Foreword

MEDICept presents this ongoing series of articles focused on the implementation and practical conduct of risk management in the medical device industry to provide practitioners with insight into how to apply risk management principles and tools to improve the performance and safety of their devices; and, as an added benefit, to maintain compliance with risk management standards.

Our team at MEDICept publishes these articles to capture best practices, to explore the more challenging aspects of maintaining risk management systems over the long term, and to elicit discussions among practitioners.

To this last point, if you have questions or comments on the issues discussed, or if you have recommendations for topics to consider in the future, please let us know: 508-231-8842.

In our last two articles, RM 5 - Assessing Severity and RM 6 – Estimating Probability of Occurrence of Harm, we discussed approaches to develop values for these two elements of risk and the challenge of completing these assessments/estimates. This article takes the next step to address the question: Are we, as a company, willing to accept the risks associated with our device given the benefits that a patient is likely to receive? This article (Part A) provides a review of the standard approach. A second article (Part B), will provide our thoughts on the challenges.

Determining Risk Acceptability – The Standard Approach

Before we jump into the challenges of determining risk acceptability, it’s important to first make sure that we have a common understanding of the key elements of the standard approach as described in ISO 14971, Medical Devices – Application of Risk Management to Medical Devices (we’ll just refer to it as “the standard”).

As a first step, it’s important to be clear on two terms: “risk evaluation” and “risk acceptability”. The standard defines “Risk Evaluation” as the “process of comparing the estimated risk against given risk criteria to determine the acceptability of the risk”. So the process involves taking the “estimated risks” (i.e., typically the results of FMEA-style analysis where you estimate severity and the probability of occurrence of harm) and evaluating those risks to determine whether they are acceptable or if risk reduction is required. Two tools described in the standard to complete this work are “risk acceptability criteria” and the “risk evaluation matrix”.

The standard calls for the risk analysis team to establish the risk acceptability criteria well before the actual risk analysis activities begin. These criteria must be established in the Risk Management Plan (either directly or by reference) and that plan must be reviewed and approved by company management. Once the plan is approved, the risk analysis team may begin its work with a clear understanding of the level of risk that management considers to be acceptable.
The risk acceptability criteria can take several forms. The two most common approaches are 1) to use Risk Priority Numbers (RPNs), and 2) to develop a risk evaluation matrix. Both are described briefly below:

- **Risk Priority Number (RPN):** Using the RPN approach, the risk analysis team multiplies the assigned “Severity” and “Probability of Occurrence of Harm” values. The product of these two values is the RPN \( S \times O = \text{RPN} \). [Note: when Detection is included in the analysis, the RPN is the product of Severity, Occurrence, and Detection \( S \times O \times D = \text{RPN} \)]. The acceptability of the resulting RPN is based on pre-established cutoff values, such as:
  - RPN < 12 = Acceptable
  - RPN ≥ 12, but < 20 = Acceptable following an investigation to identify opportunities to reduce the risk and implement risk controls if practicable (i.e., “As low as reasonably practicable”, ALARP)
  - RPN ≥ 20 = Unacceptable, design changes to mitigate risk are required.

If one were to plot the RPN acceptability criteria in a risk evaluation matrix, the result would be a symmetrical pattern. It’s symmetrical because Severity and Occurrence have the same weight. As a result, a risk with a Severity of 5 and an Occurrence of 3 (RPN = 15) is placed in the same risk category as a risk with a Severity of 3 and an Occurrence of 5 (RPN = 15) – see below.

<table>
<thead>
<tr>
<th>Severity of Harm</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Probability of Occurrence of Harm</strong></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td>Unacceptable</td>
</tr>
<tr>
<td>4</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>ALARP</td>
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<tr>
<td>2</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Acceptable</td>
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Risk Acceptability Matrix: Over time, many manufacturers found that they were not comfortable with the assumption that Severity and Occurrence have equal weight – arguing that risks with a high Severity are of greater concern than risks with high Occurrence. As a result, most manufacturers now use “asymmetrical” risk acceptability matrices to better reflect their tolerance for risk (see example below).

<table>
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<tr>
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</tr>
</tbody>
</table>

By taking this “asymmetrical” approach, companies are able to more clearly articulate their acceptance of different types of risk. In the example provided above, a risk with a Severity of 5 and an Occurrence of 3 is considered to “Unacceptable” while a risk with a Severity of 3 and an Occurrence of 5 is “ALARP”. This approach also allows manufacturers to identify any risk with a Severity of 5 as “Unacceptable” regardless of the probability of occurrence.

There are no prescribed RPN cutoff values or Risk Acceptability Matrix “patterns”. Each manufacturer is able to structure these risk prioritization tools in any way that best fits the nature and expected use of their device. In practice, the structure of these tools tends not to differ dramatically from manufacturer to manufacturer – high Severity risks are “Unacceptable” or “ALARP” and low Severity risks are “Broadly Acceptable” or “ALAR”. The differences are in the margins.

Following this standard approach, the acceptability of each individual risk identified in your Hazard Analysis or FMEA is judged using the established criteria. This evaluation is typically conducted early in the Design Control process (before the start of Detailed Design) so that there is time to implement changes needed to mitigate identified risks before getting too deep into the design process. Needed changes can take the form of design changes, protective measures, and/or information to the user (e.g., instructions, Warnings and Cautions).
Then, as part of the approval of the final drawing package, the risk analysis team reassesses the risks following the implementation and verification of risk controls. The risk analysis team uses these “post-mitigation” risk values to determine the acceptability of each individual risk. This resulting level of risk is called the “residual risk”. If the residual risk is not acceptable and further risk control is not practical, the manufacturer must conduct a risk/benefit analysis to determine whether the medical benefits of the device outweigh the residual risk.

Finally, once all controls have been implemented and verified, and the acceptability of each individual residual risk has been determined (either through a residual risk evaluation or a risk/benefit analysis), the risk analysis team must conduct an “overall” residual risk evaluation. This evaluation is based on the criteria defined in the Risk Management Plan. If the overall residual risk is not acceptable, the manufacturer must conduct a risk/benefit analysis to determine whether the medical benefits of the intended use outweigh the overall residual risk. If so, the manufacturer should be read to place the product on the market (or at least prepare a submission for the FDA or a Notified Body). If not, it’s back to the drawing board.

So, in a nutshell, if the residual risk is acceptable according to the management-approved acceptability criteria, the risk of the device is acceptable and requires no further review. If the residual risk is not acceptable, a risk-benefit analysis is required. The risk/benefit analysis typically comes into play when “Unacceptable” risks cannot be mitigated any further, but the device (as designed) could provide significant benefits to patients. For example, if a company manufactures a life-sustaining device that is only effective for half of all patients, use of the device may be warranted (even though half of all patients are expected to die) if there are no better treatment alternatives.

Assessing Risk Acceptability – The Challenges
For those of you who work with the Risk Management Standard on a regular basis, the approach for determining risk acceptability described above should seem pretty familiar. For others, hopefully you now have a general understanding of the standard approach. While this approach establishes a solid framework for building your internal risk acceptability processes, there are a few aspects of the approach that remain a bit murky and require some interpretation. The most challenging issues to deal with when applying this approach are:

- **The role of Benefits in the Risk Acceptability Criteria**
- **Independent Risks vs. Overall Risk**
- **Residual Risk Evaluation vs. Risk-Benefit Analysis**

Next Steps
In our next article “Determining Risk Acceptability – Part B”, we’ll dig deep into the three challenges described above.

If you’ve missed any of the previous articles look them up on [www.medicept.com/blog/](http://www.medicept.com/blog/).