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14. ABSTRACT Quality control (QC) is one of the most important impacts on laboratory testing - it ensures both precision and accuracy of patient sample results. The integrity of quality control samples is important to both management of overall quality as well as meeting requirements of proficiency testing. Addressing QC issues are critical to identification of potential errors with patient results, including reagent matrix effects as well as calibration misalignment of testing function. Maintaining accurate and frequent checks of laboratory sample testing through quality control is vital to ensuring patient testing is done right and produces accurate results for both the patient and physicians. Also, management of matrix effects and calibration misalignment are important aspects to observing shifting L-J charts and adjustments of accuracy over time. Continuous monitoring of quality control testing and capture of biases or trends are important factors to ensure accuracy of patient testing results. As clinical laboratory scientists, our function as managers is as valuable to the patients as our ability to analyze their samples.

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Quality control in clinical laboratory samples

By Maj. Paul R. Eden, MT (ASCP), PhD, and Maj. Cordy F. Herring III, MT(ASCP), CA CLS, MS

Laboratory testing of patient samples can be a complex procedure, depending on clinical analysis, microbiological study, or blood banking testing among other facets of the clinical laboratory. Quality control (QC) is one of the most important impacts on laboratory testing—it ensures both precision and accuracy of patient sample results. The integrity of quality control samples is important to both management of overall quality as well as to meeting requirements of proficiency testing. Addressing QC issues is critical to the identification of potential errors with patient results, including reagent matrix effects as well as calibration misalignment of testing function. Maintaining accurate and frequent checks of laboratory sample testing through quality control is vital to ensuring that patient testing is done right and that it produces accurate results.

When quality control works effectively, it is able to find and correct flaws in the analytical processes of a lab before potentially incorrect patient results are released. According to Ibrahim et al.,[1] failure of QC testing can result from "clerical, methodological, technical, PT materials stability, and random errors." (Please visit *www.mlo-online.com* to read references for this article.) By utilizing quality control practices, a laboratory self-regulates its testing and verifies that the results produced are accurate and precise. Clinical labs use management of documentation as well as incorporation of a continuous improvement process to streamline the overall quality control process.

QC samples are expected to be identical and tested identically to patient samples.[2] The purpose of repeated quality control testing is to validate precision and accuracy of the results of patient sample testing. Precision is the "degree of agreement among repeated measurements of the same characteristic on the same sample,"[3] while accuracy is how close results are to what is expected from a test. For example, a glucose quality control reagent is expected to produce results on average of 100 mg/dL. Ten repeats of that same agent produce results of 96, 98, 101, 92, 93, 88, 92, 93, 91, 90, and 98 mg/dL. These results would indicate a low bias result in the instrument.

Other ways of managing quality control include peer testing and alternative monthly review of QC trends. Clinical laboratories are frequently enrolled in clinical laboratory proficiency testing (PT) programs that are used to validate their testing protocols. These programs, for example those through the College of American Pathologists (CAP), are utilized not only to validate laboratory testing but to validate personnel training and procedures.[1] CAP's PT program utilizes samples identical to patient samples and not only validates individual laboratories but utilizes peer comparison to generate more accurate ranges for proficiency samples. Periodic review of QC results is a frequent tool for maintaining quality control of patient samples.

Although PT programs are excellent for evaluating QC performance, they can also help laboratory professionals discover issues with reagents even when controls and calibrators seem to be performing well. In early 2014, several laboratories using the same clinical chemistry analyzer failed a CAP PT survey for Hemoglobin A1Cs (HbA1C). Although the peer data showed that these laboratories were precise with each other based on the data generated, CAP reported that these laboratories had failed the survey. Investigation among the laboratories showed that controls were well within established parameters and calibrations were valid. The laboratories queried the analyzer manufacturer and expressed concerns over reagent quality. The company conducted its own internal investigation and discovered that the reagent would cause results to be 0.4% to 1.0% higher than what should be resulted. The company contacted the FDA and issued a technical bulletin alerting laboratories that patient results could be erroneous, even though calibrators and controls worked as intended. The laboratories contacted patient providers and thousands of patients so that patients could be assessed and retested.

One of the most common tools used to track laboratory quality control samples is the Levey-Jennings (L-J) chart. An L-J chart and the Westgard Rules are frequently used to verify trends, biases, or errors in quality controls. The Westgard Rules observe the normal distribution expected and identify standard deviations produced.[4-5] Implementing Westgard rules within an L-J chart can identify violation of the rules based on control limits established for the sample tested.

Many laboratories utilize L-J charts for 14- or 30-day reviews of QC testing. While daily identification of QC deviations from normal ranges ensures accuracy of sample testing, longer-term reviews are more beneficial to diagnose trends and biases in tests which could be missed on a daily basis. An additional use of the L-J chart without quality control samples is to utilize patient samples as their own controls.[6] By tracking the running averages of the patient results, a laboratorian can identify drift or problems with analyzer function that

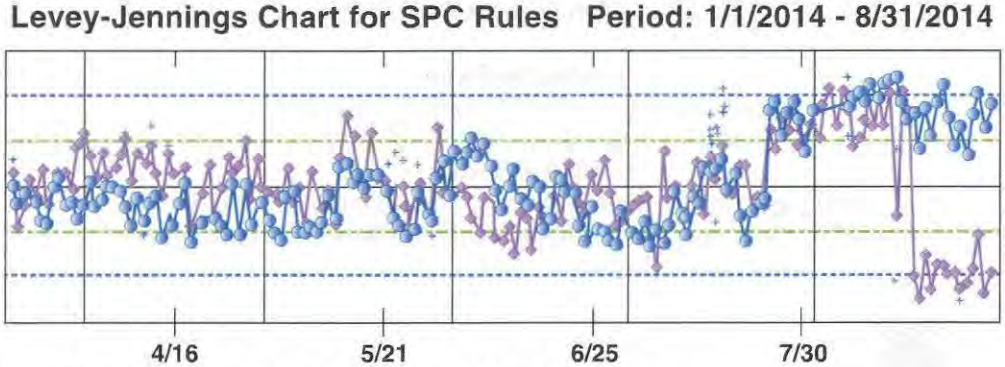

Figure 1. Levey-Jennings Chart for SPC rules—period 1/1/2014-8/31/2014

are not captured by quality control testing. Addressing concerns with QC materials as well as recall issues are common challenges for laboratory managers.

One such concern with QC materials is discovering a "matrix-related bias effect" which can skew normal results. According to Miller et al., "'matrix-related bias' [effect] refers to an effect caused by manipulation of the sample matrix during preparation of a QC material that is different from (or in addition to) the naturally occurring differences in matrix among clinical patient samples."[6] In one laboratory, the Chemistry technical supervisor discovered a matrix-related bias effect with troponin I. Troponin I tests are used for to measure troponin I proteins, which "are released when the heart muscle has been damaged, as in heart attack."[7] QC for this reagent had been steady for months within a particular accepted range. Data tracking then showed a sudden spike in values for one level of QC and a sudden drop in the other level of QC, even though both sets of QC were within range (**Figure 1**).

The Chemistry technical supervisor contacted the manufacturer and alerted representatives to a possible matrix-related bias effect with third-party materials interacting with the company's reagents. The company investigated the claim and substantiated it. Shortly thereafter, the company issued a technical bulletin advising laboratories to avoid using the third party's QC materials until the bias could be resolved. The laboratory used a different company's QC materials, and values returned to the ranges seen before the matrix effect. The labeadership was relieved to learn that the bias effect only affected quality control materials and not patient results.

In conclusion, management of quality control can ensure accuracy and precision of both quality and patient results. The focus on trends and biases is a good identification of potential changes in results that can affect accuracy of overall results. Also, management of matrix effects and calibration misalignment are important aspects to observing shifting L-J charts and adjustments of accuracy over time. Continuous monitoring of quality control testing and capture of biases or trends are important to ensure accuracy of patient testing results. As laboratorians, our function as managers is as valuable to the patients as our ability to analyze their samples. □

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