# Practical Tips to Manage Laboratory QC Data

Quality Control

## Questions and Answers

1. **Regarding the Biological Variability and TEa slide, last updated was 2014, will there be a latest version or how often is this updated or revised?**
   There are many sources of Total Allowable Error (TEa). The Ricos table was just one example. Consider the summary at Sun Diagnostics as another example compiled from several sources. https://sundiagnostics.us/wp-content/uploads/2020/02/total-allowable-error.pdf
   The Biological Variation data is now managed by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) and can be found here. https://biologicalvariation.eu/
   The Unity Real Time software also provides these Biological Variation values in the Analytical Goals and Total Allowable Error sections.

2. **Do you have any recommendations for what to do if your QC is out of control for an extended period (for example when a QC shifts due to a Reagent lot change) but you still need to process patient sample. Can you use manufacturer QC material with the insert range to maintain a service while troubleshooting?**
   Certainly the ranges and manner of troubleshooting is at the discretion of the laboratory medical director, but it is often advisable to determine why QC shifted at the reagent lot change. Consider acquiring a different lot from the manufacturer to test for possible matrix effects between the QC and a specific regent lot.

3. **Can we use 1 2s in a two-level QC?**
   The choice of QC rules and staff actions is a medical director decision. However, consider that the 1-2S rule may fail randomly 5% of the time, so the laboratory may be over-troubleshooting if the 1-2S triggers a failure rather than a warning.

4. **If you change LOT number, would you produce a new QC? Surely the QC should produce a similar value across each LOT? If it does not, should we loose confidence that our patient results are not correct/consistent?**
   I am not certain if this question is referring to reagent lot or QC lot. First QC lots, while manufactured to target specific concentrations, often have different means between QC

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lots. So, it is important to establish a new mean and acceptable range when changing lots of QC. For reagent lot changes using the same lot of QC, one expects to produce similar QC values with the established range. There occasionally can be matrix effects between different reagent lots that can lead to shifts upon implementation of the new lot. So the lab should be aware.

5. **What can you do if there is no PT/EQA or interlaboratory program in your area?**
   Most regulatory agencies require EQA for all tests. However, newer tests, laboratory developed tests or laboratories in some areas of the world may not have access to PT/EQA programs. In that instance, the laboratory can share patient samples with other local laboratories in order to compare results. We used to do this for beta-hydroxybutyrate in Massachusetts before CAP developed a PT program. Our laboratory in western Massachusetts would pull 5 samples at varying levels and send to a laboratory in Boston once every 6 months. This fulfilled the CLIA requirement for semi-annual PT for both laboratories.

6. **How do you recommend handling instruments that are high volume and multiple packs of regents are used? Are all reagent packs QC'd even if they are a closed system. For example, multiple TSH reagent packs are used in-between scheduled QC time (4 hours). Should each reagent pack be QC'd?**
   First, I'd follow manufacturer instructions, as some high volume analyzers will automatically analyze QC when shifting to a new pack of reagent. If not, you can consider running a QC sample every 25, 50, 100 patient samples. Many large labs will intersperse QC with patient samples, essentially basing QC frequency on volume of samples in order to ensure that QC is sampled on each pack of reagent, and that there are fewer patients to repeat if QC fails and requires patient look-back.

7. **If you see a shift/bias in all three levels of QC after a calibration, would you adjust the mean/ranges? What if there is a new lot of reagent?**
   If a calibration event leads to a significant shift in QC, the lab should consider that patient samples may see a similar shift in results. So, you might want to recalibrate with a new bottle of calibration to see if the shift is consistent or if the calibrator may have degraded over time (some bottles of calibrator can be stored and reused for some time after opening, which can lead to evaporation and shifts in concentration of analytes).

8. **What would you do if your mean (after collecting data) is outside the range provided by the manufacturer?**
   First, I'd ask why? If the QC is supplied by the manufacturer and paired to the analyzers, then the manufacturer supplied ranges are generally a good estimated target for the results a laboratory should expect with that lot of QC. On the other hand, if the QC is supplied from another manufacturer, then the target QC ranges may only be an

estimate and individual labs may experience differences due to matrix effect of the QC material with the instrument reagents.

9. **What are your thoughts on using moving averages as part of the quality program?**
   Absolutely. This talk focused on statistical QC, but moving averages is a different means of ensuring test system quality using patient results over time. Moving averages also can be more cost effective, as moving averages does not require purchase of QC material or staff resources managing QC data, but does require some powerful computers to compile data and run data algorithms.

10. **Calibration performed daily, before even running controls. IFU suggested that calibration was stable for 4 weeks. QC seemed to be more variable.**
    Not certain what the question is here, but depending on patient sample volume and QC frequency, multiple bottles of QC may be used within a month. So QC may show more variability due to bottle to bottle variation. This is why QC data run over several days and bottles of QC are important variables to capture when establishing ranges for new lots of QC.

11. **For smaller labs that only run analyzer QC once per day after maintenance, are patient look backs necessary for out of control assays?**
    A laboratory always wants to ensure that patient results are bracketed by successful QC. So, whenever QC fails and requires troubleshooting, depending on the issues and lab actions, some patient lookback is generally required in order to verify that patient results did not shift since the previous successful QC and due to the troubleshooting and corrective actions to get QC back in range.

12. **How often should QC be performed? Once a day or several times?**
    Depends on the test and specifically the sigma metric and most importantly local regulations. CLIA for instance, mandates at least 2 levels of QC each day of testing, but more frequent q8hr QC for hematology and blood gases. Assays with <3 sigma should attempt frequent QC with multiple rules, while those with >6 sigma can relax QC frequency and rules.

13. **Will you provide guidance on how close the results should be in determining acceptability for the patient look-back?**
    The Total allowable error limits of a test should dictate the acceptability for patient lookbacks.

14. **Do you recommend real time QC if a lab is having to trouble shoot daily**
    Real-time QC is really patient based and can incorporate moving averages and other data algorithms. Yes, I highly advocate, as both a supplement to traditional QC, and to consider as an alternative to QC where allowed by regional laboratory regulations.

Patient based moving averages can be challenging to implement, and requires IT systems to separate results from different areas (inpatient vs outpatient) or patient populations (cancer vs trauma) in order to select a set of fairly stable results to follow in real-time and signal as soon as shifts in assay performance are detected based on the rules developed by the laboratory.

15. **Is there a list of unstable quality control with analyzers?**
    Not that I know. QC supported by a manufacturer tends to perform with less variability than a third party QC supplied from a different manufacturer, mostly because the manufacturer QC performance is optimized for the manufacturers analyzers. However, third party QC offers an independent verification of test performance, independent from the manufacturer of the analyzer. These are the issues to consider when selecting a QC product.

16. **Do you have article or reference for diagram using for troubleshooting CQ , need for our policy lab thanks**
    You can pull the example I showed during the presentation, but I'd customize to your lab's preferences

17. **What should we do with some analytes which don't have biologic variability?**
    For those tests, the lab can define its own limits based on how the clinicians are using the test to treat patients, or adopt an alternative allowable limit (such as use of CAP proficiency testing limits. Take ACT coagulation test - there is no biologic variability set since the test measures heparinization, but a laboratory can set own limits (based on manufacturer package insert expected precision) or adopt CAP PT limits (+/- 3SD). When presented with 3SD tolerance limits, the lab can pull several previous surveys and determine what a 3SD range would be for a sample with clotting time in seconds close to the QC sample target. Basically, the laboratory is setting own allowable error with supporting evidence that is available.

18. **Can we use the CV of the old lot QC for the new lot and then just establish the mean for the new lot QC?**
    Correct, yes you can. I used this in the homocysteine example.

19. **If you are seeing a bias on a quality control and you have done trouble shooting and have found no error and this bias has been going on for a while, when is it ok to change your mean away from the manufacturer's suggested ranges?**
    A laboratory should establish their own QC range (based on manufacturer suggested target) before implementing the lot of QC. Once implemented, if that QC starts to show a bias, I'd compare my lab's performance against peers on an interlaboratory QC report to determine if something changed since establishing the QC range or if the initially QC range wasn't quite right to start with. Sometime measuring just 10 points over 5 days

isn't sufficient time to consider all sources of variability and shifts start to happen either due to analyzer drift or even possible degradation of analyte within the QC over time. I always tend to consider how my lab is performing in comparison to peers before making a change to the QC ranges.

20. **Our lab uses reagents "kits". This means a change in reagent lot and control lot. What is the best way to do this?**
    I know there are some analyzers that do kit their QC with the reagents and even have preset QC ranges that cannot be changed by the consumer. In these instances, I'd first follow the manufacturer instructions for use, ensure the frequency of QC is meeting federal and local regulations, and then the lab can consider supplementing the QC with a third party QC product from another manufacturer which would allow the lab to set their own ranges. Alternatively, the lab can consider patient based real-time QC or other means of controlling the testing process based on a risk assessment of the test system.

21. **What software you are using for these graph?**
    I generally use EP Evaluator or excel now for linear regressions, but have tried statistical software in the past. Several commercial products can produce graphical representations of data comparisons. For QC data, Bio-Rad Unity plots QC points automatically and graphs can be exported as adobe pdf or printed.

22. **Thank you Dr. Nichols. My question is if your interlab report says that you are out on method group, but within the peer group range. What do you recommend for a corrective action?**
    I might take no action for this, since the lab is matching peer group. Many different manufacturers can contribute to the method group and each manufacturer may show some matrix effects with that lot of QC. So, depending on the number of labs and different methods contributing to the interlaboratory summary, the method mean and range may be different from a specific manufacturer peer group.

23. **Nice lecture Dr. Nichols! Nowadays, there is substantial knowledge about QC procedures for quantitative lab assays. I was wondering if you could comment on QC tips for qualitative (yes/no; pos/neg) lab assays.**
    Qualitative assays generally show most variability around the cutoff concentration for positivity, so I'd consider picking a QC product with concentrations that bracket the cutoff rather than QC that is strongly positive and strongly negative. For drugs of abuse for instance, a lab might want to consider QC targeting +/- 20 or 25% around the cutoff concentration for that test. This way, the lab will be setup to detect smaller shifts in assay performance and the positive QC should never result negative or the negative QC result positive.

**The following questions were asked during the presentation. Please see the webinar recording for the responses.**

24. **When starting a new QC lot, do you advise to use 10 or 20 data points to estimate your new mean?**

25. **What is your recommended practice when an assay is statistically out-of-control, but within the Total Allowable Error?**

26. **What Westgard rules do you recommend that we follow? It seems that 1:2s is too restrictive?**

27. **How often should you run QC events on Point of care instruments?**

28. **If the controls and analyzer are from the same company, can we use the ranges that are preprinted that came with the controls?**