Risk Management Overview

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Outline

- Drivers for risk management
- Introduction to ISO 14971
- Key concepts in risk management
- Integrating risk management into your QMS

Global Requirements

- Where is Risk Management required?
  - United States
  - European Union
  - Canada
  - Japan

US Requirements

- The FDA Quality Systems Regulation contains requirements that add up to risk management
- Design Validation - “shall include software validation and risk analysis, where appropriate…” (21 CFR 820.30(g))
- “Manufacturers shall identify possible hazards associated with the design in both normal and fault conditions…. If any risk is judged unacceptable, it should be reduced to acceptable levels...” (Preamble to Final Rule)

US Requirements

- Requirements for complaint files define a risk management process:
  - Identify new hazards
  - Evaluate the subsequent risks
  - Control the risks you find

EU Requirements

- The essential requirements of EU directives for medical devices state that manufacturers must:
  - Eliminate or reduce risks as far as possible by inherently safe design and construction,
  - Where appropriate, take adequate protective measures, including alarms if necessary, in relation to risks that cannot be eliminated,
  - Inform users of the residual risks due to any shortcomings of the protection measures adopted.

Other Requirements

- In Canada manufacturers must:
  - Identify risks
  - Eliminate or reduce risks
  - Protect and provide information on risks that remain
  - Minimize potential failures
  - Canadian Medical Devices Regulations 1998, section 10
- Japan has translated ISO 14971 for use as a Japanese National Standard that is required for all devices marketed in Japan
- Others?

Global Harmonization Task Force

- GHTF
  - Study Group 3 Guidance:
    - Implementation of Risk Management Principles and Activities within a QUALITY Management System
  - Study Group 4 Guidance:
    - Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 2: Regulatory Auditing Strategy

www.ghtf.org

Risk Management-Globally

- “All” countries require risk management
  - Devices must be safe
  - Benefits must outweigh risks
  - Post market surveillance
    - Report adverse incidents
    - Implement effective corrective actions
    - Confirm effectiveness via feedback into risk management

Standards Drivers

- A laundry list of standards:
  - ISO 13485:2003 (Regulatory quality system)
  - IEC 60601-1:2005 (Electromedical devices)*
  - IEC 60601-1-6 (Usability)
  - IEC 62304 & AAMI SW68 (Software)
  - ISO 10993 (Biocompatibility testing, etc.)
  - Plus product-specific standards
  - Over 100 standards now reference ISO 14971
- Indirect “requirements” in other standards

What Are The Internal Drivers?

- Global marketing approach
- User requirements more easily met
- Maintain competitiveness
- Limit liability exposure

Outline

- Drivers for risk management
- **Introduction to ISO 14971**
- Key concepts in risk management
- Integrating risk management into your QMS

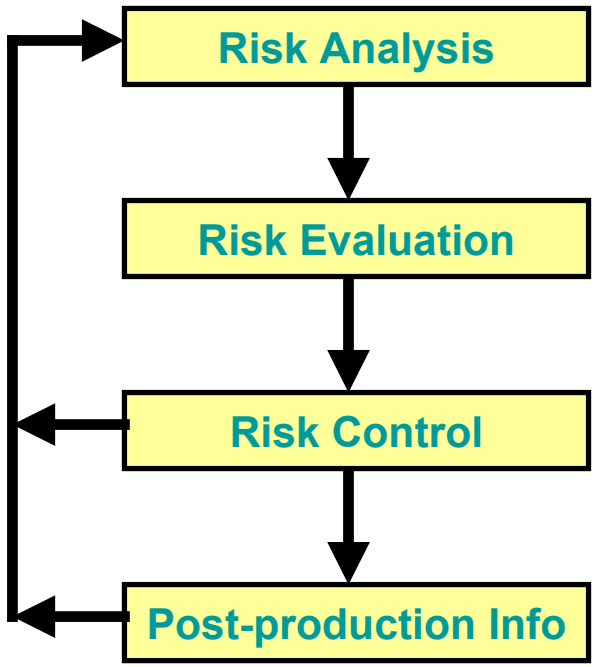
Theory behind ISO 14971

- ISO 14971 is designed as a management system standard
- Assessing risks in a structured way is good design practice
- Not all risks will be found initially, but monitoring device performance allows you to find them quickly and control them
- Documenting what you do allows you to manage risks effectively and not to repeat your previous mistakes or omissions
- **Risk management is a continual improvement process**

Precepts for ISO 14971

- There is always risk associated with the use of a medical device
- Risk acceptability is influenced by the perception of risk…what is meant by this statement?
- ISO 14971 is a “framework” for management of risks
  - Includes well-defined terminology

Risk Management a la ISO 14971



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The Role of Management

- Establish, maintain, and oversee the risk management system
- Define the **policy for determining acceptable risk**
- Provide adequate resources
- Review the results of risk management and sign off on these results
- Review the risk management process itself

ISO 14971 – Scope

- Specifies procedure for a manufacturer to
  - identify hazards
  - estimate/evaluate risks
  - control risks
  - monitor effectiveness of controls
- Applicable throughout device life cycle

ISO 14971 Does Not Specify

- Device hazards
- Acceptable risk levels
- A risk analysis tool
- How to quantify risk
- A design life-cycle model

ISO 14971 / ISO 13485

- Some parallels between Risk and Quality Management Systems:
  - Management Responsibility
  - Design control
  - Corrective and preventive action
  - Process control
  - Qualifications of Personnel
  - Etc.

Risk Management File (Clause 3.5)

- Forms part of the quality records
- Records and maintains the results of all risk management activities
- May contain pointers to the necessary documentation

Risk Management Plan (Clause 3.4)

- The Risk Management Plan includes the:
  - Scope of the plan
  - Verification plan
  - Allocation of responsibilities
  - Management review
  - Risk acceptability criteria
  - Planned production and post-production activities
- May include other items as needed, e.g., risk analysis tools to be used or method for evaluating overall residual risk

Scope

- Identifies and describes the device in sufficient detail to begin hazard identification
- Covers the life of the device from conception to complete disposition
- Ideally, should address activities at every stage of the device life cycle
- May include more than one device, if you are developing a system.

Verification Plan

- Two types of verification:
  - Implementation of risk controls
  - Effectiveness of risk controls (“measurement” of residual risk)
- Typical verification activities:
  - Design reviews
  - Prototyping
  - Testing
  - Modeling
  - Clinical studies
  - Other?

Allocation of Responsibilities

- Who does what and when, e.g.,
  - Responsible manager
  - Responsible individual(s) in Design and Development
  - For purchasing, manufacturing, etc.
  - For data analysis (including CAPA)
  - For review of new hazards or increased risk of known hazards
- Deliverable—primary person—approval

Management Review

- When, how will this be done
- May be part of routine management reviews and can refer to existing procedures for such review
  - Define in each step of your development protocol what risk activities will be reviewed and by whom, *e.g., at phase reviews with management*
  - As development progresses, risk management deliverables are updated/revised with appropriate review as needed
  - Overall residual risk acceptance and risk/benefit decisions should require senior mgmt. approval

Risk Acceptability Criteria

- Must be stated up front
- Derive from the risk management policy
- Specific to the device and its intended use

Risk Acceptability Exercise

What sources must you use?

What sources would you use?

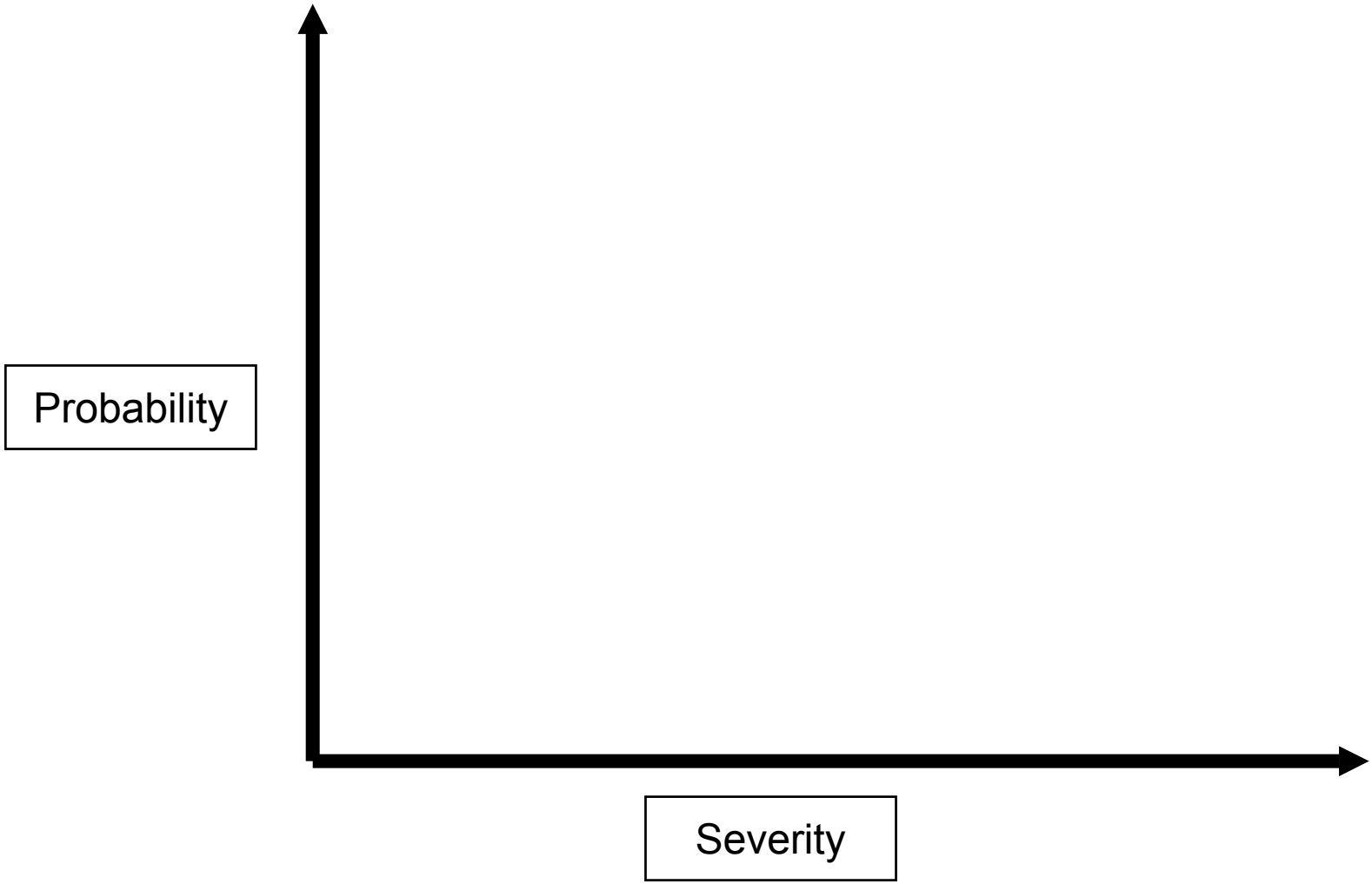
Definition of risk

- Risk has two components, probability and severity
- Each component is usually defined separately
- Risk can be defined quantitatively or qualitatively
- Quantitative estimates are harder
- Probability is fairly easy to define quantitatively
- How would you define severity quantitatively?

Example of Qualitative Levels

- Probability
  - Frequent
  - Probable
  - Occasional
  - Remote
  - Improbable
- Severity
  - Catastrophic
  - Critical
  - Serious
  - Minor
  - Negligible
- Informative guidance in ISO 14971 Annex D

Risk Chart



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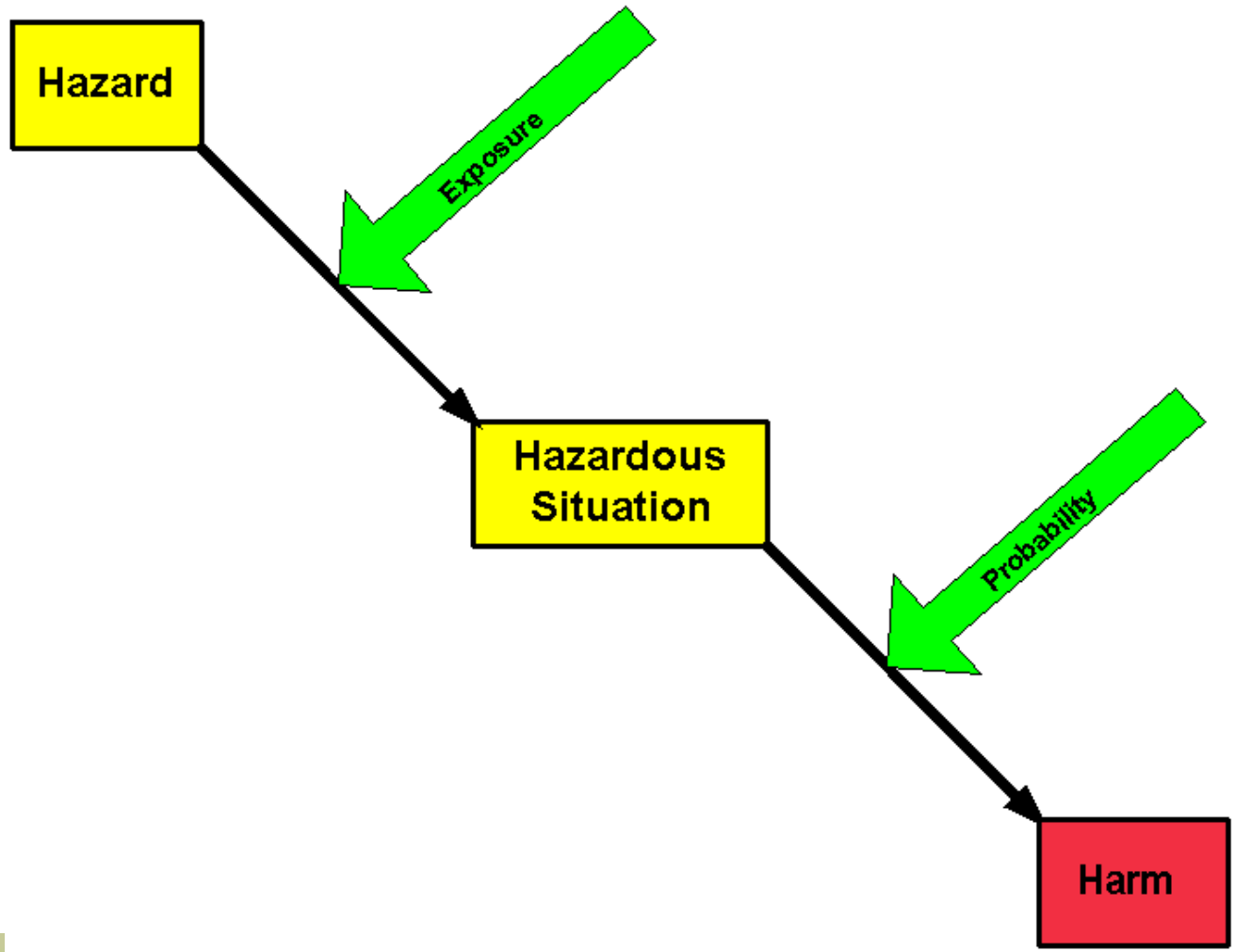
Risk Parameters Exercise

Device: Programmable dental system. Digitally control the speed, direction, and torque of a low speed dental motor. Contains a library of speed and torque settings for commonly used endodontic files and implants. Further programmable by the dentist for preferred settings.

Define the scale for harm

Define the scale for probability…what units will you use?

Use of Hazards, Hazardous Situations



Note On Intended Use

- Should have been stated in Risk Management Plan
- **Essential step**
- Must describe in sufficient detail to enable hazard identification
- Note relationship to risk acceptability… example?

Hazard Identification Clause 4.3

- ISO 14971 does not give you a list of hazards
- Annex A gives a list of questions to ask relating to safety…**use this only as a start**
- Pay particular attention to the interface between the device and the patient or the user
- Could the device be used in ways other than you intend?

Hazard Identification

- Essentially a brainstorming activity…be ruthless!
- Enlist healthcare practitioners if possible.
- Use historical examples and experience with similar devices.
- What hazards are present?
- Does a standard exist that addresses these hazards?

Hazard Identification

- Analyze both normal and fault conditions
- Consider event sequences that may result in hazards
  - EM field increments “soft” counter leading to incorrect torque setting
- List out the hazards and the hazardous situations that may occur

Hazard Identification Exercise

- Device: Programmable dental system. Digitally control the speed, direction, and torque of a low speed dental motor. Contains a library of speed and torque settings for commonly used endodontic files and implants. Further programmable by the dentist for preferred settings.
- Question C.2.1: What is the intended use and how is the medical device to be used? What other questions apply?
- What are the resulting hazards?
- What are the hazardous conditions?

Hazards and harms

- Identify the harm which may result from each identified hazard
- A hazard may result in multiple harms
- A hazard may trigger another hazard that results in harm…example?

Hazard Identification and Hazardous Situations

- What are the potential hazards with our device?
- What hazardous situations do they lead to?

- Matrix

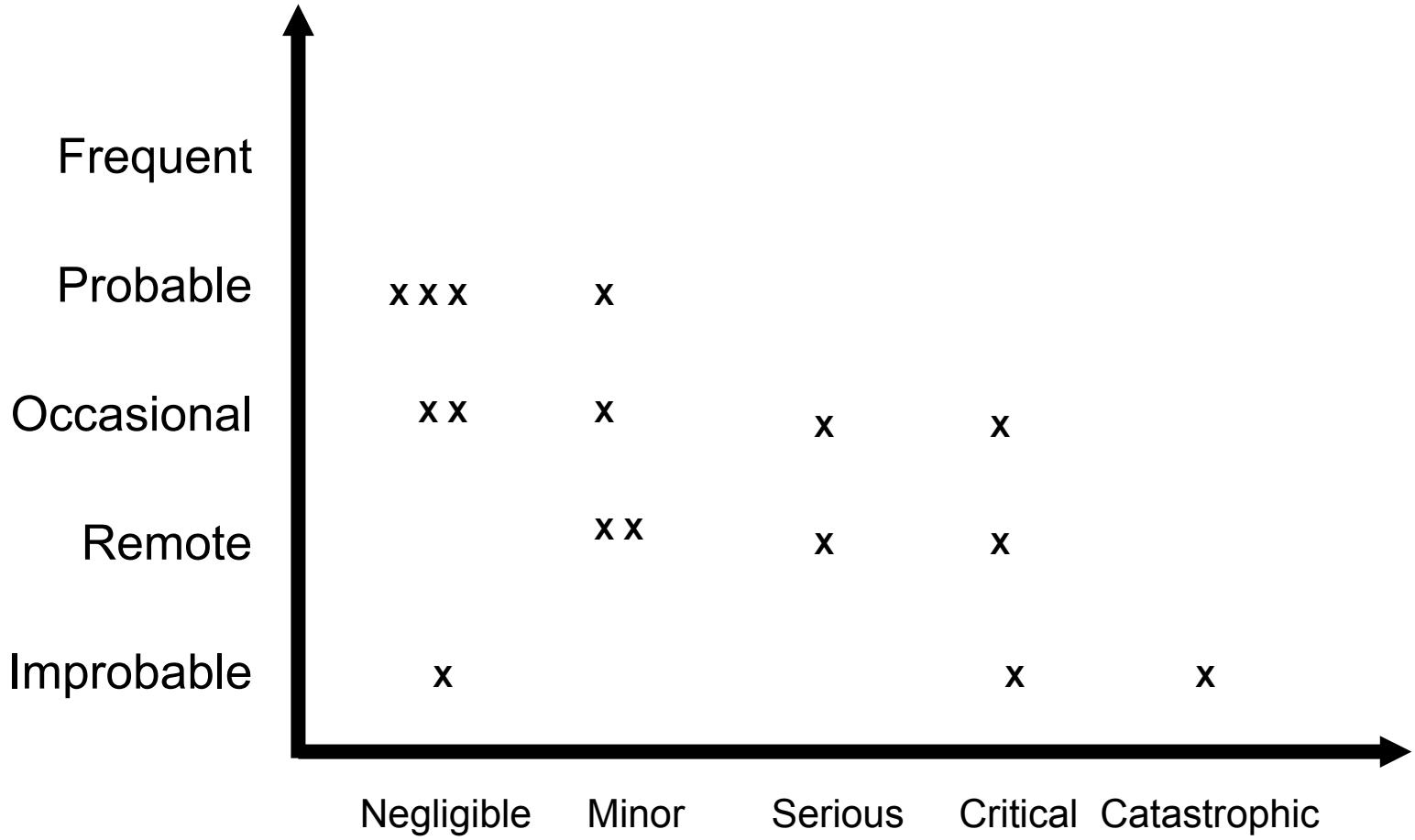
Risk Estimation Clause 4.3

- For each harm, estimate the severity and the probability of occurrence.
- Are you going to use quantitative or qualitative measures?
- Quantitative is best (sometimes necessary…why?)
- Define all qualitative measures carefully.
- Use hard data from the literature or your own files wherever possible.

Risk Estimation

- What about probabilities that you can't estimate?
  - Software failures?
  - Other systematic failures?
- These will need to be addressed separately and your risk controls severity-driven…what do we mean by this?

Risk Chart



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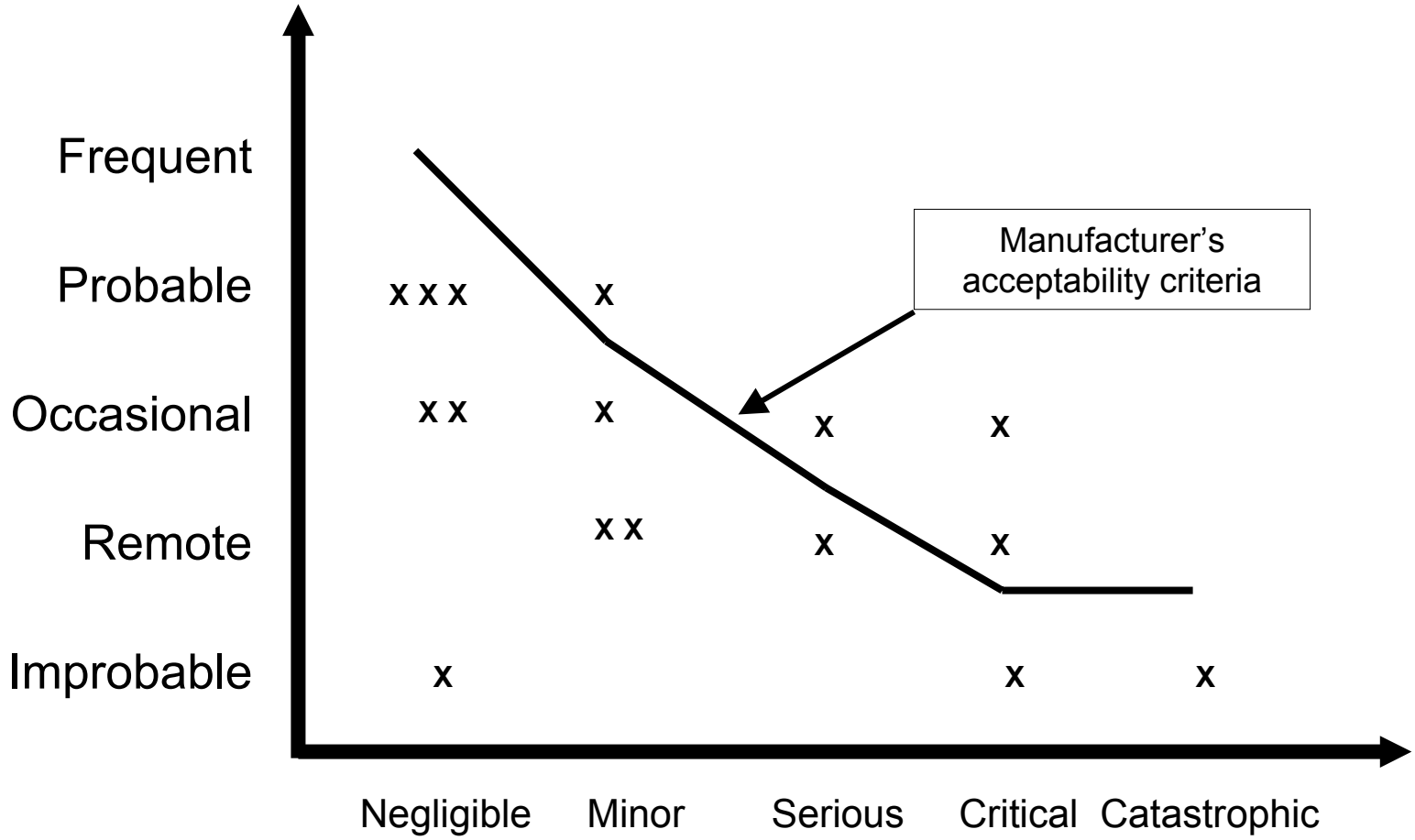
Risk Evaluation (Clause 5)

- All risks due to identified hazardous situations have been estimated
- These exceeding our risk acceptability criteria will require risk control
- Should we ignore risks that are less than our acceptability criteria?
- What do we do with the risks where probabilities cannot be estimated?

Risk Chart



Risk Control (Clause 6)

Design Goals for Risk Reduction

- Reduce each unacceptable risk
  - Reduce probability, and/or
  - Reduce severity
- Hierarchy of risk reduction options
  - Inherent safety by design
  - Protective measures
  - Information for safety

Risk Control Measures (Clause 6.2)

- Risk control measures are design requirements for:
  - Product
  - Any manufacturing or production process
  - User information
- The implementation and the effectiveness of these requirements must be verified.
- The risk management file contains the proof that this has occurred.

Option Analysis Exercise

Hazardous situation: Choose one from our traceability matrix…Matrix

Our options:

- Inherent safe design?
- Protective measures?
- Information for safety?

Other Generated Risks (Clause 6.5)

- The risk control measures have to be looked at carefully to see whether any new hazards or hazardous situations have been introduced.
- If there are new hazards or hazardous situations, they must be addressed.
- What about our previous example?

Residual Risk Evaluation (Clause 6.4)

- Once a risk control measure has been determined, the residual risk is estimated.
- If the residual risk is still judged unacceptable, then additional risk control measures must be considered.

Completeness (Clause 6.7)

- The risk management process is reviewed to make sure that, for the device in question:
  - All identified hazards are addressed
  - The risks comply with the risk acceptability criteria

Overall Risk Acceptability (Clause 7)

- Key definitions:
  - Residual Risk – Risk remaining after protective measures have been taken (Clause 2.15)
  - Overall Residual Risk – The combined impact of all individual residual risks
- Most difficult part of the risk management process
- How would you go about assessing overall residual risk?

Risk / Benefit Analysis

- If an individual or the overall residual risk exceeds the acceptability criteria, you are allowed to conduct a risk benefit analysis…**Why?**
- Questions to ask:
  - What are the medical benefits of the intended use/intended purpose of the device?
  - Do the medical benefits justify the level of risk associated with the use of the device?
- Record the justification(s) in the risk management file.

Verification Activities

- Must verify that the risk controls are present in the device (or the accompanying documents or in its manufacture, etc.)
- Must verify the effectiveness of the risk control measure, i.e., the residual risk is acceptable
- How do you verify the effectiveness of information for safety?

Risk Management Report (Clause 8)

- Produced prior to manufacture and is evidence that:
  - The risk management plan has been appropriately implemented
  - The overall residual risk is acceptable
  - Appropriate methods are in place to obtain relevant production and post-production information
- Demonstrates to the responsible manager that the product is safe for its intended use.

Production and Post-Production Information (Clause 9)

- Is user feedback (complaints) the only source for post-market information?
- What sources does the standard ask you to consider?
- May need to institute a systematic method for obtaining and evaluating post-market information
- What you do here derives from the risk management plan
- This element completes the total life cycle approach

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Key Concepts

- Risk management must occur throughout the life cycle of the device.
- Risk management must be a critical part of the Quality Management System
  - Integrated thoroughly into the QMS
  - Used to help tie all the pieces together
- Top management must play a key role
  - Policy
  - Resources
  - Review and oversight

Key Concepts

- Acceptable risks must derive from (initial) risk-benefit considerations
- Must keep current with state of the art
- Must continuously question your analysis and assumptions
- Finding out you were wrong is not disastrous, but failure to act on your findings courts disaster

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Risk Management and the QMS

- Management responsibilities
- Planning
- Design and development
- Traceability
- Purchasing controls
- Production and process controls
- Data analysis
- (CAPA)

The Role of Management

- Establish, maintain, and oversee the risk management system
- Define the policy for determining acceptable risk
- Provide adequate resources
- Review the results of risk management
- Sign off on these results

Planning

- Risk Management spans the entire life cycle of the device
- Must be incorporated into all planning activities

Design and Development

- Risk management needs to begin as early as possible in the process
- The results of risk evaluation, such as the need for risk controls, are design inputs
- The risk control measures themselves are design outputs and must be verified
- The input/output/verification cycle is iterated until risks are acceptable.
- Overall effectiveness of risk control measures that are part of the design is assessed during design validation.

Traceability

- Risk management data should be use to define which devices, components, materials and work environment conditions require traceability.

Purchasing Controls

- Risk management activities should identify hazards and evaluate risks, including those potentially introduced by suppliers early in the product realization process.
- Issue of subcontracting major components and systems (or the entire manufacturing process itself)
- Risk control measures may be part of the purchasing process, e.g., the use of high integrity components

Production and Process Controls

- Risk controls are frequently incorporated into the manufacturing process
- Need for special measuring and monitoring activities
- HACCP can be used to identify such risk control measures
- All sources of quality data should be used for production and post-production information monitoring

Analysis of Data

- Essential for an effective risk management system
- Look at:
  - Quality data
  - Service records
  - Information on competitor's devices
  - Information on similar medical devices on the market
  - Published information (recalls, Medical Device Reports, vigilance reports, etc.)
  - Scientific literature
  - Etc.

CAPA

- Even though risk management is not required for CAPA under ISO 13485, CAPA must link back into design change control through the risk management process.

Summary

- Who is involved with risk management?…everyone!
  - Management
  - Consultants
  - Design
  - Manufacturing
  - Purchasing
  - Sales and marketing
  - Service and complaint handling
  - Etc.
- Communication is the key

Thank You!

Any Questions?

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