Risk Analysis/Risk Management

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Presentation Objectives

- Discuss Quality System Regulation requirement for risk analysis
- Discuss Quality System Regulation requirements for risk based decisions
- Discuss evaluation of risk management activities during an inspection

Presentation Objectives

- Discuss links between risk analysis requirements and other subsystems

- Describe some common risk analysis and risk management methods

Risk Management Concepts in 21 CFR 820

Overview

QS Regulation VS ISO Requirements

- QS Regulation requires
  - Risk Analysis in Design Controls
  - Risk Based Decision throughout QS Regulation
- ISO System
  - ISO 13485 Quality Management System standard requires risk management within a QMS (not ISO 14971 explicitly)
  - ISO 14971 Risk Management Standard applies to <u>all aspects of the QMS</u>

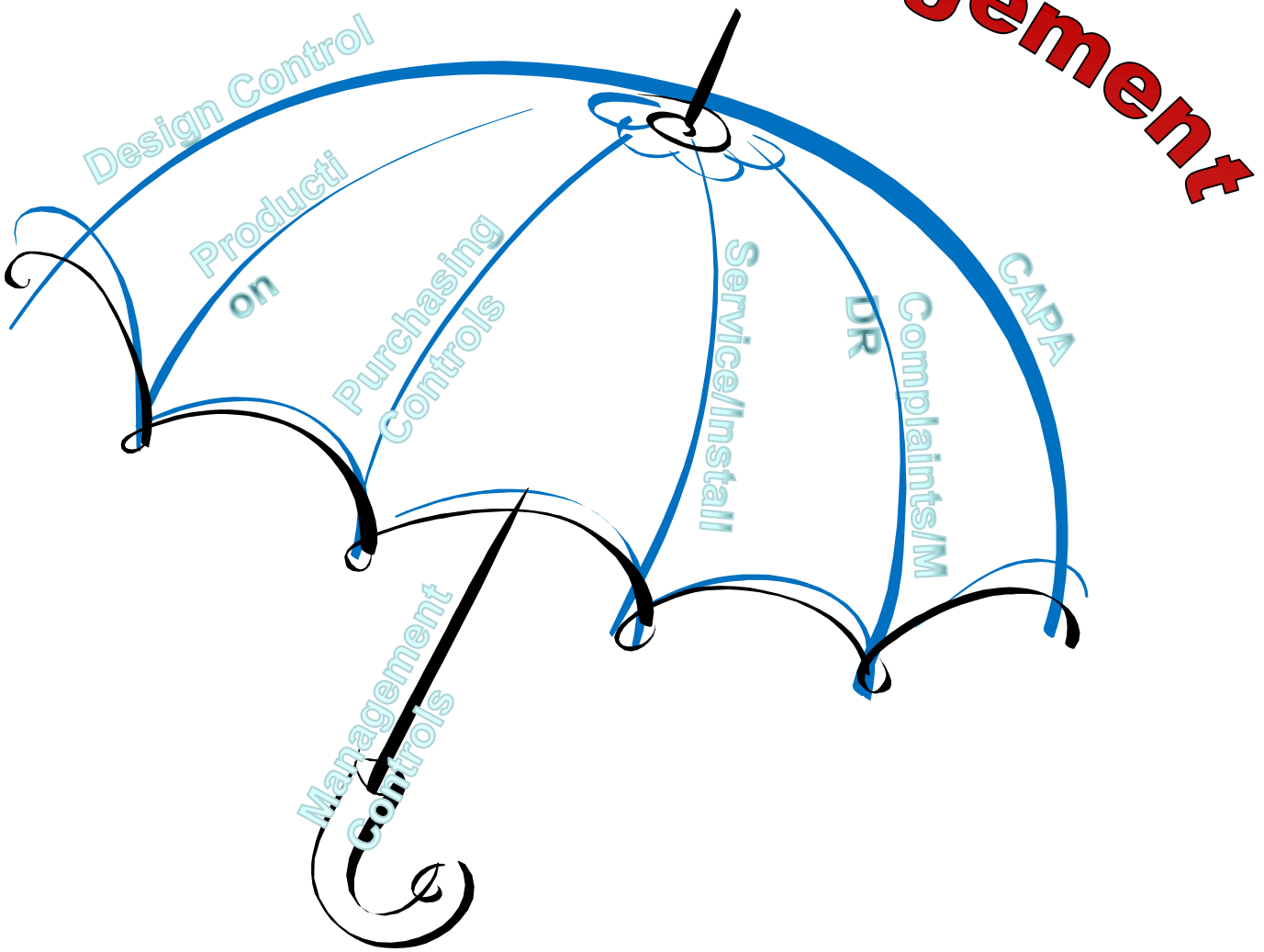
QS Regulation vs ISO Requirements

- Be sensitive to terminology differences
  - FDA Preamble: risk in terms of patient & user
  - ISO 14971: risk applies to people, property & environment
- Intentional similarities in objectives and process
- FDA Risk Analysis ≈ ISO Risk Analysis + ISO Risk Evaluation + ISO Risk Control

QS Regulation vs ISO Requirements

- Feedback Loops – similar concepts
  - FDA CAPA Subsystem
  - ISO 14971 Production & Post Production Information
- Know scope of firm's application of ISO 14971

Risk Management



Risk Management Concepts in 21 CFR 820

Design Controls Subsystem

Risk Analysis in QS Regulation

21 CFR 820.30(g) Design Validation

… Design Validation shall include software validation and risk analysis, where appropriate. …

Risk Analysis in the Preamble

… When conducting a risk analysis manufacturers are expected to identify:

- The possible hazards associated with the design in both the normal and fault conditions
- The risks associated with the hazards, including those resulting from user [use] error, should then be calculated in both the normal and fault conditions

Preamble comment #83

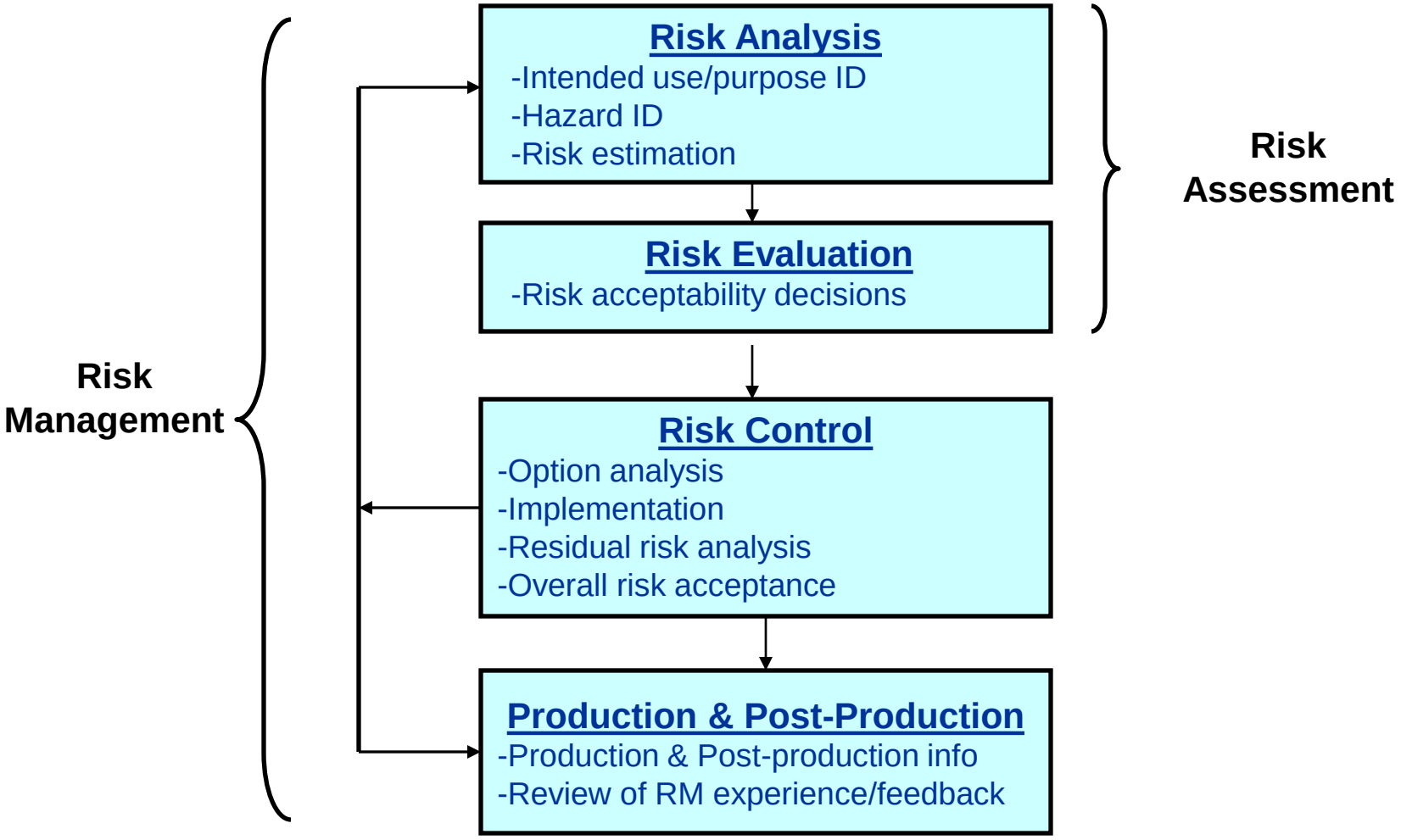
Risk Analysis in the Preamble

… When conducting a risk analysis manufacturers are expected to consider:

- If any risk is judged unacceptable, it should be reduced to acceptable levels by the appropriate means, for example, by redesign or warnings.
- An important part of risk analysis is ensuring that changes made to eliminate or minimize hazards do not introduce new hazards…

Preamble Comment #83

Risk Management Process According to ISO 14971:2006



Simplified FDA Risk Analysis and ISO Risk Management

- Define risk assessment methodology
  - Severity scale
  - Likelihood of occurrence scale
- Define risk acceptability levels
- Understand the intended use
- Identify potential hazards

Risk Based Decisions in the Preamble: Design Change Control

… Manufacturers must also conduct such tests when they make changes in the device design or the manufacturing process that could affect the safety or effectiveness as required in the original CGMP in Sec. 820.100(a)(2). The extent of testing conducted should be governed by the risk(s) the device will present if it fails …

Preamble Comment #81

Risk Management Concepts in 21 CFR 820

Production and Process Controls Subsystem

Risk Based Decisions in the Preamble: Purchasing Controls

- Establish criteria for selection, evaluation and re-evaluation of suppliers.

- Degree of supplier control … may vary with the type and significance of the product and impact on the quality of the finished device

Preamble Comment #99

Risk Based Decisions in the Preamble: Purchasing Controls

- … the extent of the specification detail necessary to ensure that the product or service purchased meets requirements will be related to the nature of the product or service purchased …

- … taking into account the effect the product or service may have on the safety and effectiveness of the finished device, among other factors

Preamble Comment #115

Risk Based Decisions in the Preamble: Acceptance Activities

- Likely to use a combination of purchasing controls and acceptance activities depending on the residual risk

- Each manufacturer must establish an appropriate assessment and receiving acceptance to ensure products and services are acceptable for their intended use

Preamble Comment #99

Risk Based Decisions in the Preamble: Manufacturing Materials

Manufacturing Materials

- When expected to have an adverse effect on product quality, … establish procedures for the removal or limited amount …

- Manufacturing materials should be controlled in a manner commensurate with their risk

Preamble Comment #31

Risk Based Decisions in the Preamble: Traceability

… FDA disagrees that the traceability determination should be based solely on economic risk …

However, to carry out the requirement of the revised provision, the manufacturer should perform risk analysis on the finished device, and subsequently on the components of such device, to determine the need for traceability

Preamble Comment #121

Evaluation of Risk Management Activities During an Inspection

Production and Process Controls Subsystem

Risk Management in Supplier Controls Procedures

- Clearly explain how the firm utilizes risk to patient and/or user to determine the level of control on the supplier including:
  - How quality requirements are established
  - How compliance with quality requirements are monitored
  - Links to design controls risk analysis, essential design outputs and design transfer
- Acceptance procedures clearly explain how risk to the patient and/or user is used to establish acceptance activities

Evaluation of Risk Management Information for a Higher Risk Supplier

- Design Risk Analysis – source of information for identifying higher risk suppliers
- Select a Higher Risk Supplier, such as,
  - Service supplier of a process requiring validation
    - Heat treatments
    - Coatings
    - Surface treatments
  - Contract manufacturer of the device or critical subassembly of the device

Evaluation of Risk Management Information for a Higher Risk Supplier

- Ensure risk to the patient and/or user has been used in establishing
  - Quality requirements for the supplier
  - Monitoring requirements for the supplier
  - Acceptance activities
- RM methodology does not have to be identical to RA in Design Control
- Link to design control information in RA, essential design outputs and design transfer

Risk Management Concepts in 21 CFR 820

Corrective and Preventive Action Subsystem

Risk Based Decisions in the Preamble: Non Conforming Product

- … Non conforming product discovered before and after distribution [should] be investigated to the degree commensurate with the significance and risk of the nonconformity

Preamble Comment #161

Risk Based Decisions in the Preamble: CAPA

… FDA agrees that the degree of corrective and preventive action

- Taken to eliminate or minimize actual or potential nonconformities must be appropriate to the magnitude of the problem and commensurate with the risks encountered.

Preamble Comment #159

Risk Based Decisions in the Preamble: CAPA

… FDA does expect manufacturers to

- Develop procedures for assessing risk,
- The actions that need to be taken for different levels of risk, and
- How to correct or prevent the problem from recurring, depending on that risk assessment

Preamble Comment #159

Evaluation of Risk Management Activities During an Inspection

Corrective and Preventive Action Subsystem

Risk Management Information in CAPA Subsystem Procedures

- CAPA Procedures explain how
  - Risk to the patient and/or user is used to
    - Triage CAPA items
    - Determine the level of investigation
    - Determine the level of verification/validation activities
  - Risk Analysis information is updated
  - Risk Analysis for a project is updated with current information

Risk Management Information in CAPA Subsystem Procedures

- Complaint Handling
  - Explain how risk to the patient and/or user is used to determine the level of investigation

- Non-conforming Product
  - Explain how risk to the patient and/or user is used to determine the level of investigation

Common Risk Analysis/Management Tools

- Failure Modes and Effect Analysis (FMEA)
  - IEC 60812
- Fault Tree Analysis (FTA)
  - IEC 61025
- Preliminary Hazard Analysis (PHA)
  - IEC 60300-3-9
- Hazard and Operability Study (HAZOP)
  - IEC 61882
- Hazard Analysis and Critical Control Point (HACCP)

Comments on Risk Tools

- Quality risk management activities are typically conducted by interdisciplinary teams
- Risk Tools should not be used as an excuse to not conduct corrective action but rather support risk-based decisions

Comments

- Poor risk management decisions will be reflected in application of risk based decisions as described in the Preamble

- ISO 14971 is the most common reference for Risk Management/Analysis and it is or will be a normative requirement in many ISO standards

Comments

- Know the limits the firm places on their compliance with any voluntary Risk Management standard

- Full compliance with ISO 14971 will meet the risk management principles in the QS Regulation
  - Design Controls Subsystem
  - Production and Process Controls Subsystem
  - Corrective and Preventive Action Subsystem

Questions?