Closed-Loop Quality for Medical Devices

MANAGING QUALITY, RELIABILITY, AND RISK THROUGHOUT THE MEDICAL PRODUCT LIFECYCLE

A PTC WHITE PAPER BY: **Jeff Milkey,** *Life Sciences Fellow, PTC* | **Mike Prudhomme**, *Senior Product Manager, Windchill Quality Solutions, PTC*

Life sciences companies have poured billions of dollars into managing product quality both in pre-market and post-market product lifecycle phases. The results are grim. Overall recall rates demonstrate that such investments have not reduced the number of adverse events, including death and impairment, that patients experience. And the FDA reports that medical device recalls grew by 282% between 2010 and 2016, an annualized growth rate of 16%.[1]

For an industry that serves human beings at their most vulnerable, these statistics are especially alarming. Why do these quality issues occur?

One answer is the siloed nature of the life sciences industry. Too often the professional independence of the engineering, quality, and regulatory departments veers into isolation. In fact, survey data shows that fewer than half of medical device manufacturers can connect what they learn from the post-market surveillance data to the rest of the engineering lifecycle.[2]

We believe that one solution to this problem lies in adopting Closed Loop Quality. This is an enterprise-wide, cross-functional discipline to improve product performance, reliability, and safety over the course of a product's life. Our white paper provides insight into best practices for adopting a Closed Loop quality approach for life sciences companies and is based on the work we have done with world's leading medical device makers, systems integrators and life sciences consultants.

Executive Summary

Companies that have successfully adopted Closed Loop Quality share common actions:

1. They established a digital thread by migrating from document-based to digital pre-market submissions. This required replacing static and paper-based DHF and DMR records with configuration and version-controlled digital records.

2. They were then able to identify potential failure more systematically throughout a system and develop controls to minimize or prevent their occurrence or effects.

3. They gave the product design and development teams visibility into post-market surveillance data. These teams then could access Complaint, CAPA and Nonconformance trends and individual submissions in the context of the products and parts they were working on. Via the digital thread, engineers received insight they could use to develop product variants and new products.

4. They adopted a risk-based approach to product quality, such as integrated FMEA codification and analysis.

Introduction

It's no secret that today's medical device and life sciences manufacturers face multidimensional challenges as they strive for high product quality. A short list: an increasingly global workforce, a widespread network of contractors and suppliers, technical complexity, and a throng of talented fast-moving competitors. Disaster can result when quality falls victim to tempting 'work arounds' that appear to address these challenges.

We believe the solution is not easy, but it is simple. Quality must be managed consistently throughout the product development process using cross-functional collaborative methods. This way, quality information from one lifecycle stage is available to relevant processes in another lifecycle stage.

Closed loop quality is a series of best practices for managing product quality, reliability and risk using methods that are integrated into the product life cycle and visible to every person with a stake in product quality.

What is Quality?

The challenge of managing quality begins with its nebulous nature. What is quality?

Does "quality" mean a high degree of safety, proven product reliability, standout performance over the lifetime of a product, exceptional value to a customer, or the unique ability to meet a specific need?

For life science companies, quality is best measured by patient outcomes. Closed Loop Quality begins by identifying desired patient outcomes associated with the product. These outcomes are mapped to requirements, which in turn are mapped to specific characteristics that are tracked throughout the product lifecycle.

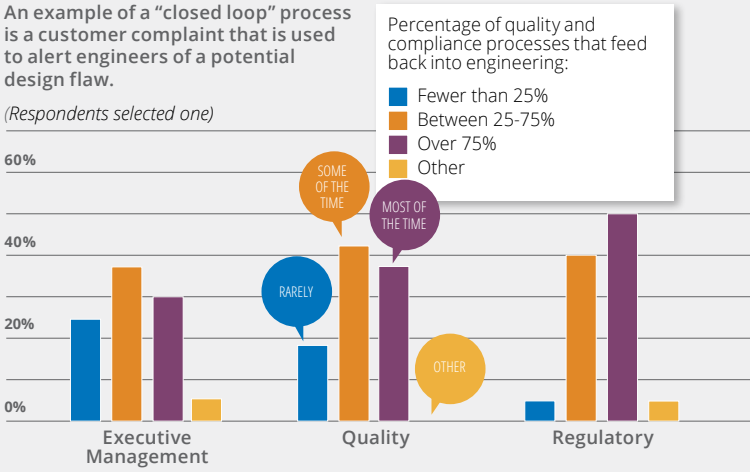
High-quality, high performing, reliable, and safe products not only boost a company's reputation, they save money in recalls, repair, replacement, maintenance, warranty, and other expensive post-market services.

The high costs of not addressing product quality for

How well does your organization currently "close the loop" from quality events to other engineering activities?

An example of a "closed loop" process is a customer complaint that is used to alert engineers of a potential design flaw.

(Respondents selected one)



Axendia Survey, "Building a Culture of Quality and Innovation in the Medical Device Ecosystem", 2018

life science companies can be measured in negative patient outcomes, including physical impairment or loss of life. Other negative outcomes include catastrophic product failures, cancelled programs, reduced profits, lowered consumer confidence, product recalls, repairs, high numbers of warranty claims, and legal liabilities.

What is Closed Loop Quality?

Closed Loop Quality is an enterprise-wide, cross-functional discipline that ensures that product performance, reliability, and safety are aligned with requirements over the course of the product development process and subsequent product life. It builds quality, reliability, and risk planning into the product lifecycle by aligning functional needs with product requirements, ensuring these requirements are met by specific characteristics, and tracking these characteristics systematically throughout development, testing, manufacture, fielded use, and service to ensure the product requirements are met at every lifecycle stage and product performance meets expectations.

According to an Axendia Medical Device Industry Survey, fewer than 40% of Medical Device Makers practice closed-loop quality.[2]

Ideally, outputs from each lifecycle stage, including analysis results, product failures, corrective actions, lessons learned, and best practices, are available to all stakeholders via objective evidence that is collected and managed at each design review. This ensures the continuous improvement of products both over the course of development and during next-generation product design.

A mature Closed Loop Quality process links together PLM, Quality, and Reliability systems and safety activities that take place across every stage of product development. In an ideal quality process one lifecycle stage informs the next and feedback from each stage is automatically fed into the other stages, creating a unified, holistic view of overall product quality.

Ideally, the closed-loop quality process will:

- Automate the workflow of quality information and feedback between product lifecycle stages.
- Enable cross-functional collaboration across multiple departments and teams responsible for product development, engineering, manufacturing, service, quality, and regulatory processes.
- Establish functional links between product requirements, product functionality, and testing activities at each lifecycle stage.
- Deliver complete management visibility into key dimensions of product safety and reliability at all lifecycle stages.
- Provide a fully documented history of product development. Enable integral quality reporting by harmonizing complaints management, CAPA and engineering change management processes.
- Improve product performance as it pertains to service with visibility to service records and data.

Why is Quality Management So Challenging?

The FDA has identified that, despite the regulations created to ensure high quality medical device products, observed quality outcomes of released products lag behind other industries and are trending worse. The basic technical problem for most medical devices is that quality metrics are not designed in to the product. While this is true for other industries, most other industries have greater ability to rapidly change the product after release.

A continuous improvement approach is more challenging in the medical device industry because any change to form, fit, or function requires re-approval from the FDA and other regulators. One of the many benefits—perhaps the greatest benefit of closed-loop quality—is the ability to bring a better product to market.

Let's examine root causes of poor quality: quality that is addressed too late; lack of accessible quality information, and fundamental misalignment of quality processes.

Quality Is Addressed Too Late, Separate from Innovation Cycle

The way most companies implement quality checks can best be described as "too little, too late, and silo'd." Without a clearly defined method to track a product's quality against its requirements throughout product development, quality checks happen too late in the development process to be effective. Another related problem is inflexibility. Over time requirements change and the ability for quality checks and balances to "go with the flow" is many times impeded by inflexible processes that make it difficult to loop back.

Quality Information Is Not Easily Accessible

Many companies implement multiple point solutions to manage product quality. These highly specialized, proprietary tools are typically limited to a single department or team. Within life science companies, product engineering, quality and regulatory departments frequently rely on disparate tool sets to manage quality. It is therefore not surprising that, when the time comes to make management-level decisions, the team is unable to reach a set of shared conclusions since a unified view of quality information cannot be easily obtained.

Even companies who are committed to providing transparent access to quality information find this impossible until they digitize product lifecycle data in the form of electronic Design History Files (DHF) and Device Master Record (DMR) records.

Consider that large life science companies may easily manage hundreds or thousands of unique products and millions of product parts. For these companies, a commitment to digital product lifecycle management is a prerequisite for associating a discrete quality event or quality trends with the appropriate product family, product and or part.

Quality Processes Do Not Work Together

When many point solutions are in place throughout an organization and used at various times during product development, the risk of misalignment is compounded. Because of their limited scope and proprietary nature, silo'd quality processes seldom communicate with one another. This can cause the time-consuming task of data entry to be replicated across several departments, resulting in a tedious, error-prone process.

Axendia Survey, "Building a Culture of Quality and Innovation in the Medical Device Ecosystem", 2018

"Lessons Learned" Are Seldom Reused

Research indicates that up to 80% of quality issues are repeat issues for which a corrective action has already been identified but does not persist.[3] This can be due to the corrective action not being formally recorded, or not being accessible in the context of the specific version of the affected product family, product and/or part.

The Virtuous Quality Cycle

Closed Loop Quality enables a structured approach to creating new products that builds on the quality intelligence acquired at each stage in the product lifecycle. In this way, innovation is made more efficient: rather than starting from scratch, the quality planning process is already equipped with a wealth of lessons learned and best practices already proven successful in establishing and sustaining product quality.

Feedback in the form of lessons learned is essential to supporting quality throughout next-generation product design. Through this feedback loop, best practices and lessons learned identified during risk and reliability analysis, product testing, design modifications, manufacturing controls, service, and fielded use can be amassed in a centralized information portal and subsequently used to "filter" a future product BOM.

Automated software processes can associate lessons learned with components, systems, failure modes, risk controls, and the like. These are then compared with the new product BOM throughout reliability analysis, service planning, and test development, saving time and supporting efficient, affordable innovation by automatically leveraging past experiences.

What's more, because innovation in the way of continuous product improvement occurs concurrently with product development throughout the lifecycle stages, more dramatic innovation is possible when it comes time to design next-generation products. Larger strides in innovation can be made during new product development because smaller steps toward quality were continuously made during the development of previous generation products.

Methodologies of Closed Loop Quality

Multiple methodologies are commonly used to perform quality, reliability, and safety-related analyses throughout the product development lifecycle from ideation through post-market surveillance.

Quality Planning

The ability to identify all functional needs of the product ahead of time and incorporate this information into each stage in the product development is key to ensuring product quality. With functional requirements of the product identified from every potential source—including The Voice of the Customer—product characteristics necessary to support these requirements may be identified and tracked to ensure they are being fulfilled. Ideally, this feedback loop persists as product requirements change in response to new market information or customer needs.

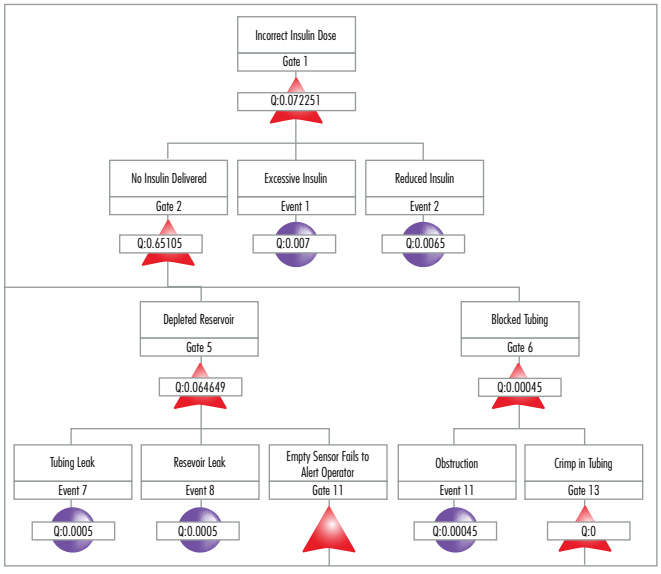
Quality planning yields immediate and long-lasting benefits. When done correctly:

- Design engineers will have criteria defining success
- Test engineers will know which characteristics to test for and what their minimum performance must be
- Manufacturing will know which aspects of the product must be controlled during production to ensure product safety and performance
- Service technicians will know which aspects of product performance to address during routine maintenance or repairs.

Quality Governance

Quality governance is the process of establishing and documenting process quality guidelines and standards. It also requires the management and auditing of these standards, to ensure they are being implemented correctly throughout the organization. Because product quality is closely linked to process quality, many companies seek not only to identify and correct product nonconformances stemming from internal and external sources, but also to establish processes that track, monitor, audit, and manage these internal and external nonconformances and the corrective actions used to address them.

For medical device makers, these process guidelines and standards conform to medical device industry directives like ISO 14971, ISO 13485, and 21 CFR Part 820 – which in turn are derivatives of more generalized ISO 9000 quality standards. In addition to providing for the intake, recording, and resolution



A Fault Tree Analysis provides a top-down, deductive analysis of risks in complex systems.

of internal and external nonconformances, quality governance provides a structured, automated, and repeatable internal process to advance these issues through a Corrective Action/ Preventive Action (CAPA) workflow to ensure they are addressed, corrected, and prevented in current and future designs. CAPAs may be tracked against the product BOM, advanced through management review steps, documented to establish an audit trail and/or meet compliance requirements, and advanced throughout the organization for supplier and training management.

Risk & Reliability Analysis

Risk and Reliability Analysis techniques are typically used by quality engineers to systematically identify potential failures throughout a system and develop controls to minimize or prevent their occurrence or effects. These fall into the subcategories identified below.

FMEA (Failure Mode and Effects Analysis)

An FMEA is a bottom-up analysis technique that identifies each failure mode beginning with the lowest-level components in the system, and examines the effects of their failures on higher levels of the system. It uses system hierarchy to trace the effects of failures up through the system in order to identify and categorize negative effects at the subassembly, assembly, and system levels.

An FMEA is an extremely flexible analysis tool that is used starting in the design stage of products and systems to identify and prevent or mitigate sources of safety risks and product failures. However, its reach also extends to the testing and manufacturing stages of product development due to its various types as well as to its powerful outputs.

Various types of FMEAs are used to identify failure modes, causes, and controls in light of the various functional requirements of the product, according to the specific components and assemblies in the system design, and in consideration of the product risks that could arise from manufacturing procedures.

Functional or System FMEA

A Functional or System FMEA focuses on the functions or requirements that a product is designed to fulfill. It identifies the required functions of the product, the ways in which the product could fail to meet these requirements–also known as failure modes–and the causes of each failure mode. This type of FMEA is used in the design stage of products and systems, is essential to quality planning, and is a key link to product testing due to its output–the Design Verification Plan or DVP (defined below).

Design or Component FMEA

Also known as a Piece-Part FMEA, a Design or Component FMEA is focused on part risk and reliability. It identifies the components, assemblies and subassemblies that make up a system in order to consider the ways in which they can fail and the effects that each of these failures can have on product operation. A Design FMEA can map to functional requirements indicated in the Functional or System FMEA. This makes it a powerful tool in an overall Closed Loop Quality solution because we are now able to connect product requirements with the parts that sustain them, the possible ways in which those parts can fail, and therefore the ways in which the product can fail to meet its requirements. A Design FMEA can also analyze the effectiveness of controls introduced to prevent part and functional failure. Important outputs from the Design FMEA are the DVP and, less frequently, Control Plans.

Process FMEA or PFMEA

A Process FMEA examines the ways in which manufacturing processes can affect device operation and product quality. It may also be applied to the way in which the tool is used, systematically identifying the consequences of improper use on device failure and/or potential hazards. The PFMEA is used to identify risks to part quality, and therefore product quality, that could be caused by the manufacturing process. The output of a PFMEA that is most commonly used is the Control Plan.

> Process FMEA proved itself as a design tool that can help identify and mitigate assembly errors before they ever occur" – ASME

Design Verification Plan, or DVP

This test plan may be produced as an output from a Functional FMEA or a Design FMEA. A DVP is used to validate the requirements of a system, and is linked to the design requirements specified in the FMEA to show whether or not that requirement has been met. It includes information about how the functional or component requirement will be met, including the specific tests, when they will be run and by whom, benchmarks for passing/failing the test, the test results, and whether the test was passed or failed.

Control Plan

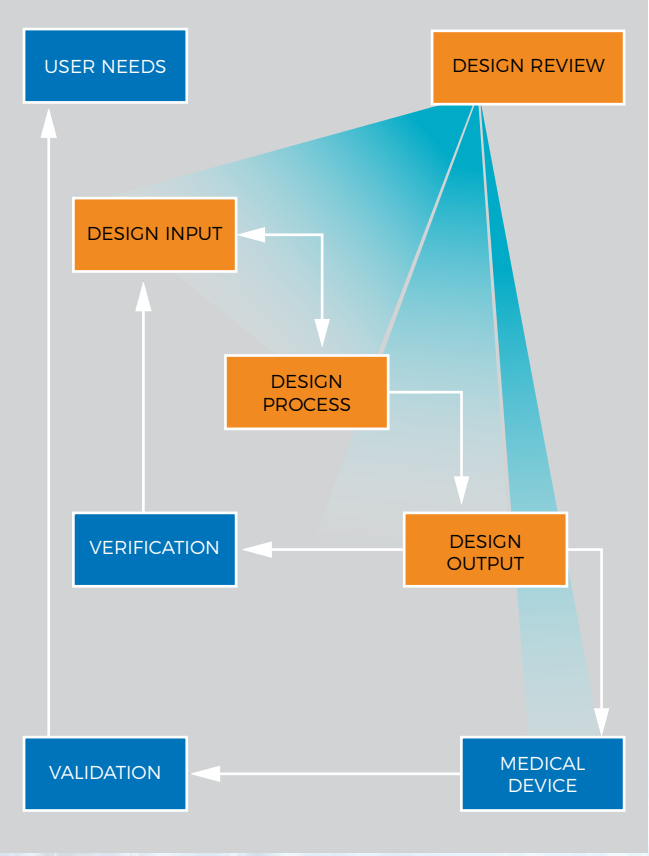
The Control Plan is a common output of the Process FMEA; because controls are implemented as part of the Design FMEA, it can occasionally be an output of the Design FMEA as well. Control Plans are used to specify and implement controls that prevent or mitigate the risks to product quality that may arise during manufacturing, as identified in the Process FMEA. For example, a Control Plan can define specific methods used to identify and minimize variations caused by the manufacturing process, ensure process control during manufacturing, and test or measure products prior to shipping to ensure specific requirements are met. The Control Plan is a living document that can be modified during manufacturing so that necessary feedback can be communicated to design or testing. This feedback can include manufacturing realities such as process limitations, machine tolerances, etc., or it may include best practices identified by manufacturing to support product quality.

Design Control

Effective design control is essential to ensuring that all team members follow a common and well governed product realization process. Life sciences leaders have discovered that PLM solutions extended with Design History File (DHF) and Device Master Record (DMR) capabilities can enable all team members to follow a common product realization process.

Effective design control allows teams to:

- Adopt a proven, consistent product realization process, preferably workflow driven
- Establish requirements that can be traced via the digital thread of PLM
- Drive the product realization process with a workflow via a product plan
- Auto-Generate accurate and up to date Design History Files (DHF) and Device Master Records (DMR)
- Leverage an integral change management system
- Understand status at regulatory milestones – and what has changed
- Manage mandatory design reviews and relevant data, action items and minutes associated with those reviews, at each gate of the process.
- Integrate with Microsoft Project to operationalize execution
- Manage design transfer to ensure accurate manufacturing BOMs



Document Control

Document management is one of the cornerstones of medical device and life science companies. Today most modern PLM systems can fulfill all of a company's document management requirements out of the box.

Comprehensive access control of all documents will protect valuable intellectual property and ensure employees only have access to the documents they are cleared to see. This includes setting access to latest released for the majority of users.

Companies today need to be able to classify documents via subtyping and also manage lifecycles, attribution and layouts. With these capabilities, it is possible to initiate processes by document type transparently and automatically.

Another mission-critical function within document control is training and training tracking. Modern PLM systems enable document cross references to people, roles, groups and organizations. The resulting matrixes are workflow enabled to auto-notify training coordinators and administrators when new documents are created that require training, documents are revised, team members leave roles and new team members join teams. People who are required to train are automatically notified with links to training in LMS systems with deadlines. These modern systems are also used for documents that require recurring reviews at specific intervals.

Another important function medical device and life science companies require is PDF publishing with watermarking and signature pages. Compliance when printing documents needs to be managed and advanced PLM systems are well suited for this task.

Companies usually have a large percentage of light touch, infrequent users of PLM systems. For this majority, a lightweight user interface is made available by many PLM providers. These lightweight user interfaces provide an intuitive user-friendly experience that promotes adoption and usage.

Post-Market Surveillance

A central function of Closed Loop Quality is to investigate the correlation between field failures and manufacturing, component, or design defects. A closed loop system can relay quality issues experienced during service and usage back to quality planning, design, testing, and manufacture in order to record and retain lessons learned and improve next-generation products. Service and use are therefore essential sources of feedback about the real-life quality and safety issues experienced by customers or service technicians, including previously unforeseen contributors to reduced product quality.

Nonconformance

Nonconformance management facilitates the handling of all associated activities in a regulated environment. Leveraging valuable internal information related to quality—including test results, manufacturing inspections, and supplier lots—nonconformance management enables initiation, evaluation, assignment, monitoring, and review of errors to ensure they are addressed in a closed-loop manner. Seamless integration with CAPA processes ensure that all reported nonconformances are addressed with corrective/preventive actions in a timely manner as part of a closed-loop, enterprise-wide quality management discipline.

Customer Complaints

Customer complaints provide for the intake, evaluation, and investigation of customer feedback for fielded products in a regulated environment. The ability to generate and electronically submit regulatory reports for the medical device field, along with seamless integration with CAPA, will ensure that customer complaints are addressed using a closed-loop process that is structured, automated, and repeatable.

CAPA

CAPA (Corrective Action/Preventive Action) enables a closed loop corrective action workflow to address the root cause analysis, corrective or preventive action identification, and resolution of product or process quality issues identified from internal or external sources. In addition to providing for the role-based workflow and management review of CAPAs. The ideal CAPA process provides role-based workflow and management review of CAPAs. It also supports monitoring, tracking, review and audit of system-wide actions, providing a single view into safety, manufacturing and performance trends over the lifespan of a product.

A mature quality management approach requires seamless integration of analysis to enable cross-functional quality activities, enterprise-level accessibility to support team collaboration, and a structured workflow to govern quality processes.

Automating Closed Loop Quality Processes

In a perfect world, medical device makers would have a complete, accurate picture of product quality as it develops and matures throughout the lifecycle. This information would:

- Unite quality-related development activities throughout the product lifecycle.
- Provide insight to stakeholders into the state of product definition at any time in the lifecycle—including engineering, product management, service, quality and regulatory stakeholders.

- Connect top management with critical information, for example using reporting and design reviews to make decisions that impact product quality, reliability, and risk.
- Help personnel across the product development process understand the quality impact of their respective activities.
- Reduce the cost of poor quality, and ensure more successful, safer and profitable products.

Mature quality practices connect quality-related activities across all lifecycle stages, including quality planning, early insight into quality, reliability, risk, cost planning, and the communication and reuse of lessons learned.

The following guidance will help your enterprise achieve clarity, visibility and agility as you automate your organization's Closed Loop Quality discipline.

The Link Between Agility and Quality

Early reliability and risk analysis can identify how well a product performs its anticipated function, and how safe it is, as early as the design stage–before a prototype is ever built. The earlier companies can determine these aspects of product quality, the less costly product changes will be. Conversely, the later in the development lifecycle changes are needed–after testing, manufacture, or, worse, after products have gone to market–the more costly they will be.

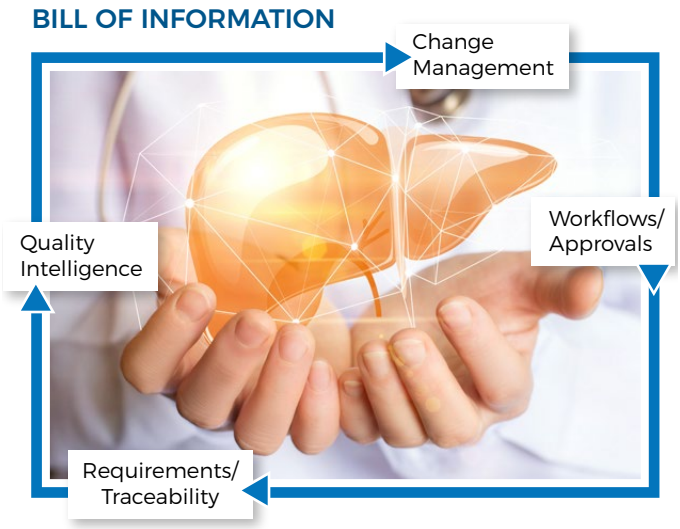
When companies break away from a linear approach to product development and expand the design phase, they not only reduce the possibilities of high-cost, late-state changes, they also increase innovation. A tolerance for "getting it wrong the first time" can be a better strategy as long as teams iterate rapidly and learn from the failures.[4]

Studies show that demanding that teams "get it right the first time" just biases them to focus on the least risky solutions.[4] In contrast, failures that are documented using a "fail early, often" approach serve the dual purpose of eliminating novel (but risky) ideas and documenting what not to try in future design activities. In the words of Thomas A. Edison, "the real measure of success is the number of experiments that can be crowded into 24 hours."

This type of progressive thinking conflicts with many companies' zero tolerance for failure and the Six Sigma methodology that strives for error free environments.

Recognizing that product development is a fundamentally different process than manufacturing helps companies improve the product development process, improving cycle times, product innovation, profitability and most importantly quality. A focus on early stage design will help decrease late stage discoveries and subsequent changes resulting in expensive and time-consuming solutions.

Fortunately, technical advances continue to reduce the cost and improve the accuracy of early-stage product experimentation. Advances in additive manufacturing, virtual reality and finite analysis in real time are accelerating company's ability to iterate rapidly.



The Expanding Role of PLM in Closed-Loop Quality

Increasingly, life science leaders recognize their PLM investments as an enterprise hub of product information supporting the disciplines of requirements and ideation, design, engineering, product management, quality, and risk and reliability. The reason? PLM is the definitive source of truth for product design information, including product versions, parts, configurations and Bills of Materials. Extending PLM to quality makes quality information actionable in the real world because

it is now linked to versioned products and parts. This aligns stakeholders through shared insight at every lifecycle stage. More importantly, it provides access to critical quality information at the earliest, requirements and design phases – when this information can have the most positive impact on product outcomes.

Choosing a PLM Solution

Choosing a PLM system is a complex undertaking. Your choice should support your product development business processes, preferred deployment architecture, and requirements for security, scalability, performance, interoperability, flexibility and maintainability. While it is beyond the scope of this white paper to fully explore selection criteria for PLM automation, below are the most important considerations.

Scalability

Whether due to acquisition or business growth, a PLM system that won't scale is a non-starter. When evaluating a PLM system, it is critical that the solution utilize a common database schema, business objects and process models. A sound and extensible architecture is mandatory for high scalability and availability without redundant infrastructure layers.

Deployment Flexibility

Another important consideration is whether to deploy on-premise or in the cloud. Companies that require on premise deployments today may very well find themselves moving to the cloud at some future date. Some PLM vendors require on premise deployment. When making enterprise decisions regarding PLM systems, be sure you have options.

Integration

Look for solutions that are open, extensible and interoperable with existing processes and technologies. No one software solution will likely meet all of your Closed Loop Quality needs and therefore the ability to interoperate will be key to success.

Accessibility

Enterprise-wide access via a web-based platform for all quality-related personnel, regardless of location, will help unify teams through a shared view of quality data. Dashboards that efficiently report high-level quality information for use by top management personnel will align executive decisions with fact-based quality metrics.

Structure

The ability to fine-tune and enforce a standards-based methodology to capture quality issues will help make your Closed Loop Quality solution both proscriptive and practical. Look for highly structured workflow capabilities to ensure the communication of quality issues to responsible personnel. Solutions that automate closed-loop quality and enable a digital thread across engineering, quality and regulatory teams will help ensure rapid response and access to lessons learned.

About Windchill Product Quality

Windchill Product Quality is PTC's leading PLM and closed-loop quality solution purpose-built for life science, medical device and bioscience innovators. It extends the industry's leading PLM platform with best-practice processes harmonized for ISO 13485, EU MDR, and FDA TPLC and 21 CFR Part 820 standards and regulations. Available in both pre-validated Cloud and on-premise deployment models, Windchill Product Quality helps teams:

- Unify engineering, quality and regulatory teams with a shared, product-centric view of the medical innovation cycle
- Adopt best practices for Design and Document Control as an integral part of your product lifecycle
- Improve quality with closed-loop Risk, CAPA/SCAR, Nonconformance and Complaint Management
- Get up and running quickly with SaaS simplicity and accelerated software validation

For more information please visit: http://www.ptc.com/industries/healthcare/windchill-product-quality

Footnotes:

[1] FAERS database (FDA Adverse Event Reporting System) Source: https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm

[2] Axendia, Drive a Culture of Quality within the Medical Device Manufacturing Ecosystem, 2018.

[3] Nick Van Weerdenburg, "Can We Improve Continuous Improvement?", Quality Digest, 2009.

[4] Thomke, Stefan, and Donald Reinersten. "Six Myths of Product Development." R1205E. Harvard Business Review 90, no. 5 (May 2012): 84–94.

J11928–Closed-Loop Quality for Medical Devices–EN–1018