Tools of Assurance : A Comprehensive Review on Quality Risk Management

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Abstract- *In the dynamic landscape of pharmaceutical industry , Quality assurance plays an important role in ensuring quality, safety , efficacy of the products as it is a continuous process various approaches can be employed to support this process and the primary goal of the quality assurance is to mitigate the risks in the industries and to deliver a product that meets customer expectation and satisfaction .*

This review article systemically explores the strategies and the tools used to mitigate the risks as Quality risk management in industry is a proactive and systematic approach that helps organizations understand, manage, and mitigate potential risks. It contributes to the overall welfare of the organization .

Quality risk management is interconnected with the regulatory requirements as it serves as an approach in ensuring product quality, patient safety and compliance with the industry standards. This study aims to provide an overview of risk management strategies, tools within pharmaceutical industries .

Keywords- Pharmaceutical industry, Quality assurance , Quality risk management .

I. INTRODUCTION

Quality assurance is defined as the concept covering all the aspects that influences the quality of product. Quality assurance ensures that the pharmaceutical products possessing the required quality is designed, developed, manufactured and are distributed and this provides a way to prevent defects and mistakes during drug product design,development, manufacturing, to ensure that the medicinal products meeting all the defined quality characters are produced and delivered to the patients .

Fig-1 QA, risk management pathway

Inadequate quality assurance cause economic risks to a company ,and it can also lead to loss of business, liability, productivity and increased expenses, and loss of reputation of the company . hence quality assurance is an important department in the pharmaceutical industries that includes describing the activities, reviewing the process, documentation , risk management and thus shows an impact on the business performance and deliver products that meet satisfaction and expectation of the customers .

Quality Risk Management : The international council for harmonization of technical requirements for pharmaceuticals for human use [ICH] Q9 [R1] deals with the quality risk management. The main purpose of this document is to provide the systemic approaches, strategies, tools used for the risk management .

Definitions :

- **Risk**-according to ICH risk is defined as the combination of the probability of occurrence of harm and severity of that harm .

- **Quality risk management(QRM)**- is defined as the systematic process for the control ,communication, assessment and review of the risks to the quality of drug product throughout the product life cycle .

Scope:

The scope of quality risk management is not only to produce a quality product but also to ensure its safety , efficacy parameters of the drug .this can be achieved by maintaining the standards following guidelines as per the regulatory requirements .the risk management is to be employed from the initial stages such as development, manufacturing, quality control , quality assurance , packaging , distribution .

Principle [2] :

The basic principles of quality risk management are

- The assessment of risk based on scientific knowledge
- Risk management should be a dynamic , iterative and responsive to change
- Documentation , level of efforts should be proportional to the level of risk
- QRM should be a continuous process.

General Quality risk management process [1,3] :

The QRM is a systematic process for evaluation, control, communication, and review of the risk to the quality of the drug product across the product life cycle and the different steps in QRM are as follows

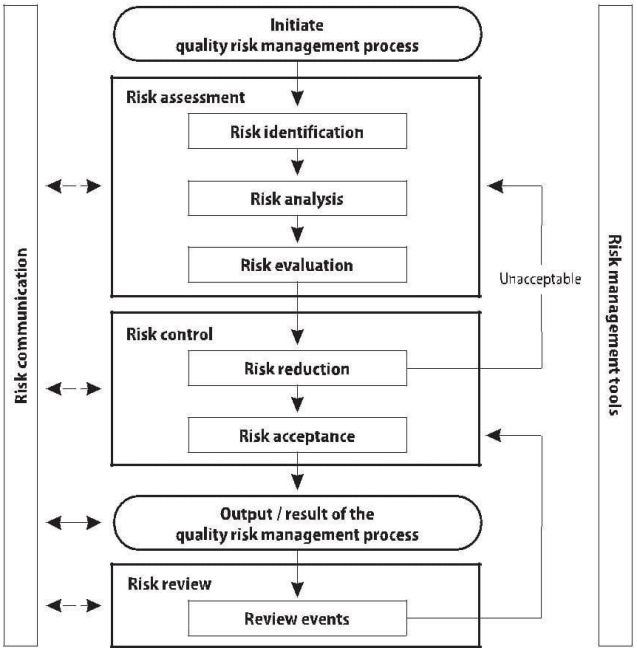

FIG-2 overview of typical quality risk management process[1]

- **Intiaite quallity risk management :**

Quality risk management should include process that can improve the decision making with respect to the risk associated and poaaible steps usd to intiate and plan a quality risk mangement process and must include the following

- Define the problem and identify the potential for risk
- Segregation of the background information on the hazard or risk
- Identify leader and necessary resounrses
- Appropriate decision making for the risk mangement .

- **Risk assessment :**

In this step identification of the hazards and the analysis and this can be achieved with a well -defined problem description or risk question such as

1. what might go wrong ?
2. what will the probability it will go wrong ?
3. what are the consequences of the risks ?

I. **Risk identification :**

Is the use of information to identify the risks this information icludes historiccal data , theortical data and this provides the basis for the further prcess .

II. **Risk analysis :**

It is the qualitative or quantitative process of linking the probability of occurance and sevrity of harms and the ability to detect the risk also factors in the estimation of risk .

III. **Risk evaluation :**

Compares the identified and analyzed risk against the given risk criteria and its considers the strength of evidence for all the fundamental questions .alternatively ,someof the risk evaluating tools use a relative risk measure to combine multiple levels of severity and its probability into an overall estimate of relative risk .

		SEVERITY OF HARM		
		LOW	HIGH	MEDIUM
Likelihood	HIGH	3	4	5
	MEDIUM	2	3	4
	LOW	1	2	3

Fig.3 Risk assessment table

- **Risk control :** this includes the decision-making process in order to reduce or to accept the risk .the purpose of the risk control is to reduce the risk to an acceptable level ;the amount of the efforts should be commensurate with the significance of the risk the decision makers make utilize of the benefit cost analysis for a better risk control .

I. **Risk reduction :** this includes the actions taken to mitigate the probability and severity of the risk .the implementation of new risk reduction plans may have a chance to increase the exiting risks or introduce the new risks so before implementing a new approach the plan has to be evaluated .

II. **Risk acceptance :** a decision to accept the risk .in regarding to some types of risks that cannot be reduced completely even after using advanced risk management techniques so , in that circumstances the risk has to be accepted at a particular level . the level of specific acceptable range will depend upon the parameters and decision is based on the cases .

- **Output/ result of quality risk management :** After execution of the quality risk management process the relevant data, information, facts and outcomes including acceptable or reducible decision all these have to be documented and approved by the decision makers [4].
- **Review events :** The risk management is an ongoing process in quality management system a proper mechanism has to be employed. The results has to be reviewed to take in account new knowledge and experience and the frequency of the risk review should be based on the level of the risk and should also include re-considerations and risk acceptance decisions[5].
- **Risk communications :** This is the sharing of information regarding the risk and risk management between the decision makers and others. The information may include about existence, nature, form, probability, severity, detectability and aspects of the risks. The communication need not be carried out for each and every risk acceptance between the industry and regulatory authorities[6].
- **Risk management tools:** The main motto of quality risk management is to reduce the risks. As of now advanced technologies, strategies are being used in mitigation of risk as in olden days. The traditional methods were employed for the risk mitigation process such as:

- Manual investigations
- Paper based documentation
- Limited data analytics
- Regular inspections

As the pharmaceutical industry is gradually evolving with increased interest so advanced tools and technologies are used for risk management process such as follows

- Basic risk management methods
- Failure mode effects analysis [FMEA]
- Fault tree analysis [FTA]
- Hazard analysis and critically control points [HACCP]
- Hazard operability analysis [HAZOP]
- Risk ranking and filtering
- Supporting statistical tools.

1. **Basic risk management methods:** Some of the basic techniques used in risk management are flowcharts, check sheets, process mapping, cause and effect diagram [Ishikawa diagram or fish bone diagram]

   - Flowcharts - This method allows for dynamic process to be represented on a paper and generally uses graphical and sequential process in risk identification.
   - Cause and effect diagram[7] - is also known as the Ishikawa or fishbone diagram. The design of this diagram looks like a skeleton of fish. Fishbone diagrams are from the right to left, with each large bone of the fish containing smaller bones containing more detail. Used to identify the problems, workout major problems

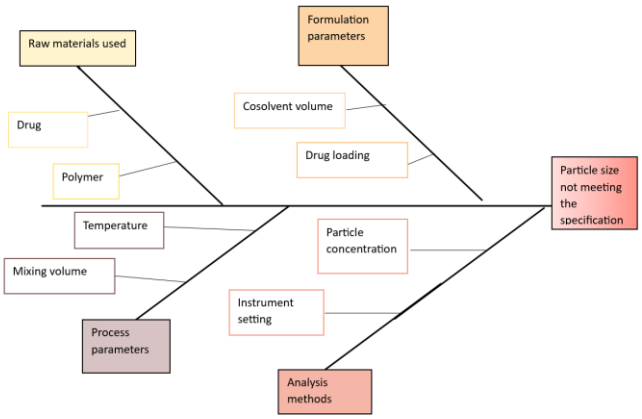

Fig.4Example of Ishikawa diagram in root cause analysis of risk

2. **Failure mode effect analysis [FMEA] [1,8]:** Is the most widespread universal accepted risk management concept. This method breaks down the analysis of the complex process into manageable steps and used to analyze the factors causing these failures. In this method first potential failure modes are identified and next the effects of the risk is analyzed . The template is as follows

Steps in process	Failure mode	Failure causes	Likelihood to occur [1-10]	Likelihood of detection [1-10]	Severity [1-10]	Risk priority number [RPN]	Actions to reduce the occurrence of risk
1.							
2.							

Potential areas of use: It is used to evaluate equipment and facilitate, analyze the manufacturing operation and its effect on product or process . The outputs or results of FMEA are used to for the further analysis or to guide as a resource .

3. **Fault tree analysis :** Fault tree analysis is a technique used in quality risk management to analyze potential failures and their causes. It helps to identify the root cause of failures and assess their impact on quality by analyzing the fault tree. We can determine the critical failure events and minimizing strategies .

Fault tree analysis	Potential areas of uses
Is an approach that assumes failure of the functionality of a process and helps in evaluating the process. It identifies the causal chains that causes the multiple causes of risk at each level in tree, combination of fault modes are described with logical operators .	Used to establish the pathway to identify the root cause of failure and is used to investigate complaints to understand the root cause of the risk analyzed and the result includes the visual representation of the failures modes .

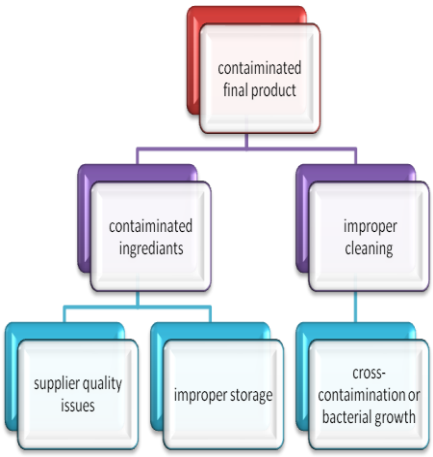

Fig-5 **E**xample of fault tree analysis

4. **Hazard analysis and critical control points [HACCP]:** is the systemic approach used in safety management . it involves identifying and assessing potential hazards and establishing the critical control points and used to analyze , evaluate, prevent, control, the risk .

Steps involved are :

1. Conduct a hazard analysis and identify preventive measures to each step
2. Establish the critical points
3. Establish the critical limits

4. Establish a monitoring system to monitor the CCP
5. Establish the corrective actions to be taken while monitoring
6. Establish system to verify that the HACCP is working effectively
7. Establish a record maintaining system .

Potential areas of use : Used to identify and manage the risk that is related to physical, chemical, biological hazards and the output of a HACCP system information that monitors important points from the entire life cycle of the product .

5. **Hazard operability analysis [HAZOP]:** is based on the theory that encounters the risk even caused by the deviations from the design or operating intentions . is a brainstorming technique also called as guide-words are applied to the parameters and uses a team of people of experts covering the design of process and its application.

Potential areas of use : is applied to manufacturing , processing , formulation and used for evaluating the safety hazards and this will facilitates the regular monitoring of critical points I the process.

6. **Risk ranking and filtering :** This helps in identifying the likelihood and potential impact of occurring the risks filtering involves the application of the criteria to prioritize risks further . by effectively ranking and filtering risks in organization can mitigate the potential threats to their operations .and this tool involves breaking down a basic risk question into as many components as required to capture factors causing risk .

Potential areas of use : This method is mainly helpful in situations in which the selection of risks and fundamental consequences are managed, and is used to analyze the qualitative and quantitative risks within same organization

7. **Supporting statistical tools :** these tools can support the risk management process and can facilitate the effective data evaluation, decision making some of the tools are as follows
    - Control charts
    - Histograms
    - Pareto charts
    - Process capability analysis .

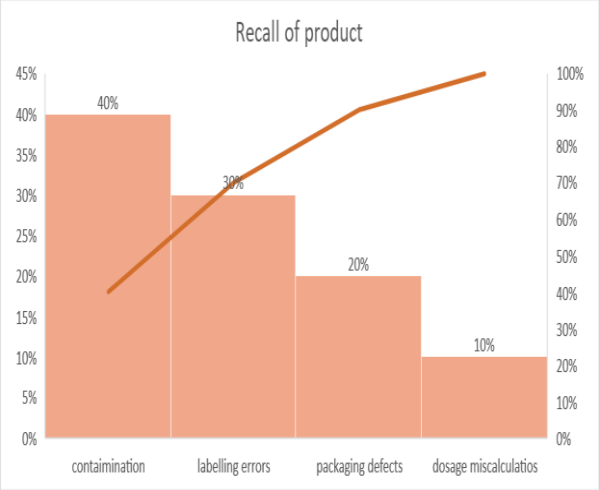

Fig-6 Example of Pareto-chart

II. CONCLUSION

Through this review article we have explored the important role of the quality assurance in maintaining product integrity, ensuring regulatory compliance, and safeguarding patient well-being. The tools of assurance, especially those employed in quality risk management, have emerged as indispensable assets in the pharmaceutical landscape. The integration of the advanced tools for risk assessment, mitigation, and monitoring becomes paramount. From Failure Mode and Effects Analysis (FMEA) to supporting statistical tools, these tools empower pharmaceutical professionals to proactively identify, evaluate, and control potential risks throughout the product life cycle. This review emphasis the symbiotic relationship between quality assurance and risk management, emphasizing their collective role in shaping the future of pharmaceutical excellence.

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