Understanding Use of Quality Risk Management

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Introductions

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Introduce Yourself

1) Name
2) Major
3) Fun Fact about YOU

MentiMeter Poll

Objectives

- Understand regulations around risk management programs
- Develop a risk question to determine the fit for purpose risk management tool
- Learn about different risk management tools and how they are used
- Practice risk management using theoretical examples and templates

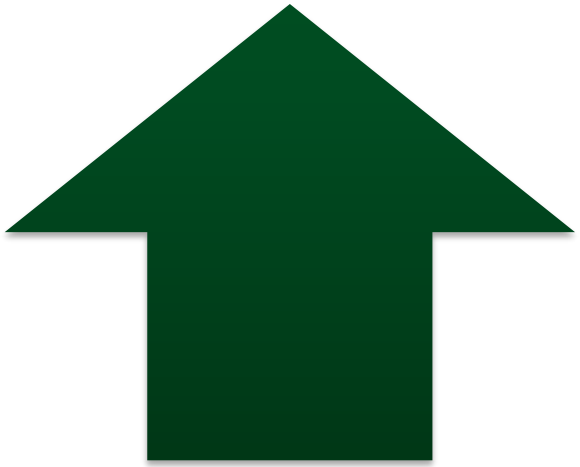
Drivers and Benefits

Introduction to Quality Risk Management (QRM)

Benefits of Quality Risk Management

- Prospectively understand process risk and ways to prevent failures before they occur
- Streamline review process through leveraging of data
- Enable an understanding of both strategic and tactical risks
- Eliminate redundancy (exception is between products where some duplication may exist)

Benefits of Quality Risk Management



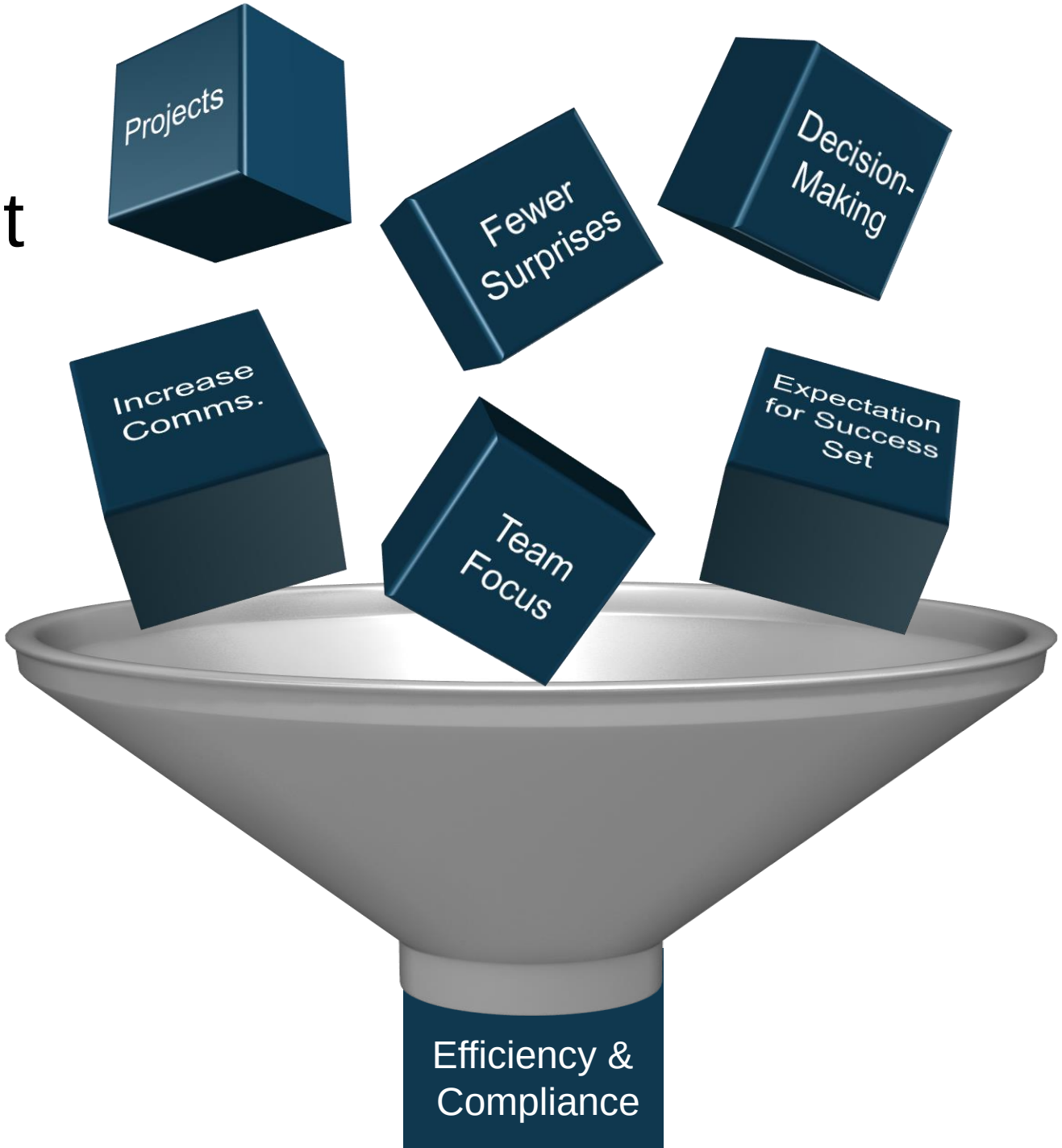
Quality Risk Management is...

- A means of consistent decision making
- Used to explore uncertainty
- Effective when communication channels are open

Quality Risk Management is NOT

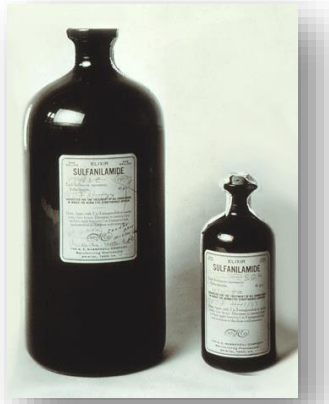
- The decision
- A means of justifying existing practices
- A substitute for sound science

Risk Management Benefits



The Regulations

History of Regulations



Brief review of regulations history…

- Elixirs, “Snake Oil Salesmen”, no controls to ensure safety
- Pure Food and Drug Act of 1906
  - Now called the Food, Drug, and Cosmetic Act (FD&C Act)
- Sulfanilamide Tragedy (1937)
  - Diethylene Glycol – Mass Poisoning
- Thalidomide Tragedy (1960s)
  - Little/No testing on pregnant women – Birth Defects

Fast forward to today…

- Various Health Authorities and Organizations

FDA U.S. FOOD & DRUG ADMINISTRATION

ICH harmonisation for better health

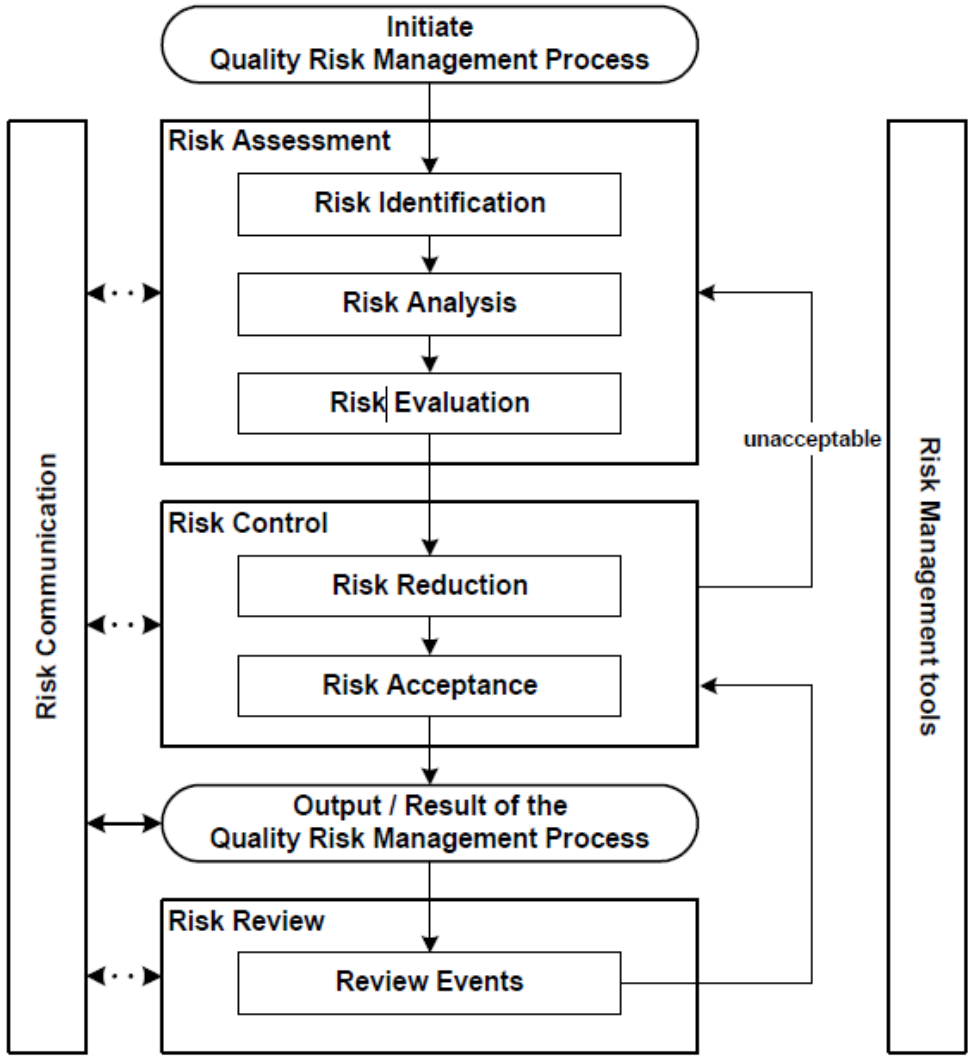
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Where QRM is required….

EU GMPs - QRM required	CA GMPs - QRM required	US FDASIA - QRM required (supply chain emphasis)	21 CFR 820 – RA/RM required (medical devices)
ICH Q8 – QRM discussed as it applies to development of finished products	ICH Q9 – QRM guideline as it applies to national authorities and the industry	ICH Q10 – QRM is an “enabler” of a PQS	ICH Q11 – QRM discussed as it applies to development of APIs and drug substances
FDA Guidance on Validation – QRM can be used to prioritize qualifications	FDA Warning Letters – QRM observations increasing	ISO 14644 Cleanrooms and Associated Controlled Environments	NOM059 – requirements connected with PIC/S Annex 20

QRM Lifecycle

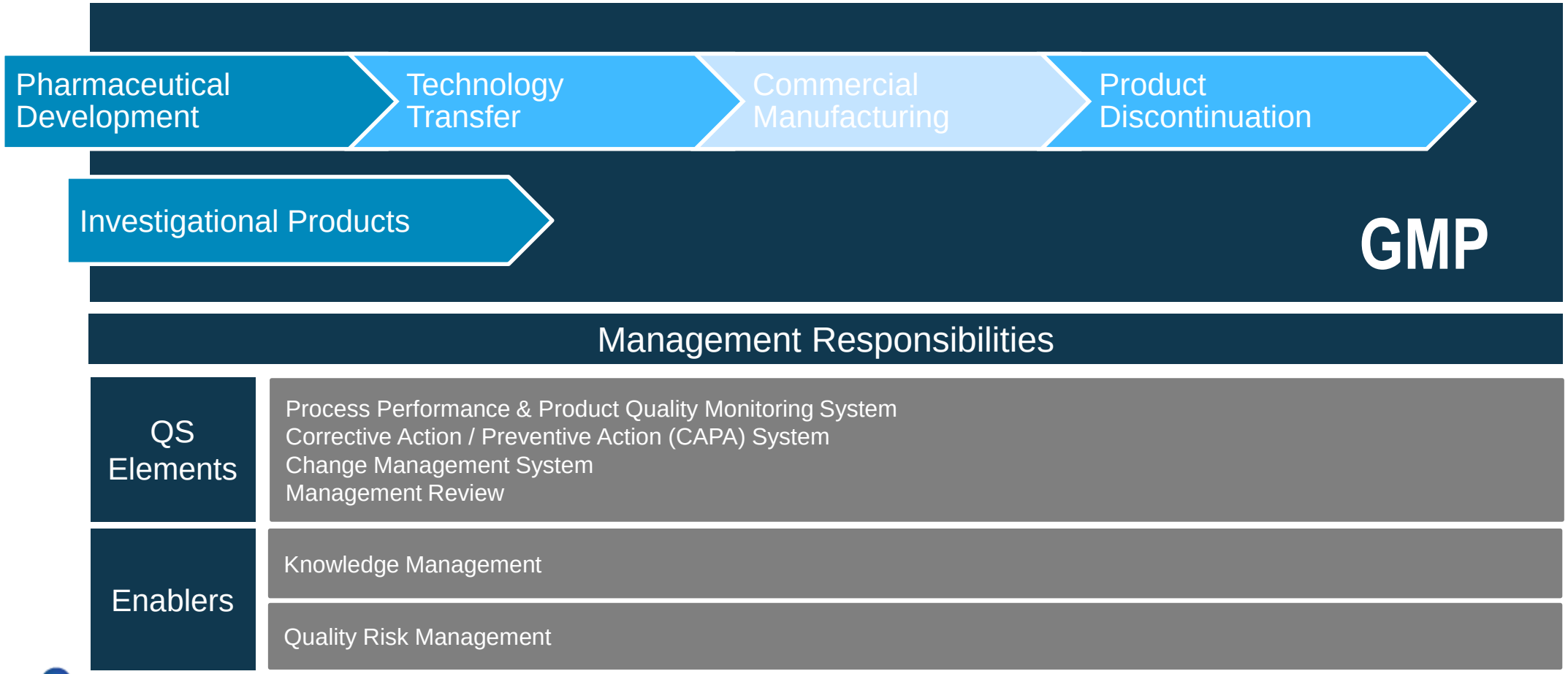
Figure 1: Overview of a typical quality risk management process



This is the Quality Risk Management lifecycle from ICH Q9.

ICH Q10: Pharmaceutical Quality System

ICH Q10 describes the pharmaceutical quality system. It positions QRM as an “enabler.”



This means that QRM helps with everything we do, from manufacturing and testing product to managing the quality system itself.

ICH harmonisation for better health

https://www.ich.org/page/ich-guidelines

Which Column Fits the Guidance?

A	B	C
“We need a risk assessment to justify…”	“Make this risk assessment conclude…”	“We need a risk assessment to determine…”
“Risk (assess) it out”	“Justify what we are already doing”	“Let’s do a risk assessment to see if we should be doing something different.”
“There’s no risk in that”	“Why bother with a risk assessment?”	“Let’s see what the risk is.”

We think in terms of risk all the time….

Are you going to go for a swim?

likelihood

Long Beach Fire (CA)
@lbfd

Follow

Shark advisory is in effect until further notice ⚠️ Please contact Lifeguard HQ: 555-BAD-SHARK for additional info. or stay tuned for updates

8:18 PM - May 10, 2017

6 30 22

severity

controls

Advisory: Shark sighted. Issued when there is a confirmed sighting of a non-aggressive shark by Marine Safety.

Warning - Aggressive shark. Issued when there is a confirmed sighting of atypical and potentially aggressive shark behavior by Marine Safety.

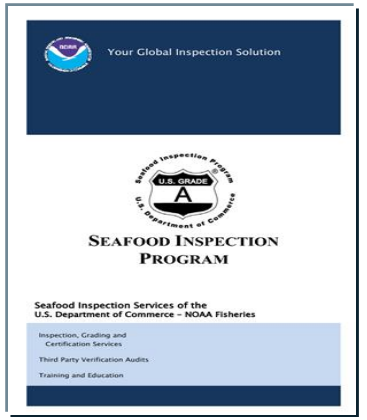
Closure - Shark attack. Do not enter. Issued following a shark attack or confirmed sighting of aggressive shark behavior by Marine Safety.

What about that new raw bar your friend raves about?

likelihood

severity

controls



Risk Communication

WARNING CUSTOMERS

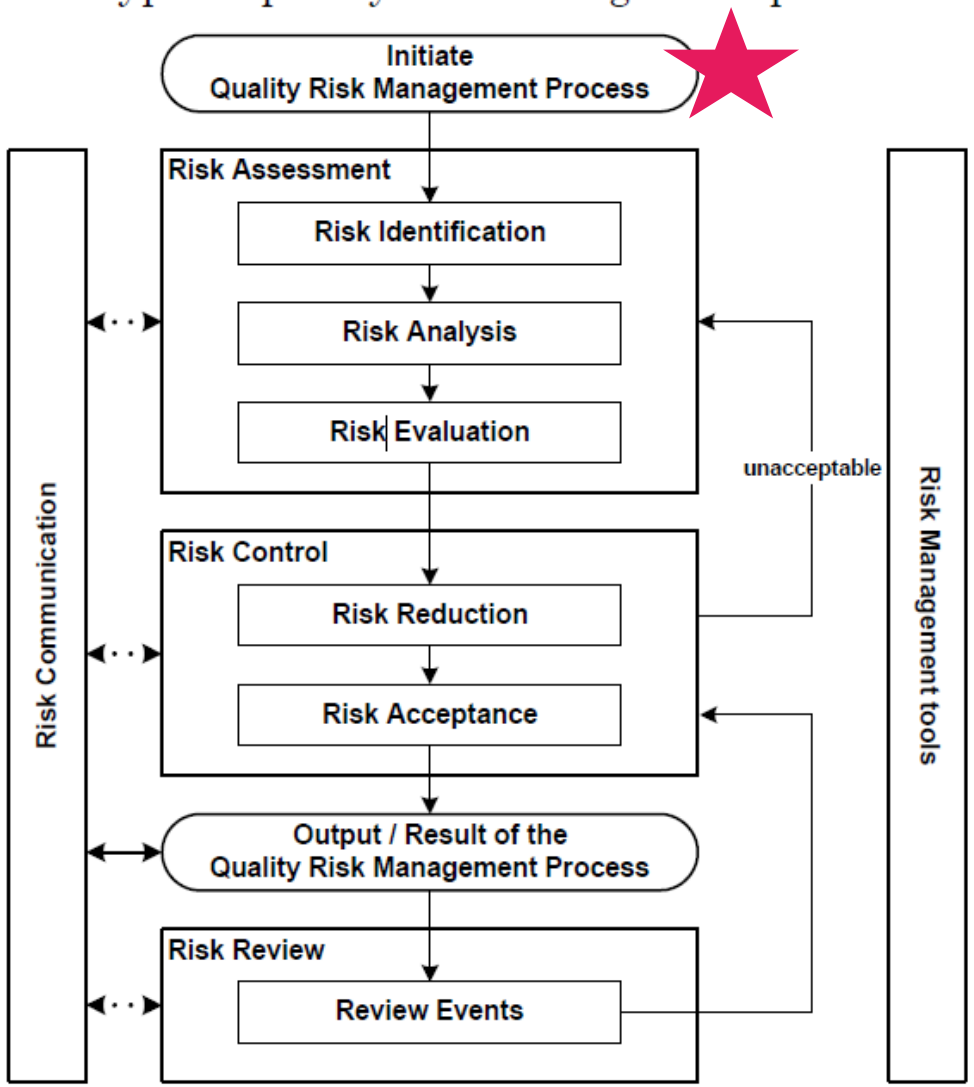
The U.S. Food and Drug Administration's 2009 Food Code allows food service establishments to serve raw or undercooked foods at a customer's request as long as the customer is informed about the risks associated with consuming undercooked food and the customer is not part of a high-risk group. In an effort to educate customers on the risks associated with consuming raw and undercooked foods, the Food Code requires all restaurants that sell raw or undercooked animal products to post a raw food warning for customers. This warning is often seen as a posted sign in fast-food or self-service restaurants or, more commonly, as a written statement at the bottom of a restaurant menu.

What is the Question?

Determining the ask from the risk assessment

QRM Lifecycle

Figure 1: Overview of a typical quality risk management process



This is the Quality Risk Management lifecycle from ICH Q9.

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

Developing a Risk Question

QRM Planning: Defining the Risk Question

What is the Risk Question?

- The question the risk assessment seeks to answer
- Provides focus for the risk assessment

Why do we care about the Risk Question?

- Essential for appropriate tool selection
- Without it, the quality risk assessment may not be appropriately focused on the risks that need to be assessed.
- Guidance for pre-work and data needed

QRM Planning: Defining the Risk Question

➢**A well defined risk question allows the team to keep its efforts within a manageable scope, no matter whether the scope is narrow or broad.**

// Problem and/or risk questions include:

- A specific risk question statement/problem statement
- Brief explanation of the risk scenario to be studied

➢**Supporting elements that should be identified include:**

// Key assumptions

// Assessment boundaries – what is in or out of scope

// Objectives

// Defining and understanding the required data to support the assessment

Start with a problem statement or objective to gain focus

Risk Question Examples

Risk questions must not imply a foregone conclusion

Avoid

- // How should I eliminate?
- // How should I reduce?
- // What are the risks of a system?
- // What are the risks of a product?

Risk questions should not be so broad that they lack specificity

Ask

- What are the risks associated with changing the 2-cc vial suppliers for filling Jansen covid vaccine?
- What are the risks of using a matrix approach for cleaning validation of Jansen covid vaccine equipment?

"What are the potential product quality risks that could result from <insert scenario here with boundaries>?"

Activity: Developing a Risk Question

Which Risk Questions below have been defined appropriately?	Yes or No? Why or Why Not?
What are the potential product quality risks associated with transferring product A to/from one commercial manufacturing site to another within the same network?	
What are the product quality risks that were introduced after installing a newly designed agitator to a fermenter?	
What are the potential product quality risks associated with choosing a new CMO?	
What are the high quality risk areas for particulate introduction in a newly constructed manufacturing room that has not yet been qualified?	

Discussion: Developing a Risk Question

Which Risk Questions below have been defined appropriately?	Yes or No? Why or Why Not?
What are the potential product quality risks associated with transferring product A to/from one commercial manufacturing site to another within the same network?	Clearly defined risk question
What are the product quality risks that were introduced after installing a newly designed agitator to a fermenter?	The risk question was developed after the change was made. Risk assessment is reactive.
What are the potential product quality risks associated with choosing a new CMO?	The risk question is not clear enough and does not include a boundary. What risks are we evaluating?
What are the high quality risk areas for viable and non-viable particulate introduction in a newly constructed manufacturing room that has not yet been qualified?	This risk question is targeted towards a risk based tool to define a program. Well constructed.

QRM Planning: Defining the Risk Question Further

Supporting elements that should be identified include:

- Problem Statement and/or Objectives
- Key assumptions
- Assessment boundaries – what is in or out of scope
- Defining and understanding the required data to support the assessment

Activity: Developing a Risk Question

Camilla Perrotta-Fowler

Exercise:

The Expected Time: 10 min

Developing a risk question

The Task: Develop a risk question associated with supporting elements using either of the scenarios:

- your favorite hobby
- a sport you play
- a daily activity in which you partake

e.g. What are the risks to making “perfect scrambled eggs” when cooking eggs over a gas stove?

The Keep in mind:

- What you want to protect/preserve (e.g. perfect scrambled eggs)
- Scope your question (e.g. “over a gas stove” vs. “on Monday mornings before work”)
  - When changing the cooking method from an electric stove to a gas stove

Exercise:

The Expected Time: 10 min

The Outcome: Everyone will have practiced generating a risk question which is the initiation of a risk assessment

Examples from the class?

Debrief:

// Was this exercise easy or difficult?

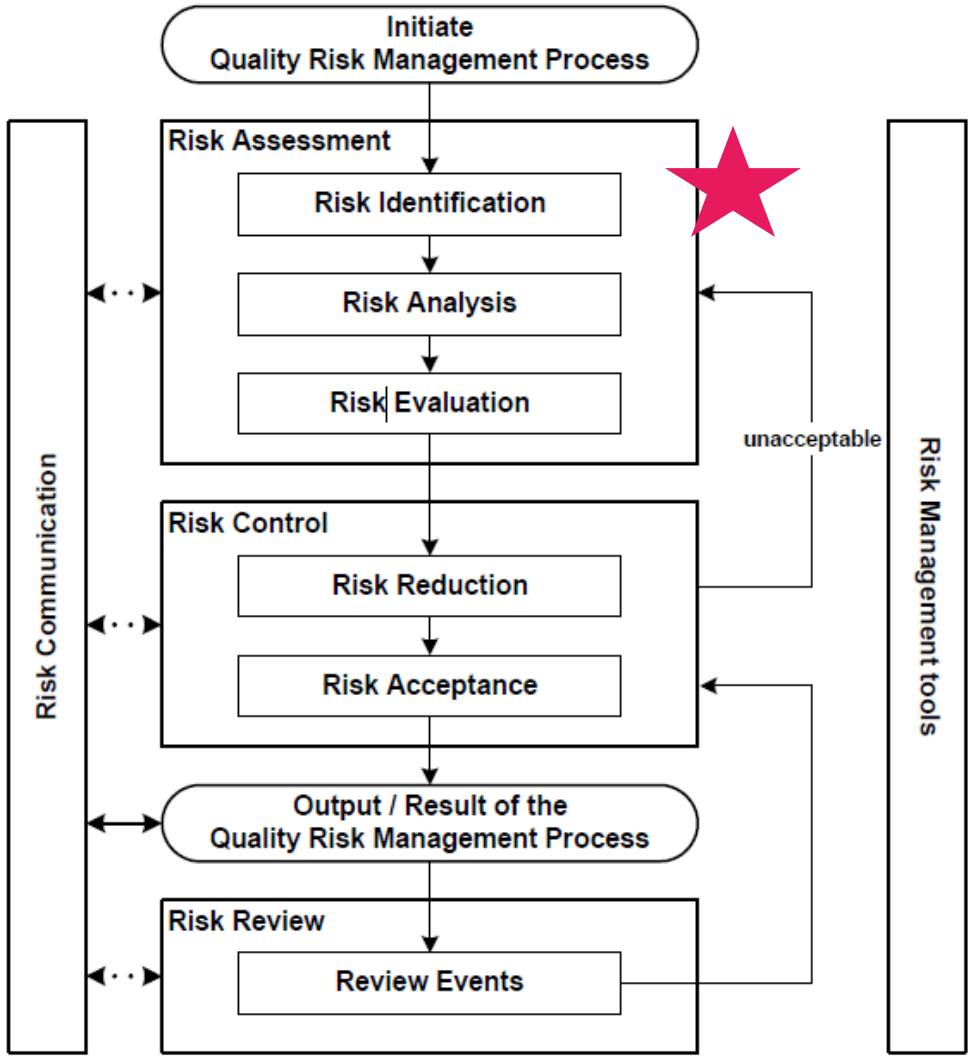
// Why do you think it’s important to scope your risk question?

Break: 10 minutes

Overview or Risk Management Tools

QRM Lifecycle- 30 mins

Figure 1: Overview of a typical quality risk management process



This is the Quality Risk Management lifecycle from ICH Q9.

Why are risk assessments important?

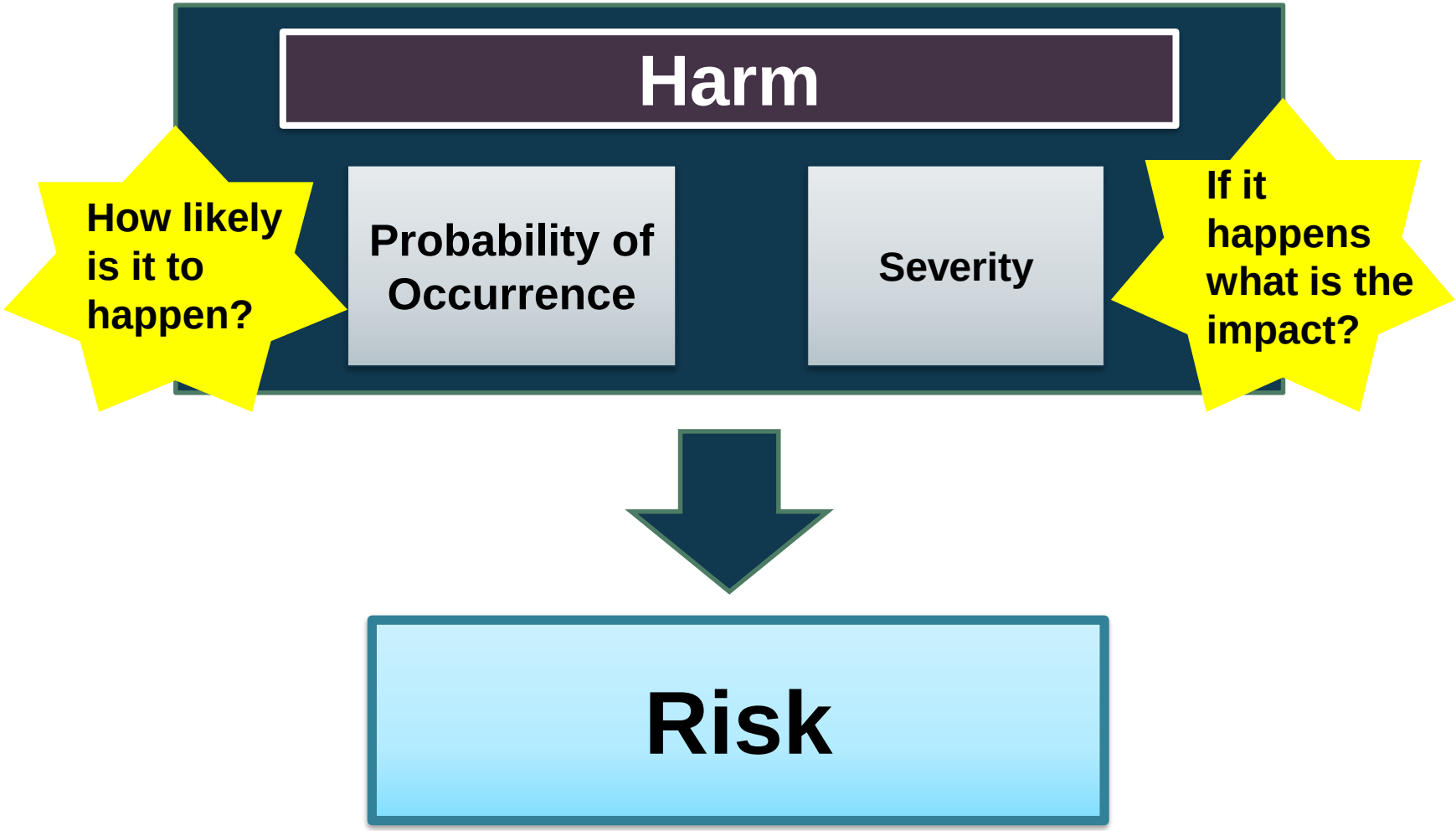
Create Awareness of Hazards and Harms

- Before a new process is being implemented
- Before new raw materials introduced
- When technology is being transferred from a building or a site

Determine if existing controls are adequate or if further mitigation is required

- Determine whether a control program is required for particular hazards
- Use a risk-based approach to prioritize recurring tasks such as periodic review or re-qualification

What is Risk?


Harm
How likely is it to happen?
Probability of Occurrence
Severity
If it happens what is the impact?
Risk

Managing Quality Risk comprises the utilization of recognized methods and tools like

- Basic risk management facilitation methods, e.g. cause and effect diagrams (also called Ishikawa or fish bone diagram)
- **Failure Mode and Effect Analysis (FMEA),**
- **Risk Identification & Control/Mitigation Matrix**
- **Hazard Analysis of Critical Control Points (HACCP)**
- **Risk-Based Impact Assessments**
- and others

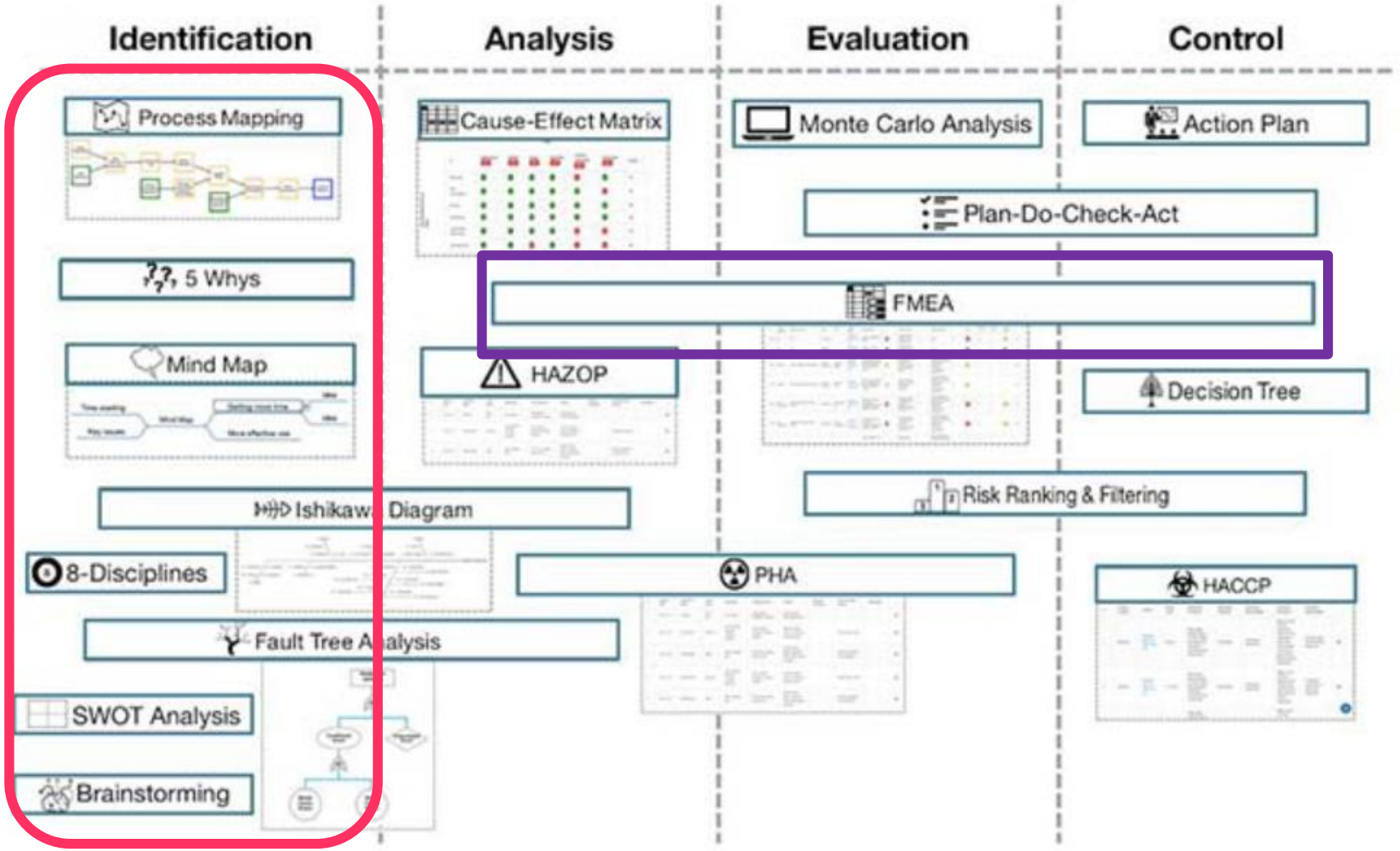


Figure 1 - Multiple tools exist to perform each of the tasks involved in risk-management. (graphic by Prof Dr José C. Menezes, CEO 4Tune Enaineerina)

https://www.gmp-compliance.org/gmp-news/quality-risk-management-is-getting-more-and-more-important

Risk Identification and Control/Mitigation Matrix

(Custom)

Risk Identification & Control/Mitigation Matrix

- Intent is to inform on any peripheral changes to various areas when a change application is introduced (Personnel, Equipment, Environment/Surroundings, Procedures, Product(s), or Others)
- During stakeholder review, representatives are expected to identify any potential additional risks and the need for further mitigation similar to identifying additional implementation plan requirements

Risk Identification and Control/Mitigation Matrix Worksheet Example

☐N/A- Provide Justification/Rationale in Conclusion Section Below

Areas of Consideration for Impact	Changes To Area	Potential Impact of Change	Current Controls	Anticipated Risks	Mitigations to Include in Implementation Plan
Personnel	☐N/A				
Equipment	☐N/A				
Environment/Surroundings	☐N/A				
Procedures	☐N/A				
Materials	☐N/A				
Product	☐N/A				
Other					

Conclusions:

(Provide rationale/justification in this section if Matrix is not required)

How to Complete

Implementation Plan + Risk Identification and Control/Mitigation Matrix

Change Requestor

Collaborate upon initiation of change on need and content of Risk Identification and Control/Mitigation Matrix (Risk Matrix)

Stakeholders/Reviewers

Align on content of Risk Matrix or rationale it is not required. If additional risks and/or mitigations are required, indicate in stakeholder review or directly in excel file content

Approvers

Ensure alignment with content of Risk Identification and Control/Mitigation Matrix alongside implementation plan. If not required, ensure alignment with rationale.

Risk-Based Impact Assessment (RBIA)

Performing Risk-based Impact Assessments (RBIA)

Why use a Risk-Based Impact Assessment?

- When the impact of a deviation is not self-evident
- When risk-based decisions regarding product disposition or next steps must be made
- When science needs the lens of risk

Performing Risk-based Impact Assessments (RBIA)

Risk-Based Impact Assessments May Help Determine Whether

- Impact is significant enough to prevent release of the affected batch/portion of batch
- Portions of the batch can be assessed and dispositioned separately
- There is potential impact to other batches not directly implicated in the deviation
- There is potential peripheral impact to facilities or equipment used to manufacture the affected batch

Performing Risk-based Impact Assessments (RBIA)

Risk-Based Impact Assessments

Will NOT:

- Help you identify root cause
- Determine CAPAs (Corrective Action/Preventive Action)
- Justify release of product if the science doesn’t support it

Performing Risk-based Impact Assessments (RBIA)

Steps: RBIA Process

Prep

- **Step One:** Determine criteria for likelihood, confidence, and severity
- **Step Two:** Determine action level table
- **Step Three:** Gather data

Assess

- **Step Four:** Determine potential impact(s) to be assessed
- **Step Five**: List supporting data/information
- **Step Six:** Estimate likelihood, confidence, and severity of each potential impact
- **Step Seven:** Determine overall risk using the Preliminary Risk Matrix and Final Risk Matrix

Act

- **Step Eight:** Determine necessary actions based on overall risk
- **Step Nine:** Document the risk-based impact assessment

Performing Risk-based Impact Assessments (RBIA)

Three factors of a Risk-Based Impact Assessment

// **Likelihood:** What is the likelihood the potential impact occurred, based on the results of the investigation?

// **Confidence:** How confident are you about the likelihood rating, based on the results of the investigation?

// **Severity:** How significant is the potential impact?

Performing Risk-based Impact Assessments (RBIA)

Likelihood Criteria for Implicated Product

What is the likelihood the potential impact occurred, based on the results of the investigation?

Ranking	Criteria
Remote	The potential impact is unlikely to have occurred.
Average	The potential impact has a moderate likelihood of occurrence.
Likely	The potential impact is likely to have occurred.

Performing Risk-based Impact Assessments (RBIA)

Simple Confidence Criteria

How confident are you about the likelihood rating, based on the results of the investigation?

Ranking	Criteria
High	High degree of confidence in the likelihood rating assigned. Presence of potential impact (nearly) **confirmed/refuted through the investigation process.**
Medium	Moderate degree of confidence in the likelihood rating assigned. Presence/absence of potential impact **can be *estimated* based on the results of the investigation.**
Low	Low level of confidence in the likelihood rating assigned. Presence/absence of potential impact **could not be confidently confirmed or estimated** based on the results of the investigation.

Performing Risk-based Impact Assessments (RBIA)

Severity Criteria: Product

How significant is the potential impact?

Ranking	Criteria
Minor	Minimal impact with no effect on product quality, safety, or efficacy.
Moderate	Moderate impact that may affect product quality but can be contained or mediated through normal proceduralized activities or defined CAPAs. No patient effects. NOTE: If assignment of a moderate severity ranking is contingent upon the execution of additional activities, these must occur prior to product release and must be disclosed in the impact assessment.
Critical	Extreme impact with effect on product quality, safety, or efficacy. Product, if used, may jeopardize the patient.

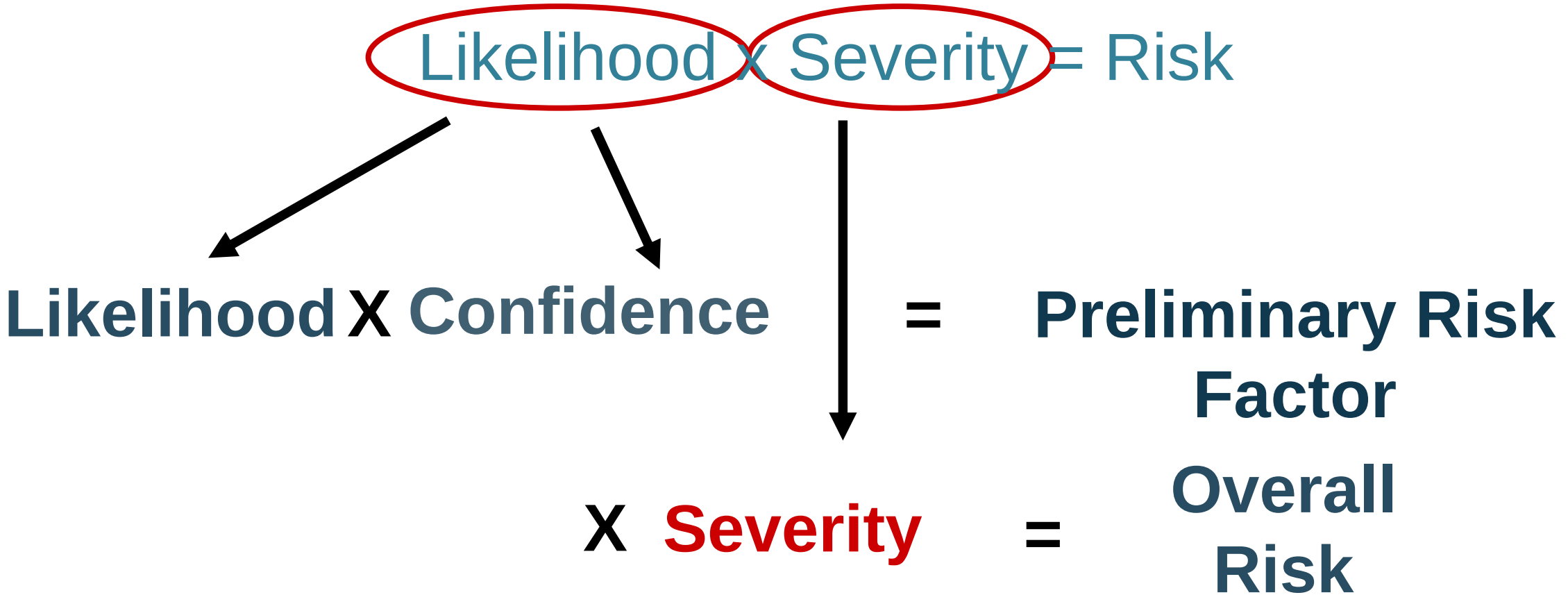
Performing Risk-based Impact Assessments (RBIA)

Step Nine: Document the Risk-Based Impact Assessment

Potential Impact	Supporting Data/ Information	L	Rationale for L	C	Rationale for C	S	Rationale for S	Preliminary Risk Level	Overall Risk Level

Performing Risk-based Impact Assessments (RBIA)

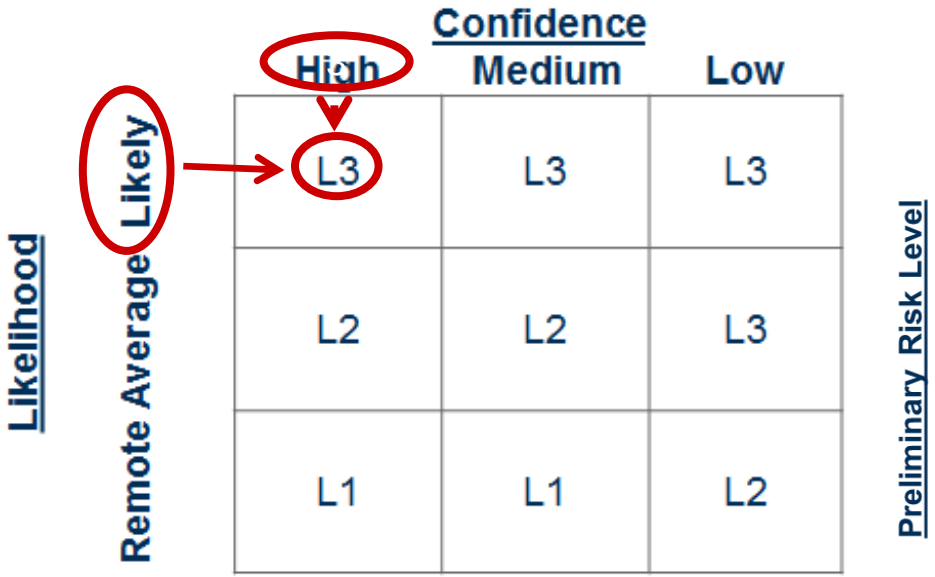
The Equation Behind RBIA



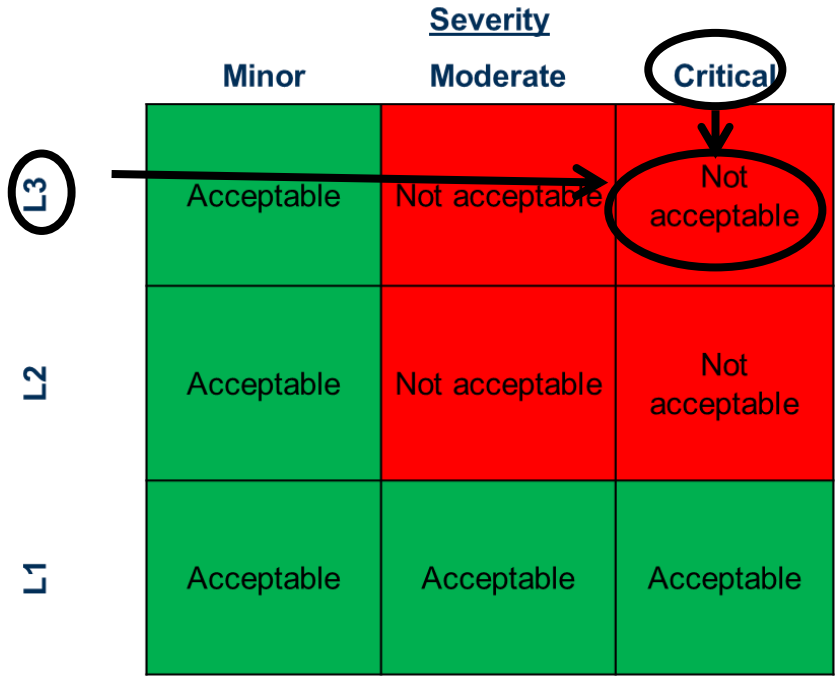
Performing Risk-based Impact Assessments (RBIA)

Step Seven: Determine Overall Risk

We have a ***likely*** likelihood, ***high*** confidence, and ***critical*** severity



The preliminary risk level is L3



The overall risk level is **Not acceptable**

Hazard Analysis and Critical Control Points (HACCP)

HACCP Overview

- HACCP is a qualitative risk assessment technique.
- It is a systematic, preventive approach to identify hazards in a process and/or system with the aim to produce a documented plan to control these scenarios.
- Focuses on physical, chemical, and biological hazards (contamination).

"… *the output of a HACCP analysis is risk management information that facilitates monitoring of critical points*…"

ICH Q9

Key Terms for HACCP

Hazard

A potential source of harm

Harm

Damage to health, including the damage that can occur from loss of product quality or availability

Control Point

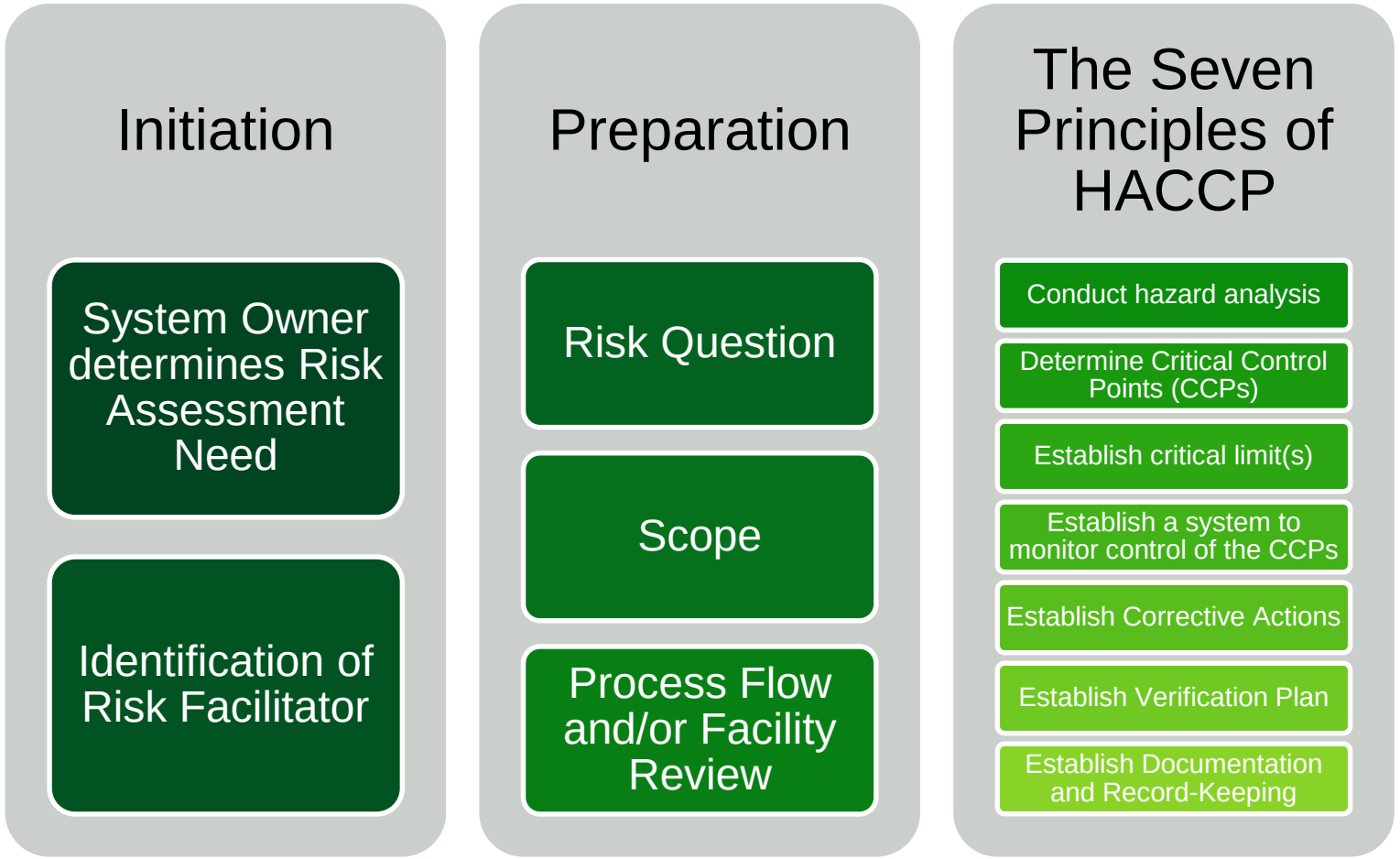
Any process step or physical location at which biological, chemical, or physical hazards require control.

What makes HACCP unique?

Like other risk management tools, HACCP employs the classical (ICH Q9) definition of risk:

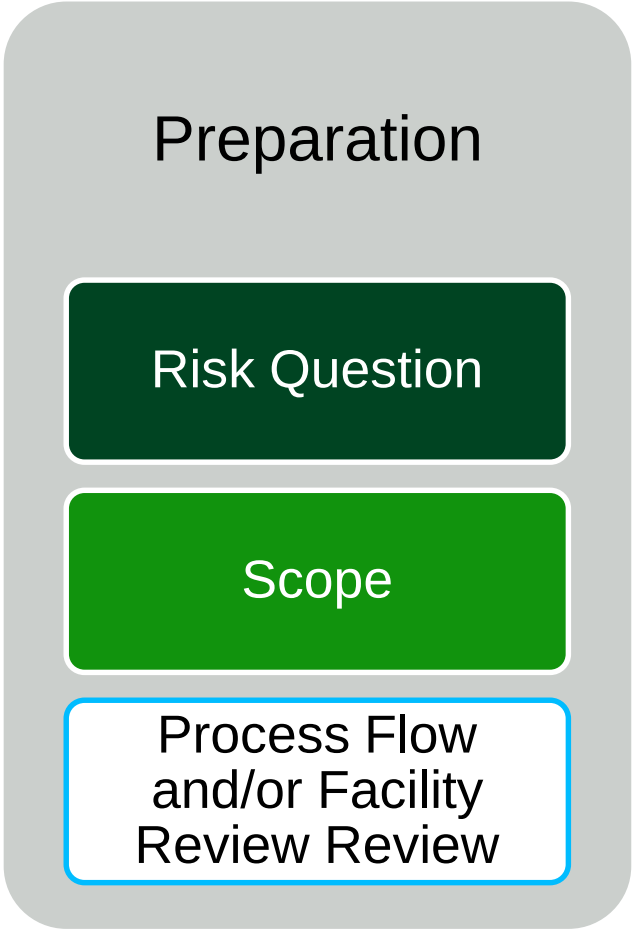
However, HACCP includes the use of a decision tree to filter risks

HACCP Process Flow

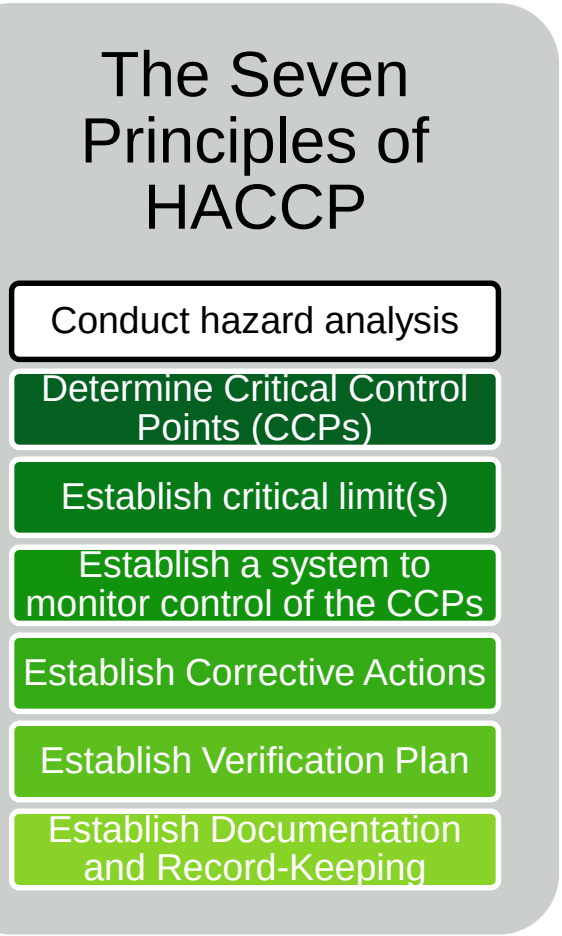


Process Flow Review and Facility Walkthroughs

- In the preparation phase of a HACCP, it is a necessity that a review of the process flow or a facility walkthrough is performed with the risk team.



Principle 1: Conduct Hazard Analysis



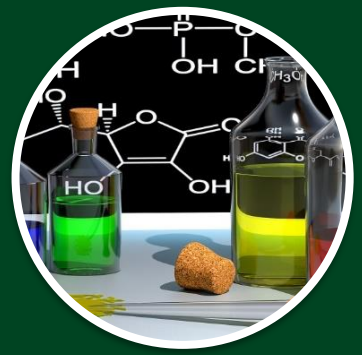
Hazard: Describes something that could go wrong, than in turn could have negative consequences. Formally defined as "potential source of harm."

Within HACCP, it is the **introduction** or **perpetuation** of contamination that is of concern!

Principle 1: Conduct Hazard Analysis

Biological Hazards

- Bacteria
- Mold
- Yeast
- Viruses



Chemical Hazards

- Chemical impurities or degradants
- Chemical properties necessary for proper processing (e.g. pH, pO2, concentration

Physical Hazards

- Particulates
- Pressure
- Temperature

Sources of Contamination

Principle 1: Conduct Hazard Analysis

Once Hazards are identified for a given process step, they are ranked for likelihood of occurrence and severity

Likelihood	
Ranking	Criteria
Remote	Remote likelihood of occurrence.
Unlikely	Failure unlikely.
Occasional	Failure moderately likely.
Likely	Failure likely
Frequent	Failure almost inevitable.

Severity	
Ranking	Criteria
Negligible	No impact to product quality.
Minor	Minor impact to product quality.
Serious	Moderate impact to product quality.
Critical	Potentially significant impact to product quality.
Catastrophic	Significant impact to product quality. Represents a risk to patient safety.

Principle 1: Conduct Hazard Analysis

The risk ranking is determined by finding the intersection of the likelihood and severity

		Severity				
		Negligible	Minor	Serious	Critical	Catastrophic
Likelihood	Frequent	Medium	High	High	High	High
	Likely	Low	Medium	High	High	High
	Occasional	Low	Low	Medium	High	High
	Unlikely	Low	Low	Low	Medium	High
	Remote	Low	Low	Low	Low	Medium

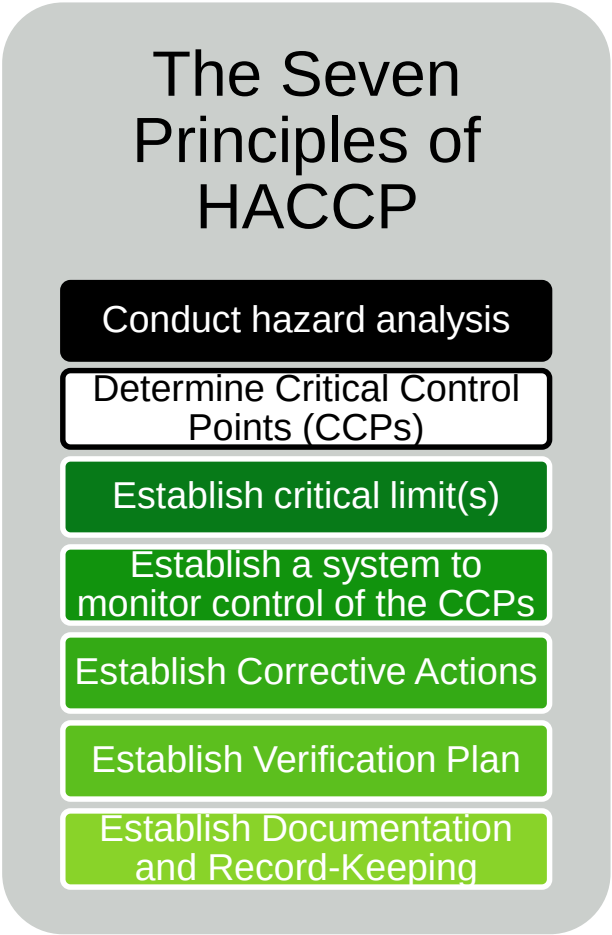
Risk Evaluation Criteria

Risk Level	Risk Acceptability/ Required Action
Low	Risk is acceptable. No further action required.
Medium	Risk must be evaluated and dispositioned as acceptable or not acceptable with appropriate rationale. Risk deemed unacceptable must be subject to risk reduction or mitigation.
High	Risk is not acceptable. Mitigation required.

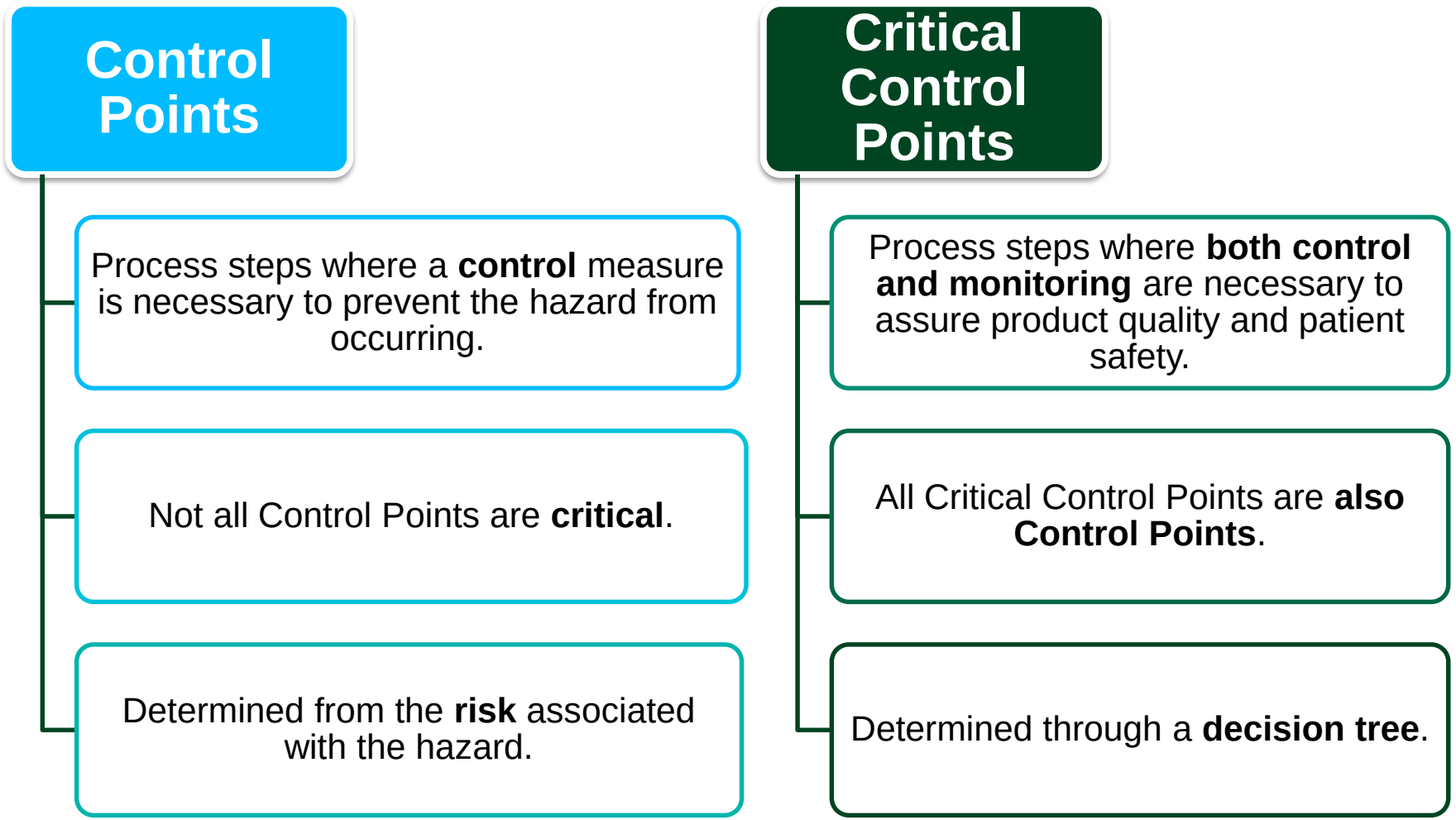
Principle 2: Determine Critical Control Points

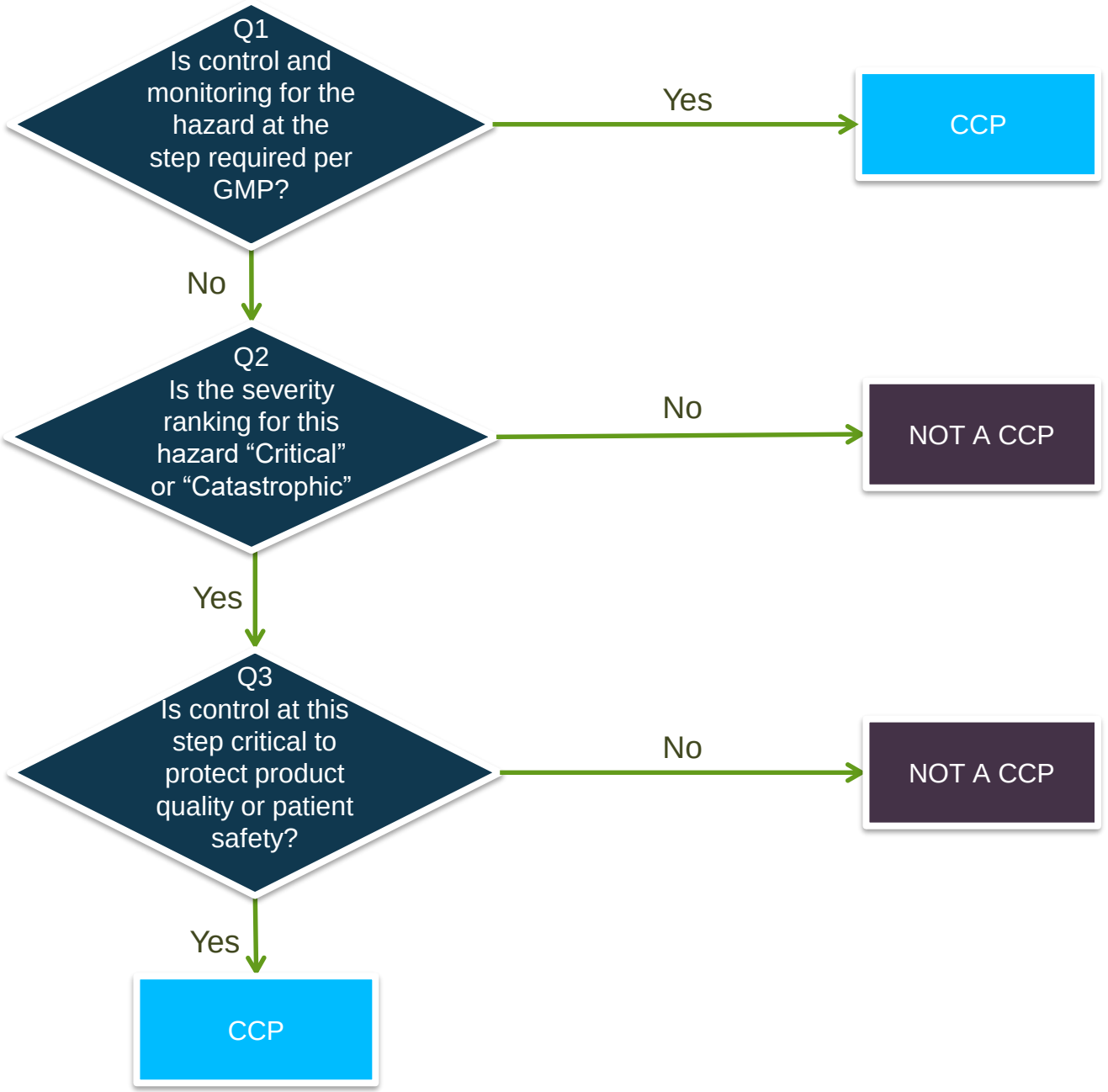
- A Critical Control Point (CCP) is a step at which control can be applied and is essential to **prevent or eliminate** a hazard or reduce it to an acceptable level.

- CCPs represents points in a process where controls should be **measured and monitored**, to ensure risk is not realized.

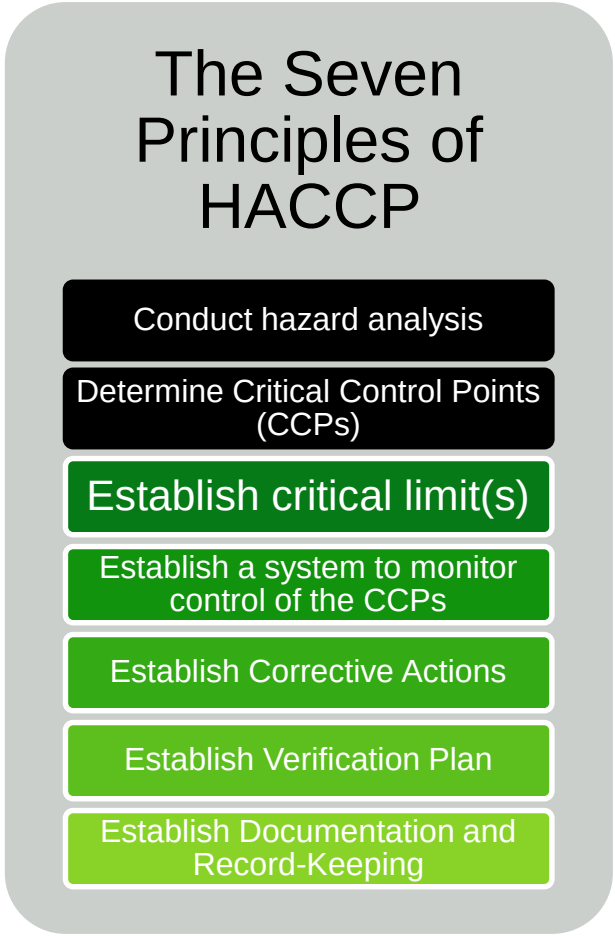


Control Points vs. Critical Control Points




Q1
Is control and monitoring for the hazard at the step required per GMP?
Yes
CCP
No
Q2
Is the severity ranking for this hazard “Critical” or “Catastrophic”
No
NOT A CCP
Yes
Q3
Is control at this step critical to protect product quality or patient safety?
No
NOT A CCP
Yes
CCP

Principles 3-7: Establish Critical Limits, Monitor, Respond, Verify, Document



- Critical Limits are set for each Critical Control Point identified in Principle 2.
- The Critical Limit is the criterion that separates **acceptability from unacceptability** (e.g. target ranges or alert/action levels) for the control.
- **Monitoring** is the act of conducting a planned sequence of observations or measurements of control parameters to assess whether **a CCP** is under control.
- If/when one or more CCPs are **outside of the Critical Limits**; the process/facility is not in control and **Corrective Actions** are needed
- On a periodic basis, data and **data trends should be reviewed** to confirm continued **effectiveness** of the monitoring program.
- The outcome of the **HACCP** must be documented in a **report**

Break: 10 minutes

Failure Mode & Effect Analysis (FMEA)

Overview of FMEA Method

FMEA begins by breaking the subject down into process steps or component parts.

For each step or part, possible Failure Modes are identified.

Each Failure Mode is then examined to determine possible Cause(s) and Effect(s), and all existing Controls.

Foundational Elements of FMEA

Foundational Elements of FMEA

Failure Mode

The manner in which a process, sub-process, or individual action could ***potentially fail to meet its performance requirements***.

Hazardous Situation

Failure Cause

The ***basic reason for failure.*** It is the cause of the Failure Mode.

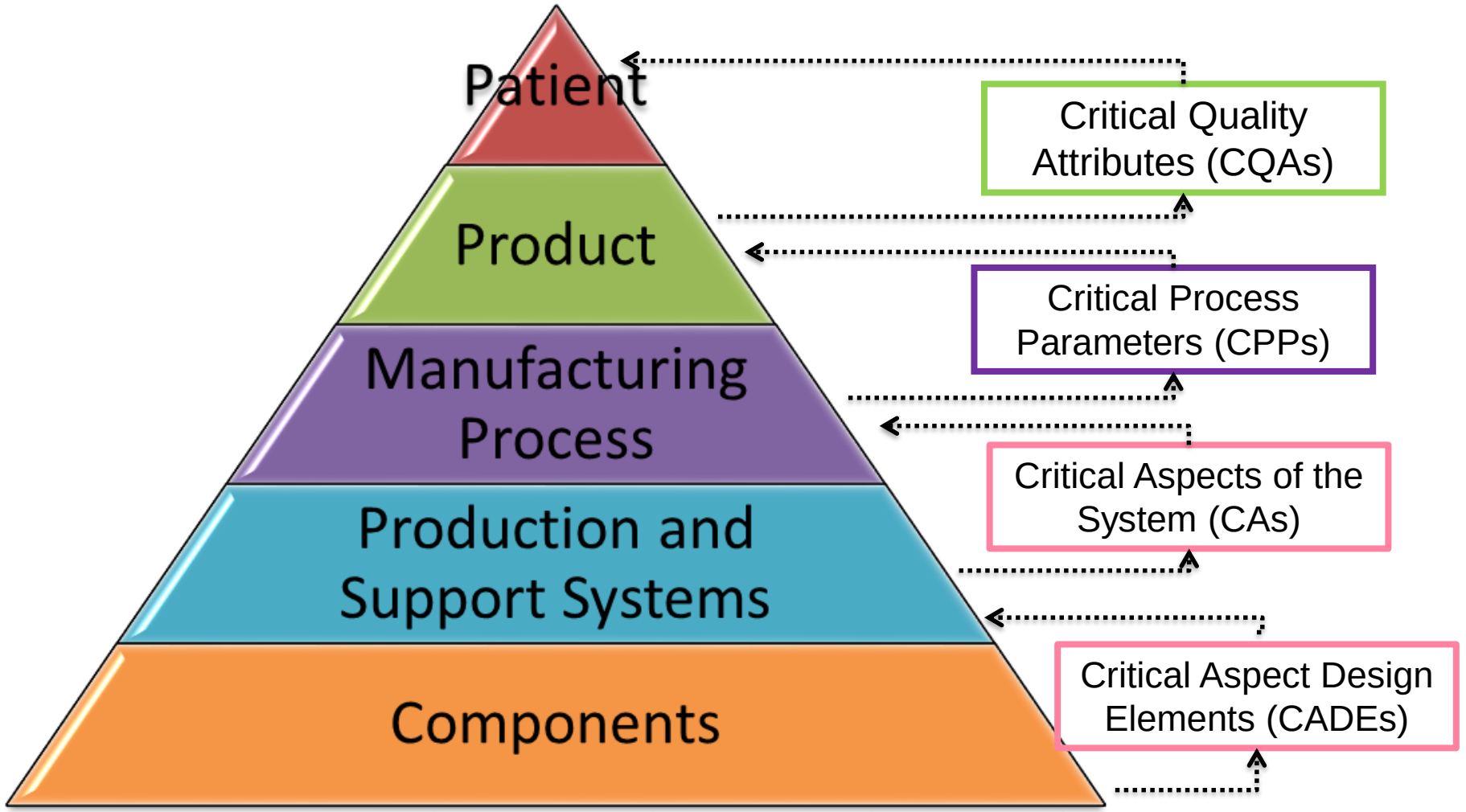
Hazard

Failure Effect

A ***consequence of the failure mode*** at the process step being assessed on the operation, functionality, or end user.

Harm

Linking the levels



Example: Process FMEA for product terminal sterilization

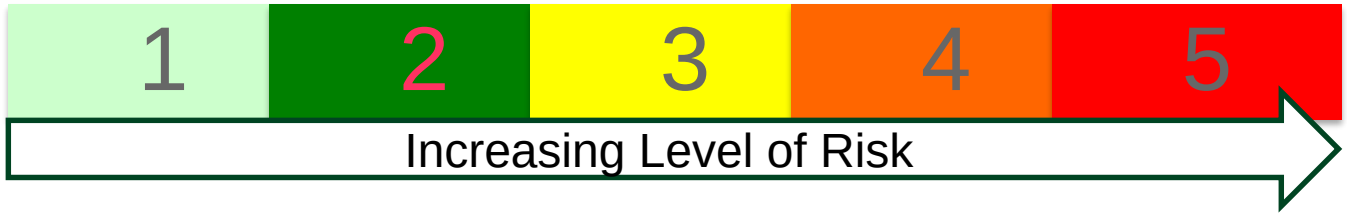
#	Failure Mode	Failure Cause	Failure Effect
1	Temperature < 121°C	Autoclave steam controller failure	Loss of sterility assurance
		Cycle (automation) failure	
2	Pressure < 2atm	Autoclave steam controller failure	Loss of sterility assurance
		Autoclave leaking	
3	Hold < 20 min	Autoclave steam controller failure	Loss of sterility assurance
		Cycle (automation) failure	
		Autoclave leaking	
4	Hold > 30 min	Cycle (automation) failure	Product degradation (viscosity OOS)

Step 1: Evaluate Risk Estimation Criteria

FMEA Execution

- **Evaluate Risk Estimation Criteria**
- Identify Failure Mode(s)
- Describe Failure Cause(s), Failure Effect(s)
- Identify Current Controls
- Assign Values
- Risk Evaluation
- Determine Proposed Mitigation Actions
- Prepare Interim Report
- Complete Mitigation and Verify Effectiveness
- Determine Residual Risk
- Prepare Final Report

- Risk estimation criteria are scales which are used to rank the FMEA elements
- Criteria are to be reviewed at the start of each FMEA with all team members
  - Ensure consistent understanding of criteria
  - Applicability to risk question and scope of the assessment
- Ratings are assigned based on the degree of applicability of a range of values
  - 1-5 scale is applied



Risk Ranking Criteria

A 1-5 Scale is used for each of the following

Severity

- Criticality of Failure Effect

Frequency

- Frequency (or Likelihood) of the Failure Cause occurring

Detectability

- Detection of the Failure Mode before it causes harm

Activity

In the following indicate if this is a likelihood or a severity criteria:

Criteria Description	Likelihood	Severity
More than 2 deviations with a 2 year interval.		
Failure almost inevitable		
Catastrophic/Critical		
5 defects within 1000		
Loss of data integrity		
Represents a risk to patient safety		
The potential impact may have extended to other batches/lots of product or the remaining portion of the batch/lot.		

Discussion

What led to the decision for L or S? Why is it important to have both? Challenges?

Criteria Description	Likelihood	Severity
More than 2 deviations with a 2 year interval.	X	
Failure almost inevitable	X	
Catastrophic/Critical		X
5 defects within 1000	X	
Loss of data integrity		X
Represents a risk to patient safety		X
The potential impact may have extended to other batches/lots of product or the remaining portion of the batch/lot.		X

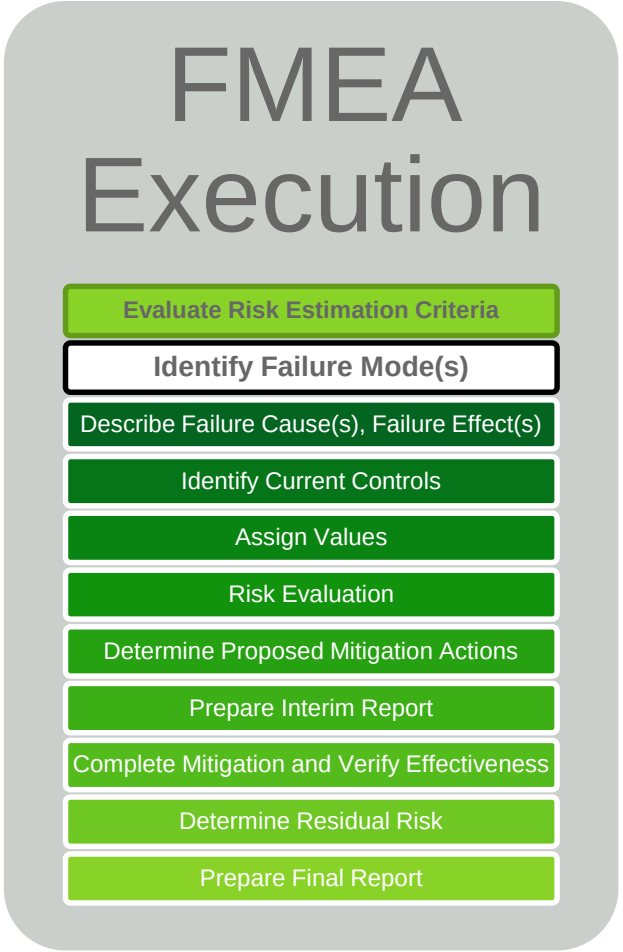
Step 2: Identify Failure Modes

Failure modes describe a way in which a

- **Component** could fail to meet specifications

or

- **Process step** could fail to perform its desired function (design intent or performance requirements; CPP failure)



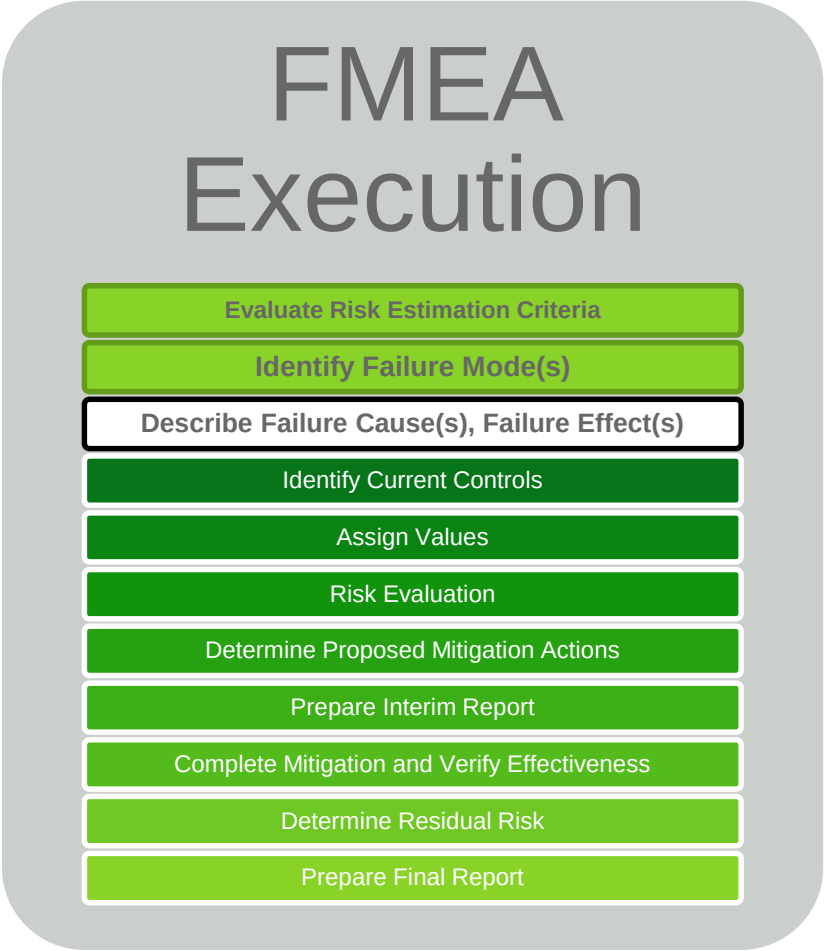
Failure Mode Identification

- Failure Modes from both *normal* and *fault* conditions should be considered:

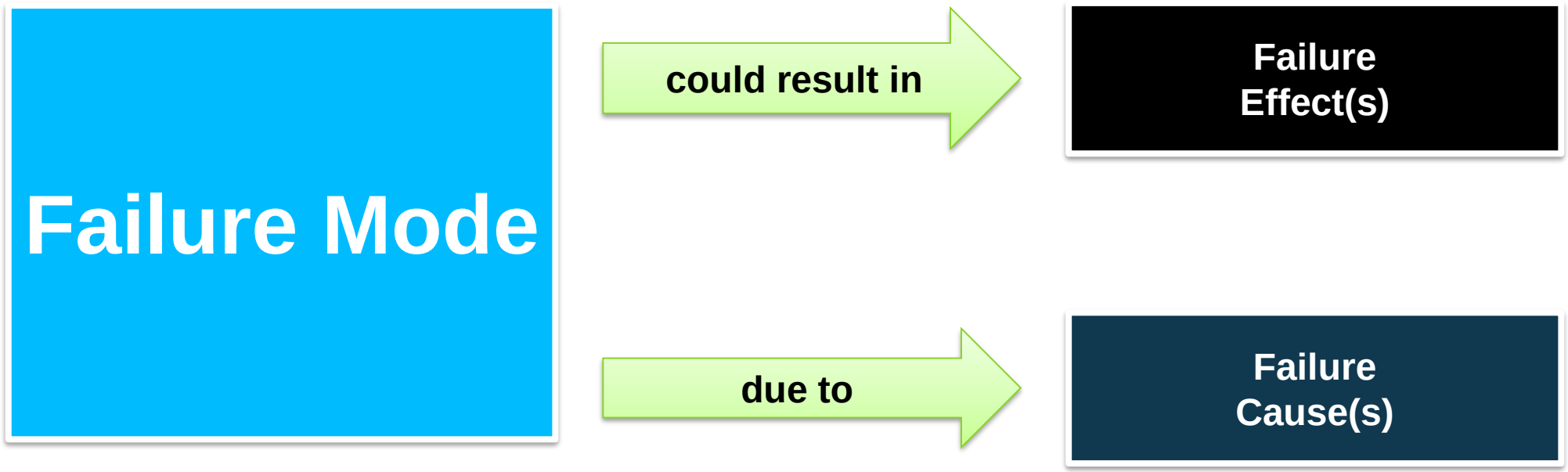
Normal Conditions	Fault Conditions
• Procedures are followed and equipment is acting as intended but a failure occurs	• Failure occurs due to a deviation from normal procedures, steps missing from procedure or equipment malfunctions

Step 3: Describe Failure Cause(s) and Failure Effects

- Failure modes are traced back to one or more potential **failure causes** with one or more **failure effects**
- **Failure causes** should be intrinsic to the application or process defined in your scope and risk question
- **Failure effects** are describes in term of what the product, system, or customer, internal or external, might experience

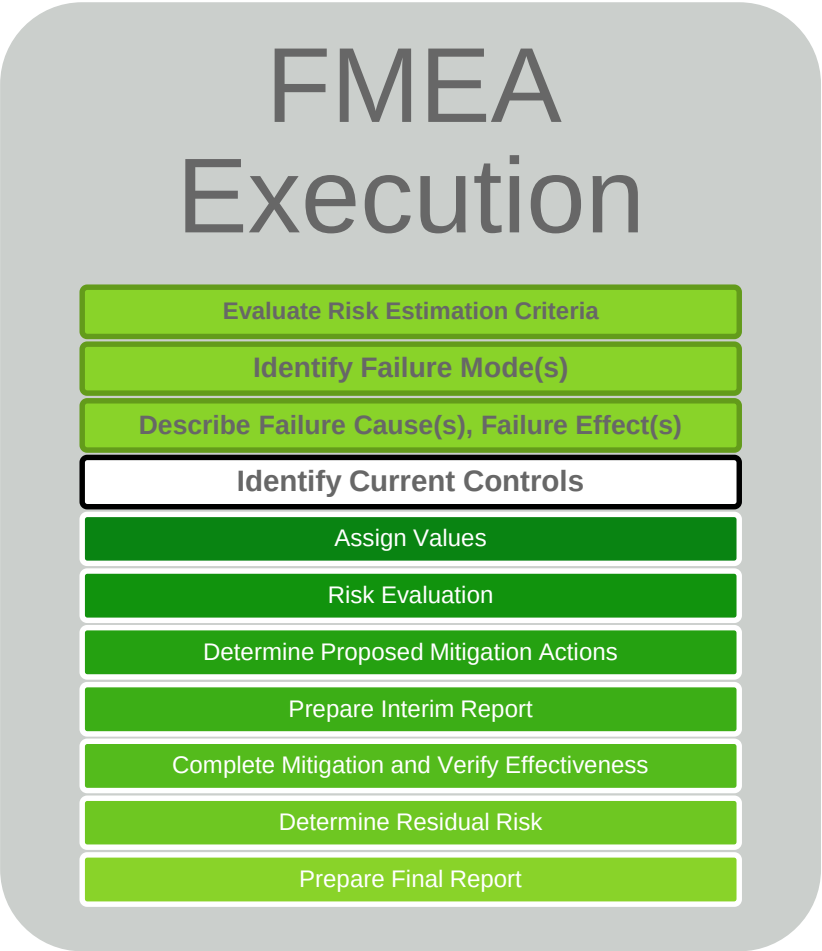


Remember the relationship between FM, FC, and FE



Step 4: Identify Current Controls

- Current Controls are controls that are already in place which may mitigate the risk or otherwise influence the components of risk (frequency, detectability, and severity).
- Current Controls can include processing steps, test procedures, characterization tests, or any means that can be used to prevent or detect a risk before an undesirable outcome occurs. (i.e. SOPs, alarms, technical reports, training etc..)



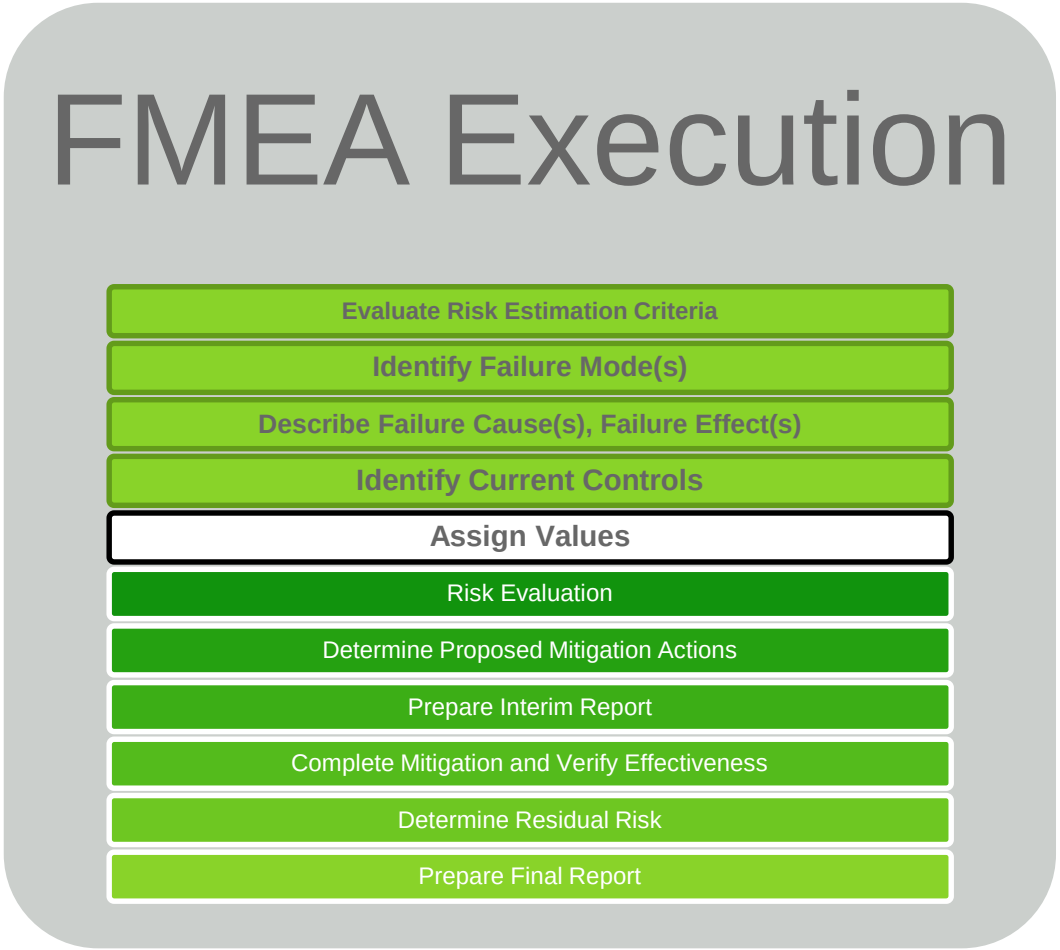
Prevention and Detection Controls

- **Prevention mechanisms** decrease the Frequency Rating Value (Failure Cause)
  - Example: A prevention mechanism for the failure cause “air contamination” in a laminar flow hood may be “use of certified HEPA filters”

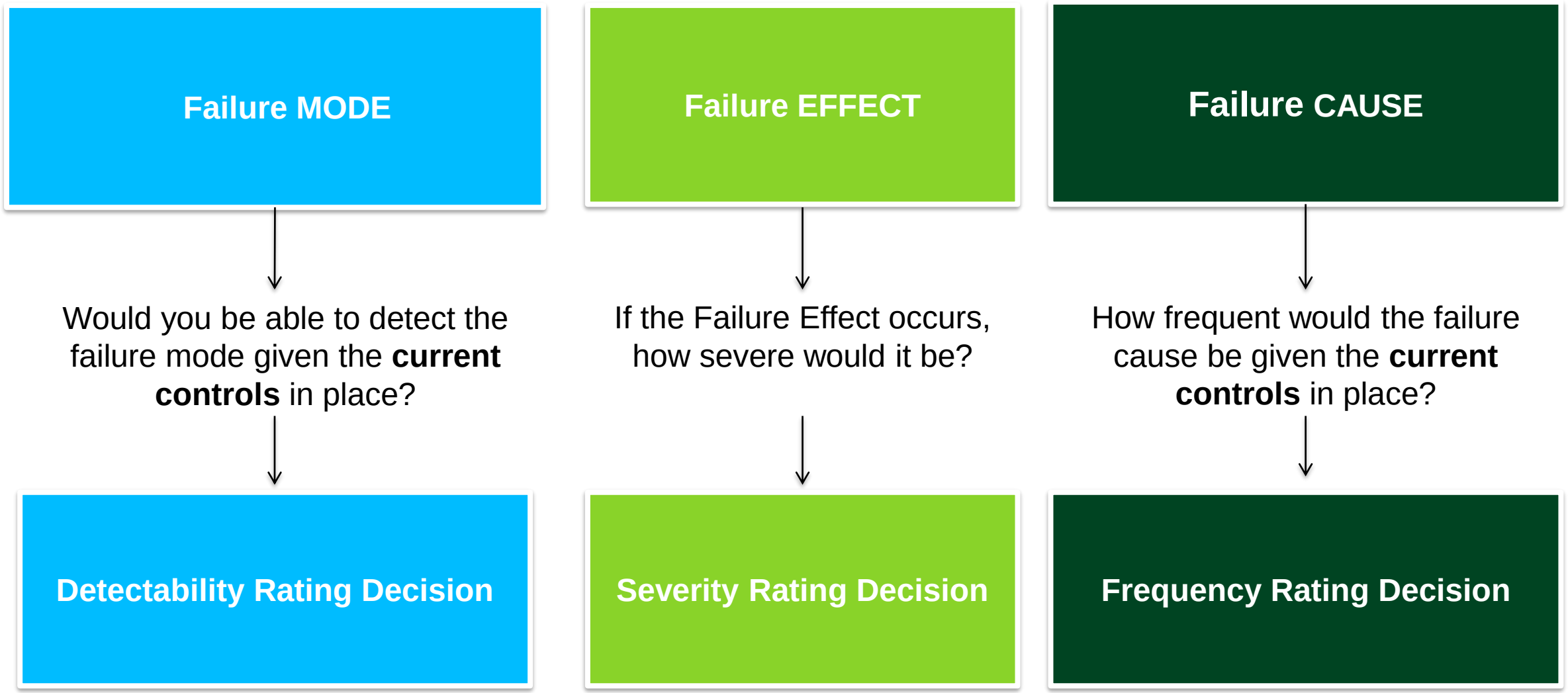
- **Mechanisms of detection** decrease the Detectability Rating Value (Failure Mode)
  - Example: A detection mechanism for the failure mode “incorrect quantities of vials” on a filling line may be “use of vial counter”

Step 5: Assign Values

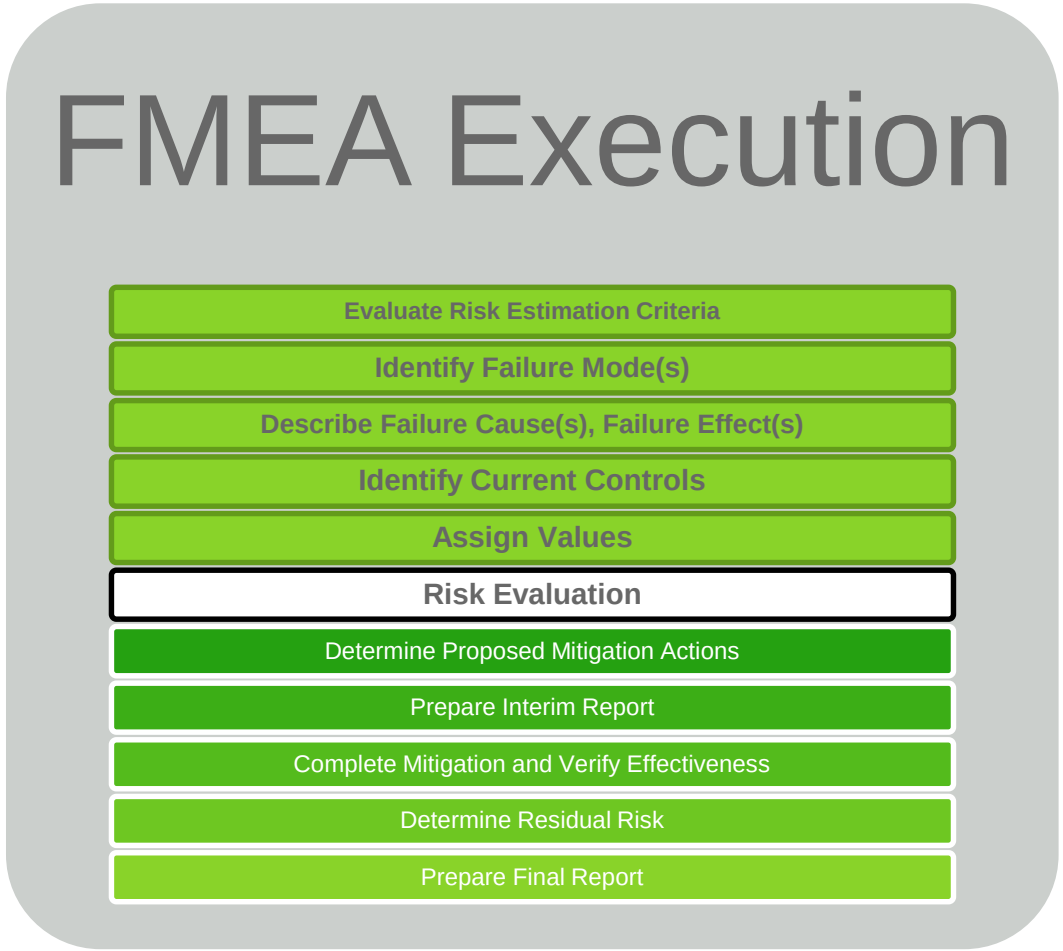
- Use the risk ranking criteria defined to assign Frequency, Detectability and Severity Scores



Recall the Risk Ranking Relationships...



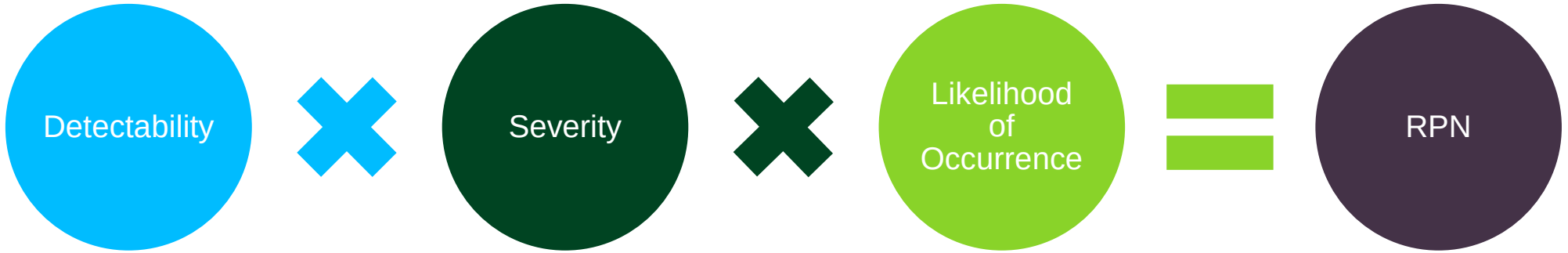
Step 6: Risk Evaluation



- Risk evaluation is the step when all the scores come together to determine the Risk Priority Number (RPN)

Risk Evaluation

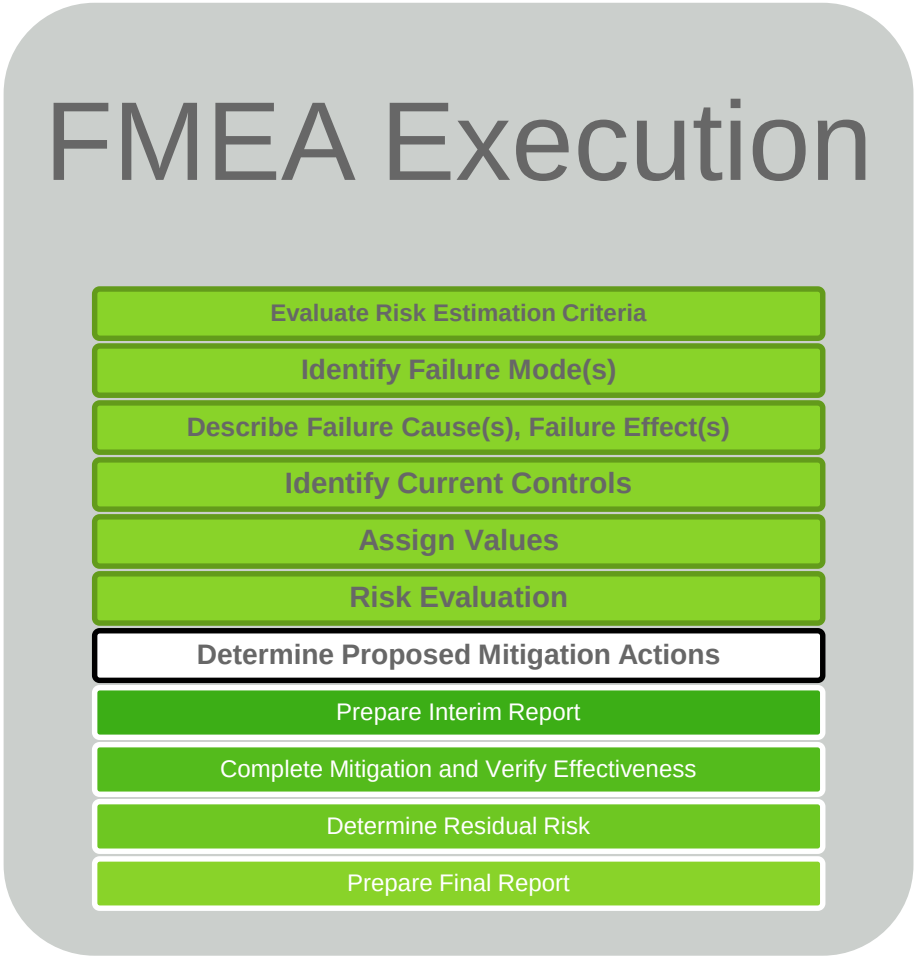
The Risk Priority Number (**RPN**) is calculated by multiplying the Frequency (1-5), Detectability (1-5), and Severity (1-5) ratings together



The resulting **RPN** is then compared to a predetermined table in order to determine which, if any, actions need to be taken.

Step 7: Determine Mitigation Strategy

- The overall RPN and individual detectability/likelihood ratings will drive the need for implementing a risk mitigation plan.



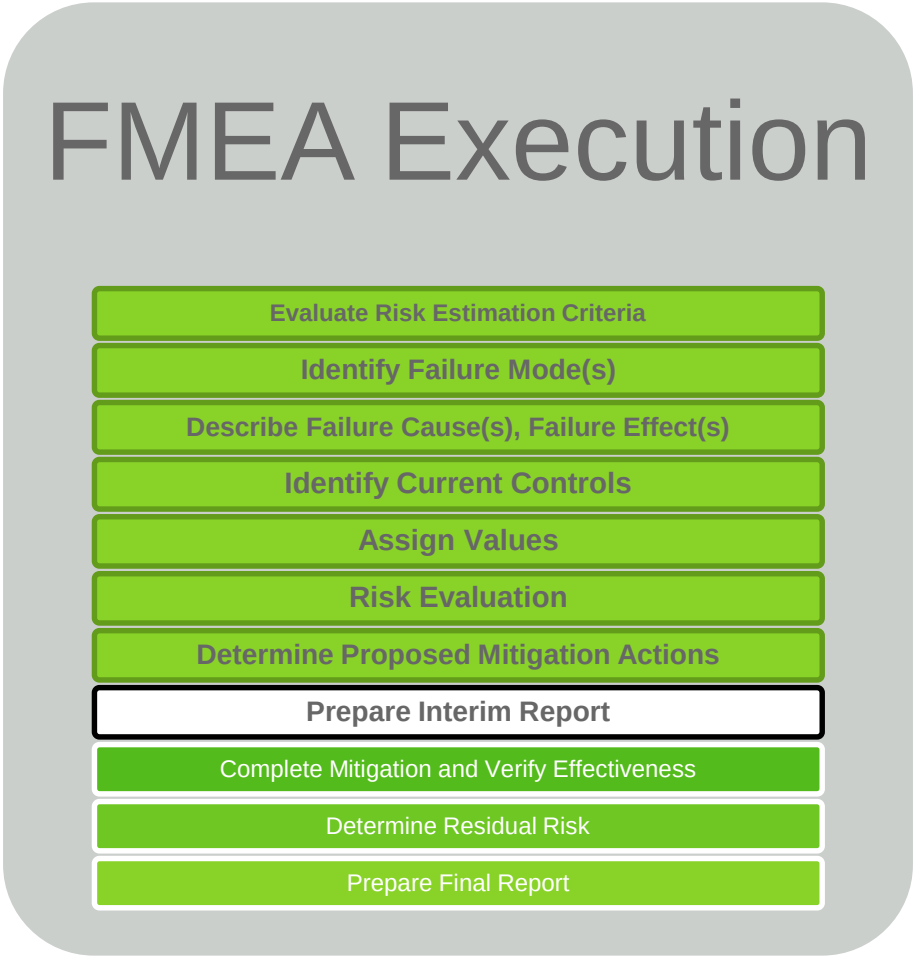
FMEA Template:

Example Excel Worksheet

Risk ID #	Current Conditions												
	Failure Mode	Detection Controls	D	Rationale for D	Failure Cause	Preventive Controls	F	Rationale for F	Failure Effect	S	Rationale for S	RPN	Mitigation Activities
												0	
												0	

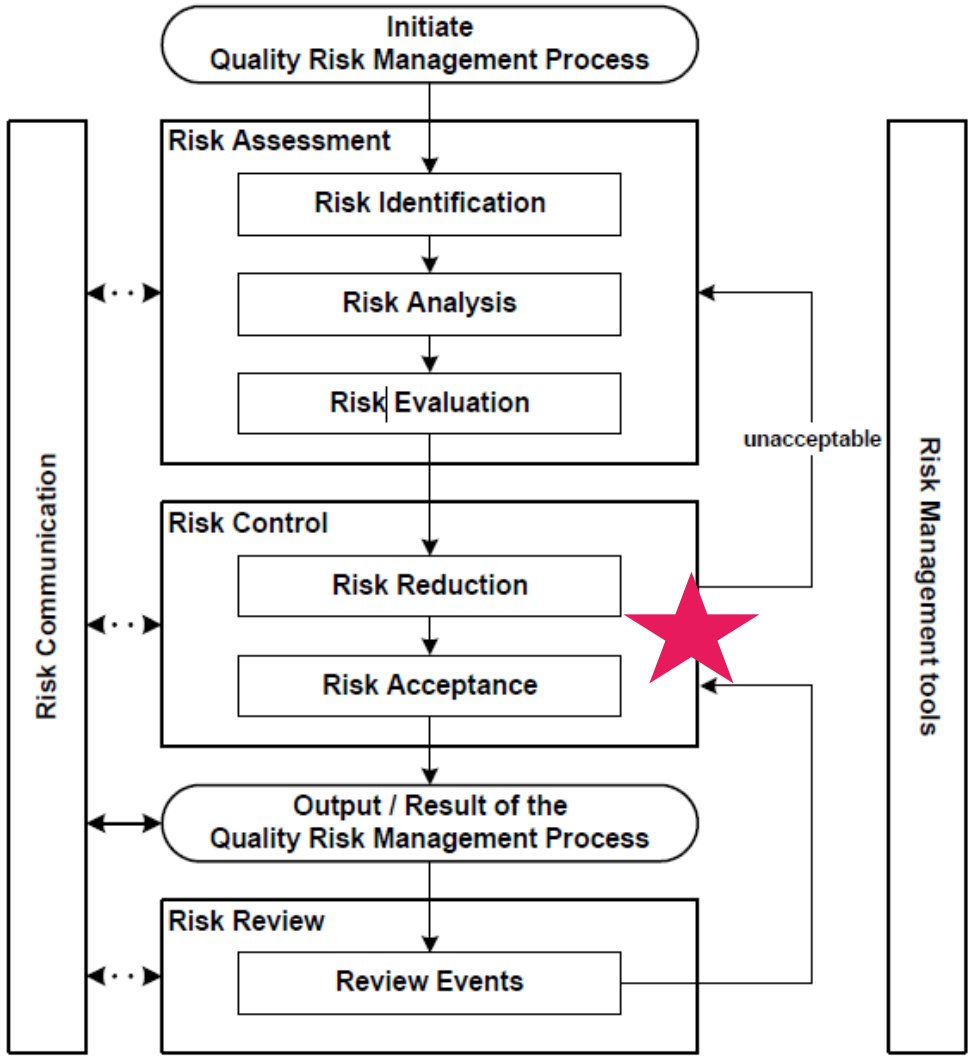
Remaining Steps: Communicate Risk, Mitigate, Accept Residual Risk

- After the risk mitigation plan has been defined, communicate outcomes and risk control
- After mitigations are done and risk reduction is complete accept resulting residual risk and finalize report



QRM Lifecycle

Figure 1: Overview of a typical quality risk management process



This is the Quality Risk Management lifecycle from ICH Q9.

Remember the Question? What is the Answer?

"What are the potential product quality risks that could result from <insert scenario here with boundaries>?"

Ask

- What are the risks associated with changing the 2-cc vial suppliers for filling Jansen covid vaccine?
- What are the risks of using a matrix approach for cleaning validation of Jansen covid vaccine equipment?

Outcome

- Acceptable and Unacceptable risks
- Mitigations required for unacceptable risks
- Data along with scientific logic indicating rationale behind acceptable risk scores
- Prioritized actions to reduce risk
- Risk-based approach for risk review intervals

The Output of the Risk Assessment = Documentation of Assessment and Risk Reduction/Acceptance (Mitigations & Controls)

Activity: Executing FMEA

Camilla Perrotta-Fowler

Activity: Executing an FMEA

Organization: Camilla's House

Processes occurring @ Camilla's House:

// Scrambled Eggs

// Scrambled Tofu (for dietary restricted guests)

// Toasted sourdough bread with butter

Process Risk Assessment: Scrambling eggs by cooking over a gas stove

Activity: Executing an FMEA

Process Risk Assessment: Scrambling eggs by cooking over a gas stove

Procedure:

1. Collect all ingredients and tools; heat pan on gas stove over medium heat
2. Crack egg on edge of bowl and drop egg in bowl; discard shells; repeat 2 more times
3. Season with salt and pepper, mix, and pour in heated pan
4. Cook in pan, constantly mixing with a rubber spatula, until light and fluffy
5. Serve on a warm plate

Activity: Executing an FMEA

Risk Question: What are the risks to making “Perfect Scrambled Eggs” by cooking over a gas stove?

The Asset: Perfect Scrambled Eggs

- Pale yellow in color
- Fluffy
- Free of debris
- Lightly seasoned with Salt & Pepper
- Single portion is 3 large chicken eggs

Activity: Executing an FMEA

Risk Question: What are the risks to making “Perfect Scrambled Eggs” by cooking over a gas stove?

Risk ID	Failure Mode	Det.	Failure Cause	Lik.	Failure Effect	Sev.	Risk Score
1							
2							
3							

Activity: Executing an FMEA

Risk Question: What are the risks to making “Perfect Scrambled Eggs” by cooking over a gas stove?

Detectability Scoring Criteria *(based on class’s collective history/experience)*

- 1 = Detected before eggs leave kitchen; have time to fix the issue
- 3 = Detected before eggs leave kitchen; cannot fix issue
- 5 = Not detected before eggs leave kitchen

Likelihood Scoring Criteria *(based on class’s collective history/experience)*

- 1 = Occurs less than 10% of the time - rarely
- 3 = Occurs half of the time - frequently
- 5 = Occurs 100% of the time – consistently

Activity: Executing an FMEA

Risk Question: What are the risks to making “Perfect Scrambled Eggs” by cooking over a gas stove?

Severity Scoring Criteria *(based on class’s collective history/experience)*

- 1 = Causes Adverse Event *(e.g. nausea)*
- 3 = Causes Consumer to stop eating *(partial batch remains)*
- 5 = Consumer eats entire batch

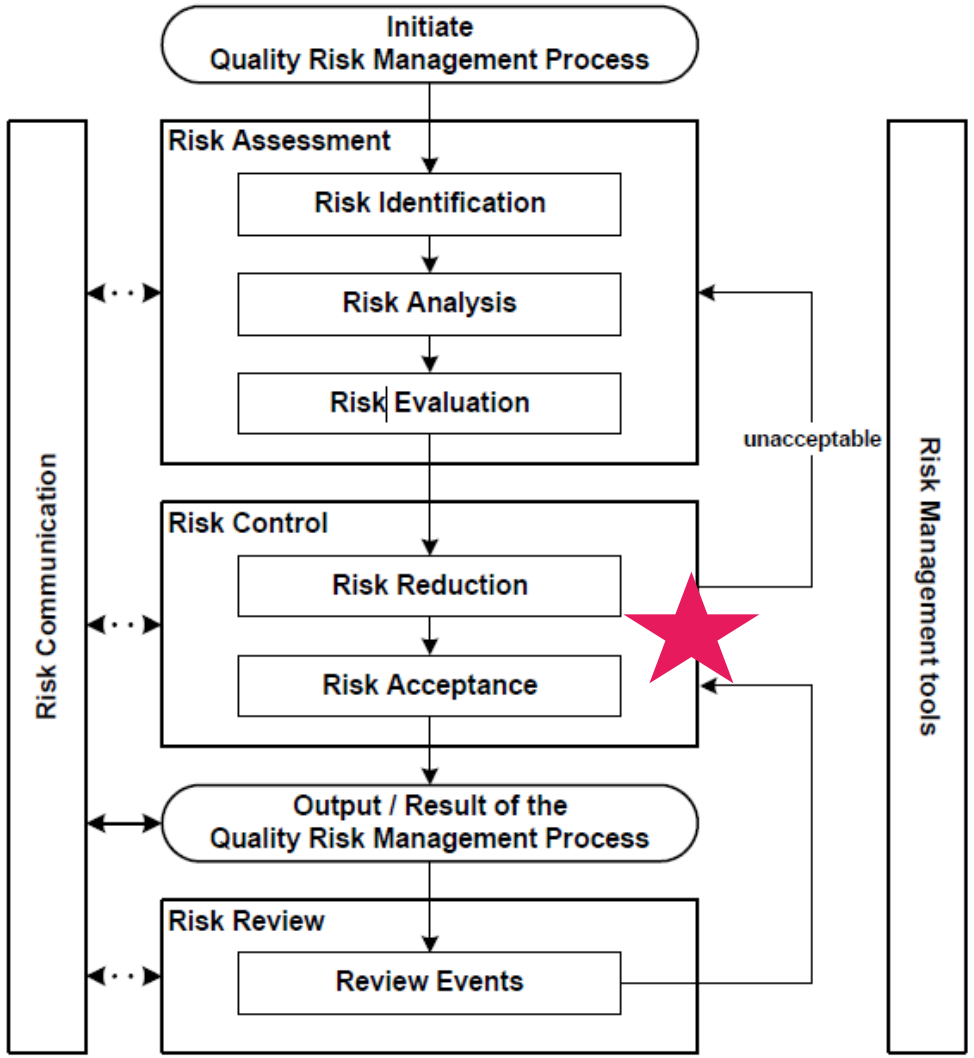
Activity: Executing an FMEA

Risk Question: What are the risks to making “Perfect Scrambled Eggs” by cooking over a gas stove?

Risk ID	Failure Mode	Det.	Failure Cause	Lik.	Failure Effect	Sev.	Risk Score
1	Egg shell in mixture before cooking	3	Broke egg on edge of bowl	5	Consumer is grossed out @ crunchy eggs	3	45
2	Egg mixture burns on bottom of eggs	5	Heat too high	3	Consumer gets sick to their stomach	5	65
3	Eggs are medium yellow (not pale yellow)	1	Naturally occurring variance with chicken eggs	3	Still looks like eggs, Consumer happily eats	1	3

QRM Lifecycle

Figure 1: Overview of a typical quality risk management process



This is the Quality Risk Management lifecycle from ICH Q9.

Close Out

Let’s reflect…

Today we covered a lot of content!

- High level introduction to QRM
- QRM Regulations
- Developed a risk question
- Learned about different risk management tools
- Practiced risk management using FMEA tool

What next?...

Back Up Slides & Definitions

DEFINITIONS

ALARP: As Low As Reasonably Practicable
Facilitator: An individual with advanced knowledge of quality risk management principles and practices who serves as a neutral arbitrator for a risk assessment
Harm: Damage to health, including the damage that can occur from loss of product quality or availability
Hazard: A potential source of harm
Event Risk Assessment: A risk assessment generated to evaluate the quality and/or compliance risks associated with an event or activity
Lifecycle Risk Assessment: A risk assessment generated to identify, evaluate, and manage the risks to patient safety, product quality, and data integrity that may arise from the introduction and ongoing operation of a process or system
Detectability: The ability to discover or determine the existence, presence, or fact of a hazard
Likelihood of Occurrence: The probability or frequency at which a hazard occurs
Risk: The combination of the probability of occurrence of harm and the severity of that harm
Risk Analysis: The determination of the risk associated with the identified hazards
Risk Assessment: A systematic process of organizing information to support risk decisions to be made within a risk management process. It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.
Mitigation Activity: A specific activity to achieve risk reduction
Residual Risk: Risk remaining after risk reduction is complete
Residual Risk Acceptance: The decision to accept residual risk
Risk Assessment Status List: An inventory of all risk assessments and associated defining criteria
Risk Communication: The sharing of information about risk and risk management between the decision maker and other stakeholders
Risk Control: The process through which unacceptable risks are reduced, acceptable risks maintained, and the residual risk is evaluated for acceptability
Risk Estimation: The assignment of ratings for likelihood of occurrence and severity (and in certain cases, detectability) to a hazard and associated harm to support Risk Analysis