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Compliance Notes

Operational Excellence: More Than Just Process Improvement

By embracing efficiency and quality, biopharmaceutical organizations can work better and achieve better work.

Life sciences companies face more pressure than ever to reduce costs and increase efficiency. The pressures are many and relentless: price constraints, global competition, product complexity, and more challenging therapeutic areas. In response, many companies have embarked on operational excellence programs. When these programs are carefully planned and executed, they can significantly improve how companies work by reducing waste, streamlining processes, increasing productivity, and assuring an uninterrupted supply of products to customers. In addition to increased efficiency and cost reduction, there is a third leg to the stool: quality and compliance benefits. With carefully designed, executed, and sustainable operational excellence programs—and with improved quality and compliance targeted as one of the goals from the outset—companies can ensure they reap the full benefits of operational excellence.

Operational excellence programs may be narrowly focused on specific processes and functions or broader in scope to encompass an entire site or multiple sites, with commensurate gains in operating efficiency and cost reduction. The following examples from undisclosed bio/pharmaceutical clients illustrate the potential benefits. One manufacturer, for example, reduced conversion cost by 22%. Another achieved increases between 15% and 40% in throughput efficiency across a variety of products. A program focused on new product introductions reduced time to market by 40%. For another manufacturer, a site-wide program generated $20 million in savings the first year and a 50% reduction in throughput time. For a vaccine maker, a simultaneous two-site initiative saved a total of $50 million across two facilities. Such transformations can yield a multiplicity of operational, organizational, and financial benefits that can be leveraged and sustained into the future. Not the least of these sustainable benefits are improved quality and compliance.

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Ian L. Uydess, PhD is a managing consultant, uydess@tunnellconsulting.com; and **Robert E. Spector** is a principal, Tunnell Consulting Inc., spector@tunnellconsulting.com.

Consider another vaccine manufacturer that faced recurring compliance problems in two key manufacturing operations. To address the problems, the organization undertook an operational excellence initiative focused on reducing human-error-caused deviations and increasing right-first-time performance in batch records. The ultimate goal was not simply to make the processes compliant, but to create sustainable improvement by training all stakeholders, not just a targeted few; increasing collaboration and partnership between operations and quality; and creating a continuing quality assurance (QA) presence on the shop floor. The absence of a QA presence coupled with the perception by shop floor personnel that QA auditors were adversaries who simply policed production were principal underlying causes of the compliance problems faced by the company. Through an extensive coaching and mentoring effort, QA personnel came to see themselves not solely as auditors (which they have to be), but as partners with the operations staff, there to help assure quality and compliance, but also to help address issues and provide guidance to help upskill shop floor personnel in their understanding and performance of cGMP/compliance.

To tackle human-error-caused deviations, the deviation management process was redesigned to bring it into line with current FDA expectations and industry best practices, and to assure that the people closest to the observation of issues were involved in the process. Instead of handing off deviation management to another department, as was done previously, the operations group took over responsibility for managing alerts and deviations in real time on the shop floor while the trail was still warm. Deviations could then be investigated in a matter of hours—not weeks—and closed faster in a scientifically sound and compliant manner. Deviation reports were made the responsibility of a single investigator with specific analytical and investigation reporting skills. The reports were then designed to connect the event and its root cause to the corrective and preventive action (CAPA), helping make recurring deviations rare.

In a parallel effort, batch records were simplified and optimized, as were a number of critical standard operating procedures, which were so difficult to follow that they each generated errors, deviations, and waste. Working together, the quality and operations groups were then able to dramatically improve the rate of right-first-time documentation. The quality function created new roles designed to partner with operations and deliver quality and compliance in real time, in-process, on the shop floor. A quality coordinator was assigned to the area with sole responsibility for compliance. Compliance specialists were created to rotate through the operations area and to spend 80% of their time on the shop floor to provide real-time, in-process batch record documentation review and mentor operations personnel on compliance issues and decision-making when deviations occurred.

MONITORING THE ENVIRONMENT

In addition, the site's environmental monitoring (EM) results showed potential contamination, but because the results were segregated in the tracking system, personnel in the area where the problem occurred were unaware that 42% of deviations were EM-related. Missed EM tests, which were responsible for much of the problem, were then reduced by addressing a key informatics interface and by moving routine testing out of operations and into EM to improve oversight. Because a significant amount of deviations were also related to positive EM test results, the quality and site sterility assurance groups worked to improve aseptic practices.

The resulting gains in efficiency were significant. At the beginning of the program, right-first-time performance in batch records stood at 32%. Within four months, the organization raised that figure to almost 60% and shortly thereafter exceeded the stretch goal for the second quarter of year two of the program. The number of errors per page dropped from a high of 3.4 to 0.9, surpassing the target of one error per page. The number of deviations caused by human error dropped to zero. In addition, improvements in EM and aseptic practices resulted in a reduction in total deviations within that operation.

Cost savings were also significant. Labor savings from this project were an estimated 4.3 effort-years of investigating and writing deviations. In addition to those labor-cost savings, the organization avoided the costs of minor and major deviations, and the cost of destroying materials and products. The estimated annual true cost avoidance was in excess of $8 million, a figure that would climb to $40 million annually if the program were rolled out to the entire site. Eliminating critical deviations avoided distribution center withdrawals and product recalls.

While the gains in efficiency and reduction in costs were significant, the outcomes in qual-

ity/compliance were crucial. The recurring problems that the company was experiencing had attracted the attention of FDA, resulting in 483 observations and, ultimately, a warning letter. Due to the importance of the manufacturer's vaccines to public health, the agency required biweekly meetings with the company for progress reports. Just three months into the program, the company was able to demonstrate to FDA that the site would be able to deliver the needed compliance improvements.

The vaccine maker's program not only generated the immediate cost, efficiency, and quality/compliance goals—all three legs of the stool—but created sustainable benefits. As a result of the program, employees were motivated to consistently strive for the highest level of quality, establishing what we called in a previous article in this space a "quality culture" (1). At the site, operational excellence is now seen as a process of continuous operational, quality, and compliance improvement, where everyone understands the organization's objectives, policies, and procedures and their individual roles in helping achieving them.

Life sciences organizations will need such hardy cultures of quality to withstand stepped-up regulatory scrutiny. FDA Commissioner Margaret Hamburg told participants at the Annual Meeting of the Generic Pharmaceutical Manufacturers Association that the agency will increasingly focus on GMPs to improve drug quality. In addition, she said that the agency is exploring the creation of a new Office of Pharmaceutical Quality charged with overseeing quality through the life cycle of the product. "To address the increasing complexity of products, we will optimize the use of staff talent and review expertise to improve consistency and regulatory certainty across the wide span of drug quality review," she said (2).

It is possible, of course, to satisfy quality and compliance imperatives by gold-plating processes and systems. However, that approach forgoes the improvements in efficiency, reliability, and the reductions in costs biopharmaceutical organizations can ill afford to sacrifice. And the result of gold plating will be less a quality culture than a sort of "quality castle" that depends more on implementing costly fortifications than on developing quality-conscious people. At the other extreme, myopically focusing only on process and efficiency improvements in the design and implementation of OpEx programs—particularly regarding cost reduction and "right sizing" staff—can result in increased quality and compliance issues that, if not addressed early, can cripple an organization and lead to serious and expensive remediation efforts. By taking an approach to operational excellence that simultaneously embraces efficiency and quality, biopharmaceutical organizations can make sure they get the best of both worlds: working better and better work. ◆

REFERENCES

1. I. Uydess and C. Meyers, "Developing and Sustaining a Quality Culture," *BioPharm Intl* 24. 20-22 (2011).
2. M. A. Hamburg, Annual Meeting Generic Pharmaceutical Manufacturers Association, Orlando, Fla., Feb. 22, 2013.