2014 MEDCON CONFERENCE
Risk Management Overview

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Presentation Goal

To provide an overview on the application of risk management prior to Case Study

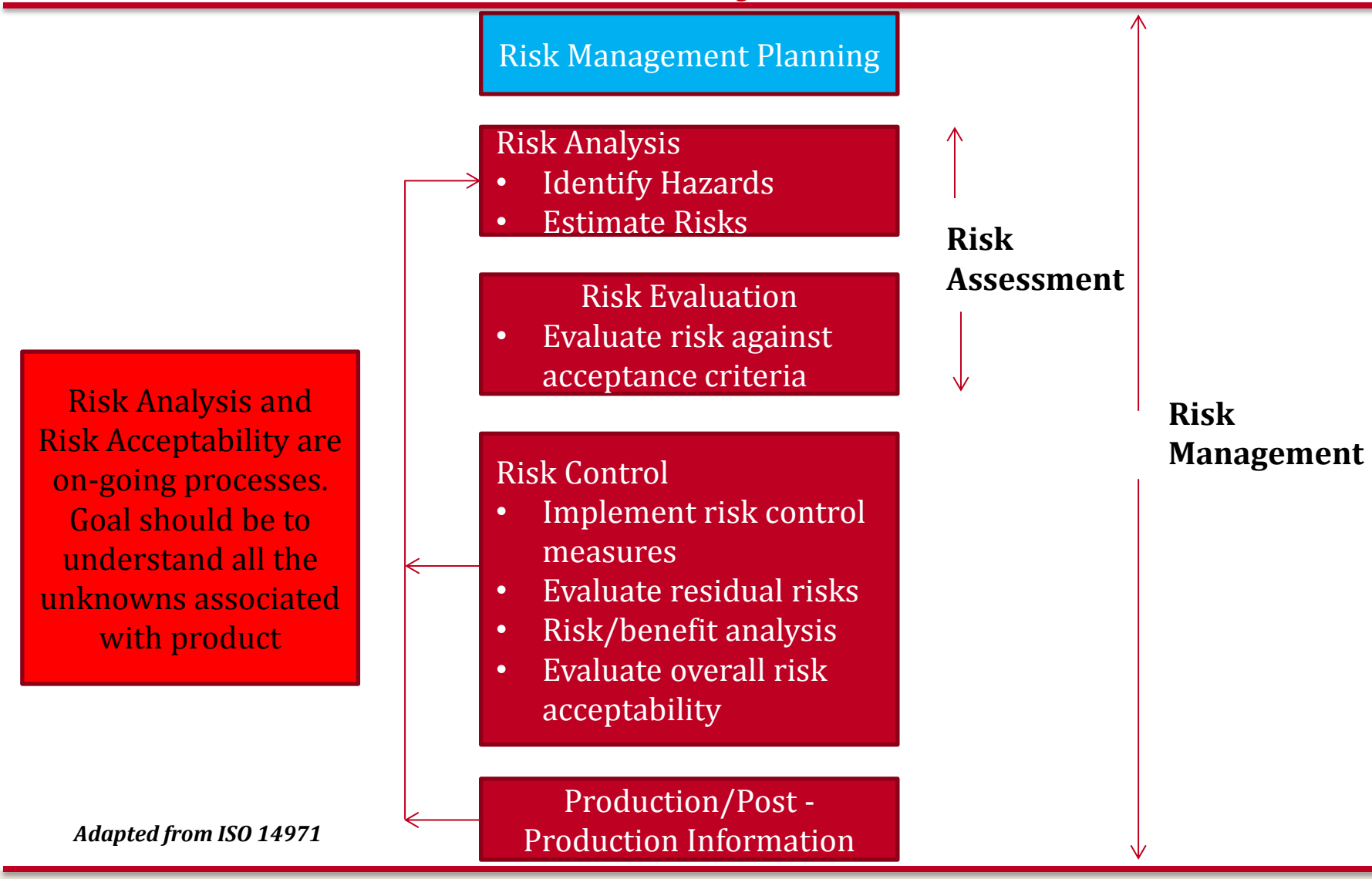
Key Terms and Definitions

Term	Definition
Harm	Physical injury or damage to the health of the people, or damage to property or the environment
Hazard	Potential source of harm
Hazardous Situation	Circumstance in which people, property, or the environment are exposed to one or more hazard(s)
Risk	Combination of the probability of occurrence of harm and the severity of harm
Residual Risk	Risk remaining after control measures have been taken
Risk Analysis	Systematic use of available information to identify hazards and to estimate the risk
Risk Management	Systematic application of management policies, procedures, and practices to the tasks of analyzing, evaluating, controlling, and monitoring risk

Source: ISO/IEC Guide 51:1999

Clear understanding of terminology and definitions is critical

Risk Management Process Throughout Product Lifecycle



Risk Management Plan

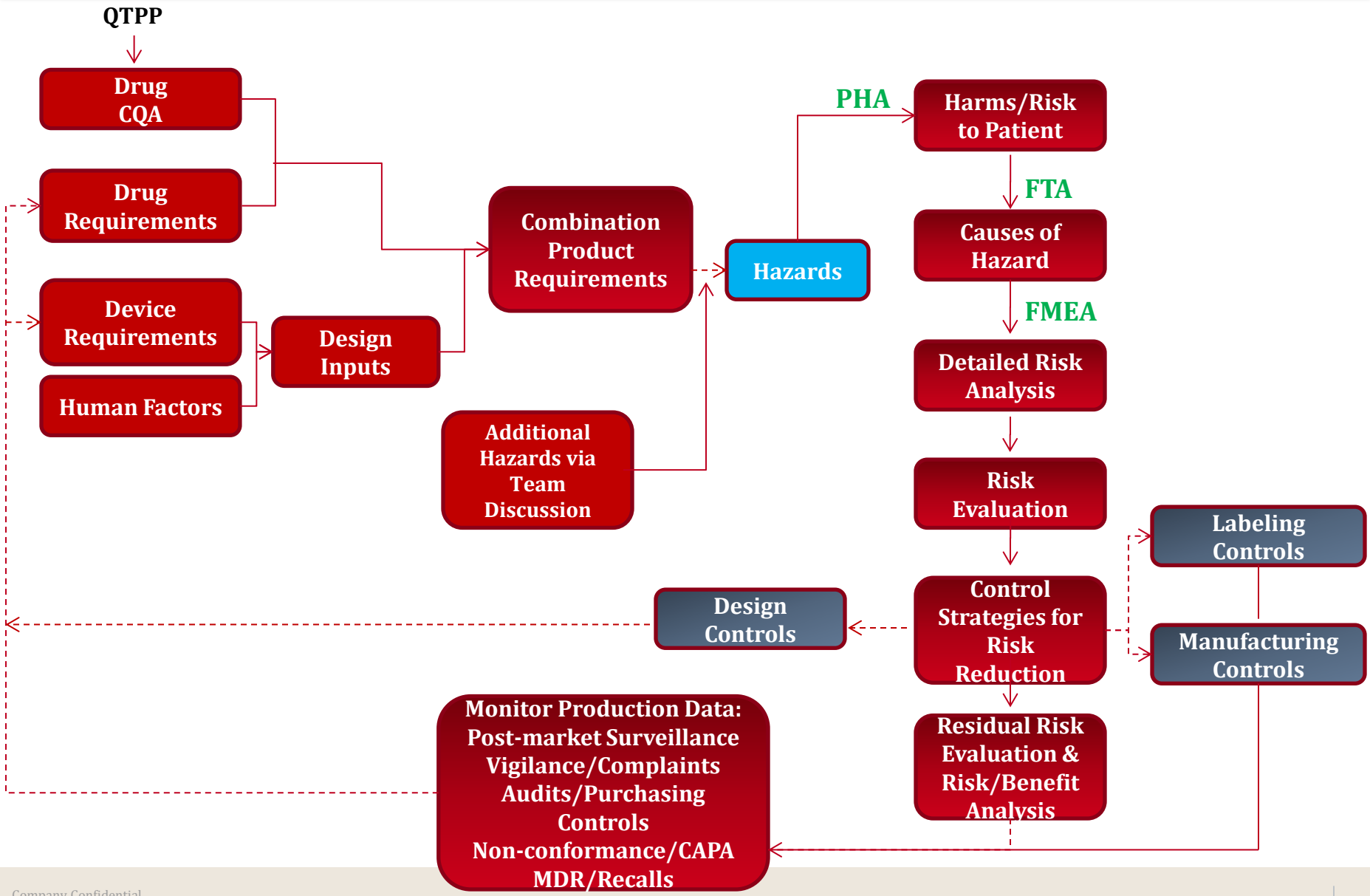
- Ensure appropriate governance (including escalation) and clearly defined roles and responsibilities
- Identify standards and policies to be used
- Define risk ratings, risk grids, risk acceptance criteria
- Define risk management deliverables including Human Factors studies (Formative and Summative)
- Verification activities and traceability
- Plan for post-launch risk management

Risk Management Plan

Make Sure Your Plan is Inclusive as Possible

- Your Risk Management Plan should address the management of all Risks. For example:
  - Design
  - Delivery Device Design (Mechanical)
  - Packaging
  - Labeling
  - Instructions for Use
  - Clinical Trials
  - Component and subassembly manufacturing
  - Component and subassembly handling, storage and shipping,
  - Device assembly operations
  - Device handling, storage and shipping
  - Device packaging and labeling operations
  - Finished product storage and handling at distribution centers
  - Finished Product shipping
  - Handling, storage and dispensing/purchasing of product
  - Product Use
  - Product Disposal
  - Product Discontinuation
  - Other areas, as indicated in product supply chain

Integrated RM Strategy for Device/Combination Product



Risk Analysis –Identification of Hazards

Known and foreseeable hazards in both normal and fault conditions

- Team brainstorming – past experience
- Intended use/medical device characteristics
- Human Factors
- Requirements – i.e. failure to meet requirements
- Literature/standards
- MDRs, recalls, complaints, safety alerts

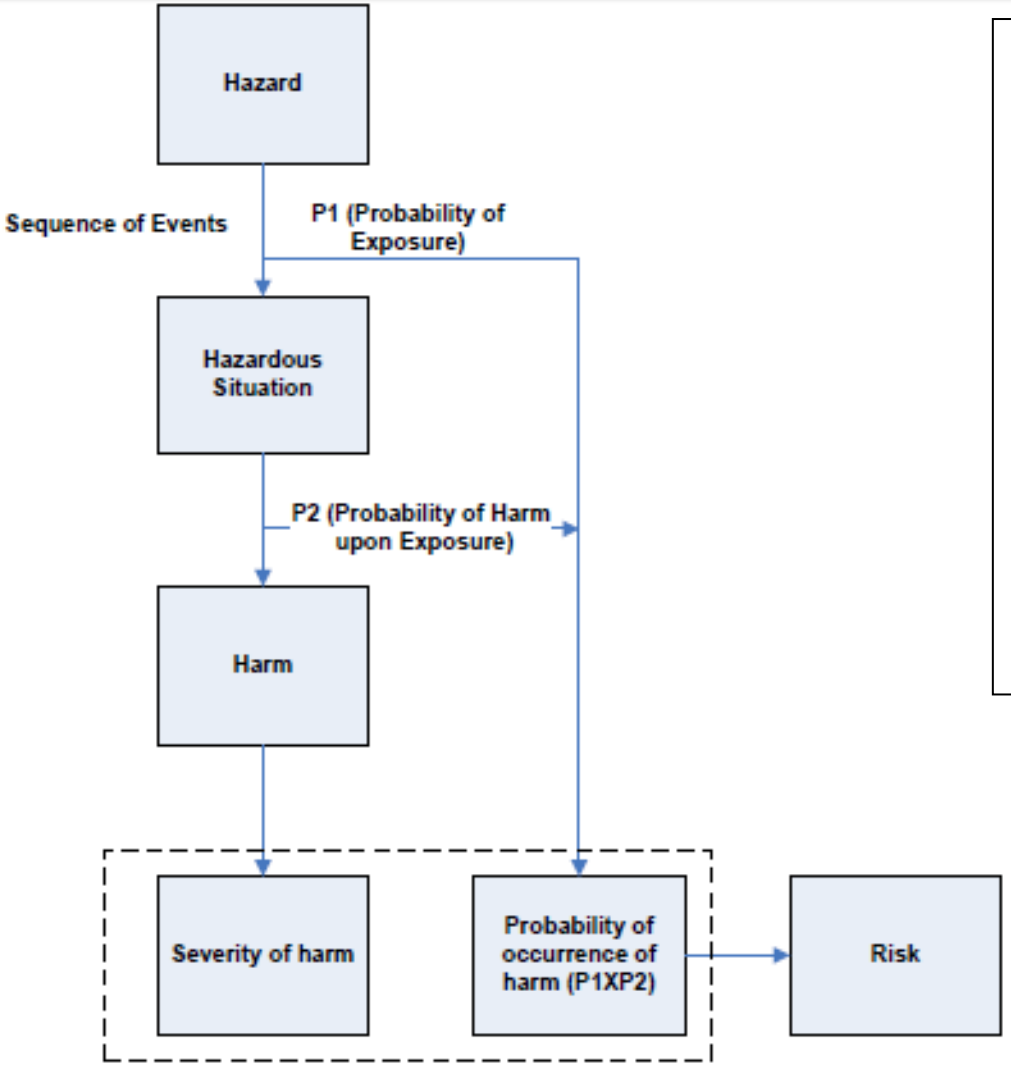
Unknown Hazards???

Risk Analysis – Estimation of Risks

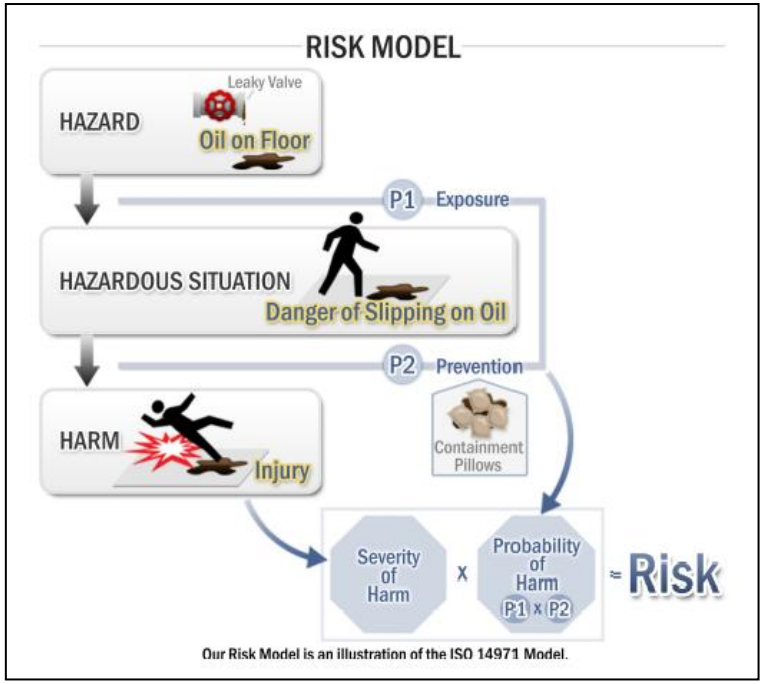
- Risk is estimated as a combination of probability of occurrence of harm and severity of harm
- Severity of harm does not change throughout the product lifecycle
- Probability of occurrence of harm may change during the lifecycle of the product

Monitor production/post-production data to re-estimate risk and ensure residual risk remains acceptable
More than just patient safety, don't forget about Compliance

Probability of Occurrence of Harm



Adapted from ISO 14971



Not all hazards result in harm. A hazardous situation must be present for harm to occur. Document rational and references used to support probability overrides

Risk Analysis Tools

Examples:

- Preliminary Hazard Analysis - PHA
- Fault Tree Analysis - FTA
- Failure Mode and Effects Analysis – FMEA
- Hazard and Operability Study – HAZOP
- Hazard Analysis and Critical Control Point – HACCP
- Human Factors

FMEA does not identify combination fault conditions and does not identify normal condition hazards. A combination of risk tools need to be used throughout product life cycle. Recommend top down, bottom up approach

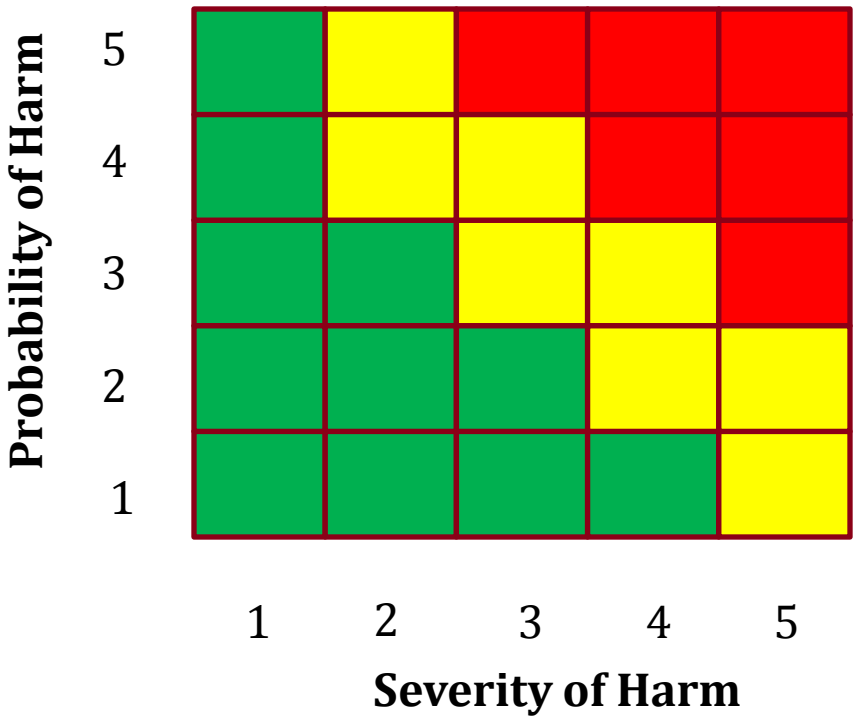
Risk Ratings Definition

Severity of Harm	Description (Patient Impact)
1 Negligible	dissatisfaction
2 Minor	temporary and non-debilitating state of pain/discomfort e.g. upset stomach, headache, minor wound
3 Moderate	injury that is not permanent but may require minor medical intervention e.g. dizziness, infection requiring antibiotics, minor episodes of stomach cramps
4 Major	injury that is permanent or requires major medical intervention e.g. birth defects, disfigurement, organ damage and severe stomach cramps requiring hospitalization
5 Severe	Life threatening or resulting in death

Probability of harm	Description
1 Improbable	unlikely to occur, not expected
2 Remote	unlikely, but can resonably be expected to occur
3 Occasional	occurring at irregular or infrequent intervals
4 Probable	likely to occur
5 Frequent	common, repeated or occurring often

Note: The description column just provides examples of Severity and Probability of Harm rating

Risk Grid



Acceptable
Marginally Acceptable
Unacceptable

Severity of Harm

1 Negligible
2 Minor
3 Moderate
4 Major
5 Severe

Probability of Harm

1 Improbable
2 Remote
3 Occasional
4 Probable
5 Frequent

Preliminary Hazard Analysis (PHA) - Example

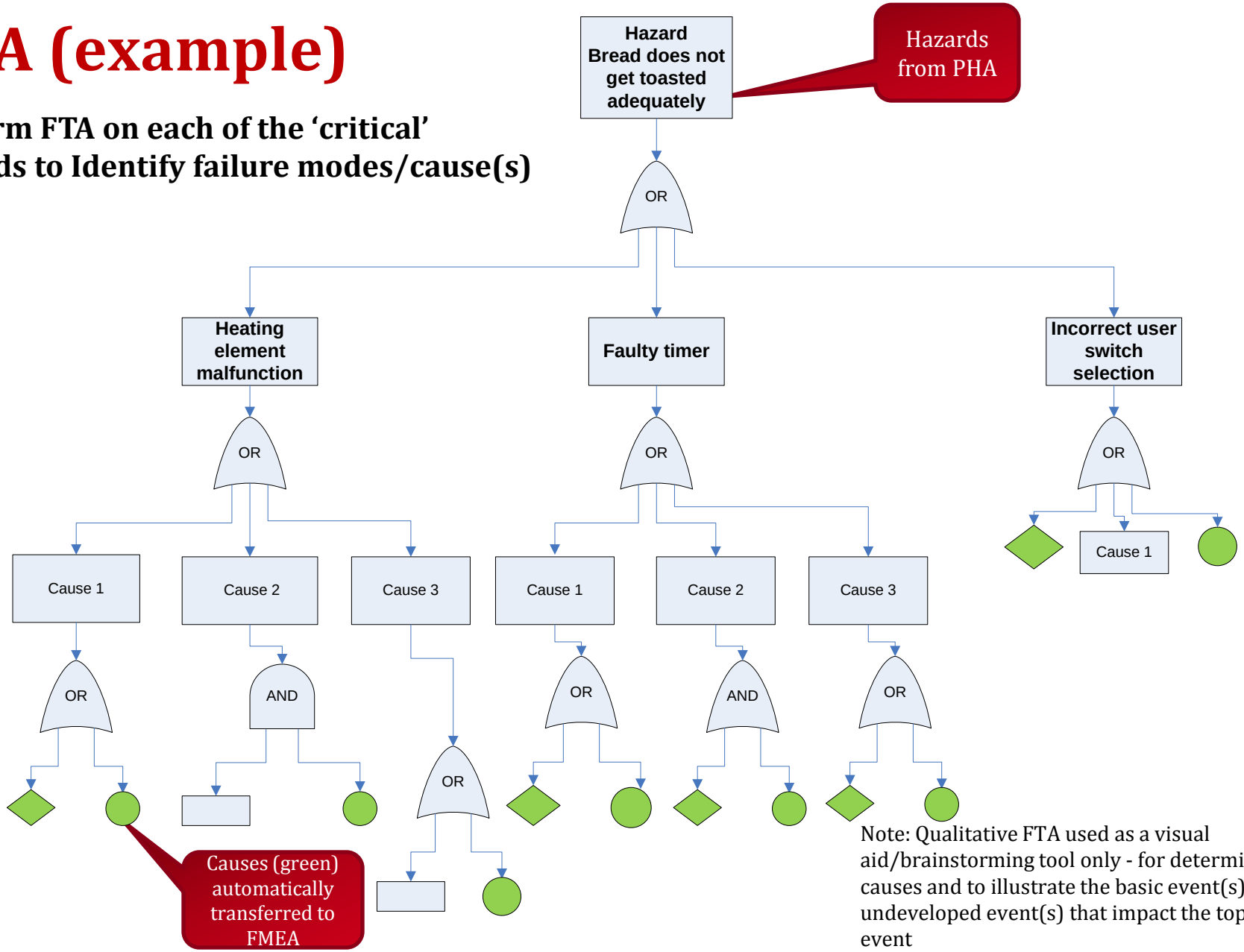
Hazard: failure to meet the requirements

Requirement	Hazards	Harm	Severity of Harm	Probability of Occurrence of Harm	Risk	Risk Reduction?	Recommended Preliminary Control Strategy	Comments
1. Bread should pop-up after toasting	Bread does not pop-up	User dissatisfaction	1	4	**Acceptable**	No		
2. Bread toasting level	Bread is not toasted adequately/ correctly	User dissatisfaction from burnt bread/ inadequately toasted bread	2	4	**Marginally Acceptable**	Yes	Design controls	
3. Toaster must be designed to minimize burn, electric shock and fire hazards	Hot exterior surfaces	Minor Burns from touching hot surfaces	2	4	**Marginally Acceptable**	Yes	Safety instructions in user manual	
	Fire	Second degree burn requiring major medical intervention	4	2	**Marginally Acceptable**	Yes	Design controls Safety instructions	
	Electric shock	Electrocution	5	3	**Unacceptable**	Yes	Design controls Safety instructions	

Note: PHA should be conducted at the initial stages of the design control process for the device

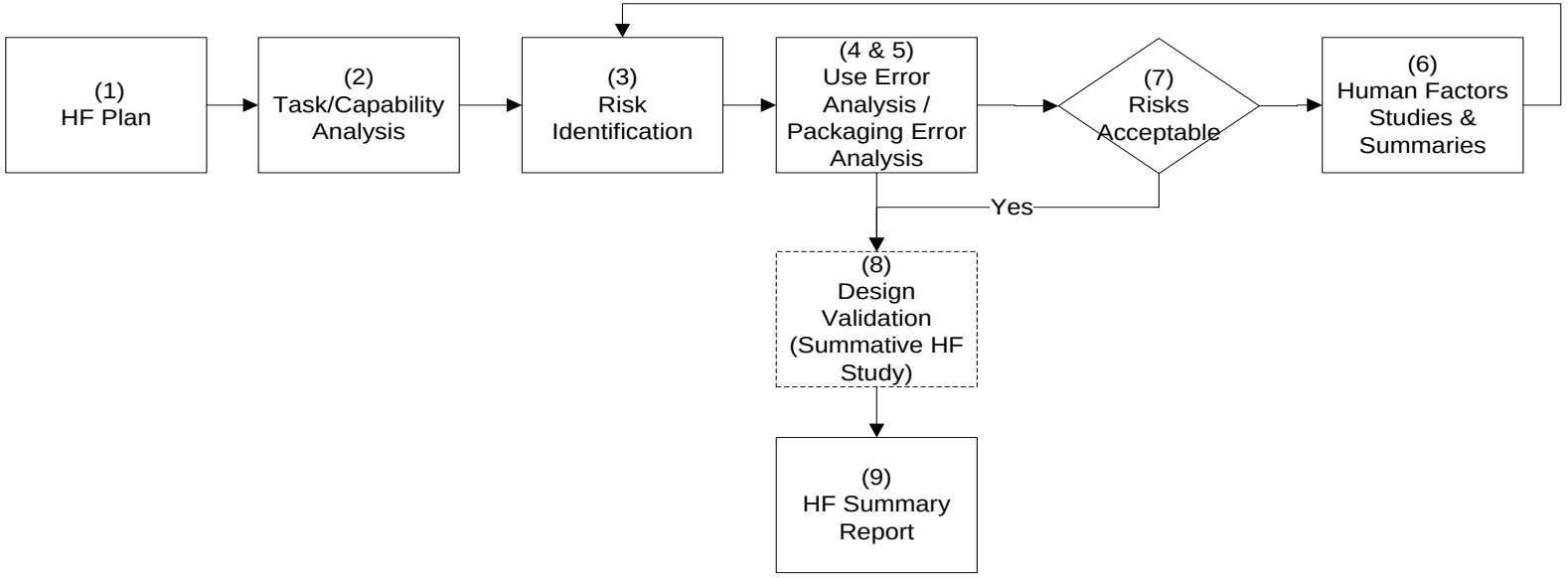
FTA (example)

Perform FTA on each of the 'critical' hazards to Identify failure modes/cause(s)



Note: Qualitative FTA used as a visual aid/brainstorming tool only - for determining causes and to illustrate the basic event(s)/ undeveloped event(s) that impact the top level event

Human Factors – Normal Use/Foreseeable Misuse Hazards



- Ensure study participants are representative of the user population including users with potential impairment
- Explore each use error or near miss in detail -What was person thinking? What can be done to avoid error or near miss?
- Analyze results, look for trends across study groups

FMEA Risk Ratings Definition

Occurrence (O) Rating

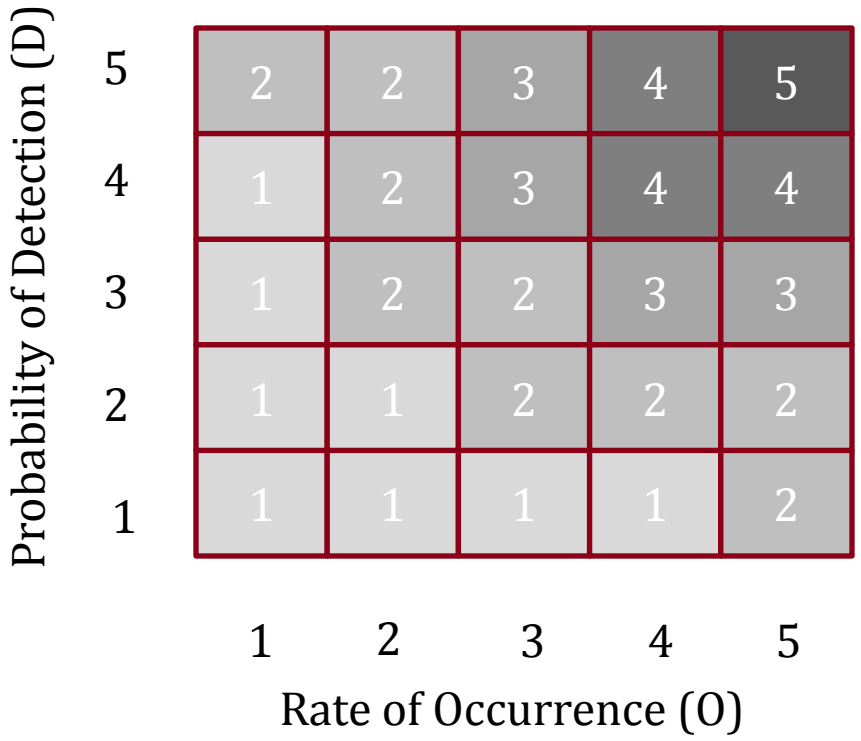
Rating	Description
1 (Very Low)	Remote probability of occurrence
2 (Low)	Low probability of occurrence
3 (Moderate)	Moderate probability of occurrence
4 (High)	High probability of occurrence
5 (Very High)	Very high probability of occurrence

Note: Consider reporting units: days of use, manufacturing units etc.

Detection (D) Rating

Rating	Description
1 (Very High)	Controls almost certainly will detect the existence of a failure
2 (High)	Controls have a good chance of detecting the existence of a failure
3 (Moderate)	Controls may detect the existence of a failure
4 (Low)	Controls more likely will not detect the existence of a failure
5 (Very Low)	Controls very likely will not detect the existence of a failure

Risk Grid to Calculate Probability of Harm (for use with FMEA)

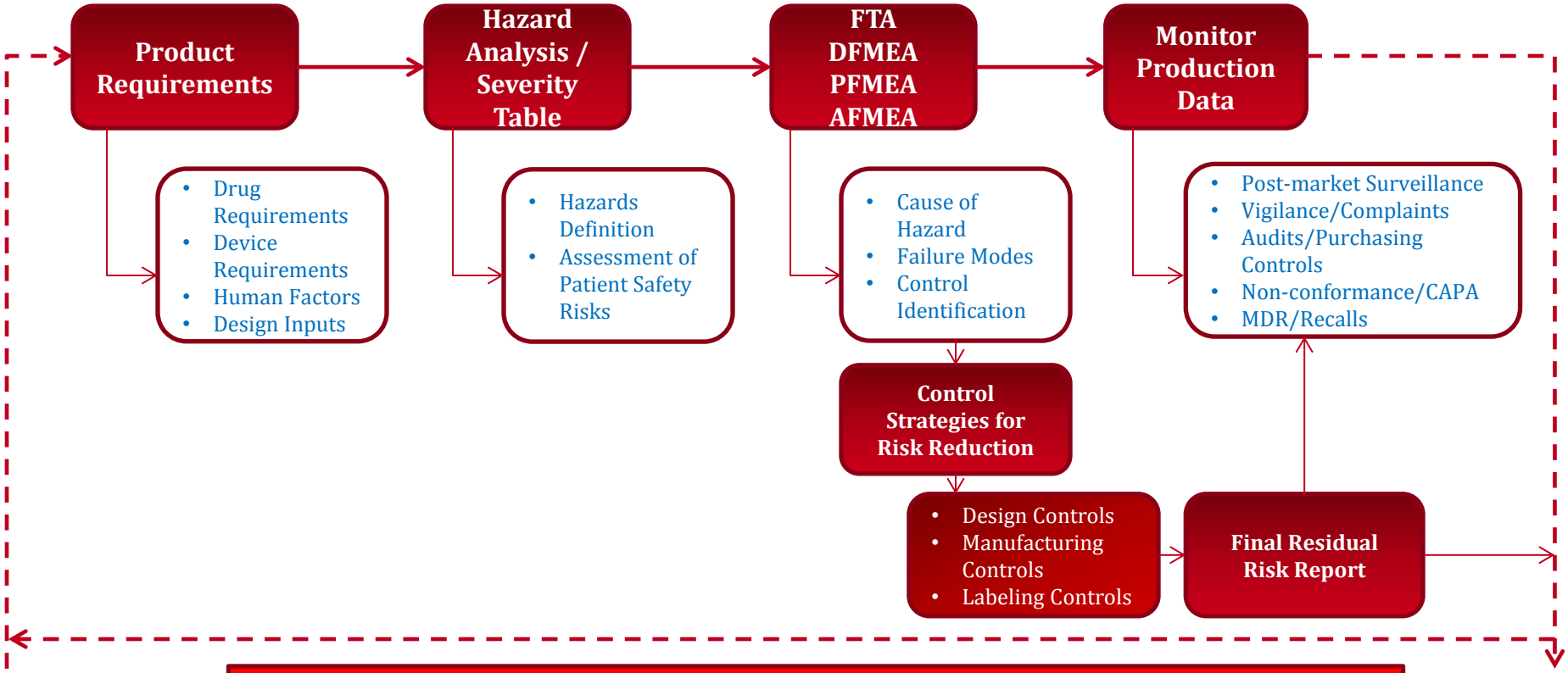


Once the probability of harm is calculated using this grid, use the PHA risk grid to compute FMEA risk level

FMEA (example- ratings are for illustration purposes only)

Product Reqs	Potential failure mode (Hazard)	Potential failure effect (Harm)	Severity	Max. Severity	Step	Potential causes of failure	Current Controls	O	D	Risk level	Risk reduction required (Y/N)	Additional controls	O	D	Residual risk after additional controls
1. Toaster must be designed to minimize burn, electric shock and fire hazards	Hot exterior surfaces	Minor Burns from touching hot surfaces	2	2	Station 1	Cause 1	xyz	4	5	Marginally Acceptable	Y	Design change	2	2	Acceptable
	Fire	Second degree burn requiring major medical intervention	4	4	Station 2	Cause 2	xyz	2	3	Marginally Acceptable	Y	Design change	1	1	Acceptable
2. Bread toasting level	Bread is not toasted adequately/ correctly	User dissatisfaction from burnt bread/ inadequately toasted bread	2	2	Module 1	Cause 3	xyz	5	4	Marginally Acceptable	Y	Process change	2	1	Acceptable
					Module 4	Cause 4	xyz	4	4	Marginally Acceptable	Y	Process/ Design change	3	1	Acceptable

Integrated Risk Management Strategy for Device/Combination Products



Traceability between controls and requirements and verification/validation of implemented controls is key

Post-Launch Risk Management

- Risk management does not stop after design transfer is completed
- Monitor production/post-production data to reassess risk estimates
- Ensure residual risk continues to be acceptable
- Production/Post-Production data: Post-market surveillance, Vigilance/Complaints, Audits, Non-conformance/CAPA, MDR/Recalls etc.

Apply Risk Management throughout life cycle of product, using multiple tools and frequently re-assess residual risk