What's New in Laboratory Statistical Quality Control Guidance? The 4th Edition of CLSI C24, Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions

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In laboratory medicine, our main goal is to improve patient health by providing laboratory results that support medical decisions. To meet this goal, the laboratory needs to report accurate results that enhance care and minimize patient risk. Analytical goal setting helps the laboratory assure that when their measurement procedures are operating in their stable, in-control state, the patient results they report will be fit for their intended use. The laboratory's QC plan is designed to assure that even when test system failures occur, the risk of patient harm due to erroneous reported results is kept to acceptable levels.

The CLSI C24 document first published as an approved guideline in 1991 has been a popular and useful resource to help laboratories design, implement, and assess their QC practices. The 4th edition of CLSI C24 titled *Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions* has just been completed (*1*). As chair of the C24, 4th edition, document development committee, my goal, as I expressed it to the committee at our first meeting, was to keep the content that was still applicable and relevant to the modern laboratory, modify or enhance content where necessary to bring it in line with current laboratory thinking and practice, and add content related to those laboratory and health care issues that have risen in importance since the publication of the 3rd edition of the document in 2006. The result of the committee's work has produced a 4th edition that is approximately twice the size of the 3rd edition. This overview will briefly highlight some of the changes and additions included in the 4th edition.

The publication in 2011 of CLSI EP23, *Laboratory Quality Control Based on Risk Management*, marked a change in perspective regarding the purpose and goals of laboratory QC (*2*). Many of the changes in the 4th edition of the C24 document were initiated to align it more closely with the concepts and principles espoused in EP23. The EP23 document describes a risk management approach to laboratory QC that seeks to identify all possible failure modes in the laboratory, rank the identified failure modes in terms of their risk, and then establish policies and procedures to prevent or reduce the risks to acceptable levels. Risk is defined as the combination of the probability of occurrence of patient harm and the severity of the harm.

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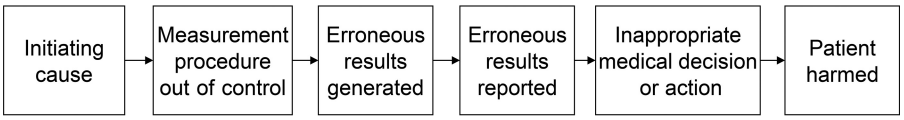

Fig. 1. A model of the sequence of events leading to patient harm caused by an erroneous reported patient result due to an out-of-control condition in a measurement procedure.

This approach places the focus of laboratory QC squarely on the patient. The purpose of laboratory QC is to mitigate patient risk. The goal of laboratory QC is to devise and implement a QC plan that mitigates patient risk to an acceptable level.

Figure 1 is similar to a figure that appears in the CLSI EP23 document that displays a sequence of events that starts with the occurrence of an out-of-control condition in a measurement procedure and ends in patient harm. The figure provides a model that can be used to relate how a laboratory's QC practices affect the risk of patient harm. First, there is the chance that an out-of-control condition occurs in a laboratory's measurement procedure. An out-of-control condition will increase the likelihood that erroneous patient results are generated. An erroneous patient result is defined as a result with measurement error that exceeds the allowable total error requirement for the analyte, as specified by the laboratory or some other body. If erroneous patient results are reported, this creates a hazardous situation for the patient. Finally, how the analyte is used in the patient care decision-making process will influence whether or not the erroneous result leads to inappropriate actions causing patient harm. Statistical QC has its impact on this sequence of events beginning with the occurrence of an out-of-control condition and ending with the reporting of erroneous patient results.

Some notable changes and additions to the 4th edition of the C24 document include the following:

- Introduction of additional QC performance metrics that more directly relate to patient risk.
- Expanded guidance on setting QC target values (means) and measurement procedure SDs.
- A greater focus on the frequency of QC events and the relation to patient risk.
- More emphasis on recovering from an out-of-control condition including approaches to identifying and correcting reported erroneous patient results.

The classic QC performance metrics used to evaluate statistical QC are the probability that a QC rule will reject when an out-of-control condition exists (usually referred to as the probability of error detection) and the probability that a QC rule will reject when the measurement procedure is in control (the probability of false rejection). These are useful measures for evaluating and comparing the ability of QC rules to detect out-of-control conditions when the QC rules are evaluated, but they neither provide information about the potential consequences of the frequency of QC events, nor do they provide a direct assessment of the QC rule's ability to limit the number of erroneous patient results reported during an out-of-control condition. The 4th edition of the C24 document adds discussion of QC performance metrics related to the following:

- The expected number of patient results affected by an out-of-control condition before it is detected.
- The expected number of affected patient results containing measurement errors that

exceed their quality requirements (erroneous results).

- The expected number of erroneous patient results that are reported and create hazardous situations for patients.

These performance measures can be computed using mathematical or simulation approaches similar to those used to compute a QC rule's probability of error detection.

While choosing among alternative QC rules can affect the probability of detecting an out-of-control condition when the QC rule is evaluated, choices about how frequently QC events occur have much more potential influence on the number of erroneous patient results that are reported due to an out-of-control condition. Only recently has more attention been paid to providing guidance on the appropriate frequency of QC evaluations to manage patient risk. As discussed in the 4th edition of C24, a laboratory's decisions regarding the frequency of QC testing should consider the following:

- The reliability of the measurement procedure, i.e., the rate of occurrence of out-of-control conditions.
- The analytical imprecision and bias of the in-control measurement procedure relative to quality goals.
- The rate of patient testing, i.e., the number of patient results expected between QC events.
- The power of the laboratory's QC procedures to detect out-of-control conditions.
- The expected time between reporting of a patient result and when it will be acted on.
- The potential severity of harm if an erroneous patient result is acted on inappropriately.

Traditionally, the study of QC has mainly focused on the ability of various QC strategies to detect out-of-control conditions as quickly as possible. Much less attention has been paid to strategies for effectively recovering from an out-of-control condition once it has been detected. Recovery includes both actions taken to troubleshoot and resolve the detected out-of-control condition, as well as actions taken to identify and correct any reported erroneous patient results. While there is not as much peer-reviewed literature studying the merits of different strategies for recovering from an out-of-control condition, the 4th edition of C24 has significantly expanded the coverage of this topic and provides useful ideas and approaches for responding to an out-of-control QC event, troubleshooting an out-of-control condition, and retesting affected patient specimens.

As its title implies, the C24 document covers principles and definitions related to statistical QC for quantitative measurement procedures. As such, and consistent with previous guideline editions, C24 does not recommend a specific QC strategy for any individual device or technology. Likewise, while a number of the QC performance metrics discussed in the document require computer software to compute, the guideline neither makes recommendations nor gives examples of the use of any specific software.

The objective of the latest edition of the C24 guideline was to provide a helpful roadmap for designing, assessing, and implementing a statistical QC strategy that is consistent with the patient risk concepts introduced in CLSI EP23. We believe that this edition of C24 achieved this objective and provides an important complement to risk management principles and activities.

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2. CLSI. Laboratory Quality Control Based on Risk Management; Approved Guideline. CLSI guideline EP23-A™. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.