Medical Device Risk Management

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"It does not do to leave a live dragon out of your calculations, if you live near one."

- J.R.R. Tolkien -

The Current State of ISO 14971

ISO 14971:2019 released

- Recognized by FDA 23 December 2019
- FDA transition period to 22 December 2022
- Aligned with EU MDR and parallel implementation is encouraged

ISO TIR24971:2020 released

Risk Management Process, Plan, and RMF

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Risk Analysis

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Risk Evaluation

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Risk Control

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Risk Acceptability (including Benefit / Risk)

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Review and Report

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Post-Production Monitoring

KING & SPALDING

Significant Changes to EN ISO 14971:2007 (...and what this means to you) (1)

Definition of "Harm" Revised

Removed the word "physical"

- "injury or damage to the health of people, or damage to property or the environment"
- 2019 language in Forward: "It is explained that the process described in ISO 14971 can be used for managing all types of risks associated with medical devices, <u>including those related to data and systems security</u>."
- 2019 Annex A.2.1: "Risks related to data and systems security are specifically mentioned in the scope, to avoid any misunderstanding that a separate process would be needed to manage security risks."
- <u>Impact</u>: Cybersecurity and privacy risks may now be considered "harm" subject to 14971

Significant Changes to EN ISO 14971:2007 (…and what this means to you) (2)

"Benefit" Defined — Alignment with MEDDEV and FDA Guidance

- "positive impact or desirable outcome of the use of a medical device on the health of an individual, or a positive impact on patient management or public health | Note 1 to entry: <u>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 public health impact</u>."

- Better alignment with MEDDEV 2.7.1/1 Revision 4 ("Clinical Evaluation: A Guide for Manufacturers and Notified Bodies Under Directives 93/42/EEC and 90/385/EEC") and FDA Guidance (e.g. "Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions")

- <u>Impact</u>: May alter the objective of Risk-Benefit Analysis, with new definition

Significant Changes to EN ISO 14971:2007 (...and what this means to you) (3)

RBA -> BRA

Benefit – Risk Analysis Elaborated

- 2007 language: "If this evidence does not support the conclusion that the medical benefits outweigh the residual risk, then the risk remains unacceptable."
- 2019 language: "If this evidence does not support the conclusion that the medical benefits outweigh this residual risk, then <u>the manufacturer may consider modifying the medical device or its intended use</u>. Otherwise, this risk remains unacceptable."
- Annex D moved to TR 24971
- Annex ZA language removed (required RBA in all instances – regardless of acceptability)
- <u>Impact</u>: (1) BRA now clearly driven by acceptability; (2) by adding the design change language and thus linking to post-market data, continuous evaluation of benefit-risk is necessary (recurring theme)

Significant Changes to EN ISO 14971:2007 (...and what this means to you) (4)

"Reasonably Foreseeable Misuse" Defined

Intentional and Unintentional in Scope

- "use of a product or system in a way not intended by the manufacturer, but which can result from readily predictable human behavior | 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: <u>Reasonably foreseeable misuse can be intentional or unintentional</u>."
- Definition includes use error, as well as reasonably foreseeable abnormal misuse
- <u>Impact</u>: This may expand the instances of reasonably foreseeable misuse included in risk analysis

Significant Changes to EN ISO 14971:2007 (...and what this means to you) (5)

Risk Control Measures Clarified

Same Priorities, with Clarified Definitions

- "Inherently safe design <u>and manufacture</u>"
- "Information for safety and, <u>where appropriate, training</u>"
- <u>Impact</u>: Design transfer activities and training activities may be necessary in risk control measures before evaluating residual risk

Significant Changes to EN ISO 14971:2007 (...and what this means to you) (6)

Usability and Intended Use Elaborated

Better Alignment with IEC 62366-1

- Added definition of "accompanying documentation" (for disclosure of residual risk), which includes "instructions for use, technical description, installation manual, quick reference guide, … auditory, visual, or tactile materials and multiple media types"
- Definition of "use error" broadened beyond acts or omissions leading to a "different medical device response" to now include any action (or lack of action), which results in a "different result than that intended"
- Considerations for intended use elaborated (i.e. "intended medical indication, patient population, part of the body or type of tissue interacted with, user profile, use environment, and operating principle") and tied to use specifications, as defined by 62366
- Impact: More use considerations may be needed during risk analysis and risk control implementation

Significant Changes to EN ISO 14971:2007 (...and what this means to you) (7)

ALARP

It's back!

- 2007 language: "The as-low-as-reasonably-practicable approach can be used as part of risk control options analysis (6.2). Risks for which the probability cannot be estimated would normally use the as-low-as-reasonably-practicable approach."
- 2012 Annex Z language: "Accordingly, manufacturers and Notified Bodies may not apply the ALARP concept with regard to economic considerations." (Used MDD language as justification)
- 2014 NB Interpretation: "This disregard of economic considerations when reducing risk is not coherent with the Medical Device Directives' objective as stated in, for example, the following recital of Directive 93/42/EEC"
- 2019 language: "The manufacturer's policy for establishing criteria for risk acceptability can define the approaches to risk control, for example reducing risk as low as reasonably practicable, reducing risk as low as reasonably achievable, or reducing risk as far as possible without adversely affecting the benefit-risk ratio."
- Impact: If the organization has moved too far down the "as far as possible" road, consider re-evaluating using a reasonable "as low as reasonably practicable" approach

Significant Changes to EN ISO 14971:2007 (...and what this means to you) (8)

Residual Risk

Clarified

- Unacceptable residual risks now drive "<u>consideration</u>" of additional risk controls, where 2007 language required "application" of additional risk controls (Mandate to <u>consider benefit vs. risk</u> stronger, when evaluating unacceptable residual risk)
- Unacceptable risk disclosure consideration removed from individual residual risk section and kept in overall residual risk section
- <u>Impact</u>: (1) benefit-risk analysis may need to include more discussion of unacceptable residual risks; (2) current disclosure statements may now be more systemic, as opposed to line-by-line discussions of individual unacceptable residual risks

Significant Changes to EN ISO 14971:2007 (...and what this means to you) (9)

Post-production Activities Expanded

- Post-market surveillance: Clarified sources of data to be reviewed (i.e. production, user, installation, maintenance, supply chain, state-of-the-art)
- What are you looking for? (new hazards / hazardous situations, altered risk profile, changes in state-of-the-art)
- What is the outcome of post-market surveillance? (risk profile re-evaluation, design changes, management evaluation of the risk management process)
- Impact: Risk management process may now need more detail regarding the handling of post-production data and the outcome of reviews thus linking to process improvements and other elements of the QMS (be clear on the feedback loop)

14971 in the Era of EU MDR (1)

Risk Management Process
• Specific risk management process elements mandated (i.e. risk management plan, risk analysis, risk estimation / evaluation, risk controls, post-market monitoring, risk re-evaluation) • Risk controls language almost identical to 14971

ALARP?
• "As low as reasonably practicable" language included in discussion of chemical, physical, and biological risks (Annex I, Section 10.2) • Risk reduction clearly addressed in terms of acceptability (Annex I, Sections 4 and 10.2) • "As far as possible" included regarding risk reduction in design and manufacture (Annex I, Section 4(a)) and use-related risks (Annex I, Section 5(a))

14971 in the Era of EU MDR (2)

Residual Risk

- 14971: "If the <u>overall</u> residual risk is judged acceptable, the manufacturer shall decide which residual risks to disclose and what information is necessary to include in the accompanying documentation in order to disclose those residual risks."
- EU MDR: "Manufacturers shall inform users of <u>any</u> residual risks."

Post-market Monitoring

- "evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on <u>hazards and the frequency of occurrence</u> thereof…"
- This may drive greater consideration of P_1 (probability of hazardous situation) / P_2 (probability of causing harm) method of evaluating probability since many current methods assume occurrence of the hazardous situation leads to harm
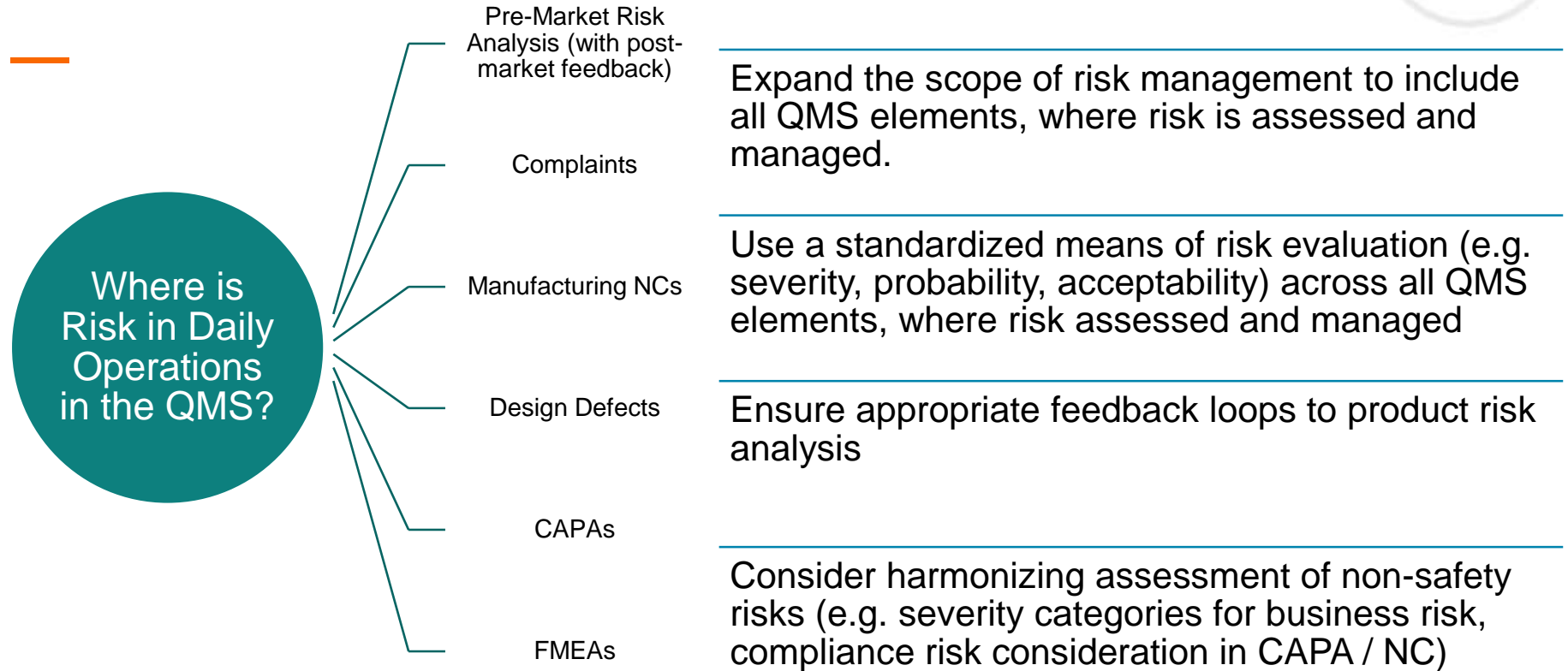
What is this 24971 thing?

Originally released in 2013, with a 2016 revision

- 26 pages
- Light guidance regarding use of international standards in risk management, risk acceptability, post-market feedback loop, information for safety vs. disclosure of risk, and evaluation of residual risk
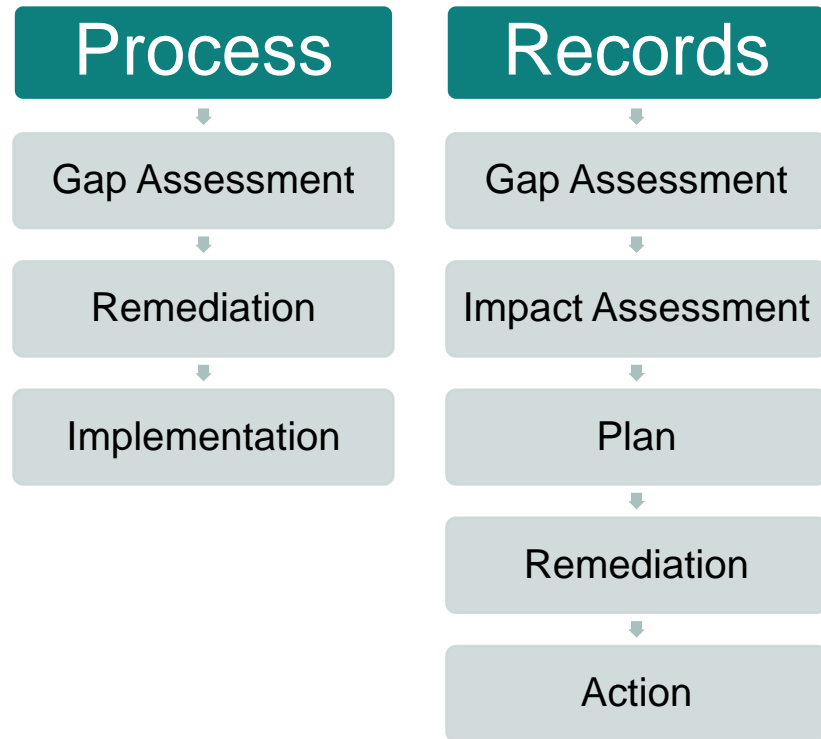
Updated in 2020 to complement ISO 14971:2019

- 99 pages
- Guidance for each stage of risk management
- Eight annexes addressing various topics including those from 2013/2016 (e.g. security-related risk, IVD, risk analysis techniques); many moved from previous 14971 versions

Risk Management: It's Not Just for Design Controls

Where is Risk in Daily Operations in the QMS?

- Pre-Market Risk Analysis (with post-market feedback)
- Complaints
- Manufacturing NCs
- Design Defects
- CAPAs
- FMEAs

Expand the scope of risk management to include all QMS elements, where risk is assessed and managed.

Use a standardized means of risk evaluation (e.g. severity, probability, acceptability) across all QMS elements, where risk assessed and managed

Ensure appropriate feedback loops to product risk analysis

Consider harmonizing assessment of non-safety risks (e.g. severity categories for business risk, compliance risk consideration in CAPA / NC)

The Transition

Process

- Gap Assessment
- Remediation
- Implementation

Records

- Gap Assessment
- Impact Assessment
- Plan
- Remediation
- Action

A Few Considerations

- Consider a CAPA-like process
- Use detailed & comprehensive impact assessment
- Consider grandfathering
- Avoid the "remediate as the design changes" fallacy
- Remediation may result in a change to the risk profile, new hazards (e.g. privacy, intentional misuse), new benefit / risk ratio, new risk controls, new BRD ratio, etc.
- Recognize the potential for disclosure, correction / recall post-remediation

A word of caution...

Watch over-use of probability tables... especially in post-market

Actual Case:

- Design issue resulting in frequent servicing causes nine serious injuries (including one death) among service staff over 18 months

- Four CAPAs are requested and submitted to the CAPA Review Board for consideration over this period

- All Four CAPAs are rejected since risk analysis for this issue shows a low probability and a risk profile of "acceptable"

Moral:

- Using pre-market estimates of risk to drive investigations, containment, corrections, and corrective actions around post-market data and events (especially serious injuries / death) may lead to significant impacts on the safety of your device

- Real-time and periodic updates of risk analyses (and risk profiles) are necessary based on post-market data and events (Statistics evaluating actual vs. predicted are also helpful)

- Investigations, containments, corrections, corrective actions, and feedback to risk management related to post-market adverse events are expected by the US FDA and are now codified in the EU MDR

Questions?