A DATA-DRIVEN APPROACH TO QUALITY RISK MANAGEMENT

Going Beyond Compliance to Boost Quality for Medical Devices

Honeywell

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MANAGEMENT SUMMARY

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The international medical device industry has enjoyed tremendous growth. This growth has driven innovation for complex medical devices that have broadened the treatments available to patients with complex diagnoses and other conditions.

For example, minimally invasive procedures have provided medical benefits to patients such as less bleeding, trauma, and scarring compared to invasive or open procedures and surgeries. Robotic and navigation-enabled surgeries have improved trajectory and depth visualization for surgeons, resulting in reduced soft tissue damage and reduced pain for patients. Innovations in instrumentation and implants have provided effective treatments and corrections for complex spinal deformities.

These innovations have increased the complexity in how medical devices are designed and manufactured, while also increasing the diversity in usage environments of those same complex products. Alongside this growth and innovation has come the increasing reports of serious adverse events.[1] In fact, serious adverse event reports have outpaced the medical device industry growth since 2001. Further, over half of all medical device recalls have been due to design flaws and manufacturing issues of medical devices.

There has also been an increasing transparency into comparative quality between medical device manufacturers, including an increasing media focus on medical device quality.[2] The medical device market rewards manufacturers who have higher perceived quality, such as less recalls and higher achievement of benefits. "In the past decade, an average of one company per year has seen a 10 percent drop in share price after a single, major quality event (e.g., a major product recall)."[1] This increasing transparency of quality has strongly influenced buying choices across the industry by healthcare providers and by patients[2] , thus making medical device quality not only a regulatory expectation, but one that differentiates one medical device manufacturer from another.

To systematically reduce harm to patients and users, proactively detect signals and trends, and continuously improve quality and safety of medical devices through real world evidence, quality risk management must successfully integrate risk communication throughout the quality management system.

Alongside this integration comes the benefits of fast quality decision making with proactive solutions for medical device professionals. This paper provides insights into the methods and benefits of digitally integrating a quality risk management program to the quality management system.

While the contents of this paper reference international standards and regulations that are specific to medical devices, the basic principles of quality risk management being integrated throughout the quality management system are ones that can be employed by any manufacturer, including manufacturers of pharmaceuticals, diagnostics, and other medical products.

RISK MANAGEMENT: TOUGH AND GETTING TOUGHER

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New regulations are bringing more scrutiny from regulators on the risk management processes for medical devices and combination products. The European Union Medical Device Regulation (EU MDR) and ISO 14971:2019 requirements are bringing the full burden of risk management to medical devices and combination products.

Risk management in the new era is a big undertaking. It spans all lifecycles of product development and means tracking practically every system and process in your enterprise, including:

- Product planning, design, and changes
- Manufacturing activities
- Clinical evaluation plans and reports
- Regulatory submissions and labelling
- Post-market surveillance

And to be effective, all your risk management efforts must be interconnected.

Information must be handed off between departments in a way that keeps complexity from leading to confusion. These teams include personnel from quality, regulatory affairs, clinical affairs, R&D engineers, manufacturing engineers, distribution and supply chain personnel, and many more that all speak about similar topics in different ways. It's a lot to ask of cross-functional teams from every part of your organization to coordinate so much data frequently enough to be useful when they are working in siloes.

"Both ISO 14971 and 21 CFR Part 820 take a total life cycle approach to management of risks associated with medical devices and expect that manufacturers will incorporate post market data into their device risk management process, including new and changes to existing risks identified after the device is on the market. " – FDA[5]

WHAT YOU NEED FROM RISK MANAGEMENT

- Reduce harm to patients using your products
- Detect signals and identify trends for effective root cause analysis and decision making
- Improve quality and safety continuously
- Ensure acceptable quality
- Resolve process and product deviations and nonconformances quickly
- Expedite approvals and market authorization
- Comply with standards and regulations
- Minimize the resources required for all of the above

DO THESE SOUND FAMILIAR?

The constantly evolving expectations of risk management over the years have resulted in many manufacturer's developing a complex, ineffective risk management processes. These changes span over three decades and include the European Directives (MDD, AIMDD, IVDMDD), ISO 14971-1:1998, ISO 14971:2000, ISO 14971:2007, and EN ISO 14971:2012 with content deviations. Most recently, the EU MDR and ISO 14971:2019 have added to the burden of manufacturers staying on top of changing regulatory expectations for medical device risk management.

Compliance with the EU MDR and ISO 14971:2019 from planning to production and post-product information collection requirements will take a lot of resources and will fail to deliver high quality if your company relies on outdated risk management methods.

Old, manual ways of doing risk management are simply not good enough anymore—they will consume too many resources, slow down decision making, and not deliver the quality improvement and risk reduction that you need to compete.

HERE ARE SOME OF THE HALLMARKS OF RISK MANAGEMENT THAT JUST ISN'T GOOD ENOUGH TO KEEP UP:

Standalone failure modes and effects analysis that are tracked in manual record systems such as Word or Excel

Risk scoring in different parts of the product lifecycle is subjective or undefined, leading to variable outcomes

Risk management takes significant time from quality, R&D, operations, supply chain, distribution, clinical, and regulatory affairs staff

Risk review is done quarterly or monthly instead of continuous signal analysis and trend detection

Risk analysis is linked manually to the quality management system—or it isn't linked at all

Risk analysis, analysis, evaluation, control, review, and post-market decision making all start from scratch for each new product and process

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SIGNS OF A WEAK LINK BETWEEN RISK MANAGEMENT AND THE QUALITY MANAGEMENT SYSTEM

Using Different Risk Terminology across the Quality Management System

The medical benefits associated with use of a medical device include an inherent degree of risk, and the core of risk management is ensuring that patients and users have the freedom from those risks that are considered to be unacceptable.

To do this, the Risk Management process includes data and inputs from many various highly specialized teams. But effective risk management is hard to do when different teams use different terms or different standards for the exact same problem. This makes it difficult for teams that are tasked with relating complaints and CAPA with risk management data as part of understanding significance and spotting signals and trends to act quickly when a significant failure occurs or occurs unacceptably frequently.

If the terminology that your risk management team uses to describe what failures are and how severe they are is different than the terminology your complaint handling team uses, you may think you need to take action when you really don't. Or worse, you may not take corrective action, or issue a product recall, when you really need to.

It's vital to use consistent severity and occurrence definitions to ensure that residual risks in your risk management file align with how they are documented in your post-market surveillance processes. If you can do that, it becomes very easy to determine if an observed risk has already been evaluated for acceptability in the existing risk management file.

COMPLIANCE CORNER:
EU Medical Device Regulation (Regulation EU 2017/745) – Annex 1 GSPR 2 Evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; and if necessary, amend control measures.

NOT USING CONSISTENT AND PRECISE NUMBERS

Without quantitative occurrence rates, you cannot evaluate trends to identify if you need to take corrective action to reduce risk.

All too often, a risk management file will use vague descriptors for expected or acceptable failure frequencies, such as "remote" or "frequent," without any quantitative numbers or rates. This leaves the teams conducting post-market surveillance scrambling to determine whether the actual (observed) risks are acceptable or not acceptable. Are the frequencies of the risks that they're seeing the same as those considered acceptable in the risk file, or not?

If risk management doesn't make decision making easy once the product is launched, what's the point of it? How do you justify taking a risk-based approach if your risk management file doesn't give you sufficient information and decision-making criteria to actually manage risk when real world evidence is received?

If the prediction in a risk file is a precise failure frequency of 1 in 100 times at a precisely defined severity, and post-market surveillance reveals a frequency of 1 in 250 times at that severity, then it is instantly clear that no immediate correction or corrective action is needed. This doesn't just lead to faster action on patient safety, it saves staff time and other resources.

SILOED OR PERIODIC TREND REVIEWS

A long-standing practice for many medical device manufacturers is to have a recurring review board meeting, whether it is captured within Management Review, or a product specific meeting, to collect data and analyze trends of products through complaint rates or nonconformance rates. Quality teams wait until those board meetings to collect data. If these review boards are quarterly, how long is an adverse trend occurring before it is brought to the attention of subject matter experts and management? In this gap of data collection and analysis, whether it is a month or a quarter, time is being wasted to react to these trends. Furthermore, the reviews of these trends are limited in scope due in part to data management limitations, analysis limitations, and resourcing of quality teams, resulting in less data being available to make critical decisions on quality and safety.

If these describe your risk management efforts today, your efforts are not sufficient—and they may be hindering your ability to manage risks of your products as effectively as possible.

Many companies are capable today of doing risk management just well enough to stay compliant most of the time, fending off warning letters and adverse audit findings but keeping their heads above water... but they will be outcompeted by companies with effective, digital risk management. Effective risk management process locks down compliance and adds significant quality decision making value, while consuming far fewer resources.

ASK YOURSELF:

How can existing data be used to better understand existing risk profiles and improve new products? What is the value of identifying an adverse trend early and implementing risk control? Or worse, what is the impact of failing to identify a safety signal when one truly does exist? These consequences can range from business impact of costly manufacturing rework, to compliance and brand impacts from a safety related recall.

DIGITAL RISK MANAGEMENT IS THE SOLUTION

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We're in the era of big data.

At its heart, risk management is a big data problem and the information revolution has solved it. The solution is a digital risk management system that goes beyond minimal compliance, has automated ties to existing quality management processes, uses consistent qualitative and quantitative descriptors, provides automatic signal and trend detection, and enables proactive and predictive risk management.

A digital risk management system overcomes all of those challenges and enables continuous quality improvement that can set you apart from the competition.

A digital risk management system is a centralized, enterprise-wide collaborative space for cradle-to-grave risk management records and activities. A good digital risk management solution will offer cloud storage and reliability, and will comply with 21 CFR Part 11 and EU GMP Annex 11.

With an automated digital risk management system, you can:

- Lower risk
- Increase efficiency and reduce costs
- Improve patient safety
- Increase quality-led responsiveness in your manufacturing, supply chain, and distribution ecosystems

The following pages discuss its key features.

Digital risk management is an entirely different way to manage risk than traditional processes.

PERFORM DEEPER ANALYSIS: THE IMPORTANCE OF DATA-BACKED, QUANTIFIABLE RISK MANAGEMENT

A digital risk management system doesn't just get through the usual risk management activities faster and with fewer resources, it enables risk management that is more effective for the safety of the end user and patient.

IDENTIFY SIGNALS AND ADVERSE TRENDS ACROSS THE QUALITY MANAGEMENT SYSTEM

A digital risk management system achieves risk management efficiency and enables better decision making by standardizing risk management terminology across the Quality Management System. Instead of requiring staff to collect and analyze information from a spreadsheet or separate files, subject matter experts can utilize their time for deeper analysis in a centralized location. Let's take a closer look at how this is possible.

There are multiple processes within the quality management system that impact, or are impacted by, risk management activities: complaints, nonconformances, deviations, corrective and preventive actions (CAPAs), and change control to name a few. Complaints and nonconformances are sources of real-world data that can be used to improve existing risk evaluations, while CAPAs and change control can be used as pathways to drive post-market risk reduction, but all these activities have a risk management link that triggers timely decision making.

"The first step is to establish a system to collect and review relevant production and postproduction information. This system must include appropriate methods for the collection and processing of data, which can include statistical methods for trend analysis. " – BSI[6]

For example, medical device manufacturers have high volumes of complaint records that each identify reported failures and harms. This is the very same type of information that is assessed in the risk management files. A risk management process that is digitally integrated with the complaints process allows for the sharing of that relevant information, including failure modes and harms. Not only can a complaint record be linked with the appropriate risk file, pre-determined categories of complaint type and severity from the risk management file can indicate as to whether the reported complaint has identified a new risk that is not identified in the current risk management file, among other instances that requires a review of the risk management file:

- New hazards or hazardous situations
- New harms or greater than expected severity of risk
- Higher than expected P1, P2, and Occurrence of Harm values
- Breaches of statistical techniques that include automatic central tendency and control charts evaluating raw number, or rates, of complaints and quality events of a specific time period

Further, a combination of similar complaints may indicate an adverse trend, and because a digital risk management solution can allow you to correlate complaint to residual risks in the risk management file, the comparison between expected frequencies versus observed frequencies of risks becomes that much easier to determine if action is required or not. An increase in the same type of failure mode for a product may breach the accepted probability of a hazardous situation occurring, while an increase in a single type of harm may breach the accepted probability of harm as documented in the risk management file. In either case, the proper personnel are able to take a deeper look at these adverse trends as soon as possible and take timely action to reduce risk. Earlier, this paper discussed recurring review boards that analyzed trends. So instead of waiting for a quarterly meeting, adverse trends can be flagged more efficiently for appropriate staff to review.

DIGITAL INTEGRATION OF TOP-DOWN AND BOTTOM-UP RISK ANALYSIS

Digital risk management provides incredible advantages by not only providing risk analysis tools such as hazards analysis and failure mode and effects analyses (FMEA), but by linking those complex analyses to establish a complete, holistic risk management workflow.

FMEAs can include analyses of the manufacturing process (pFMEA), design (dFMEA), and use (uFMEA) of a medical device and they systematically evaluate consequences of those single fault failure modes, along with the occurrence and detectability of those consequences[7].

COMPLIANCE CORNER:

ISO 14971:2019 Section 10.3 The manufacturer shall review the information collected for possible relevance to safety, especially whether previously unrecognized hazards or hazardous situations are present or an estimated risk arising from a hazardous situation is no longer acceptable.

This is often referred to as a "bottom-up" risk analysis as each process step, part, or procedure is evaluated in progressive levels of the functional system[8].

FMEAs, however, are founded on the principle that a harm can only occur if there is first a failure in the process, design, or use of a product. Both ISO 14971:2019 and EU MDR have made it clear that the risks associated with a medical device also need to be identified in normal conditions (i.e. no-fault conditions), this is because hazardous situations (and ultimately a harm) can occur even where there are no faults.

This is where the Hazard Analysis supplements the FMEA, and further complies with ISO 14971 and EU MDR. The Hazard Analysis identifies hazards and hazardous situations, associated harms and occurrences, and resulting risk control, verification, and evaluation of risk activities. The probability of the hazardous situation occurring (P1), probability of a hazardous situation leading to a harm (P2), and the probability of occurrence of harm (P=P1*P2), along with the severity of harm are documented on the Hazard Analysis. Further, the outputs of the FMEA can be linked to the Hazard Analysis by identifying which failure modes are causing which hazards and hazardous situations, thus the Hazardous Situation becomes a "top-down" analysis as it first identifies the risk on the end user or patient at the highest system level, and then drills down to find the lower system level faults that cause those risks.

Process FMEAs, for example, have been a risk analysis tool used by manufacturers for decades. However, many manufacturers are not systematically including the effects of process failures into the evaluation of the overall residual risk. This link between the Hazard Analysis and FMEA is difficult to implement when these analyses live in different documents that are manually maintained by different teams. Further, this link is even more difficult to maintain through the constant manufacturing changes that companies implement to drive efficiency.

By digitally integrating failure modes from the FMEA to hazards/hazardous situations in the Hazard Analysis, engineers can now trace a top-level hazard down to the specific failure or failures that caused the hazard, allowing for effective root cause identification and risk control activities that reduce risk to the end user and patient. Furthermore, these links can be maintained during the post-market lifecycle phase of a product.

PROACTIVELY MANAGE RISK FOR NEW PRODUCTS

Data-driven risk management during the design and manufacturing development process allows for safer new or next generation products.

A top-of-the-line digital risk management system allows you to efficiently and effectively gather risk insights.

New product development teams can derive insights from relevant complaints, nonconformances, and CAPAs. The

analysis into historical performance of manufacturing processes and designs and the ultimate insights from that data are hindered by the vast amount of data available, coupled with the fast pace of new product development projects and short project timelines. Leveraging historical risk knowledge becomes a business value when it leads to shortened time to market by utilizing real world evidence that focuses risk control activities on where it's necessary

What is the value of identifying systematic manufacturing nonconformance across multiple product lines and international sites? What is the value of identifying common use or technique errors across similar product lines? The use of these digital technologies allows for insights from data across product lines, across manufacturing plants, and across divisions of a business. These insights drive risk reduction activities that include newer products having:

1. Inherently safe design and manufacture
2. Protective measures in the design and manufacture
3. Information for safety for users

A holistic review of these sources of data, without the need for burdensome data gathering by experts, allows new product development teams to efficiently and effectively establish design and manufacturing process inputs to make for a safer new product based on lessons learned from previous products' post-market surveillance.

Furthermore, project teams can save time and resources when building a risk analysis for similar new products, or product line extensions, with the ability to leverage portions of an existing risk analysis into a new risk analysis. The system identifies failure modes of process, design, or use from the risk registry that are common to the new or enhanced product under consideration.

THE USE OF ARTIFICIAL INTELLIGENCE

When the clues to a problem are hidden in massive data sets, there is no substitute for a powerful system that leverages artificial intelligence to categorize events and find correlations.

The application of Artificial intelligence, in the context of medical device risk management, is not to replace human involvement (i.e. autonomous intelligence). PricewaterhouseCoopers[9] model on the types of artificial intelligence are key here, and the

application of Artificial Intelligence for medical device risk management can be classified as Assisted and Augmented Intelligence. Assisted Intelligence helps humans perform tasks faster, and Augmented Intelligence helps humans make better decisions.

With the vast amount of data available throughout the QMS that is used in the risk management process, the applications of auto-categorization and autocorrelation can augment and assist quality teams. Auto-categorization can suggest classifications of complaints and quality events across the QMS. Autocorrelation can rapidly search through all available current and historical data to instantaneously identify correlations, trends, and patters that may have been previously invisible to quality personnel.

For example, in a standalone complaints process, incoming complaints are reviewed to determine complaint classification, reported severity, and a determination on regulatory reporting (e.g. Medical Device Reporting to the FDA). However, the complaint handling unit would not identify unacceptable risks, and instead, days or weeks go by until the complaint is forwarded to a subject matter expert who can then review the relevant risk file and make a determination on acceptability. By applying auto-categorization to a complaint record, the identification of a high or unacceptable risk as compared to the risk management file can be done prior to a complaint record being reviewed, thus allowing for prioritization of these specific complaint records.

On the same example of complaints, by automatically correlating similar complaint records together, an AI-enabled risk management solution can make a disposition on whether the frequencies are an expected or adverse trend as compared to the risk management file accepted frequencies. Both auto-categorization and auto-correlation support human decision-making on product quality and patient safety by getting through minor, less severe issues faster and uncovering urgent, more sever issues sooner.

This is crucial because the volume of complaints and other quality records is constantly growing. In fact, 66% of quality leaders indicated "sufficient staffing/resourcing" is a top quality system challenge[10]. You can achieve a much higher level of quality and patient safety when you can act without delay. And it saves engineers from performing individual root cause analyses and investigations for every failure, saving considerable resources.

66%

of quality leaders indicated "sufficient staffing/resourcing" is a top quality system challenge

COMPLIANCE CORNER:

EN ISO 13485:2016 Section 7.3.3.c Inputs relating to product requirements shall include applicable output(s) of risk management.

CHOOSE THE BEST DIGITAL RISK MANAGEMENT SYSTEM

5

The best risk management systems increase patient safety, enable higher quality, and require fewer resources. And by flagging issues faster and more reliably, they reduce harm.

TrackWise Digital® Risk Management is such a system. As a comprehensive risk management solution that effectively integrates with the TrackWise Digital Quality Suite, it is best in class and goes beyond achieving compliance.

It enables a systematic approach for risk analysis, evaluation, control, review, and post-market decision making that is fundamental in managing the risks of pharmaceutical products, combination products, and medical devices. It also features a robust data model that digitally integrates the top-down and bottom-up risk assessment methodologies, as well as provides an overall residual risk visualization on a risk matrix that is kept up to date with information received throughout the QMS and TrackWise Digital®. And it makes the development, implementation, and maintenance of a risk management program in accordance with ICH Q9, ISO 14971, and EU MDR that is less time and resource intensive.

Regulatory compliance is the foundation of risk management, but not its highest level of achievement.

Source

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