Quality: the next six months

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The eclectic mix of participants in the forum had a surprisingly singular focus when it came to the topic of quality in clinical laboratories. All sensed that the time is right for a transition from laws, rules, and inspections to a true quality-based system. Such a system can achieve the goals, implicit and explicit, that are the rationale for the multiplicity of regulations affecting today’s laboratories. A true quality-based system has great potential benefits to laboratories, regulators, and manufacturers, and ultimately to our true customers, the patients. The benefits include lower costs, superior products, and better test results; in short, better patient care. This transition will be possible only through formation of a “Quality Alliance,” composed of those skilled in the “theory” of quality—laboratory personnel, manufacturers, and regulators, acting as one to implement the quality system. The Quality Alliance requires a team of individuals with different skills, aligned as one, for the purpose of achieving a common goal. On the basis of views expressed in this Forum, our collective future will be defined by the evolving Quality Alliance, an alliance focused on true quality systems in clinical laboratories.

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This Clinical Chemistry Forum, “Quality for Tomorrow,” addressed both the long- and short-term aspects of laboratory quality. Quality in this context is a noun, a concept and a philosophy, and not an adjective. Our challenge was to concentrate on the changing laboratory environment and how quality, in the fundamental sense, will affect clinical laboratory testing in the short term—the next 6 months. This focus can be summarized in the themes of two Forum presenters: (a) “a quality laboratory system (test or method) is characterized by the fundamental quality designed into the product and into the production processes” and (b) “manufacturers seek to produce quality products because ultimately they are easier to support in the field and are more profitable.” From these two perspectives came the Forum’s conclusion that, as the laboratory’s diagnostic products evolve into true quality-based systems, the regulatory burden of the laboratories, the manufacturers, and the regulators will be minimized.

The prevailing theme of the conference participants is that an uneasy partnership is forming between regulators, manufacturers, and clinical laboratories. Our term for this is the “Quality Alliance,” which is forming because the time and circumstances are right. Several of the Forum’s presenters seemed to suggest that in the long term, today’s entire regulation-oriented clinical laboratory system may be replaced by a true, quality-driven process. The 1996 Clinical Chemistry Forum may be a catalyst in the process.

We can restate the premises on which the Quality Alliance is based: (a) quality can be designed into the laboratory operation, into diagnostic products, and into the protocols for their use, (b) quality can be built into manufacturers’ production processes, and (c) the inherent quality of the products can be the primary factor in meeting regulatory goals. In the short term, these regulatory goals are only loosely associated with patient/physician needs; in the future, they will be derived from explicit knowledge—i.e., quality requirements. In a Quality Alliance-driven environment, regulators will recognize the built-in, quality-driven features of testing devices included to achieve and document regulatory goals. Laboratories will function without abject adherence to antiquated, irrelevant, or misapplied “rules” or protocols. Deming understood this principle, in effect recognizing what we have termed the Quality Alliance throughout his writings. For example, he demanded that all participants look for the “win–win” in every situation and realize that in a true quality-driven system there can be no losers, only winners [1]. True quality makes winners of manufacturers, regulators, laboratories, and the ultimate customer, the patient.

This concept of a quality system and the Quality Alliance behind it can be illustrated by the practical example of an in vitro diagnostic testing device. The entire analytical system, beginning with product design,
through the manufacturing process (including the in-process testing) and the protocols for end use, can be optimized to meet regulatory requirements or, better yet, the quality goals behind them. If quality is built into each step, the possibility of an erroneous test result becomes virtually zero. This is not an impossible dream; in fact, it is quite feasible. Consider the three-stage life cycle of a product:

At the product design stage, a system is created that either performs perfectly or clearly fails. Such systems incorporate a clear quality indicator. When the system fails, the preferable indicator is “no result” produced. Some of today’s diagnostic products, qualitative and quantitative tests with built-in process controls, are beginning to incorporate this concept. While they represent substantial progress toward a quality system, we still are at the elementary stage of development. In the future, there would be no reason why both qualitative and quantitative test devices could not include the appropriate measurements and numbers of in-process controls to ensure true, analytical quality. Once quality control becomes an integral part of the process design, the data/information can be evaluated automatically, and a degree of confidence, based on a quality requirement, can be assigned to the test result before reporting it or making a decision to suppress the result.

At the manufacturing stage, a process is created that ensures error-free testing devices, in the sense that they are fully functional or, on the basis of a quality specification, that the test results are completely suppressed as discussed above. The ability to integrate internal process controls, i.e., function checks, and meaningful quality control makes this a viable possibility. While Deming suggests that “inspecting quality into the product at the end of the production line is a poor strategy,” appropriate in-process product testing throughout manufacturing is critical to creating the future clinical laboratory test systems [2]. When the manufacturing process for products achieves a status where its “error” contribution is truly negligible, the manufacturer’s role in the Quality Alliance will be to document that product is error-free, i.e., performs to “6 Sigma” specifications. To date, manufacturers, understandably, have not been forthcoming with data on their product defect rates, which are the components of error attributable to the various stages in the manufacturing process. However, if the needs of the ultimate customers (patients), intermediate customers (analysts), and the regulators are to be met, this information is an essential step in building a total quality-based clinical laboratory test system. The in-use quality-control algorithms, i.e., sampling plans, must be based on the measured defect rate. In this situation, options including one control per week and acceptance testing of an entire shipment will replace the presently required two controls per day. This is equivalent to eliminating the final “inspection at the end of the line,” a quality-control process not necessary in a true quality system. These data, or the absence of defect rates, appropriately used by all Quality Alliance partners, are critical to the process.

Finally, at the regulatory stage, only a true Quality Alliance will be able to foster a profound, quality transformation. The regulators will be challenged to show that their standards are both consistent with the regulatory intent of the CLIA amendments of 1988 (CLIA’88), the Food Drug and Cosmetic Act, good manufacturing practices, and good laboratory practices and are true quality-based criteria. This profound knowledge is based on three critical factors—the existence of a database capable of defining a quality standard for clinical practice, the assumption that one can translate this information into a quality standard for the whole system (manufacturing and laboratory use), and that true quality performance can be monitored. To date, this has not been accomplished. CLIA’88 sets no true quality standards within its requirements—except proficiency testing [3]. Instead, CLIA’88 relies, appropriately, on the judgment of laboratory directors to define acceptable quality-control performance. The CLIA’88 rules do require, as a minimum specification, the analysis of two controls per test per day. They do not address the question of whether two controls are adequate to meet or far exceed the regulatory intent (to ensure quality).

The regulators’ emphasis must change from one of enforcing minimal regulations, which supposedly ensure quality, to assessing whether the testing process, considering all its components, adequately meets defined quality goals. In short, a change of focus, from “how we got here” to “where we are,” and ultimately, to “where we want to be” must occur. The regulators are focused on a very important, but very elementary step in the quality process. They cannot be expected to certify even rudimentary compliance without creating criteria (i.e., two controls per test per day) and inspecting for actual data. The future quality system will be data-driven, but it will not consist solely of quality-control data from the laboratories. Instead, much of it will be created by the manufacturers from in-process product testing, and will be supplemented by external (laboratory) controls. In many of today’s unit-test systems, controls will become integral to the actual patient testing process [4-6].

The concept of a Quality Alliance does not ignore the laboratory or testing stage. In the Deming sense, the laboratory (analyst), clinician, and patient are all customers of the Quality Alliance. Speaking as laboratorians, we must remind our colleagues, if they haven’t noticed, that analysts are becoming spectators in the testing process. Whether through use of the large “slide- or pack-

1 Nonstandard abbreviations: CLIA’88, Clinical Laboratory Improvement Amendments of 1988; HCFA, Health Care Financing Administration; FDA, Food and Drug Administration; CAP, College of American Pathologists; JCAHO, Joint Commission on Accreditation of Healthcare Organizations; COLA, Commission of Office Laboratory Accreditation; AQA, Alternate Quality Assurance Survey.
states, i.e., those with “deemed” status from HCFA and Office Laboratory Accreditation (COLA)—and some care Organizations (JCAHO), and the Commission of professional societies—College of American Pathologists enforce the requirements.” The latter group includes regulations and policy, as well as those “subcontracted to Food and Drug Administration (FDA), to make regula-
ing include those empowered by federal law, the Health Care Financing Administration (HCFA), the CDC, and the Commission of Laboratory (JCAHO), and the Commission of Alliance. This means explicitly linking our professional goals to truly meeting patient needs. In this area, we may be the “indispensable ingredient.”

The Regulatory Picture

In the present environment, regulators of laboratory testing include those empowered by federal law, the Health Care Financing Administration (HCFA), the CDC, and the Food and Drug Administration (FDA), to make regulations and policy, as well as those “subcontracted to enforce the requirements.” The latter group includes professional societies—College of American Pathologists (CAP), the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), and the Commission of Office Laboratory Accreditation (COLA)—and some states, i.e., those with “deemed” status from HCFA and the proficiency testing providers [7-9]. The forum has been remarkable in that the “empowered” federal regulators have indicated strongly that future CLIA’88 policies will reflect, as HCFA has stated, a “kinder and gentler” approach. The federal regulators have even suggested that the original intent of CLIA’88 was to be not a heavy-handed regulatory device but a process to weed out a few bad laboratories while protecting the interests of the vast majority of good laboratories. This assertion is supported by factual data. After 4 years of CLIA’88 enforcement, only a few laboratories have been shut down because of failed inspections. Many laboratories, after several inspection cycles, have demonstrated “zero defects.” The inspection experience has led HCFA to propose and implement the Alternate Quality Assurance Survey (AQAS), which permits selected laboratories with no deficiencies on the previous inspection to self-inspect on the basis of quality-assurance principles [10]. The AQAS can be recognized by Quality Alliance members as significant progress toward a true, quality system. At present, the AQAS process has begun its initial cycle. On the basis of a few observations, a truly quality-assurance-based self-inspection requires more effort than an on-site visit from an inspector.

In the short term, we must consider pressing quality problems. The issue of emerging technologies is not adequately addressed by the current regulations. Inspectors and those organizations with deemed status have complained that they were required to contract with HCFA to enforce the provisions of CLIA’88, which include unequivocal mandates such as “two controls per test per day.” HCFA does not have a mechanism outside of the complex and arduous rule-making procedure to change the regulatory requirements nor does it have the means to “excuse” adherence to the existing regulations. This is a quality-inhibiting bottleneck. The flurry of activity from October 1995 through March 1996 on the use of “electronic controls” is the quintessential example of this problem [11]. A series of HCFA “interpretations” indicated they were not acceptable, they were acceptable, they were under some circumstances acceptable, and finally that the original interpretation was correct but the issue was under review. regulator’s interpretations of existing rules seem to be a poor means of modifying or adapting regulatory protocols. On the electronic control issue, we are back where we started with no clear future direction from federal regulators. In the near future, HCFA has promised yet another revision of the CLIA’88 regulations, but this too is unlikely to be the long-anticipated “final” rule.

The above is not an ineffective Quality Alliance nor a problem with the federal regulators. The problem is the process. In many ways, today’s participants in the Quality Alliance, manufacturers, laboratories, professional organizations, and even states, have forced one partner, the regulators, to continue using an antiquated, cumbersome, and very slow moving rule-making process to promulgate or change regulations [12]. The process resulted from mistrust on all sides. It did not emanate from a quality process in which all stakeholders focused first on a common vision. To achieve the benefits of a true Quality Alliance, we must recognize, first, that there are no second-class partners. Only then can a fundamental transition to a true quality-driven regulatory process occur.

Unit-Use (Single-Test) Devices

Soon, changing concepts of quality will focus on unit-use or single-test devices. These devices are used in both the laboratory and point-of-care setting and may take the form of a disposable “kit” of materials, a cartridge, or a cassette designed to analyze a single sample. These devices usually contain an internal, integral quality-control system that may include both “electronic checks” and actual control materials that interact with the analytical process. The electronic checks may assess the performance of the electronic circuits of the instrument or they may include more-comprehensive function checks that evaluate the system’s temperature, sample flow, electronic stability, and sensor response and guard against such analyst mistakes as low sample volume. The built-in quality-control systems range in complexity from the simple “positive/negative,” i.e., “test worked/test failed,” to sophisticated, quantitative measurements providing numerical responses to the analyte concentrations in the control. Many devices automatically record these data, produce quality-control charts, calculate statistics, and apply sophisticated quality-control algorithms to the data.

For every member of the Quality Alliance, these unit-
use devices add a new dimension to the discussion of quality and quality-control procedures in tomorrow’s laboratories. The devices represent a unique opportunity, even at this somewhat primitive stage of development, to create a breakthrough in providing quality test results to patients and meeting regulatory mandates. The regulators (HCFA, CDC, and FDA), as well as those inspecting laboratories and enforcing the CLIA’88 regulations (CAP, JCAHO, COLA, states), have expressed an interest in maximizing the quality control/quality assurance potential built into unit-use devices.

The issues of cost, efficiency, and applicability within the laboratory are relevant to any discussion of quality control and quality assurance strategies for unit-use devices. However, the major rationale for creating alternative strategies is that the unit is destroyed in the testing process. While traditional analysis of external, liquid controls (in the context of CLIA’88 regulations, “two controls per test per day”) furnishes information on the specific unit-use device, it does not, theoretically, provide data on the next unit or the entire lot. For these types of products, the alliance partner owning the manufacturing process must design total quality-control systems to qualify the entire lot. Some inspectors are beginning to recognize variations of this approach.

Reconsider the sequential logic behind the Quality Alliance: (a) design the product to incorporate the necessary, relevant elements of quality assurance, (b) control the manufacturing processes to ensure low or zero-defect rates, (c) establish, through manufacturing process control, the product’s integrity, i.e., conformance to specifications, and (d) integrate on-board controls that truly provide fail-safe indicators of performance. “Fail-safe,” in this case, means that the unit-use device either works correctly or fails completely. Some devices are moving toward this concept. They measure analytes as sophisticated as troponin, blood gases, and other potentially critical substances such as electrolytes and glucose in the self-contained, unit-test format.

Although these important first steps are themselves milestones, in the authors’ view the level of quality assurance envisioned in the context of the Quality Alliance is not yet present in most of today’s unit-use devices. Regulators, particularly JCAHO and COLA, and more recently CAP, have accepted alternative quality-assurance approaches for the unit-use devices; others are reevaluating their own alternative requirements. We are confident that within the next 6 months, there will be a movement by all inspectors to accept alternatives on the basis of built-in quality-control systems of the devices. However, before the Quality Alliance can propose and fully implement new, theoretically sound approaches to quality assurance, their efforts must emanate from manufacturers’ product defect rate information. Laboratories and regulators cannot do this alone nor can manufacturers. The key is to “begin at the beginning.” This means beginning with outcome-based quality standards and integrating the interests of all the stakeholders.

Optimistically, in the next 6 months, we may see new (actually modified) CLIA’88 regulations. It will be interesting to observe how many of these ideas related to unit-use alternative quality-control/quality-assurance practices are included. Concurrently, we suggest that there also will be an increased emphasis on the part of inspectors to interpret the existing regulations in the context of “a particular laboratory situation,” a change that will permit reliance on the unit-use device’s built-in quality-control systems. What is unlikely is final implementation of CLIA’88’s “September 1, 1994, rule,” first extended to September 1, 1996, and now postponed indefinitely, allowing manufacturers to petition FDA for acceptance of their customized quality-control/quality-assurance practices [13]. This is unfortunate because the NCCLS-sponsored 1990 CLIA Congress, which provided a forum for comment on HCFA’s initial, proposed CLIA’88 regulations, specifically sought to ensure that regulations did not impede incorporation of new ideas, technologies, and quality-control approaches.

The concept of a Quality Alliance will, of necessity, reengineer the entire regulatory process. We recognize HCFA for its recent efforts to find a reasonable accommodation on the electronic control issue. The situation warranted action, and HCFA attempted to do the right thing. The lack of resolution demonstrates the need to rethink quality-control/quality-assurance approaches, the need to utilize new kinds of information from manufacturers, specifically product defect rates, and the need for a new streamlined process for modifying the regulations. The present formal, rule-making process is not the answer and proves that Deming had it right—one partner in any Quality Alliance cannot do it alone. Quality must always begin by seeking a win–win solution for everyone. Design of a true, quality-based system, involving all of the participants as true partners, is the only solution.

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