into three different categories.

1. "Laboratory Type" instruments used in a point of care environment. Examples: "Full size" blood gas, and column HbA_{1c} analysers.
2. "Cartridge Based" instruments. Examples: Cartridge based blood gas analysers, HbA_{1c}, and INR analysers.
3. "Strip Based" instruments. Examples: Electrochemical or reflectance strip based glucose meters and INR analysers.

QC Requirements by Instrument Type

The categories will help determine how the QC program should be tailored to effectively control the PoCT system.

1.Full size laboratory derived analyser

In these instruments the manufacturer has placed their technology investment in the analyser as a whole and any QC program must reflect this fact. Multi-level daily QC samples, combined with regular QA samples and a rigorous preventative maintenance program will form the backbone of any QC program.

2.Cartridge Based

Cartridge instruments provide a greater challenge. In most cartridge based systems, the manufacturer has placed their principal technology investment in the test cartridge. In many systems, it entirely contains the specimen, the calibrator, the reagent and the detection system and is THE entity responsible for the analysis of the specimen. In these cases the "analyser" is actually an "electronic reader" converting minute changes in voltage or current produced by the test cartridge into human readable numbers. These instruments can offer incredible flexibility. A single instrument can measure a prothrombin time one minute and then, by simply changing a disposable cartridge, instantly becomes a blood gas analyser! As the sample never touches the "analyser", the need for routine "analyser" maintenance is reduced or removed.

This very flexibility can render effective QC more difficult, particularly when the test range crosses traditional departmental testing boundaries. When running traditional wet QC samples on such instruments one is really only checking the performance of that (one) disposable cartridge. Test reproducibility is provided by the quality certification of the cartridge manufacturing process. Increasingly these systems provide for some type of "electronic" self check of the analyser component, which may be a simple circuit and display check, or may involve the use of an optical or electronic check cartridge. In better systems, check devices perfectly mimic a real specimen cartridge, and thus provide a very comprehensive instrument check.

In these cases, it could be argued that this electronic control is no different to running a real cartridge with a known control, and is thus all the QC that the "analyser" part of the test system requires.[5]

Any given cartridge within a lot will have identical calibrators, reagent and detectors to its fellows, and so provides exactly the same testing environment independent of the "analyser" component.

In these systems the QC efforts should concentrate on the cartridge itself, and the test system, as a whole, rather than the "analyser" per se.

In another cartridge analyser variant, the cartridge is designed to perform multiple patient analyses rather than single use. Because the cartridge is sealed, this system can allow for some very sophisticated inbuilt QC systems. Every variable, bar the test sample, is effectively fixed for the life cycle of the cartridge.

Such analysers combine the convenience of use of a laboratory type instrument with many of the advantages of a cartridge based system. They may be treated as a cartridge based instrument for QC purposes although the inbuilt QC systems may approach or even exceed those of conventional analysers.

3.Strip Based Instruments

Strip based instruments are in many ways similar to cartridge based systems. However, in this category of instrument, minimal costs and simplicity of operation have been the desired manufacturing outcome, as many of these instruments are intended for direct lay consumer purchase and use.

Once again QC practices must be altered to compensate. The manufacturer's technology investment is in the test strip. Everything related to the test is contained within the

strip, however, rather than being self calibrating, strips are usually calibrated by lot. The calibration factor for each lot is commonly introduced into the reader by a microchip or bar code. The reader design is stripped down and can usually perform only a single, or perhaps two related tests. The reader electronics rarely contain instrument self checks beyond a simple continuity, battery and display check. Usually there is no provision for separate "analyser" calibration. Faulty "analysers" are usually simply replaced.

Despite the apparent simplicity of "strip" systems, due to the lack of a separate "analyser" QC device, and the lack of inbuilt calibrators on the strips, QC requirements for strip systems should actually be more stringent than for many cartridge based instruments, in order to ensure and maintain good control of the system.

Tailoring a QC program for a PoCT System.

When designing a QC program for a PoCT system it is important to be aware of the type or mix of PoCT instrument(s) you intend to use in the system and exactly what part of the "instrument" you are checking when running a QC or QA specimen. This knowledge can significantly affect how the data should be interpreted, and what action should be taken if unacceptable results are obtained. We need to refer to our types as described above.

1.Bench top Blood Gas Analysers

PoCT Benchtop Blood Gas analysers and other laboratory derived instruments must be controlled and maintained in a similar manner to their laboratory counterparts, as we have already discussed.

2.Cartridge and strip based analysers.

Due to the large degree of heterogeneity in this instrument class, constructing an effective cartridge or strip based analyser QC program requires some initial detective work on the instruments to be used. Unfortunately "one size" does not always fit all! The following questions are intended to be suggestive, rather than a comprehensive guide for the reader.

- Can the "analyser" component perform multiple test types or is it designed to perform a single test only?
- Are the cartridges/strips single use or multiple use?
- Do the test cartridges/strips contain all the components necessary to perform the test?
- Do the cartridges/strips, require separate (lot) calibration or are they self-calibrating?
- If the cartridge is multi-use, does the initial calibration step last the life of the cartridge or must it be repeated at regular intervals?
- Does the sample ever touch the "analyser" itself or is it completely contained within the cartridge/strip?
- Can the analyser component be checked independently with a separate electronic or optical check cartridge?
- Does the analyser have other built in self check capabilities?
- What are the manufacturer's recommendations for QC and maintenance? Does the analyser have moving components which wear, or which must be routinely repaired or replaced?
- Must the manufacturer's calibrators and QC materials only be used, or can third party ones also be used?
- What are the manufacturer's recommendations for storage of the cartridges/strips?
- What are the local and national regulatory requirements?

A Suitable QC Program for a Cartridge Instrument might be:

Cartridges are QC checked on delivery with multiple levels of the manufacturer's, or a manufacturer recommended QC material. This basic check ensures that cartridges perform to specification, and were not damaged in transit. Different lot numbers and cartridge types in the delivery must be checked separately, and a randomly selected "representative" sample should be tested. Once this check has been performed, it should not be necessary to QC the cartridges again, even if they are used in multiple analysers within a geographical group, providing the storage is consistent with the manufacturer's recommendation. The "analyser" component is checked with the manufacturer's electronic QC cartridge on every day of use prior to patient testing being performed. If the analyser does not feature an electronic check cartridge, then additional single level cartridge controls may be necessary on every day of use (see QC program for strip based systems below).

It is recommended that a QA sample (if available) is run at least monthly, on at least one analyser within a group. Many operators prefer to use the one which is used to QC cartridge deliveries. This QA sample checks that storage conditions for the cartridges are correct, and secondarily checks operator performance. Arguably, cross checks between multiple analysers may not be required in this type of system because essentially all the cartridges within a lot number are identical and should perform identically, no matter on which "analyser" they are run. The analyser component of the system is controlled separately by the electronic check cartridge and does not affect the cartridge result if operating correctly. Cross checks or additional QA programs may be required if an "analyser" does not feature an electronic check cartridge.

A downside of this type of QC "program" is that very few QC "points" per lot are produced, rendering the production of a

traditional Levy–Jennings QC plot impractical and making it difficult for a laboratory to produce its own QC ranges for each cartridge lot. This forces a degree of reliance on manufacturer recommended ranges, which might be considered undesirable for a laboratory instrument.

For this reason, some authorities have suggested for cartridge PoCT, a QC system based on continual comparative patient results with a laboratory.[4] Such systems although innovative and worthy of attention, would rely on constant ready access to a laboratory and thus be more useful in a large hospital setting, than for PoCT in rural and remote areas.

A Suitable QC program for a Strip Based System might be:

Strips must be stored in accordance with the manufacturer's recommendations. Strips are checked with multiple levels of the manufacturer's recommended QC material at delivery, and every day of analyser use. It is necessary to perform a QC every day of use because the reader has no independent electronic QC check unlike many of the cartridge based analysers. Without this daily check, a faulty "analyser" could produce incorrect results for quite some time before being identified by a QA sample. As the analysers are tested daily, it is possible to use Levy-Jennings type QC monitoring, although in practice this is not commonly used on such instruments due to the lack of suitable software links and the reliance on tedious manual transcription.

A manufacturer recommended or third party QA sample is run at least monthly on every analyser at the site. This QA checks the storage conditions of the strips, the continuing correct functioning of the analysers and the operator performance. The QA reports are used to target analysers and areas which continually produce results which fall outside of acceptable limits.

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