HACCP- QUALITY REVIEW ON RISK MANAGEMENT TOOL FOR FOOD INDUSTRY AND BIOSAMPLES

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ABSTRACT

Background: Biosamples are extremely important to the pharmaceutical sector, hence ICH criteria should be followed when storing them. Conducting a risk assessment using specific tools, such as risk assessment methodologies, is one of the essential components of clinical trial (CT) preparation that adheres to the idea of quality-by-design.**Design:** In current history, Quality risk management (QRM) plays a crucial part in the production of pharmaceutical products as well as healthcare. Quality risk management effectively provides inventive information to the industries in order to make proper decisions which will also act as proof to the authorities about the capacity of the company to manage future hazards.**Results: T**he need for monitoring and evaluating the quality risk management tools conducted. Therefore, the present study will help to understand the importance of HACCP and errors to the general community which will, in turn, improve the quality of the use of medicine and healthcare facilities.**Conclusions:** Many businesses use Hazard Analysis and Critical Control Points (HACCP), a risk management method. It is a modern tactic that can help to reduce hazards in the manufacturing and food industries.

KEYWORD: HACCP, food industry, biosamples, clinical trials

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BACKGROUND

The Hazard Analysis and Critical Control Point (HACCP) technique is a Procedure that contains the base for the food safety assurance in a contemporary lifestyle.HACCP preposition and exertion are behind the capacity of the delineate.Clinical and non-clinical biological samples (biosamples) are stored and analyzed under circumstances that ensure stability during each phase of the methodology, ensuring the analyte concentrations. Because if the biosamples are contaminated at any point before the findings from the pharmacovigilance modelling may be impacted, specimen administration in a controlled clinical diagnostic is perhaps among the greatest crucial and difficult parts of supporting clinical and non-clinical studies.The processing and storage of CT data should be done in accordance with the Good Clinical Practice (GCP) guidelines mentioned under International Conference on Harmonization (ICH), which ensures that the data can be reproduced and verified accurately. There are currently more and more methods accessible to establish risk management measures for CTS, as this is one of the prerequisites, the development of systems and techniques to guarantee the integrity of each CT element(1). Among them deployment is the adoption aligned toward danger strategy, which enables us to discover, evaluate, and mitigate the dangers of improper usage of CT resources, particularly

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blood and urine bioassays collected and held at the CTS(2).

HACCP chronicle Proceed at the end of 1959, when the National Aeronautics and Space Administration (NASA) commissioned the Pillsbury enterprise to fabricate food products for service by astronauts during space missions. The stringent safety requirements imposed on these foods were a reflection of deep concerns in NASA about the potential consequences of foodborne sickness among astronauts in space, as well as of food particles interfering with flight systems (Stevenson and Bernard, 1995).Large pharmaceutical companies currently employ the guideline mentioned under ICH Q9 series, whichsummarizes the most widely used best practices and principles for risk management(3).The paper includes highly helpful learning programs for failure modes and effects analysis, risk ranking and filtering tools(4-6),hazard operability analysis (HAZOP)(7), hazard analysis and critical control point (HACCP)(8). The works of O. M. Zaliska, V.Ye. Dobrova, K. O. Zupanets, and K. L. Ratushna take scientific study on the use of risk aversion approaches into consideration. Although a great range research, the hunt for novel, extremely successful risk management strategies for use in the field of CT is still ongoing(1-9).

The pharmaceutical sector continues to underutilize the HACCP approach of quality risk management, which enables not merely to limit but also to stop from reoccurring risky elements, hence avoiding the quality failure of CT findings. Hazards and Critical Control Points Analysis, or HACCP, is a reliable scientific tool and methodical methodology that offers broad recommendations for ensuring the characteristics of data by analyzing critical control points to minimize risks to a considerable extent(10).

This method is highly useful as it relates to the CTS enables the identification of specific dangers and the establishment of crucial components of continuously keep an eye on them and avert any oscillations that can result in the loss or destruction of CT data.

INTRODUCTION

Food companies frequently employ Hazard Analysis and Critical Control Points (HACCP) as a proactive risk reduction strategy to improve product safety and safeguard public health (11). It thoroughly and methodically examines the numerous risk variables contributing to food pollution during the food manufacturing and processing processes.Then, the hazardous factors causing food pollution are controlled at the critical control points, the control effects are monitored at the same time, and the control methods are corrected and supplemented whenever necessary based on the analysis of the hazards that can be effectively prevented, reduced, or eliminated(12).

Requirement of high-level risk management

The use of quality risk management has become crucial in healthcare companies. Every manufacturing procedure and pharmaceutical has associated dangers.Throughout the pharmaceutical sector, lowering these issues are the cornerstone toa high standard risk management because the characteristics of the manufactured finished product causes direct impact on the health of the patient.The pharmaceutical business has had official access to ICH Q9 QRM for more than ten years. When ICH Q9 was put into effect, the risk-based strategy started to gain more and more traction. QRM should be integrated into daily operations to create a culture where quality is prioritized while making choices, hence reducing quality risks. By proactively identifying and reducing quality risks, QRM ensures and verifies that the product consistently meets positive risk balance.Additionally, reasons of deviation

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should be identified and chosen for ongoing improvement (13-14).

The following steps compose good risk management processes. As follows:

1. QRM Process Initiation: Quality risk management must involve systematic procedures designed to streamline, enhance, and organize decision-making linked to risk. The actions listed above can be used to build and start a strong risk management strategy.
    - Describe the problem or danger in question, taking into consideration any potentially relevant assumptions.
    - Compile historical data or information that is pertinent to the evaluation of the possible hazard's risk.
    - Create a schedule and suitable criteria for making important decisions for the QRM process(15).
2. Risk Assessment: Identifying hazards and analyzing and evaluating the risks connected to their exposure are both included in the idea of risk assessment.
    - Basic questions like these can be really helpful:
    - What possibly could go terrible, then?
    - How likely is it that something will go inappropriate?
    - Lastly, what will happen as a result?

- **Risk identification:** Probabilities and consequences of recognizing risks while using risk-related information. Information can take several forms, including historical data, stakeholder concerns, and theoretical analysis. This stage forms the basis for the remaining strategy.

Risk analysis: Through risk analysis, the risk associated with the recognized dangers is assessed. This process establishes a link between the likelihood and the gravity of the harm. In certain risk management strategies or instruments, the ability to notice harm (detectability) significantly adds to the risk calculation.

Risk evaluation: is used to establish whether a particular risk or hazard satisfies acceptable standards after it has been identified and examined(16,17,18).

3. Risk management: Risk management includes minimizing risk or accepting risk by making wise decisions. The risk control aims to reduce the risk to a level that is acceptable. To control the risk, matching work must be done depending on how serious the hazard is.
    - **Risk reduction:** Risk reduction stresses methods for lowering or even eliminating quality risk whenever it exceeds a given threshold. In order to reduce the likelihood of harm occurring, the following actions are taken: actions taken to reduce the likelihood that harm will be severe.
    - **Accepting risk:**Risk acceptance refers to the choice to do this. Even the most effective risk management techniques might not be sufficient to totally eliminate risk for some types of injury. In such situations, it is genuinely possible to state that a

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competent risk management approach is implemented and the risk is minimized up to a predetermined range. These predefined ranges are established using a number of variables (19,20).

4. Risk communication is the sharing of knowledge regarding risks and prevention with other decision-makers and other stakeholders. The results of the risk management strategy must be effectivelydescribed with reference.
5. Examine: The evaluation of risk management outcomes, which considers both new material and expert opinion, gives assurance that nothing has changed that could have an impact on theQRM convictions, results, and conclusions. The inspection of the quality management process can also spot a number of issues with the product's quality, including its safety(21-24).

Several quality hazards can cost a company money and even damage its brand. In these circumstances, risk management is a useful tool. By identifying and eliminating failure, which ultimately results in internal and external cost modes deduction, it helps a company become more cost-effective. It also provides workers with the tools and guidelines they need to make wise decisions more quickly by providing a perspective through which scientific knowledge and data demonstrates that aids in determining different options and taking potential outcomes into account. Previously, the risk to the product's operation and quality was assessed using flow charts, complaints, and checklists.Regulatory authorities have currently created a risk management plan or strategy that uses tools for statistics and management.

Of all the tools outlined, FMEA is the one that is utilized the most frequently. However, many pharmaceutical companies view it as a standalone quality risk management system and just use failure mode and effect analysis(25,26). Figure 1 indicates the level of risk management process.

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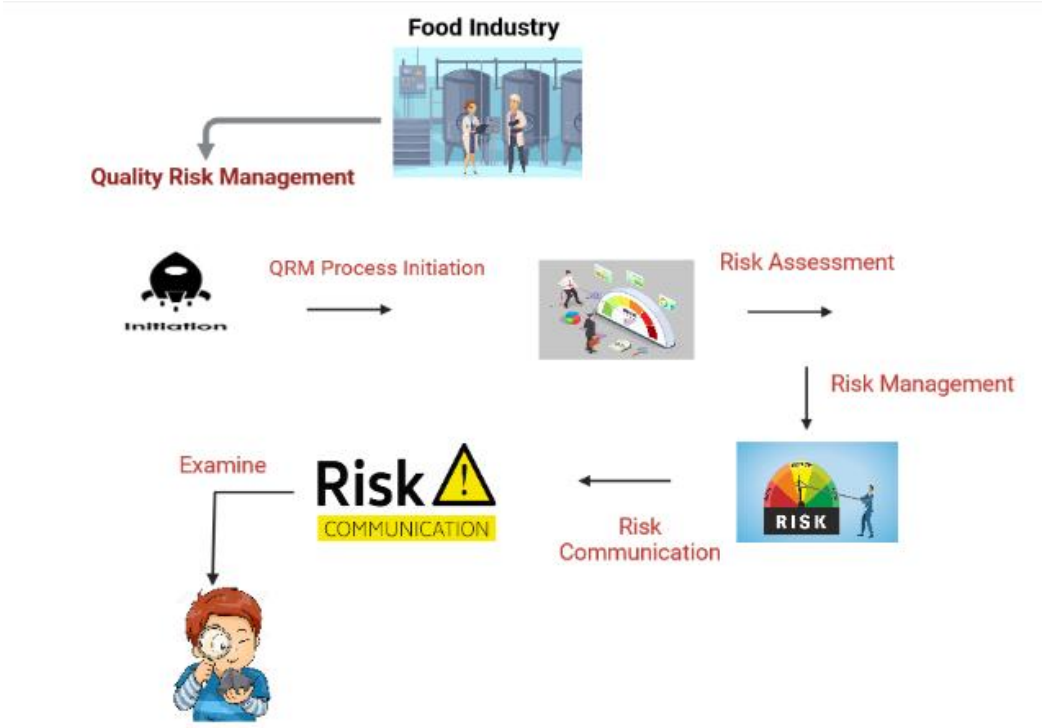

Figure 1: indicates the level of risk management process.

HAZARD ANALYSIS AND CONTROL CRITICAL POINTS

HACCP, a quality risk management tool, is a proactive technique to detect, assess, and create control measures intended to prevent or eradicate hazards.

By using the investigation, evaluation, and safety monitoring concerns, the HACCP technique, which is systematic in nature, enables the manufacturing of dependable and safe pharmaceuticals or healthcare goods. The HACCP methodology aims to eliminate or reduce risks that might occur throughout the pharmaceutical production process by preventing identified hazards. By confirming the essential steps and techniques utilized in the production of completed products in accordance with GMP, the quality threats are somewhat reduced. HACCP, therefore, addresses both GMP and the safety of factory personnel (27,28,29).

OBJECTIVES

Making safe products is the main goal of the HACCP system. Another function of HACCP is to lessen or perhaps do away with the need for endpoint testing, which may be tedious and time-consuming.

- An organization can develop and distribute high-quality, lower-risk products with the proper application of HACCP.
- As a result, enterprises primarily in the food and pharmaceutical industries are emphasizing on routine audit and inspection to ensure appropriate reliability on HACCP(30).

When HACCP is used in conjunction with several other quality techniques, the potential dangers that may arise during the manufacturing of pharmaceutical products can be reduced to a greater extent. These dangers may be chemical, biological, or physical elements that, if not avoided, have the potential to be harmful(31).

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A business can develop and distribute high-quality, lower-risk products with the proper application of HACCP. The scientists also discovered that poor HACCP implementation can cause financial harm(32).As a result, companies mostly engaged in the food and pharmaceutical industries are focusing on regularly scheduled audits and checks to ensure appropriate HACCP system execution(33,34).

MANAGEMENT OF BIOSAMPLES

To enable accurate interpretation of CT data, biosamples should be created, handled, and stored in accordance with the relevant good manufacturing practice (GMP). They ought to be utilized in keeping with the established methodology(1). The protocol must be followed exactly, and additional information from a laboratory manual or standard operating procedure (SOP) should be used if more information is needed.

The primary risk management techniques have been described, and the adoption of the HACCP approach to guard against loss of data and the fabrication of clinical trials outcomes has been justified using scientific in general procedures (synthesis, retrospective analysis, systematization, and comparison).

Assessment and control of quality risks are carried out in the pharmaceutical sector utilizing internal procedures or well-known risk management technologies indicated in Figure 2.The primary tools are described in the section below(4,5,35-39).

Since biological samples are temperature-sensitive pharmaceuticals, the HACCP principles can also be used to guarantee the calibre of the clinical triallike those. Inadequate biological sample storage creates a risk for the accuracy and dependability of the CT results. By utilizing HACCP-analysis to examine the circumstances and the condition of their frozen storage equipment, it is guaranteed to identify the major risks and create countermeasures that use temperature as the primary CCP (40).

Seven principles form the foundation of the HACCP system, which should be executed in twelve steps(41). Let's have a look at a potential HACCP implementation algorithm at the CTS to manage hazards during the storage of biological samples for the CT.

A list of all potential risks must be compiled according to the first HACCP principle. The same risks that apply to any product apply to CT biological samples as well. Physical hazards include improper storage and freezing-thawing, mechanical risks include shaking and resistance, chemical risks include adding insufficient reagents, reducing their activity, and biological risks include the establishment of metabolites as a result of thawing biosamples (contamination and accidental insect invasion into test tubes).

Identifying the CCP is the second HACCP tenet. It is advised to identify sites (places), processes, or computerized operations at this stage that can be regulated to obliterate risks or reduce the possibility that they will materialize. The primary CCP in the event of insufficient biological sample backups is the thawing-freezing and loss of clinical trial information to the analytical laboratory's final analysis of biosamples.

Setting critical limits for CCP is the third HACCP tenet. With the use ofrefrigerators that may be set to very low and low temperatures, biological blood samples, blood fractions (serum, plasma), and urine can be stored between 80 and 130 degrees Celsius(12,42,43).

Therefore, establishing a plan for the HACCP system's implementation along with defining the critical control points for ongoing surveillance at the CTS enables effective temperature stability risk management for biological samples breaches and the loss of CT data.

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Because of this, the HACCP method is applied as a risk management tool in clinical trial quality management, based on cross-links with the ISO 9001, which is a more effective application of either ISO 9001 or HACCP alone, and results in an improvement in satisfaction with the quality of clinical trials materials storage and organizationof the staff work at the clinical trial simulation(41).

DIFFICULTIES OR OBSTACLES TO THE SUCCESSFUL INTEGRATION OF HACCP

Despite the fact that HACCP systems are highly regarded, it has been noticed that the pharma industry has not totally adopted HACCP systems. The system's lack of adoption is explained by the existence of hurdles, which may make it difficult to use. The HACCP framework won't be used widely in the pharmaceutical industry or reach its full potential unless the restrictions are addressed. The term "barriers" refers to all the actions, attitudes, and convictions that impair the comprehension of the HACCP concept as well as its application and retention. Here, some of the obstacles have been covered(44,45,46).

1. Due to the lack of enough resources, practical knowledge, and qualified employees for HACCP implementation, pharmaceutical firms that are small to medium-sized may find it difficult to adopt HACCP, whereas comparatively large companies may find it simpler to do so (47,48).
2. A lack of monitoring and incentive on the part of employees - Maintaining the HACCP system's functionality depends heavily on staff motivation. Staff supervision at all times is crucial for the proper operation of HACCP. The HACCP system's motivated employees play a significant role in implementing and maintaining the HACCP framework, particularly with regard to the needs for ongoing surveillance and reporting(49).
3. One of the main challenges brought on by the lack of employee training for HACCP is the lack of workers with expertise and awareness of the system. Typically, training sessions are designed with specific staff members or groups in mind, taking into account their level of technical expertise and level of responsibility throughout the HACCP process. Personnel can now use the HACCP idea in their own processes thanks to this (50,51).

Small pharmaceutical businesses sometimes struggle to support the implementation of HACCP due to their limited purchasing power, which also makes it difficult to persuade or sufficiently pressure suppliers to adopt the HACCP system (52).The Figure 3 indicates difficulties or obstacles to the successful integration of HACCP.

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Figure 3: Difficulties or obstacles to the successful integration of HACCP.

BENEFITS OF IMPLEMENTING HACCP IN THE PHARMACEUTICAL INDUSTRY

There are no restrictions on the benefits of HACCP. Because of its adaptability and compatibility, HACCP can be implemented in practically any place. The following are the primary benefits of using HACCP:

- In addition to enhancing the safety of pharmaceutical products, the adoption of HACCP has other benefits, including better resource management and quick fixes for product safety issues. The HACCP system can adapt to changes in operational procedures or advances in technology.
- The system's major benefactors are consumers because it ensures the production of products that are safe and of high quality.
- Improved awareness and training could lead to a decrease in operational errors made by people.
- A HACCP framework enables improved process control, higher staff commitment, and fewer failures.
- Consumer trust and confidence rise, and the possibility of a product recall is reduced, which lowers the cost of the good (53-56).The Figure 4 indicates Difficulties or obstacles to the successful integration of HACCP.

Figure 4: Difficulties or obstacles to the successful integration of HACCP.

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CONCLUSION

A high level of the CTS's procedure management is made possible by the implementation of the HACCP system, which complies with ISO 9001-2015 requirements. This results in cost savings and improved biological sample quality at the CTS. It would undoubtedly necessitate the initial expenditure of some additional funds, but over time, the improved CT quality assurance would more than offset this.As a result, this strategy is actually being used at the CTS in the present.

Although the quality of pharmaceutical products has significantly improved, there are still many issues that need to be taken into account. Quality Risk Management provides assurance that the risks are well managed and additionally aids the drug sector in making consistent and traceable decisions that will lessen the risk through consistent use of tools and routine evaluation. Risk identification, analysis, evaluation, and the creation of risk management strategies are all part of the systematic process known as risk management. It employs a variety of methods that are widely used in the pharmaceutical industry, but it has been found that there is an excessive reliance on retroactive measures, which deal with problems after they have already occurred rather than preventing problems in the first place.

The ideal approach for risk management in the pharmaceutical industry is HACCP as a potential toolbecause preventing hazards that could cause a product recall and other quality problems is the main focus rather than inspecting the final product. Everyone benefits from the HACCP approach because it is economical, results in less product loss, and also ensures the safety of the pharmaceutical product. This includes consumers and pharmaceutical companies. In order to reach the goal of business, it is advised that pharmaceutical businesses use tools like HACCP to reduce losses and product rejections due to poor quality.

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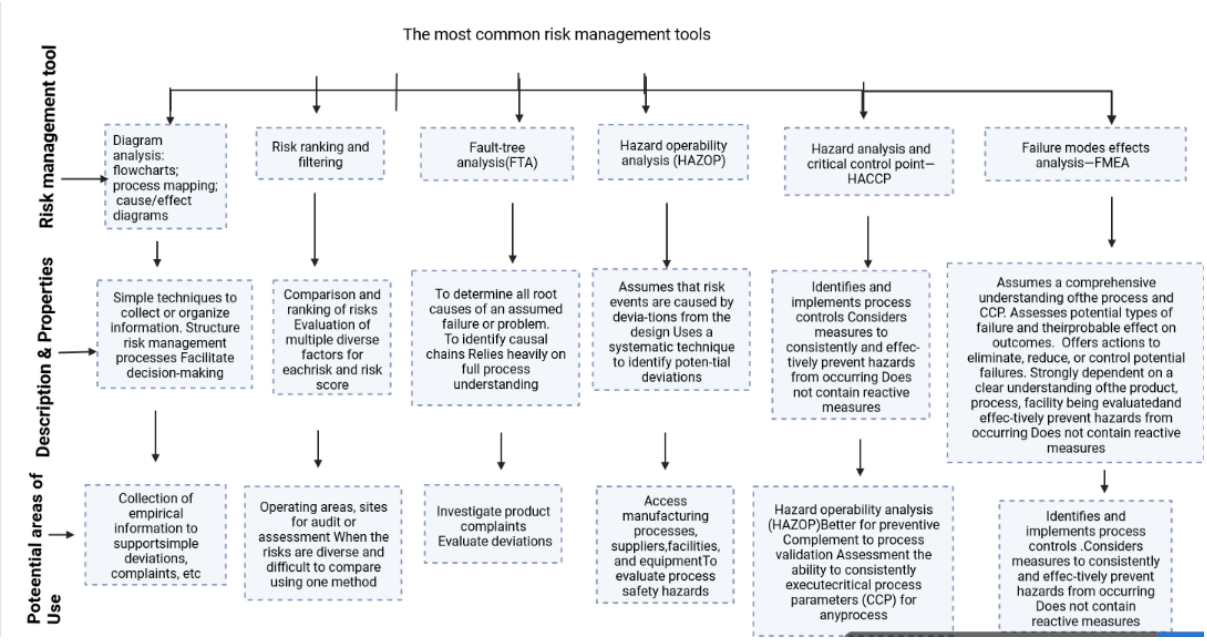

Title of the Table-1: Typical strategies include the following:

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