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COMMENTARY

Individualized Quality Control Plan (IQCP): Is It Value-Added for Clinical Microbiology?

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The Center for Medicaid and Medicare Services (CMS) recently published their Individualized Quality Control Plan (IQCP [https://www.cms.gov/regulations-and-guidance/legislation/CLIA/Individualized_Quality_Control_Plan_IQCP.html]), which will be the only option for quality control (QC) starting in January 2016 if laboratories choose not to perform Clinical Laboratory Improvement Act (CLIA) [U.S. Statutes at Large 81(1967):533] default QC. Laboratories will no longer be able to use "equivalent QC" (EQC) or the Clinical and Laboratory Standards Institute (CLSI) standards alone for quality control of their microbiology systems. The implementation of IQCP in clinical microbiology laboratories will most certainly be an added burden, the benefits of which are currently unknown.

In 1967, the Clinical Laboratory Improvement Act (CLIA '67) (1) set guidelines regulating laboratories that performed Medicare billing and/or engaged in interstate commerce. Prior to that time, there were few regulations for laboratories. Generally, CLIA '67 affected large hospital and independent laboratories, while physician office laboratories and small laboratories were essentially left unregulated. CLIA '67 required these large laboratories to adhere to quality control (QC), proficiency testing (PT), test performance, and personnel standards.

Partially in response to public furor over deaths attributed to false-negative Pap smear readings, Congress passed the Clinical Laboratory Improvement Act of 1988. CLIA '88 (2) set forth new regulations for personnel standards, specimen management, QC, PT, and quality assurance (QA) for all entities performing laboratory testing and mandated that testing must follow manufacturers' recommendations. After the implementation of CLIA '88, the Centers for Disease Control and Prevention (CDC) and The Centers for Medicare and Medicaid Services (CMS) had several meetings in order to identify improved and more efficient ways to perform QC, but these meetings reportedly met with limited success.

CMS published their Quality Systems Regulations in 2003, which updated all QC requirements. At that time, instead of changing the regulations to address new, emerging technology, CMS decided to introduce "equivalent QC testing" (EQC). EQC primarily refers to those test systems that utilize internal controls. CLIA '88 had already established what is referred to as "default QC" testing, which involves the inclusion of 2 levels of external controls on each day of testing (both a positive and a negative control for qualitative tests and 2 levels of positive controls for quantitative tests). EQC, as an alternative to CLIA default QC, gave laboratories the option of using both external and internal controls in their total QC testing process. EQC was designed to minimize the frequency of external QC that was required to control laboratory test systems, help reduce costs and resources for laboratories, and acknowledge technological advances. Clinical microbiology laboratories recognized EQC as an effective program and adopted EQC successfully. However, there were concerns expressed by some in industry and in laboratories, as well as by other experts, about the rigidity and the limit of scope with EQC. In 2005, CMS reached out to the Clinical and Laboratory Standards Institute (CLSI) to facilitate the development of a scientific, objective consensus guideline. A meeting called "QC for the Future" was held and attended by representatives from accrediting organizations, industry, professional organizations, and governmental agencies. Stakeholders expressed concerns at this meeting that manufacturers did not provide laboratories with sufficient information regarding QC and that a one-size-fits-all requirement for QC would not work with all new technologies. Due to this concern, CMS asked the CLSI to develop a QC evaluation protocol that led to the 2011 publication of CLSI document EP23, *Laboratory Quality Control Based on Risk Management* (3). This document uses a risk assessment approach to the management of policies, procedures, and practices for the tasks of analyzing, evaluating, controlling, and monitoring risk. It defines QC as the set of operations, processes, and procedures designed to monitor the measuring system to ensure the results are reliable for the intended clinical use. CLSI document EP23 also describes good laboratory practice for developing and maintaining a quality control program for medical laboratory testing using recognized risk management principles. CMS incorporated the key concepts of CLSI document EP23 into the CLIA interpretive guidelines (IG), and in 2014, CMS announced that laboratories could either comply with CLIA default QC or develop what they were calling an Individualized Quality Control Plan (IQCP [https://www.cms.gov/regulations-and-guidance/legislation/CLIA/Individualized_Quality_Control_Plan_IQCP.html]). These two options would

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apply to all nonwaived tests and would become effective on 1 January 2016.

In October 2014, a memo notifying laboratories that references to CLSI documents would be removed from the CMS IG was issued (4). The revised CMS IG released in May 2015 contain no references to CLSI. CMS stated that this action had nothing to do with the implementation of IQCP but was due to the fact that the CLSI documents must be purchased and are not freely available to the public.

CMS describes IQCP as "voluntary"; however, EQC and CLSI standards alone will soon no longer be an option for the clinical laboratory. As of 1 January 2016, laboratories will only be able to choose to use default CLIA QC (2 levels of controls each day of patient testing) or develop their own IQCP. For clinical microbiology, this does not seem very "voluntary"; for example, performing daily QC for antimicrobial susceptibility testing (AST) or a self-contained multiplex molecular assay is not feasible or reasonable.

Developing an IQCP involves a review of the entire testing process, beginning with specimen collection (preanalytic) and continuing through the analysis of the specimen (analytic) until the final test result is reported (postanalytic). There are three components to an IQCP: risk assessment (RA), quality control plan, and quality assessment, and there are five components that must be evaluated in the RA (specimen, test system, reagents, environment, and testing personnel) as part of the IQCP for each test system. In addition, laboratories may identify additional risk factors to consider and are not limited to these five components. One other facet of the RA is to note both the frequency of occurrence and impact of possible laboratory errors. The frequency of errors can be determined by reviewing historical data; however, the accurate determination of patient harm resulting from these errors is highly variable and a nearly impossible task. For example, reporting a falsely susceptible antibiotic result could lead to a devastating outcome in a patient with a severe infection being treated with that drug; however, if this error occurred with an antibiotic that would not be considered for this patient due to the likelihood that alternative agents would be more effective, the impact of this testing error would be minimal to none.

CMS states that IQCP is a new, flexible QC option that provides the opportunity to tailor QC to your unique testing environment and patients and will establish the appropriate quality practices which will reduce the likelihood of errors occurring in your laboratory. In addition, CMS mandates that the data referenced in the IQCP must support the rationale for the number, type, and frequency of QC testing performed, yet it also indicates that QC for a commercial test cannot be less than that recommended by the manufacturer. For laboratories accredited by the College of American Pathologists (CAP), it should be noted that the most recent version of the CAP checklist will require testing of an external control every 31 days (5). Thus, regardless of how rigorous your IQCP, CMS and CAP will not allow you to use your own data to truly "individualize" your IQCP.

On 2 September 2015, ASM's Committee on Laboratory Practices wrote a letter to Andrew Slavitt, Acting Administrator for CMS, stating that we as clinical scientists rely on published literature, statistically derived data, and evidence-based medicine to guide our practice (http://www.asm.org/index.php/whatsnew-policy/137-policy/documents/statements-and-testimony/93728-iqcp-cms). The letter requested data from CMS to support the notion that applying IQCP to clinical microbiology tests would improve patient outcomes. These data are critical to help clinical microbiologists understand the value in IQCP and to further motivate us to allocate resources to this time-consuming effort. If there are no data or evidence that IQCP helps to effect positive patient outcomes, requiring clinical microbiology laboratories to implement IQCP or return to CLIA default QC in lieu of EQC and CLSI guidance was not supported by the ASM Committee on Laboratory Practices.

Although CMS's IQCP program has been developed to address quality issues for new technology and offers a less rigid method for QC practices than EQC, considering the unique aspects of clinical microbiology ("exempt" media, microorganism identification, and susceptibility testing, etc.), IQCP will not necessarily improve or enhance the quality of testing or patient outcomes. However, through the efforts of CLSI, CAP, and the American Society for Microbiology (ASM), several data-supported standards and guidelines have been developed that address QC of tests and test systems. Several decades ago, it was recognized that testing of QC strains by the user for commercially prepared media demonstrated few QC failures and imposed a substantial financial burden on microbiology laboratories. Subsequently, CAP conducted three surveys among clinical microbiology laboratories (1984, 1988, and 2001) to determine the failure rates of commercially prepared media. CLSI document M22-A3 on QC for commercially prepared microbiological culture media includes data from these three CAP surveys (6, 12). These data demonstrated that retesting of many types of commercially prepared microbiological culture media with QC strains in-house will not improve the quality of patient results. The most recent survey, in 2001, evaluated over 260,000 lots of over 32 million pieces of media. These surveys used an extrapolated failure rate of $\leq$0.5% in order to consider media exempt from retesting by the user; any media that had failure rates above this were considered nonexempt and must undergo CLIA default QC testing. The power in these numbers is obvious, and there is ample evidence to categorize media as being exempt or nonexempt. Following the CLSI M22-A3 standard for commercial media, which is evidenced based, should be sufficient without the need for the development of an IQCP.

In addition, CLSI standards M07-A10 (*Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*; approved standard, 10th edition) (7), M02-A12 (*Performance Standards for Antimicrobial Disk Susceptibility Tests*; approved standard, 12th edition) (8), and M100-S25 (*Performance Standards for Antimicrobial Susceptibility Testing*; 25th informational supplement) (9) for *in vitro* susceptibility testing allow for less frequent QC than does CLIA default QC. The QC recommendations in the CLSI standards are supported by data demonstrating that following CLIA default QC (daily testing of QC strains) will not improve the quality of patient results for laboratories that have documented satisfactory performance with a specified amount of daily QC testing. For these laboratories, testing each new lot/shipment of materials before or concurrent with first use followed by weekly QC testing is sufficient. "System" errors would likely be identified with initial QC testing of a lot/shipment. "Random" errors can occur 5% of the time (95% confidence limits) and may be observed with daily or weekly QC testing. A discussion of the statistical considerations that support the CLSI recommendations for frequency of QC testing is available (10). Again, following the CLSI statistically based standard for antimicrobial susceptibility QC testing should be sufficient, and it is unclear how

the development of an IQCP will improve the quality of reporting patients' results.

Likewise, for commercial microbial identification systems (MIS) that use two or more substrates, CLIA '88 requires QC testing with positive and negative reactivity controls for each substrate with each batch, lot number, and shipment of reagents. Due to the refinement and advancement of MIS, this requirement has become difficult and costly for clinical microbiology laboratories and has not been shown to prevent errors when testing patients' isolates. MIS have proven reliability based on peer-reviewed scientific publications and are manufactured by companies that must meet quality standards and applicable regulations. In 2005, at the suggestion of the Clinical Laboratory Improvement Advisory Committee (CLIAC), ASM conducted a survey of clinical microbiology laboratories to determine the QC failure rates of MIS in a random selection of laboratories. Nearly 300 laboratories provided data for nearly 10,000 lots of MIS. These data showed that the failure rate due to the MIS itself was less than 0.1%. ASM recommended that these data be used by CLSI for the development of a QC testing guideline for MIS. CLSI convened a subcommittee composed of laboratorians, manufacturers, and government representatives (CDC, CMS, and the Food and Drug Administration) to determine if and when a streamlined approach to MIS QC could be developed. The result was CLSI document M50-A, *Quality Control for Commercial Microbial Identification Systems* (11), which provides practical guidelines for laboratories to ensure the quality of their microbial identification results when using commercial MIS. Following the CLSI evidence-based guideline for QC of MIS should be sufficient without the need for the development of an IQCP.

As stated in the ASM letter to CMS, the reason why CMS removed references to the CLSI documents for antimicrobial susceptibility testing (CLSI documents M100, M02, and M07), streamlined QC of identification tests (CLSI document M50), and QC of media (CLSI document M22) is understood. However, it is unlikely that the development of an IQCP for these tests will discover that additional QC will lead to improved patient care. For decades, the QC recommendations in the CLSI documents have effectively identified problems in clinical microbiology testing systems for which they are designed. The need to justify the reliability of these CLSI QC recommendations now seems little more than an exercise. It should be noted that these guidelines, along with the tenets of EQC, can still be used by clinical microbiology laboratories as a component of an IQCP. Most clinical microbiology laboratories in the United States have access to CLSI documents, and the continuation of their use should be a stand-alone option for microbiology laboratories. Following CLIA default QC or the development of an IQCP could be an alternative for laboratories that elect not to follow the recommendations of the CLSI. Laboratories must allocate resources to educational materials/activities, and it should be their choice as to whether to procure CLSI documents and/or pursue IQCP for their testing systems.

Errors in laboratory medicine can certainly have significant effects on patient care, and we in the clinical microbiology community clearly support quality improvement measures which have the potential to positively impact patient outcomes. We also understand that there are common errors in microbiology that need to be managed; however, it is difficult to see how the implementation of IQCP and the elimination of both EQC and the use of recommendations in CLSI standards and guidelines will have a positive effect for our patients. Again, as stated in the ASM letter to CMS, there are many tests in clinical microbiology where additional QC testing does nothing to prevent reporting erroneous results on patient's isolates or samples. For example, daily QC testing with antimicrobial susceptibility tests will not prevent a laboratory from reporting results from a mixed population of organisms. Similarly, testing commercially prepared exempt media with QC strains will not prevent a technologist from choosing a poor quality portion of a sputum sample for plating onto a blood agar plate. Likewise, daily external QC of self-contained molecular test systems that have internal controls also does not mitigate the risk of cartridge-specific errors or inadequate specimen collection. It would be more prudent for CMS to focus on measures that might be of greater benefit to patients and clinical microbiology than generating an IQCP. In fact, developing an IQCP for these and perhaps other clinical microbiology tests might give laboratories a false sense of security that other "quality" measures are unnecessary. Surveying clinical microbiology laboratories for their most common errors/failures that lead to erroneous laboratory results, working to find ways to better understand the reasons for these failures, and then making recommendations for possible pathways toward improvement would perhaps be a better approach. To this end, our clinical microbiology community is more than willing to have its members assist CMS in this endeavor. Undoubtedly, our goals are common and we all wish to optimize the use of our resources and talents to best serve our patients.

All five of the CLSI documents mentioned here are available and used by most clinical microbiology laboratories in the United States; they are data driven, evidence based, and have proven efficacy. Likewise, the use of EQC for the past decade for our diagnostic microbiology test systems has proven reliable. IQCP will soon be the law of the land for clinical microbiology laboratories; time will tell if it improves our ability to decrease adverse patient outcomes.

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