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The Future of Risk Management in Medical Device

How to Leverage a PLM Backbone and Machine Learning for a Modern, Closed-Loop Approach to Risk

Medical device manufacturers must follow a highly structured and rigorous risk management process, mandated by the FDA, EU and ISO. To track risk-related data over the entire product lifecycle, companies currently use a variety of risk management solutions, from sophisticated software packages to simple spreadsheets and shared drives.

Given the increased regulatory rigor, it's more important than ever to have a closed-loop risk management program built on an automated and integrated data management tool that tracks risk over the entire product lifecycle. This means closing the loop to integrate risk data with a global product lifecycle management (PLM) solution that acts as the backbone of product data and process governance.

The challenge – implementing global PLM is not easy. Getting to an ideal end-state can take years. **But for companies considering (or part way through) a PLM implementation, closing the loop for risk management should be addressed simultaneously.**

Machine learning and analytics can be leveraged here as well, helping to analyze risk and quality data to minimize post-market problems, predict outcomes and even prescribe actions to prevent future quality-related issues.

Layering advanced analytics on top of structured quality and product data stored in PLM can help companies move from corrective risk management to predictive risk management, speeding time-to-benefit during a PLM implementation and greatly extending the value. Machine learning can also be used to verify the risk controls are working correctly, improving the safety and efficacy of the products themselves.

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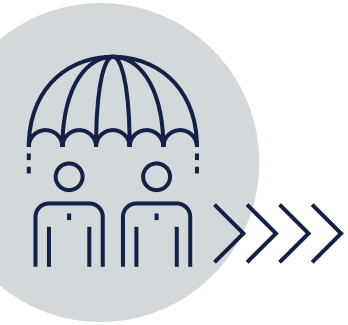


Regulatory requirements continue to evolve and get stricter all the time. While this makes it more important than ever to effectively and efficiently manage risk, the need is not new. In fact, the word 'risk' is used multiple times in 21 CFR Part 820. Since Part 820 was released, regulators and standards bodies have put increasing focus on risk management and the science behind it. Experts worldwide have since recognized ISO 14971 as the standard by which medical device manufacturing companies should operate.

Today's Risk Management Challenges

Despite the increased focus, leading risk management practices are not implemented routinely in PLM due to more foundational elements like change management, BOM management, regulatory reporting and quality management taking priority. This is a missed opportunity for the industry, because those that can do this well will generally be ahead of most of their peers. Even for companies where sophisticated risk management is implemented, information is trapped in siloed systems, which makes it difficult to analyze, escalate and resolve safety issues.

Without these capabilities, there's no way to evolve to more mature risk management by predicting and avoiding these issues. Things are now more challenging from a business governance perspective as well. More than ever, businesses are acquiring each other, which makes the enterprise technology landscape for large companies complex and broad, even for basic company functions.

This often means that risk management capabilities are out-prioritized as a key building block for a global PLM system, even as regulations get tougher and more rigorous.

Moving Forward: The Benefits of Emerging Technology

Today, companies are trying to balance new technology with sound process governance. Emerging technologies like machine learning and advanced analytics have evolved over recent years, becoming easier to use and understand. Here's how recent technology improvements drive more rapid, comprehensive business value:

1. The maturity of risk-based capabilities means that usability, data entry and traceability mapping is easier than ever
2. The emergence of role-based apps enables key users to focus on specific tasks rather than requiring them to learn a more complex solution like PLM
3. The availability of smart connected systems or mashups means that it's not necessary to immediately migrate all data to one centralized system before making progress - mashups bring data together from multiple systems
4. Predictive analytics and artificial intelligence allow users to draw deep insights from well-structured risk data, especially when integrated with a broader ecosystem of quality and regulatory information

Benefits of Closing the Loop with Risk Management in PLM

Risk Management 101: Don't Forget the Basics

ISO 14971, ISO 13485, ISO 9001, FDA Case for Quality, EU MDR and several other regulations and standards have been updated to incorporate risk-based approaches beyond product realization.

Risk is considered in the context of the safety and performance of the medical device and in meeting regulatory requirements. Many of these standards and regulations place greater emphasis on risk-based quality management systems (QMS) throughout the supply chain and product lifecycle, as well as device usability and post market surveillance requirements.

It's become critically important to prove safety and efficacy based on actual post market surveillance data. Implementing a closed-loop QMS with direct feedback to product development teams drives significant benefits to product quality and reduces the cost of poor quality.[3, 5] Companies close the loop when they use Harm, Hazards and Failure Mode and Effects Analysis (FMEA) risk codes to validate that product changes are still applicable during post market stages.

Leading medical device manufacturers are using FMEA, 5-Why and Hazard Analysis as their main risk management techniques.[13] They integrate risk data, regardless of source, into their PLM solution to harmonize design control, process control and post market surveillance components. This supports the regulatory emphasis on improved trending, management review and escalation of risk management-related issues after release to manufacturing and the market.

Leading Practices for Integrating Risk with PLM

Before companies begin to integrate risk management into their core PLM system, they must better understand the context of risk management and how risks are first evaluated. This leads to appropriate controls to eliminate or reduce the overall safety risk, because those controls are verified and validated as appropriate during the entire product lifecycle (concept, development, release to manufacture, post market and obsolescence).

Using the following ISO 14971 illustration, companies can align the organization with the four phases of risk management: definition, analysis, evaluation and control.

PHASE 1 Define Acceptable Risk	**Step 1. (ISO 14971) Risk Management Plan:** Define acceptable & unacceptable levels of risk
PHASE 2 Identify and Analyze Risk	**Step 2. Risk Analysis:** Identify risk Estimate risk level (a quantitative process)
PHASE 3 Evaluate Risk	**Step 3. Risk Evaluation:** Evaluate estimated level of risk for acceptability/unacceptavility based on Risk management plan
PHASE 4 Control Risk and Monitor Effectiveness of Controls	**Step 4. Risk Control:** Analyze control options, implement controls, evaluate residual risk, risk/benefit analysis, review effects of controls, review completeness
	Step 5. Overall Residual Risk
	Step 6. Risk Management Report
	Step 7. Production and Post-Production Monitoring

The Risk Management Plan

During the initial stages of product development, medical device manufacturers can store the risk management plan in PLM, along with design, supplier and process information. Collectively, this synergized data can be used to more efficiently manage product registrations, governance procedures and design history files.

The risk management plan should describe:

- Scope of the risk management activities based upon the product risk classification and distribution channels
- Intended use of the product(s)
- All risk management activities planned throughout the product lifecycle
- Roles and responsibilities
- Criteria for a product's risk acceptability and risk control measures
- How post-production info - which includes nonconformances, audit issues, complaints, corrective and preventative actions (CAPAs) and supplier corrective actions (SCARs) - will be captured and fed back into risk management activities for the product

Managing Risk and Reliability in PLM

All risk and reliability documentation for fault tree, FMEA, reliability, etc. should be output in the tool of choice and then managed in PLM. This provides flexibility in the approach, and value is not dependent on how sophisticated (or not) current risk and reliability solutions are.

Ultimately, the risk acceptability matrix (example at right) defines the manufacturer's probability of occurrence ranking versus severity of risk, graphically highlighting acceptable, unacceptable or review regions.

	Severity				
Probability (of occurrence of harm)	Negligible	Minor	Serious	Critical	Catastrophic
Frequent	MEDIUM	MEDIUM	HIGH	HIGH	HIGH
Probable	LOW	MEDIUM	HIGH	HIGH	HIGH
Occasional	LOW	MEDIUM	MEDIUM	HIGH	HIGH
Remote	LOW	LOW	MEDIUM	MEDIUM	MEDIUM
Improbable	LOW	LOW	LOW	LOW	LOW

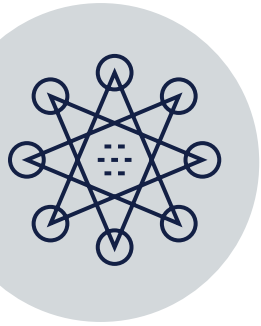
Once the risk analysis is complete, design and process FMEAs can be stored in the PLM system to ensure that they can be shared amongst different products and that they are available to use as part of the post market surveillance process. This needs to be harmonized between risk evaluation (phase 3) and control (phase 4).

In general, there are two approaches here: simply storing the risk acceptability matrix in PLM as a document or managing it as a set of structured data. The latter is more complex but provides a much finer level of control and can be useful in driving better business logic, control, automation, and traceability. It also enables better decision making based on advanced analytics and machine learning, especially when there are multiple data sets that also contain historical data.

The leading practice recommendation is to invest in a PLM system that allows management and/or importing of Harm, Hazard and FMEA codes so they can be used to prioritize corrective action in a closed-loop fashion.

With this data in PLM – and therefor available in a global architecture – risk controls can be put in place and compared to the residual risk (which is almost always a factor) in order to create a safety net for unpredicted risks. Some manufacturers do this with documents and some use control plans as part of their ERP and/or MES solutions. As a leading practice, this should be harmonized with the design, process and supplier controls in the PLM system. This is much easier if the more sophisticated approach to risk data management is taken (i.e. liberate from a document into structured data).

Leveraging Machine Learning for Predictive Risk Management and Control Verification



By leveraging descriptive and diagnostic analytics for all this rich data, companies can compare emerging issues with the risk matrix to provide engineering teams with real-time visibility into post-production quality and performance.[15] Taking this further, predictive analytics can be used to detect design or process failures before they can occur, and prescriptive analytics can even recommend preventive actions. While descriptive and diagnostic analytics have been around for a long time, the ability to predict and prescribe is newer and much more impactful.

Many medical device manufacturers are making moves to capitalize on the Internet of Medical Things (IoMT) and smart connected products, and to use predictive analytics to improve healthcare outcomes, driving huge business value.

When FMEA, 5-Why and Harm Hazard Analysis are managed in the PLM architecture, companies can compare expected versus actual outcomes. Product and process FMEAs can be associated with audit issues, nonconformances, complaints, CAPAs and SCARs. They can be compared to the critical to quality (CtQ) design and process characteristics to determine if there are any new failure modes present. Any systemic or high-risk failure mode that violates the risk acceptability matrix can be immediately prioritized for corrective action. Combining leading practice risk management techniques in PLM with machine learning can synergize the benefits of a closed-loop quality system.

By leveraging machine learning for all this rich data, companies can compare emerging issues with the risk matrix to provide engineering teams with real-time visibility into post-production quality and performance.[15]

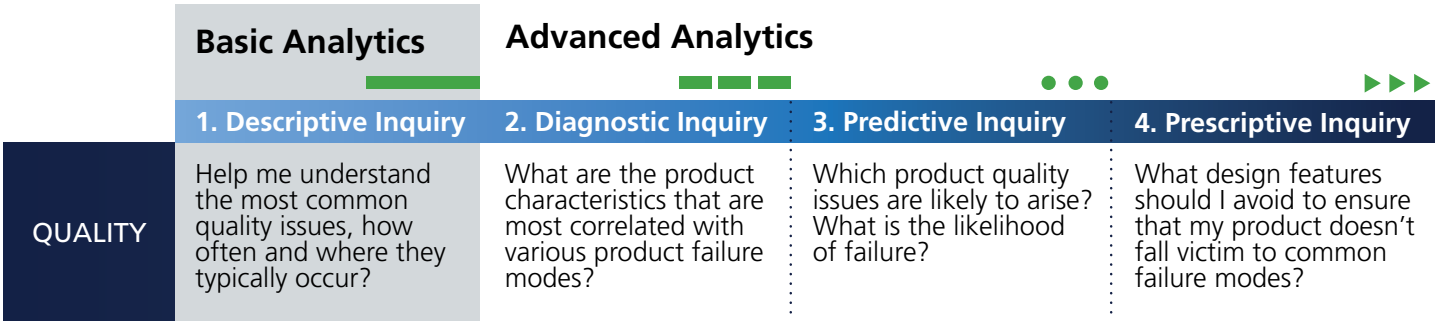
Predictive analytics leverages machine learning to apply advanced analytics to data generated from connected medical devices. It empowers better decision making based on data from medical grade wearables, connected imaging devices, and monitoring devices connected via the IoMT. The insights generated by linking connected medical device and health data sets can play a key role in helping health systems to reduce costs and improve quality, identify populations at risk, connect with consumers and better understand performance.[16] It will be incumbent on medical device companies to take advantage of these forms of artificial intelligence, combined with IoMT, in order to reduce risk and avoid patient harm.

An Advanced Analytics Example

There is no doubt that advanced analytics will play a key role in synergizing efforts throughout the ecosystem of buyers, payers and manufacturers of medical device products. This supports the industry transition from 'sick care' to 'well care' and outcome-based reimbursement models.

The graphic below shows the types of quality-related questions a manufacturer can readily answer with an application of advanced analytics called product lifecycle intelligence (PLI). Maturity moves from left to right, starting with the most basic understanding of what happened (descriptive), why it happened (diagnostic), what will happen (predictive), and what recommendations will optimize future outcomes (prescriptive).

It's important to note that PLI can drive data-driven insights to answer similar questions for other business functions, including R&D, manufacturing and supply chain.



Here's an example. A patient with a heart condition uses a smart connected wearable device (enabled by IoMT) that tracks real-time analytics to support closed-loop healthcare. The patient, the manufacturer and the healthcare provider all receive real-time information to make better risk management decisions and improve patient outcomes.

With thousands of connected heart monitors in the field, we can see our four types of analytics in action. Descriptive analysis shows that the data is coming back intermittently, and a diagnostic inquiry determines that this is due to poor fitting of the device, most commonly in young children. A predictive inquiry indicates that signal quality is likely to get worse, or at best to remain intermittent. Prescriptive analysis recommends sending an alert to all three parties – patient, manufacturer and provider – that it's a priority to check the fit of each patient's device.

And the story doesn't end there. With a connection between these analytics and PLM data, the manufacturer can see that failures in this 'poor fit' category do not correlate with what was predicted in the FMEA (there's a high incidence in the field, while the FMEA says there's a low likelihood). The closed-loop system can trigger a CAPA request process for consideration in PLM, which forces the manufacturer to review the entire data set. The manufacturer can then issue a change to the product that results in better fitting monitors for children.

The Ideal End State: What Closed-Loop Risk Management Looks Like

Prevention is the key to reducing risk, lowering the cost of poor quality, and increasing the safety and effectiveness of medical device products. It's usually better to implement a preventive action versus a corrective action as part of a CAPA process. Closed-loop risk management in PLM enables these preventive measures and lowers overall risk.

To get to this end state, the preferred approach is to include design features and process controls to prevent events that lead to safety-related issues. Based upon the level of risk posed, other approaches may also be appropriate.

Here are three safety risk control system strategies *(in order of preference):*

1 Design for Minimal Risk

With this strategy, the system design encompasses principles that eliminate or minimize the potential for safety risk. Companies use a PLM system with integral QMS and post market surveillance risk-based info. This is the most complete closed-loop methodology for designing out previous failures, safety issues and nonconformances.

2 Protective Measures

If a safety risk cannot be eliminated or adequately reduced through design techniques, it should be reduced with protective safety design features or methods. This system strategy detects safety-related conditions and produces a warning signal to alert medical personnel. In some cases, audio and visual alarms may be appropriate for the operational environment.

3 Developing Labeling, Operational Procedures and Provide Training

Labeling and training should be used as a last resort if the two methods above won't work. In this strategy, standard operating procedures (SOPs) are applied to tasks that have potential safety impacts and require training and qualification of operations personnel. The use of 3D CAD and augmented reality can significantly increase the first-time right manufacturing rate as well as assembly efficiency gains.

Closing the Loop with a Safety Risk Management Report

According to the certified biomedical auditor handbook, the results of the risk management process are to be provided in a safety risk management report.

The report should provide the following data:

- Identification and description of the safety risk
- Risk control requirements
- Severity of risk
- Probability of risk
- Estimation of residual safety risk
- Mode of risk control (software, hardware, labeling, etc.)
- Method to verify risk control measures
- Competitive product risks and failures[18]

This data is typically split across multiple siloed systems. **With PLM at the core, and with enabling digital technology that can pull data from multiple systems, companies can more quickly and easily aggregate accurate reports. Advanced analytics can then be leveraged to understand key insights that regular reports don't expose, such as which features or data influences specific goals the most.**

The Journey to Closed-Loop Risk Management

According to the FDA, despite the regulations created to ensure that high quality medical device products are produced, the observed quality outcomes are not good as compared to other industries and are trending worse.[17]

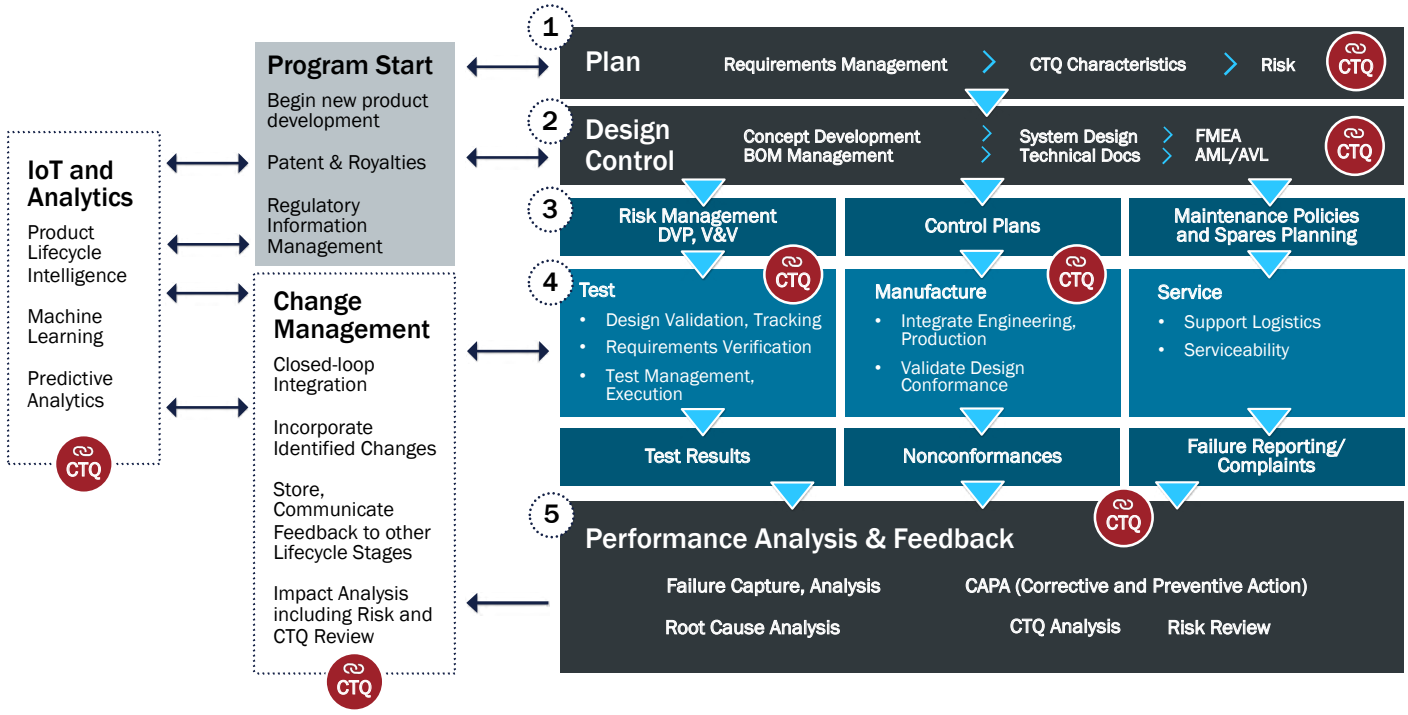
The basic technical problem that makes this difficult is that quality metrics are not designed into the medical device product development process. This is mostly because of the industry's traditional use of paper-based compliance. Companies in other industries may be paper-based too, but they can make more rapid product changes after release. This continuous improvement approach is much more difficult in medical device because any change to form, fit or function requires re-approval from the FDA and other regulators.

Every medical device manufacturer needs to implement a program for evaluating device performance after it has been released for manufacture. The evaluation program should assess customer complaints for possible safety relevance including:

- Whether previously unrecognized hazards are identified
- Whether the original risk assessment it still valid or not
- Whether estimated risk from the safety hazard is no longer valid

The ideal, closed-loop solution shown below focuses on connecting predictive failure analysis in requirements, early stage design, detailed design and manufacturing processes to generate a quality path for the design. This is done using FMEA outputs directly against CAD models to identify and predict the way the product could fail and its harm / hazard impact, and then uses that information to generate the CtQs, design verification plan (DVP) and control plans. These failure modes are used to monitor post market surveillance issues which should be integral with the PLM artifacts. When failures are observed in the field, these are immediately visible to the entire enterprise, providing vital information and feedback to engineering, manufacturing and procurement.

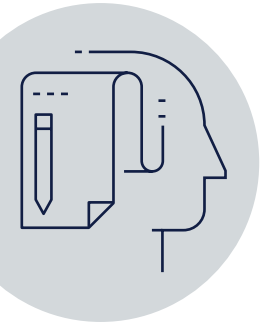
Closed-Loop Risk Management & Tracking of Critical to Quality Characteristics



Today's most innovative companies are using role-based app connectors, along with IoT and analytics, to help enable this closed-loop vision and create a competitive advantage over traditional risk management methods.

For now, these tools can be a competitive advantage, but they will soon become expected and enforced by regulatory bodies as an additional way to improve patient safety.

Getting Started with a Pragmatic Approach



A comprehensive safety risk management program is essential, and doing it right can result in more effective design control decisions along with reduced maintenance costs, regulatory risk and liability. With early identification of safety risks, companies can also support a more focused program for verification and validation activities.

Current risk management system maturity is irrelevant. Companies must harmonize risk management data with PLM processes and data, whether they use document-centric tools like Microsoft Word, Excel and PowerPoint or more sophisticated solutions like automated risk and reliability software.

Emerging technology like advanced analytics, machine learning and role-based apps can be layered in, moving companies from corrective risk management to predictive risk management.

All companies want to better understand, balance and quantify risk when bringing devices to market, in turn optimizing the safety and efficacy. **The journey to closed-loop risk management requires a pragmatic approach with a roadmap that leads to more refined levels of automation over time versus a big bang approach. With this approach, value can come early and often throughout the journey – not just at the end.**

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