Risk Analysis for Medical Devices

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My goal for today?

Teach you about the risk management process used with all medical devices

Why me?

- Previously worked at Stryker as project leader to develop a novel medical device
- Now work directly with FR orthopedic implant manufacturers on EN translation projects, including risk analysis documents

THE BIG SPREADSHEET

	B	C	F	G	H	I	K	M	N
	Risk analysis						Risk eval.		Risk con
	Hazard	Reasonably forseeable sequence or combination of events	Hazardous situation	Harm	Po	Severity	Acceptable?	Risk control options and rationale	Risk control measure
	Virus	DISPOSABLE is contaminated during UNPACKING.	Patient is exposed to virus.	Infection leading to death	3	5	N ACC	Design cannot be inherently safe by design, nor can protective measures be applied to prevent users from touching sterile disposable when unpacking.	Label the device as sterile. Provide information in the instructions for use on how to unpack and not to touch disposable without using sterile procedure.
	Bacteria	TUBING is kinked during STERILIZATION.	Patient is exposed to bacteria.	Bacterial infection	2	4	ACC*	Tubings cannot be removed, thus design cannot be inherently safe by design, however	An outer stiff tubing/spring shall be applied to tubing. The tubing shall be fixated to packing material to

Agenda

Big picture

ISO 14971 standard

Risk management process

Sample medical device

Big Picture

- Use of any medical device entails some degree of risk
- Acceptability of this risk affected by stakeholder's perception of this risk:
  - Cultural background, educational level
  - Patient's health condition
- Safety: freedom from unacceptable risk

Big Picture

- Why perform risk analysis?
  1) It's the right thing to do
  2) Ensures that device is safe
  3) Identifying problems in device's design before distribution eliminates costs associated with recalls
  4) Provides some measure of protection from product liability damage awards
  5) Helps to identify any unsafe devices on market and correct deficiencies
  6) Required by law

Big Picture

- In the USA:
  - Medical Device Good Manufacturing Practices Regulation, 21 CFR Section 820.30 (Design Controls) calls for:

    "§820.30(g) Design validation….

    Design validation shall include software validation and risk analysis…"

Big Picture

- In Europe:
  - Manufacturer required by the Directive to perform a formal risk analysis within its quality management system
  - European Directive 93/42/EEC on Medical Devices
  - Preferred standard to use: ISO 14971
- In Japan:
  - Risk analysis report according to JIS 14971 (ISO 14971)

Agenda

Big picture

ISO 14971 standard

Risk management process

Sample medical device

ISO 14971:2007 Standard

- Application of risk management to medical devices
- Provides framework for risk management process

- Risk: combination of the *probability* of occurrence of *harm* and the *severity* of that *harm*

ISO 14971 – Definitions

- Harm: physical injury or damage to health of person, or damage to property or environment
- Hazard: potential source of harm
- Hazardous situation: circumstance in which people, property, or the environment are exposed to one or more hazard(s)
- Severity: measure of the possible consequences of a hazard

Agenda

Big picture

ISO 14971 standard

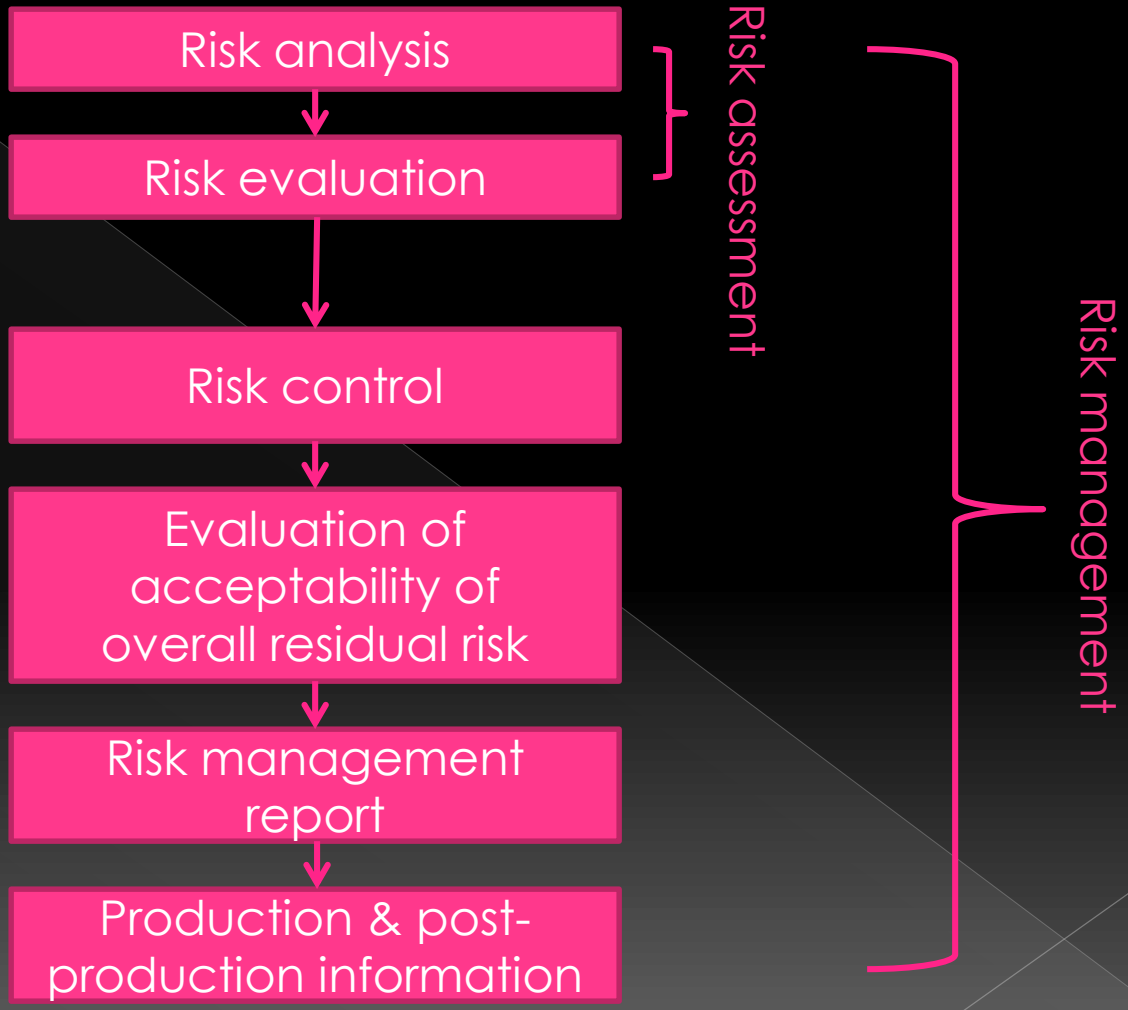
Risk management process

Sample medical device

Risk Management Process

- Manufacturer responsible for
  - identifying hazards associated with device
  - estimating & evaluating the associated risks
  - controlling these risks
  - monitoring effectiveness of controls
  - assessing whether residual risk(s) are acceptable
  - regularly reviewing new data wrto these risks
- Manufacturer maintains risk management file to provide traceability

Risk Management Process



Based on Figure 1 in ISO 14971:2007

Agenda

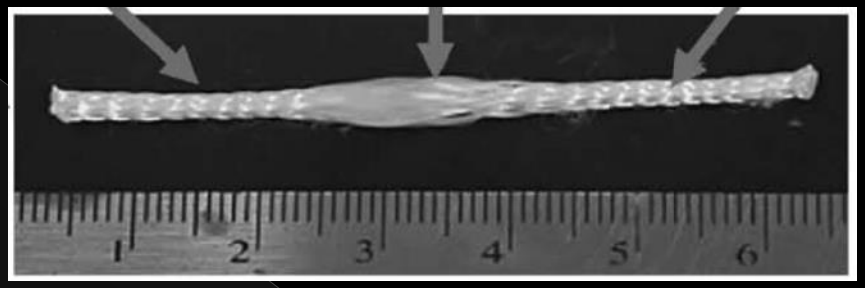
Big picture

ISO 14971 standard

Risk management process

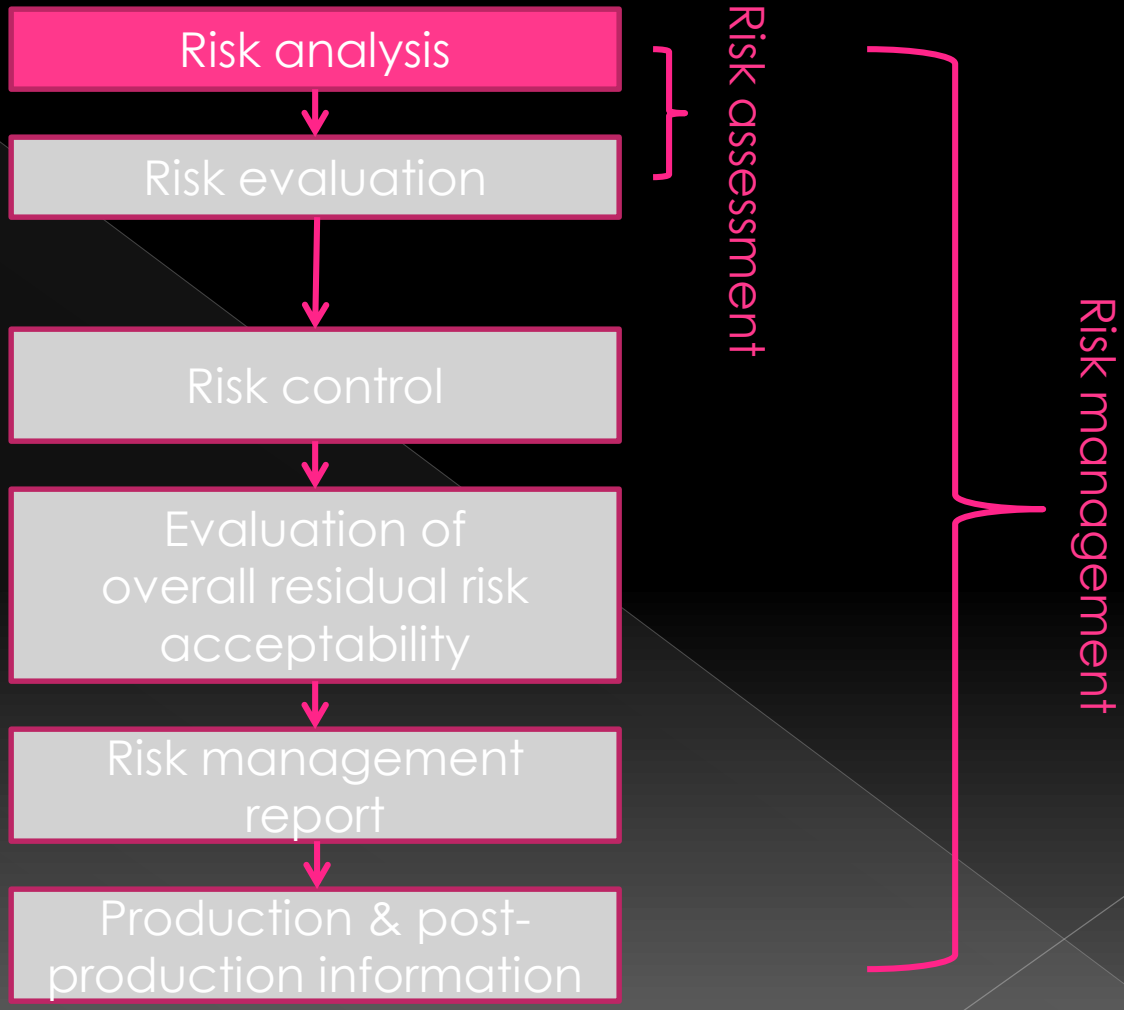
Sample medical device

Sample medical device – SILKNEE



- New medical device undergoing preclinical development
- Indication: replacement of torn ACL (knee ligament)
- Made from silk that is braided into a small rope
- Available in different lengths
- Will be implanted by an orthopedic surgeon
- Target market: athletes with knee injury

Process – Risk analysis



Process – Risk analysis

- Definition from ISO 14971
  - Systematic use of available information to identify hazards and to estimate the risk
- Steps
  1) Defined intended use and identify characteristics related to safety of device
  2) Identify hazards and hazardous situations
  3) Estimate risk(s) for each hazardous situation

SILKNEE – Intended use

- Intended use
  - Replace torn ACL following knee injury
- Characteristics that could impact safety of device (questions in ISO 14971 Annex C)
  - Will device be implanted?
  - Is energy delivered to or extracted from patient?
  - Is the device sterile or will it be sterilized by user?
  - Are measurements being taken?
  - Is maintenance or calibration needed?
  - Does the device have a shelf life?

SILKNEE – Hazards identification

- Compile list of foreseeable hazards → potential sources of harm
  - Energy hazards
    - electromagnetic, radiation, thermal, mechanical
  - Biological and chemical hazards
    - bacteria, viruses, cleaning agents, biocompatibility
  - Operational hazards
    - function, errors in use
  - Information hazards
    - labelling, instructions for use, warnings, maintenance

SILKNEE – Hazard identification

Energy	Biological/chemical	Operational	Information

Hazard: potential source of harm to patient or user

SILKNEE – Hazard identification

Energy	Biological/chemical	Operational	Information
	Allergens in silk		Incorrect storage
	Residue from EtO sterilization	Not correctly secured inside knee	
	Denatured silk	Wrong length	Implant is reused

Hazard: potential source of harm to patient or user

SILKNEE – Hazardous situation

Hazard	Hazardous situation	Harm
Wrong length implanted		
Denatured silk		

Hazardous situation: circumstance in which people, property, or the environment are exposed to one or more hazard(s)

Harm: physical injury or damage to health of person, or damage to property or environment

SILKNEE – Hazardous situation

Hazard	Hazardous situation	Harm
Wrong length implanted	No tool to estimate required length of SILKNEE	
Denatured silk		

Hazardous situation: circumstance in which people, property, or the environment are exposed to one or more hazard(s)

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SILKNEE – Hazardous situation

Hazard	Hazardous situation	Harm
Wrong length implanted	No tool to estimate required length of SILKNEE	Knee too tight Knee is loose Revision
Denatured silk		

Hazardous situation: circumstance in which people, property, or the environment are exposed to one or more hazard(s)

Harm: physical injury or damage to health of person, or damage to property or environment

SILKNEE – Hazardous situation

Hazard	Hazardous situation	Harm
Wrong length implanted	No tool to estimate required length of SILKNEE	Knee too tight Knee is loose Revision
Denatured silk	Box containing device was forgotten outside in Miami on November 4th (Temp: 88F, RH: 76%); that device is implanted in patient	

Hazardous situation: circumstance in which people, property, or the environment are exposed to one or more hazard(s)

Harm: physical injury or damage to health of person, or damage to property or environment

SILKNEE – Hazardous situation

Hazard	Hazardous situation	Harm
Wrong length implanted	No tool to estimate required length of SILKNEE	Knee too tight Knee is loose Revision
Denatured silk	Box containing device was forgotten outside in Miami on November 4th (Temp: 88F, RH: 76%); that device is implanted in patient	Allergic reaction Device fails inside knee Revision

Hazardous situation: circumstance in which people, property, or the environment are exposed to one or more hazard(s)

Harm: physical injury or damage to health of person, or damage to property or environment

SILKNEE – Estimate risk

- Risk estimation has two components:
  - probability of the hazardous situation occurring
  - consequences of that harm → severity
- Estimate probability of hazardous situation occurring
  - Historical data, experimental data, production data
  - Expert judgement
- Categorize severity of harm
  - Continuum of levels set by manufacturer

- Note: probability aka likelihood

SILKNEE – Estimate risk

- Qualitative analysis: describe probability and severity of risk associated with each hazardous situation

Table D.1 — Examples of qualitative severity level

Common terms	Possible description
Significant	Death or loss of function or structure
Moderate	Reversible or minor injury
Negligible	Will not cause injury or will injure slightly

Table D.2 — Simplified examples of qualitative probability levels

Common terms	Possible description
High	Likely to happen, often, frequent
Medium	Can happen, but not frequently
Low	Unlikely to happen, rare, remote

SILKNEE – Estimate risk

Risk #	Hazard	Hazardous situation	Prob. of occurrence	Harm	Severity of harm
1	Wrong length implanted	No tool to estimate required length		Knee too tight Knee is loose Revision	
2	Denatured silk	Device exposed to high heat & humidity		Allergy Device fails inside knee Revision	

SILKNEE – Estimate risk

Risk #	Hazard	Hazardous situation	Prob. of occurrence	Harm	Severity of harm
1	Wrong length implanted	No tool to estimate required length	High	Knee too tight Knee is loose Revision	Moderate
2	Denatured silk	Device exposed to high heat & humidity	Medium	Allergy Device fails inside knee Revision	Moderate

High probability: Likely to happen, often, frequent
Medium probability: Can happen, but not frequently

Moderate severity of harm: reversible or minor injury

SILKNEE – Estimate risk

- Qualitative 3 x 3 risk matrix

Severity levels

Probability levels	Negligible	Moderate	Significant
High			
Medium			
Low			

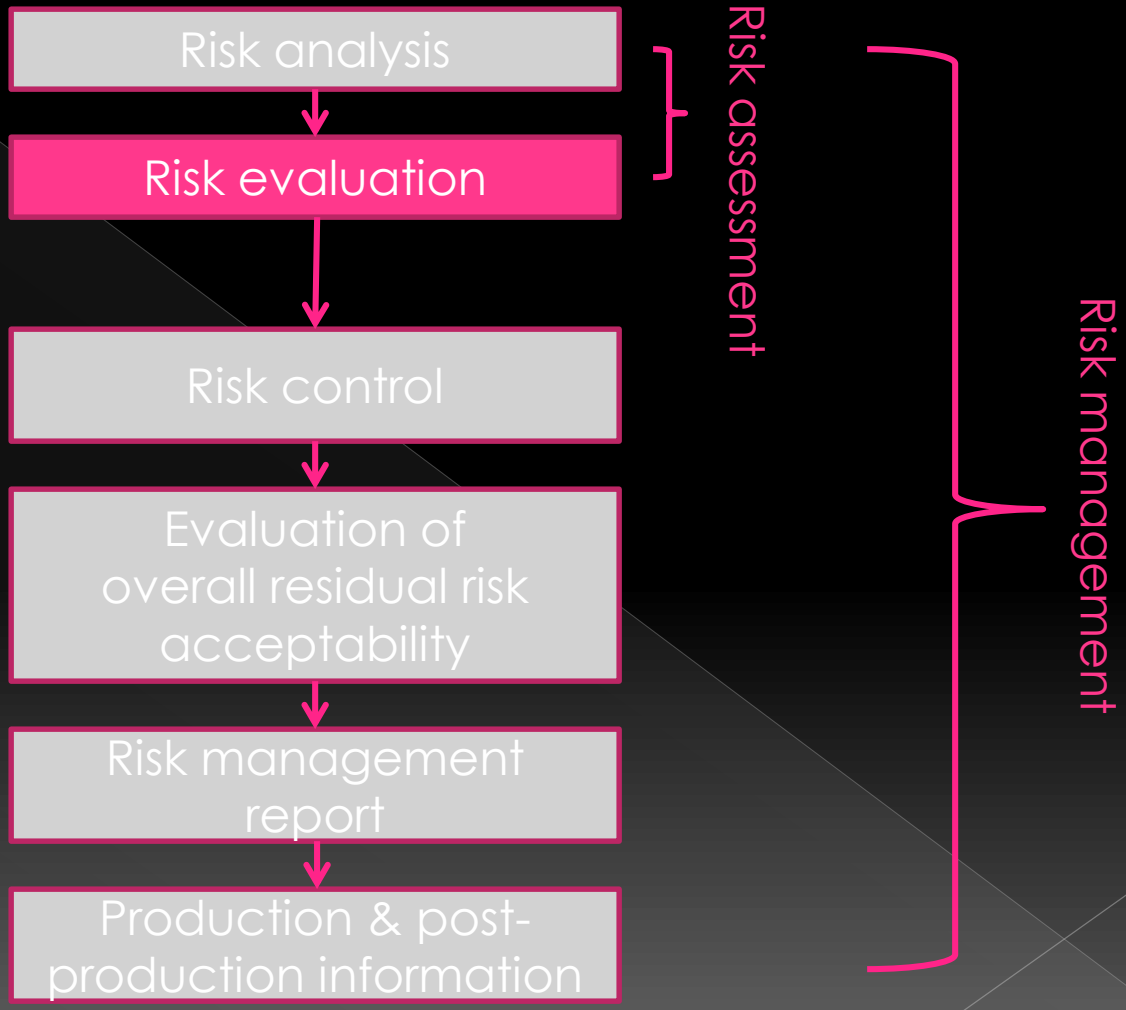
SILKNEE – Estimate risk

- Qualitative 3 x 3 risk matrix

Severity levels

Probability levels	Negligible	Moderate	Significant
High		1	
Medium		2	
Low			

SILKNEE – Risk evaluation



Process – Risk evaluation

- Definition from ISO 14971
  - Process of comparing estimated risk against given risk criteria to determine acceptability of the risk
- For each identified hazardous situation, manufacturer decides if risk reduction is required based on its risk acceptability criteria defined in its risk management plan
  - Criteria applied by persons not involved in design and development of device

Process – Risk evaluation

- Manufacturer determines risk acceptability
  - ISO 14971 does not specify acceptable risk
  - Guidance provided in Annex D
- Methods to determine acceptable risk
  - Use applicable standards
  - Compare risk levels with devices already in use
  - Evaluate clinical data
  - Take into account state of the art
- Also take perception of risk into account

SILKNEE – Risk evaluation

- Application of acceptability criteria

Severity levels

Probability levels	Negligible	Moderate	Significant
High			
Medium			
Low			

Key

unacceptable risk

acceptable risk

SILKNEE – Risk evaluation

- Application of acceptability criteria

Severity levels

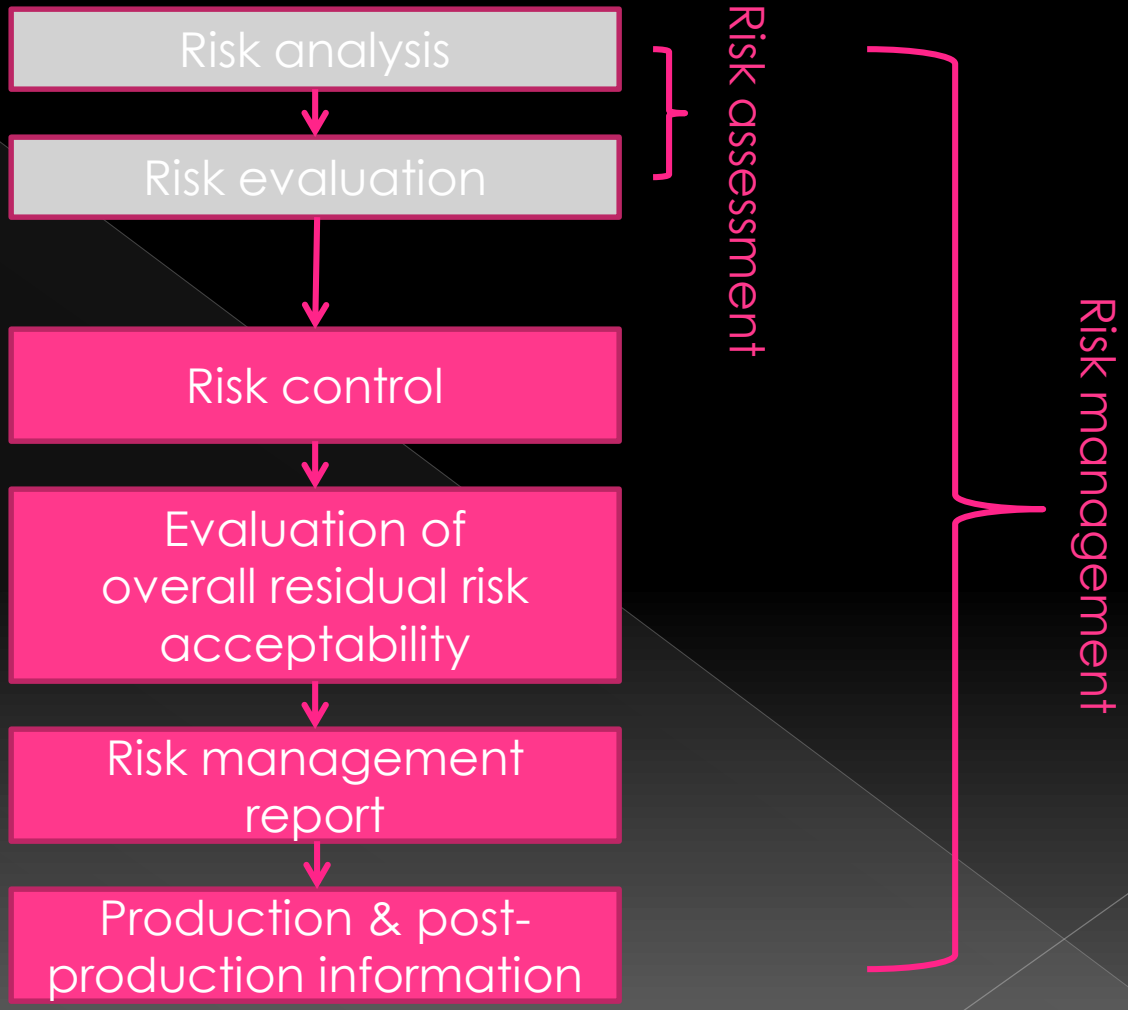
Probability levels	Negligible	Moderate	Significant
High		1	
Medium		2	
Low			

Key

unacceptable risk

acceptable risk

What's next in the process?



Process – Risk control

- Definition from ISO 14971
  - Process in which decisions are made and measures implemented by which risks are reduced to, or maintained at, specified levels
- Steps
  - Analysis of risk control options
  - Implementation of risk control measure(s)
  - Residual risk evaluation
  - Risk/benefit analysis
  - Risks arising from risk control measures
  - Completeness of risk control

SILKNEE – Risk control measures

Risk #	Hazard	Hazardous situation	Acceptable risk?	Risk control measures
1	Wrong length implanted	No tool to estimate required length	**No**	
2	Denatured silk	Device exposed to high heat & humidity	**No**	

SILKNEE – Risk control measures

Risk #	Hazard	Hazardous situation	Acceptable risk?	Risk control measures
1	Wrong length implanted	No tool to estimate required length	**No**	X-ray template to measure length Length gauge for inside knee
2	Denatured silk	Device exposed to high heat & humidity	**No**	Packaging Warnings on outer label about storage conditions

Process – Evaluation of overall residual risk acceptability

- Residual risk (RR)
  - Risk remaining after risk control measures have been taken
- Is the overall RR of the device acceptable?

SILKNEE – Risk control measures

Risk #	Hazard	Hazardous situation	Acceptable risk?	Risk control measures	Acceptable RR?
1	Wrong length implanted	No tool to estimate required length	No	X-ray template to measure length Length gauge for inside knee	Yes
2	Denatured silk	Device exposed to high heat & humidity	No	Packaging Warnings on outer label about storage	Yes

Process – Evaluation of overall residual risk acceptability

- Does data suggest that the medical benefits of the intended use outweigh the overall residual risk?
  - If evidence supports conclusion that medical benefits outweigh overall RR, then overall RR can be judged acceptable
  - Otherwise, overall RR remains unacceptable

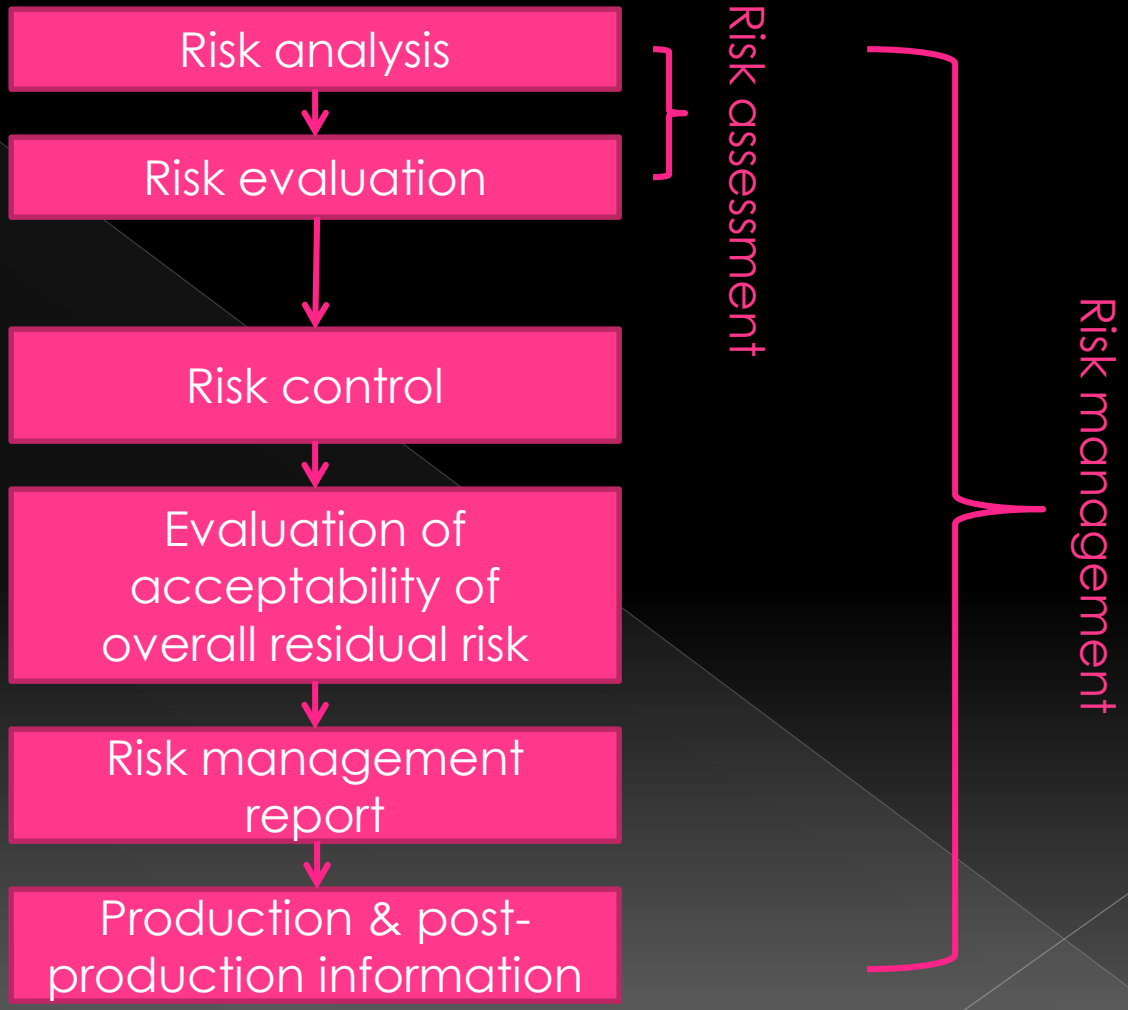
Process – Risk mgmt report

- Before device can be approved for sale
- Manufacturer reviews risk management process
  - Risk management plan has been appropriately implemented
  - Overall residual risk is acceptable
  - Appropriate methods in place to obtain relevant production and post-production information
- Results recorded in risk management report

Process – Production and post-production information

- Collect and review information about device in production and post-production
- Collect and review publicly available information about similar medical devices to evaluate:
  - if previously unrecognized hazards or hazardous situations are present
  - if the estimated risk(s) arising from a hazardous situation is/are no longer acceptable
- Impact on safety?

Risk Management Process



Based on Figure 1 in ISO 14971:2007

Summary

- Risk analysis required by law to protect patients, but also benefits manufacturer
- Dynamic activity throughout the device's life cycle
- ISO 14971 standard is the key to the process
- 2012 version requires that all risks are reduced to levels that are "as low as reasonably possible"

Questions?

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