Consideration of Reasonably Foreseeable Misuse in a Biological Evaluation

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Disclaimer – the content of this presentation reflects the views of the presenter and not those of Smith + Nephew

Agenda

- Reasonably foreseeable misuse - concepts from industry
- What constitutes "systematic" reasonably foreseeable misuse
- Potential impact on device categorisation
- Integration with the ISO 14971 risk management process

Background

- Consideration of reasonably foreseeable misuse (RFM) added to ISO 10993-1:2025
- Mixed feedback:
  - Some consider reasonably foreseeable misuse has always been in scope of ISO 10993
  - Others are concerned about possible testing of the device to account for improbable use scenarios
- ISO/TC 194 WG 1 developing guidance document

ISO 14971 - Reasonably Foreseeable Misuse

- ISO 14971 defines reasonably foreseeable misuse as “Use of a product or system in a way not intended by the manufacturer, but which can result from readily predictable human behaviour”

Should be included in the risk management file

In scope of usability engineering, IFU and user training

Requires risk controls

- Inclusion in risk management process = mandatory
- ISO 10993 biological risk management is a subset of medical device risk management
  - Logical to consider the biological risk associated with reasonably foreseeable misuse?

Established elsewhere in industry

Usability Engineering	**IEC 62366-1:2015**: RFM to be identified during usability engineering formative & summative tests **FDA Guidance**: RFM to be evaluated, including warnings on labelling
EU MDR	**EU MDR 2017/745 Annex I**: Consider risks of RFM throughout device lifecycle
Post-Market	**EU MDR Annex 14b**: PMCF studies should be designed to detect RFM **GHTF SG2*** – RFM considered in adverse event reporting

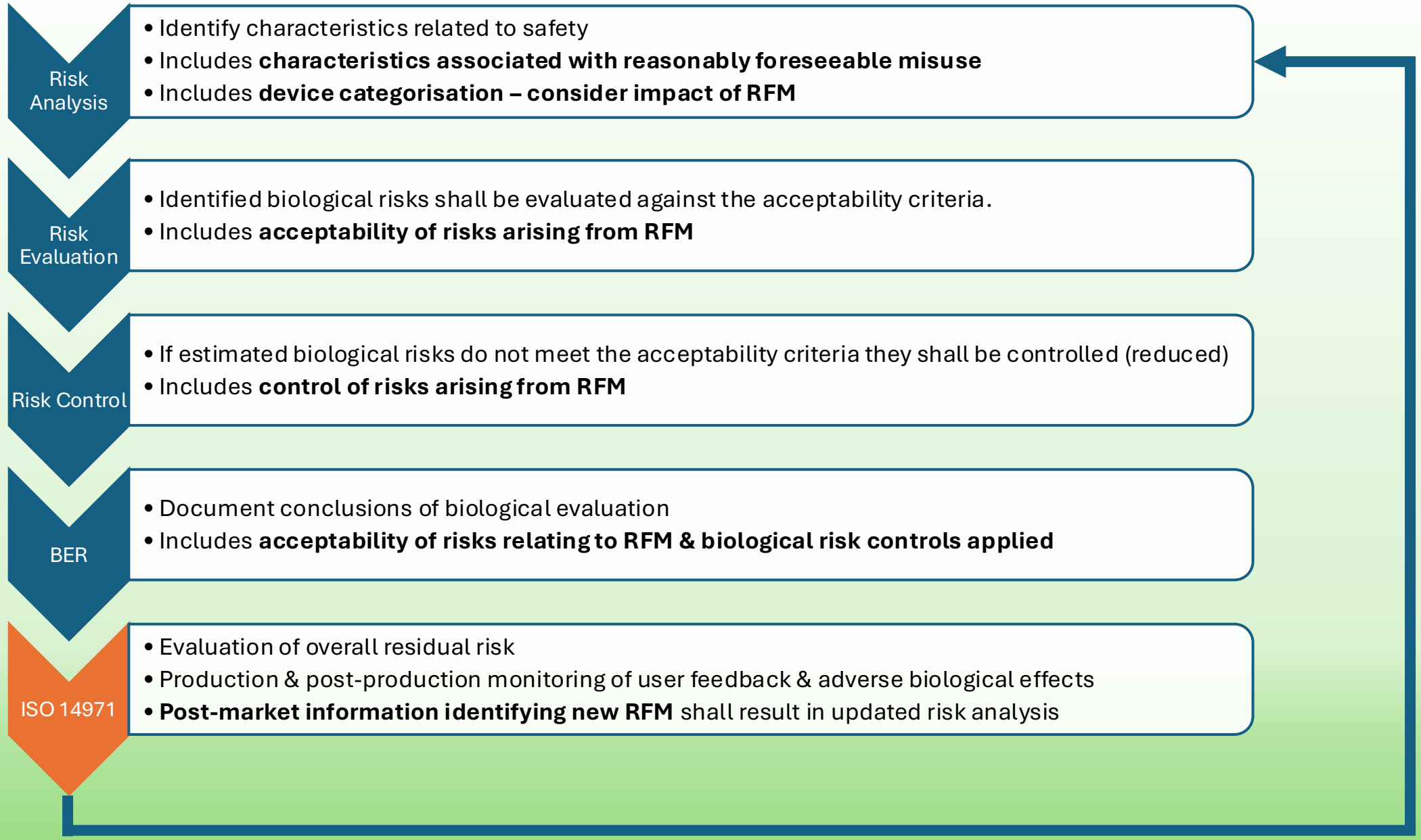
*Medical Devices: Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices – GHTF/SG2/N54R8:2006 Study Group 2 Final Document

What does ISO 10993-1:2025 say?

Aligns with ISO 14971 definition

"Use of a medical device in a way not intended by the manufacturer, but which can result from readily predictable human behaviour"

- Biological evaluation plan should include RFM (Clause 5)
- Biological risk analysis requires categorisation of the device to include reasonably foreseeable misuse (Clause 6.1)
- RFM should be considered as part of biological risk control (risk reduction) activities
- Risk acceptability, including RFM, should be included in the BER


Risk Analysis
• Identify characteristics related to safety
• Includes **characteristics associated with reasonably foreseeable misuse**
• Includes **device categorisation – consider impact of RFM**
Risk Evaluation
• Identified biological risks shall be evaluated against the acceptability criteria.
• Includes **acceptability of risks arising from RFM**
Risk Control
• If estimated biological risks do not meet the acceptability criteria they shall be controlled (reduced)
• Includes **control of risks arising from RFM**
BER
• Document conclusions of biological evaluation
• Includes **acceptability of risks relating to RFM & biological risk controls applied**
ISO 14971
• Evaluation of overall residual risk
• Production & post-production monitoring of user feedback & adverse biological effects
• **Post-market information identifying new RFM** shall result in updated risk analysis

Risk Analysis

Device Categorisation Clause 6.4.1

- “The intended use…shall be documented…should include the **intended medical indication, patient population, part of body or type of tissue**…the categorisation enable identification of potential biological effects…”
- “**Categorization** of the medical device **shall…consider the potential impact of reasonably foreseeable misuse** in accordance with ISO 14971, where there is information available (e.g. post-market surveillance data, clinical literature) to suggest that the device can be used outside of its intended use, and this misuse is identified as being **systematic**”.

What constitutes “systematic”?

- “Foreseeable misuse” all misuse that can be imagined - not necessarily probable.
- “Reasonably foreseeable misuse” is **a subset of foreseeable misuse** that is predictable and more likely to occur.
- **“Systematic”** terminology used in ISO 10993-1:2025 but not other standards
- Purpose:
  - **Focus on real risks** and not theoretical cases
  - Ensure risk controls are established only for realistic scenarios

Risk Analysis

Systematic Reasonably Foreseeable Misuse can be…

- …considered as misuse that occurs in a **consistent, repeatable and predictable** manner.
- …predicted during product development though usability engineering studies, experience of similar products or related methods.
- …evidenced through post-market surveillance activities including complaints investigation, clinical reports, user feedback etc.

Systematic Reasonably Foreseeable Misuse can be…

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Determination that RFM is "systematic" likely to require input from a cross-functional team as part of ISO 14971 processes

Device Categorisation – RFM Examples

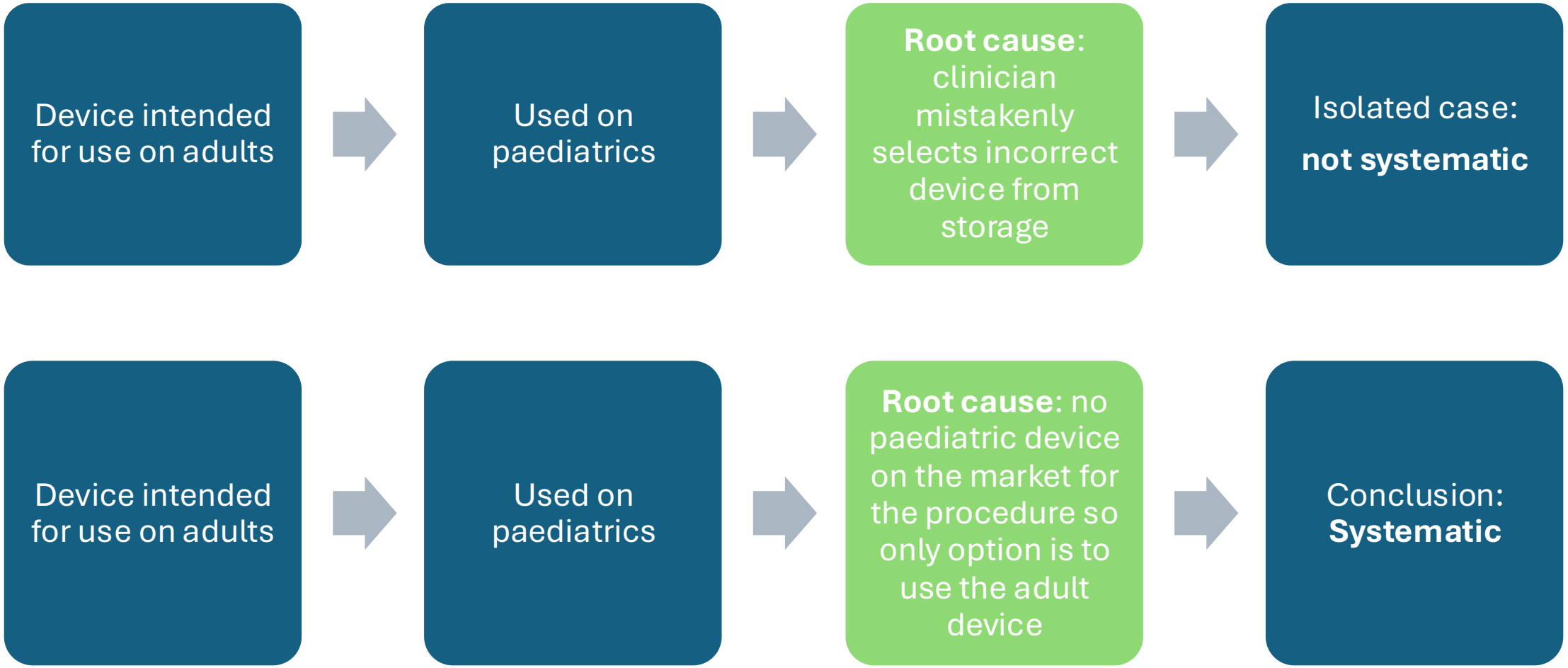
10993-1 Clause 6.4.1

- Use for longer than intended by the manufacturer
- Use at a different body contact site
- Use in a different patient population

Patient population doesn't directly impact device category but is to be documented as part of broader categorisation activities

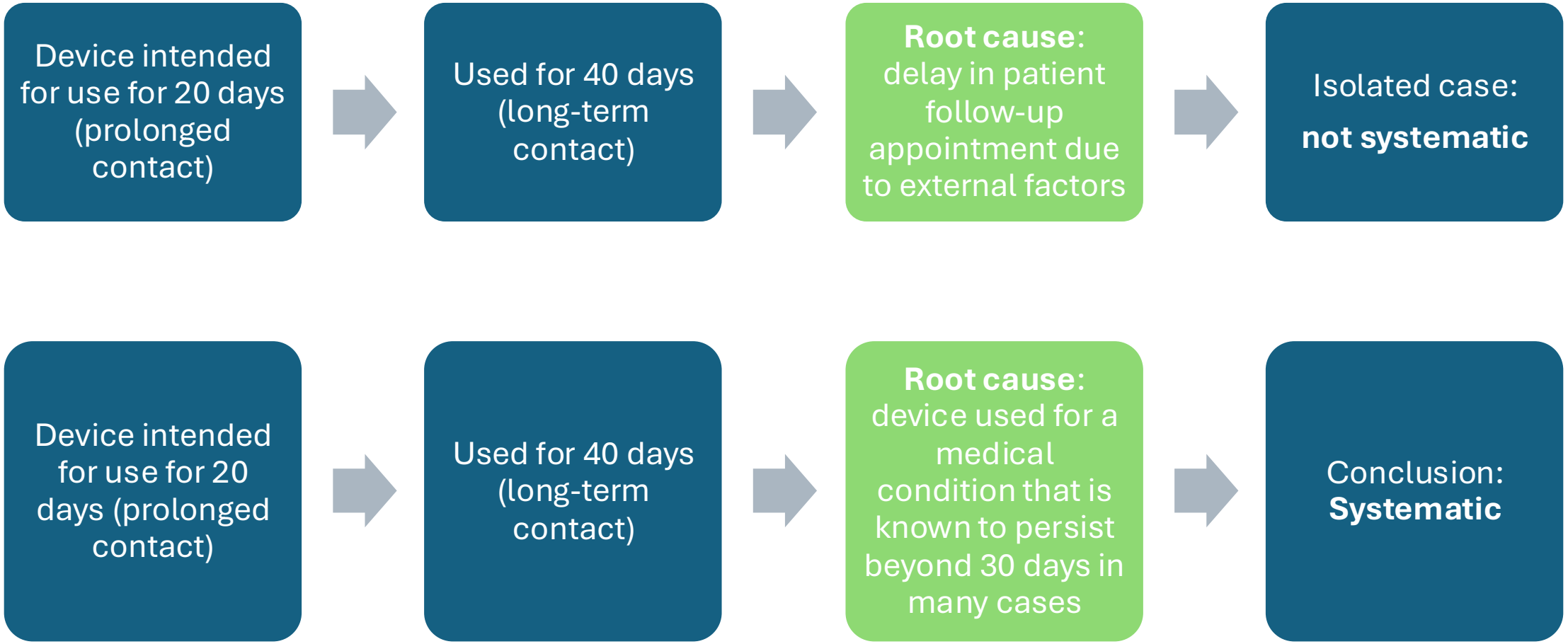
Risk Analysis

Example – use on different patient population



Risk Analysis

Example – use for longer than intended



Risk Analysis

Risk Analysis

- The impact of a new device category due to RFM should be considered:
  - Additional biological effects not previously in scope?
  - Different population for TRA?
  - Longer exposure period for biological tests?
  - Alternative extraction conditions for extractable studies?
  - Increased tissue exposure – is TRA protective?
  - Others?
- Additional data may need to be gathered or generated to determine the new biological risks arising from reasonably foreseeable misuse

Risk Analysis

Risk Analysis

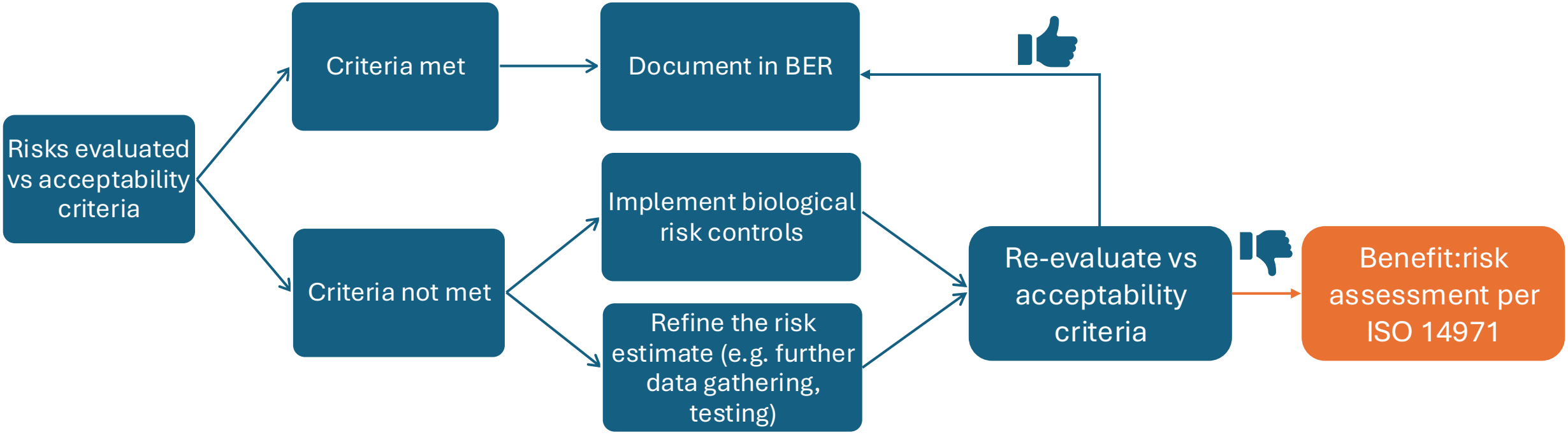
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New testing may not be needed – the biological risk could be determined based on existing data, use of similar devices, literature data etc

Risk Evaluation

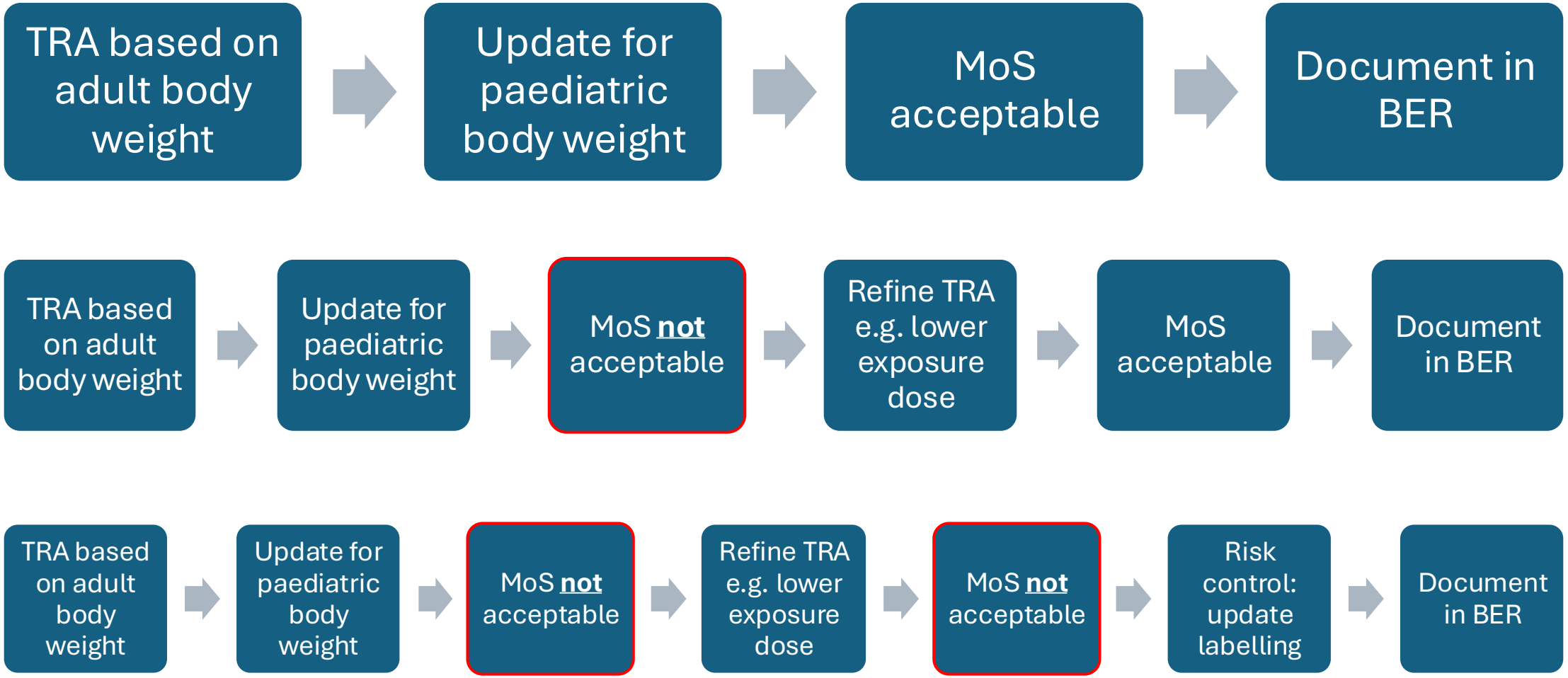
Risk Acceptability

- Biological risks – including those from RFM - must be evaluated against pre-defined criteria to determine their acceptability



Risk Analysis

Risk Acceptability: Adult → Paediatric



Risk Control

Biological Risk Control

Includes risks arising from reasonably foreseeable misuse

- Biological risks that do not meet the acceptability criteria shall be controlled
- Hierarchy of risk controls:
  1. Safe by design
  2. Protective measures
  3. Information for safety
- ISO 10993-1:2025 Clause 8 item C notes: “information for safety and…training to users (e.g. contraindications for susceptible individuals, **warnings about biological risks from reasonably foreseeable misuse** or a risk of biological harm)”

Risk Control

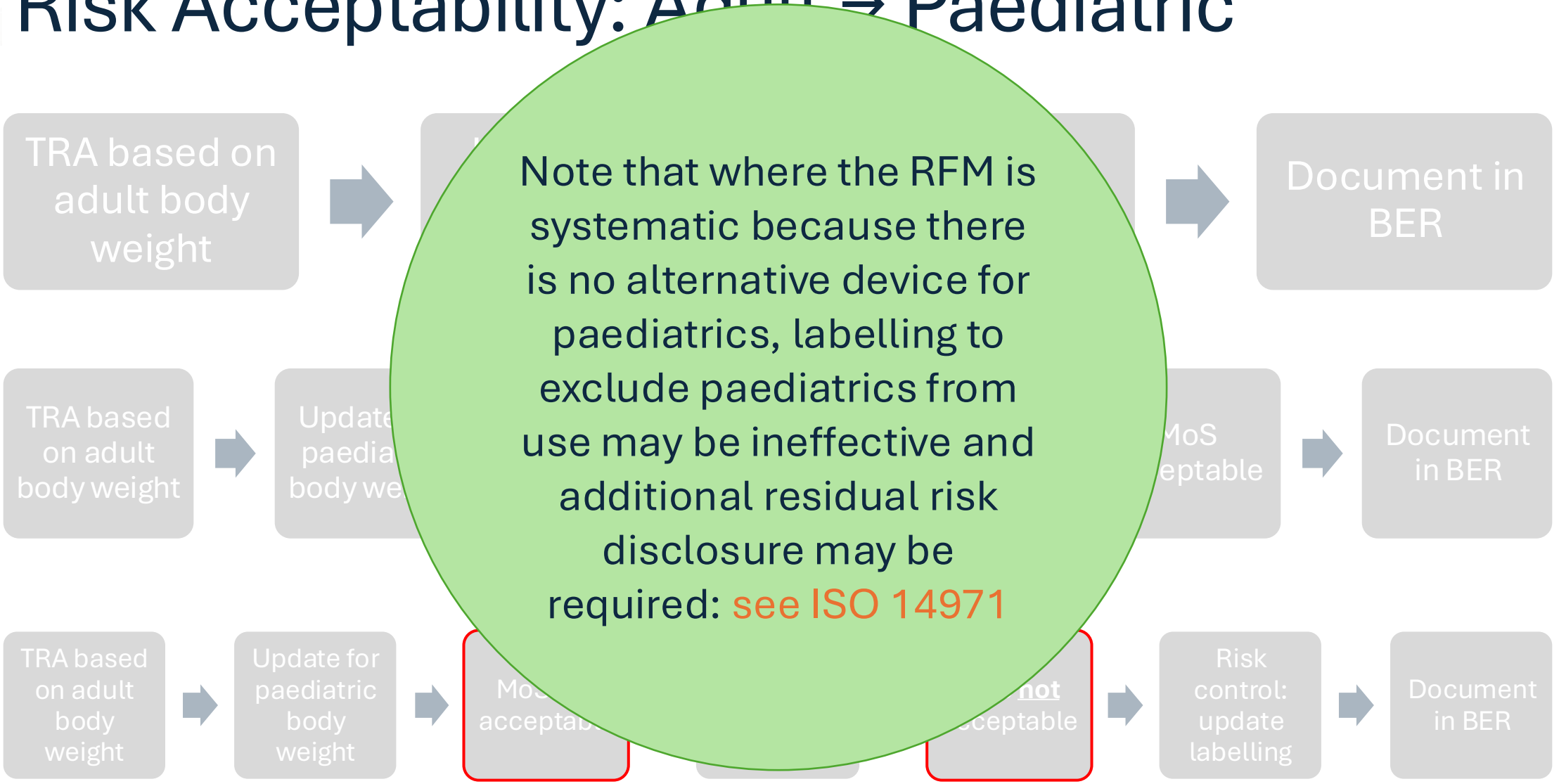
Biological Risk Control Examples

More detail on general risk control in ISO/TR 24971:2020 7.1

Safe by design	• Substitute with a material showing more favourable toxicity profile
Protective measures	• Barrier or seal around hazardous constituents
Information for safety	• Labelling changes to contraindicate for susceptible populations • Residual risk disclosure – provide further detail to users regarding the potential harms arising from the misuse scenario • Providing user training

Risk Analysis

Risk Acceptability: Adult → Paediatric



BER

Document in BER

- Conclusions of the overall biological evaluation shall be documented in the Biological Evaluation Report, including:
  - Criteria for risk acceptability of the medical device, including RFM
  - Outcome of the biological risk evaluation
  - Risk controls applied
  - Residual risks

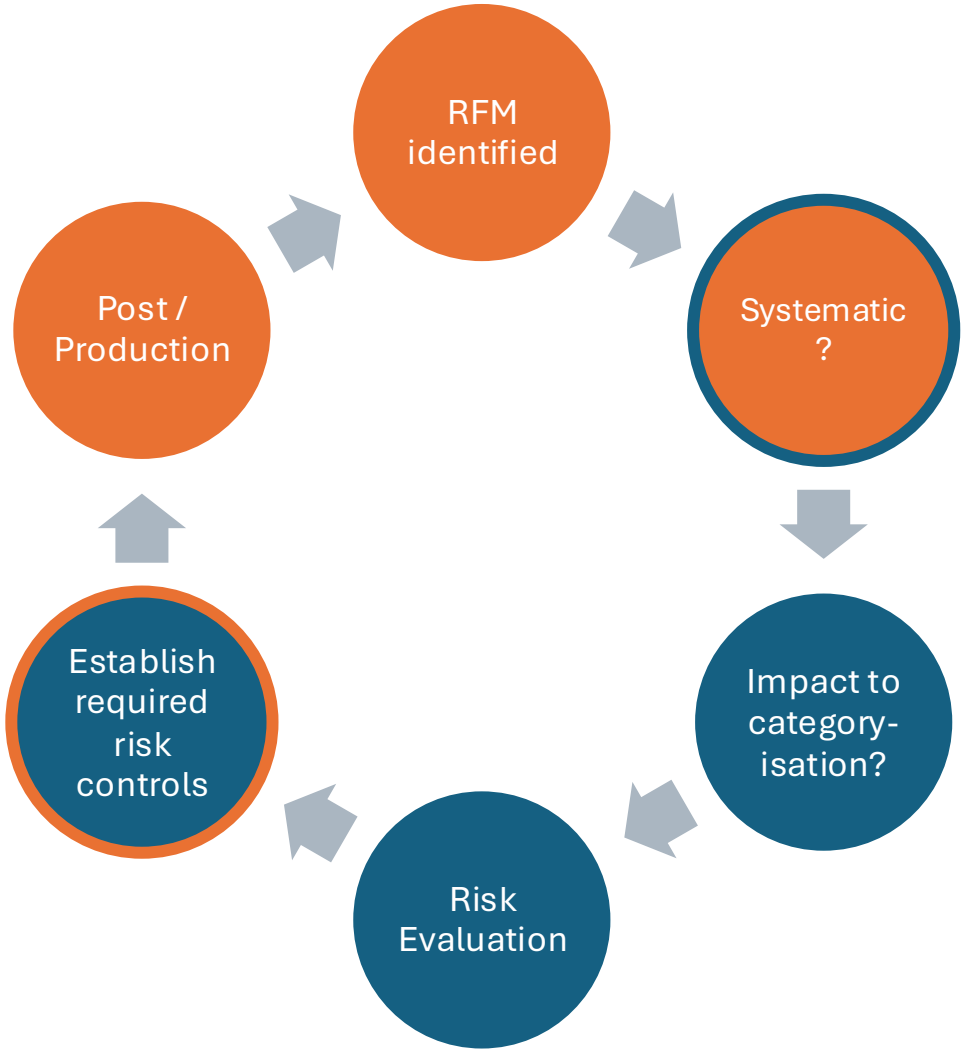


ISO 14971 Process

- Benefit:risk assessment
- Production & post-production activities

ISO 14971

Integration with risk management processes



- RFM included in the biological evaluation should also be documented in the risk file
- A cross-functional team of experts may input to decision on “systematic”
- Biological risk acceptability = align with the criteria in the ISO 14971 risk management plan
- Decision-making on risk control measures can be supported by a cross-functional team
- Outputs are documented in the BER → risk management file

Summary

- Reasonably foreseeable misuse – well established across industry
  - ➡ Allows closer alignment with related standards
- Use of “systematic” allows focus on real risks – not theoretical
- Evaluating the impact to device categorisation does not automatically lead to new testing
- Biological evaluation of RFM forms part of the ISO 14971 process & improves patient safety

Thank you