Four Critical Process Automation Steps that Reduce Life Science Regulatory Compliance Cost

by Jonathon Thompson

Executive summary

The cost of regulatory compliance violations is growing in the life sciences industry. In the US alone, more than $10 billion in fines were levied against pharmaceutical companies over a recent two year span. These costs are avoidable. New, modern approaches to automation control now enable companies to exercise much tighter compliance discipline, thus avoiding regulatory penalties. This paper reviews four best practices for easing these compliance cost issues.

998-2095-10-30-14AR0A4

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Introduction

Regulatory compliance in the life sciences industry is difficult to maintain when production operations are partly or completely manual. Under such circumstances solid data is not being gathered on an ongoing basis and processes are not being verified at all times. In the event that reports are required to prove compliance, they are difficult and costly to generate and take a long time to produce. A senior executive from a major life sciences organization has recently commented that it can take up to six weeks to answer a simple question such as, "Was a particular batch made with a given ingredient?"[1]

In addition to this lack of automation, regulatory agencies around the globe are continuing to evolve their compliance expectations for life science operations. This evolution differs region by region and life science companies with global reach are being required to address these variable expectations. The clear direction for the regulatory agencies is towards more scientific understanding of both the product research *and the process used to produce the product* from the time it moves out of the laboratory. This discipline is expected to be integrated into the manufacturing facility to ensure the ongoing quality of the process. In the past, government agencies were only interested in testing product quality only after the product had been manufactured. The US Food and Drug Administration (FDA) and other organizations have made Quality by Design (QbD), a major initiative in recent years[2].

Failure to address these challenges is resulting in higher costs for life sciences firms. With the public spotlight on corporate product quality issues, a compliance failure in life sciences can be devastating to a company. In the U.S. pharmaceutical industry alone, a recent two-year span saw 74 settlements with federal and state governments totaling 10.2 billion dollars—an average of more than 135 million per settlement.[3] Beyond the direct costs of fines and penalties, quality problems cause long-term harm to a brand, undermining the consumers' trust and eroding sales. This is a problem even for manufacturers in less critical markets; in life sciences, where the stakes can be life and death, brand trust is essential for business success. **Figure 1** highlights the high costs of life science industry compliance in the US.[4]

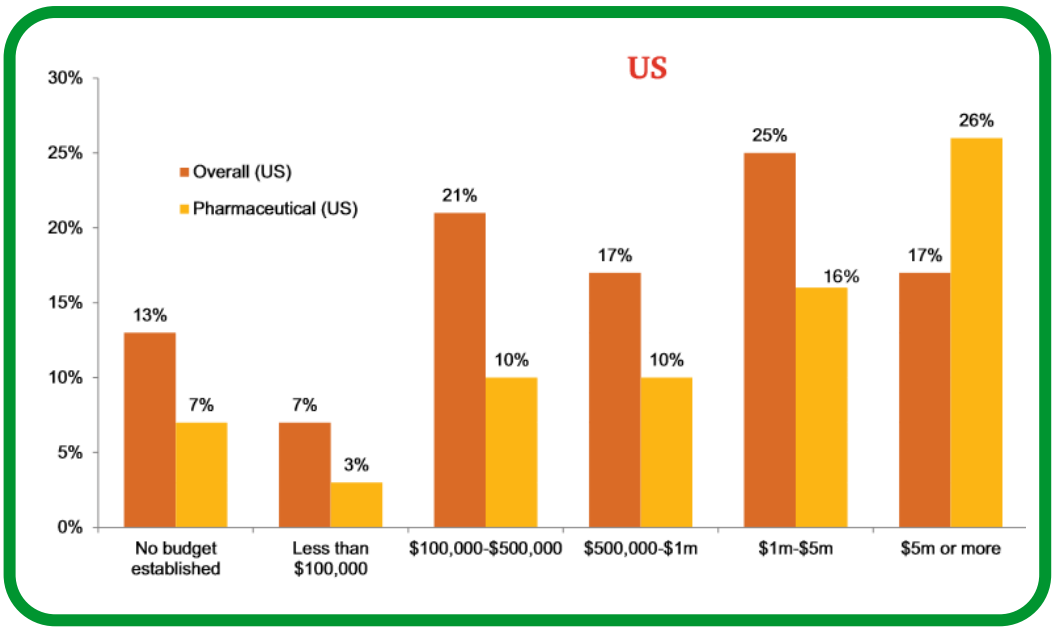

Figure 1
US pharmaceutical firms are more likely to spend $5 million or more annually on compliance activities than are companies in general

[1] Paul McKenzie, "Data and the Connected Supply Chain," OSIsoft User Conference, 2013

[2] Anurag S Rathore, Helen Winkle, "Quality by design for biopharmaceuticals," Nature Biotechnology, 2009

[3] Almashat and Wolfe, "Pharmaceutical Industry Criminal and Civil Penalties: An Update", www.citizen.org, September 27, 2012

[4] "Addendum to State of Compliance 2013 Survey Pharmaceutical and Life Sciences Industry Report," PwC, 2013 (http://www.pwc.com/us/en/risk-management/assets/pharma-addendum.pdf)

These challenges are driving life science companies to take a closer look at the various processes within their operations and to explore new technologies that will enable better compliance. For example, Amgen, a leading biotechnology firm, has posted on its website that it "has adopted the Quality by Design (QbD) principles, which further integrate quality control into the manufacturing process."[5]

Other companies are also moving rapidly to automate. According to the publication *Plant Engineering*, "In recent years, manufacturing execution systems (MES) and process control systems (PCS) have gained wide acceptance in pharmaceutical and biotech industries due to the adoption of industry standards and technology advancements."[6]

So how are these forward-looking companies achieving this transformation to new process control automation? While these new technology upgrades impact the entire operation, four key initiatives deserve special attention because they are critical to maintaining proper regulatory compliance. These four areas include:

1. Automation of manual operations
2. Standardization of processes across work sites
3. Availability of data and information
4. Establishment of a roadmap for innovation

By focusing on these four initiatives, companies can make significant strides towards meeting the expectations of regulatory bodies and improving compliance—while improving production efficiency, profitability, and maintaining competitive edge.

Four steps to success

For life sciences companies preparing to embark on modernization initiatives that include automated production processes, goals must be specific and must focus on essential issues.

The following four steps to successful automation have been established through experience and best practice at leading life sciences companies. However, each manufacturer will face some unique challenges, and not all life science companies will agree on a solution. Nevertheless, most life science manufacturers will benefit by keeping these four steps in mind as they move through their manufacturing transformation (see **Figure 2**).

Step 1: Automation of manual operations

Automation, by its very nature, is all about removal of the need for a manual process. Therefore, automation of operations is a first priority.

But the task of automating processes is not as simple as it first might seem. Some operations can be fully automated. For example, instead of using a manual switch that a human operator must activate for every step in a particular batch process, a computer could run the entire sequence—with or without human supervision.

However, other processes may always require a human operator, such as a quality inspection in a medical device company. In these cases, automation can be used to improve compliance by providing a computer interface that the operator must interact with. This guides the worker, and ensures and verifies proper processes. It also captures data that can be leveraged for generation of compliance reports, quality investigations, and continuous improvement programs.

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[5] www.amgenbiotech.com/pdf/Delivering%20High%20Quality%20Products%20Through%20Quality%20Processes.pdf

[6] Ronald E. Menéndez, Darrell Tanner, "Manufacturing Control Systems Bridge Production and IT," Plant Engineering, May 1, 2008 (http://www.plantengineering.com/single-article/manufacturing-control-systems-bridge-production-and-it/069774961d34e9fccbf0c9cb4eaf66a5.html)

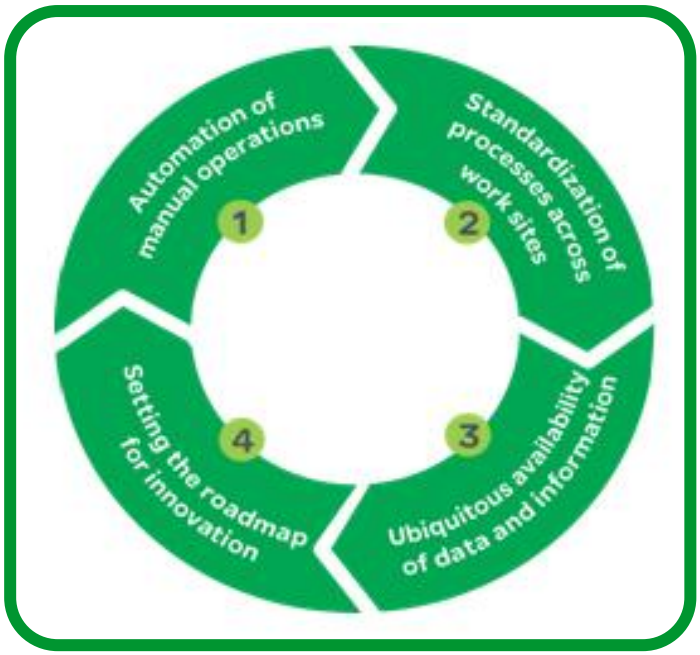

Figure 2
Implementation of four key steps can help companies plan a path to modern operations

The importance of automating as many processes as possible becomes clear when current manual methods that are used in most plants today are compared with the new, improved automated process. Below is a simple example of the difference:

- **Manual:** In a typical life sciences company, products are released by the quality team after reviewing the batch records, comprised of thousands of pages of data. These records must be reviewed by quality experts in their entirety, which can take weeks to complete.

- **Automated:** By contrast, in an automated factory, the approach to quality is on the front-end, not the back-end. Automation is used to design quality into the product, and then verified by process conformance that is ensured by automation and the continuous capture of process data. This allows "release by exception," so instead of reviewing thousands of pages and holding up shipment, the quality team only needs to investigate a batch when an exception in the process has occurred. In other words, as long as the process is followed and verified, the quality of the product is assured.

  This approach aligns with International Conference of Harmonization (ICH) Q11, which emphasizes quality processes. (The ICH, comprised of regulatory authorities in Europe, Japan and the United States, has issued a series of guidelines since 2005 designed to encourage modernization. The most recent, ICH Q11, "formally began the agency's push to instill the concepts of scientific understanding and risk management as a basis for product design and quality."[7] ICH Q11 process validation guidelines are designed to encourage automation and the building of quality into products, instead of testing for quality after the fact.) Also, it should be noted that automation improves quality and compliance by enabling continuous improvement, based on the historical data that can be captured and analyzed.

Eliminating manual operation also reduces the risk for operator error. Manual processes are known to be error prone: The top 20% of FDA 483 violations are largely due to failure to establish or follow written procedures[8] —a problem typical of manual operations, but rare in automated ones.

[7] "Global Pharma Outlook for 2014", pharmapro.com, Apr 22, 2014 (http://www.pharmpro.com/articles/2014/01/global-pharma-outlook-2014)

[8] Paula Felps, "Manufacturers Can Reduce 483 Observations Through Automation But The Barriers Are High,"(http://life-sciences.real-time-answers.com)

Automation also reduces the reliance on worker knowledge, which makes it easier to transfer best practices from one plant to many, eases training requirements, and provides a solution to the aging knowledge worker retirement issue in life sciences manufacturing.

Automation will also enable companies to take full advantage of mobile technology, which can be used for mobile data collection and visualization to support better decision-making at all times—not just when workers are physically at their stations or desks.

Step 2: Standardization of processes across work sites

Automating a single plant will provide many of the advantages described above. However, the real mission for life sciences manufacturers is to automate across the enterprise in a standardized way. This standardization will help to scale the benefits accrued from automation in the following ways:

- **Addressing regulatory expectations** - Regulatory agencies no longer view each manufacturing site as a separate entity. Rather, they take a more holistic view of companies and their operations. If one location has a compliance issue, it is assumed that this issue might exist across the network. By the same token, if one location is using best practices in technology there is an expectation that this proliferates across the company.

"If one location has a compliance issue, it is assumed that this issue might exist across the network".

- **Managing complexity** - Standardization is becoming a necessity for compliance simply because of the complexity of global manufacturing today, with the same products being produced in multiple facilities, and supply chains that stretch across regions and continents. For example, Johnson & Johnson reports that they have some 18,000 raw material SKUs and over 2000 product SKUs.[9] Keeping track of every detail of so many products is nearly impossible with paper systems, and the company points out that many of their compliance and recall problems stem from confusion—such as the wrong label or cap—rather than from actual products themselves. These problems are largely solved by standardized automation, which yields global consistency, reduced process and product variation around the globe, and greater product quality and compliance.

- **Proliferating best practices** - Without standardization, no effective way exists to capture, define, and deploy processes with the kind of consistency and science-based approach that is necessary. By standardizing, life science manufacturers can be certain that best practices are in fact instituted and maintained at every site. Note that standardization does not mean that all processes are exactly the same everywhere, since local regulations and requirements may vary; but it does mean that processes are deployed on common technology platforms and that any variations are carefully managed and tracked.

- **Maintaining competitiveness** - New life sciences plants being built in emerging markets are more highly automated and standardized than their European and North American counterparts. This is a trend that will no doubt continue, making it increasingly difficult in the years ahead for manufacturers to compete without standardized automation of production.

It should be noted that there are two aspects to standardization: One is choosing a technology platform that has the capability and scalability to be expanded throughout an enterprise. The other is the ability of an enterprise to maintain a long term commitment and to push through business process standardization as a major initiative.

Step 3: Ubiquitous availability of data and information

Automation creates an information loop where data moves from factories to decision-makers and back to the factories again with improved efficiency. Thus, it's important to

[9] Paul McKenzie, "Data and the Connected Supply Chain," OSIsoft User Conference, 2013

have an automation strategy that focuses on providing the right information to the right people, at the right time. **Table 1** highlights the list of affected stakeholders that should be actively involved in shaping the automation data sharing strategy.

Table 1
Key stakeholders that will consume the flow of data created through plant automation

Stakeholder	Requirements
Operators	• Real-time updates to all operators • Availability of a mobile interface • Information delivered will have to be formatted to address the user need • Simplified information for single operator • Detailed and aggregated information for supervisors
Engineering / Tech services	• Real-time alerts about equipment performance, • Aggregated data to use for process analysis and trending.
Quality team	• Real-time delivery of alerts and quality indicators for fast reaction to deviations • Aggregated data for analyzing quality trends.
Management	• Local aggregated data for up-to-the-minute plant floor updates • Enterprise data for comparison of facilities • Big data and on-demand KPI reports from across the production and supply chain • Drill-down capability.

The automation of manual processes increases information access which in turn improves compliance through better control and management. This simplifies regulatory reporting and improves responsiveness to investigations. When limited to manual operations, answering a simple question such as “What batch was this raw material used in?” can take weeks; with automated production systems, the answer can be available immediately.

In addition, new serialization laws are being widely adopted around the world. These new laws require pharmaceutical manufacturers to track and trace products with a much greater level of detail. The U.S. Senate passed the Drug Quality and Security Act in 2013, which will require “unit level traceability for all drugs manufactured in the U.S.” within a decade. Serialization laws have also been passed in Turkey, India, China, Brazil, Argentina and South Korea, and it’s expected that every major pharmaceutical market will have formal regulations regarding serialization in place by 2017.[10] This trend is a strong driver of automation, since global product genealogy is, practically speaking, impossible without automated production and record-keeping.

Step 4: Setting the roadmap for innovation

Cultural barriers within the organization can pose a major roadblock to progress. Old habits and resistance to change can make it difficult to adopt a culture of innovation. Below are some suggestions for overcoming these challenges and staying current with automation technology:

Cost-justify the transition - While compliance may be a major driver for change, multiple financial arguments can be made for adopting new production technology. It has been reported that the pharmaceutical industry wastes as much as $50 billion a year due

[10] “Global Pharma Outlook for 2014”, pharmapro.com, Apr 22, 2014 (http://www.pharmpro.com/articles/2014/01/global-pharma-outlook-2014)

to inefficient manufacturing processes[11], most of which can be addressed through automation. Below are several examples:

- Production automation reduces quality control costs by enabling "release by exception" (as described earlier), while improving compliance verification through reporting and data analysis.
- Automation reduces the frequency and cost of non-compliance events when they occur. In some companies, investigating a single deviation in a batch can cost $15,000 or more using manual methods. Within an automated system fewer deviations occur due to greater control of processes.
- Market leaders are embracing the new technologies and leaving competitors behind. Companies like Johnson & Johnson, for example, have committed to enterprise-wide manufacturing transformation.

(To learn more about the financial advantages of production automation, download the Schneider Electric white paper "*Improving Process Efficiency and Business Performance in Life Sciences Plants*").

Preach continuous improvement - Regulatory bodies over the years have promoted a view of manufacturing that was stable and static. Now, however, regulations are changing in response to the global, connected world and companies are expected to flexible and to improve their processes through the use of technology. Though challenging to the industry, in the long run it will result in higher-quality, safer products. The aim—fully supported and encouraged by regulatory bodies—is to deploy best practices and to show continuous improvement.

"At one time, any major change within the industry was deemed a risk. Now, the opposite is true. Not changing is considered the greater risk."

Emphasize risk management - At one time, any major change within the industry was deemed a risk. Now, the opposite is true. *Not* changing is considered the greater risk. Modernized plants reduce risk in new ways. For example, processes can be modeled and simulated utilzing a computerized process before going live, and then implemented with confidence. Within the realm of automated systems, it is no longer necessary to shut down a production line in order to test and validate a process change. This enables the deployment of best practices and continuous improvement.

Propose a phased approach - Life sciences is unlike most other industries, and corporate decision-makers will want to see a careful approach to technology innovation that does not cause disruption and confusion in the organization. Best practice is to develop a detailed, phased approach to implementation that will prove and verify the plan at every stage. Phased strategies can take many forms, and will depend on each company's goals and resources. Typically, a company will automate a single production line or facility as a pilot—often this is done in the best performing plant in the company, where there is high confidence in the skills and experience of the workers.

Seek outside help - The scope of transforming manufacturing to automated systems should not be underestimated. Life sciences manufacturers will probably need the help of vendors and consultants to lay out a practical, low-risk, and cost-effective roadmap for production automation. Many consultancies specialize in life sciences automation, and large solution providers offer consultant services as well. Third-party experts can help establish goals and expectations, guide companies through the decision process, choose appropriate technologies, and help implement the new systems.

[11] Shula Neuman, "Pharmaceutical industry wastes $50 billion a year due to inefficient manufacturing," Washington University in St. Louis, Oct. 9, 2006 (http://news.wustl.edu/news/Pages/7912.aspx)

Conclusion

An evolving regulatory climate is forcing companies to address outdated technology and processes. The globalization of life sciences operations is opening the industry to the use of more modern technologies in the emerging markets. This is shining a light on the existing operations in the established markets, and giving regulatory bodies a new measuring stick by which to judge these facilities. Increasingly, regulators are expecting global life science operations to be based on modern and standardized operations across the enterprise.

As a result of these strong pressures, life science manufacturers are beginning to embrace automation as a quality solution. In Europe, for example, sales of automation and control solutions have grown by 50% in the last 5 years.[12] An executive at Johnson & Johnson has stated that his company is moving to global, standardized, automated approach to manufacturing processes, largely for quality reasons.[13]

With the advantages of production and process automation becoming clear, from both a regulatory and an economic perspective, the life sciences industry will continue its adoption of automation solutions for manufacturing. The four keys steps discussed in this can help companies plan a path to modern operations that will improve efficiency and compliance. Such implementations will provide a competitive advantage against those companies that choose to delay.

About the author

Jonathon Thompson is Director of Compliance Consulting with Schneider Electric. Jonathon has more than 15 years of experience working in the Life Sciences, with previous roles in Information Technology, Quality, Validation and Operations. He has specialized in the improvement of operational efficiency of the Life Sciences supply chain through the implementation of technology. He is currently focused on helping customer create the Factory of the Future.

[12] "Automation market in European Pharmaceuticals to reach $1.4 billion by 2013", Frost & Sullivan, April 22, 2014

[13] Paul McKenzie, "Data and the Connected Supply Chain," OSIsoft User Conference, 2013