

Application of Risk Management Principles for Medical Devices

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Risk Management Activities



Learning Objectives

- Discuss the reasons for conducting risk management activities for medical devices
- Identify when to use risk management activities for medical devices
- Explain techniques for the application of risk management principles

Reasons for Conducting Risk Management Activities

Why Conduct Risk Management Activities?



Why conduct risk management activities?

To ensure safety of the device throughout the product lifecycle

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To identify device design problems prior to distribution

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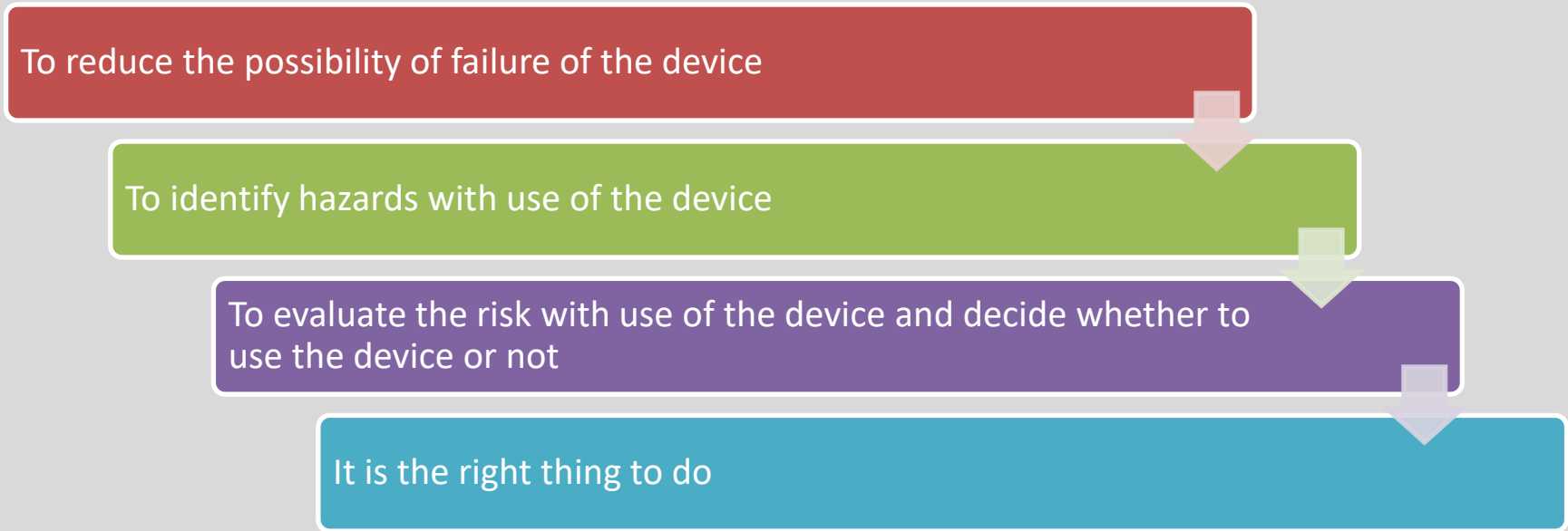
Risk analysis is a regulatory requirement

A purple rectangular box with rounded corners and a white border, containing the text "Risk analysis is a regulatory requirement". A white downward-pointing arrow is attached to the bottom right corner of the box.

FDA regulatory submissions require risk analysis information

A teal rectangular box with rounded corners and a white border, containing the text "FDA regulatory submissions require risk analysis information". A white downward-pointing arrow is attached to the bottom right corner of the box.

Why conduct risk management activities?



When To Use Risk Management Activities for Medical Devices

When to Use Risk Management Activities

- When implementing a quality system to:
 - Conduct risk analysis, where appropriate, as required
 - Make risk-based decisions including:
 - Identifying design outputs essential for proper functioning of device
 - Defining type and extent of control to be exercised over product, services, suppliers, contractors, and consultants

When to Use Risk Management Activities

- When implementing a quality system to:
 - Make risk-based decisions including:
 - Describing necessary process controls
 - Documenting major equipment used for validated processes, where appropriate
 - Determining necessary approvals for in-process acceptance activities

When to Use Risk Management Activities

- When implementing a quality system to:
 - Make risk-based decisions including:
 - Determining need for investigation of nonconforming product
 - Conducting internal audits
 - Identifying valid statistical techniques required for establishing, controlling, and verifying the acceptability of process capability and product characteristics

When to Use Risk Management Activities

- By FDA to make risk-based decisions related to:
 - Device classifications
 - Recall classifications
 - Inspectional decisions
 - Enforcement activities

Application of Risk Management Principles

Risk Management Process

- AAMI/ANSI/ISO* 14971:2019 Medical devices-Application of risk management to medical devices (ISO 14971)
 - Used to conduct risk analysis activities as required by regulation
 - Systematic approach to conducting risk management activities

*AAMI =Association for the Advancement of Medical Instrumentation

ANSI = American National Standards Institute

ISO = International Organization for Standardization

Risk Management Process

- AAMI/ISO TR*24971:2020-Medical devices- guidance on the application of ISO 14971
 - Provides guidance on the application of ISO 14971

*AAMI =Association for the Advancement of Medical Instrumentation
ISO = International Organization for Standardization
TR = Technical Report

Risk Management Process

AAMI/ANSI/ISO 14971:2019

Medical devices- Application of risk management to medical devices

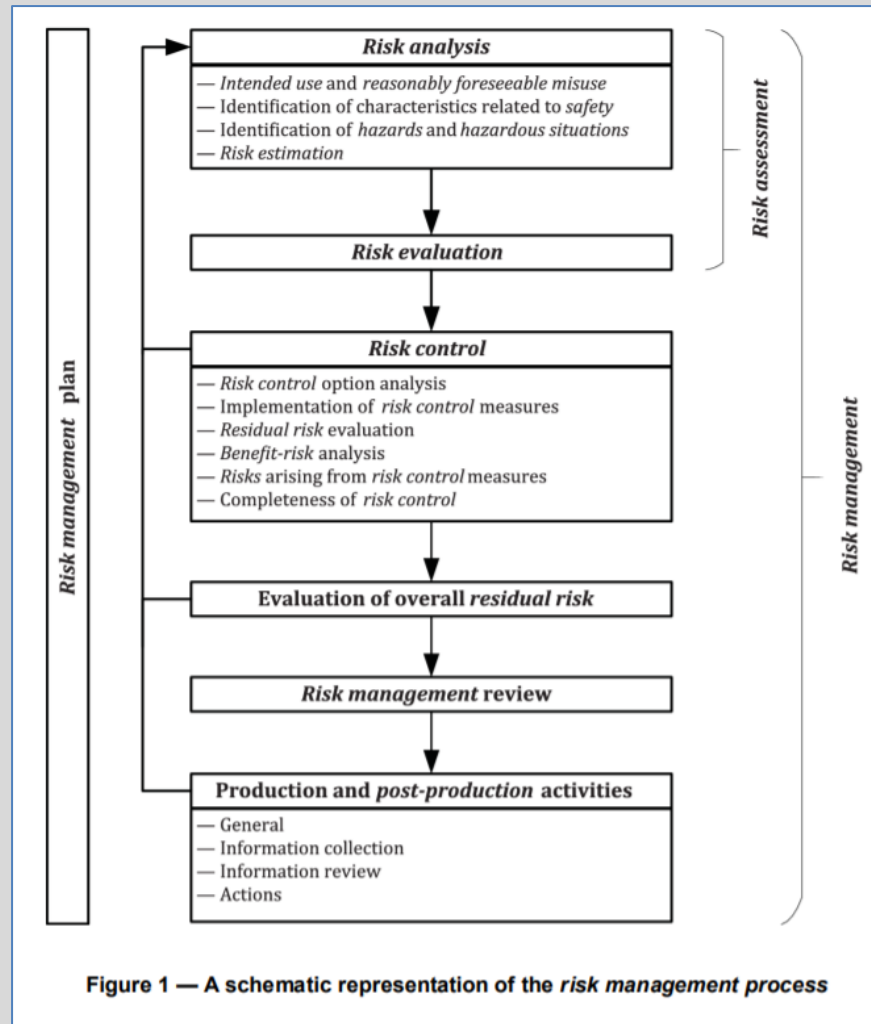


Figure 1 — A schematic representation of the risk management process

Risk Management Techniques

- Preliminary Hazard Analysis (PHA)
- Fault Tree Analysis (FTA)
- Failure Mode and Effects Analysis (FMEA)
- FDA Benefit-Risk Analysis

Risk Management Techniques

Preliminary Hazard Analysis (PHA)

- Used in risk analysis as a means of identifying hazards and hazardous situations
 - Few device design details known
 - Conducted early in device development
 - Useful in prioritizing hazards

Risk Management Techniques

Preliminary Hazard Analysis (PHA)

- List possible hazards
 - Brainstorm for possible hazards
 - Use previously published literature
 - Use information in international standards

Risk Management Techniques

Preliminary Hazard Analysis

| # | Hazard | Hazardous situation | Harm | Severity | Probability | Risk control |
|---|------------------------------------|--|--|----------|-------------|---|
| | Patient gets incorrect test result | Doctor believes result is accurate and administers insulin | Hypoglycemia; Patient suffered a seizure | S-4 | P-3 | Redesign test; build in internal control; change chemical |

Risk Management Techniques

Fault Tree Analysis (FTA)

- Used in risk analysis as a means of analyzing hazards identified
 - Top-down method
 - Estimate fault probability
 - Identify single fault that result in hazardous situations
 - Identify common faults that result in hazardous situation

Risk Management Techniques

Failure Mode and Effect Analysis (FMEA)

- Used in risk analysis as a means of identifying and evaluating individual fault modes
 - Bottom-up method
 - Starts with causes and works toward effects
 - Estimates fault probability
 - Identifies single fault that result in hazardous situations

Risk Management Techniques

Failure Mode and Effect Analysis (FMEA)

- Answers the question, “What happens if...?”
- Requires device detail to be known

Risk Management Techniques

FDA Benefit-Risk Analysis

- Used to assess medical device risk once all measures to reduce the risk have been applied
 - Decision to rework or use “as is” a nonconforming product
 - CDRH guidance documents available
 - Framework for medical device decision making

Risk Management Techniques

FDA Benefit-Risk Analysis

- Considers several factors when assessing benefits and risk for:
 - Determinations in Premarket Approval Application (PMA) and De Novo classification
 - Determining substantial equivalence in Premarket Notifications [510(k)]
 - Determinations for Investigational Device Exemption (IDE)
 - Product availability, compliance, and enforcement decisions

FDA Benefit-Risk Analysis

| Benefit Factor Considered | PMA/De Novo Determination | 510(k) Substantial Equivalence Determination | IDE Determination | Availability, compliance, and enforcement decisions |
|---|---------------------------|--|------------------------|---|
| Type of benefit | X | | X | X |
| Magnitude of benefit | X | X | X | X |
| Probability or likelihood of participant experiencing one or more benefit | X (Probability) | X (Probability) | X (Probability) | X (Likelihood) |
| Duration of effects | X | X | X | X |
| Patient Perspective on Benefit | | | | X |
| Benefit factors for healthcare professionals or caregivers | | | | X |
| Medical Necessity | | | | X |

FDA Benefit-Risk Analysis

| Risk Factor Considered | PMA/De Novo Determination | 510(k) Substantial Equivalence Determination | IDE Determination | Availability, compliance, and enforcement decisions |
|---|---------------------------|--|-------------------|---|
| Severity of Risk or Harm | X | X (Harmful events) | X | X (Harm) |
| Probability or Likelihood of risk(s) or harmful event | X (Probability) | X (Probability) | X (Probability) | X (Likelihood) |
| Probability of patient experiencing harmful event | | X | | |
| Distribution of nonconforming devices | | | | X |
| Duration of harmful events, risk, or exposure to population | X (Harmful events) | X (Harmful events) | X (Risks) | X (Exposure to population) |

FDA Benefit-Risk Analysis

| Risk Factor Considered | PMA/De Novo Determination | 510(k) Substantial Equivalence Determination | IDE Determination | Availability, compliance, and enforcement decisions |
|---|---------------------------|--|-------------------|---|
| False-positive or false-negative results | X | X | | X |
| Patient tolerance of risk | | | | X |
| Risk factors for healthcare professionals or caregivers | | | | X |
| Risk management | | | X | |
| Residual risk | | | X | |

FDA Benefit-Risk Analysis

- Additional factors to consider (*not all inclusive*):
 - Uncertainty
 - Mitigations
 - Detectability
 - Patient perspectives
 - Patient Impact
 - Firm compliance history
 - Postmarket data
 - Availability of alternative treatments or diagnostics

Example: Benefit-Risk Analysis

- Product Availability, Compliance, and Enforcement Decision:
 - Human chorionic gonadotropin (hCG) device
 - Detection of hCG in urine to aid in early detection of pregnancy
 - Indicated for over-the-counter (OTC) use
 - Healthcare provider noticed higher rate of positive results, but not confirmed positive in blood sample
 - Higher rate of false positives than expected
 - Malfunction identified in specific lots
 - Lay users unable to detect malfunction
 - Many other pregnancy test on the market

Example: FDA Benefit-Risk Analysis

- Benefits
 - Helps patient determine whether patient is pregnant
 - Benefit reduced due to potential lack of test accuracy

- Risks
 - Unnecessary prenatal care
 - Delayed medically necessary treatments

Example: FDA Benefit-Risk Analysis

Worksheet Assessment: Factors considered

- Patient tolerance for risk and perspective on benefit
 - Patient like having OTC test for pregnancy
 - FDA does not have data on patient tolerance
- Mitigation
 - Firm did not identify a mitigation to address this risk
- Patient impact
 - Impact on patient if device was not available in the marketplace
 - Similar devices available without additional risks

Example: FDA Benefit-Risk Analysis

- Product availability, compliance, and enforcement decision
 - **No need to support continued availability of affected lots**
 - Benefit to patients is low
 - Risk moderate due to delay in medically necessary treatment
 - Firm notified retailers and distributors to remove affected lots
 - Firm submitted report to FDA per 21 CFR 806
 - FDA classified action as a Class II recall

Other Risk Management Techniques

- Risk Acceptability Chart
 - For evaluating risk (initial and residual risk)
- Risk Control Option Analysis
 - For controlling risk
- Risk Management Report
 - To capture relevant review of production and postproduction risk information

Summary

- Risk management activities are essential throughout the product life cycle
- PHA, FTA, FMEA, and FDA Benefit-Risk analysis are different types of risk management techniques
- Manufacturers should use more than one risk management technique in their risk management process

Resources

| Slide Number | Cited Resource | URL |
|--------------|--|---|
| 6, 7 | ANSI/AAMI/ISO 14971:2019 Medical devices – Applications of risk management to medical devices | www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/detail.cfm?standard_identification_no=40369 (for purchase from standards organization) |
| 15, 16, 17 | 21 CFR 820 Quality System Regulation | www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=820 |
| 19 | ANSI/AAMI/ISO 14971:2019 Medical devices- Guidance on the application of ISO 14971 | https://www.iso.org/standard/74437.html (for purchase from standards organization) |
| 20 | Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions | https://www.fda.gov/regulatory-information/search-fda-guidance-documents/factors-consider-regarding-benefit-risk-medical-device-product-availability-compliance-and |
| 20 | 4 CDRH Benefit-Risk Guidance documents: | https://www.fda.gov/regulatory-information/search-fda-guidance-documents |

Industry Education: Three Resources for You

1. CDRH Learn: Multi-Media Industry Education

- Over 200 modules
- Videos, audio recordings, power point presentations, software-based “how to” modules
- Mobile-friendly: access CDRH Learn on your portable devices

www.fda.gov/CDRHLearn

2. Device Advice: Text-Based Education

- Comprehensive regulatory information on premarket and postmarket topics

www.fda.gov/DeviceAdvice

3. Division of Industry and Consumer Education (DICE)

- Contact DICE if you have a question
- Email: DICE@fda.hhs.gov
- Phone: 1(800) 638-2041 or (301) 796-7100 (Hours: 9 am-12:30 pm; 1 pm-4:30pm EST)
- Web: www.fda.gov/DICE

Your Call To Action

- Identify when to evaluate risk and conduct risk management activities early
- Identify and utilize resources available for conducting risk management activities
- Make sure you use the appropriate risk management technique/tool for managing risk

