International Research Journal of Education and Technology
ISSN 2581-7795

ICH Q9-Basics Quality Risk Management approach in Qualification of Pharmaceutical Equipments: A Review

[1]Dr. Shiba Morris, [2] Ms. Arati Tamta and [3] Mr. Munish Sharma

[1] Associate Professor, Pharmaceutical Quality Assurance, Gyani Inder Singh Institute of Professional Studies, Dehradun, Uttarakhand India,

[2]Assisstant Professor, Pharmaceutical Quality Assurance, Gyani Inder Singh Institute of Professional Studies, Dehradun, Uttarakhand India

[3]Research Scholar, Pharmaceutical Quality Assurance, Gyani Inder Singh Institute of Professional Studies, Dehradun, Uttarakhand

----------***----------

Abstract - The aim of the present work is to identify and evaluate the risk factor involved in Qualification of PLC operated System and to provide risk mitigations. Risk assessment involved various tools and techniques to identify, evaluation communication and control techniques to minimize affect of risks related to the safety, quality, reliability or durability of a product to be processed in PLC operated conta blender and to get maximum benefits & compliance of cGMP from PLC system.

Risk assessment approach in qualification of PLC Operated Cont blender includes operational parameters & others functions of equipment which may have impact on patient safety, product quality and data integrity. The scope of this document is to identify the Risk involved in qualification of PLC operated conta blender.

The advantages of risk assessment leads to providing assurance and documented evidence that equipment will perform as per predefined parameters and produce same results during every operation and developing suitable control systems in the PLC operation procedure of conta blender.

The goal of Risk assessment is to determine the criticality of the system to the process (with respect to product efficacy or patient safety.

Risk assessment based qualification approach provide assurance & acceptance criteria for the PLC Control system & its supporting automation that "Conta Blender (1200 Ltrs)" installed will perform as per quality & cGMP procedure in the processing environment. & control system

Risk is the combination of the probability of occurrence of harm & the severity of that harm.

Keywords: Quality Risk Management, Risk- based approach, Patient safety, and Product quality.

1.INTRODUCTION

Quality risk management in the pharmaceutical sector is used widely in various compliances and operations but still it is limited in usage & there is a lot of scope for utilization of risk management techniques & tools in equipment & process qualification. In addition, the application of quality systems has been understood by pharmaceutical regulators and it has become a statutory guidance as per ICH, FDA, EMA & other regulatory authorities.

Risk may be defined as the severity & probability of any harm that might occur due to result of failure.

However, it is difficult to give a single definition for risk due to different understanding of every human being. Risk factors are evaluated differently by every evaluator. Each stakeholder uses his own perception for potential harms; give a unique probability for harm that might happen. It results in different attribute for severity for every harm. For pharmaceuticals, there are various stake

holders e,g Regulatory agencies, Marketing agencies, Industry owners, patients and medical practitioners. The main purpose of QRM principles are the safety & efficacy of medicines.

The medicinal products, supplements, always go through some quantum of risk. Product quality should be taken into consideration throughout the product lifecycle & all critical product quality must be evaluated & remain consistent till expiry of shelf life.

Additionally, quality risk management provides better decision making process during any quality concerns. Rational decisions provide regulators a better assurance of a organization's ability to handle potential quality risk .[1,3]

It is not mandatory to use a guided risk management tools and systems. The informal risk management processes using internal methods are also acceptable. Applying quality risk management system does not guarantee regulators obligation to comply with set standards. It does not replace inspection requirements & other relevant communications between medicinal manufacturing industry and pharmaceutical regulators.

Principles of Quality Risk Management [1,2]

Four primary principles of QRM are:

1. Scientific &
2. Patient safety.
3. Rational oriented.
4. Properly Documented

3. Control,
4. Communicate
5. Review of risks .[4,5]

General Quality Risk Management Process

1. Risk Management is:
2. Scientific process to evaluate,

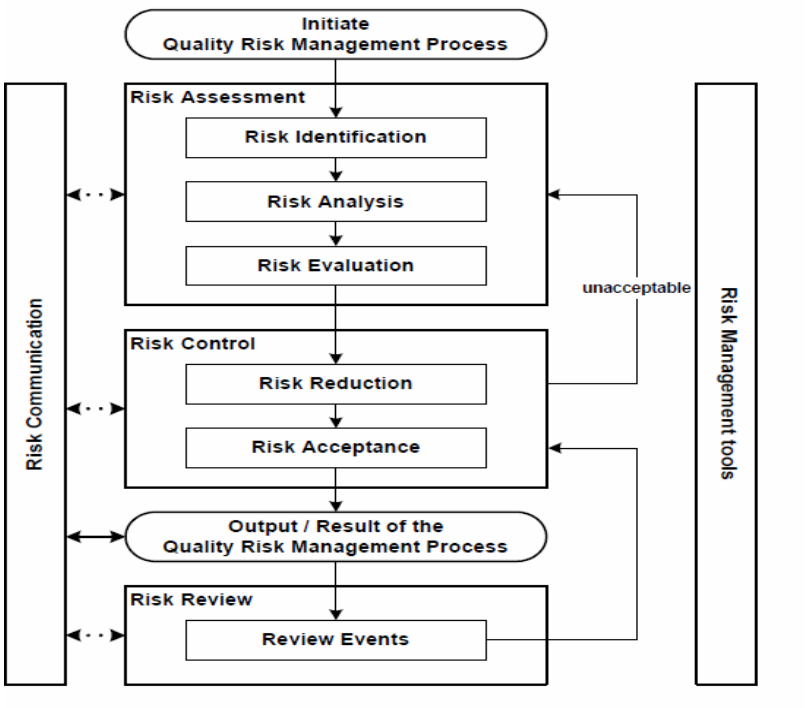


Figure 1: Overview of a typical Quality Risk Management process [1]

Initiating a Quality Risk Management Process

Risk Assessment

Risk assessment should include Following:

1. risk identification,
2. Risk analysis and
3. Risk evaluation.[5]

Basic theory of risk assessment.

4. What might go wrong?
5. How much probability to go wrong?
6. What are the consequences if go wrong?

Risk identification involved

1. Information to identify hazards w.r.t to risk. E.g. History trend of failure, Operational breakdown.
2. Risk identification includes "What might go wrong?" question, evaluating possible hazards.

Risk analysis involved

1. Ability to identify hazards.
2. Probability of occurrence.
3. Severity of hazards.

Risk evaluation involved

1. Comparison of risk as per risk criteria & Relevance of evidence.

Steps Involved In the Risk Assessment [5,6]

1. Collect & organize the information.

- Collection of information,
- Review of reference documents & identify assumptions based aproaches.
- Utilization of Tools to scrutinize the information.
- Setting of limits of the risk management

2. Risk Question:

- outline the risk
- Identification of risk factors
- Severity of the issue.

3. Choose Tool different tools include-

- Basic risk management (flow diagrams, check point).
- Failure Mode Effects Analysis
- Failure Mode Effects and Criticality Analysis.
- Fault Tree Analysis.
- Hazard Analysis and Critical Control Points.
- Hazard & Operability Analysis.
- Preliminary Hazard Analysis.
- Risk Ranking & Filtering.
- Supporting statistical tools.

4. Identification of involved all Risks Factors and Hazards related to safety of the patient.

5. After hazards reorganization: Classify them as: Man/Machine/Material/Method
6. Define the Risk Components &give them ranking[s][4]

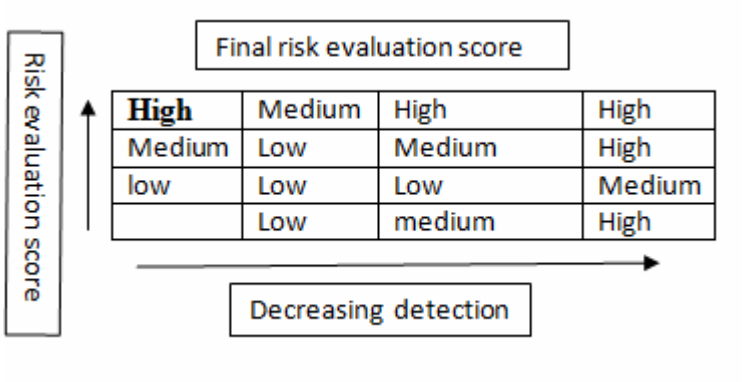
RISK = PRIORITY * DETECTABILITY * SEVERITY

Severity means Criticality of failure w.r.t product quality.

Priority means Complexity of process understanding

Detection - Identification or history.

International Research Journal of Education and Technology
ISSN 2581-7795



7. Evaluation of risk for each hazard.
8. Determine acceptance & mitigation of risks[6,7]

9. Setting of Action limits.

- A level or value above for action requirement..

10. Apply the tool

- Analyze the risks
- Quantify risks as per levels for severity, probability and detection to get the risk score.

➢ Conclude actions requirements as per risk score..

Risk Control

Risk control includes:

- Decision making to downgrade risk .
- Application of control systems to reduce risk to significant acceptable level. [12,13]

Risk control shall involved following points :

➢ What is risk acceptable level?
➢ What actions required for reduce or eliminate risks?
➢ What are the benefits, risks and resources?
➢ Are new risks introduced to system by controlling previous risks?

Risk reduction Involves:

1. Efforts to reduce harmful events of risks.
2. Lowering down the risk by implementation of appropriate tools.
3. Evaluation of process to identify new evolved risks.

Consider measures/actions that could:[6]

1. Reduce the severity

➢ Identify failure modes &take significant precautions to avoid reject, recall

2. Reduce the probability

➢ Inspect the defect in every batch to reduce Quality complaint

3. Increase the detection

➢ By use of automated systems for better control.

Risk acceptance includes

1. Decision for accepting those risk which are not possible to eliminate completely..

Risk Review includes

1. Risk review involve reconsideration of risk acceptance decisions

Risk Communication includes

1. Risk Information sharing must be done through proper communication channel and properly documented.

Discussion

Table 1: Common Risk Management Tools[2]

Risk management tool	Description/attributes	Potential applications
Basic tools		
Diagram analysis Flowcharts Check sheets Process mapping Cause/effect diagrams	organize data, structure RM processes facilitate decision making	Compilation of observations,
Risk ranking and filtering	Method to compare and rank risks	Prioritize operating areas or sites for audit/assessment diverse and difficult to compare using a single tool
Advanced tools		
tree analysis (FTA)[8]	identify all root causes failure or problem process understanding to identify causal factors	Investigate product complaints Evaluate deviations
Hazard operability analysis (HAZOP)[9]	identify potential deviations from normal	Access manufacturing processes, facilities and equipment Commonly used to evaluate process safety hazards
Failure modes effects analysis (FMEA)[10]	Assesses potential failure Output is a relative "riskscore" for each failure mode	Evaluate equipment and facilities;

Conclusion

The principal purpose of this document is to identify and evaluate the risk factor of PLC System and also provides its mitigations. The purpose of the risk assessment is to minimize affect the safety, quality, reliability or durability of a product and to get maximum benefits of cGMP from PLC system.

PLC system provides basic operational control to conta blender and also provides assurance that all programmable logics will perform as per their intended functions.

Risk assessment will help in identification of possible risk associated with Qualification of Conta blender and identification of failure associated with those risks. A proactive mitigation plan during qualification will prevent and control reoccurrence and eliminates the chance of failure during commercial manufacturing.

References:

1. Guidance for industry "Q9 Quality Risk Management" by US department of Health and Human Services, Food and drug Administration, Center for Drug and Evaluation Research, June 2006.
2. WHO Guideline on Quality Risk Management A draft guidance August 2010.

3. Implementation of ICH Q9 in the pharmaceutical field an example of methodology from PIC/S 2010.
4. Prashant kumar katiyar-International journal of pharma world research(an international quarterly pharmaceutical research journal) risk analysis and risk management in pharmaceuticalindustry prashantkumarkatiyarvol 1 2010.
5. Risk assessment and quality control by By Max Williams, MPA, November 2012.
6. Quality Risk Management- the pharmaceutical experience ann'omahony 11 november 2011.
7. kelvin CPharmaceutical engeneeringvol 28 no 3 GAMP 5- A Quality Risk Management Approach may/june 2008.
8. *Health and Safety Briefing*, Fault Tree Analysis, Pg. No. 26, Dec. 2006.
9. *IEEE Xplore*, Data Management Tool for Aiding the Hazard and Operability AnalysisProcess, Page(s):1 – 4, Aug. 2006.
10. Failure Mode and Effect Analysis: *FMEA from Theory to Execution*, D. H. Stamatis.2nd Edition 2003.
11. WHO Technical Report Series No. 908, 2003, Application of Hazard Analysis andCritical Control Point (HACCP) methodology to pharmaceuticals.
12. Risk Management: Guidelines and Best Practices Missouri Information Technology Advisory Board Project Management Committee Risk Management Subcommittee November 2003.
13. Risk Management - Vocabulary - Guidelines for Use in Standards, Internationalorganization for standardization, Jan 1, 2002.
14. International Organization for Standardization. ISO 14971:2007 Medical devices - application of risk management to medical devices. www.iso.org.