**Document approval**

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**Table of Contents**

[1 Purpose 3](#_Toc130376337)

[2 Scope 3](#_Toc130376338)

[3 Responsibilities 3](#_Toc130376339)

[4 Definitions, terms, and abbreviations 4](#_Toc130376340)

[5 Workflow 6](#_Toc130376341)

[5.1 General 6](#_Toc130376342)

[5.2 Risk Assessment 8](#_Toc130376343)

[5.2.1 Risk Identification 8](#_Toc130376344)

[5.2.2 Risk Analysis 8](#_Toc130376345)

[5.2.3 Risk Evaluation 8](#_Toc130376346)

[5.3 Risk Control 8](#_Toc130376347)

[5.3.1 Risk Reduction 8](#_Toc130376348)

[5.3.2 Risk Acceptance 9](#_Toc130376349)

[5.4 Risk Review 9](#_Toc130376350)

[5.5 Documentation and Communication 9](#_Toc130376351)

[6 Applicable documents 9](#_Toc130376352)

[*7* Appendices 10](#_Toc130376353)

[8 Document revision history 10](#_Toc130376354)

# Purpose

The purpose of this Standard Operating Procedure (SOP) is to ensure the high quality and safety of final products by providing a systemic approach to Quality Risk Management and identify and control potential Risk throughout various stages of a product’s manufacturing lifecycle.

# Scope

This SOP is valid at Organisation Name for the whole Organization. The respective training shall be given in accordance with **SOP-10 Training Management**.

# Responsibilities

Responsible for the content of this SOP is e.g., Quality Management Director*.*

|  |  |
| --- | --- |
| **Role** | **Definition /Task** |
| Project Manager/Leads | * Work with Departments Leads to determine when a Risk Assessment is necessary * Ensure that this SOP is followed when carrying out a Risk Assessment * Assemble the project team and ensure the project team consists of experts of the Departments involved, SMEs, and individuals who are knowledgeable about Risk Management process and tools * Leading the Team and manage the Risk Management process including development, creation, and documentation of the Risk Management plan |
| Department Heads / Team Leads | * Control Risk for areas for which they have direct oversight / responsibility * Determine when a Risk Assessment is necessary |
| Quality Organization | * Provide guidance to the project team Management tools and techniques * Maintain and ensure compliance with procedure * File and retain related Risk Management records |

# Definitions, terms, and abbreviations

| **Term/abbreviation** | **Definition at Organisation Name** |
| --- | --- |
| Risk Priority Number (RPN) | A priority ranking for the actions to be implemented based on the severity, impact, and detectability. Each category is ranked from 1 to 3 with 3 being severe/critical and one being uncritical. The final RPN is calculated by multiplying the three factors. All items with RPN lower than 8 are considered acceptable, while 8-27 require some form of mitigation. |
| Corrective and Preventive Action (CAPA) | It is a systematic approach that includes actions required to correct, prevent recurrence, and eliminate the cause of potentially non-conforming products and other quality problems. |
| Detection | The means of Detection of the Failure mode by maintainer, operator or built-in Detection system, including estimated dormancy period (if applicable). |
| Failure cause and/or mechanism | Defects in requirements, design, process, quality control, handling or part applications, which are the underlying cause or sequence of causes that initiate a process (mechanism) that leads to a Failure mode over a certain time. A Failure mode may have multiple causes. |
| Failure effect | Immediate consequences of a Failure on operation, function or functionality, or status of some item. |
| Failure mode | The specific manner or way by which a Failure occurs. It is the result of the Failure mechanism (cause of the Failure mode) and should clearly state the end state of the failure. |
| Failure | The loss of an intended function of a product, equipment, system, devices, or processes under predefined conditions. |
| Fault Tree Analysis (FTE) | FTE is an approach that assumes Failure of the functionality of a product or process. This tool evaluates system (or sub-system) Failures one at a time but can combine multiple causes of Failure by identifying causal chains. |
| Failure Mode Effects Analysis (FMEA) | The FMEA is a design tool used to systematically analyze postulated component Failures and identify the resultant effects on system operations. It is a systematic, proactive method for evaluating a process to identify where and how it might fail and to assess the relative impact of different Failures, in order to identify the parts of the process that are most in need of change. |
| Occurrence | How often an event can occur, frequency. |
| Risk / Benefit Analysis (RBA) | RBA determines if the benefits of the new process/product or change to a process/product outweigh the overall Residual Risk. |
| Residual Risk | Residual Risk is the Risk that remains after all reasonable efforts to identify and eliminate some or all types of Risk have been made. |
| Risk | The combination of the probability of Occurrence of harm and the Severity of that harm. |
| Risk Acceptance | The decision to accept Risk, mostly an outcome of low-risk implications or preset mitigation strategies. |
| Risk Analysis | The estimation of the Risk associated with the identified hazards. |
| Risk Assessment | A systematic process of organizing information to support a Risk decision 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 |
| Risk Communication | The sharing of information about Risk and Risk Management between the decision maker and other Stakeholders. |
| Risk Control | Actions implementing Risk Management decisions. |
| Risk Evaluation | The comparison of the estimated Risk to given Risk criteria using a quantitative or qualitative scale to determine the significance of the Risk. |
| Risk Identification | The systematic use of information to identify potential sources of harm (hazards) referring to the Risk question or problem description. |
| Risk Management | The systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating and reviewing Risk. |
| Risk Reduction / Risk Mitigation | Actions taken to lessen the probability of Occurrence, the Severity of that harm or increase its detectability. |
| Risk Review | Review or monitoring of output/results of the Risk Management process considering (if appropriate) new knowledge and experience about the Risk. |
| Severity | The consequences of a Failure mode; Severity considers the worst potential consequence of a Failure, determined by the degree of injury, property damage, system damage and/or time lost to repair the Failure. |
| Stakeholder | Any individual, group or organization that can affect, be affected by, or perceive itself to be affected by a Risk. Decision makers might also be Stakeholders. For the purposes of this guideline, the primary Stakeholders are the patient, healthcare professional, regulatory authority, and industry. |
| Subject matter expert (SME) | A professional who has advanced knowledge in a specific field and can provide guidance and strategy. |

# Workflow

## General

This Risk Assessment process can be applied but is not limited to evaluation and decision-making regarding the implementation of or changes to the following:

* Drug product
* Active Pharmaceutical Ingredient (API)
* Packaging / Labeling
* Processes / Systems
* Operations
* Distribution
* Regulatory Inspection
* Validation
* Other decision making where Risk is inherent

Diagram, schematic

Description automatically generatedA Risk Management Process includes the following elements ([***Figure 1***](#_bookmark6)):

***Figure 1: Risk Management Process***

In preparation to perform the Risk Assessment address the following items upfront:

* Define the problem and/or risk question, including pertinent assumptions identifying the potential for risk;
* Assemble background information and/ or data on the potential hazard, harm or human health impact relevant to the Risk Assessment;
* Identify a leader and necessary resources;

Specify a timeline, deliverables, and appropriate level of decision-making for the risk management process.

## Risk Assessment

### Risk Identification

Risk Identification may come from Quality Organization, Project Leads or Department Heads / Leads.

In order to properly identify Risk, it is important to collect any relevant data that may help identify Risk including new or revised standards, nonconforming material reports, supplier’s CAPAs, product complaints, customer inquiries, service reports, historical data, informed opinions, etc.

**Step 1:** Determine key differences in the changed/new state (proposed) from a point of reference or the original state.

* *What might go wrong?*
* *How high is the probability / likelihood it will go wrong?*

**Step 2:** Focus on the possible effects of the key differences from Step 1.

* *What are the consequences?*

**Step 3:** How likely can the failure be detected?

Detailed instructions on the execution and risk scoring are part of **Failure Mode Effects Analysis (FMEA) Form**.

### Risk Analysis

Analyze the Risk associated with the problem by determining the likelihood and consequence of the identified Risks.

The ability to detect the harm should also factor into the estimation of Risk.

Several tools are available to perform Risk Analysis. Although not required, it is recommended to use a Failure Mode Effects Analysis (FMEA) for Risk Analysis (see **Failure Mode Effects Analysis (FMEA) Form**). Alternative methods are permissible as deemed suitable by the stakeholders. It is mandatory that alternative analysis also includes clear identification and evaluation of the risks, mitigation actions and strategies to control them, and a conclusion with an acceptance statement.

### Risk Evaluation

During the Risk Evaluation identified Risk is compared against a given Risk criteria. Depending on the Risk Priority Number (RPN) mitigation actions will be implemented. A verification to assess the acceptability of the remaining risk will be noted. In the case other evaluation methods are used the same principles apply, only without any reliance on the RPN.

## Risk Control

### Risk Reduction

After identifying the risks and applying RPN, the members of the Risk Assessment team decide on actions to mitigate the Severity of the Risk, probability of harm or to improve detectability. Mitigation actions may include, but are not limited to:

* appropriate work instructions and SOPs
* train operators on the new procedure or equipment (ensure documentation)
* restrict access or exposure
* qualify equipment, operators and validate procedures (e.g., cleaning, production process)

All proposed mitigation measurements shall be managed according to **SOP-07 CAPA Management** and reflected in associated Risk Assessment records for traceability.

### Risk Acceptance

Risk Acceptance can be a formal decision to accept the Residual Risk post mitigation actions.

## Risk Review

A Risk Review should be conducted to take into account new knowledge, experience, and events that may impact the original Risk Management decision. The frequency of any review should be based upon the level of Risk. Risk Review might include reconsideration of Risk Acceptance decisions.

## Documentation and Communication

When completed, the Risk Management plan should include:

* background information and context (e.g., the Risk environment);
* the scope of the change or project proposed;
* the scope of the planned Risk Management activities;
* the strategy for managing the Risks. Describe the approach, responsibilities (and assignments), activities, timelines, and tools;
* methodology of any Risk calculation tools, including Risk Severity, probability, and acceptability;
* risk analyses and all Risk Evaluation tools utilized (e.g., FMEAs, Fault Tree Analysis);
* review of the Risk Management plan by the Head of the Department impacted, and other relevant Stakeholders, as necessary and approval by Head QM;
* records demonstrating the implementation and verification of the Risk Control measures and/or the acceptance of Risk.

Upon completion, the approved Risk Management plan is forwarded to QM for filing and retention.

# Applicable documents

SOP-07 CAPA Management

SOP-10 Training Management

EMA/CHMP/ICH/24235/2006 ICH guideline Q9 on quality risk management

# Appendices

The following appendix is an integral part of this SOP:

Appendix Failure Mode Effects Analysis (FMEA) Form

# Document revision history

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| --- | --- | --- | --- |
| **Version** | **Valid from** | **Description of the revision** | **Reason for the revision** |
| 1 | See header | Document created | QMS implementation |