IMPORTANCE OF QUALITY MANAGEMENT SYSTEM IN PHARMACEUTICAL INDUSTRY:A REVIEW BASED CASE STUDIES

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ABSTRACT:

The topic of this thesis is quality management in pharmaceutical industries. This is an important topic because drugs or pharmaceutical products are directly delivered to the customers' bodies, so the drug product must maintain their identity, purity, safety, and ultimately appropriate product quality. Many research has been conducted on this issue in order to discover the significance of quality management in pharmaceutical industries administrative systems as independent factors on competitive policies utilized in industrial facilities as dependent variables. Studies have focused on themes that are closely related to pharmaceutical product quality management.Several polls and literature studies were conducted as part of the pharma quality management study to identify gaps in pharmaceutical in order to enhance the quality system. Based on the result of a pharmaceutical company's performance. It was determining that individuals are well-informed and trained to do their particular activities and tasks, which have been determined based on their qualifications and experiences.

Keywords: Quality; Safety; CAPA; OOS; OOT; change management.

Introduction:

Management is required for all organizations, regardless of their size, type, or activities. Management is not limited to company organizations; even non-business organizations must manage their activities. Management is a widespread and well-regarded role. A manager is an individual or a group of people who assume responsibility for running a company. They plan, organize, direct, and control all of the organization's important activities. Management does not

perform the task. They encourage people to complete the task and coordinate all efforts to achieve the organization's goals.

A quality management system helps a corporation to develop procedures and structures that are effective, efficient, transparent, and easy in order to achieve continuous compliance. Furthermore, the company's operation will profit from enhanced quality, reduced expenses, inspection preparedness, and increased customer satisfaction.(1)

The Indian pharmaceutical sector has made enormous strides in terms of infrastructure development, technological base creation, and product diversity. Despite the fact that it is undergoing reorganization, it continues to demonstrate its presence and drive to thrive in a changing environment. The business currently manufactures bulk pharmaceuticals for all main therapeutic classes. This has been made possible by superior scientific and technical staff, as well as pioneering efforts in process development. During 1997-1998, the total output of API medications and formulations was anticipated to be Rs. 26280 billion and Rs. 120680 billion, respectively. During the 1990s, the growth rate for API medications was roughly 15% and 20% for formulations. The export performance is likewise impressive, with an increasing rate that exceeded over 20 percent in 1997-98. Nonetheless, the scope is to increase the volume of exports is tremendous. (2)

The current pharmaceutical quality management system is based on an internationally harmonized guidance ICH Q10, which has been produced by the Experts Working Group (Quality) of the International Conference on Harmonization of the Technical Requirements for Registration of Pharmaceuticals for Human Use and the USFDA and is in the final stages of popularity by the regulatory bodies of the European Union, Japan, and the United States and describes a model for a pharmaceutical quality management system.(3)

Evolution of Quality in Industrial Sector:

Initially, everyone's attention was solely on accepting or rejecting produced items based on requirements following inspection, with little thought given how to avoid these faults. Early in the 1920's, statistical theory was applied to preserve the quality aspect of goods, and in 1924, Dr Shewart created the first attempt to build a quality control chart, which was subsequently

improved by Dr Deming and became known as the basic concept of statistical process control (SPC) in the 1940's.

Quality management practices were established and applied by Japanese businesses in the 1950s, and by the 1960s, quality control and management had become an option for every nation. In 1969, Feigenbaum presented a report at a conference, and for the first time, the phrase overall quality was used to refer to broader concerns such as planning, organization, and managerial accountability. Ishikawa delivered a paper in which he explained how complete quality control differed in Japan, referring to companywide quality control and detailing exactly how everybody at a company, from top management to laborers. must learn and engage in quality control. Quality management became mandatory in the majority of Japanese enterprises in 1970.[(4)]

The term quality management system was coined by the western world in 1980, and a component of this is total quality management, which has become a very important phenomenon in most health care systems or industries in order to rectify and eradicate mistakes in order to achieve zero defect products. In the twenty-first century, several nations made quality management systems necessary in order to assist organizations in achieving exceptional performance and delivering zero faults. [(5)]

Scope of QC and QA:

Quality assurance (QA) and quality control (QC) are critical components of every health care organization. Their goal is not just to test, but also to generate superior final products. The quality of health-care goods has become a major consideration for the World Health Organization and the International Conference for Harmonization, with the goal of marketing drugs in a safer and more effective form. Quality control entails inspecting the level of quality of goods and methods used in their production. QC and QA are in charge of inspecting all elements of a product. For example, QC of aerosol includes documentation of checking in propellant, container, valve, quality and life span active concentrate, and so on, whereas QA is checking products which are moved by QC department. They will double-check all of the limits and equations that were approved by QC. QA professionals are the highest paid personnel in the pharmaceutical industry. Working in any pharmaceutical sector requires knowledge of management and analytical skills. It is extremely serious labor to produce zero-deficiency goods of great quality, safety, and efficacy. (6) However, many basic learners are confused by the

difference between quality control and quality assurance. To help them understand the extent of the QC & QA is represented below in the Table 1.

S.NO	Criteria	Quality Assurance	Quality Control
1	Focus	To prevent defects with a focus on the process.	To identify defects in the finished product.
2	Goal	To improve development and test processes so that defects don't arise	To identify defects after a product is developed and before it's released.
3	How	Establish a good quality management system &assessment of its adequacy with continuous monitoring.	Finding sources of quality problems to continually meet customer's requirement.
4	What	Prevention of quality problems through planned and systematic activities.	Analytical techniques used to maintain the product quality and process
5	Responsibility	Everyone on the team.	Of a specific team that tests the product for defects.
6	As a tool	QA is a managerial tool	QC is a corrective tool

Table 1: The difference between quality assurance and quality control

The Top Ten Responsibilities of the Pharmaceutical Quality Unit:

1. To establish the quality system
2. To audit compliance to the quality system
3. To establish procedures and specifications
4. To establish manufacturing controls
5. To perform laboratory tests or examinations
6. To review and approve or reject all things cGMP
7. To ensure investigation of nonconformance
8. To keep management informed
9. To describe responsibilities in writing

10. To remain independent

Comprising of quality system in pharmaceutical company:

1) SOP (standard operating procedure)
2) Validation
3) Quality management system
4) Training

A quality management system (QMS) is a group of operational procedures aimed at constantly satisfying and meeting the needs of customers. It is stated in terms of the organizational structure, rules, guidelines, steps, and resources required to put quality management into practice. Early methods used simple statistics and random sampling to emphasize predictable results of an industrial product manufacturing chain. [7,8]

Focus turned to team interaction and dynamics, particularly the early signaling of issues via a continuous improvement cycle, as laborsinputs were often the most expensive inputs in most industrialized cultures during the 20th century. Since investor and customer happiness and perceived quality are increasingly correlated with these variables in the 21st century, QMS activities have tended to merge with sustainability and transparency programmed. The ISO 9000 family of standards is likely the QMS regime that is used the most commonly in the world; the ISO 19011 audit regime is applicable to both and deals with quality and sustainability and their integration. In addition to complementing ICH "Q8 Pharmaceutical Development" and ICH "Q9 Quality Risk Management, it incorporates the principles of good manufacturing practice (GMP) laws and ISO quality ideas. [9,10]

It is an extra piece of advice that is part of the technical standards for ICH registration of medicines for human use and is not in the form of a requirement. It improves the standard and accessibility of medical care globally. It strengthens the connection between drug development and manufacturing operations and promotes innovation and ongoing improvement. The FDA's primary rules, such as 21 CFR Part 2117, are the source of the definition commonly used quality management systems for the pharmaceutical business.[11]

A quality management system typically consists of four facts:

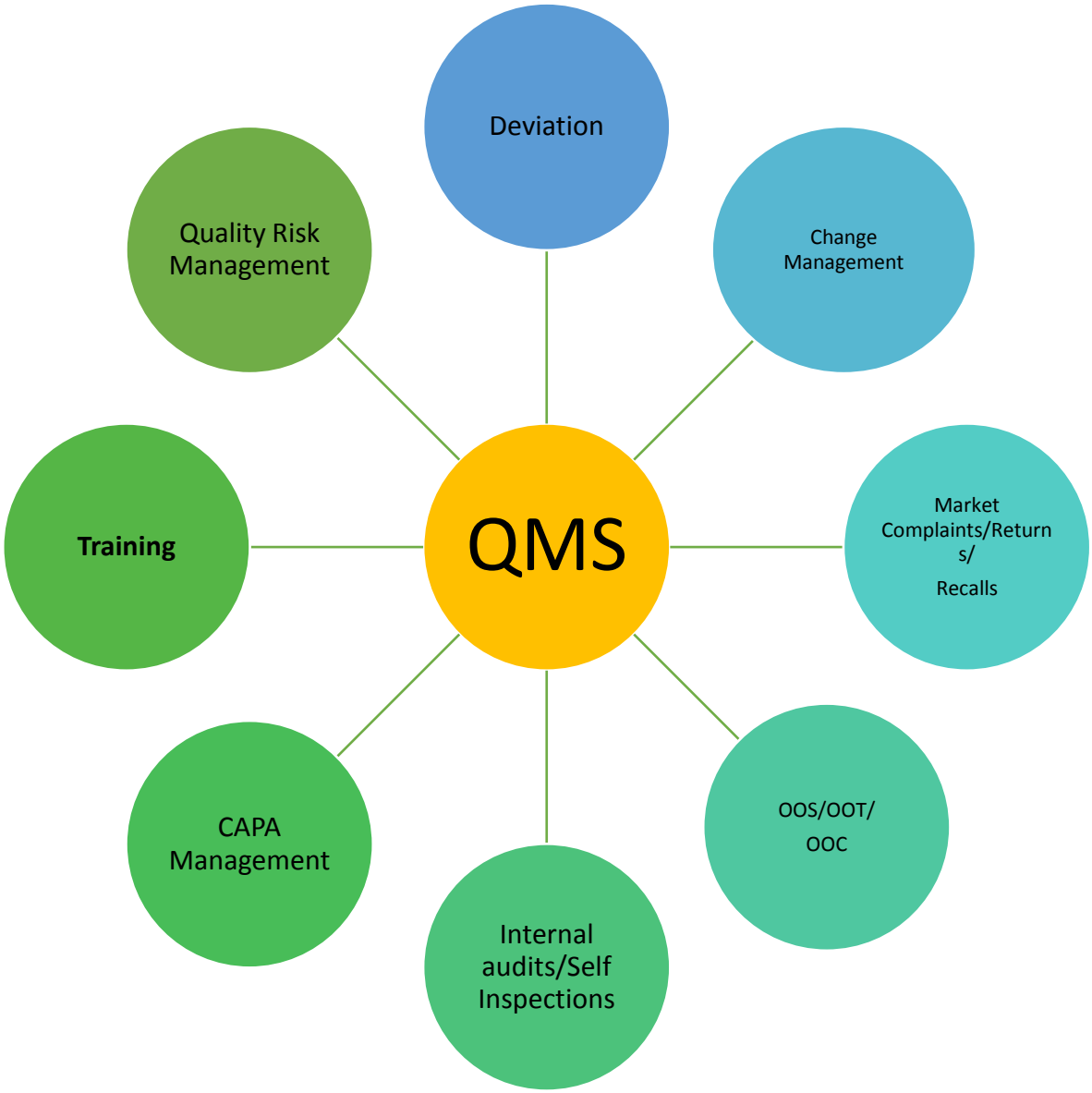
- **Quality planning –** process of translating quality policy into processes, procedures, and instructions to achieve measurable objectives and requirements
- **Quality assurance –** planned and methodical activities executed as part of a quality system to provide confidence that process, product, or service requirements for quality are being satisfied
- **Quality control –** act of monitoring, appraising, and correcting a process, product, or service to ensure requirements for quality are being satisfied
- **Quality improvement –** process of analyzing performance and taking methodical, systemic actions to improve it.

Essential Principles of Quality Management System:

Change Management/ Change Control, Out of Specifications (OOS), Out of Trend (OOT), Corrective & Preventive Actions (CAPA) and Deviations, Product Recall, Returned Product, Market Complaints, Internal Quality Audit are all important in every organization to achieve the goal of quality and safe products. This current review emphasizes the importance of the above principles with some case studies as examples, and the importance of these aspects of the quality management system was strictly considered by the Pharmacy Council of India, which resulted in a new Maters of Pharmacy course named pharmaceutical quality control and quality assurance, in which the course practical of the first semester is named Quality Assurance Practical-I, and one of the practical is case studies on the quality management. [(12)]

Elements of Quality Management System (QMS)

QMS TOOLS



Definition of QMS Tools:

1. Change Control:

A formal system by which qualified representative of appropriate disciplines review proposed or actual changes that might affect the validated status of facility, systems, equipment or processes.

Temporary Change:

A change (departure from any established procedure/system/process) initiated for the evaluation of proposed procedure/system/process, which has been taken with prior approval to achieve the desired output, allowed for one time change and limited to a particular batch. For example, change in batch size, manufacturing equipment, etc.

Permanent change:

A change initiated based upon scientific rational or historical GMP data or data generated through temporary changes. Permanent changes mean the changes that remain in effect till the next required revision or modifications.

Major Change:

Change that has a significant impact on quality and / or safety of the final product. Changes, proposed for improvements to process, materials, product and procedures which may have impact upon the identity, quality, purity, strength, stability, safety and efficacy or physical characteristic of the product. Notification to agency required.

Moderate Change:

A change that is likely to have an impact on the quality of the product, but does not make any significant change in the final quality of the product.

Minor Change:

Changes, which does not have impact on the quality attributes like identity, quality, purity, strength, stability, safety, efficacy or physical characteristic of the product.

2. Deviation Management:

Departure from an approved instruction or established standard.

Procedure:

Deviation shall be classified as:

1) Planned deviation
2) Unplanned deviation

1)planned deviation:

Deviation with prior approval

2)unplanned deviation:

Any deviation, which occurred eventually in the due course of process.

The QA head shall review the deviation and asses the quality impact on the product based on the assessment, deviation shall be categorized as:

1)Minor

2)Major

3)Critical

MINOR: Deviation, which does not have impact on identity, strength, efficacy and purity of the product.
MAJOR: Deviation, which may have indirect impact on identity, strength, efficacy and purity of the product.
CRITICAL: Deviation, which may have direct impact on identity, strength, efficacy and purity of the product.

3. Corrective Action & Preventive Action:

Correction:

Correction refers to repair, rework, or adjustment and relates to the disposition of an existing nonconformity.

Corrective Actions:

A corrective action is to eliminate the cause of a detected non-conformity or other undesirable situation. There can be more than one cause for non-conformity. Corrective action is taken to prevent recurrence. Corrective action may arise from manufacturing deviations, OOS (Out of Specification) investigations, complaints, audit findings, recalls, etc. The process includes:

1). Reviewing and defining the problem or non-conformity.

2). Finding the cause of the problem.

3). Develop an action plan to correct the problem and prevent a recurrence.

4). Implementing the plan.

5). Evaluating the effectiveness of the correction.

Preventive Actions:

A preventive action is a process to eliminate the cause of a potential non-conformity or other undesirable situation. There can be more than one cause for a potential non-conformity. Preventive action is taken to prevent occurrence. Preventive action may result from trending of in process data, of analytical data, of audit findings, trending of root causes for non-conformities or complaints, from annual product reviews, quality risk analyses, etc. The process includes:

1). Identify the potential problem or non-conformance.

2). Find the cause of the potential problem.

3). Develop a plan to prevent the occurrence.

4). Implement the plan.

5). Review the actions taken and the effectiveness in preventing the problem.

4. Out of Specification:

OOS – All suspect results, that fall outside of the predetermined limits or acceptance criteria established in the specification, are defined as Out of Specification results.

5. Out of Trend:

OOT – The Result that may be within specification but show significant variation from the historical results.

OOS (Out of Specification) is the comparison of one result versus predetermined specification criteria while OOT (Out of Trend) is the comparison of many historical data values versus time. OOS investigation focus on determining the truth about that one value while OOT investigation focus on understanding non-random changes.

6. Market Complaints:

A market/consumer complaint is the notification that a product in commercial distribution (which also includes physician sample),

- May be in violation of the laws or regulations administered by the FDA.
- May have caused illness, injury or death.
- Is alleged to have caused problems not covered by the above.

7. Product Recall:

Recall refers to the withdraw of specific batch(es) of the product from the market.

8. Returned Product:

- Returned Product: Any product, which is returned without a quality defect from the market, shall be considered as returned product.
- Rejected Product: Any product, which is returned with quality defect from the market, shall be considered as rejected product.

9. Internal Quality Audit:

Internal Audit:

A planned and systematic examination and check of a system, procedure or operation by internal auditor in order to monitor compliance, the effectiveness of established standards, to take corrective measures where required and provide for improvement.

Auditor:

An individual or group of persons those who are responsible for conducting the evaluation.

Auditee:

A representative from respective area/section of the department being evaluated.

10. Out of Calibration:

In simple terms it may be defined as "failure to meet the acceptance criteria during the calibration process".

METHODOLOGY:

Methodology is about anything that has to do with procedures or techniques of investigation, that is, the set of techniques used in one piece of research. It is all about the methods used in the study of the research. Methodology is essential in gathering relevant information thereby giving effective and reliable representation.

Quality is a universal concept and concern for every item or article of use, be it a house-hold item, home appliance, personal care products, machinery purchased from the market, cars for personal or commercial use, foods and food products or medicines for animal and human consumption. No one wants to compromise quality on any item they use. Quality assurance therefore is the process or the end of the process of vouching for the integrity of a product to meet the standard for the intended use. Quality assurance is an obligation automatically imposed on the manufacturer of any product to ensure that it meets the needs of the end-user in the measures intended for use.

Quality, safety, efficacy, reliability, strength and or durability etc. For the end-user, the benchmark of quality is perfection they cannot allow less than 100%.

Poor quality medicines are not only a health hazard, but a waste of money for both governments and individual consumers. A poor-quality medicine may contain toxic substances that have been unintentionally added a medicine that contains little or none of the claimed ingredient will not have the intended therapeutic effect.

Most countries will only accept import and sale of medicines that have been manufactured to internationally recognized GMP. Governments seeking to promote their countriesexport of pharmaceuticals can do so by making GMP mandatory for all pharmaceutical production and by training their inspectors in GMP requirements.

The methodology of this research is broken down into the following framework:

1. Definition of problem
2. Objectives
3. Hypothesis
4. Method adopted
5. Population and sample
6. Data collection

Change Management / Deviation Management:

Change management or deviation management can be defined as a systematic approach deals with transformation of organizations objectives, manufacturing process or the protocols. The main aim of this change management also known as restructuring management is to implement strategies for effecting, controlling and the change and to help the people to adapt to the new system. This includes structured protocols to request a change and also a proper step to request and follow them up. Even it is a part of quality management system to eradicate the errors of failures and to make the products success. The implementation of the deviation management in many pharmaceutical companies like Astra Zeneca lead to a successful product at minimum cost with high quality.[(13)]

The restructuring management can be better understood by taking an case study from AstraZeneca, which clearly explained that the success of any management is by understanding the background and challenges, the challenges faced by this pharmaceutical MNC is fewer new products from this company, expiring patents, increase in cost towards production of new products, more competition with less margin on sales and change in marketing strategies. In order to face these challenges, the Astra Zeneca, Sweden implemented restructuring management skills like agreed with white collar trade unions about a compulsory redundancy package in 2006, agreed with all trade unions about a voluntary redundancy package in 2007, agreed with all unions about a check list for the reorganization & redundancy Process (aligned to our Project Management Framework) in 2008, Global process in AstraZeneca for Restructuring Selection in 2009.

These challenges can be faced successfully by Astra Zeneca with the implementation of Management team with focus on change and restructuring, Project organization with people from HR and line to plan and support all activities, With planning and a change program running during four years, Developed a process to plan and manage resources internally and continuous dialogue with trade Unions, including training in AstraZeneca processes.[(14)]

Out of specification (OOS):

OOS can be defined as those results of any procedures which may fall out of specified limits, which are represented in the official monograph or compendia, the frequent arising of OOS in any procedure indicates that protocols / sops are not in control which result in rejection of final products which will be an ultimate loss for any company including pharmaceutical industries. So that it is an important criterion to address the OOS results. This can be eradicated by laboratory investigation by changing the errors in the standard operating procedures and to address by quality control officer by additional laboratory testing.[(15)]

In a deep study, the OOS can be eradicated in three phases- Phase I: Laboratory investigation, Phase II: Full scale investigation and Phase III: Review of product development. This OOS can be easily understood by taking the case study of apotex (Commercial Stability Program-Medicinal Products), the main aim of this program is to address the stability issues associated in

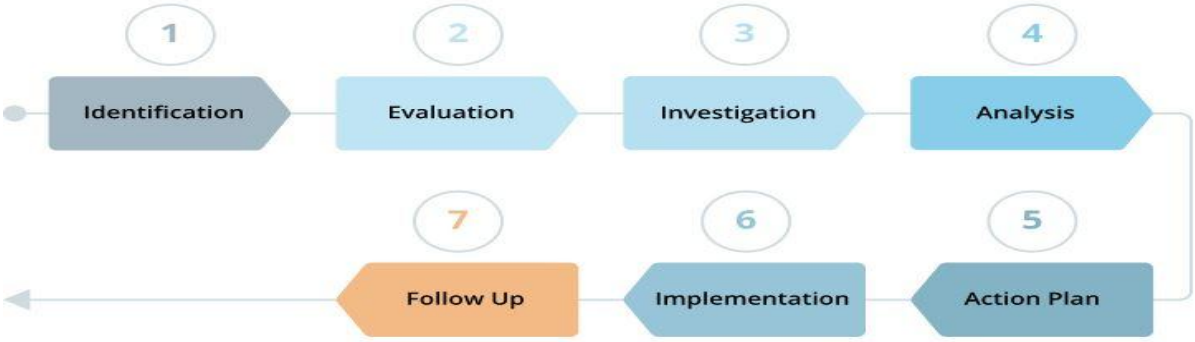
the formulation with the marketed package. It is addressed in this case study that investigation of OOS is an important criterion and reporting immediately the OOS results to the authorities is an important agenda by the laboratory quality control staff.[16]

Out of Trend (OOT)

The Astra Zeneca defines OOT as an out of trend is an important regulatory or quality assurance parameter that is must to be addressed in a pharma industry in order to reduce the errors and to deliver a stable pharma product. This can be defined as an out-of-trend (OOT) result is a stability result that does not follow the expected trend, either in comparison with other stability batches or with respect to old results or existed results, this a challenge in pharmaceutical companies always to identify OOT stability data and how to address this out of trend stability results. The identification of out of trend results is a very challenging task in the degradation and impurity analysis. The implementation of an OOT procedure for commercial stability batches.[17,18]

Corrective and Preventive actions (CAPA):

The CAPA is an important quality management principle can be defined as a corrective action to eliminate detected nonconformity and as an action to prevent the occurrence of non-conformity. The CAPA can be better understood by the help of CAPA five step process explained by Tonya White-Salters which is represented in the below flowchart.



The CAPA can be analyzed with its subsystems, The CAPA can be better understand with the help of case study of Massachusetts specialty pharmacy of Washington where a toxic fungus contaminated the steroidal injection led to death of 25 people in various states. The FDA investigated this case and clearly expressed their opinion that implement of CAPA in every

pharmaceutical MNCs is very much essential to prevent these types of mishaps and can produce zero defect and safe products to customer at economical rates.[19]

Case studies on QMS tools:

1.Case study for Change Management:

Introduction of SAP [SYSTEM APPLICATION PROGRAME] in the premises.

Existing status:

Systems without SAP software were followed in the premises, hence there is no data traceability and there is a difficulty in analyzing & retrieving the data in the respective departments.

Proposed changes:

The SAP system must be implemented to all the respective departments [Warehouse, Production, QC, QA, Finance, Purchase, and Commercial]

Reason:

To have a better control and data traceability.

Classification:

Major

Action Required:

- New server to be procured with the required specifications
- SAP software must be installed to all the respective departments.
- For implementing the SAP system SOP must be prepared by respective department.
- Data collection for respective departments shall be done and it must be synchronized with the collected data.
- Training can be imported to all the departments.

Review, Evaluation and Assessment of change:

The proposed changes shall be explained to the Respective departments and shall get approval from them.

Respective Departments:

1. Warehouse
2. Production
3. Finance
4. QC
5. Purchase
6. Commercial
7. QA

Categorization:

Permanent

Review, Evaluation and Assessment by QA:

Systems without SAP software were followed in the premises were replaced with the new SAP systems, required action has been taken, reviewed, implemented and found satisfactory and the same was submitted to all the respective departments.

2.Case study for Deviation Management:

Origin of Deviation: Facility modification

Type: Planned deviation

The secondary packaging material stored in the warehouse I is shifted to warehouse II due to the flooring modification carried out in warehouse I. During this period, the following will not be followed in the warehouse I: Area cleaning will not be performed as per the SOP and will not be recorded. The temperature monitoring for packaging material storage area will not be done. Dispensing of packaging material will not be done at the warehouse. The newly received materials which need to be stored in the warehouse I is shifted to warehouse II.

Reason/justification for deviation:

To carry out flooring work at the warehouse I. Area cleaning for the warehouse will be done. Temperature monitoring will be done as per the SOP. Dispensing of the materials will be done as per the SOP in warehouse II. Transfer of all materials from warehouse I to warehouse II will be done in a closed container.

Final disposition of deviation by QA department:

This planned deviation was for storing of secondary packaging materials in warehouse II due to flooring modification in warehouse I. As per this deviation: Training was given to all the personnel involved to execute the deviation.

Before shifting material, the area was cleaned and the temperature was monitored and recorded as per SOP. During this period following was not done in the warehouse I. Area cleaning and temperature monitoring were not done. Impact assessment: Warehouse II was cleaned and the temperature was maintained before transferring the material from warehouse I. Appropriate conditions was maintained. Materials were shifted and stored with care. After the completion of flooring modification in warehouse I, the area was cleaned and the materials were shifted back from warehouse I to warehouse II in a closed container. The planned deviation is completed.

3.Case Study for CAPA:

TITLE:

During manufacturing of Glucosamine Hydrochloride, in Charcoal treatment process, reaction mass was stirred at 28º instead of 30º to 35º.

Investigation details

Review of raw material quality and quantity:

Analytical results of the respective input materials were reviewed and found meeting the predetermined specification. All the raw materials were charged as per the standard quantity provided in the approved Batch Manufacturing Record.

Review of batch manufacturing record

Process parameters:

All the process parameters of respective batch were reviewed from the executed batch manufacturing record and noted that all the process operations were executed as per the BMR. However, at specified operation, the reaction mass was stirred at 28º. During charcoalization, The reaction mixture should be 30° to 35º as approved BMR. Since, the reaction mass was maintained below 30°.

In process controls:

In process controls are reviewed and found all are meeting the pre-determined in process specification as per the BMR. No abnormalities were identified during reaction monitoring.

Personnel Evaluation:

Concerned personnel involved in the batch manufacturing were inquired with respect to the temperature discrepancy and found no operational deviations occurred. Training records of respective personnel involved for the execution of the batch were reviewed and observed that they are enough experienced and trained on manufacturing process of specific API stage

Summary of investigation

Based on the above review it is noted that the reaction was maintained below 39° due to the boiling point of the process solvent i.e., Dichloromethane. However, further operations were reviewed and no abnormalities noted and all the in-process samples met the specification without any abnormalities.

Root Cause

During charcoalization, the reaction mixture should be 30° to 35º as approved BMR. Since, the reaction mass was maintained below 30°.

Impact on other batches

The output and quality of subject batch were reviewed and found to be well within the limits. No abnormalities identified with respect to other process operations. Hence, there is no impact on the subject batch quality due to said discrepancy. However, there were no further manufacturing of said API stage. Hence, there is no impact identified on other batches.

Details of Corrective & Preventive action

Correction:

As per approved BMR Reaction mass should maintained at 30º to 35º but it was maintained at 28º

Corrective and preventive action:

As the occurred deviation is due to process solvent boiling point, it is proposed to revise the batch manufacturing record of said API stage by modifying the temperature at specified operation as 25° to 30° instead of 30º to 35º.

4.Case Study for Out of Calibration:

Title: Out of Calibration Equipment in the manufacturing process:

Type: Unplanned Deviation

Immediate actions taken after identifying Deviation:

It was identified after the production of a few batches so we need to find out whether the operations were stopped or not. After that it is mandatory to inform the status to the Quality

Assurance Personnel. The Quality Assurance team will ensure that the affected material/batch numbers (part quantity or full quantity) was identified and segregated separately.

Root cause analysis

Out of Tolerance:

The first thing to be considered is to check the calibration certificate when out of tolerance occurs. QA should understand that what went wrong and check the data in the calibration report and must check that what should be the reason for out of tolerance. After the reason identified the must analyze the risks. **For example**: The weighing balance reading is not tarred as zero before weighing and the product was weighed with that and then it causes deviation.

When did this happen?

Finally, check when was the measurement shown by the instrument accurately and the due date for calibration and previous calibration date.

Where is the instrument used?

You have to check where the instrument is used, such as production department or warehouse, etc. check whether the logbook is maintained for the instrument and is it maintained properly and entered after every use.

How is it used?

The last step is to identify how the out of tolerance instrument was being used. Determine what all measurements were being made at the location. This information will likely be found in the operator's work instructions or end users procedures or an engineering specification. The objective of this step is to determine that whether the out of tolerance instrument could have affected any of the products manufactured or the services that are provided by this instrument, in this time frame, in this location, for these measurements. This can be achieved by reviewing the documentation process

Corrective and preventive action

Corrective action:

Products which are not shipped must be separated instantly for testing. Re-inspection should be done for the products which are stored in the warehouse. If a product is already shipped, then it should be recalled. If a customer utilizes the product as the raw material and has not yet used it for production, then you can test or inspect in their site itself. If there is no proper equipment for testing then you have to recall.

Preventive action:

1. You have to calibrate the instrument regularly at periodic intervals.
2. Calibration data must contain the following data:
3. Is the calibration within the range?
4. Is it out of calibration?
5. Can calibration be extended for a longer time?
6. Whenever it's calibrated, is it within the specified limit?

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