Accelerating the Development of Medical Devices: The Value of Proactive Risk Management

For medical-device manufacturers, fast-tracking product development requires controls and processes that address risks early on, reduce exposures, and improve the odds of success in the marketplace.

Executive Summary

For medical-device manufacturers worldwide, risk management must be preemptive and detailed. The U.S. Federal Drug Administration (FDA) requires adherence to the industry’s current risk-management standard (ISO 14971: 2007-Application of Risk Management to Medical Devices), which specifies a process for identifying, assessing and controlling risk. These requirements apply throughout the life of a medical device.¹

While statistics show that 60% of risk management takes place in the detailed design phase, only 30% of medical-device companies employ it during concept development.² Spotting risks after problems arise, at the validation stage, is a reactive approach that in our view is sub-optimal. Identifying hazards and working to mitigate them during the initial phases of new product development can help alleviate issues down the road.

There is also the possibility of running into risks prior to concept development, when companies gather customer, technology and regulatory requirements. If appropriately managed, these exposures can be effectively dealt with very early in the product lifecycle. This can result in “risk-proof concepts” driven by four risk-mitigation strategies: risk limitation, risk transfer, risk avoidance and risk acceptance.³ Using these four strategies, companies can evaluate risk effectively and reduce the time and cost associated with new product development (NPD).

This white paper offers a proactive approach that medical-device companies can use to identify, treat and resolve risks upstream, in the earlier stages of product development, by categorizing them as requirements or constraints. Our method is based on best practices and the experience we have gained in numerous client engagements across the medical-device field.

Risk Prioritization, Mitigation & Cost

In the global medical-device industry, proactive risk management is critical to maximizing value and fast-tracking new product development upstream.

Risk prioritization, mitigation and cost are three interlinked dimensions typically used to deal with this issue. They play a major role in determining if risk should be limited, transferred, avoided or
accepted. Figure 1 illustrates how these strategies can be applied, depending on the priority of the risk and the cost involved to control it. Usually, managing a high risk consumes more costs. In this situation, companies can attempt to split the risk by applying various combinations of the aforementioned strategies. Similarly, risks that are deemed limited, transferrable, avoidable, or acceptable must be sorted. Once this is done, the actions required to limit and/or avoid the risk can be proposed.

Risk analysis as such is not a primary activity, but part of the risk-assessment phase. Prior to risk assessment, business needs and intended use must be confirmed. At this point, various requirements are gathered, followed by risk assessment and evaluation. In our view, defining intended use, analyzing preliminary hazards and evaluating risk before the detailed design phase are upstream activities. The concept we propose emphasizes accelerating new product development (NPD) by controlling risk during this stage, as described in the following section.

Upstream Activities
Upstream activities include the following tasks:

- **Defining intended use.** Intended use is the basis for any medical-product design, and the reference for all design activities that follow. Intended use or indication for use can apply to a clinical condition that a device is intended to help diagnose, treat, reconstruct or improve upon. Once defined, the next step is to gather requirements.

- **Requirements-gathering analysis.** Requirements and intended use go hand in hand, since the design of a medical device is constructed around requirement specifications. A predicate study of an equivalent, or virtually equivalent, model and a benchmarking analysis can also be useful when gathering technical requirements. Regulatory requirements are based on industry standards, specific geographic regulations, functional requirements, the class of the device, intended use and the user environment.
• Developing a risk management plan. An effective risk management plan typically relies on numerous strategies to define various risk scenarios, acceptability criteria and targets so that risks can be resolved or headed off early on. Sufficient time and effort should be given to evaluating realistic scenarios and timelines rather than making assumptions. (New products typically fail due to improper planning, unrealistic timelines, infrastructure shortcomings, communication disconnects among cross-functional teams, and/or insufficient knowledge of the product and product standards. Using non-conformed medical devices can result in any number of hazards, including inherently risky medical treatment, device failures/malfunctions and poor interactions between the device and users. If risk management is viewed as a mere formality, mainstream risk identification can be overlooked—often requiring companies to revisit their risk-management tools. A risk-management expert is expected to anticipate all the foreseeable consequences and events that can occur during the entire NPD process.

Incorporating human factors engineering (HFE) into risk management can help identify most device- and use-related hazards (see Figure 2).

Identifying Device and Use-Related Hazards

HFE aligns the design of devices, systems and working conditions with the capabilities and requirements of users. This takes place in the development stage, which must take into account a device's technologies, human interactions, the environment in which the technology will be used, potential dangers and, of course, the criticality of patient care.

• Risk evaluation. The risk-evaluation process can involve qualitative decision making or a quantitative assessment applying probabilistic and statistical tools. Depending on the depth and complexity of the assessment, practitioners can use a number of tools: comparison matrix (CM); fault tree analysis (FTA); event tree analysis (ETA); failure mode and effects analysis (FMEA); hazard analysis and operability study (HAZOP); or a hazard analysis critical control point study (HACCP) (see Figure 3).

Figure 3 (next page) depicts a risk-management tools matrix that can be applied in various stages of product development. An Ishikawa diagram can be used in almost all phases to identify associated risks. PHA (preliminary hazard analysis) can be employed in design planning, retrofitting design development and to enhance existing designs, for example. CM, REM and FMEA can be used once risks have been identified, and applied in various phases to determine marketing, design and process exposures. HACCP and HAZOP can be employed in different stages once risks are ascertained.
Problem Definition

If upstream activities related to risk management are wrongly perceived as adding less value, they may be deemed unworthy of further exploration. In fact, it is likely that risk-management practitioners consider FMEA as the only significant tool they need, and ignore attempts to assess risk until the design has matured. Low-risk medical devices (whether used in hospital settings or business/safety-related environments) do not apply to this discussion.

Managing Risk at Every Stage

New product development typically starts with identifying a set of risks (negative voice of customer, unknown vulnerabilities from a new technology or mechanism, a first-in-market challenge, for example). Apart from these concerns, there are the risks associated with usability, energy interactions, regulatory mandates and system integration, which must be analyzed before product design begins and prior to the concept phase. In Figure 4, the slope (red line) in the first two phases means that risks are identified, but not assessed and controlled.

Proactive Risk Management

Figure 3

A Subset of Risk Management Tools Used in Product Development

<table>
<thead>
<tr>
<th>Risk Management Tool</th>
<th>Design &amp; Development Planning</th>
<th>Design Input</th>
<th>Design Output</th>
<th>Design Verification &amp; Validation</th>
<th>Design Transfer</th>
</tr>
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<tr>
<td>Fault Tree Analysis</td>
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<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Failure Mode &amp; Effects Analysis</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

Figure 4

Proactive application of risk management reduces the volume of risks. Gap: Risks transferred or converted to requirements. More iterations in the design cycle as more risks are encountered. Less iterations and fewer risks through a proactive approach.
To clarify, consider this scenario: A customer is unhappy with the weight of a portable medical device. If the device engineer doesn’t address this issue during the concept phase, rework will be required at a later stage – carrying the risk forward. Risks that can be addressed in the initial phases of product design are represented in the larger slope in Figure 4 (previous page).

The wavy lines in Figure 4 represent rework. In our experience, this is usually caused by delaying the implementation of risk-mitigation strategies. For example, if the housing of a medical device is burned in a “heat distortion” or “burn out” test, changing the material will be proposed – potentially leading to changes in the design. Earlier in the process, the material did not suit the thermal requirements – forcing the team to find an alternative. Dealing with risk effectively in each phase can reduce the time and costs associated with overall design-implementation and rework. As mentioned earlier and illustrated in Figure 5 below, this involves four main strategies: risk limitation, risk transfer, risk avoidance and risk acceptance.

**Primary Risk Strategies**

- **Risk Transfer**
- **Risk Avoidance**
- **Risk Limitation**
- **Risk Acceptance**

Figure 5

To address the risks cited earlier, we recommend the following:

- **Requirements-gathering and analysis**: This is the stage where MDD companies confirm requirements based on a device’s intended use, applicability and class. This helps assure the viability of the input during concept and design. Once requirements are collected, we recommend a preliminary analysis to help anticipate and detect hazards, confirm their primary cause, and more accurately identify and quantify risk (see Figure 6, next page). During this initial stage, risks can be ranked as high, medium or low. Each risk must then be analyzed to determine if it is limited, should be transferred, avoided or accepted.

As discussed, the application of risk-mitigation strategies in the requirements-gathering phase involves the following:

**Risk Limitation**

Consider a portable medical device that projects readouts on a display screen. If there is a potential issue regarding visibility, it could have been detected much earlier at the requirements-gathering phase. Action items for limiting the
level of risk could then be determined and addressed. For example:

- Adjusting the angle of the screen.
- Enlarging the size of the screen font.
- Adjusting the clarity of the screen.

**Risk Transfer**
A risk-transfer strategy can be applied in cases that require a third party. A medical device that involves a pump has a high level of risk during the design and development stage. Managing risk can be time-consuming and costly. It makes sense to transfer the task to a capable external source.

**Risk Avoidance**
In some instances risk should be avoided at all costs. For example, an MRI machine emits powerful magnetic fields that must be carefully controlled during the imaging process to protect the patient, as well as the medical staff, in the MRI suite. Risk avoidance is a top priority, and a strategy that must be applied at every stage of design and development.

**Risk Acceptance**
A risk acceptance strategy is appropriate when, for example, a medical device permeates sensible heat (heat that alters a body’s temperature without causing harm).

**Prepared and Proactive**
Addressing risk through the aforementioned strategies can head off hazards and set requirements before concept development — affording the opportunity to apply actions at the initial phase of NPD.

During requirements-gathering, risks are validated at the unit level, since the design is in the very early stages. By taking a proactive approach to risk management, companies can transfer risks, convert them into requirements, or eliminate them — reducing the number of potential and real hazards they have to deal with. Risks converted to action items become input for product requirement specification (PRS), which serves as the basis for concept generation.

**Concept Generation and Selection**
In order to convert a risk into an action item, it must first be analyzed to determine its root cause. If the issue that originated at the subsystem level is identified at the component level, failures or accidents could be attributed to various factors. To mitigate these risks, we use tools such as fault tree analysis (FTA) and event tree analysis (ETA), as shown in Figures 7 and 8 on the following pages. These can be applied in parallel during the concept phase.
Implementing the four strategies described here (limitation, transfer, avoidance and acceptance) can further reduce the number of risks. This raises the question, “If these strategies can be applied at once, in a single phase, why apply repetitively?” The answer is that the risks analyzed at each stage of product development become more detailed as product development progresses through different phases. Take the example of the risk that “readings are not visible on a display screen.” While this could be considered a high risk during the requirements-gathering phase, it could not be classified as a design requirement because the problem could be traced to various root causes. These risks should be analyzed and identified through a fault tree analysis, which can confirm the cause of the risk, be it due to the inclination of the display screen, the screen’s level of clarity, or a hardware or software issue, for example.

New risks should be managed alongside mitigation strategies. “Inclination of the display screen” could be converted to a requirement; hardware and software problems could be transferred to the appropriate vendor. “Display screen not clear” could be dealt with either by accepting or avoiding the risk. A risk-avoidance strategy might involve adding an extra shield to avoid dust accumulation and an extra layer of protection, for example. These measures are then converted into requirements, which can be applied to the concepts. If needed, further analysis can be carried forward.

This process not only reduces the volume of risks, but also ensures that the right tools are employed to mitigate them in the early phases of product design. It would be unwise and ineffective to analyze a risk through fault tree analysis when there is no possibility of various fault modes. Similarly, FMEA cannot be used for risk identification, since its purpose is to evaluate risk.

Not all risks identified at the conclusion of requirements-gathering can be managed through FTA; Those that require more detailed analysis using tools like FTA and ETA are handled during the concept phase, which does not entail much risk. However, the comparative decrease in risk is the result of a proactive, rather than reactive, approach to risk mitigation.

**Detailing Design & Optimization**

In the requirements-gathering phase, risk is typically analyzed at the product level, whereas in the concept phase, it is assessed at the subsystem and component levels. Risk analysis is handled from the top down until the concept phase. The next step is analyzing risk from the component level to the top levels (i.e., from bottom to top) using FMEA, HACCP and HAZOP tools. In this stage of product development, failures are converted into action items. Risk limitation and risk avoidance strategies are generally deployed during this stage.

Through FMEA, risk priorities are quantified and action items identified against it. For example, a medical device that takes input from a user through a button can experience various communication failures, which are initially analyzed using FTA. The results indicate “improper assembly of buttons,” “buttons hard to operate” and “loose connection between the button and the board.”
These issues can be drilled down further in FMEA. For instance, the anticipated failure “buttons hard to operate” can be resolved with another, more appropriate material or through a design change. “Loose connections” and “improper assembly” can be avoided through poka-yoke features, which provide a fail-safe method for preventing errors.

A good practice for companies to follow during the decision-making process or when proposing an action item in a failure mode and effects analysis is to refer to industry publications, databases and technical forums that offer relevant information on a product or product failures. Addressing risks through appropriate use of risk-controlling tools can help MDD companies move forward with more confidence and less assumptions, which lessens the risk of product failure in the validation phase.

Apart from the business requirement and intended use, risk quantification and action items that are identified through the tools we described will play a major role in developing a detailed, risk-averse design. Figure 8 shows how the four strategies we cited can be applied to reduce the volume of risks using a failure mode and effects analysis. At this point, risks are already identified and processed; we only evaluate risk in this phase.

The design engineer will ensure that the design is incorporated, and identify the necessary action items to avoid risk. Once the design is completed, the team creates a virtual design, which often reveals that additional changes are needed. At this stage, iterations to the design should be minimal, but nonetheless help ensure that risks are limited and avoided.

The fewer assumptions made, the less the risk of product failure in the validation phase.

Design Verification & Validation
No matter how effectively proactive risk assessment is embraced and executed, possibilities still exist for risks to flow into the validation phase. This issue can originate at the risk-transfer and risk-acceptance stage, or be the result of poor design assumptions. Here, the goal is to address all risks and bring in a solution without modifying the overall design.

The objective is to correlate risk with real-world scenarios and assess how they could have been proactively mitigated early on using the tools we cited earlier.

These examples help build confidence in the significance of upstream risk management tools, which can reduce the time and cost of new product development (see Figure 9, next page).

Looking Forward
The FDA has set huge expectations for medical device companies on the risk-management front. These expectations can be met by applying new concepts and theories to make the process more effective. Potential areas of investigation include:

• Addressing the need for a risk-management model in line with ISO 14971, which is capable of controlling risk at each and every phase.

Failure Mode & Effects Analysis

<table>
<thead>
<tr>
<th>Risks Identified</th>
<th>Severity</th>
<th>Occurrence</th>
<th>Detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantify Risks Based on RPN</td>
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</tbody>
</table>

Apply Four Strategies

- Risk Transfer
- Risk Avoidance
- Risk Limitation
- Risk Acceptance

Action Items

Figure 8
### Proactive Risk Management

<table>
<thead>
<tr>
<th>S.no</th>
<th>Risks that can be converted to action items before FMEA</th>
<th>Application of Upstream tools</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Problem Detected in the Downstream Process</td>
<td>Foreseeable Consequences/Causes</td>
</tr>
</tbody>
</table>
| 1    | A medical device uses a rubber keypad or common base to communicate user input. | The user’s input is incorrect. | - Ineffective communication caused by human error at the back end.  
- Tactile buttons are adjacent to one another; while using one button, the user mistakenly activates another. | Inappropriate functionality. | A fault tree analysis (FTA) could have helped avoid these consequences.  
Output from a preliminary hazard analysis (PHA) could be used to identify and resolve the issue through appropriate action items. | - Rubber keypad base should have sufficient distance between buttons – helping to eliminate the potential for error.  
- If possible, see that keypad buttons do not share a common base.  
- Alternative keypads with high response and low error rates can be used.  
- Control critical dimensions of the rubber pad.  
- Perform a lifecycle test of the rubber pad. |
| 2    | A medical device uses tubes for transporting fluid (liquid or air). | Fluid leakage. | - Degradation of tubes.  
- Unexpected pressure of the fluid.  
- Improper maintenance.  
- Chemical reaction between the tubes and the fluid. | Exposure to reactive fluids (alkalis/ acids), Exposure to high-pressure fluids. | A fault tree analysis (FTA) could have helped avoid these consequences.  
Output from a preliminary hazard analysis (PHA) could be used to identify and resolve the issue through appropriate action items. | - Material selection should consider reactive fluids.  
- Assembly of the tubes should withstand worst-case scenarios identified. |
| 3    | An enclosure ruptures after being used for only a short period of time. | Enclosures fail due to lack of stability to bear the vibrational load. | Considering the possibility of many root causes, FTA is used. | Structural instability. | Action items identified by using FTA:  
- Inappropriate material.  
- Vibration not considered a primary noise factor.  
- Enclosure not designed for worst-case situations  
- Manufacturing defect.  
- Sudden variation in vibration due to malfunctioning pump. | - Appropriate material selection.  
- Thorough design considerations.  
- High-quality pump with good durability. |
| 4    | A medical device shows low accuracy/high error or deviation. | Errors due to improper calibration. | - Use of non-standard calibration device.  
- Improper method of calibrating.  
- Defective calibrating device. | Inappropriate output/functionality. | Foreseeable consequences are not many using FTA. | Employ a high-quality calibrating device. |
| 5    | Exposed plug-in points or USB port. | Users experience shock. | - Earth leakage current  
- Enclosure leakage current.  
- Patient leakage current. | Current leakage. | The output from FTA can be used as action items here. | |

**Figure 9**

- Managing risk upstream – from requirements-gathering to concept-generation – to reduce the time and costs involved in new product development.
- Applying risk management in conjunction with design controls.

- Applying all necessary risk-management tools at all levels to avoid and overcome hazards.

When properly applied, these practices can minimize the probability of unexpected or harmful events and improve a company’s overall benefit-risk profile.
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Reference


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