Use of Production and Post-Production Information in Risk Management

July 13, 2022

LCDR Tom Peter

Investigator/Medical Device Specialist

OMDRHO Division 1 (East)

Disclaimers

This communication is consistent with 21 CFR 10.85(k) and constitutes an informal communication that represents my best judgment at this time but does not constitute an advisory opinion, does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the Agency to the views expressed.

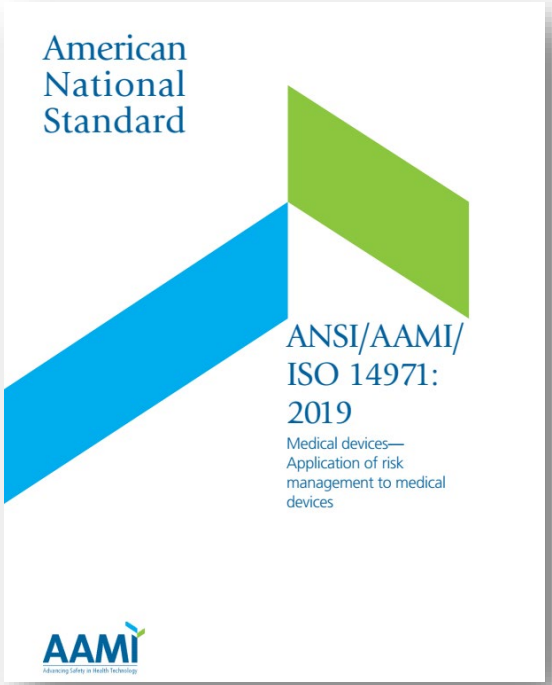
Objectives

1. Discuss the use of production and post-production 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

Why is Monitoring Important?



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?

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 **risk analysis**, where appropriate…*

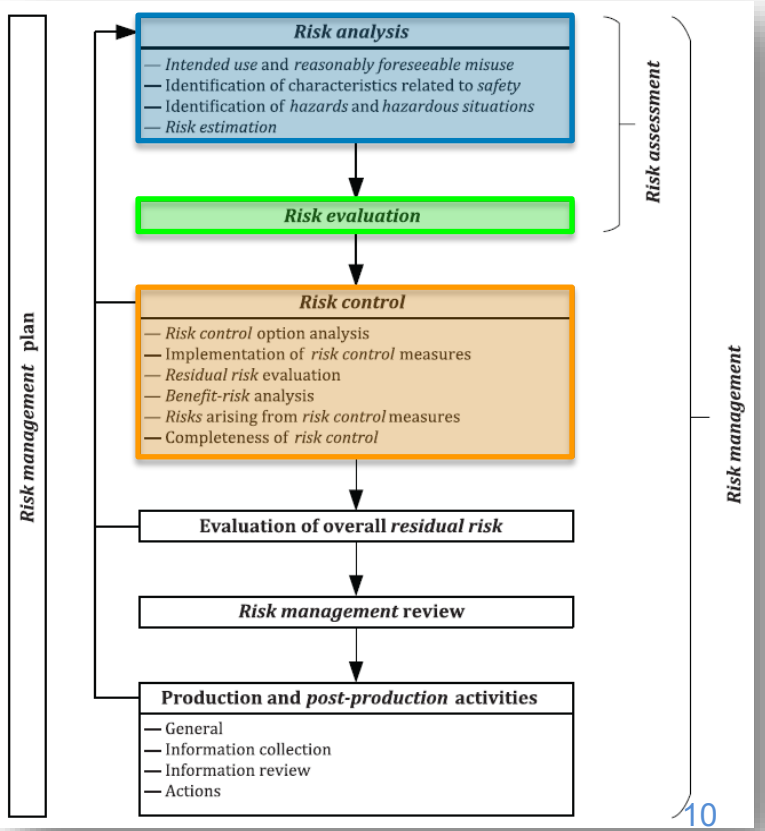
21 CFR 820.30(g)

- 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



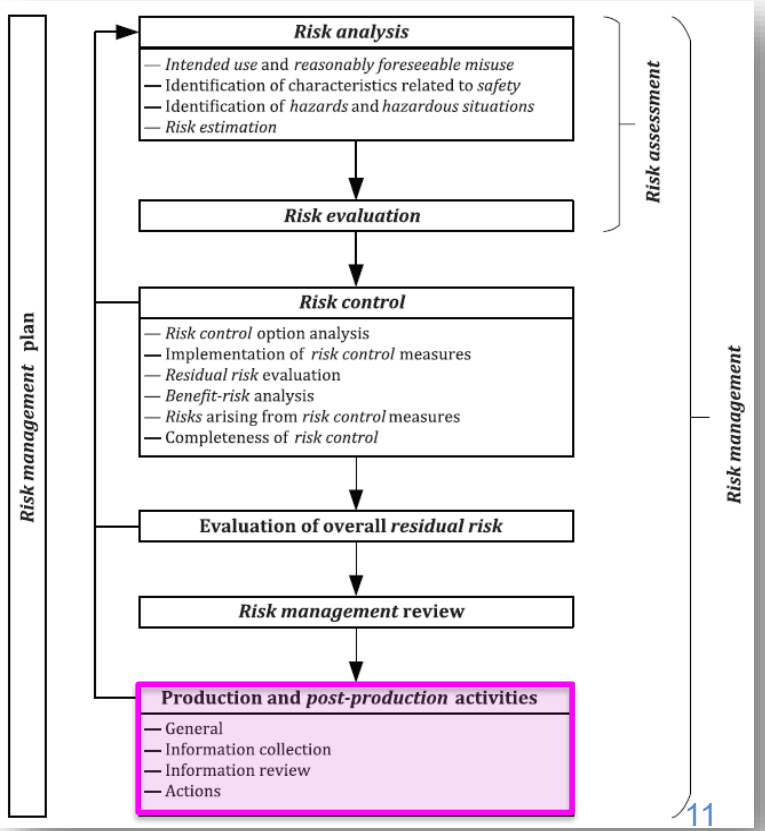
QSR Preamble and Risk (2/2)

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…

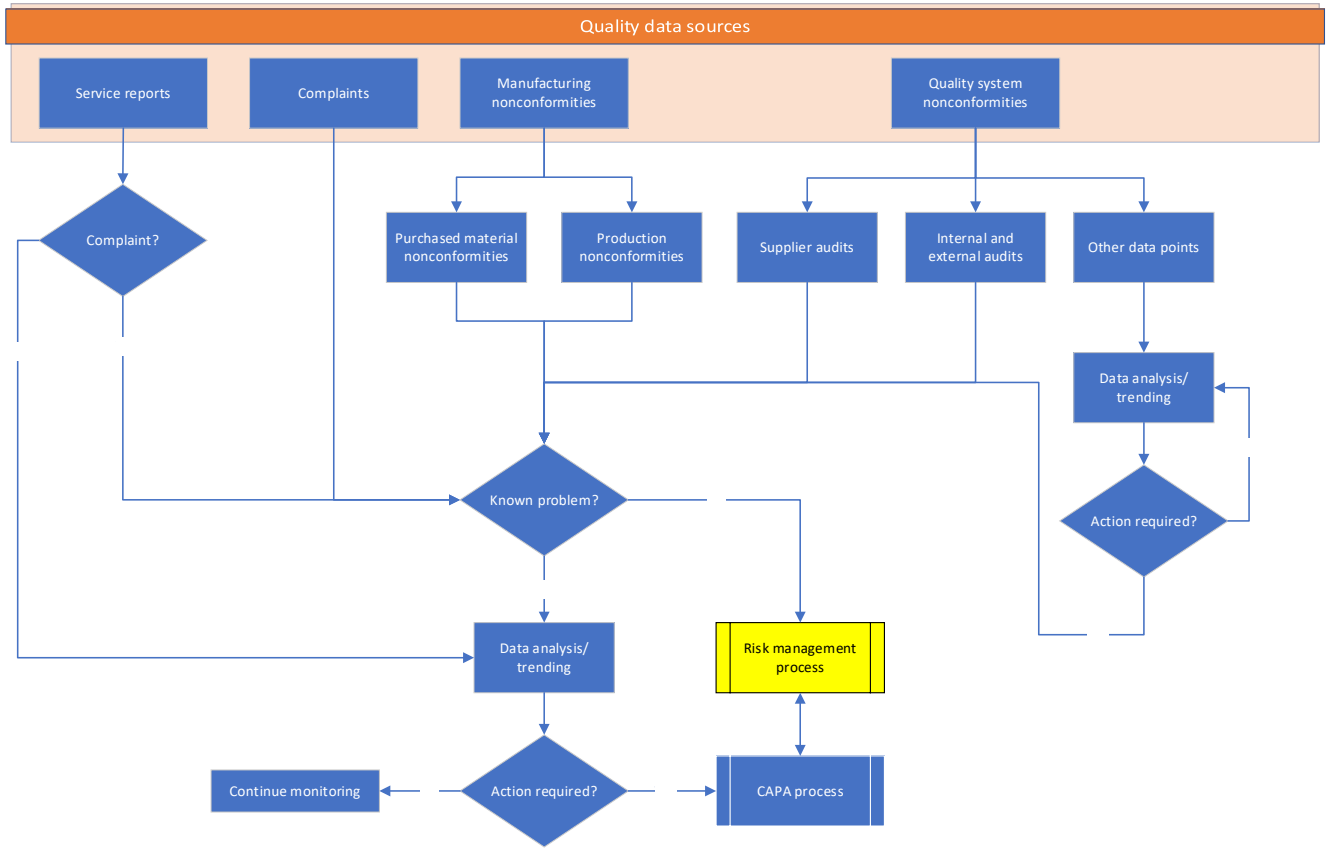
QSR Preamble Comment #159

Also consider:

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

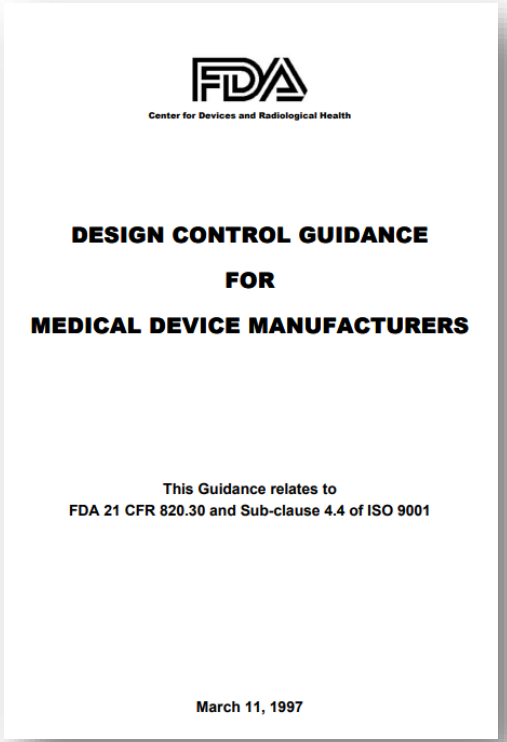


GHTF Risk Management Guidance



A Word on Manufacturing Risk

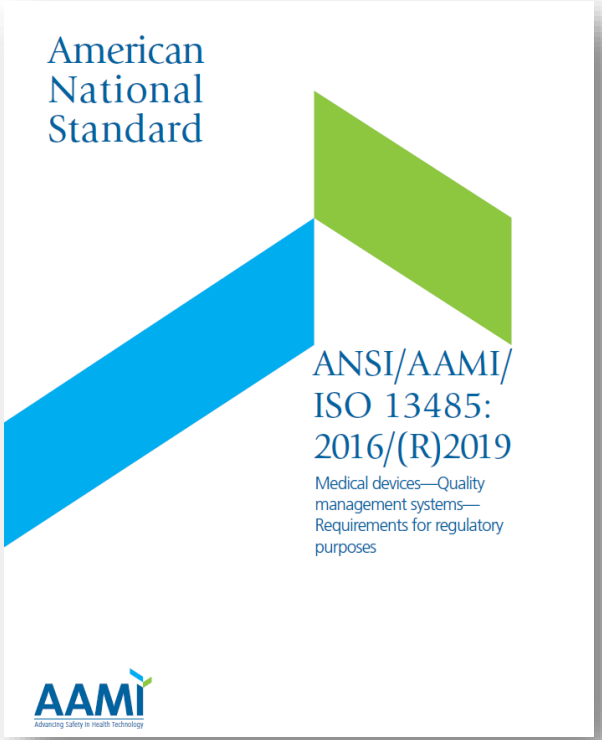
FDA Design Control Guidance for Medical Device Manufacturers (March 1997)



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

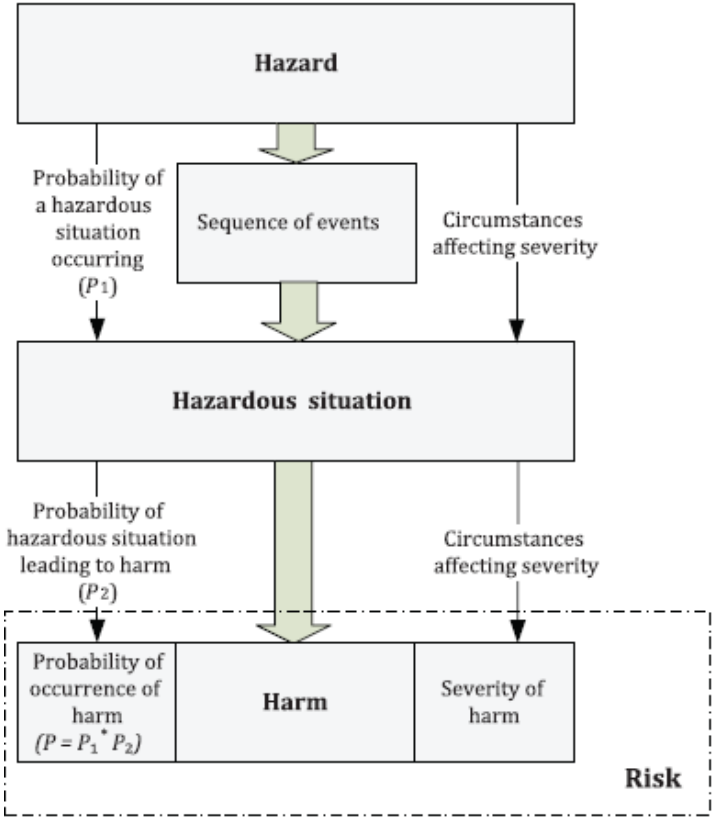
ISO 13485 Requirements

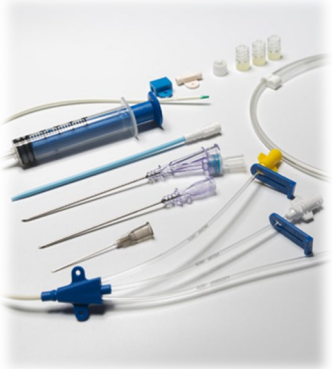
ISO 13485:2016, Subclause 8.2.1



Risk Management Terms

Risk	Combination of the probability of occurrence of harm and the severity of that harm
Harm	Injury or damage to the health of people, or damage to property or the environment
Hazard	Potential source of harm
Hazardous situation	Circumstance in which people, property or the environment is/are exposed to one or more hazards





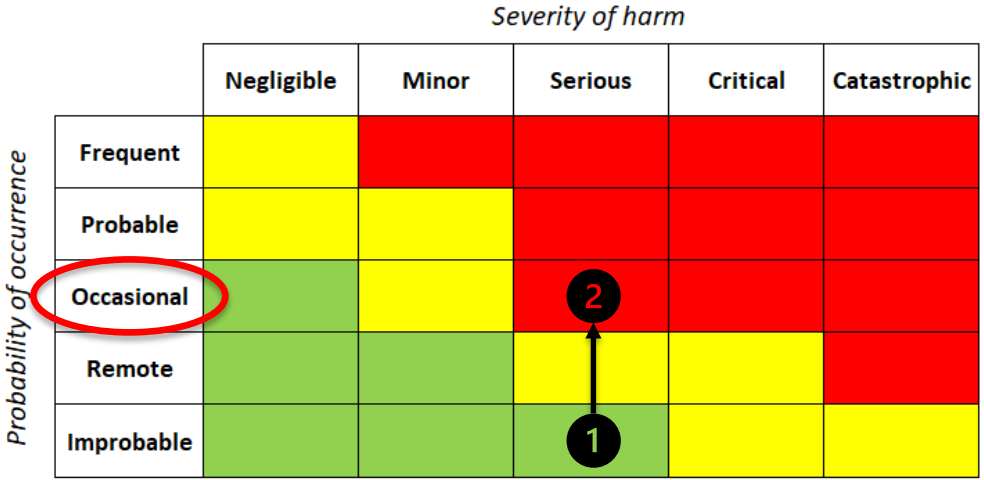
SCENARIOS

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

Hazard	Hazardous situation	Harm	INITIAL RISK EVALUATION			Risk Controls	FINAL RISK EVALUATION		
			Severity	Occurrence	Risk		Severity	Occurrence	Risk
Lubricants used in machining operations	Excessive lubricant remains on device	Adverse biological response	Serious	Probable	Unacceptable	Cleaning process validation	Serious	Improbable	Acceptable



1. Estimated risk per RMF
2. Risk observed via data analysis

Unacceptable risk

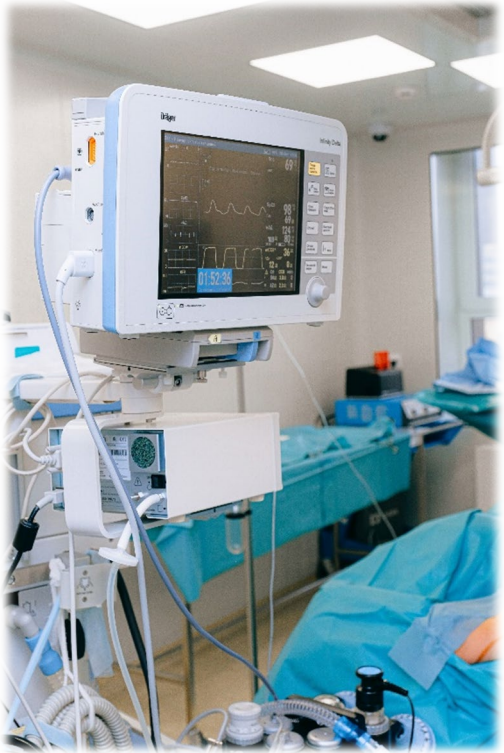
Requires justification

Acceptable risk

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…

Hazard	Hazardous situation	Harm	INITIAL RISK EVALUATION			Risk Control	FINAL RISK EVALUATION		
			Severity	Occurrence	Risk		Severity	Occurrence	Risk
Inaccurate measurement	Ingress of cleaning agent → corrosion → component failure	Unintended or inappropriate medical treatment	Serious	Probable	Unacceptable	Redesigned housing	Serious	Improbable	Acceptable

Design change

Effectiveness confirmed through design V&V

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

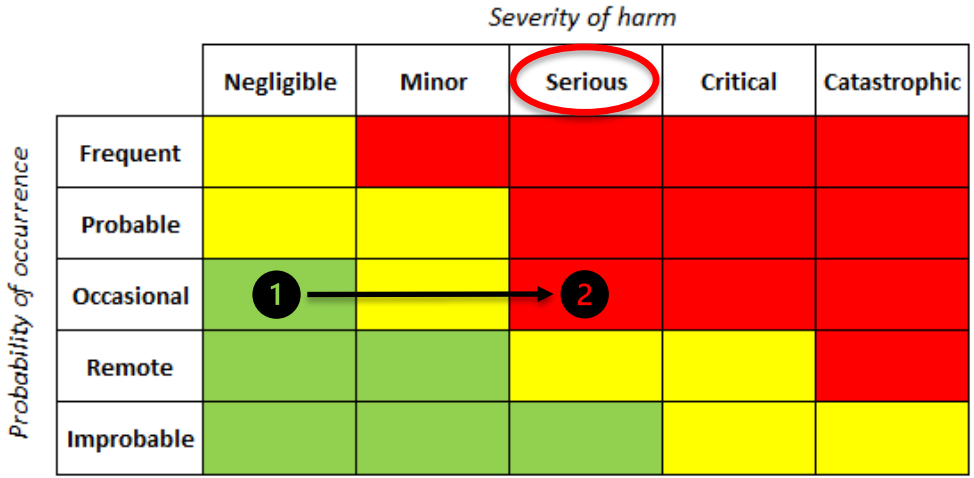
Scenario #3: MDR Database (MAUDE)

- *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.*

Scenario #3: MDR Database (MAUDE)

Risk Management File prior to data analysis…

Hazard	Hazardous situation	Harm	INITIAL RISK EVALUATION			Risk Control	FINAL RISK EVALUATION		
			Severity	Occurrence	Risk		Severity	Occurrence	Risk
Mechanical forces of normal use	Failure of solvent bond → component dissociation	Negligible injury	Negligible	Probable	**Requires justification**	Validated manual bonding process	Negligible	Occasional	**Acceptable**



1. Estimated risk per RMF
2. Risk observed via data analysis

Unacceptable risk

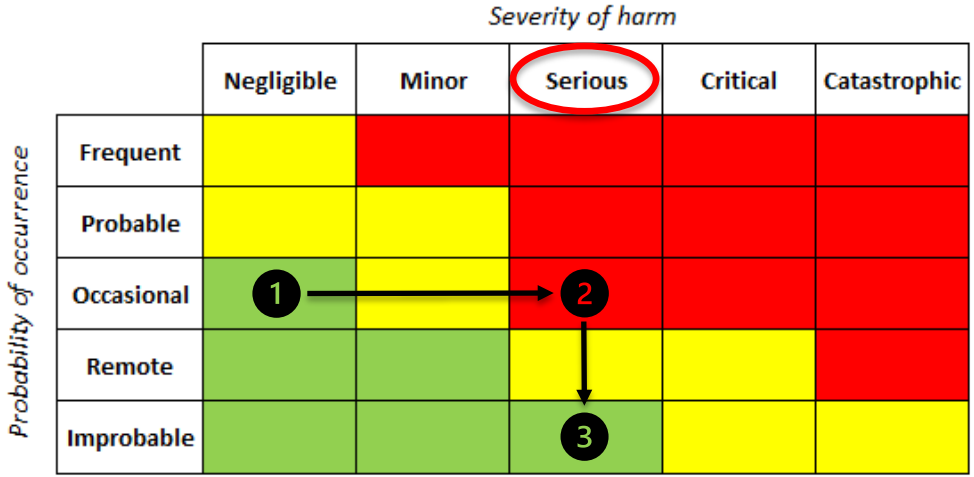
Requires justification

Acceptable risk

Scenario #3: MDR Database (MAUDE)

…Risk Management File after additional mitigation

Hazard	Hazardous situation	Harm	INITIAL RISK EVALUATION			Risk Control	FINAL RISK EVALUATION		
			Severity	Occurrence	Risk		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**



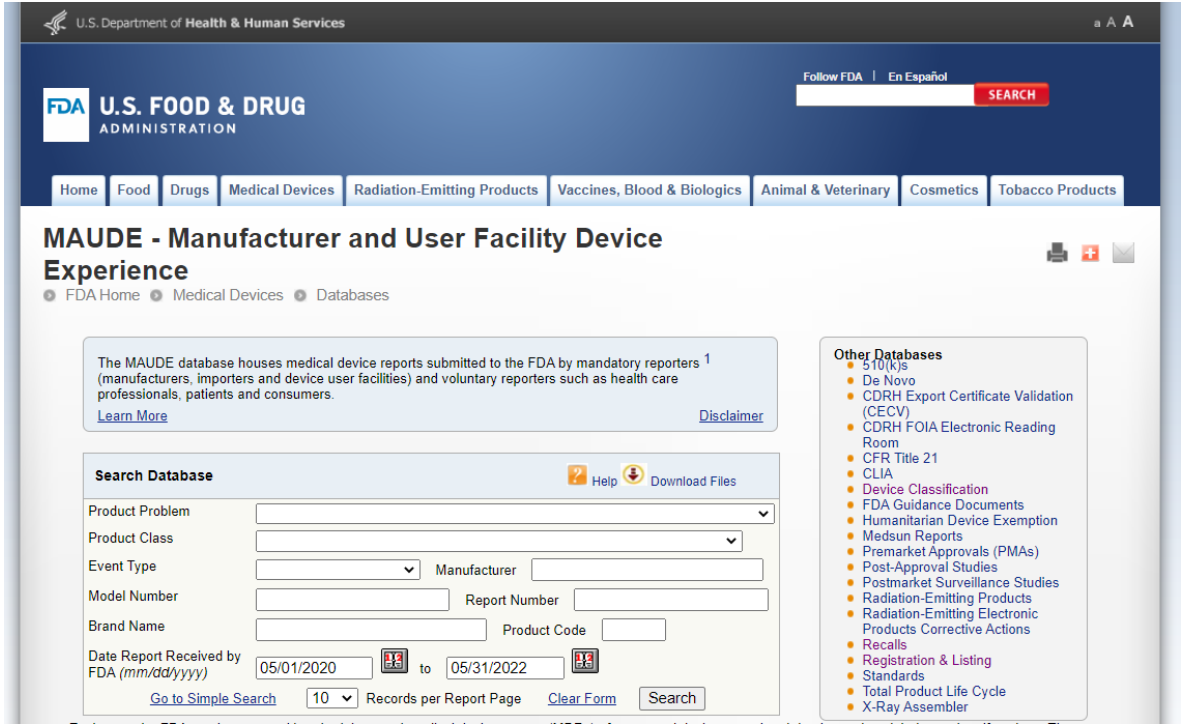
1. Estimated risk per RMF
2. Risk observed via data analysis
3. Risk after additional mitigation

Unacceptable risk

Requires justification

Acceptable risk

Scenario #3: MDR Database (MAUDE)



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


FDA
U.S. FOOD & DRUG
ADMINISTRATION