44th Annual ASQ North Jersey Spring Quality Conference

MEDICEPT
Trusted Solutions, Rapid Response

Integrated Lifecycle Model of the QMS & RMS for Successful Post Market Surveillance

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MEDIcept, LLC

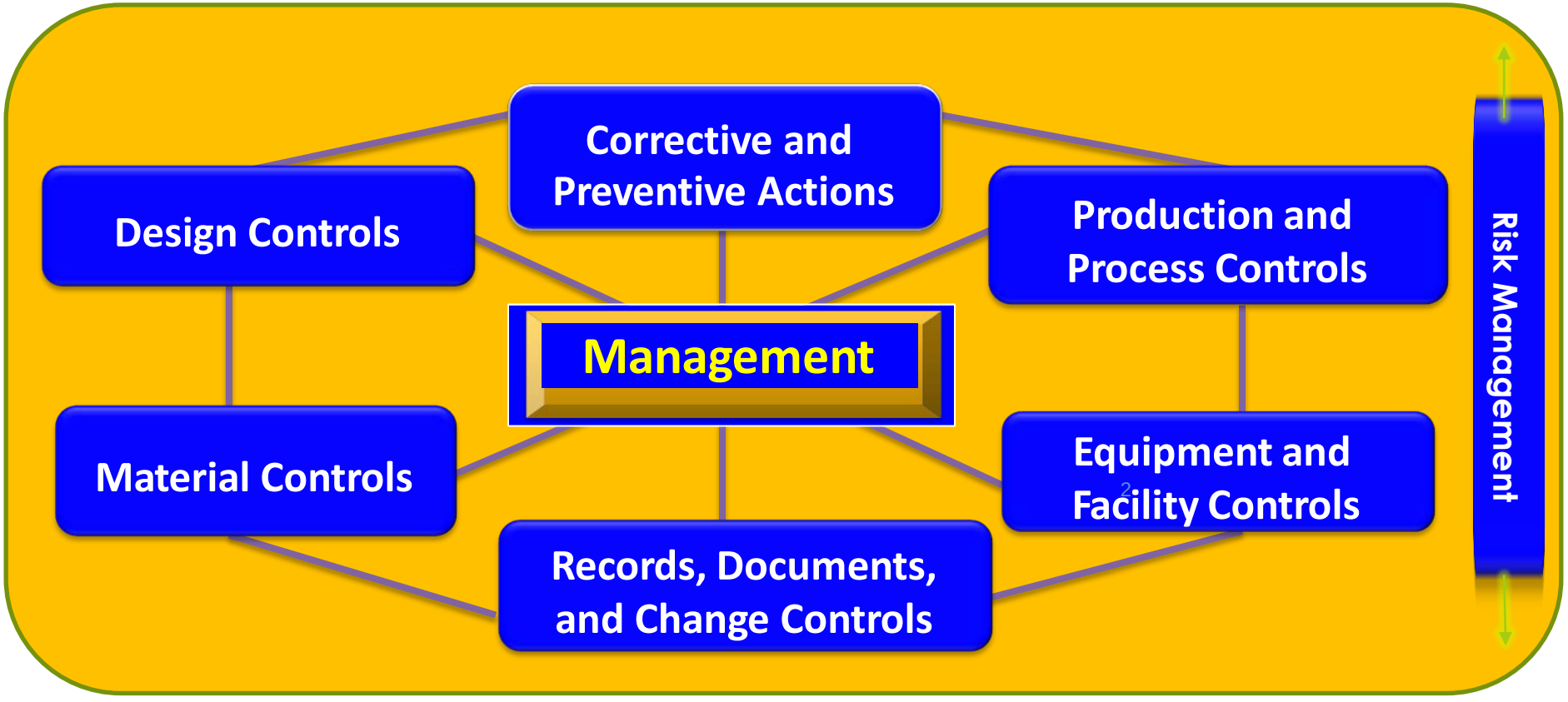
Key Takeaways

Recognize that substantial changes within your Quality Management System will be necessary in order to comply with new global regulatory expectations for Risk Management

Identify the correlation between quality management systems, risk management, clinical evaluation and other post market surveillance activities

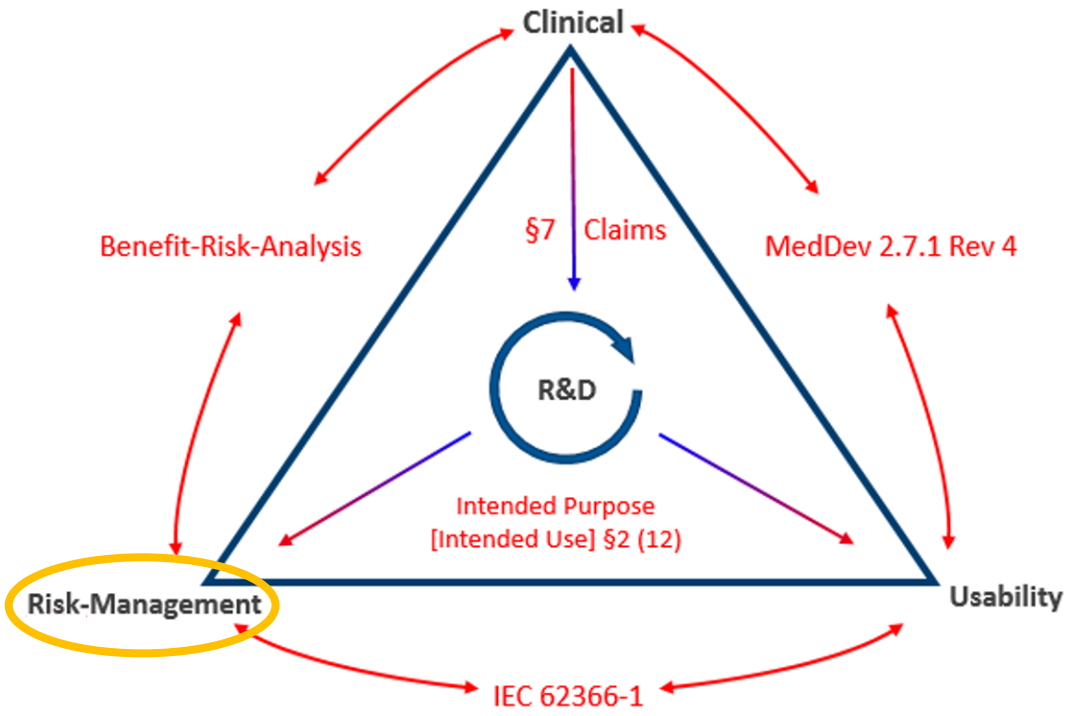
Reflect on the importance of coordinating efforts within your company related to these requirements to ensure the approval and certification/recertification of your products

Subsystems of a Quality System



EU MDR/IVDR

EU MDR/IVDR



EU Medical Device Regulations requirements:

ANNEX I

GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

CHAPTER I

GENERAL REQUIREMENTS

1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.

Achieve the performance intended . . . suitable for their intended purpose . . . and shall not compromise:

- the clinical condition or safety of the patient
- the safety and health of users
- acceptable risks when weighed against the benefits to the patient
- taking into account the generally acknowledged state of art

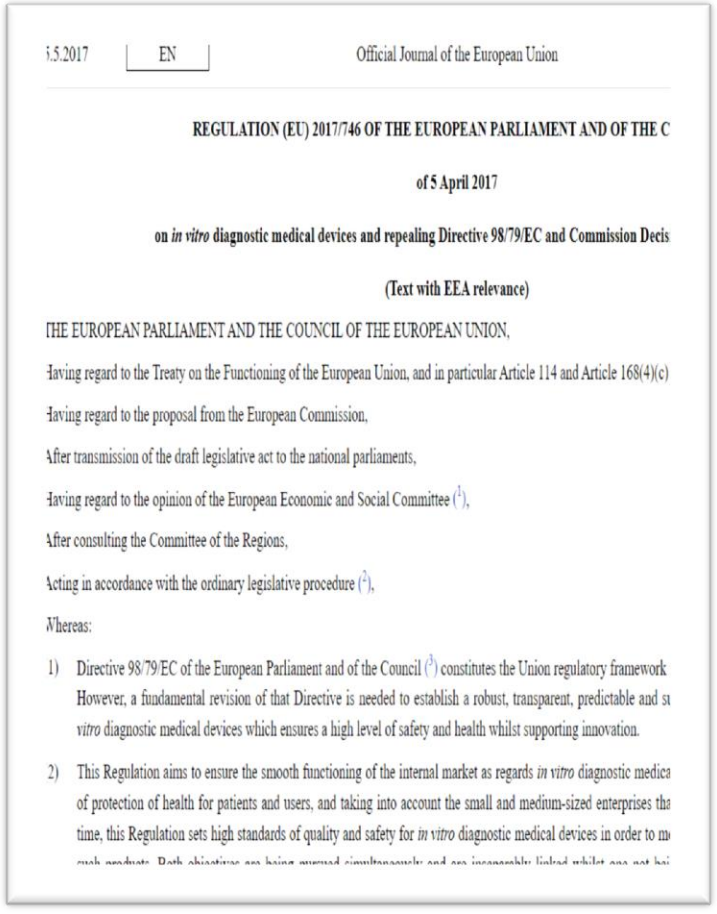
Risk Management - Focal Point for Regulatory Purposes and Update on ISO 14971:2019

EU MDR 2017/745
EU IVDR 2017/746

Regulatory Requirements

"Risk" is referenced 160 times
"Risks" is referenced 83 times

EU 2017/746 (EU IVDR)



5.2017 EN Official Journal of the European Union

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE C

of 5 April 2017

on *in vitro* diagnostic medical devices and repealing Directive 98/79/EC and Commission Decis

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c)

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee [1],

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure [2],

Whereas:

1) Directive 98/79/EC of the European Parliament and of the Council [3] constitutes the Union regulatory framework However, a fundamental revision of that Directive is needed to establish a robust, transparent, predictable and su *vitro* diagnostic medical devices which ensures a high level of safety and health whilst supporting innovation.

2) This Regulation aims to ensure the smooth functioning of the internal market as regards *in vitro* diagnostic medica of protection of health for patients and users, and taking into account the small and medium-sized enterprises tha time, this Regulation sets high standards of quality and safety for *in vitro* diagnostic medical devices in order to m

Whereas (13)

The requirement to reduce risks as far as possible should be fulfilled taking into account the generally acknowledged state of the art in the field of medicine. (EU IVDR)

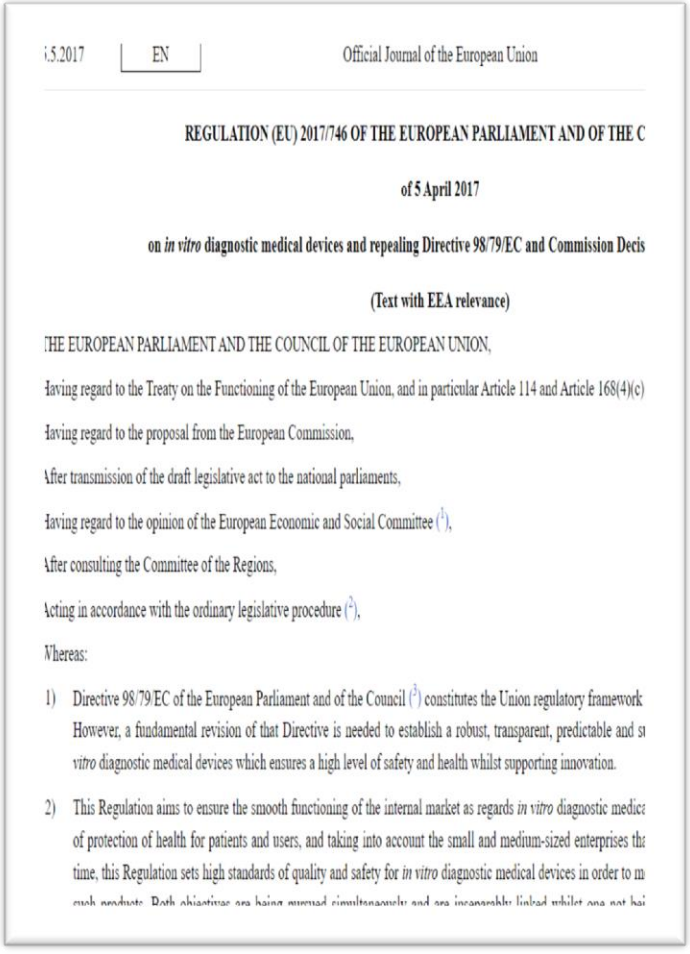
Whereas (32)

The risk management system should be carefully aligned with and reflected in the performance evaluation process for the device, including the clinical risks to be addressed as part of performance studies, performance evaluation and post-market performance follow-up. The risk management and performance evaluation processes should be inter-dependent and should be regularly updated.

EU 2017/746 (EU IVDR)

Whereas (75)

Manufacturers should play an active role during the post-market phase by systematically and actively gathering information from post-market experience with their devices … Relevant data and information gathered through post-market surveillance, as well as lessons learned from any implemented preventive and/or corrective actions, should be used to update any relevant part of technical documentation, such as those relating to risk assessment and performance evaluation, and should also serve the purposes of transparency.



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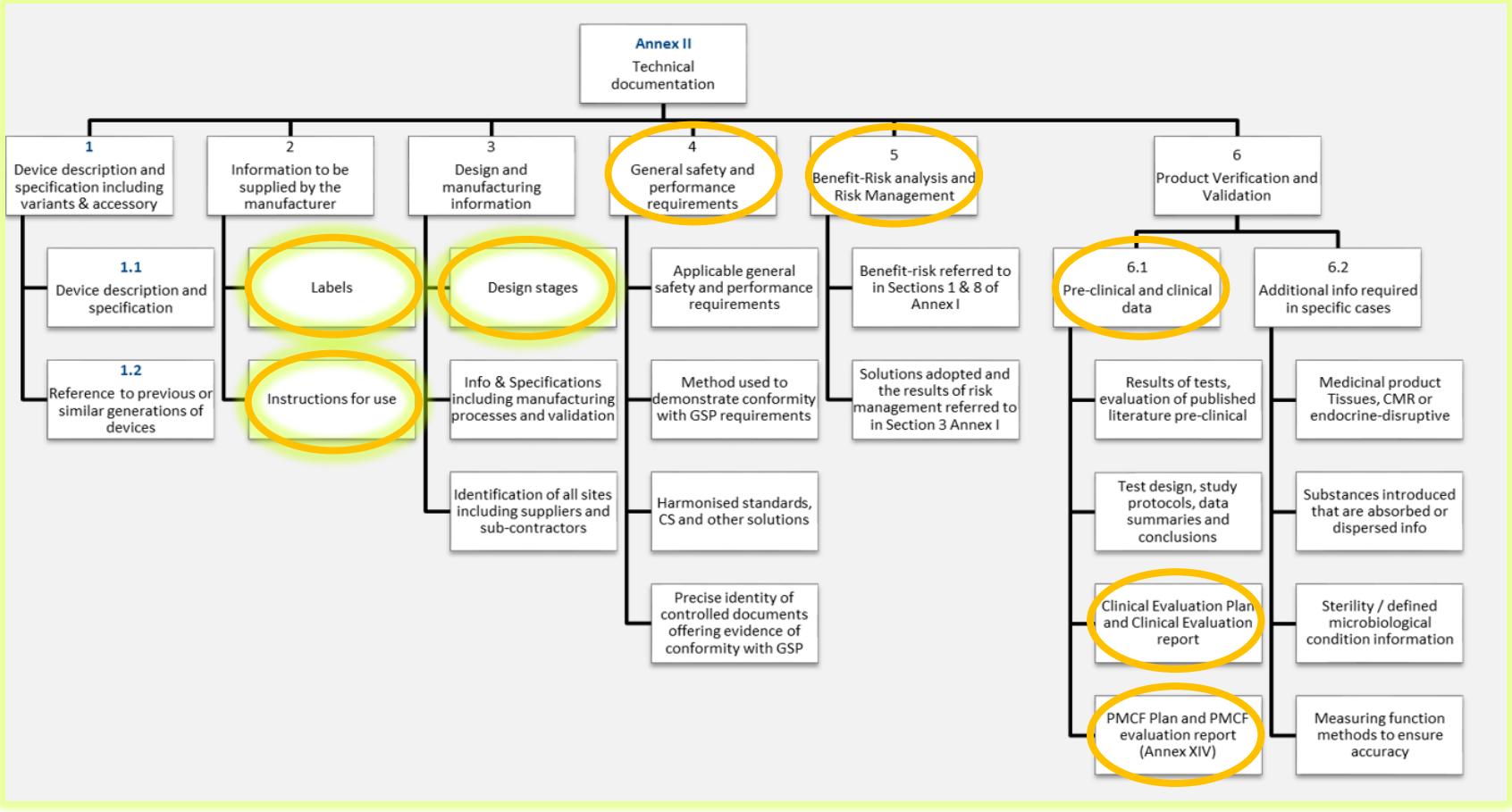
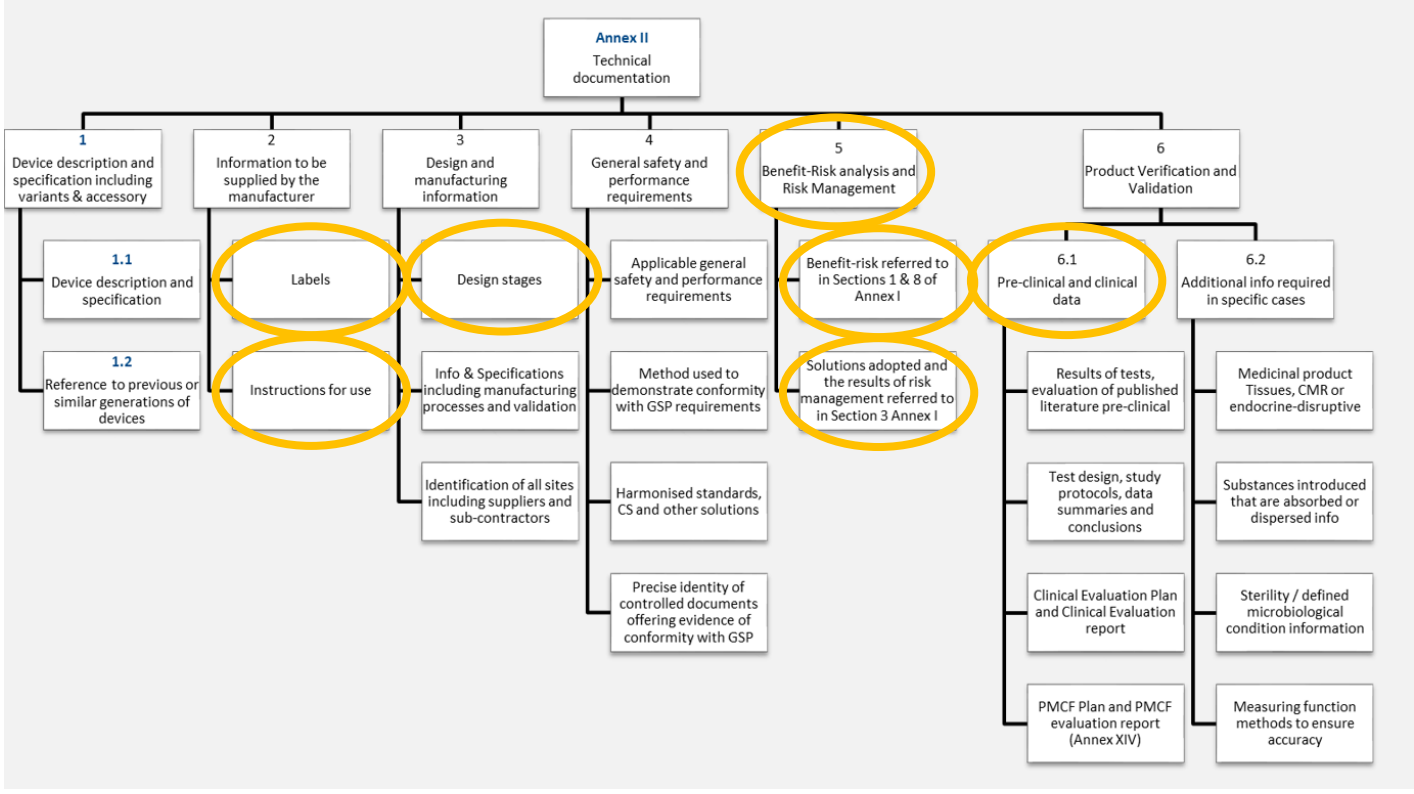
Technical Documentation

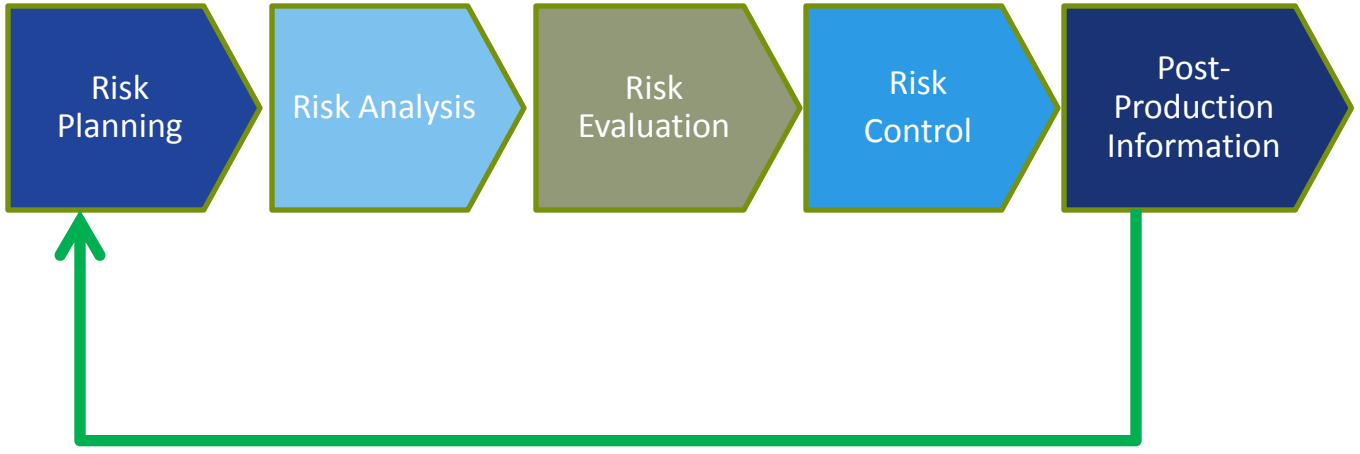


General Safety and Performance Requirements – GSPRs



What is Risk Management?

Risk Management is the "systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating and controlling risk."



Where Do You Consider "Risk"

Throughout Total Product Life Cycle

Where Do You Consider "Risk"

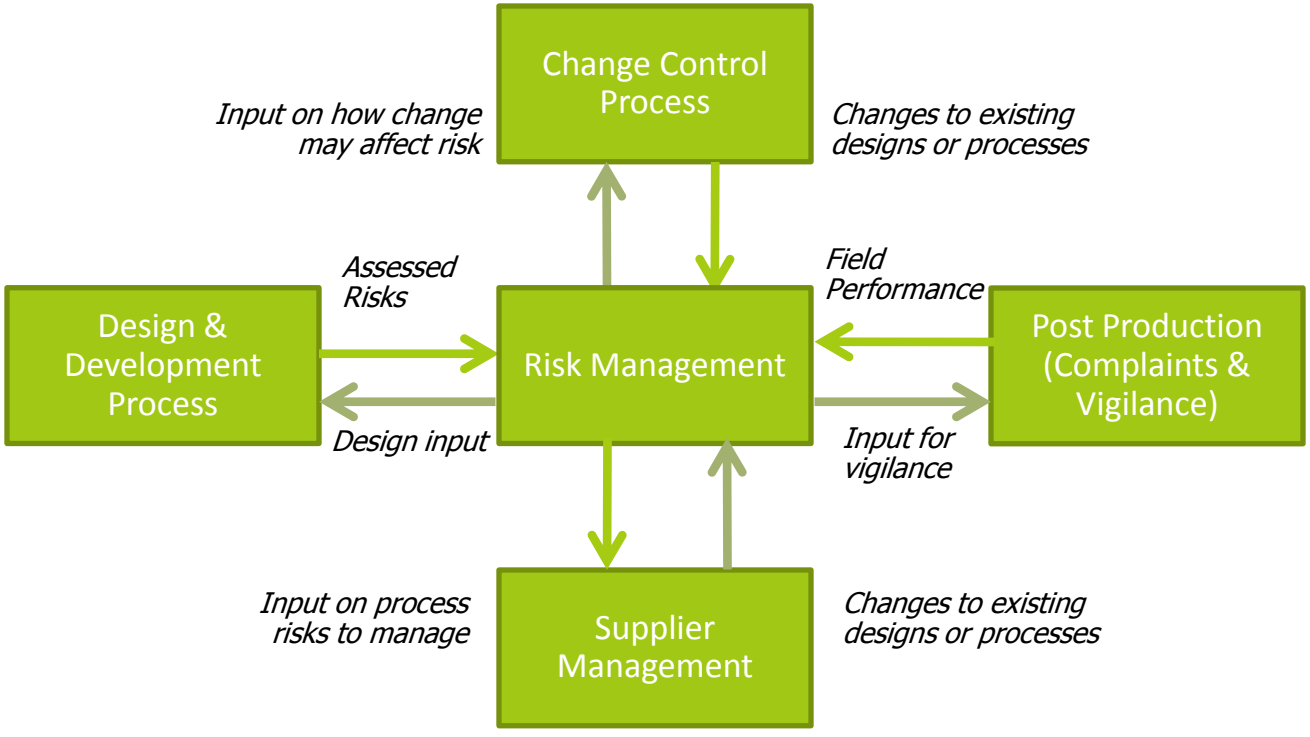
Throughout Total Product Life Cycle

Where Do You Consider "Risk"

Throughout Total Product Life Cycle

What's Involved?

- Risk Management begins during the design and development
- Process and is maintained throughout the life of the device.



Risk Based Decisions

Risk management requirements are described in the following standards:

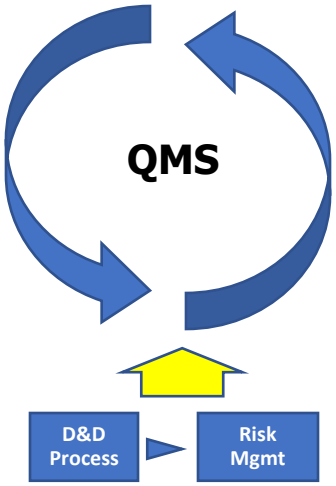
ISO 13485 , section 7.1 Planning of Product Realization	ISO 14971, section 4.1 Risk Management
The organization shall document one or more processes for risk management in product realization. Records of risk management activities shall be maintained.	Where a documented product realization process exists, it shall incorporate the appropriate parts of the risk management process.

ISO 13485 also requires that the following activities be managed in a manner that is "***proportionate to the risk involved***":

- 4.1.5 Outsourced processes
- 4.1.6 Validation of computer software
- 7.4.1 Purchasing process
- 7.4.3 Verification of purchased product
- 7.5.6 Validation of processes for production and service provision

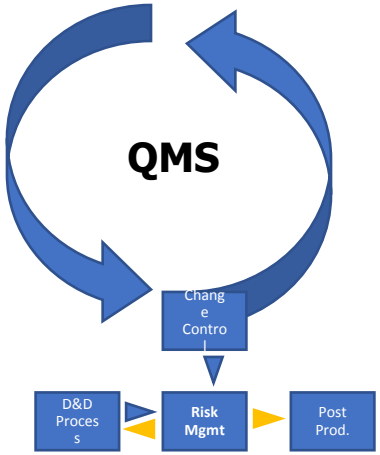
Introduction: Risk Management Stages of Development

Stage 1
Separate Analysis



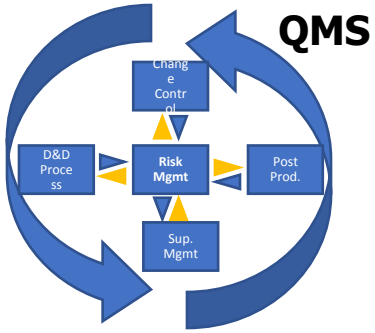
- Completed as a separate project – often after the fact.
- Included in regulatory submission, limited further use.
- Prepared and owned by specialized team.

Stage 2
Supporting Role



- More integrated into development process.
- Outputs used to support a few other QMS processes.
- Broader team involved in developing and using the data.

Stage 3
Integrated Process



- Fully integrated into the QMS.
- Outputs guide decisions across the QMS system.
- All relevant teams provide into to, and make use of, risk information.

GHTF GUIDANCE DOCUMENT – QMS+RMS

GHTF SG3 - Risk Management Principles and Activities within a QMS - May 2005

GHTF/SG3/N15R8

GHTF

FINAL DOCUMENT

Title: Implementation of risk management principles and activities within a Quality Management System

Authoring Group: GHTF Study Group 3

Endorsed by: The Global Harmonization Task Force

Date: May 20, 2005

Abraao Carvalho, GHTF Chair

This document was produced by the Global Harmonization Task Force, a voluntary international group of representatives from medical device regulatory authorities and trade associations from Europe, the United States of America (USA), Canada, Japan and Australia.

The document is intended to provide *non-binding* guidance to regulatory authorities for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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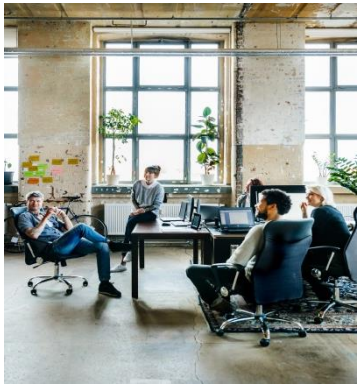
Risk Management File and/or Design History File

The Risk Management File contains records and other documents created during risk management activities for the medical device throughout its life cycle from initial conception until final decommissioning and disposal.



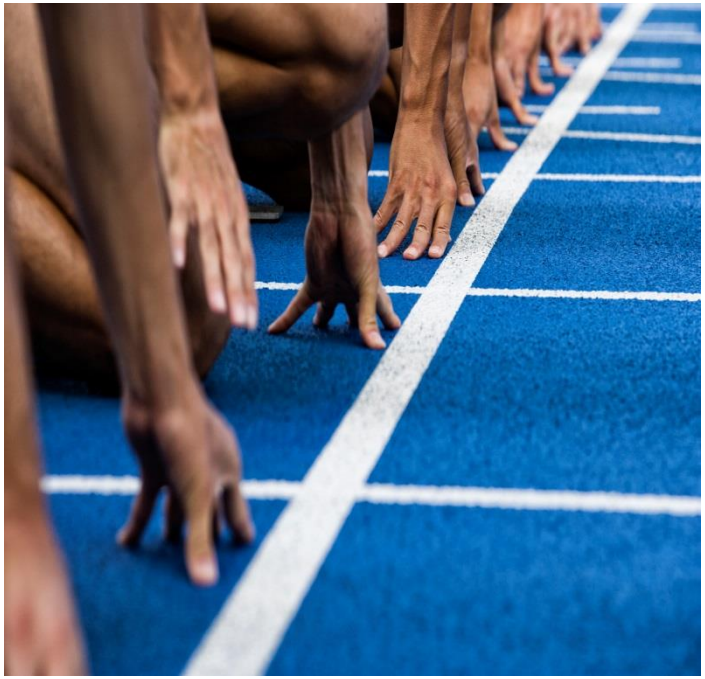
- Risk Management Plan
- Risk Assessments
- Risk Management Report
- Production and Post-Production Records

The risk management file is a logical construct. ***It is not necessary that the risk management file physically contains all the required records and related documents. The records and related documents can be part of files required by other systems such as the manufacturer's quality management system.*** The records and related documents can exist in any format or media (hard copy, electronic records, etc.). [TIR24971, Section 4.5]

Risk Management: Timeframe

When do you start . . .

And when are you done?



Product Development Process

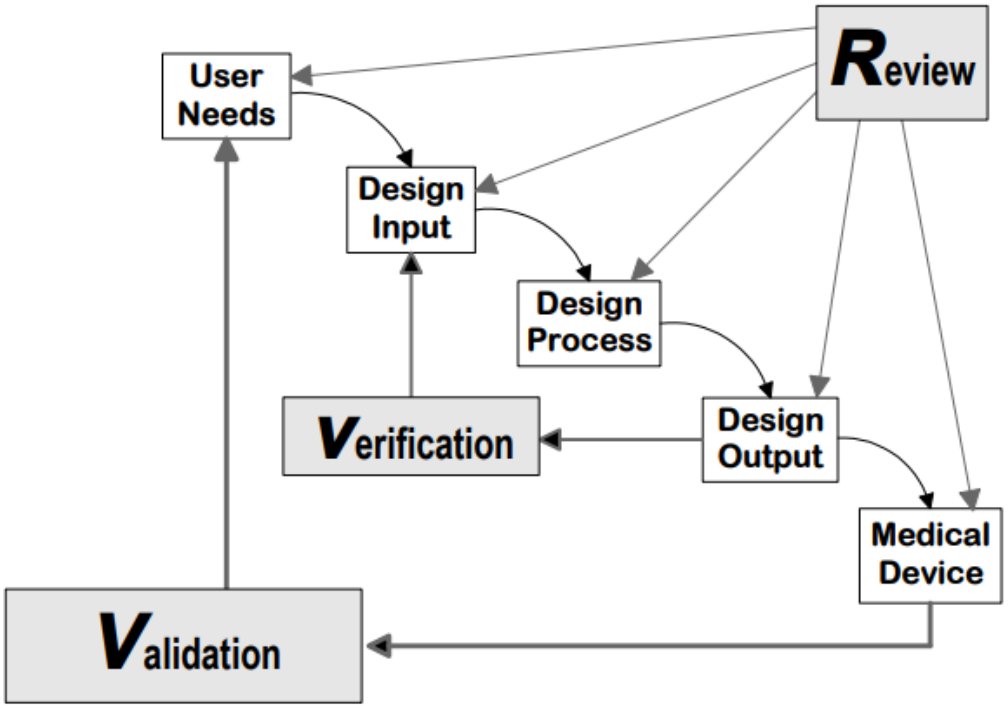


Figure 1 – Application of Design Controls to Waterfall Design Process (figure used with permission of Medical Devices Bureau, Health Canada)

Source: FDA, Design Control Guidance for Medical Device Manufacturers (1997)

Product Life Cycle

From the early conception phase

Throughout Design Control

Through Design Transfer and Release

Through Revision Control

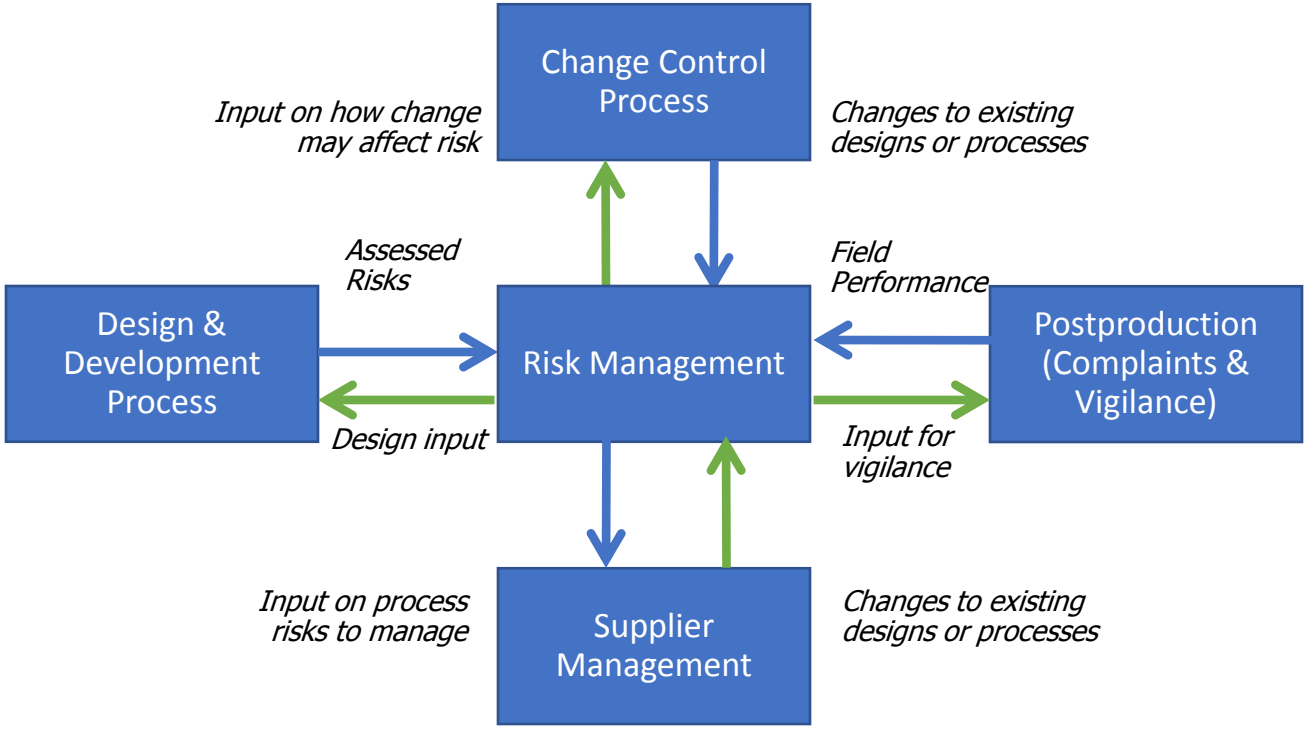
Through Corrective and Preventative Action

Through complaints

To obsolescence and removal

Ongoing Updates

Risk Management begins during the design and development process and is maintained throughout the life of the device.



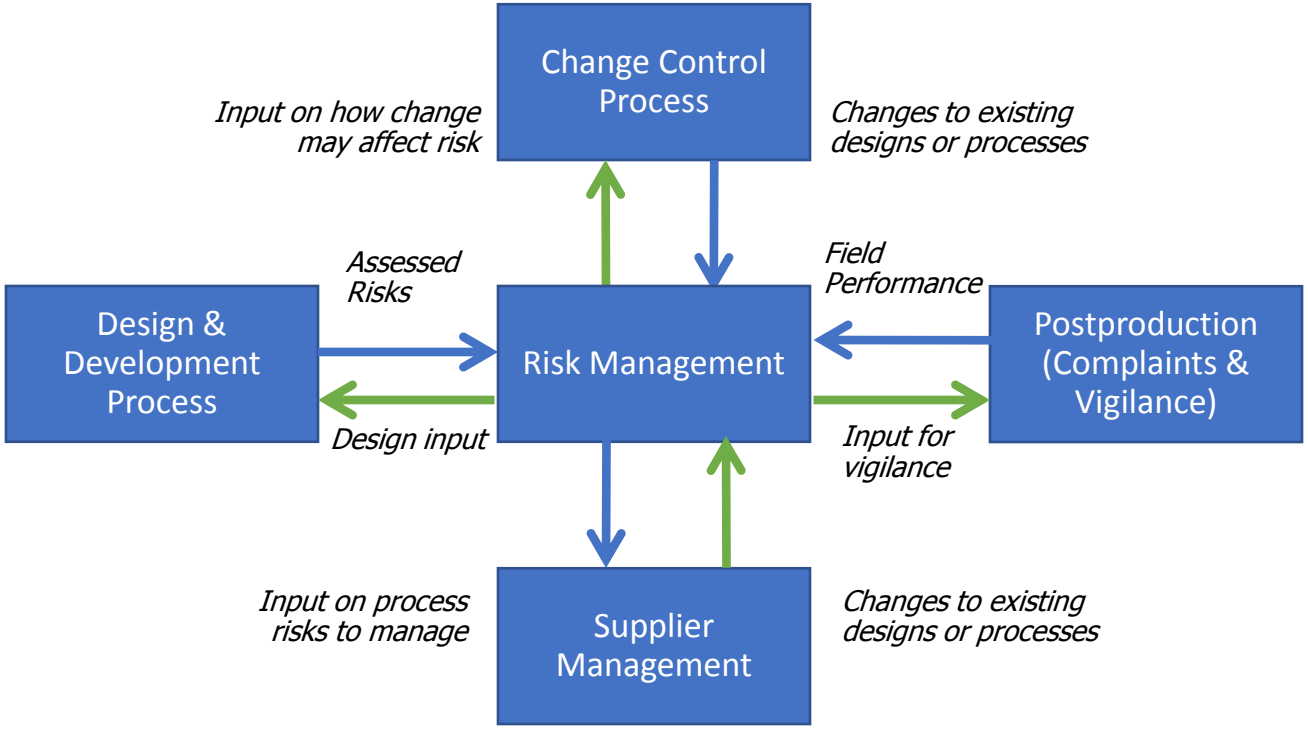
Postproduction Information

The risk management process is a truly repetitive closed-loop process.

- No amount of modeling can substitute for an actual device in the hands of actual users.
- Scheduled review of the released product should be described in Risk Plan.

Postproduction Information

Continual integration of postproduction information is required to ensure the effective, ongoing management of risk.



International Standards

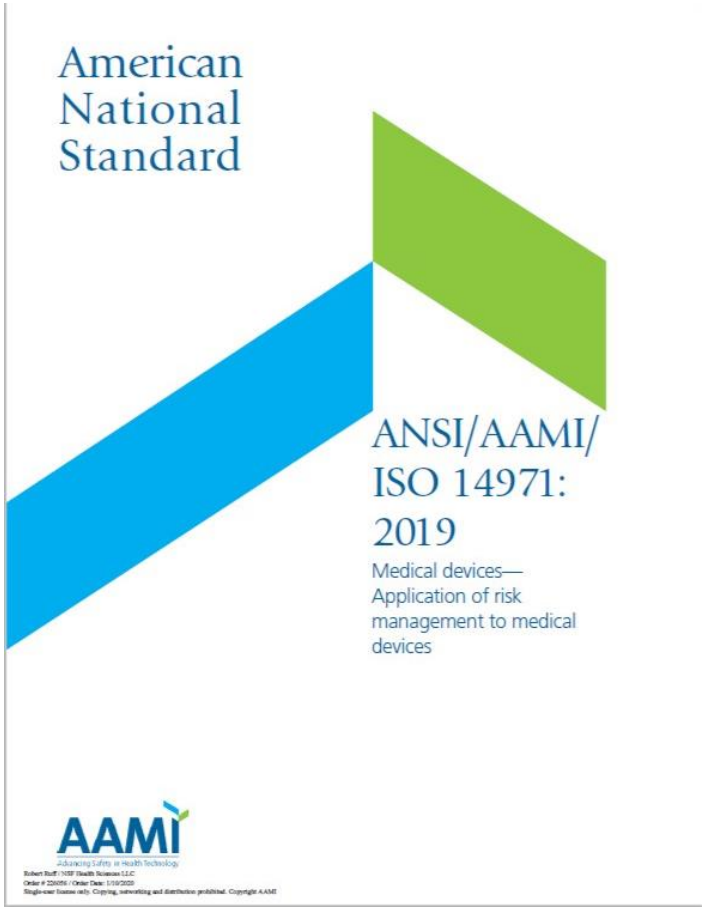
The Importance of Definitions

- Understanding basic terms and definitions vital to ensure that everyone is talking about the same thing during risk discussions!
- Definitions come mostly from the International Organization for Standardization (ISO) 14971:2019 standard

Disclaimer when looking at definitions of risk terms:

- Understand context and nuance as they relate to the specific guidance documents or standards etc. and where they are used.
- Note different definition of Risk in ISO 31000 – causing all kinds of potential problems for the medical device industry!

Terms & Definitions



Terms & Definitions

3.18 *RISK*

Combination of the probability of occurrence of HARM and the severity of that HARM.

3.4 *HAZARD*

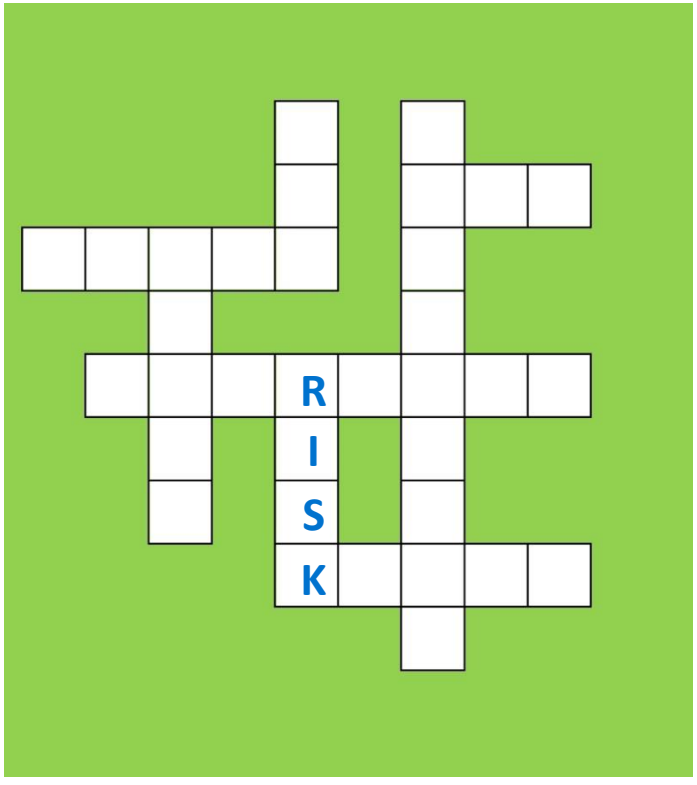
Potential source of HARM.

3.3 *HARM*

Injury or damage to the health of people, or damage to property or the environment.

3.24 *RISK MANAGEMENT*

systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating, controlling and monitoring RISK.



Terms & Definitions

3.2 *BENEFIT*

positive impact or desirable outcome of the use of a *medical device* (3.10) on the health of an individual, or a positive impact on patient management or public health

Note 1 to entry: *Benefits* can include positive impact on clinical outcome, the patient's quality of life, outcomes related to diagnosis, positive impact from diagnostic devices on clinical outcomes, or positive impact on public health.

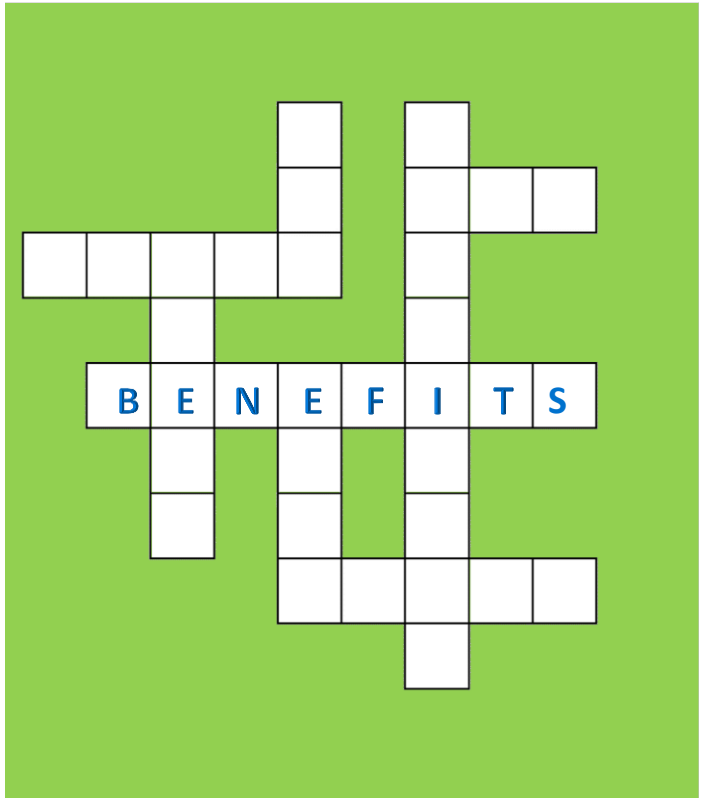
3.15 *REASONABLY FORESEEABLE MISUSE*

use of a product or system in a way not intended by the *manufacturer* (3.9), but which can result from readily predictable human behaviour

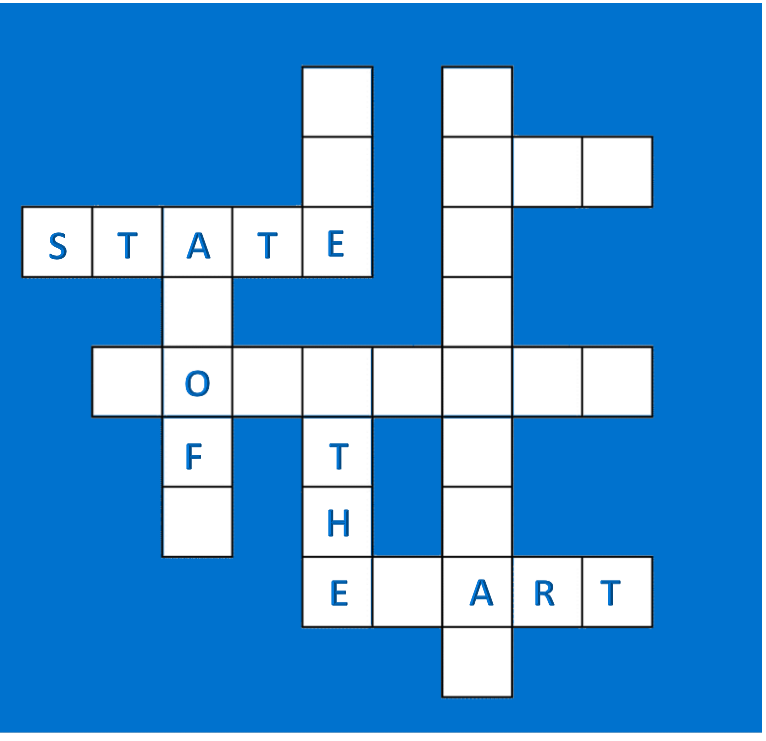
Note 1 to entry: Readily predictable human behaviour includes the behaviour of all types of users, e.g. lay and professional users.

Note 2 to entry: *Reasonably foreseeable misuse* can be intentional or unintentional.

[SOURCE: ISO/IEC Guide 63:2019, 3.8]



Terms & Definitions



3.28 *STATE OF THE ART*

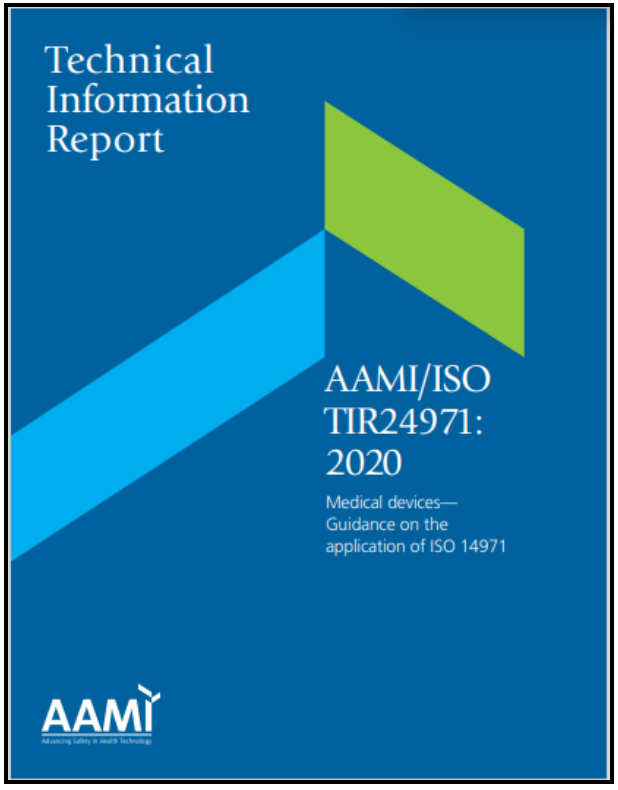
developed stage of technical capability at a given time as regards products, *processes* (3.14) and services, based on the relevant consolidated findings of science, technology and experience

Note 1 to entry: The *state of the art* embodies what is currently and generally accepted as good practice in technology and medicine. The *state of the art* does not necessarily imply the most technologically advanced solution. The *state of the art* described here is sometimes referred to as the "generally acknowledged *state of the art*".

IMPORTANT GUIDANCE

ISO TIR24971:2020 – Medical Devices – Guidance on the Application of ISO 14971

- **Contains many of the Annexes that were in earlier versions of the standard.**

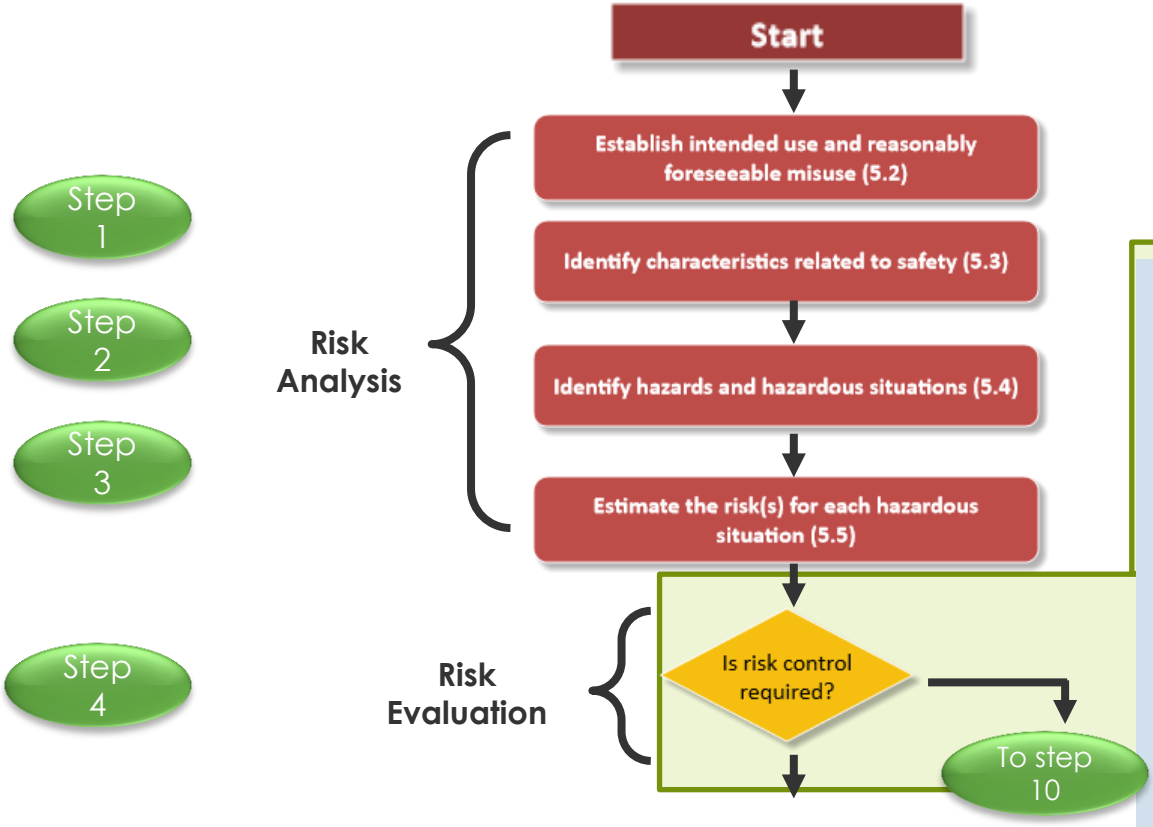


ISO TIR 24971:2020 – Medical Devices – Guidance on the Application of ISO 14971 (99 pages)

- **Additional guidance on:**
  Risk analysis, Risk evaluation, Risk control, Evaluation of overall residual risk, Risk management review, and Production and post-production activities.
- **Annex A:** Identification of hazards and characteristics related to safety
- **Annex B:** Techniques that support risk analysis
- **Annex C:** Relation between the policy, criteria for risk acceptability, risk control and risk evaluation
- **Annex D:** Information for safety and information on residual risk
- **Annex E:** Role of international standards in risk management
- **Annex F:** Guidance on risks related to security
- **Annex G:** Components and devices designed without using ISO 14971
- **Annex H:** Guidance for in vitro diagnostic medical devices.

Risk Management Process

Risk Assessment Clauses 5.2 – 5.5 and Clause 6



NOTE EU Content deviation 1
All risks regardless of their dimensions, need to be reduced as much as possible

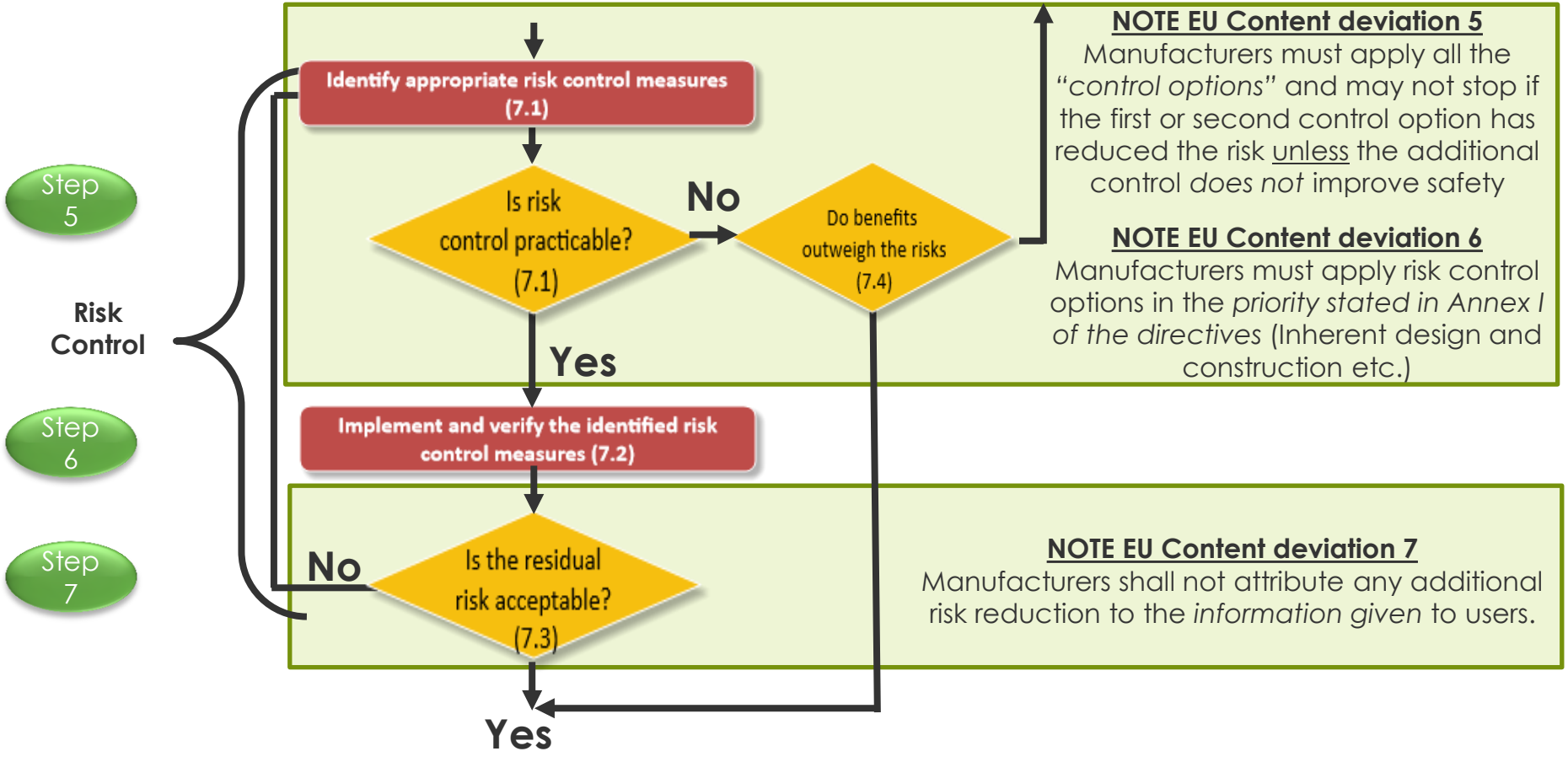
NOTE EU Content deviation 2
Manufacturers *may not* apply any criteria of risk acceptability without high degree of protection & positive benefit-risk ratio

NOTE EU Content deviation 3
Manufacturers *may not* apply the ALARP concept with regard to economic considerations

Adapted from ISO 14971:2019 Figure 1 , Clause 4.1

Risk Management Process
Risk Control Clauses 7.1 – 7.4

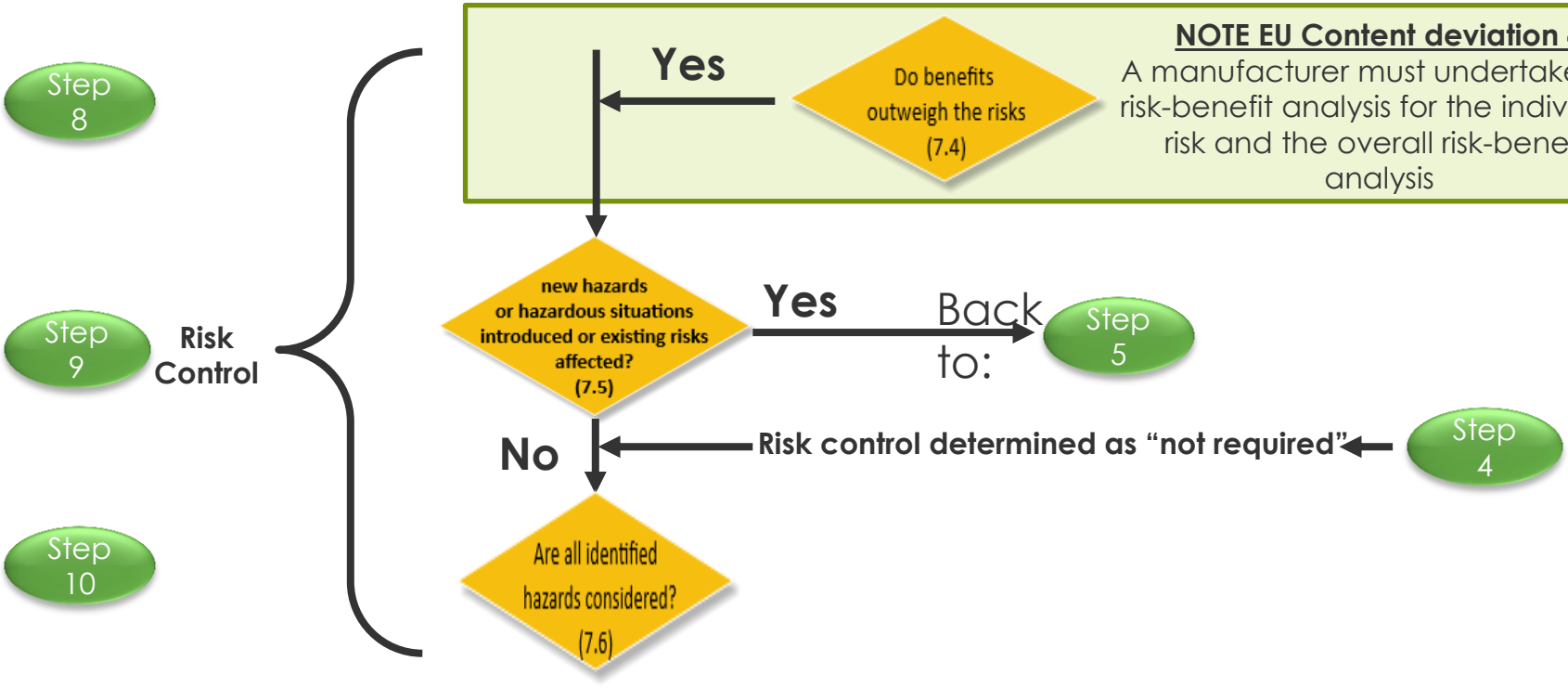
Modify the device or intended use (go back to 5.2). Otherwise, risk remains unacceptable



Adapted from ISO 14971:2019 Figure 1 , Clause 4.1

Risk Management Process

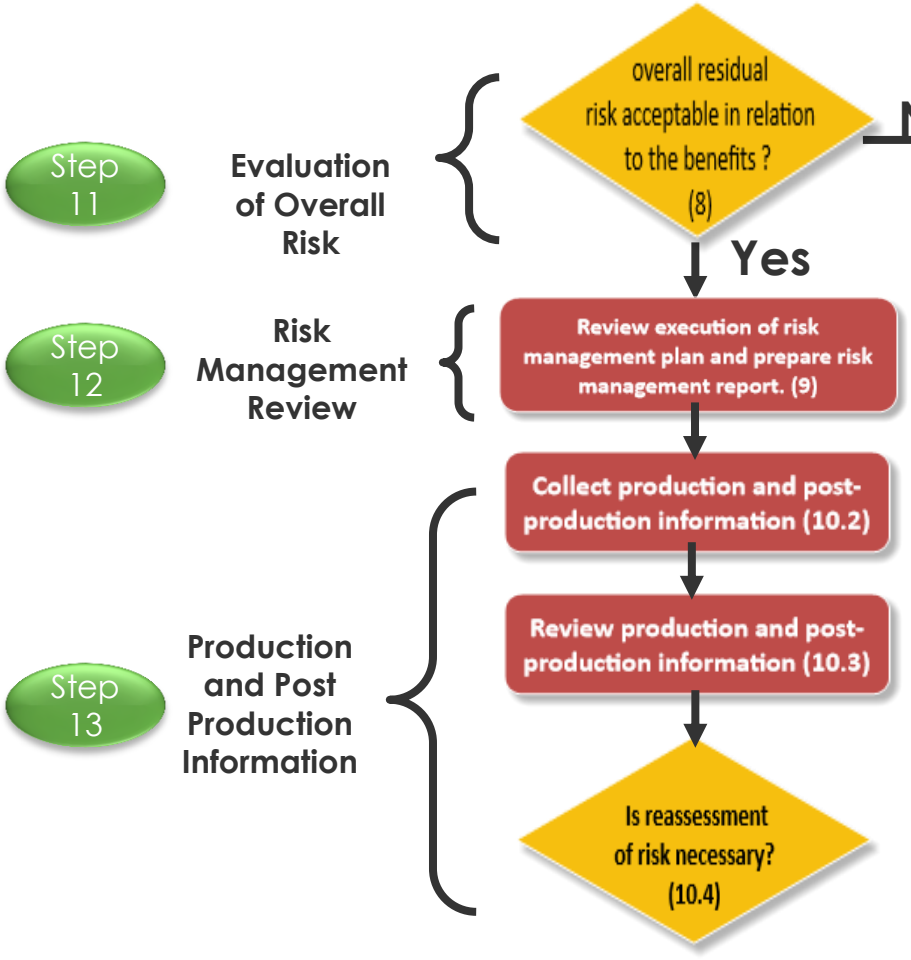
Risk Control Clauses 7.4 – 7.6



Adapted from ISO 14971:2019 Figure 1 , Clause 4.1

RM Process

Risk Acceptability and Update Clauses 8-10.4

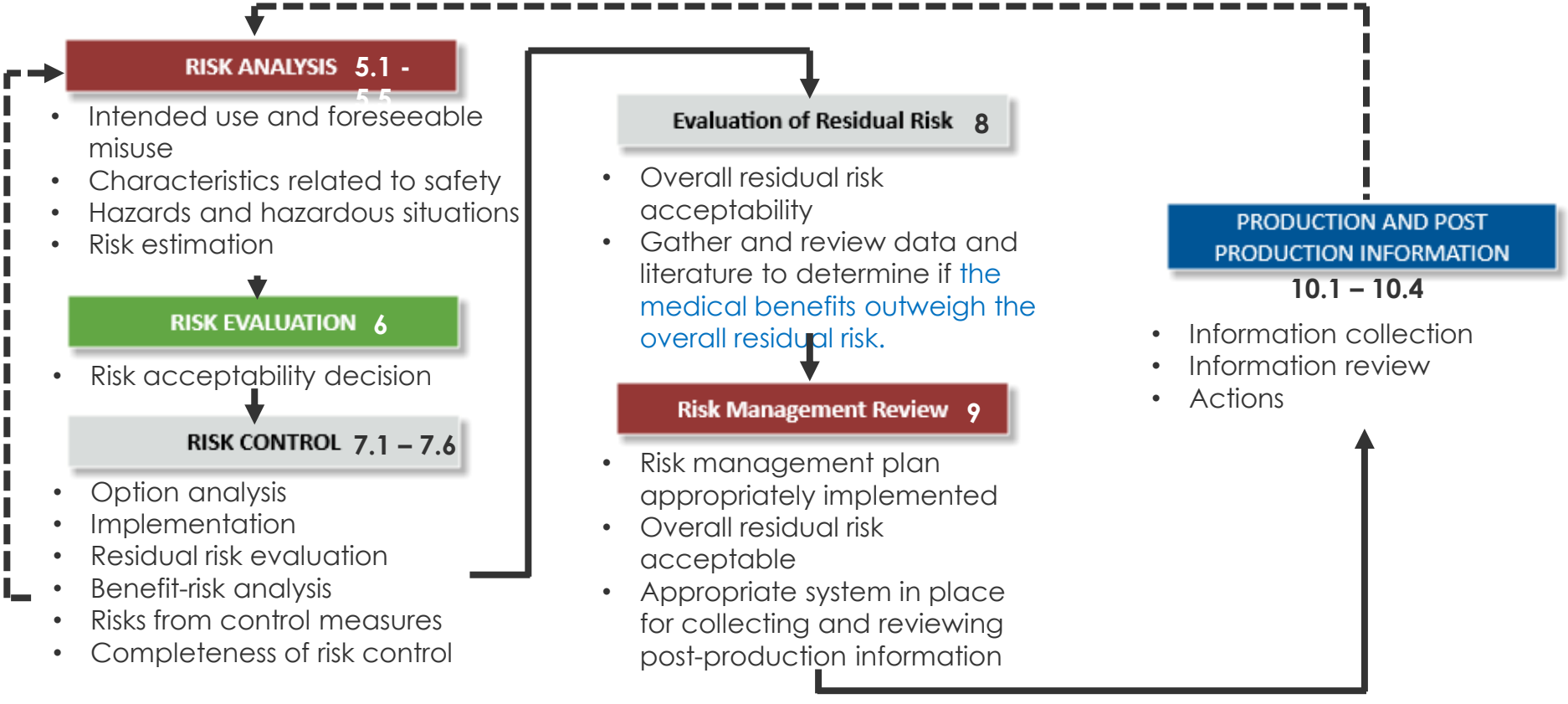


Consider implementing additional risk control measures (go back to 7.1) or modifying the device or its intended use (go back to 5.2). Otherwise, the overall residual risk remains unacceptable.

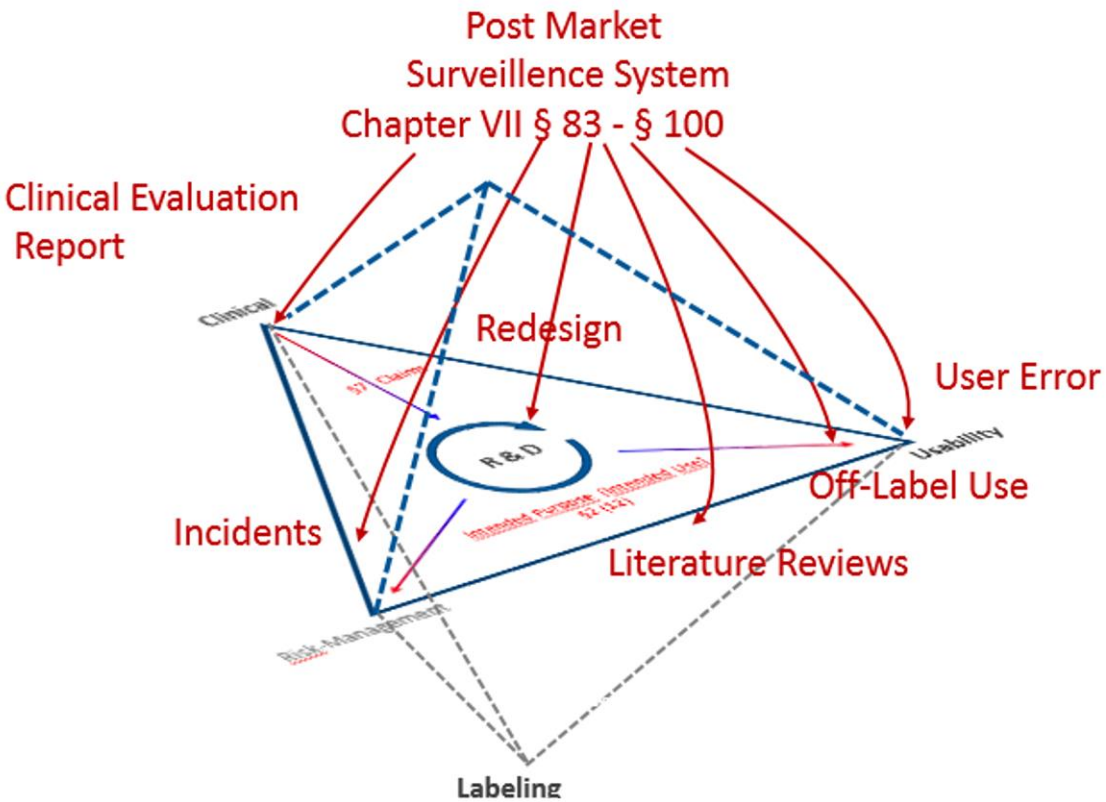
Adapted from ISO 14971:2019 Figure 1 , Clause 4.1

ISO 14971: 2019
Risk Management Process

Device Risk Management Plan 4.4



EU MDR/IVDR



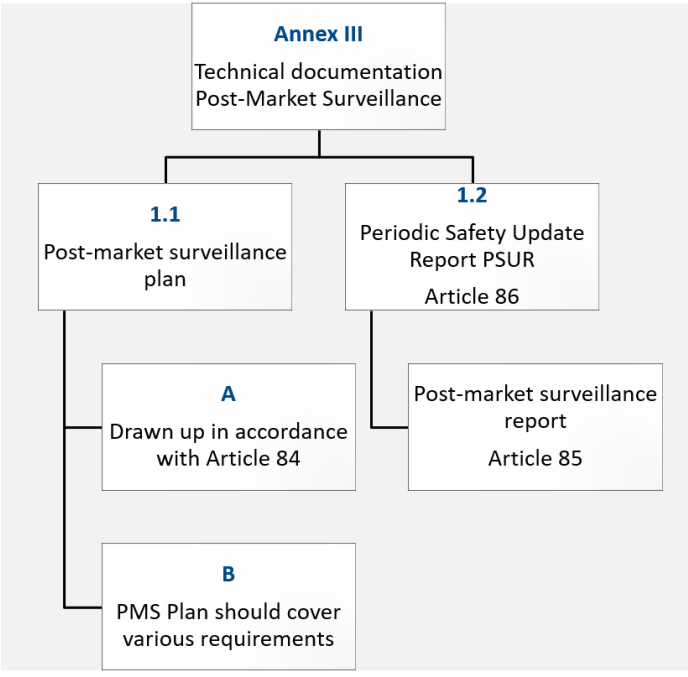
EU 2017/745 (EU MDR)
EU 2017/746 (EU IVDR)

Annex III – Technical Documentation On Post-Market Surveillance

The technical documentation on post-market surveillance to be drawn up by the manufacturer in accordance with Articles 83 to 86 shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular the elements described in this Annex.

(b) The ***post-market surveillance plan*** shall cover at least:

- suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I;



Clinical Evaluation

Manufacturers are required to implement and ***maintain a PMS system that routinely monitors the clinical performance and clinical safety of the device as part of their quality management system***. The scope and nature of such PMS should be appropriate to the device and its intended purpose.

Post-Market Clinical Follow-up (PMCF) Requirements

PMCF shall be understood to be a continuous process that updates the clinical evaluation [...] and shall be addressed in the manufacturer's post-market surveillance plan.

When conducting PMCF, the manufacturer shall proactively collect and evaluate clinical data from the use in or on humans of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence.

[Regulation (EU) 2017/745 Annex XIV Part B (5)]

Post-Market Clinical Follow-up (PMCF) Requirements

PMCF Objectives

Gather clinical data to:

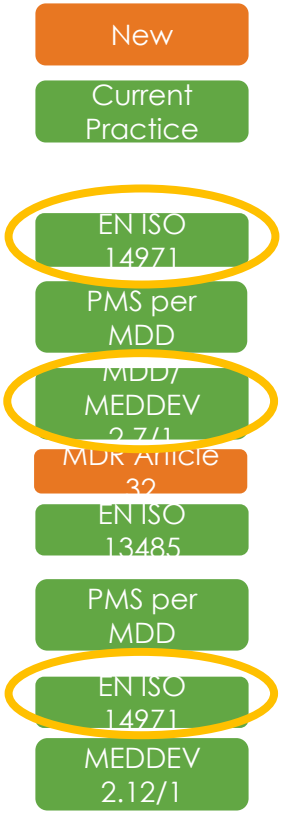
- Confirm the safety and performance of the device throughout its expected lifetime
- Identify previously unknown side-effects and monitoring the identified side-effects and contraindications,
- Identify and analyze emergent risks on the basis of factual evidence,
- Ensure the continued acceptability of the benefit-risk ratio, and
- Identify possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

[Regulation (EU) 2017/745 Annex XIV Part B (6)]

PMS Requirements – The PMS System

Data gathered by the manufacturer's post-market surveillance system shall in particular be used:

- **to update the benefit-risk determination and to improve the risk management;**
- **to update the design and manufacturing information, the instructions for use and the labelling;**
- **to update the clinical evaluation;**
- **to update the summary of safety and clinical performance;**
- **for the identification of needs for preventive, corrective or field safety corrective action;**
- **for the identification of options to improve the usability, performance and safety of the device;**
- **when relevant, to contribute to the post-market surveillance of other devices; and**
- **to detect and report trends.**



[Regulation (EU) 2017/745 Article 83]

Post-Market Surveillance

Feedback (ISO 13485:2016, 8.2.1)

As one of the measurements of the performance of the quality management system, the organization shall gather and monitor information relating to whether the organization has met customer requirements. Methods for obtaining and using this information shall be documented.

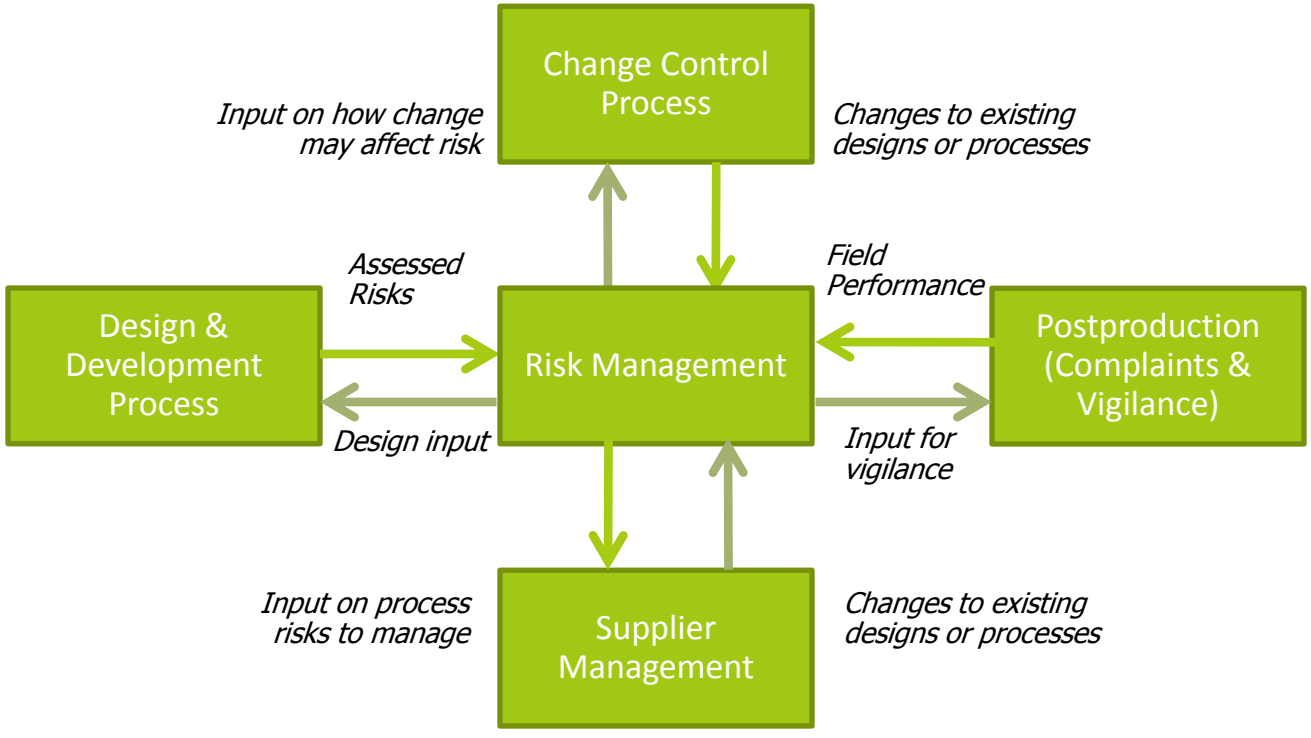
The organization shall document procedures for the feedback process, which shall include the provisions to gather data from production, as well as post-production activities.

The information gathered in the feedback process shall serve as potential input into risk management for monitoring and maintaining the product requirements, as well as product realization or improvement processes.

If applicable regulatory requirements require the organization to gain specific experience from post-production activities, the review of this experience shall form part of the feedback process.

Postproduction Information

Continual integration of postproduction information is required to ensure the effective, ongoing management of risk.

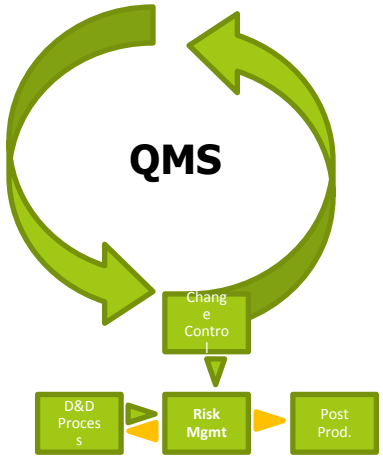


Risk Management Systems + Quality Management Systems

Stage 1
Separate Analysis

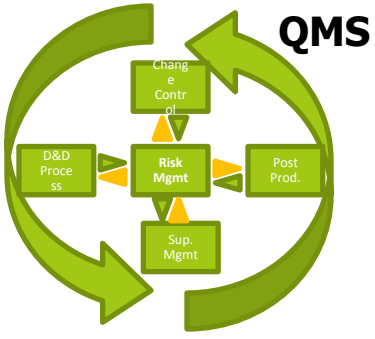
- Completed as a separate project – often after the fact.
- Included in regulatory submission, limited further use.
- Prepared and owned by specialized team.

Stage 2
Supporting Role



- More integrated into development process.
- Outputs used to support a few other QMS processes.
- Broader team involved in developing and using the data.

Stage 3
Integrated Process



- Fully integrated into the QMS.
- Outputs guide decisions across the QMS system.
- All relevant teams provide into to, and make use of, risk information.

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