PROTOCOL FOR RISK ASSESSMENT OF PROCESS SIMULATION STUDY

PROTOCOL
FOR
RISK ASSESSMENT
& MITIGATION
OF
PROCESS SIMULATION
STUDY

Facility: PLANT

LOCATION:…….....

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1. Protocol Approval

This is a specific protocol for Risk assessment and Mitigation of Process Simulation Study which has to be carried out in Sterile Plant.

Prepared By:

Name	Designation	Department	Signature	Date

Checked By:

Name	Designation	Department	Signature	Date

Approved By:

Name	Designation	Department	Signature	Date

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2.0 Overview

2.1 Objective:

The Objective of this Protocol is to adopt a systematic process for the assessment, control, communication and review of risk associated with the Process Simulation study which is to be carried out in the sterile Plant …….

2.2 Purpose and Scope

The purpose of this Protocol is to outline a scientific and practical approach for decision making process by applying a suitable tool of risk assessment covering all aspects of risk associated with Process Simulation study.

2.3 Risk Assessment Team

- Production Executive/Officer/Manager
- Quality control Executive/Officer/Manager
- Projects Engineer/Sr. Engineer/Manager
- Maintenance Executive/Officer/Manager
- Quality Assurance Executive/Officer/Manager

2.4 Responsibility

S.No.	Department	Designation	Responsibility
1.	Production	Executive /Officer/ Manager	Review of Protocol & report To Provide the all relevant information that are required while undergoing Risk assessment process i.e. Quantity, Packaging etc.
2.	Quality control	Executive /Officer/ Manager	Review of Protocol & report To provide information about the availability of Analytical methods Pharmacopeia reference and finally reviewing the testing procedures
3.	Maintenance	Executive /Officer/ Manager	Review of Protocol & report To assist the risk assessment team about the technical queries of facility & equipments
4.	Projects	Executive /Officer/ Manager	Review of Protocol & report To assist the risk assessment team about the technical queries of facility & equipments & also provide provisions for further reduction of associated risk with facility & operations

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S.No.	Department	Designation	Responsibility
5.	Quality Assurance	Executive /Officer / Manager	Preparation of Protocol & report To review all the Procedural controls both in-house and vendor To conduct audits to assess the quality management system and manufacturing facility Final approval of Protocol & report By head quality Assurance

3. Introduction:

Risk analysis for Process Simulation study shall be done by considering the below mentioned factors

- The Risk Impact on the Process
- The Risk impact on the Process Equipment
- The Risk impact on the Aseptic Environment of the Plant
- The Risk impact on the Product Quality & Sterility
- The Risk impact on the regulatory compliance
- The Risk impact on customer

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4. Quality Risk Management Process

Risk assessment is a systematic process of organizing information to support a risk decision to be made within a risk management process. Its consists Identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards

Quality risk assessment begins with a well defined problem description or risk question.

For risk assessment process three fundamental questions are considered

- What might go wrong?
- What is likely hood **(Occurrence)** it will go wrong?
- What are the consequences **(Severity)?**

- **Risk Identification**

  Risk Identification is systematic use of information to identify hazards referring to risk questions or problem description. Information may include historical data theoretical analysis, informed opinions and concerns of stakeholders. Risk Identification will be conducted by reviewing the types of events that might occur in both normal and unusual situations. This may be done by challenging the normal presumptions, and considering the possibilities of unanticipated situations. For each risk event, the underlying (root) cause should be determined that will create the potential risk occurrence.

  Risk Identification addresses the "what might go wrong" question including identifying the possible consequences. This provides the basis for the further steps in quality risk management process.

- **Risk Analysis**

  Risk analysis is the estimation of risk associated with the identified hazards.

  It is the quantitative or qualitative process of linking the likelihood of occurrence and severity of harm and sometime the detectability of harm is also consider during estimation of risk.

- **Risk Evaluation**

  Risk Evaluation compares the identified and analyzed risk against the given risk criteria. Risk evaluation considers the strength of evidence for all three of fundamental questions. Risks are ranked by scoring various criteria with appropriate numerical ratings, adding to scores to determine the overall score of each risk, and sorting the risks into descending order based on each score. A risk scoring threshold is established, over which risks must be mitigated using adequate design and/ or process controls that will protect the system. Those risks that fall below the threshold are either unmitigated or scheduled for later mitigation. An additional threshold or characteristic of risk can be used to determine the differentiation of non- mitigation versus postponed mitigation.

- **Risk Control**
  Risk control includes decision making to reduce or mitigate risk. The purpose of risk control is to reduce the risk to the acceptance level
  The risk control is done by considering the following question
  - Is the risk above an acceptable level?
  - What can be done to reduce or eliminate risk?
  - What is appropriate balance among benefits, risks and resources?
  - Are new risk is introduced as a result identified risk being controlled?
- **Risk Reduction**
  Risk reduction focuses on processes the mitigation or avoidance of quality risk when it exceeds the acceptable level. Risk reduction includes action taken to mitigate the severity, occurrence or probability of harm and the processes that improve the detectability of harm. It is the part of risk control strategy and involves
  - Engineering Control
  - Procedural Control
  - Manual control etc.

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5.0 Risk Assessment for Process Simulation Study

5.1 Risk Assessment Legend

A. Severity

Ranking	Effect	Criteria
10	Hazardous	Hazardous effect without warning. Safety related. Regulatory non-compliant.
9	Serious	Potential hazardous effect. Able to stop without mishap. Regulatory compliance in jeopardy.
8	Extreme	Item inoperable but safe. Customer very dissatisfied.
7	Major	Performance severely affected but functional and safe. Customer dissatisfied.
6	Significant	Performance degraded but operable and safe. Non-vital part inoperable. Customer experiences discomfort.
5	Moderate	Performance moderately affected. Fault on non-vital part requires repair. Customer experiences some dissatisfaction.
4	Minor	Minor effect on performance. Fault does not require repair. Non-vital fault always noticed. Customer experiences minor nuisance.
3	Slight	Slight effect on performance. Non-vital fault notice most of the time. Customer is slightly annoyed.
2	Very Slight	Very slight effect on performance. Non-vital fault may be noticed. Customer is not annoyed.
1	None	No effect.

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B. Probability or Occurrence

Ranking	Possible Failure Rates	Probability of Failure
10	≥ 1 in 2	Almost certain
9	1 in 3	Very high
8	1 in 8	High
7	1 in 20	Moderately high
6	1 in 80	Medium
5	1 in 400	Low
4	1 in 2,000	Slight
3	1 in 15,000	Very slight
2	1 in 150,000	Remote
1	1 in 1,500,000	Almost impossible

C. Detection

Ranking	Detection	Likelihood of Detection by design control
10	Absolute Uncertainty	No design control or design control will not detect potential cause
9	Very Remote	Very remote chance design control will detect potential cause.
8	Remote	Remote chance design control will detect potential cause.
7	Very Low	Very low chance design control will detect potential cause.
6	Low	Low chance design control will detect potential cause.
5	Moderate	Moderate chance design control will detect potential cause.
4	Moderately High	Moderately high chance design control will detect potential cause.
3	High	High chance design control will detect potential cause.
2	Very High	Very high chance design control will detect potential cause.
1	Almost Certain	Almost certain that the design control will detect potential cause.

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5.2 Risk Assessment Tool – Failure Mode effect Analysis (FMEA)

5.2.1 Risk Identification

Risk assessment team shall identify all possible failure modes of Process simulation Study by reviewing the various aspects of facility design & operational features, Provisions and Adopted procedures. The risk identification involves three aspects

1. **Identification of Failure Mode of Process simulation study**
    a. Failure of Equipment
    b. Failure of Process
    c. Failure of Provisions
    d. Failure of Procedures etc.

2. **Identification of Potential cause**
    a. Operator Error
    b. Equipment Malfunctioning
    c. Instrument malfunctioning
    d. Non availability or Non rational Procedures
    e. Inefficient Provisions for operations etc.

3. **The consequences i.e. End results of failure mode**
    The failure Mode may leads to
    a. Poor process Performance
    b. Poor Product Quality
    c. Deterioration of Aseptic conditions required for sterile manufacturing
    d. Regulatory non compliance
    e. Unsafe operating conditions
    f. Unsafe environmental conditions etc.

4. **Justification**
    The identification done for the risk shall have scientific rational and must be justified for its validity. The below mentioned table shall be used for Risk Identification process.

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Justification
	Risk Identification			

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5.2.2 Risk Analysis

Risk Analysis is the second step of risk identification Process. It involves the assessment of the

1. Severity of the Consequence of failure Mode
2. The Probability or Occurrence of Failure mode by reviewing effectiveness of the existing Design control
3. The its detectability under the existing design control

Base upon the analysis Risk priority number will be assigned to the particular failure Mode as per the formula

RPN = Severity X Occurrence X Detection

Each index ranges from 1 (lowest risk) to 10 (highest risk). The overall risk of each failure is called Risk Priority Number (RPN) and the product of Severity (S), Occurrence (O), and Detection (D) rankings: RPN = S × O × D. The RPN (ranging from 1 to 1000) is used to prioritize all potential failures to decide upon actions leading to reduce the risk, usually by reducing likelihood of occurrence and improving controls for detecting the failure

The below mentioned table shall be used for Risk Analysis process.

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Severity	Probability	Detection	Risk Priority Number	Existing Design Control
				(S)	(P)	(D)	RPN=S x P x D	
	Risk Analysis						Risk valuation	

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5.2.3 Risk Reduction or Mitigation

The Risk Reduction or Mitigation is the Third step of Risk assessment process. if the Existing design control cannot lead the risk priority number to the acceptable level then additional design control shall be worked by providing

1. New or Improved Provisions or Procedures
2. Modification in the existing facility design
3. Additional resources
4. Improved control strategy etc.

The additional design control shall be appropriately worked out to reduce the risk to its acceptable level. The below mentioned table shall be used for the Risk Reduction or Mitigation process

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
							RPN=S x P x D					**RPN=S x P x D**

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5. Acceptance Criteria:

The Risk Priority Number shall be within the range 0<RPN<100

6. Risk Control Strategy:

S.No.	Risk Priority Number	Risk Decision	Risk control strategy
1	0<RPN<100	Risk Acceptable	No control is required
2	100<RPN<500	Risk Reduction	Additional Procedural Control
			Manual Control
			Documentary Evidence
3	500<RPN<1000	Risk Reduction	Rugged Procedural control
			Additional Manual Control
			Auditing
			Engineering controls (if Possible)

7. Report Preparation and Approval

The report shall be prepared by evaluating all possible risks and finally shall be approved by Quality Assurance head

8. References:

1. Risk Management Master Plan
2. ICH Q9