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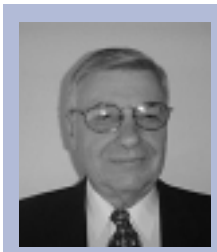
Where's the Baby and Who Threw Out the Bathwater?

Over a number of years, the resources allocated by the FDA to infrastructure development and maintenance have declined, while the performance time pressures have escalated. The most striking example of these phenomena was the 1977 jettisoning of the executive secretariat function of the Association of Official Analytical Chemists (now AOAC International) from the bosom of the FDA. That AOAC secretariat function had been part of the FDA and its predecessor organizations back to the time of Harvey Wiley.[1] Since its founding by state chemists in 1884, its mission has been to develop regulatory analytical methods, establish uncertainty assessments, and provide a broad-based public peer-reviewed credentialing process for regulatory methods. Over the years, the AOAC has added other services to support quality analysis (see www.aoac.org). The critical role of the AOAC in the FDA, apart from the method development aspects, was the training and the peer-reviewed credentialing of the laboratory staff through the analytical method collaborative study process. (It should be noted that the Method Committee Members were not only from FDA but also from the USDA, U.S. EPA, and the corresponding Canadian regulatory agencies.) When the secretariat was in the FDA, all FDA laboratory staff members were automatically members of AOAC. The annual meeting was dominated by the FDA and other U.S. and Canadian governmental regulatory analysts presenting their method developments along with statistical assessments of uncertainty. Virtually all FDA analysts at that time—chemists, microbiologists, entomologists, etc.—participated in these processes. In order to advance professionally in the laboratory, it was almost mandatory to have at least one method developed and credentialed through the processes. To advance to a supervisory position, it was a virtual requirement to have served as a General Referee or scientific mentor to a number of analysts who were developing and collaboratively studying regulatory methods.

As noted above, the bathwater was thrown out in 1977. Unfortunately, no coordinated effort was initiated at the time to keep the method development and very creditable peer-reviewed credentialing procedures that had for many years provided the foundations for the FDA laboratory quality systems. This type of staff competency development and peer-reviewed credentialing process along with proficiency testing is important not only to our concepts of the cGMP requirements, but also to address ISO accreditation attributes. As the FDA moves to establish a credentialing and accreditation process for its testing and inspection functions, many of these processes will need to be resurrected. Mr. Dennis Baker, former Associate Commissioner for Regulatory Affairs, stated:



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> [M]ission statement of ORA: Achieve effective and efficient compliance of regulated products through high-quality, science-based work that results in maximizing consumer protection. In the area of Field Science . . . develop a lab Quality Management System that conforms to ISO Draft International Standard 17025 "General Requirements for the competence of testing and calibration laboratories." The ISO 17025 will be incorporated as part of ORA's Quality Management System (QMS) . . . internal quality system based on ISO 9000 quality standards, which will become the ORA-wide quality information base for system-wide evaluation and assessment. The QMS will be integrated across all ORA work products and processes: investigative, scientific, and enforcement activities. The QMS will strive to improve dissemination of scientific and management policy and preserve institutional knowledge through a unified document management system and also build a framework for managing other initiatives. Training is one area that is important both to ORA and to the states and local agencies. As a part of our training initiative we are continuing to implement our certification of investigators initiative. We have certified 100 device investigators at Level II and we have begun the process of certifying investigators in blood banks and in seafood products. We will continue to implement these specialties in 2000, and will begin implementing drug and cooperative program certifications in the near future. Our goal is to eventually make these certification programs available to the state and local agencies.
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> (Note: The ISO 17025 standard was adopted essentially unchanged from the draft referred to in this presentation. Presentation given by Mr. Dennis Baker, FDA/Associate Commissioner for Regulatory Affairs, at the AFDO Annual Meeting, published in March 2000, Journal of AFDO.)

Training and certification programs of this type are essential for the FDA to establish consistent, predictable, and well-controlled assessments and evaluation of the regulated industries. In addition, to "make these certification programs available to the state and local agencies" would help harmonize the regulatory environment of the U.S. in those areas in which there are jurisdictional overlaps and accessions. These issues must be adequately addressed for the success of any mutual recognition agreement, whether it be international or in the U.S.

These same concepts are required to build and sustain a quality system that, additionally, should be extended throughout the Agency. However there is no free lunch. It is well known in the industry that a quality system requires a resource outlay on the order of 10–20% of operating resources. It is also known that the lack of a quality system or a predictable delivery system, which is in control, is not a regulatory issue per se, but rather a sustainable business requirement. A well-defined, ordered, and predictable business structure that is in control can better withstand buffeting and changing environments. On the other hand, a poorly defined, poorly ordered, and unpredictable business structure that is out of control does not have resilience and is susceptible to major shakeups, both economically and managerially. In the highly regulated FDA industries, a parallel phenomena enters the good business model; an unpredictable and disordered regulatory agency is an anathema to good business practices regardless of how well their internal quality systems are maintained. All predictable ordered systems are the result of a systematic effort to provide education and training, including competency assessments to ensure that all staff members possess the required knowledge and skills to competently and consistently perform their assigned tasks. This, unfortunately, is not the result of a one-time event, but rather the outcome of an ongoing commitment to keep the organization poised for change in an orderly fashion. Putting the regulated industry and the regulators on the same page, behaving predictably in a controlled fashion, so that conscientious producers of regulated products can effectively compete in a quality marketplace is critical to keeping operating costs at a minimum, while at the same time successfully protecting the public interest.

"IF THE FINANCIAL AND COMMUNICATION INDUSTRIES ESTABLISH BROAD-BASED HARMONIZATION, THE REGULATED INDUSTRY AND REGULATORS ALSO SHOULD BE ABLE TO SIMILARLY ACHIEVE AND RECOGNIZE A COMMON SET OF COMPETENCIES AND PROGRAMS TO ESTABLISH AND ASSESS THEM."

These concepts will be critical not only to the Center for Drug Evaluation and Research (CDER, Rockville, MD), but also to the other Centers as they move forward to strengthen the scientific framework of the Agency. The CDER has announced an effort to establish a stronger scientific risk-based interpretation for the cGMP regulations and their implementation. For the success of such an undertaking, appropriate training programs along with competency assessments and credentialing will be essential. A useful model for developing such a training program was defined recently as a part of the activities of the CDER Process Analytical Technology (PAT) Advisory Committee (see the PAT course description at www.fda.gov/ohrms/dockets/ac/02/slides/3869S1_08_Training%20Course-Morris.doc). In this exercise, the competencies necessary to perform both review and inspections of the PAT implementations were first compiled and then the education program was drafted to establish those competencies. This same development model should be established to bring about a smooth, orderly transition to addressing new technologies and other institutional quality system changes. This type of activity is especially important in the Chemistry, Manufacturing, and Controls (CMC) assessment functions. Striking technology assessment possibilities were identified in the PAT Committee manufacturing discussions, and similarly, there are other rapid CMC assessment technology changes underway, especially in the biotechnology fermentation and pharming processes.

However, as noted previously, there is no free lunch or quality system building. The FDA will need 10–20% of operating resources to establish and maintain a proper quality system that will have the required resilience and flexibility not only to revisit the cGMP implementation, but also to address the myriad of new products and technologies being introduced. In addition to this jump-start training program, an ongoing refresher or sabbatical program will need to be established to keep staff members better informed about the impacts of change in the regulated industry. In the academic environment, sabbatical programs provide an opportunity to refresh and upgrade the intellectual base of the faculty, thereby strengthening and energizing the education process. This sabbatical or every seventh-year intellectual refocus period to allow rejuvenation has its roots stretching back to Biblical days and has been sustained in academia because of its utility. (For a discussion of the ancient sabbatical time period, see www.britannica.com/eb/article?eu=119914&tocid=68351&query=sabbatical. Also see http://sabbaticalhomes.com/, where one can let one's home and rent another to accommodate one's sabbatical leave period at another housing location. Helpful hints on how to plan and deliver this intellectually stimulating event can be found at http://omni.cc.purdue.edu/~alltson/sabbat.html.) The academic refreshment programs, along with standardized examinations and accreditation processes, are attempts to keep the academic quality system for teaching and research in good stead. (For a discussion of academic accreditation by peer review, see www.aaup.org/Issues/ACCRED/index.htm.) The typical sabbatical is one semester at full-pay every seventh year of one-year at half-pay. The sabbatical program quality system directly costs one-fourteenth resource or 7% (one semester every seventh year or one-fourteenth of resource). This amount should also be built into the FDA quality system development program. However, the regulatory sabbatical should not be a happenstance undertaking, but rather be designed to improve specific competencies, as was the PAT training program.

The FDA proclamations on improving the scientific framework of the regulatory environment are laudable, but these proposals can succeed only if Congress and the regulated industry also provide strong support, not only with stakeholder input, but also with the additional 10–20% of resources required to implement and properly sustain the activity. In addition, broad-based stakeholder developed competency and credentialing criteria should be established through a transparent process. The competency assessment and credentialing process should be also broadly based through peer review. As noted above, this is not a one-time event, but rather a consistent institutional commitment to quality performance. As quoted by W.E. Deming, "The commitment to quality must begin with the highest level of institutional management and extend from there to all other levels in the organization."

In the globalization arena, there is a continuing drive to harmonize various dimensions of economies and regulations. As we look at success stories, we find credit/debit cards that will work in credit-charge devices and ATM machines throughout the world. The size of the cards, location of the magnetic strip, magnetic coding standards, numerical imprints, etc., have been magnificently standardized and harmonized. Our computers and telephones issue audible tones to "dial" through the communication systems of the world using tone standards that are universally linked to the numbers 0–9. If the financial and communication industries can establish broad-based harmonization, the regulated industry and regulators also should be able to similarly achieve and recognize a common set of competencies and programs to establish and assess them. Training and quality systems will be essential for this to occur. However, harmonization and mutual recognition agreements should not be the primary driver. The primary driver should be the strengthening of the Agency's regulatory quality systems to help ensure more consistent, predictable performance, not only in inspection, but also in review functions that ultimately will produce a cost savings to the regulated industries and the regulators as well. However, it will not be cheap or happen instantaneously and, unless all parties pull together to make these laudable objectives a reality, they may wither and disappear in the ongoing deluge of demands on the FDA's already stretched resources.

Reference

1. Helfrich K. The great collaboration: The first 100 years of the Association of Official Analytical Chemists. Washington, DC: AOAC, 1984.