

Use of Production and Post-Production Information in Risk Management

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Objectives



- 1. Discuss the use of production and postproduction information in risk management
 - What is it?
 - Why is it important?
- 2. Relevant regulatory requirements
- 3. Reinforce concepts through scenarios

Introduction



- Risk management does not end with design and development
- Manufacturers must continue to ensure that device benefits to outweigh risks throughout the TPLC
- Monitoring production and post-production information may result in:
 - Identification of unforeseen hazardous situations
 - Refinement of risk estimations

FDA Why is Monitoring Important? American National Standard ANSI/AAMI/ ISO 14971: 2019 Medical devices-Application of risk management to medical devices AAMÌ

ISO 14971:2019, Clause A.2.10



Examples of Data Sources

PRODUCTION

- Supplier performance monitoring
- Production process monitoring
- Inspection and test results
- Environmental monitoring
- Internal and external audit results

POST-PRODUCTION

- Complaints
- Customer feedback
- Adverse events
- Installation and servicing
- Clinical studies
- Scientific literature
- Media sources

Consider the subject device and other devices with similar intended uses or operating principles

Additional references: ISO/TR 24971 and GHTF SG3/N18

Why Should You Monitor?

FDA

- 1. Serves as a means of preventive action
- 2. Keeps risk management file current
- 3. It's the right thing to do
- 4. Required by regulations and standards

Important References

- **21 CFR 820**: *The Quality System Regulation*
 - QSR Preamble
- **ISO 13485 (2016)**: Quality management systems Requirements for regulatory purposes
- ISO 14971 (2019): Application of risk management to medical devices
- ISO/TR 24971 (2020): Guidance on the application of ISO 14971
- **IEC/TR 80002-1 (2009):** Guidance on the application of ISO 14971 to medical device software
- GHTF SG3/N15R8 (2005): Implementation of risk management principles
- and activities within a Quality Management System
- **GHTF SG3/N18 (2010):** *Guidance on corrective action and preventive action and related QMS processes*
- FDA Guidance (2016): Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions

QSR Requirements

• The QSR only mentions "risk" once:

Design validation shall include software validation and <u>**risk analysis**</u>, where appropriate...

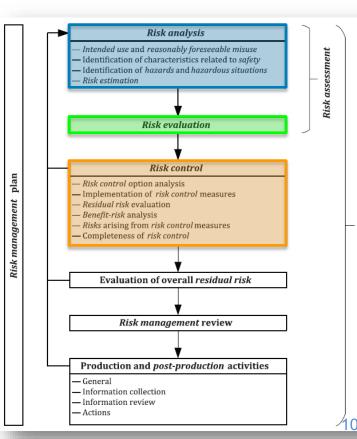
21 CFR 820.30(g)

- QSR preamble discusses additional expectations:
 - Risk evaluation
 - Risk control
 - Production and post-production activities

QSR Preamble and Risk (1/2)

When conducting a risk analysis, manufacturers are expected to *identify* possible hazards associated with the design in both normal and fault conditions. The risks associated with the hazards, including those resulting from user error, should then *be calculated in both normal and fault* conditions. If any risk is judged unacceptable, it should be reduced to acceptable levels by the appropriate means, for example, by redesign or warnings.

QSR Preamble Comment #83



Risk management

QSR Preamble and Risk (2/2)

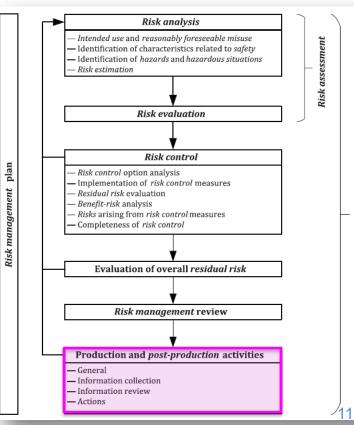
FDA

FDA cannot dictate in a regulation the degree of action that should be taken because each circumstance will be different, but FDA does expect the manufacturer to develop procedures for assessing the risk, the actions that need to be taken for different levels of risk, and how to correct or prevent the problem from recurring, depending on that risk assessment...

QSR Preamble Comment #159

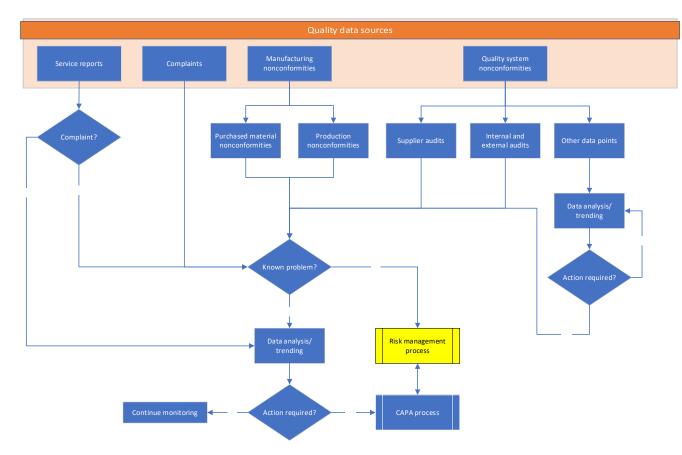
Also consider:

- 21 CFR 820.100(a)(1): Data analysis
- 21 CFR 820.100(a)(3): Identifying actions needed



Risk management

GHTF Risk Management Guidance



FDA

A Word on Manufacturing Risk

FDA Design Control Guidance for Medical Device Manufacturers (March 1997)



FDA

DESIGN CONTROL GUIDANCE

FOR

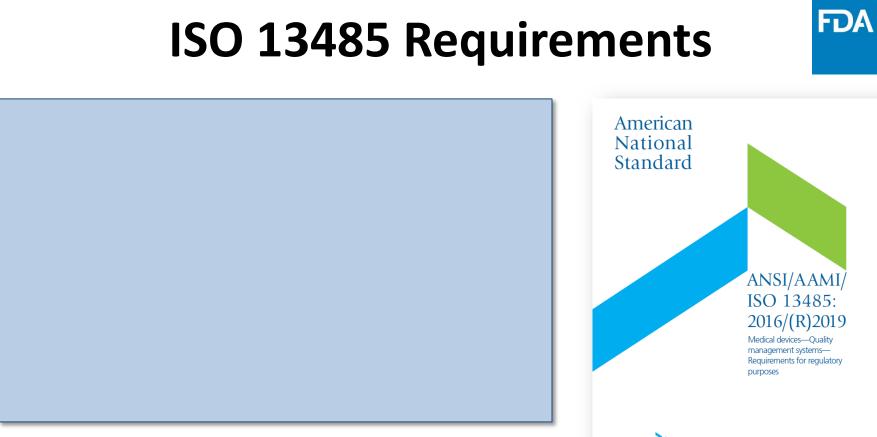
MEDICAL DEVICE MANUFACTURERS

This Guidance relates to FDA 21 CFR 820.30 and Sub-clause 4.4 of ISO 9001



"Risk analysis" per 21 CFR 820.30(g) includes analyzing risks attributable to **manufacturing**.

March 11, 1997



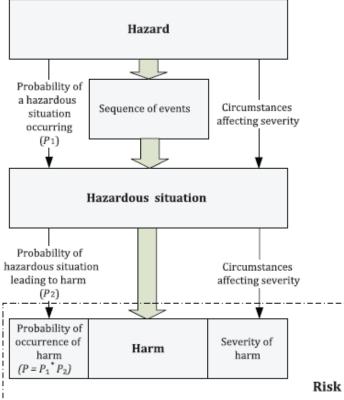
ISO 13485:2016, Subclause 8.2.1



Risk Management Terms



Risk		Combination of the probability of occurrence of harm and the severity of that harm	Prob	ability of	Ha	zard	
Harm	1	Injury or damage to the health of people, or damage to property or the environment	a ha sit oc	zardous uation curring (P1)	Sequence	e of events	Circ
Hazar	rd	Potential source of harm		•	Hazardou	s situatior	1
Hazar situat		Circumstance in which people, property or the environment is/are exposed to one or more hazards	hazardo leadin	ability of ous situation g to harm	on		Circ







SCENARIOS

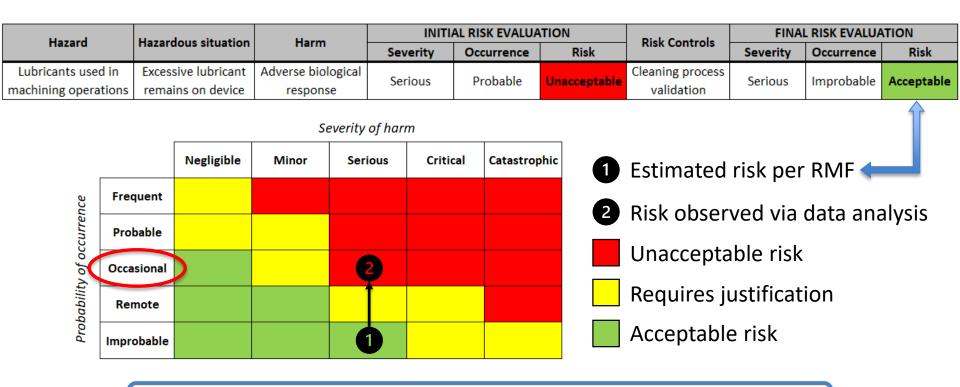
Scenario #1: Nonconforming Product

- A Material Review Board meeting was convened at an implantable spinal device manufacturer due to an emerging trend of NCRs opened for visibly contaminated devices.
- The RMF shows that biological risks due to contamination were already identified and mitigated by a validated final cleaning process.



Scenario #1: Nonconforming Product





NCR data indicates risk has not been effectively mitigated

Scenario #2: Customer Complaints

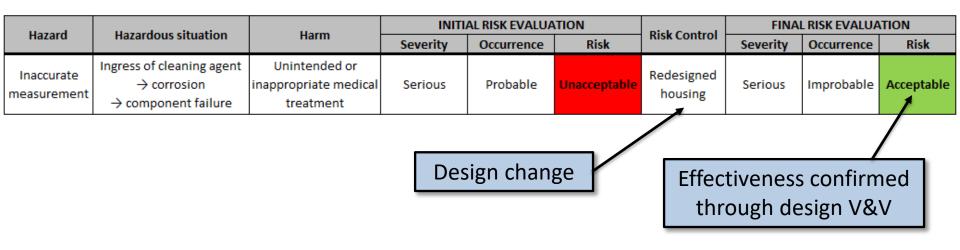
- During a routine quality data review meeting, a manufacturer of patient monitoring systems observed an adverse trend of complaints for inaccurate readings.
- Investigation of returned devices determined the cause to be component failure due to moisture ingress.



Scenario #2: Customer Complaints



New entry to Risk Management File...



Additional mitigation likely needed for distributed product (*e.g.*, recall)



- During routine monitoring of MAUDE data, a manufacturer of IV catheters learns of an event where components broke apart, leading to serious patient injury.
- Previously, the RMF had indicated that component dissociation could only lead to negligible harm.





Risk Management File prior to data analysis...

Hererd	Hazardous situation	Harma	INITL	AL RISK EVALUA	TION	Dick Control	FINA	RISK EVALUA	TION
Hazard	Hazardous situation	Harm	Severity	Occurrence	Risk	Risk Control	Severity	Occurrence	Risk
Mechanical forces of normal use	Failure of solvent bond → component dissociation	Negligible injury	Negligible	Probable	•	Validated manual bonding process	Negligible	Occasional	Acceptable



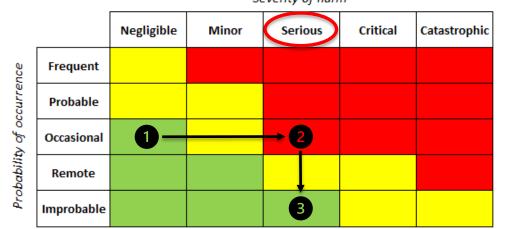
Severity of harm

- Estimated risk per RMF
- 2 Risk observed via data analysis
 - Unacceptable risk
 - Requires justification
 - Acceptable risk



...Risk Management File after additional mitigation

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Hazard	Hazardous situation	Harm	Severity	Occurrence	Risk	Risk Control	Severity	Occurrence	Risk
Mechanical forces of normal use	Failure of solvent bond → component dissociation	Serious injury	Serious	Probable	Unacceptable	 (1) Validated automated bonding process (2) non-destructive tensile test 	Serious	Improbable	Acceptable



Severity of harm

- Estimated risk per RMF
- 2 Risk observed via data analysis
- **3** Risk after additional mitigation
 - Unacceptable risk
 - Requires justification
 - Acceptable risk



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https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm

Summary



During this presentation, we discussed:

- 1. The use of production and post-production information in risk management
 - What is it?
 - Why is it important?
- 2. Relevant regulatory requirements
- 3. Scenarios to reinforce concepts

