

*Review article***Quality Risk Management (Q9): An Overview****Abhishek Maithani***, Kumar Gaurav*Department of Pharmaceutics, Guru Gobind Singh Khalsa College of Pharmacy, Yamunanagar 135001 Haryana, India.***ARTICLE INFO:****Article history:**

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ABSTRACT

The goal of the CGMPs for the 21st Century initiative such as advancing science and technological innovation. Update guidance based on regulatory experience since 1987. Quality Risk management emphasizes on risk management and maintaining quality during commercialization. Quality Risk management also emphasizes the role of objective measures and statistical tools & analyses and emphasizes knowledge, detection and control of variability and gives assurance on consistent of quality/productivity throughout life cycle of product.

1. Introduction

Quality risk management is integral to an effective pharmaceutical quality system. It can provide a proactive approach to identifying, scientifically evaluating, and controlling potential risks to quality. It facilitates continual improvement of process performance and product quality throughout the product lifecycle. ICH Q9 provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality. Quality is degree to which a set of inherent properties of a product, system, or process fulfills requirements, Risk is the combination of the probability of occurrence of harm and the severity of that harm, and risk management is the systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating, and reviewing risk[1].

2. Scope

This guidance provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality. These aspects include development, manufacturing, distribution, inspection, and submission/review processes throughout the lifecycle of drug substances, drug products, biological and biotechnological products (including the use of raw materials, solvents, excipients, packaging and labeling materials in drug products, biological and biotechnological products).

3. Principles of quality risk management

Two primary principles of quality risk management are:

- The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient.
- The level of effort, formality, and documentation of the quality risk management process should be commensurate with the level of risk.

4. Quality risk management process

Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the drug product across the product lifecycle. A model for quality risk management is outlined in the diagram (Figure 1). The emphasis on each component of the framework might differ from case to case but a robust process will incorporate consideration of all the elements at a level of detail that is commensurate with the specific risk.

4.1 Initiating a quality risk management process

Quality risk management should include

- Define the problem and/or risk question, including pertinent assumptions identifying the potential for risk

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- Assemble background information and/or data on the potential hazard, harm or human health impact relevant to the risk assessment
- Identify a leader and critical resources
- Specify a timeline, deliverables, and appropriate level of decision making for the risk management process[2].

4.2 Assessment of risks

Evaluate the following measures for their effectiveness • Working personnel and their threat to product quality

- Equipment and there threat to product quality
- Facility/ utilities and their threat to product quality.
- Environment control and their threat to product quality.
- Materials and their threat to product quality.
- Methods and procedures and their threat to product quality.
- Any change taking place in facility, system, equipment, utilities, process, methods, supply chain and documentation.
- Evaluate existing control measures for their effectiveness.

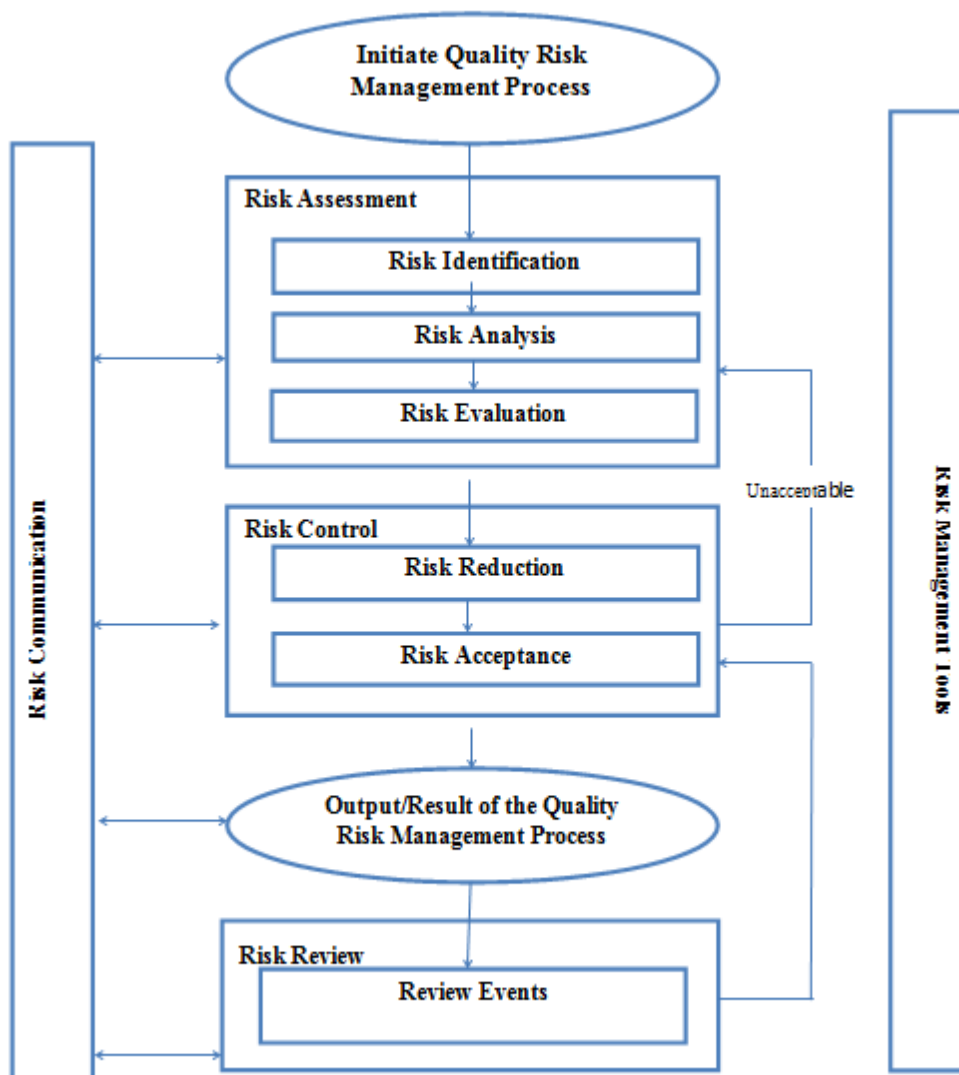


Figure 1: Model for quality risk management

4.3 Identification of threats

The risk assessment shall be conducted by a multi-discipline team and the composition of the team shall depend on the nature of the topic that is being risk assessed. The risk assessments undertaken with respect to equipment, facility, procedure, material, process and environment are some of examples of quality risk management.

To identify the threats the following points should be considered.

Personnel: Training, Education Competence, reporting relationship communication, tampering theft and substitution.

Equipment: Type design, condition, capability, location, installation, operation, maintenance and calibration. It refers to the design specification.

Facilities: Site lay-out, utilities, maintenance, dedication and hygiene.

4.4 Methods and procedures

Checking, Content, alterations, distribution, utilization, condition, change control, storage, trends, handling planned preventive maintenance and breakdowns care must be taken while preparing the validation protocols and any major change applied to the system considering the safety aspect to minimize the risk.

4.5 Materials

Identity, Status control, Quality, handling, specifications, security arrangements, counterfeiting control and material condition.

4.6 Environments

Physical effect of climatic and storage conditions (temperature, time, humidity, rain, light, vibration), pest infestation, cross-contamination and damage by fire or flood.

4.7 Identify the GXP risk (X-warehouse, manufacturing and laboratory)

A system functions or sub-function shall be assessed against a series of GXP criteria that are appropriate to the steps it performs or processes it impacts on:

Material managements:

- Raw and packing materials error
- Labeling errors
- Handling errors
- Storage errors

Process:

- Equipment functionality
- Facility
- Process parameter
- Batch/ Lot traceability

- Batch status
- Labeling error
- Quality of in-process or finished products
- Handling error
- Storage condition

Quality control:

- Receipt of samples and integrity
- Facility of each area wet area, instrumentation area, stability area etc.
- Environmental condition
- Operation and calibration errors
- Training
- Manpower
- Stability of solutions and others

4.7 Risk analysis

Risk analysis is the estimation of the risk associated with the identified hazards. It is the qualitative or quantitative process of link among the likelihood of occurrence and severity of harms. In some risk management tools, the ability to detect the harm (detectability) also factors in the estimation of risk.

4.8 Risk evaluation

Risk evaluation compares the identified and analyzed risk against given risk criteria. The risk to product quality is a function of consequences and likelihood of the threat. A judgment should be made on the severity of the consequences and the likelihood of the adverse event occurring, taking in to consideration any current measures that are in place each of these can be identified low, medium and high. The source of severity shall be assessed by probability and detectability of risk. The following approaches shall be followed.

A. Assign severity

- High severity – Event that is expected to have a very significant negative impact. The impact shall have significant long term effects and potentially catastrophic short term effects.
- Medium severity – Event that is expected to have a moderate impact. The impact shall have short to medium term detrimental effects.
- Low severity – Event that is expected to have a no impact.

B. Assign severity of occurrence

- High Probability – Fault event is perceived to be highly likely.
- Medium Probability – Fault event is perceived to be reasonably likely.
- Low Probability – Fault event is perceived to be Unlikely.

Addressing the risk class: Risk class shall be defined based on the severity and probability of risk. Priority to address the risk class shall depend on the detectability level and risk class.

C. Assign Detectability

- High Detectability – Fault event is perceived to be highly likely. High Detectability will lower the risk.
- Medium Detectability – Fault event is perceived to be reasonably likely.
- Low Detectability – Fault event is perceived to be low. Low Detectability will increase the risk.

4.9 Risk control

Risk control includes decision making to reduce and/or accept risks. The purpose of risk control is to reduce the risk to an acceptable level. The amount of effort used for risk control should be proportional to the significance of the risk. Decision makers might use different processes, including benefit-cost analysis, for understanding the optimal level of risk control.

5.0 Assign Risk Priority

- High – Equipment that has direct impact on product and its failure leads to product failure and loss.
- Medium – Equipment that has direct impact on product and its failure may leads to product failure and loss.
- Low – Equipment that may have some impact on product quality attributes and may not leads to product failure and loss.

5.1 Risk communication

- Risk communication is the sharing of information about the risk and risk management between the decision makers and others.
- Department Shall Communicate At Any Stage of The Risk Management Process.
- The output / result of the quality risk management process should be appropriately communicated and documented.
- Communication might include those among interested parties e.g.-regulatory and industry with in a company, industry or regulatory authority, etc.
- The included information might relate to the existence, nature form probability severity acceptability control treatment detectability or other aspects of risk to quality.
- Communication need not be carried out for each and every risk acceptance, but based on the severity and if resulting into

quality issue, then it is to be communicated to external body/ Customer.

- Communication conserving quality risk management decisions might be affected through existing channel as specified in regulation and guidance between the industries and regulatory authorities.

5.2 Risk review

The output/results of the risk management

Process should be reviewed to take into account new knowledge and experience. Once a quality risk management process has been initiated, the process should continue to be utilized for events that might impact the original quality risk management decision, whether these events are planned (e.g., results of product review, inspections, audits, change control) or unplanned (e.g., root cause from failure investigations, recall).

5.3. Risk management tools[3-5]

- Basic risk management facilitation methods (flowcharts, check sheets, etc.)
- Failure Mode Effects Analysis (FMEA)
- Failure Mode, Effects, and Criticality Analysis (FMECA)
- Fault Tree Analysis (FTA)
- Hazard Analysis and Critical Control Points (HACCP)
- Hazard Operability Analysis (HAZOP)
- Preliminary Hazard Analysis (PHA)
- Risk ranking and filtering
- Supporting statistical tools

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