HOW TO EFFECTIVELY IMPLEMENT THE NEW ISO 14971:2019 & MAINTAIN YOUR CURRENT RISK FILE

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WELCOME TO TODAY'S TRAINING SESSION!

POLL QUESTION

My Quality System (QMS) is based on:

A) ISO 13485

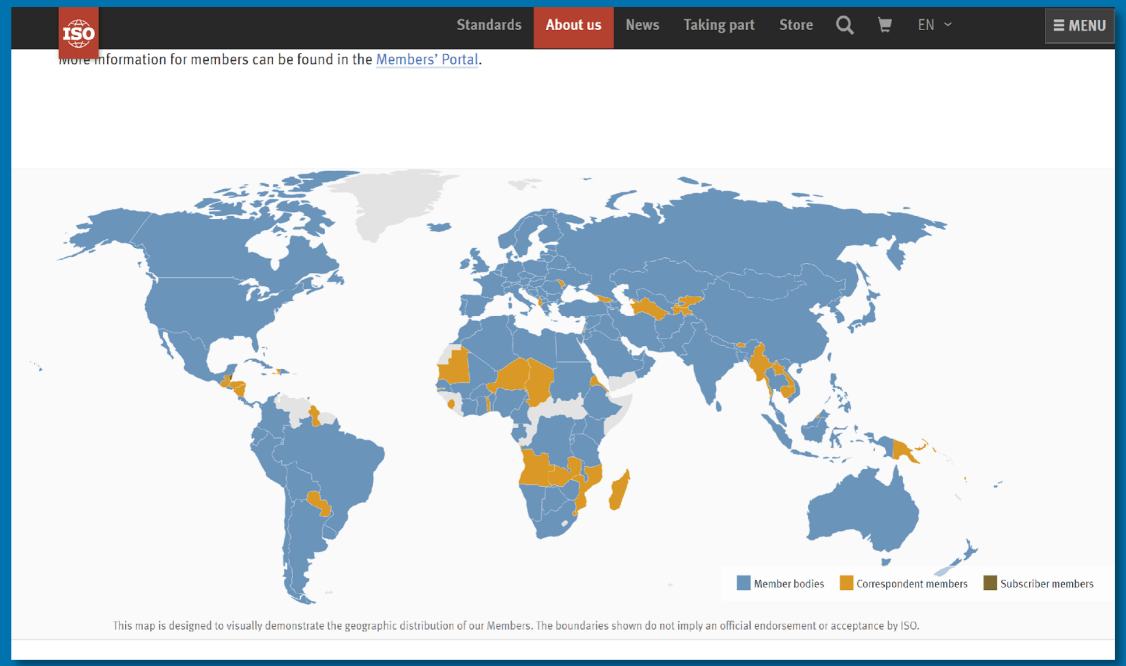
B) 21 CFR part 820

C) ISO 13485 **and** 21 CFR part 820

D) Other

ISO – INTERNATIONAL STANDARDS ORGANIZATION

- ISO develops & publishes International Standards. They are **not** a governing body or a regulatory agency.
- ISO is an independent, international organization with a membership of 165 national standards bodies.
- ISO standards are internationally agreed by experts. Think of them as a formula that describes the best way of doing something. (reference iso.org)



WHAT IS ISO 14971 AND HOW DOES IT APPLY TO MY COMPANY?

ISO 14971:2019 - Medical Devices — Application of risk management to medical devices.

- “medical devices” include active, non-active, implantable, and non-implantable medical devices, software as medical devices and in vitro diagnostic medical devices.
- Defines **a standard process for identifying risks associated with medical devices at all stages in a device's life cycle**, from product design to procurement to production and post-market use
- This standard contains risk process concepts which can be utilized across multiple industries including but not limited to medical device, invitro-diagnostics, pharmaceuticals, biotech and even automotive and other non-medical related fields, despite the fact it was written for medical devices.

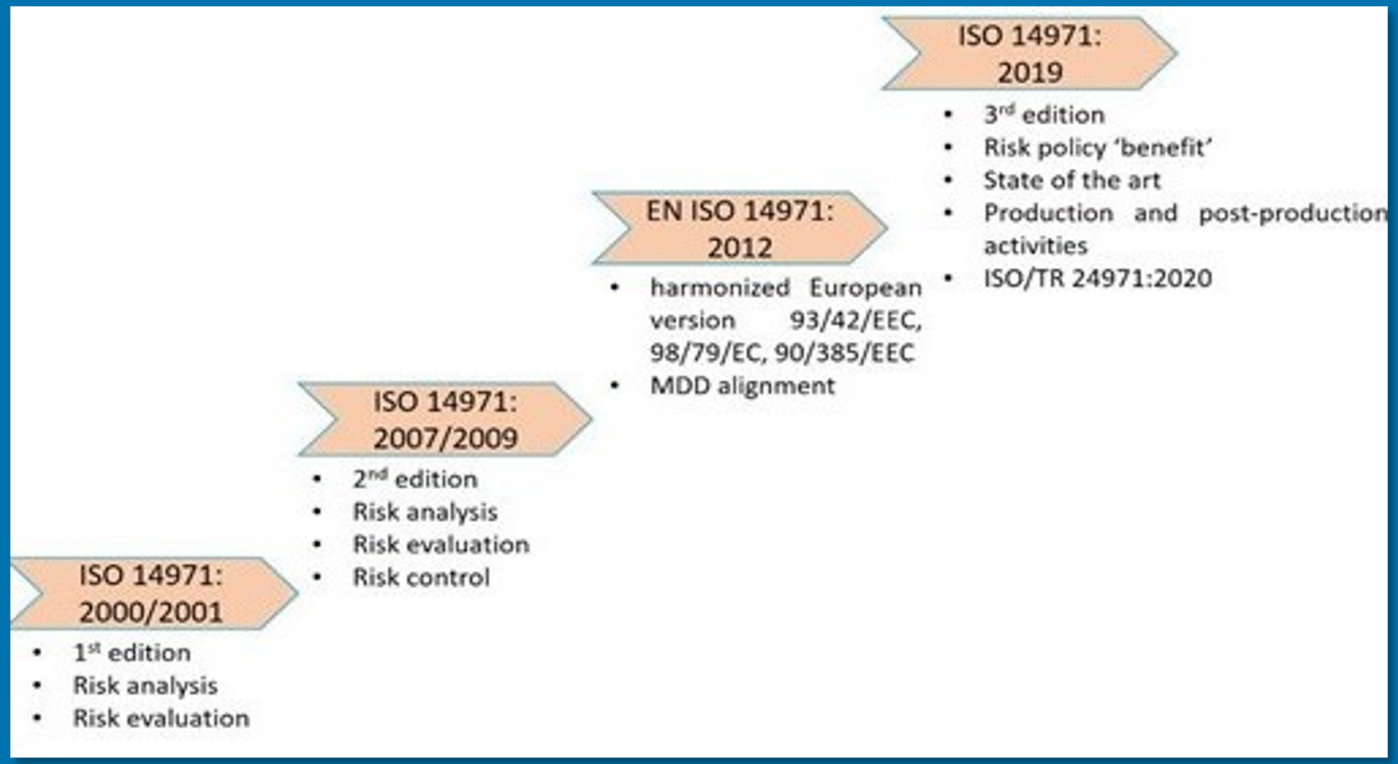
WHAT IS TR 24971:2020 AND HOW DOES IT RELATE TO ISO 14971?

ISO/TR 24971:2020 Medical devices — Guidance on the application of ISO 14971

- Provides detailed guidance on how to use the standard most effectively, the recently published technical report – ISO/TR 24971
  - Clarifies the requirements of the standard.
  - Contains recommendations and practical examples.
  - Follows the same structure and the same clause numbering as ISO 14971:2019.
- This document provides guidance on the development, implementation and maintenance of a *risk management* system for *medical devices* according to ISO 14971:2019.

EVOLUTION OF ISO 14971 STANDARD

Why was the standard updated?



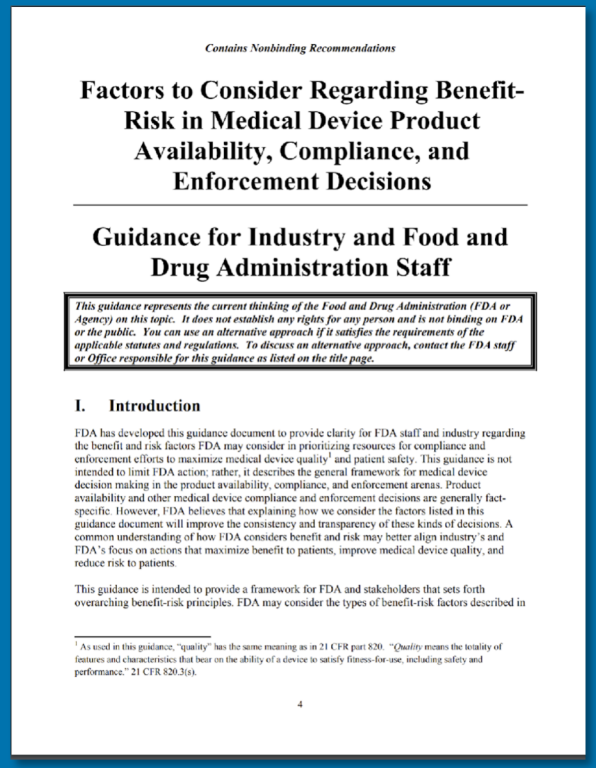
WHERE DOES ISO 14971:2019 FIT IN?

- If your QMS is mapped to ISO 13485:2016
  - Section 7.1 in ISO 13485, you shall establish documented requirements for risk management throughout product realization.
  - Note 3. further it says "See ISO 14971 for guidance related to risk management"
- GHTF references ISO 14971 for Risk Control and Risk Management
- FDA is harmonized with ISO 14971:2019
- EU MDR (2017/745) and IVDR (2017/746) changes are aligned with this standard

U.S. FDA AND ISO 14971

Per the U.S. FDA

- ISO 14971 is an FDA-recognized consensus standard
- Assuring conformity with this standard may help device manufacturers meet the requirements specified in the design controls section (21 CFR 820.30) and other sections of 21 CFR Part 820.
- Both ISO 14971 and 21 CFR Part 820 take a total life cycle approach to management of risks associated with medical devices and expect that manufacturers will incorporate post market data into their device risk management process, including new and changes to existing risks identified after the device is on the market.



Contains Nonbinding Recommendations

Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions

Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

FDA has developed this guidance document to provide clarity for FDA staff and industry regarding the benefit and risk factors FDA may consider in prioritizing resources for compliance and enforcement efforts to maximize medical device quality[1] and patient safety. This guidance is not intended to limit FDA action; rather, it describes the general framework for medical device decision making in the product availability, compliance, and enforcement arenas. Product availability and other medical device compliance and enforcement decisions are generally fact-specific. However, FDA believes that explaining how we consider the factors listed in this guidance document will improve the consistency and transparency of these kinds of decisions. A common understanding of how FDA considers benefit and risk may better align industry's and FDA's focus on actions that maximize benefit to patients, improve medical device quality, and reduce risk to patients.

This guidance is intended to provide a framework for FDA and stakeholders that sets forth overarching benefit-risk principles. FDA may consider the types of benefit-risk factors described in

[1] As used in this guidance, "quality" has the same meaning as in 21 CFR part 820. "*Quality* means the totality of features and characteristics that bear on the ability of a device to satisfy fitness-for-use, including safety and performance." 21 CFR 820.3(s).

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TIMING OF ISO 14971:2019 GLOBALLY

USA

In the US, FDA requires device manufacturers to align with ISO 14971:2019 by the end of the transition period December 25, 2022, after which time FDA will no longer accept the previous ISO 14971:2007 version.

Europe

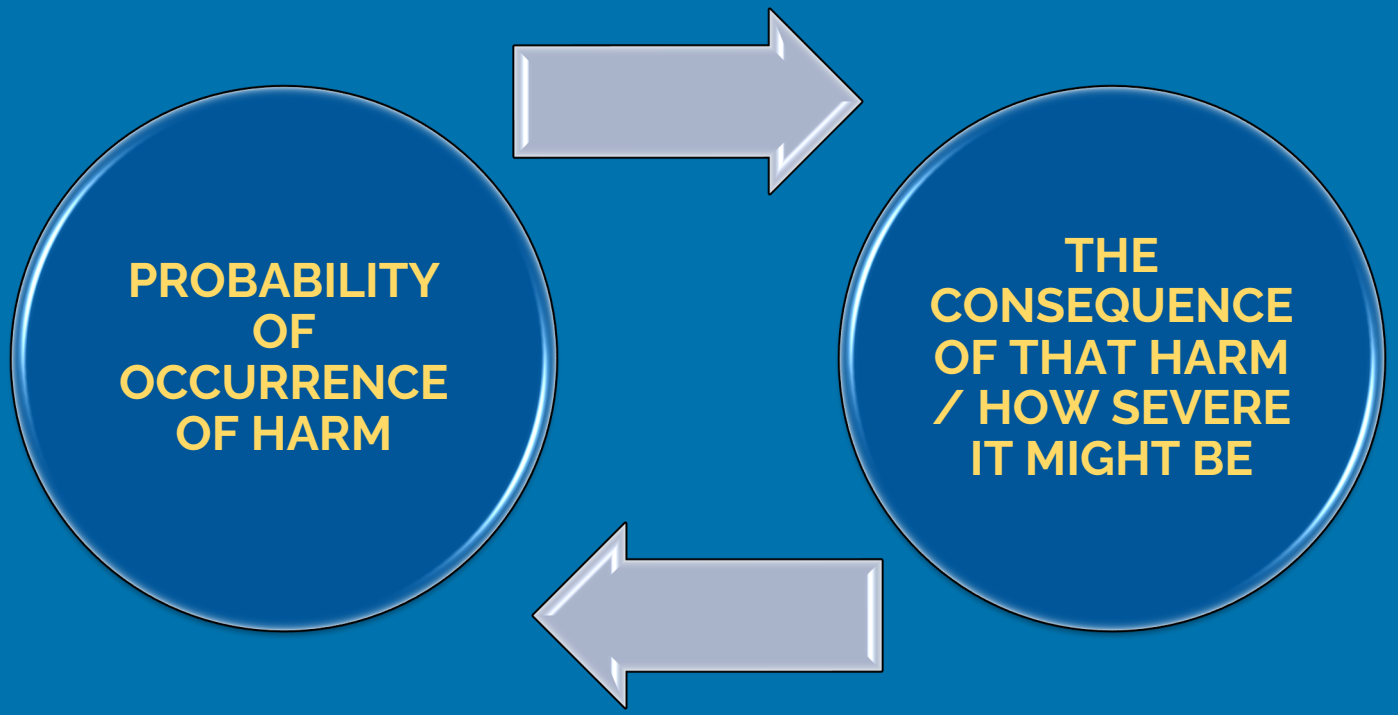
In Europe, ISO 14971:2019 (EN version) aligns with the Medical Device Regulations (MDR) and In Vitro Diagnostic Regulation (IVDR) safety and performance requirements. The date for MDR (26 May 2021) is in effect and IVDR (26 May 2022) is quickly approaching.*

- Note that Covid-19 pandemic has proposed some tiered implementation delays due to Notified Body availability, but these dates apply for new products.

Globally

Globally, ISO 14971:2019 is considered the international standard for risk management and is referenced, if not endorsed, by all other major markets that require the application of risk management including, Australia TGA, Brazil, Health Canada, and Japan MHLW.

KEY COMPONENTS OF RISK



KEY DEFINITIONS

HARMS	Injury or damage to the health of people, or damage to property or the environment
HAZARDS	Potential source of harm
BENEFIT RISK ANALYSIS	Evaluate if the benefit of the intended use outweighs the residual risk
RESIDUAL RISK	Risk remaining after all the risk control measures have been implemented
RISK ANALYSIS	Systematic use of available information to identify hazards and to estimate the risk

NEW DEFINITIONS

BENEFIT	A positive impact or desirable outcome of the use of a medical device on the health of an individual or the positive impact on patient management or public health.
REASONABLY FORSEEABLE MISUSE	If misuse of a product can result from “predictable human behavior” than you need to take into account in your risk analysis. Reasonably foreseeable can be intentional or unintentional and include those why in the world would someone do that scenarios and applies to both professional and layman users.
STATE OF THE ART	Developed stage of technical capability at a given time as regards, products, processes and services based on the relevant consolidated findings of science, technology and experiences

RISK BENEFIT - NEW CONCEPT

The standard emphasizes that manufacturers need to demonstrate that the benefits outweigh the risk, & the risks have been mitigates to as low as possible.

Examples of benefits:

- Positive impact on clinical outcome
- Patient's quality of life
- Outcomes related to diagnosis
- Positive impact from diagnostic devices on clinical outcomes
- Positive impact on public health

TR 24971 PROVIDES CLARIFICATION AND EXAMPLES OF RISK BENEFIT DECISION

OVERVIEW OF CHANGES TO THE UPDATED STANDARD

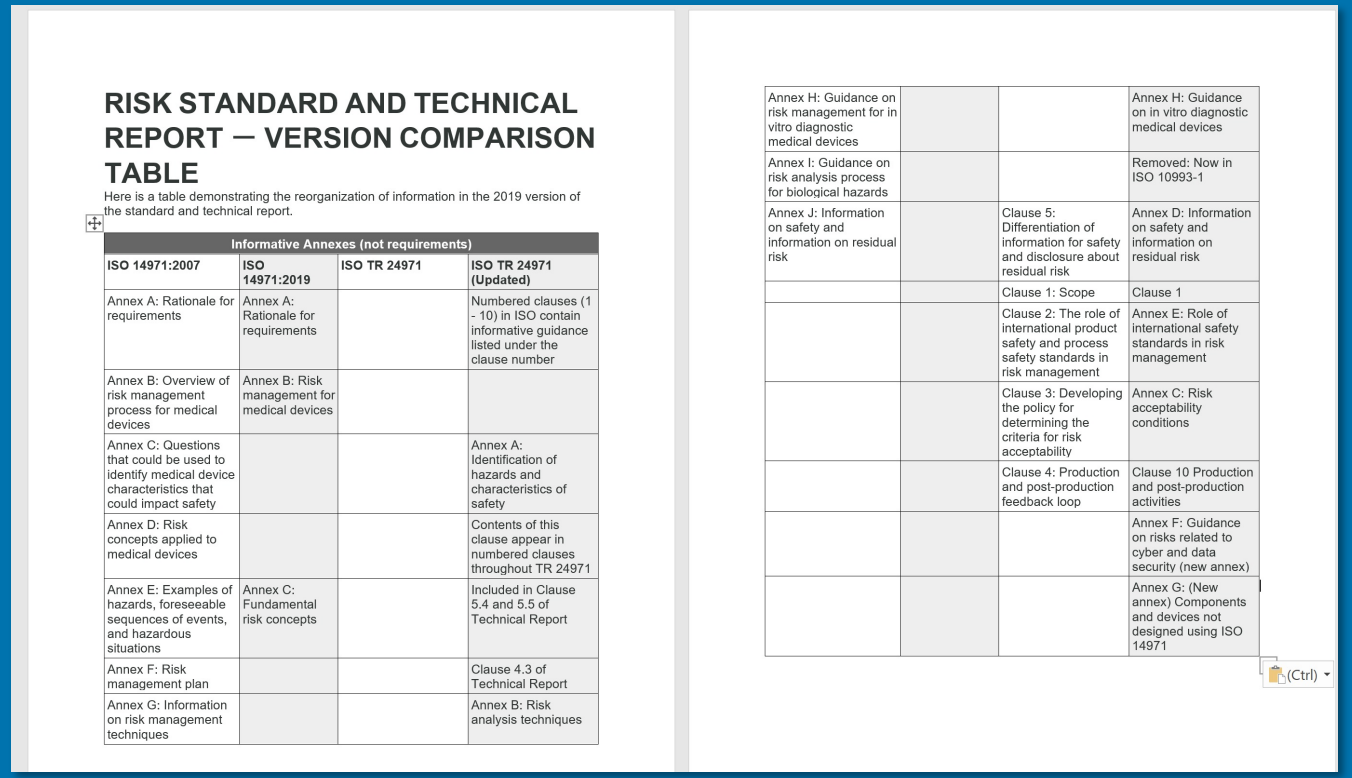
1. Normative References - Clause 2 is new
2. Terms and definitions - new definitions for Benefit, reasonably foreseeable misuse, state of the art, and harm and some other modified definitions to align with updated standards
3. Risk Management Plan added (Clause 4.1)
4. Update to Risk Analysis (Clause 5.4)
5. Benefit risk analysis (clause 7.4)
6. production and post production activities (clause 10) - specifically addresses the risk management in post market surveillance
7. Annex A- rationale for requirements
8. Annex B- Risk Management Process
9. Annex C - Examples of hazards, foreseeable sequences, events and hazardous situations

OVERVIEW OF TR 24971

- Annex D - Risk Concepts
- Annex F - Risk Management for Cybersecurity (new)
- Annex G - Risk Management File (new)
- Annex H - In Vitro Diagnostic (IVD) Devices (revised)

REORGANIZATION OF INFORMATION IN THE 2019 VERSION

If your company has been using multiple versions, this comparison chart may be helpful.



RISK STANDARD AND TECHNICAL REPORT — VERSION COMPARISON TABLE

Here is a table demonstrating the reorganization of information in the 2019 version of the standard and technical report.

Informative Annexes (not requirements)			
ISO 14971:2007	**ISO 14971:2019**	**ISO TR 24971**	**ISO TR 24971 (Updated)**
Annex A: Rationale for requirements	Annex A: Rationale for requirements		Numbered clauses (1 - 10) in ISO contain informative guidance listed under the clause number
Annex B: Overview of risk management process for medical devices	Annex B: Risk management for medical devices		
Annex C: Questions that could be used to identify medical device characteristics that could impact safety			Annex A: Identification of hazards and characteristics of safety
Annex D: Risk concepts applied to medical devices			Contents of this clause appear in numbered clauses throughout TR 24971
Annex E: Examples of hazards, foreseeable sequences of events, and hazardous situations	Annex C: Fundamental risk concepts		Included in Clause 5.4 and 5.5 of Technical Report
Annex F: Risk management plan			Clause 4.3 of Technical Report
Annex G: Information on risk management techniques			Annex B: Risk analysis techniques
Annex H: Guidance on risk management for in vitro diagnostic medical devices			Annex H: Guidance on in vitro diagnostic medical devices
Annex I: Guidance on risk analysis process for biological hazards			Removed: Now in ISO 10993-1
Annex J: Information on safety and information on residual risk		Clause 5: Differentiation of information for safety and disclosure about residual risk	Annex D: Information on safety and information on residual risk
		Clause 1: Scope	Clause 1
		Clause 2: The role of international product safety and process safety standards in risk management	Annex E: Role of international safety standards in risk management
		Clause 3: Developing the policy for determining the criteria for risk acceptability	Annex C: Risk acceptability conditions
		Clause 4: Production and post-production feedback loop	Clause 10 Production and post-production activities
			Annex F: Guidance on risks related to cyber and data security (new annex)
			Annex G: (New annex) Components and devices not designed using ISO 14971

(Ctrl)

POLL QUESTION

My Company is ___ % complete implementing the new ISO 14971:2019

A) 0% complete, we have not started

B) 20% complete

C) 50% complete

D) 80% Complete

E) 100% complete, we have completed implementing the standard

SAMPLE HAZARDS/HARMS TABLE FROM STANDARD

Cybersecurity Examples:

Hazard	***Harm***
Data without encryption	Potential for unauthorized access
Software updates without Authenticity confirmation	Potential for unauthorized Version
Data confidentiality	Loss of Patient Privacy
Data Access	Loss of Patient Data

WHAT IS A RISK FILE AND WHAT GOES INTO IT?

Risk Management File

- Risk Management Team
  - Cross functional team with subject matter expertise
  - Risk Manager recommended
- Risk Management Plan
- Risk Analysis & Risk Evaluation/Control
  - FMEAs
  - Fault Tree Analysis
- Risk Reviews
- Risk Management Report & Medical Benefits Assessment

CONCEPTUAL CHANGES FROM EARLIER VERSIONS

What are the changes?

- Creation of Risk Management Plans.
- Reduction of risk to As Low As Possible. (no more ALARP)
- Labeling/Training does not reduce risk score.
- Must take into account reasonably for-seeable misuse
- Focus on state of the art.
- Focus on post market surveillance.
- Focus on medical benefit assessment.
- Evaluate residual risk.

What is the impact of these changes?

- Gap assessments of previously scored risk files to address these difference, will need to compare new standard to current company processes
- May cause some remediation work for older products (rescoring, testing, etc.)

TYPICAL ISO 14971: 2019 QMS CHANGES:

Helpful Checklist

- Update your risk procedures for
  - Add the definition of benefit to your procedure.
  - Update to the new definition of harm (remove "Physical").
  - Check that cybersecurity risks are included in your risk analysis when applicable.
  - Add the definition of reasonably foreseeable misuse to your procedure.
  - Update definition of residual risk in your procedure (replace "taken" with "implemented").
  - Add definition of state-of-the-art to your procedure.
  - Add risk management plan to the process
  - Define and document the policy for establishing criteria for risk acceptability in the risk management procedure. See ISO/TR 24971:2020 for guidance.
- Add "method to evaluate the overall residual risk…" to your risk management plan or risk management plan template.
- Replace reference to Annex C with questions relating to the safety of the medical device, with a reference to ISO/TR 24971
- Update the wording relating to risk evaluation. The standard no longer says "decide…if risk reduction is required", but instead "evaluate the estimated risks and determine if the risk is acceptable or not".
- Update risk control options to: a) inherently safe design and manufacture b) protective measures in the medical device itself or in the manufacturing process c) information for safety and, where appropriate, training to users.
- If you have previously written that information for safety cannot reduce the risk, you can now remove that statement with reference to c) above and the new MDR. NB. It is still the least effective risk control and you still need to verify the effectiveness of the information for safety.
- Update risk benefit analysis to benefit risk analysis.
- If you have used the methods and techniques for overall residual risk from the previous versions of ISO 14971 and ISO/TR 24971, update to the new methods and techniques that are mentioned in 8.3 of ISO/TR 24971. a) The benefits related to the intended use weighed against the overall residual risk b) Visual representations of the residual risk c) Compare medical device under consideration to similar medical devices on the market d) Experts evaluate the overall residual risk in comparison with the benefit e) Further investigations
- Update production and post-production information to production and post-production activities.
- Implement the steps from production and post-production activities steps; collect, review, take actions.

HOW DO PRODUCT RISK FILES TIE INTO THE QUALITY MANAGEMENT SYSTEM?

Risk Management Files are living files

- The risk management files are developed during the design control development process of the product and are updated throughout the life of the product – this is tied closely to the requirements and the useability information
- Post market surveillance data needs to feed back into the FMEAs and the risk management report
- Design changes require risk file impact evaluation and updates as necessary
- CAPAs require product risk file impact evaluation and updates as necessary

DEVELOPMENT OF PRODUCT RISK FILES DURING TYPICAL DESIGN CONTROL PROCESS

Risk Deliverables for Typical Design Control Milestones for Development			
Design Goal	**Design Input**	**Design Output**	**Launch Design**
Identification of Cross-function Risk Management Team **(RMT)**	Identification of preliminary design risks identified in **FMEA** files/FTA files without risk controls completed (example use FMEA, design FMEA, cybersecurity, manufacturing process FMEA)	Post verification and validation, tying the risk controls and evaluation to update the risk analysis files	Review Risk Management File and update any analysis files with latest information.
Identification of Risk Manager to drive Risk File Development	Ensuring that risks related to requirements are identified	Risk ratings are scored and evaluated through documented risk reviews	Creation of a Risk Management Report (RMR) and Medical Benefits Assessment **(RMR)**
Creation of Risk Management Plan **(RMP)**	Documented Risk Reviews are initiated and placed in the Risk Management File	Identify any servicing risks on locked design (ex. Service FMEA) and include operating instructions/method sheets/servicing information	Update supporting documentation as necessary
Creation of Intended Use Statement and State of the Art Definition for the Product and identified of any risks associated with the IUS	Update supporting documentation as necessary	Update supporting documentation as necessary	Identification of how to tie in QMS processes to maintain the RMF current

DESIGN PROJECT EXAMPLES OF TYPEICAL RISK MANAGEMENT FILE DELIVERABLES

New Instrument

- Risk Management Plan, Design FMEA, process FMEA, software FMEA, service FMEA, Risk Management Report

New Software

- Risk Management Plan, Cybersecurity FMEA, design FMEA, process FMEA, Risk Management Report

New Assay

- Risk Management Plan, Design FMEA, process FMEA, Risk Management Report

POLL QUESTION

Do you struggle with getting post market surveillance data incorporated back into your product risk files?

A) Yes

B) No

POST MARKET SURVEILLANCE AND RISK FILE UPDATES

The updated regulations for Europe have more of an emphasis on post market surveillance.

Where can you find post market surveillance data?

- Literature searches on your product
- Customer complaints
- Similar product issues
- Field action data/Recall data
- Trend reports/product quality teams monitoring product performance

POST MARKET SURVEILLANCE AND RISK FILE UPDATES

1. Are new risks identified by the post-market data that need to be evaluated and incorporated into your risk files?

2. Does the data collected support the existing risk ratings (severities, detection, probability of occurrence) or does it cause any to change?

Tip: Improvements in your complaint handling system and customer complaint data collection methods can help with this and make your product risk files more robust.

POLL QUESTION

My company evaluates risk as part of a Design Change Request?

A) Yes

B) No

DESIGN CHANGES AND RISK FILE UPDATES

Key Concept: Design Change = Risk Increase

When you are doing a design change it will fall into one of the following:

- Replacement of an existing component due to obsolescence – typically targeting “Like for Like” or similar functional replacement.
- Improvement of design by typically changing out a component for a different one.
- Change of process.

You should only make a change when the Benefits offsets the Residual Risk

DESIGN CHANGE RISK ASSESSMENT EXAMPLES

Example: Part Obsolescence / Part Change

- Is the part replacement "like for like?"
- Are any new risks being introduced as a result of the change? (new size, new material, new connections?)
- Are changes to processes needed, and does that introduce new risk?

How to document this?

- A formal review with subject matter experts (cross functional team)
- It is also important to document that there is no impact to the file to demonstrate that the review has been done and considered.
- The record becomes part of the formal risk management file

CAPAS/NCRS AND PRODUCT RISK FILE UPDATES

Root Cause analysis and risk-based system analysis are the backbone for CAPA and non-conforming product investigations.

How does this tie into the product risk file?

- CAPAs and NCRs require root cause investigations and
- Usually, a step in the process is to see if the nonconformance is addressed by risks in the product risk management file
- Product Risks need to be assessed to see if new risks should be added or updated in the risk management file

KEY TAKE AWAY INFORMATION

- Make sure you know the implementation dates of ISO14971 for your impacted region
- Gap assess existing risk files and procedures for updates caused by standard changes.
- Evaluate risk as part of produce development and as part of product/process changes.
- Incorporate post market data into your risk file.
- Include new definitions such as “benefit”, “reasonably foreseeable misuse”, and “state of the art.”
- Create/update risk documentation during appropriate development and on market phases (see table.)

BEST PRACTICES

- Update your Complaint Evaluation procedures to create categories (or buckets) for root cause that align with your risk file.
- When developing a new product create a risk file that will grow with your product. Remember the risk file is a living thing.
- Be sure to show the design change (or improvement) has created a benefit and reduces risk (i.e. the benefit has offset any residual risk)
- Use of Standardized tools, and Standardized Harms and Hazards; create consistency in the maintenance of the risk management files.

KEY REFERENCES

- ISO 14971: 2019 Medical Devices - Application of risk management to medical devices
- ISO TR 24971:2020 Medical Devices - Guidance on the application of ISO 14971
- ISO 13485: 2016 Medical Devices- Quality Management Systems – Requirements for Regulatory Purposes
- International Standards Organization www.ISO.org
- US FDA 21 CFR Part 820 Quality System Regulation
- "Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance and Enforcement Decisions", Guidance for Industry and FDA Staff , Dec 27, 2016
- FDA Guidance, Factors To Consider When Making Benefit- Risk Determinations in Medical Device Premarket Approval and De Novo, August 2019
- "Implementation of Risk Management Principles and activities within a Quality Management System" GHTF Study Group 3, May 20, 2005
- "Risk Management & the Total Product Life Cycle", Katelyn Stuab-Zamperini, FDA, June 23, 2021
- "Greenlight Guru –What are the changes to ISO 14971:2019 and ISO TR24971", Jon Speer April 12, 2020
- Greenlight Guru Medical Device QMS Software , https://www.greenlight.guru/

THANK YOU!

DO YOU HAVE ANY QUESTIONS?

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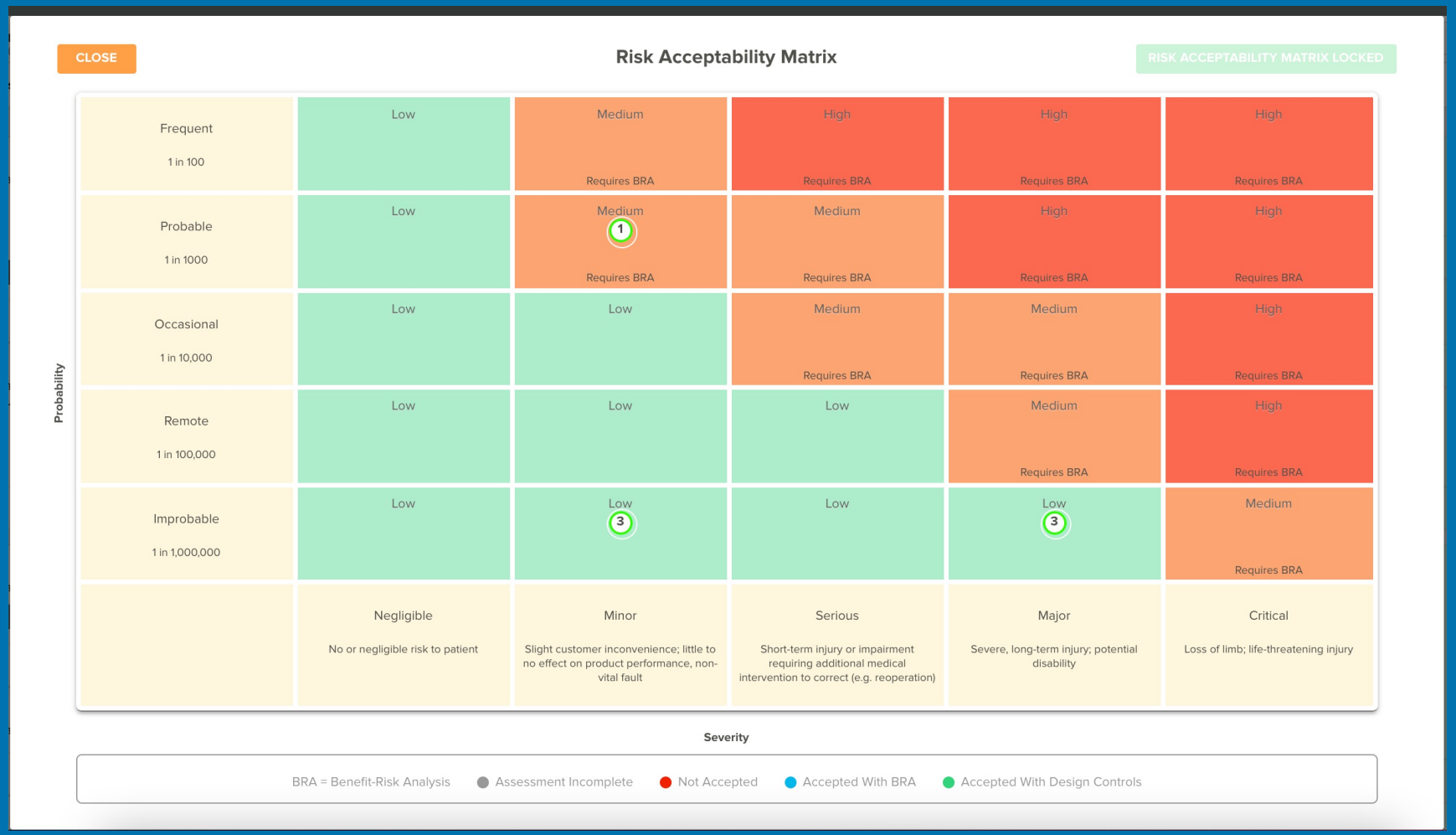
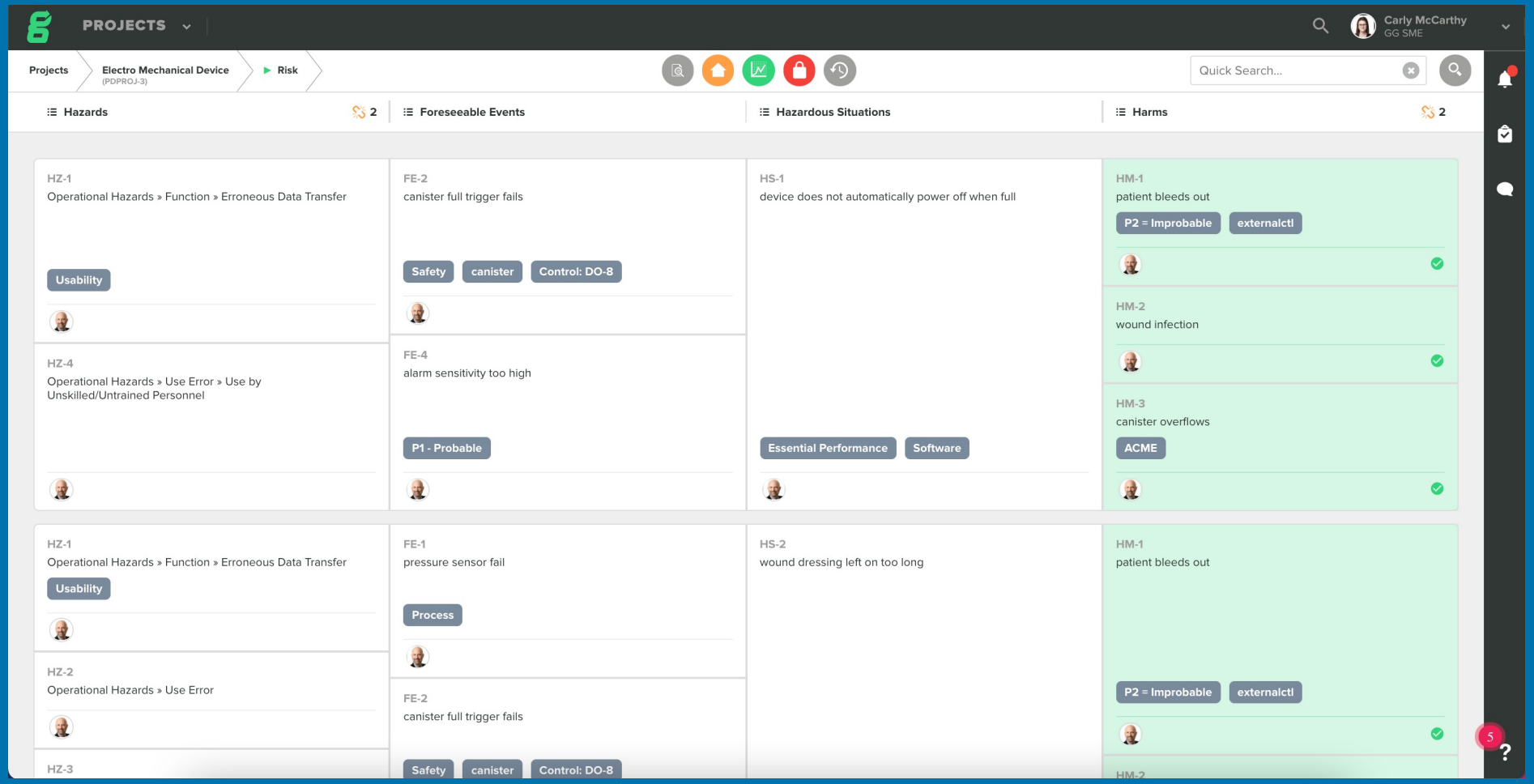
BACKUP SLIDES


CLOSE
Risk Acceptability Matrix
RISK ACCEPTABILITY MATRIX LOCKED
Probability
Frequent
1 in 100
Low
Medium
Requires BRA
High
Requires BRA
High
Requires BRA
High
Requires BRA
Probable
1 in 1000
Low
Medium
1
Requires BRA
Medium
Requires BRA
High
Requires BRA
High
Requires BRA
Occasional
1 in 10,000
Low
Low
Medium
Requires BRA
Medium
Requires BRA
High
Requires BRA
Remote
1 in 100,000
Low
Low
Low
Medium
Requires BRA
High
Requires BRA
Improbable
1 in 1,000,000
Low
Low
3
Low
Low
3
Medium
Requires BRA
Negligible
No or negligible risk to patient
Minor
Slight customer inconvenience; little to no effect on product performance, non-vital fault
Serious
Short-term injury or impairment requiring additional medical intervention to correct (e.g. reoperation)
Major
Severe, long-term injury; potential disability
Critical
Loss of limb; life-threatening injury
Severity
BRA = Benefit-Risk Analysis
Assessment Incomplete
Not Accepted
Accepted With BRA
Accepted With Design Controls


PROJECTS
Carly McCarthy
GG SME
Projects
Electro Mechanical Device
(PDPROJ-3)
Risk
Quick Search...
Hazards
2
Foreseeable Events
Hazardous Situations
Harms
2
HZ-1
Operational Hazards » Function » Erroneous Data Transfer
Usability
FE-2
canister full trigger fails
Safety
canister
Control: DO-8
HS-1
device does not automatically power off when full
HM-1
patient bleeds out
P2 = Improbable
externalctl
HM-2
wound infection
HZ-4
Operational Hazards » Use Error » Use by Unskilled/Untrained Personnel
FE-4
alarm sensitivity too high
P1 - Probable
Essential Performance
Software
HM-3
canister overflows
ACME
HZ-1
Operational Hazards » Function » Erroneous Data Transfer
Usability
FE-1
pressure sensor fail
Process
HS-2
wound dressing left on too long
HM-1
patient bleeds out
P2 = Improbable
externalctl
HZ-2
Operational Hazards » Use Error
FE-2
canister full trigger fails
Safety
canister
Control: DO-8
HZ-3
HM-2
5