

Application of Risk Management Principles

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Hello everyone, thank you for joining this presentation. My name is Tonya Wilbon, and I am the Branch Chief for the Postmarket and Consumer Branch within the Division of Industry and Consumer Education. This presentation will focus on the application of risk management principles for medical devices.

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Some of you may think that risk management activities may look similar to the image on this slide: sketchy; crowded; uncertain; and even perhaps overwhelming. Hopefully this presentation today, will provide you with knowledge, tools, and techniques to understand and successfully reduce, control, monitor, and/or accept risk when the benefits outweigh those risks associated with the use of a medical device.

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For this presentation, the learning objectives are to: discuss the reasons for conducting risk management activities for medical devices; identify when to use risk management activities for medical devices; and the final learning objective is to explain a few techniques used to apply risk management principles for medical devices.

If you understand the reasons why you should conduct risk management activities, you would perhaps be more willing to do so and feel less overwhelmed.

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Let's begin by reviewing some of the reasons for conducting risk management activities.

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At some point during the total product life cycle specifically during design, manufacturing, and or production of a medical device, you will have to conduct risk management activities and make risk-based decisions. This is critical to manufacturing a safe and effective medical device.

The next two slides will provide a few specific examples of reasons for conducting risk management activities for medical devices.

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One of the first and most obvious reasons why you conduct risk management activities, is to ensure safety of the device throughout the product lifecycle. Risk management activities ensure the safety of the device by reducing, controlling, and monitoring risk associated with the use of medical devices.

You conduct risk management activities to identify device design problems prior to distribution. This will assist in eliminating costs associated with recalls due to faulty device designs That could result in device failures.

The fact that risk analysis is a regulatory requirement is another reason to conduct risk management activities. Risk analysis (one element of the risk management process) is specifically required in the Quality System regulation under the design validation requirements of, Title 21 Code of Federal Regulations, or CFR, Part 820.30(g).

You conduct risk management activities also because certain regulatory submissions, such as a Special 510(k), required by the FDA call for inclusion of risk analysis information.

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Additional reasons why you should conduct risk management activities include to reduce the possibility of your device failing by also identifying hazards that could result in harm from use of your device; to evaluate the risk and make an informed decision as to whether you want to accept the risk of using that device or not; and to put it plain and simple, it is the right thing to do, to identify, evaluate, control, and monitor the risk associated with use of your device. Remember, the use of every medical device has some risk.

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I am sure we all would agree that it is important to understand why you should use risk management activities. Well, it is equally important to identify when to use risk management activities within a Quality System or Quality Management System or in general. Risk management activities occur throughout the total product lifecycle of a medical device.

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Risk Management activities within a Quality System control the safety and performance of the device throughout its total product lifecycle; they demonstrate control over all risk associated with use of the device.

You should use Risk Management activities when implementing a Quality System to conduct risk analysis, as required. FDA's response to comment #83 in the preamble to the QS regulation further clarifies that manufacturers must identify possible hazards and the risk associated with those hazards to reduce the risk to acceptable levels.

You should also use risk management activities or the results of risk management activities when implementing a quality system to make risk-based decisions including identifying design outputs that are essential for the proper functioning of the device as required by 21 CFR 820.30(d). This ensures controls are in place for those outputs that can cause the device to fail if they do not meet specification.

Additional risk-based decisions include defining the type and extent of control to be exercised over the product, services, suppliers, contractors, and consultants according to 21 CFR 820.50(a). For example, to ensure the supplier will provide critical products that meet required specifications.

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You should also use risk management activities when implementing a Quality System to make risk-based decisions. The next two slides list a number of examples of decisions that you may make. For example, describe the necessary process controls needed to ensure the device meets specifications and performs as intended per 21 CFR 820.70(a). Document major equipment used for validated processes, where appropriate, to ensure you qualify that the equipment will operate as intended according to 21 CFR 820.75(b). Determine necessary approvals for in-process acceptance activities as required by 21 CFR 820.80(c). Note: this critical decision is needed to ensure unacceptable product is not used that could negatively impact the finished device.

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Determine the need for an investigation of nonconforming product to make decisions about the disposition of those products per 21 CFR 820.90(a).

Decide when to conduct internal audits (or how often) and decide how detailed of an audit is needed to ensure product consistently meets specifications or processes consistently perform as intended.

And identify valid statistical techniques required to establish, control, and verify the acceptability of process capability and product characteristics per 21 CFR 820.250.

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In accordance with the relevant laws and regulations in the United States Federal Food, Drug, and Cosmetic Act, or the FD&C Act, and its implementing regulations as described in its guidance, FDA regularly uses risk management principles to make risk-based decisions. These are risk-based decisions related to device classifications, recall classifications, inspectional decisions, such as when to conduct an inspection and the type of inspection to conduct, and enforcement activities.

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Risk management is not just one activity. It entails using perhaps several techniques to obtain risk information and thus complete the risk management process. The next few slides will provide examples of risk management techniques that can be used in the application of risk management principles.

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The Association for the Advancement of Medical Instrumentation, or AAMI, the American National Standards Institute, or ANSI, and the International Organization for Standardization, or ISO, standard 14971: 2019, here after referred to as ISO 14971, titled Medical devices- Application of Risk Management to Medical Devices, is the international standard for medical devices, accepted around the world and recognized by the FDA, that is used to establish a risk management process. It is used to conduct risk analysis activities as required by the Quality System regulation.

It is a systematic approach to conducting risk management activities and specifies risk terminology, risk principles, and a process for risk management of medical devices, including software as a medical device and In Vitro Diagnostic devices.

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The AAMI/ISO Technical Report, or TR, 24971:2020, titled, Medical devices- guidance on the application of ISO 14971 is another helpful international document for applying risk management principles. It provides guidance on the application of ISO 14971 to assist manufacturers in the development, implementation, and maintenance of a risk management process for medical devices that aims to meet the requirements of ISO 14971.

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As previously indicated, ISO 14971 is an international standard that is widely used and has proven to be very informative when it comes to the application of risk management principles. Here is a diagram of the overall risk management process that is included as Figure 1 of this standard. As you can see, risk analysis is a subset or element of the entire Risk Management Process. The steps in the risk management process can be performed iteratively or in multiple steps.

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Now, here is a list of a few examples of different techniques or tools you can use to support risk management process and apply risk management principles. They include Preliminary Hazard Analysis, or PHA; Fault Tree Analysis, or FTA; Failure Mode and Effects Analysis, or FMEA. These and additional techniques can be found in Annex B of TR 24971:2020.

In addition, FDA conducts a Benefit-Risk Analysis to apply risk management principles and make risk-based decisions. FDA has issued several guidance documents regarding these risk management principles and techniques.

Due to time restraints, I am unable to provide examples for each one of these, but I will highlight the characteristics of each.

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Preliminary Hazard Analysis or PHA is used in risk analysis as a means of and with an objective of identifying hazards, hazardous situations, and events that can cause harm. Usually, little is known about the device design and this technique is typically conducted early in device development. A PHA is very useful in prioritizing hazards.

Performing a Preliminary Hazard Analysis results in the identification of the probabilities or the likelihood that a hazardous situation will occur and the probabilities that a hazardous situation will lead to harm. It results in qualitative evaluation of the extent of possible harm or how severe is the harm and the identification of possible risk control measures.

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When conducting a PHA, you begin with listing possible hazards. You can accomplish this by: brainstorming for possible hazards; using previously published literature and/or using information in international standards.

You can list hazards when conducting a PHA by considering characteristics such as materials used, equipment used, use environment, and layout interfaces among system components.

This PHA technique can be useful in identifying essential design outputs.

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Here is an example of using the principles of a Preliminary Hazard Analysis.

You can use questions to identify characteristics or hazards that could impact safety as well as the other characteristics previously listed. Annex A of ISO 24971:2020 has questions, factors or characteristics to consider that you can use as a starting point.

This information obtained after analyzing each hazard can be captured in a chart or table as shown on this slide. For each hazard identified, you identify and document the hazardous situation, the possible harm, the severity of the harm and the probability of the hazard and hazardous situation leading to harm, using the already defined risk severity chart and risk probability chart; and the identification of possible risk control measures. There are numerous examples of probability and severity charts already created that you can use if it is applicable to the possible harms that could result from use of your device.

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Another technique is the Fault Tree Analysis or FTA. It is used in risk analysis as a means of analyzing identified hazards. It uses a top-down method to estimate fault probability and identifies single faults that result in hazardous situations as well as common faults that result in hazardous situations. The results are represented pictorially in a tree form or a fault mode using connectors such as “AND” or “OR”.

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Failure Mode and Effect Analysis, or FMEA, is also used in risk analysis to identify and evaluate individual fault or failure modes. It is a bottom-up method that starts with the causes and works towards how this will affect or impact device use. You have to be somewhat familiar with the device to use this technique to understand how the device could fail.

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FMEA is not restricted to failure of device design and can include failures in manufacturing and assembling of components or PFMEA. It can be useful in dealing with use error and answers the question, “What happens if...?” we get an incorrect result such as a false positive. FMEA does require some understanding of the device.

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FDA uses a Benefits-Risk Analysis technique to assess the medical device risk once all measures to reduce the risk have been applied and only acceptable residual risk remain. The benefit-risk analysis helps to decide to rework or use the device “as is” with the risk you are unable to reduce further. There are several CDRH guidance documents available that provide the framework for medical device benefits-risk decision making.

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When conducting a benefit-risk analysis, FDA considers several factors to assess the benefit and risk of a device for determinations in Premarket Approval Application, or PMA, De Novo classification, substantial equivalence in Premarket Notifications, or 510(k), with different technological characteristics, investigational device exemption, or IDE, as well as determinations for product availability, compliance and enforcement decisions.

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This slide includes a list of factors FDA may consider when assessing the extent of benefit of a device when making benefit-risk determinations during premarket review process and when determining product availability, compliance and enforcement decisions. As noted in the table not all of the same factors are considered when making certain risk-based decisions. For example, the benefit factor of patient perspective on benefit and medical necessity are only considered when determining product availability, compliance and enforcement decisions.

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The next two slides include a list of factors FDA considers when assessing the extent of risk of a device when making benefit-risk determinations during premarket review process and when determining product availability, compliance, and enforcement decisions. Again, as noted in the table, not all of the same factors are considered when making risk-based decisions during this premarket review process and when determining product availability, compliance, and enforcement decisions. For example,

severity of risk or harm is considered during premarket review process and when making product availability, compliance and enforcement decisions. However, distribution of nonconforming devices risk factor is only considered when making product availability, compliance and enforcement decisions.

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This slide lists the additional risk factors FDA considers when conducting Benefit-Risk Analysis.

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In addition to the specific benefit and risk factors FDA considers when conducting a benefit-risk analysis, there are several additional factors that are also considered to assess the risk of the device in general. This is not an all-inclusive list of the additional factors to consider. The list is included in each of the guidance documents pertaining to making benefit-risk determinations.

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Let's review an example of a benefit-risk analysis completed to make a risk-based product availability, compliance, and enforcement decision, specifically a product availability decision.

This example involves a human chorionic gonadotropin (or hCG) device. The hCG device is intended to detect hCG in urine to aid in early detection of pregnancy and is indicated for over-the-counter (OTC) use.

The healthcare provider noticed a higher rate of positive results, but the positive results were not confirmed in blood samples, thus the device yielded a higher rate of false positives than expected by the manufacturer. The manufacturer identified a malfunction in specific lots and noted that the lay user is not able to detect this malfunction.

It is noted that there are other devices on the market for detecting pregnancy.

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FDA conducted a Benefit-Risk Analysis as outlined in the guidance document, "Factors to consider regarding benefit-risk in medical device product availability, compliance and enforcement decisions." The benefits and risks were identified as listed on this slide. It is noted that the benefit was reduced due to the potential lack of test accuracy.

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The assessment was completed using the worksheet included in the guidance document for documenting responses to the questions listed for each factor considered. The factors for benefits and risks considered included, among other factors considered, patient tolerance for risk and perspective on benefit, mitigation, and patient impact and the results were documented. It was documented that for patient impact, there are similar devices available without additional risks.

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After all of the risk information was gathered and documented on the Assessment worksheet, it was determined that there was no need to continue to support product availability. FDA and the manufacturer agreed the risk outweighed the benefit of this device remaining available on the market and decided to recall the device. The firm submitted a correction and removal package to the FDA in accordance with 21 CFR 806 and FDA classified the recall as a Class II recall.

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So, as I indicated earlier, you may need to use more than 1 risk management technique throughout your quality system or in general when implementing risk management activities.

Here are a few more examples of risk management techniques that can be used as well: Risk Acceptability Chart—for evaluating risk, both initial and residual risk; Risk Control Option Analysis- for controlling risk; and Risk Management Report, to capture relevant review of production and post-production risk information.

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In summary, risk management activities are essential throughout the product life cycle and not just required during design validation.

Preliminary Hazard Analysis, Fault Tree Analysis, Failure Mode and Effects Analysis, and FDA Benefit-Risk Analysis are different types of risk management techniques and tools that can be used in the risk management process.

And finally, manufacturers should use more than one risk management technique in their risk management process.

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Here is a list of resources that were applicable to this presentation.

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This slide lists three additional resources for industry education: CDRH Learn where this presentation will be posted; Device Advice; and our Division of Industry and Consumer Education.

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Let's conclude this presentation with Your Call to Action.

Your Call to Action is to: identify when to evaluate risk and conduct risk management activities early, identify and utilize resources available for conducting risk management activities; and ensure you use the appropriate risk management technique and/or tool for managing risk with your device.

This will ensure your devices are safe and effective.

Thank you for viewing this presentation.
