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Ingenuity for life

Siemens Digital Industries Software

Improving market presence, manufacturing processes and product quality with manufacturing operations management

The need for good business practices

This white paper outlines the business value of focusing on quality rather than compliance, and the technology infrastructures required to close the loop on product quality.

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Introduction

Quality and compliance professionals are paying close attention to regulatory bodies signaling the end of the Compliance Era. The Med-Tech industry needs to be prepared for this new reality. The U.S. Food and Drug Administration (FDA) is shifting its focus from “compliance only” to “quality always.” The timing is no coincidence, as recalls are on the rise and companies are reporting an increased rate of product changes over the next two years. Since medical devices are in a constant state of evolution – providing new capabilities, addressing defects, adapting to changing markets or regulatory demands and reacting to competitive threats – companies that actively manage products using closed-loop systems and technology are able to simultaneously address these issues and drive improvements across the manufacturing process.

While giant mounds of paper (GMPs) have historically driven compliance activities, they do not drive profitability. What does drive profitability are good business practices (GBPs). Innovators who focus on GBPs over GMPs have implemented relevant technology infrastructures needed to close the loop on product quality. These include manufacturing operations management (MOM) solutions that ensure the right products are manufactured the best way possible and support improved product quality and continuous improvement. This white paper outlines the business value of focusing on GBPs over GMPs and the benefits of avoiding the game of “regulatory Whack-a-Mole.”

This white paper is derived from and based upon primary research on *The Future of Change and Configuration Management in the Med-Tech Industry* conducted by Axendia. For the purpose of this white paper, a closed-loop process is a system in which the desired output depends on input and feedback elements. For the Med-Tech industry, closed-loop processes must start with R&D/ideation, support manufacturing operations and include post-market surveillance/obsolescence.

The terms “innovators” and “laggards” are also used throughout. Respondents to Axendia’s survey who strongly agreed that they have a closed-loop change and configuration management (C&CM) process were categorized as innovators; those who strongly disagreed were categorized as laggards.

See the Definitions section for additional details.

Background

Although the terms are often used interchangeably throughout the industry, quality and compliance are not the same. Quality is an investment that should pay dividends. Innovators who are focused on building a culture of improved product quality for the benefit of patients are enhancing their product design and manufacturing processes. These companies also benefit from better-informed regulatory practices and are ultimately changing the very nature of their interactions with the FDA in relation to quality and compliance.

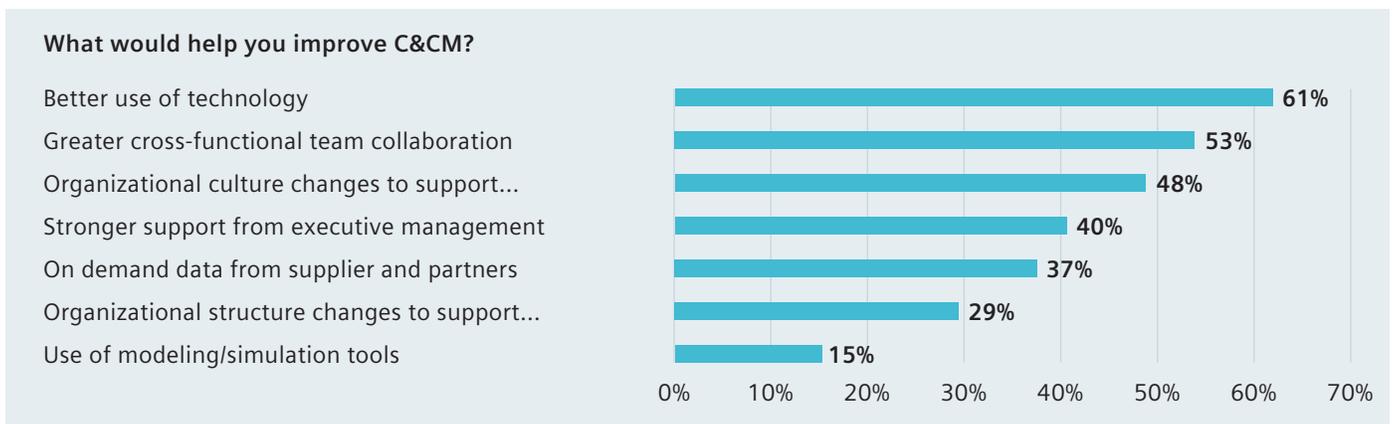
By showing the FDA their commitment to quality by facilitating e-inspections, quality-focused companies can expect fewer disruptions to their businesses via onsite FDA audits and inspections. Integrated systems and better use of technology, including MOM, product lifecycle management (PLM) and manufacturing execution systems (MES), can provide key metrics and intelligence that the FDA will be requesting to support quality metrics.¹

Actively managing products across the total product lifecycle (including design, manufacturing and service management) drives improvements in product quality and accelerates new product introductions in a timely and cost-effective manner while supporting regulatory compliance. Axendia’s survey revealed that, without better use of technology, Med-Tech organizations struggle to close the loop on C&CM. A closed-loop C&CM

process provides a standardized, effective and efficient way to manage approved design and configuration changes to products, processes and documentation and then transfer them for efficient, fully traceable and error-free manufacturing execution.

An integrated PLM and MOM infrastructure results in a dynamic system providing digital continuity to allow people to follow the product, not the documents. This permits full traceability downstream or upstream (for example, from ideation and design to sourcing materials, through manufacturing and ultimately to patient outcomes). It can also be used to support regulatory changes to enable more efficient adoption of innovative technologies, regulatory evaluation, both in review and inspection, and throughout the product lifecycle.

An integrated PLM, MOM infrastructure system results in a dynamic system providing digital continuity to allow people to “follow the product, not the documents.”



Source: *The Future of Change and Configuration Management in the Med-Tech Industry*, 2016, Axendia Inc.

Recalls are on the rise

To gauge the business value of closed-loop processes in support of product quality and in a globalized ecosystem, it is important to understand the cost of recalls. While medical device manufacturers are focused on bringing innovative high-quality products to market, many organizations are in recall denial, believing that recalls affect other companies, not them.

Unfortunately, the number of recalls is on the rise. Analysis shows a 97 percent increase in the annual number of medical device recalls for the 10-year period, increasing from 604 recalls in FY 2003 to 1,190 recalls in FY 2012.²

Axendia's analysis of published recall data shows that a single major recall could pay for the implementation of closed loop processes and systems for the entire Med-Tech industry.

For example:

- Recall charges at a major orthopedic company exceeded \$1.5 billion net of insurance recoveries.³
- Another company reportedly spent nearly \$1 billion on recalled hip implants.⁴
- The same company was reported to have reached a \$4 billion settlement on hip implant lawsuits.⁵
- A major Med-Tech company reported a special pretax charge of \$400 million to \$600 million to cover infusion pump recall costs.⁶

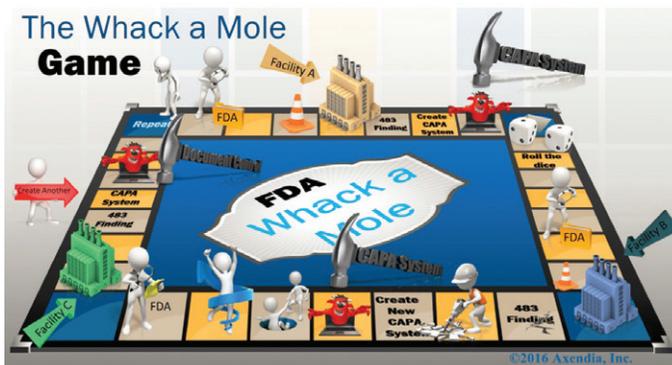
Axendia's research shows that the cost of implementing closed-loop C&CM processes and technology would be:

- Five to 10 percent of the cost of a recall
- One to two percent of the total litigation costs resulting from a recall

The regulatory “Whack-a-Mole” game

The great incentive for strategic action is often a warning letter or a recall. Many companies do not invest in systems or technologies because of the cost and the disruption to the business. These are real concerns that every company struggles to balance when considering an investment in technology.

- Close a CAPA (70 percent)
- Regulatory requirements/mandates (52 percent)
- Fix defects (48 percent)
- Customer inquiries/complaints (43 percent)



According to the Whack-a-Mole approach to regulatory enforcement, inspections would lead to findings for a site (for example, 483 for corrective and preventive action at facility A). That facility would then react by implementing a corrective and preventive action (CAPA) system at that site. Yet the implementation only addressed a regulatory or quality issue at one facility without seeking to address issues before they occurred company-wide. The goal was to simply respond to the finding and avoid the next “whack.”

Had these organizations focused on company-wide process improvements rather than merely closing CAPAs, they could have avoided the subsequent finding. However, systems are continuously implemented as standalone silos, with the primary purpose of avoiding the next finding during the next inspection or at the next site. This approach does not scale as innovation cycles become increasing shorter and products become increasingly complex.

Such an inspection and regulatory action approach has put the industry in a reactive and firefighting stance, and the FDA is recognizing this. When survey respondents were asked “What are the primary drivers for implementing process and documentation changes at your organization?” the top answers were reactive in nature:

The solution is to avoid focusing on procedural quality and change the focus to product quality. Taking a remedial approach is extremely counterproductive in an industry that manufactures on a global scale and within varying regulatory frameworks. Quality and compliance issues can vary from site to site, but by implementing MOM across the enterprise, companies can ensure that consistent processes are followed to drive quality and continued improvement initiatives, while at the same time documenting compliance with regulatory requirements. With this shift in mindset, compliance becomes a by-product of an innovative quality culture.

Companies that focus on GBPs over GMPs use technology to actively manage products across the total product lifecycle (including design, manufacturing and service management), which drives improvements in product quality and accelerates new product introductions in a timely and cost-effective manner while supporting regulatory compliance.

Integrated MOM and PLM infrastructures ensure that the right products are manufactured the best way possible and support a closed-loop feedback process for continuous process and product improvement. Closed-loop C&CM processes allow the business to focus on making sure that critical business information will be available to customers, suppliers, regulators and other entities that are permitted to see and use data from those functions. They focus on making sure that information is presented in the right context, available and therefore usable.

Investing in MOM and PLM infrastructures that support closed-loop systems leads to:

- Streamlined end-to-end processes that result in operational efficiencies and reduce waste
- Predictable processes that reduce opportunities for errors and field actions
- Improved quality outcomes and compliance with global regulatory frameworks

Compliance and quality are not the same

Can you distribute poor-quality products while complying with all applicable regulatory requirements?

Certainly. After all, you can conduct a recall of poor-quality products in compliance with all applicable regulations. The focus should always be on manufacturing the highest-quality devices, while at the same time ensuring compliance to applicable regulations.

The FDA's top medical device official agrees. Jeff Shuren, M.D., J.D., director of the FDA's Center for Devices and Radiological Health (CDRH), put it this way: "...one device manufacturer can meet FDA requirements and still make a poor-quality device; whereas, a second manufacturer may not comply with all FDA requirements and yet make a high-quality device."⁷

This begs the question: has the FDA's traditional compliance-based enforcement approach become a disruptor? Has it driven the Med-Tech industry to focus intensely on compliance, and become an obstacle to improving quality?

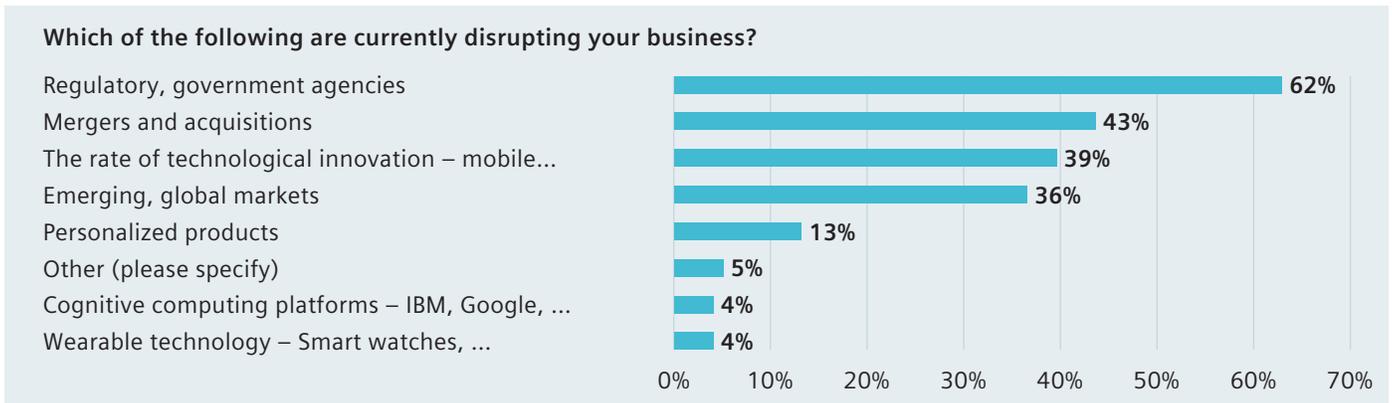
When asked to identify business disruptors to the Med-Tech industry, the majority of all respondents selected "Regulatory, government agencies" (62 percent) as the top disruptor.

Generally, when regulatory or government agencies ask for information, there is tremendous disruption to the business. It's all hands on deck to manage the inspection, gather requested information and respond to inquiries. However, there is a clear distinction in the level of disruption that regulatory and government agencies have on innovators versus laggards. While government agencies represent the top disruptor for both, 64 percent of laggards identified regulatory and government agencies as a top business disruptor compared to only 40 percent of innovators.

Although the terms are often used interchangeably in the Med-Tech industry, regulatory compliance and quality are not equivalent. While GMP drive compliance activities, they do not drive profitability or ensure product quality. What does drive profitability and product quality is good business practices.

Compliance should be a by-product of well-designed and executed processes – improved quality and consistent processes that reduce opportunities for errors, nonconformances and field actions.

- Compliance is the price of entry into the Med-Tech market (an expense)
 - Collecting documented evidence of compliance with regulatory requirements is an overhead cost for Med-Tech companies.
 - Regulatory compliance is a baseline all Med-Tech companies who are marketing medical devices must achieve.
 - Do your primary business objectives revolve solely around compliance?
- Quality is an investment that should pay dividends
 - Improvements in quality drive enhanced and predictable product performance.
 - Streamlined processes result in operational efficiencies and reduce waste.
 - Investing in product quality lowers costs and improves profitability.



Source: *The Future of Change and Configuration Management in the Med-Tech Industry*, 2016, Axendia Inc.

Building a culture of quality

The Case for Quality (CfQ), under the management of the Medical Device Innovation Consortium (MDIC), represents a unique forum for medical device stakeholders including the FDA, Med-Tech companies, healthcare providers and payer organizations to work together to foster a new culture of quality in the medical device industry. CfQ includes top officials from the FDA as well as leading experts representing a cross-section of the medical device industry, each committed to advancing product and manufacturing quality and ensuring that regulatory policy and practice are aligned and transparent.

“...one device manufacturer can meet FDA requirements and still make a poor-quality device whereas a second manufacturer may not comply with all FDA requirements and yet make a high-quality device”

Jeff Shuren, M.D., J.D.,
Director FDA's CDRH

CfQ aims to improve product quality for the benefit of patients by enhancing product design and manufacturing processes, better informing regulatory practices and changing the very nature of interactions between FDA and industry in relation to quality and compliance.

This new culture requires a paradigm shift where compliance is the baseline and improved product quality is the goal. This calls for a new approach to product design, manufacturing and regulation that drives the focus on product quality and patient safety. To support this cultural shift, CfQ stakeholders are working to identify and disseminate evidence-based, critical-to-quality practices across the medical device lifecycle that correlate to higher-quality outcomes.

Building on its shared commitment with industry, FDA CDRH is continuing to make Case for Quality a strategic priority for 2016-2017.⁸ The agency is working to identify policies and practices within the agency itself that encourage adoption of critical-to-quality practices.

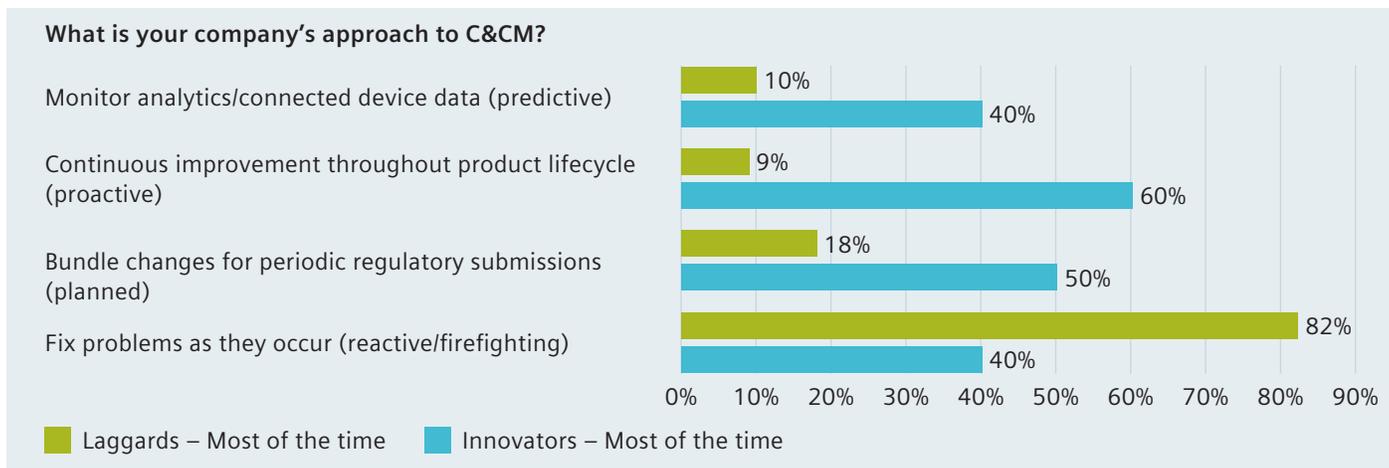
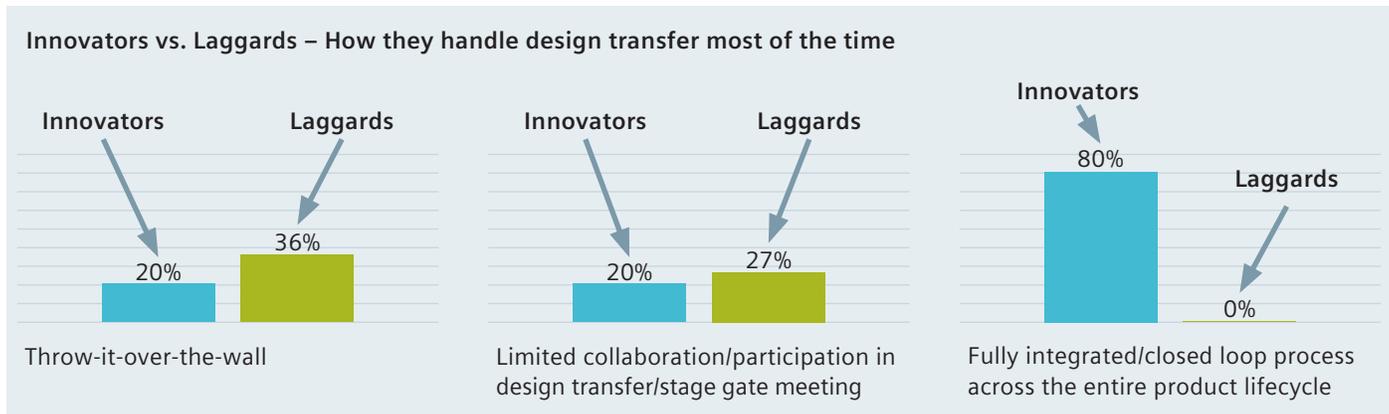
For more information about the Case for Quality movement visit <http://mdic.org/cfq/>

Closing the loop across the entire product lifecycle

Respondents to Axendia’s survey who strongly agreed that they have a closed-loop C&CM process were categorized as innovators; those who strongly disagreed were categorized as laggards.

Axendia’s research revealed that 80 percent of innovators stated that most of the time they handle design transfer with a fully integrated/closed-loop process across the entire product lifecycle. However, 20 percent are still using a “throw-it-over-the-wall” approach, and that number increases to 36 percent for laggards.

While innovators approach product and process change management as a proactive, predictive and planned activity, laggards are in a reactive/firefighting mode. Another tell-tale sign of an industry operating in the compliance era is the relatively small number of respondents who are monitoring analytics and connected device data. With the implementation of integrated systems in support of 21st-century manufacturing strategies, companies who operate globally would be better able to address issues before they occur.



Source: *The Future of Change and Configuration Management in the Med-Tech Industry*, 2016, Axendia Inc.

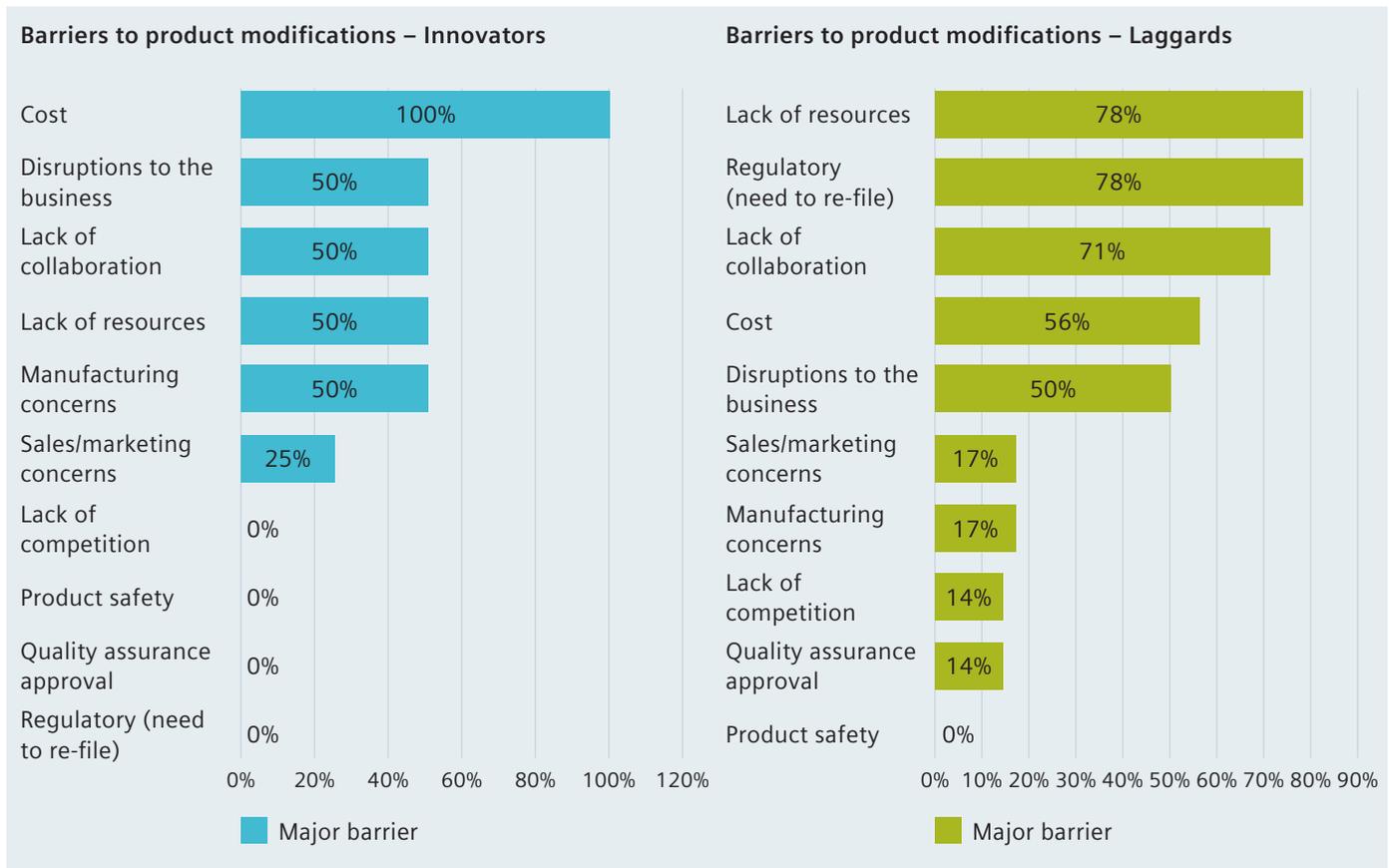
Overcoming the effect of regulatory inertia

The risk associated with product changes often drives Med-Tech organizations to avoid making product enhancements. When asked to classify major barriers to implementing product modifications, 79 percent of respondents listed regulatory (the need to re-file). Often, Med-Tech organizations find it difficult to distinguish between changes categorized as medical device enhancements versus those that would trigger a device recall.

While the FDA has issued guidance on this topic,⁹ many companies choose to err on the side of caution and

often bundle changes into a regulatory submission rather than make product modifications. This is due to the concern that if a change is considered a correction rather than an enhancement, it would lead to the real possibility that the existing product may be subject to recall – a very costly consequence.

The only barrier to product changes selected by a majority of innovators was cost – with 100 percent. However, not a single innovator identified regulatory (need to re-file) as a major barrier to making product changes.



Source: *The Future of Change and Configuration Management in the Med-Tech Industry*, 2016, Axendia Inc.

Recommendations and conclusion

It is clear that innovators understand the value of continuous improvement to ensure that their products remain safe and effective over their lifecycles. By building a culture of improved product quality for the benefit of patients, they are simultaneously enhancing their product design and manufacturing processes.

The contrast between innovators and laggards illustrates the gaps that exist between a closed-loop process and an open-loop process. Innovators, who focus on GBPs over GMPs, have implemented relevant technology infrastructures needed to close the loop on product quality. These include a MOM solution that ensures that the right products are manufactured in the best way possible and supports improved product quality and continuous improvement.

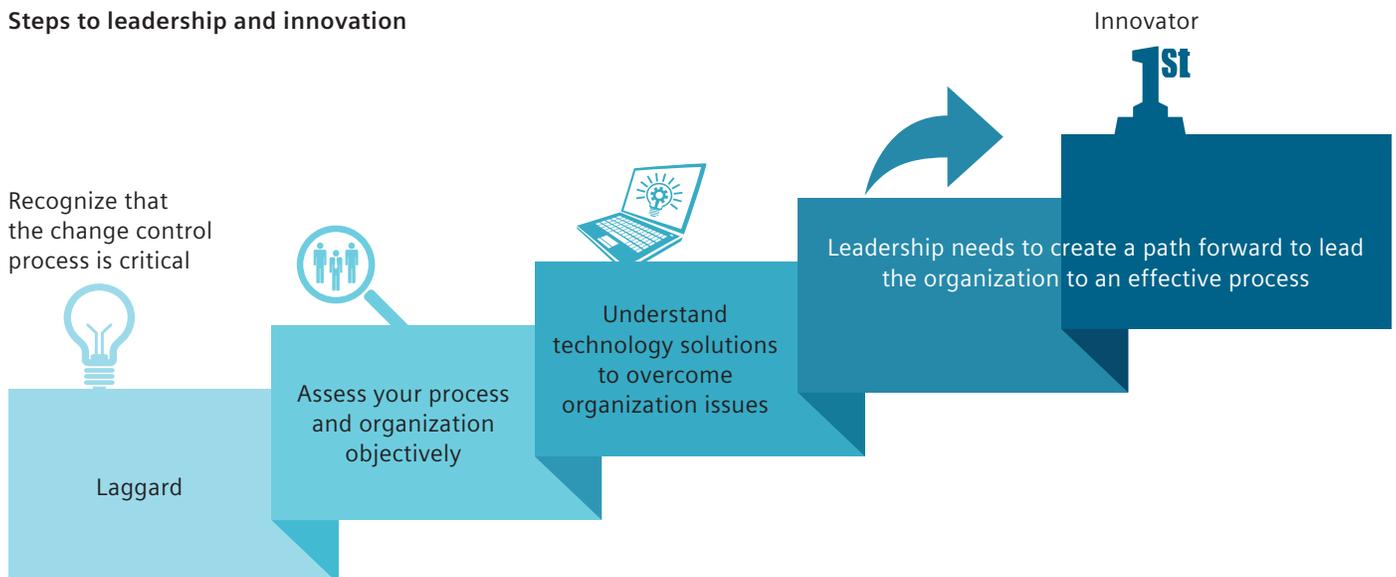
To become more effective, Med-Tech companies must gain the ability to connect decision loops across the total product lifecycle and from outside of their own walls. To this end, they must implement strategies, processes and technology that support a harmonized, integrated and closed-loop approach.

This will facilitate response to product, supplier and process changes as well as customer inquiries, adverse events and regulatory findings.

The implementation of a closed-loop C&CM strategy supports improved product outcomes while simultaneously enabling shorter innovation cycles that are driven by closed-loop integrated processes and systems that allow for real-time decision making based on intelligence.

The FDA is quickly recognizing that the industry's intense focus on compliance is a major contributor to rising recalls and regulatory action that ultimately can impact patient outcomes. In the same way that CAPA and procedural quality systems have dominated for the past 15 years, industry must now plan for and implement closed-loop systems. Integrated PLM and MOM solutions that support this approach should be considered core platforms for future C&CM success. A metrics-driven FDA will demand a smarter industry supported by 21st-century systems.

Steps to leadership and innovation



Source: *The Future of Change and Configuration Management in the Med-Tech Industry*, 2016, Axendia Inc.

Definitions

Throughout this study and white paper the following definitions were used:

Open-loop system: a system in which the desired output only depends on the input signal.

Closed-loop system: a system in which the desired output depends on the input and the feedback element.

Innovators and laggards: According to *Diffusion of Innovations*,¹⁰ innovators are those willing to take risks, have the highest social status, have financial liquidity, are social and have closest contact to scientific sources and interaction with other innovators. By contrast, laggards are the last to adopt an innovation. Laggards show little to no opinion leadership and typically have an aversion to change. Laggards generally tend to be focused on traditions.

To evaluate the impact of closed-loop change and configuration management processes, Axendia explored the difference between those survey respondents that “strongly agreed” with the assertion: that “we have a closed-loop system for change and configuration” from those who “strongly disagreed” with that assertion.

In this distribution, Axendia labeled respondents that strongly agreed as innovators and those that strongly disagreed as laggards.

Axendia defines **Closed-loop change and configuration management (C&CM)** as a collaborative and concurrent approach that allows medical device manufacturers to leverage information for better decision-making, thus yielding more effective, higher quality, and safer medical devices.

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