WHITE PAPER

Elevating the Quality of QMS in Life Sciences: The Age of Digital eQMS

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Introduction

The shift to today's digital era has been in process for decades. In fact, we are approaching the post-digital age where technology is bringing new and powerful capabilities to organizations that are completely reshaping their businesses. Not only are new digital products emerging in the marketplace at warp speed, but today's manufacturing mindset just assumes that digitally based processes upstream are essential to churning out increasingly advanced products.

The post-digital age

Perhaps nowhere is this more evident than in the life sciences industry where at the furthest point downstream -- the delivery of quality healthcare - we have become largely reliant on digital technology, from the use of health apps, wearable monitors and sensors, point of use diagnostics, and other platforms built to identify medical conditions, monitor and maintain our health, and aid disease diagnosis and management.

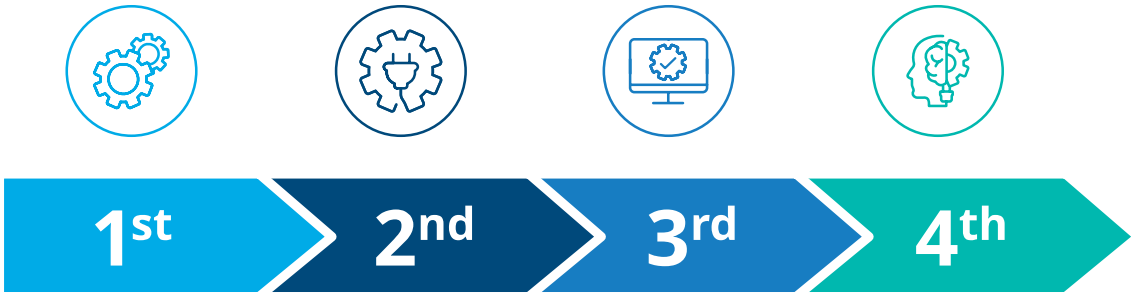
As digital technology becomes more prevalent in the life sciences industry along the entire lifecycle continuum, from R&D and manufacturing to the patient bedside, successful integration of all things digital will be crucial. Embedded within the entire spectrum, Quality professionals need to embrace data and technology to drive innovation, while improving overall quality from end to end to improve patient outcomes and product efficacy.

Today, life sciences organizations are implementing Digital Enterprise Quality Management Systems (eQMS) with the objective of harmonizing policies, processes, procedures, and documentation in the effort to ensure quality is built into every step of their operations. As simple as this may seem to accomplish based on the constant presence that technology has among us today, a true transition from a paper-based quality management system (QMS) to digital-based QMS is proving to be a challenge for many organizations. A shift in culture and a better understanding of how digital technology "thinks" are essential to leveraging the abilities and functionality of digital eQMS.

This paper will review why life sciences industry professionals are implementing digital eQMS within their operations and how they can best make that transition. The organizational impact with regard to culture and training, data management, validation and security, and the impact of artificial intelligence

(Al)/machine learning (ML), will also be explored, along with how digital eQMS improves product safety and patient outcomes, and results in cost savings both within the manufacturing organization and as it's passed down along the healthcare continuum.

A primer on Industry 4.0



To fully understand digital eQMS, it's important to take a quick look at the concept of Industry 4.0, or the Fourth Industrial Revolution, and its components. Industry 4.0 can be broadly defined as the trend towards automation and data exchange in manufacturing. It is essentially a digital industrial revolution that includes cyberphysical systems, the Internet of things (IoT), and cloud computing, to name a few of its components.

Industry 4.0 has introduced to manufacturing the concept of the "Smart Factory," a collaborative, digitally based environment that is integrated, both vertically and horizontally in real time, across an organization's extended supply chain. The Smart Factory includes cyber-physical systems which create virtual representations of the physical world, allowing for interaction between people and machines. This is evident in the "Big Three" of this digital ecosystem: AI and machine learning and big data analytics. Additionally, IoT as a whole digitally collects and exchanges data across multiple sources, including some we use every day.

The existence of digital eQMS, which has arisen out of the Industry 4.0 initiative, must live within this digital ecosystem. Everything in the digital ecosystem should be integrated, connected, and collaborative if digital eQMS is to contribute to an organization's bottom-line benefits and meet its full purpose as the backbone of a successful life sciences manufacturing operation.

As the concept of the Smart Factory continues to take hold, the evolution of technology within the life sciences industry will continue to require that quality management systems become digitized. This concept can be intimidating to those tasked with overseeing the compliance of their organization and the safety of its products.

That said, as the life sciences industry continuously embraces quality, not just for the purpose of regulatory compliance, but to provide better products to the patients that need them, it is increasingly recognizing the benefits of automating quality management operations - better efficiency and consistency. Subsequently, the move to automation requires quality teams to move on from their traditional quality management approaches and undergo an internal cultural shift.

Overall, the shift to digital requires departmental, operational, and functional walls to be broken down, and that often requires conversations about change management and employee training - investments and related costs can't be relegated to technology and equipment only. Most people aren't comfortable with change, at least not when they are in the midst of it. Regardless of how flexible administrators attempt to be, or how well the benefits and procedures related to change are communicated, there will be challenges.

Digital cultural shifts

It's critical to involve employees in the change process itself by asking for their insight into such topics as obstacles they might have faced prior to change, and obstacles they anticipate in the face of change, and incorporating these concerns into any necessary training along the way to change.

Case Study:

Harmonize, don't standardize, across the organization

At a large, a multinational medical equipment manufacturing company headquartered in England, leadership built their digital eQMS system with input from all key stakeholders, spanning across each of the company's divisions around the globe. They took a bottoms-up implementation approach to ensure that everyone's voice was accounted for and all division-based requirements were captured appropriately. Components of the system were then tested, and feedback was provided over the course of about eight months. This approach helped with achieving buy-in among staff members and to help everyone to embrace the system as an overall team effort, i.e. harmonizing versus standardizing. The system had buy-in from everyone, as they felt a sense of ownership. This was not an initiative pushed by an IT Department or management agenda. The so-called 'fear of the unknown' slowly became less of a concern as staff were trained on the product and protocols. The rollout became that much easier to conduct through
early participation.

Finally, from a cultural perspective, quality must be an integrated process in both the short term during any eQMS conversion, and the long term. Quality is not a "department." Everyone must be part of the quality solution, not just overseers of results, if truly safe, effective, quality products are to be available consistently to improve the lives of many.

Intro of digital QMS

Aside from the cultural change and adoption of a new mindset, deploying a digital QMS is not always an easy feat for the quality management function, considering the genesis of day-to-day quality operations was founded in paper documentation. Today, real- or

near-time analysis of decisions is critical to product quality and patient safety. Digital eQMS needs its own rules-based engines, AI and machine learning algorithms, and connectivity, if it's going to keep pace with industry.

It is said, "If Quality didn't document it, it didn't happen." So, Quality needs to figure out a new, faster way to document events as they occur and make decisions. Quality must still analyze history and look at trends as a part of its processes. However, the immediate recording of quality events and data, combined with technology is the only way to become proactive, preventative, and predictive. Quality-oriented organizations need to be "right now" and future-focused, as opposed to focusing on the rear-view mirror, fixated on history. When technology is properly implemented, it will support this new quality orientation and help to drive innovation and continuous improvement.

Accomplishing this new future-focused orientation requires quality processes themselves to be reexamined, along with the technology that is needed to drive any change required within the organization's processes.

In an attempt to quickly make the technical leap, many organizations shifting to digital eQMS will start by simply automating their current paper processes. This approach, however, has the tendency to build many

of the inefficiencies of a paper processes into the new digital process, including serial processing and approval cycles, process delays, print control and management, and the re-keying of data from forms filled out by hand.

So, how can technology make processes faster and less costly while improving quality? How can technology help with maintaining compliance? It is a journey, not an "overnight fix", and all constituents in this industry should initiate this evolution because it will take time. There is no shortcut to success.

Typically, the bigger the organization, the more harmonization of different quality processes and systems is necessary. The good news is that if issues are approached appropriately, and change management disciplines are employed, desired benefits can be realized as soon as the first module of the quality system is implemented. This is a very measurable action, as are some of the resulting benefits, such as reduced costs, including cost of quality, more streamlined processes and shortened cycle times, increased flexibility, and reduced time to market.

Investing beyond the digital

Quality must embrace data and technology and use them to drive innovation while improving overall product safety, efficacy, and at the end of the day, patient care.

With the ongoing digital age comes an explosion of data., Transforming numbers into meaningful information that drives actions and decisions quickly is critical not just to the organization's processes but to ROI of the digital initiative. Establishing a metrics baseline for one's investment, and then continuously monitoring and measuring those metrics against the investments based on the benefits derived, is the only way to manage the rapid pace of the digital era and support continuous improvement and innovation.

Therefore, when assessing the cost of converting to a digital eQMS, it is necessary to view required investments through a lens that focuses not only on technology, but to also consider the investment in additional company resources, including staff, materials, training, change management and continuing education, when undergoing such a long-term initiative.

Key considerations for the digital world of eQMS - data volume, security, validation

So, what happens when the organization has buy-in to go digital, the cultural shift is in motion, and it's time to begin the implementation? With the massive amount

of data coming from various sources, both internal and external, multiple considerations come into play, even when working with electronic-based systems.

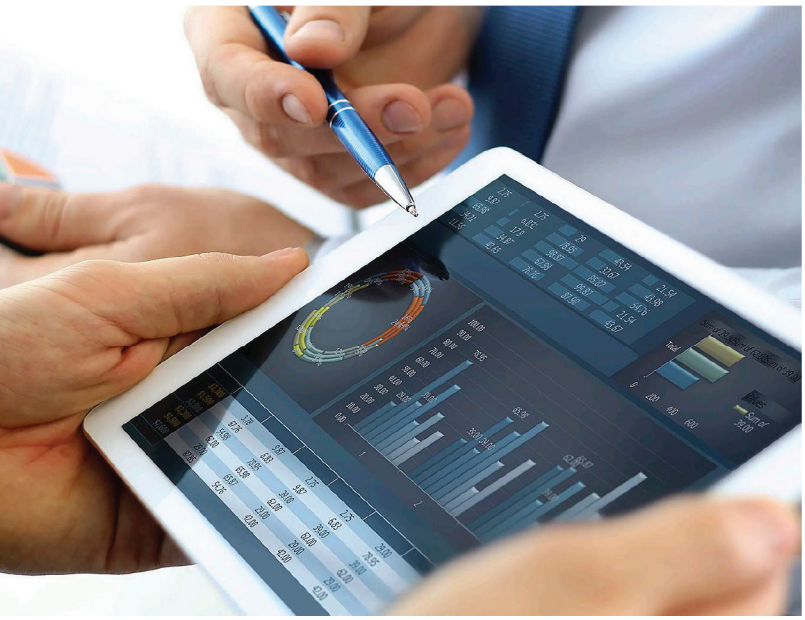
- Data volume - how do we keep track of all of this?
- Data security- how do we protect all of this?
- Data validation - how do we know this is accurate?

These factors require examination before launching a digital eQMS platform.

The security concerns associated with the massive rise in data volume coming into any eQMS make it easy to understand why industry professionals place data protection as a top-of-mind issue, whether related to protected health information (PHI) or personally identifiable information data (PII), location data, or merely data integrity in general. Data security and data integrity cannot be afterthoughts.

Each digital eQMS component must also go through validation for purposes of meeting requirements associated with the U.S. Food & Drug Administration (FDA) and other governing regulatory bodies around the globe. Validation is a high-impact area when it comes to AI and machine learning. As life science products and software take in massive amounts of data over time, they learn and adjust. And as a given system cross-references, correlates, and assimilates data, it can recognize new patterns, store these patterns, and then use the patterns in future learning. These complex algorithms and methods can generate results at record speeds that may not have been anticipated. That said, similar to the notion that automation of paper processes can be the entry path into

digital integration, traditional validation methods are very likely to fall short in regard to the technology of today and in the future. Traditional validation processes are geared towards the objective of demonstrating that products and processes are always going to achieve expected results. However, in the digital "intellectual" eQMS world, it's highly likely the organizations will, at some point, experience the unexpected.



Another validation challenge can be remaining in compliance continuously during any digital eQMS initiated change because digital systems can update frequently and quickly. Due to the rapidly changing technology environment we're in, a risk-based approach to validation is recommended. Organizations should work with their vendors to identify as early as possible new features and functions, and then outline the risks of those features and functions so they can be assessed based on the organization's risk profile. As vendors update their systems, these risks must be continually re-assessed. Review release notes early enough in the cycle to get a comprehensive perspective of what's being introduced, tested, finalized, and everything in between, including an ongoing assessment of risks.

Regulating technology in the digital era

In their best attempt to keep pace with technology, regulators are striving to balance new, innovative solutions that can improve health with concerns about patient safety and privacy.

Bakul Patel, the director of Digital Health at the FDA, has been quoted as saying, "We've been trying to translate the current regulation paradigm for digital, but what we have today and what we're going to have tomorrow are not really translatable. We need to take the blinders off and start with a clean sheet of paper."[1] In 2019, at the MedCity INVEST Conference in Chicago, Patel told the audience, "No regulator in the world can keep up with the volume of new software being created."[2] FDA officials agree, as is evident by the organization's Digital Health Software Precertification (Pre-Cert) Program,[3] a program designed to help the development of future regulatory models that will provide more streamlined and efficient oversight of software-based medical devices. Pre-Cert, spearheaded by Patel, was developed by manufacturers who have demonstrated a robust culture of quality and organizational excellence, and who are committed to monitoring real-world performance of their products once they reach the U.S. market.

Regulations and guidance are already coming from regulatory bodies in regards to Technology and AI/ML. Guidelines on clinical decision support software and for software as a medical device during clinical evaluations are being issued. Prior regulations and policies have also included a general wellness policy for low-risk devices addressed by the 21st Century Cures Act. The use of real world evidence to support regulatory decision making is also important draft guidance, and adaptive designs for medical devices have been part of clinical studies. This does not comprehensively cover the regulations associated with technology in life sciences, however. The impact of regulations during this digital era and the continued use of AI and machine learning is going to be significant.

The digital eQMS implementation

Quality itself should have a rules-based automated workflow engine, which can be helpful during the digital eQMS transition for people who ask, what's next? Typically, the next step is continuing to integrate with the organization's other enterprise software solutions. As that occurs, and as massive amounts of new data are introduced into the ecosystem, it becomes more important that the organization prioritize trending, and become predictive and prescriptive. In that vein, establishing an alert system for all need-to-know parties utilizing the software is an early necessity of the digital eQMS "journey," especially for global organizations and those that have employees working in remote locations.

Visibility and transparency are vital to this concept, and when it comes to electronic forms and records, or any collaborative digital tool or documentation program, establishing a real-time alerts/notifications system is the way to promote both vital aspects.

Notifications should be geared to both the positive and negative aspects of any workflow by letting others know, for example: when certain checkpoints are completed and what upcoming checkpoints will need to be completed; regulatory red flags and audits; deadlines for regulatory related issues and other due dates; pre-market product concerns; and, of course, anything relative in the post-market space. Notifications and alerts should also be delivered in a variety of ways concurrently for management purposes, such as via desktop and mobile apps, to further foster a preventative approach beyond being corrective only in nature.

Another consideration during the COVID-19 pandemic, is the increase of remote virtual working (which is extensive) for both internal and external resources. Secure access is critical to systems, and data is critical to continued operations. With the inability to vet and monitor third parties through on-site audits, inclusion of third parties in your organization's eQMS is also paramount to the quality and safety of your products. Allowing outside parties directly into a quality management system, where there's potential intellectual property that should not be deliberately or accidentally accessible, should generally be avoided. But given the challenges that are inherent with remote working, offering some type of participation in the digital eQMS can be navigated with the proper tools such as portals. For both internal and third-party eQMS participants, organizations must have written guidelines, appropriate training, and security measures implemented.

It's also important to recognize that with the digital era's sophisticated and advanced techologies being implanted and extended, organizations may want to put some focus on natural language processing (NLP). This subfield of linguistics, computer science, and AI addresses the interactions that occur between devices and humans, particularly related to how systems process and analyze large amounts of natural language data. It's possible, and probably warranted, that regulations will be more intimately developed to further improve the reach of quality and transparency. In fact, regulations could already exist in the fine print.[4]

Finally, as mentioned previously, when implementing digital eQMS, focusing on the people as well as the technology is critical. One additional component to consider is the integration of the digital eQMS to other solutions. These solutions will include your organization's ERP, MES (sensors, too), Supply Chain, PLM, and Lab systems to name a few. In particular, don't forget the internet. These integrations need to be stable, secure, and bi-directional to achieve a truly digital ecosystem within your organization.

Benefits of digital eQMS

With a well-planned, carefully executed project for digital eQMS, your organization will see value as soon as you stand up one module of a digital quality system. The ability to extend the maturity of an organization's quality footprint, by both improving organizational culture and achieving process excellence through the digital eQMS journey, is the most significant benefit. And the higher an organization ascends the quality maturity ladder, the more it reduces its Total Cost of Quality.

Quality maturity is driven by people and processes and fueled by technology. In the beginning stages of maturity, processes are manual and typically reactive. They're also mainly compliance-driven, as opposed to being driven by quality improvement. As organizations increase in their maturity, the focus moves to prevention and the organization becomes better able to anticipate and manage risks. This can be driven and supported by integrated collaborative quality and other enterprise systems. In higher stages of quality maturity, companies become more proactive and can harmonize processes across the enterprise to better manage third-party quality measures. At the highest level of maturity, a true culture of quality with end-to-end processes is in place, as is the ability to continuously sustain and improve overall quality.

LEVEL 5 LEADER	Emphasis on long-term growth and predictive/prescriptive measures that continue to evolve overall quality and operational excellence **Cost of quality: 3-7% of revenue.**
LEVEL 4 HARMONIZED	Achieve market leadership by leveraging innovative technologies focusing on leading versus lagging indicators and engraining quality into the culture of the company. **Cost of quality: 8-11% of revenue.**
LEVEL 3 INTEGRATED	Improve by building quality performance into the corporate structure and extend proactive measures outside the four walls to reach suppliers and other value chain constituents. **Cost of quality: 12-17% of revenue.**
LEVEL 2 CONTROLLED	Improve by tightly integrating quality systems, processes, and programs across the organization and advancing the focus from problem correction to problem prevention. **Cost of quality: 18-24% of revenue.**
LEVEL 1 DEVELOPING	Improve by tightly integrating quality systems, processes, and programs across the organization and advancing the focus from problem correction to problem prevention. **Cost of quality: 25-40% of revenue.**

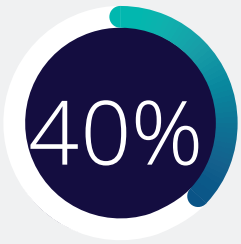
Source: LNS Research, 2017

Harmonization, cultural shifts, integration, and collaboration are all elements of digital transformation. But they're also the same themes that drive quality maturity, reflecting the value of investing in a digital eQMS.

A successful digital eQMS implementation results in tangible and intangible benefits in a life sciences organization. Industry leaders and analysts have charted benchmarks and determined quality improvement metrics including (but not limited to):

Improved operational efficiencies of up to 50%

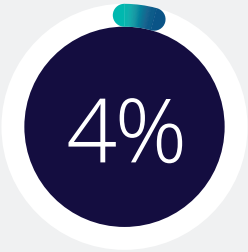
Reduced costs of up to 40%



Increased revenue of up to 40%

Reduced non-conformance in manufacturing of up to 12%

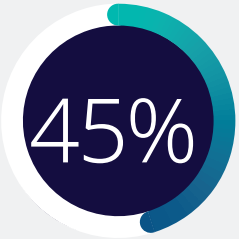
Increased/improved overall equipment effectiveness of up to 10%



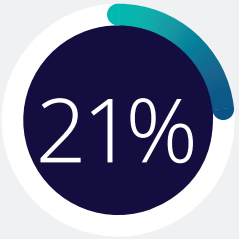
Improved operational efficiencies of up to 50%

Reduced costs of up to 40%

Increased revenue of up to 40%



Reduced non-conformance in manufacturing of up to 12%



Increased/improved overall equipment effectiveness of up to 10%

Conclusion

Regardless of how seamlessly an organization's integration of digital eQMS with other enterprise solutions may operate, the digital age requires a cultural and thought paradigm shift on many fronts. Traditional methodologies to validate and achieve compliance are likely to fall short moving forward in the digital age. As we are still in the midst of the digital era, nobody knows exactly what those methodologies are going to be or what they'll look like. There is still more to be learned as the technology and the implementation of that technology to solve business problems in the digital era is evolving at a rapid pace. And that could be the new standard for any business investment tied to quality throughout the healthcare industry.

SmartSolve®, a digital QMS from IQVIA, helps life sciences organizations maintain efficient and compliant quality management systems. SmartSolve's integrated platform enables quality to become a centralized hub for continuous improvement throughout your business. Contact IOVIA to learn more.

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As QMS Regulatory and Product Management Leader for IQVIA, Kari Miller is responsible for driving the strategic product roadmap, and delivery of industry best practices and regulatory compliance solutions for quality management. Kari has more than 25 years of experience delivering software solutions for life sciences. She brings that knowledge to her current team as they focus specifically on translating market and industry requirements into industry-leading enterprise quality management solutions that meet the needs of the heavily regulated life sciences QMS market. Kari earned a Bachelor of Science in Business Administration and a Bachelor of Science in Psychology from Marian College of Fond-du-lac, Wisconsin.

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