International Journal of Frontiers in
Life Science Research
Journal homepage: https://frontiersrj.com/journals/ijflsr/
ISSN: 2783-0470 (Online)

(REVIEW ARTICLE)

Check for updates

Importance of quality management system in current scenario

Prachi Soni, Dhara Patel, Grishma Patel *, Tejas Patel and Dhananjay Meshram

Department of Quality Assurance, Pioneer Pharmacy Degree College, Vadodara, Gujarat, India.

International Journal of Frontiers in Life Science Research, 2022, 02(02), 016–025

Publication history: Received on 11 February 2022; revised on 09 April 2022; accepted on 11 April 2022

Article DOI: https://doi.org/10.53294/ijflsr.2022.2.2.0038

Abstract

A review was conducted by analysing many publications and they were concerned with the pharmaceutical quality directly and with the general quality practices. The content of those sources was analysed and some guidelines were identified which include WHO guidelines, FDA guidelines, EU guidelines and ICH guidelines. Upon reviewing the previously highlighted guidelines and the practices that are widely applied in the pharmaceutical industry, some topics were identified and reviewed like quality risk management, quality by design, corrective actions and preventive actions, process capability analysis, Six Sigma, process analytical technology, lean manufacturing, total quality management, out of trend, out of specification and HACCP.

Keywords: Quality management system; OOS; OOT; Elements; Principle

1. Introduction

The quality in the pharmaceutical industry has become a very important topic. Evolution of Quality in Industrial Sector During the early days, every one focus is only to accept or reject the manufactured goods based on the specifications after inspection and not trail was made how to prevent these defects. Since the world has gathered together to harmonize its practices and guides and the launching of the FDA current good manufacturing practices – the cGMP; for the 21st century – there has been a growing awareness for the significance of the quality of the pharmaceutical products. In the present scenario the context of Quality has emerged as an important factor. People are wise enough to choose things that assure to fulfil their demands. If we precisely define Quality, it means meeting the specifications that are summarized keeping in mind the demand of today's fast changing world. If we talk of Pharmaceutical Industry, quality becomes an unavoidable thing. Quality management in pharmaceutical industries, is an important subject because the drugs / or pharmaceutical products are directly delivered to the customers body system, thus identity, purity safety and ultimately appropriate quality of product are strongly essential. There are numerous guidelines worldwide that has made some sort of rules and specifications which must be followed by every pharmaceutical industry. To maintain quality in pharmaceutical products, Quality Management System is followed. In the 21st century, the quality management systems became mandatory in many countries to help the organization aimed at helping organizations, to achieve excellent performance and to achieve the delivery of zero defects.

2. Principle of quality management system

As the international Standard for quality management, ISO 9001 has been developed by experts from around the world to help you put quality at the heart of your organisation. ISO 9001 builds upon seven key principles. By following these principles, you will be able to reap the rewards of greater consistency, better customer satisfaction and stronger

* Corresponding author: Grishma Patel
Department of Quality Assurance, Pioneer Pharmacy Degree College, Vadodara, Gujarat, India.

performance. These principles are the basis of the ISO 9000 suite of quality standards, including ISO 9001:2015. In short, the seven principles of quality management are:

- Engagement of people
- Customer focus
- Leadership
- Process approach
- Improvement
- Evidence-based decision making
- Relationship management

3. Elements of pharmaceutical quality management system

There are four elements of a Pharmaceutical Quality System. The drug manufacturer can incorporate these elements as per product life cycle requirements, and there is no fixed scheme for applying these elements.

- Process performance and product quality monitoring system
- Corrective action and preventive action (CAPA) system
- Change management system
- Management review of process performance and product quality

3.1 Process Performance and Product Quality Monitoring System

The process monitoring system is an integral part of an organization's efforts in delivering a quality product. It shows the company's commitment to sustained resources and control. Risk assessment techniques can be used to detect shortcomings in-process components. Specialized tools and feedback can also be used to perform analysis on given parameters. An example could be detecting faults with the inspection system in Blister Packaging Machines. The inspection system is designed to detect empty pockets. Sometimes external factors affect the system, such as the accumulation of dust particles on the camera lens. In this case, the inspection system can accept all or just some empty blisters. The inspection system is checked randomly by both production personnel and the Quality Department to identify faults or malfunctions. Luckily, a tool like Issue Management Software by Simpler QMS, automates data collection, routing, and escalation of overdue activities. This makes the performance and safety monitoring of your products and processes much easier.

3.1.1 Corrective Action and Preventive Action (CAPA) System [4, 5]

Corrective Action and Preventive Action (CAPA) is a system for identifying the causes of the fault and preventing them from recurring in the future. The CAPA can be applied in case of complaints from both inside and outside the organization.

The CAPA structure and format can be different from organization to organization, but mainly it consists of the following information:

The department where process deficiency is found

- Fault detail and its implications
- A possible effect of fault on process or product
- Corrective Action to remove the problem
- Preventive action to prevent recurrence of the fault
- Due date to implement the corrective and preventive actions
- Next review date to assess the effectiveness of corrective action
- See the illustrated CAPA process below.

Identification → evaluation →Investigation →Analysis →Action Plan→ Implementation →Follow up

After necessary Corrective and Preventive actions are applied, the CAPA is sent again to auditors for approvals. Upon approval, the CAPA is closed, and the format is made part of the records.

For example, during a routine audit, the Job Description (JD) of one of the employees was out of date. The auditors initiated CAPA and gave time to make the JD available in the department. The respective department contacted the Human Resource (HR) department regarding the JD. When JD was available, the respective department filled the CAPA by stating the problem and proposing corrective action to avoid a similar condition in the future. The CAPA was presented to the auditors for approval. After approval, the CAPA format was made part of the records presented to regulatory bodies upon investigation.

The process presented in the example above can easily be automated with CAPA Management Software. It automates data collection, routing, follow-ups, notifications, approvals, and escalation of overdue activities allowing you to manage Corrective and Preventive Actions more effectively.

3.1.2 Change Management System

Different standards such as ISO and ICH promote innovation in existing processes to increase product quality. Pharmaceutical companies must have Change Management System to study, monitor, adapt, and approve the change. If the change is implemented after regulatory filings, the change in the respective process or procedure is submitted to the regulatory body for review and approval, as per the regulations.

For example, the supply chain department proposes to change the packaging size to reduce logistics costs. The quality department analyses the packaging requirement in light of accredited regulatory bodies and approves the change. The engineering department analyses the current equipment and its system to apply the change. After approvals from these departments supply chain orders the new packaging material size to implement in a small number of products. When these small quantities of products are prepared, the supply chain checks for its success and communicates it to all relevant departments. After approval from the supply chain, the production department updates its standard operating procedure (SOP) and communicates it to the Quality and Engineering department. The change is made official in change control format, with necessary approvals from the Production, Quality, and Engineering departments. The change is then reviewed by higher management to made part of the company's policy and process.

Fortunately, Change Management Software by Simple QMS makes the change management process a whole lot easier. It allows you to automatically track changes to SOPs, instructions, products, and product processes. Using the software, you can easily send changes through the approval process, and ensure that changes are implemented [6, 9].

4. Management Review of Process Performance and Product Quality

Management review is a process of reviewing process and product quality across various management hierarchy levels to escalate urgent quality and product problems. The purpose of management review is to propose improvements in product quality and process.

The management review includes the following:

- The commitment made to regulatory bodies
- Customer complaints
- Nonconformances
- CAPA review
- Audit findings
- Process performance
- Any pending matter or follow-up from previous management review

5. General practices recently applied in pharma industry [9, 12]

QMS and protocols are important in every organization to achieve the target of quality and safe products and this will work on the following:

- Total Quality Management (TQM)
- Six sigma
- QRM
- QbD

- Process capability analysis
- Change control/Change Management
- Out of specification (OOS)
- Out of trend (OOT)
- Corrective and Preventive actions (CAPA)
- Hazard Analysis and Critical Control Point
- Process analytical technologies
- Lean Manufacturing
- ISO

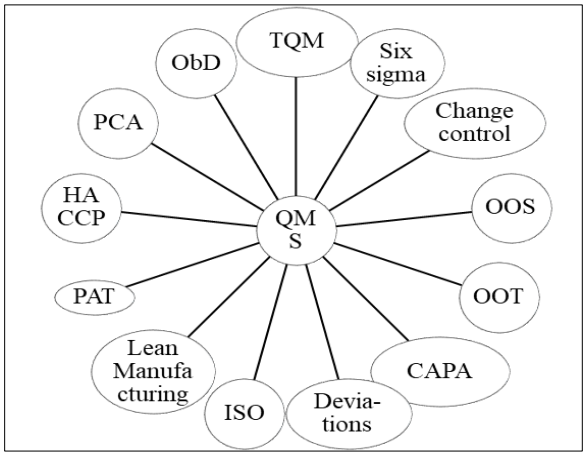

Figure 1 Principles of QMS

5.1 Total Quality Management (TQM)

TQM is a joint effort of an organization to improve quality at every level. TQM consists of efforts of organization to install and make an environment in which an organization unceasingly improves its ability to deliver high quality products and amenities to consumers.

The key elements of TQM approach are:

- Focus on the customer
- Employee involvement
- Continuous improvement

TQM is a complex approach which is used for quality management among various branches of pharmaceutical industry i.e., research and development, production and marketing.

5.2 Six Sigma [13, 14]

The six sigma can be defined as the method of continuous improvement intended at reducing defects which can be used along with lean management principles. The essentiality of lean management and six sigma principles are must in a pharmaceutical company in order to provide a zero-defect product which have safety and efficacy towards the customer. Today, many companies in different industries, both large and small, implement six sigma and lean together to improve efficacy of design, manufacturing, business processes and intellectual property in reducing costs. This implementation of six sigma and lean management together improves the total quality of the pharmaceutical and medical device industry with a minimal cost. This even resolves the matter of unnecessary cost that limits profitable innovation. To combat the situation of unstable and turbulent market in time of crisis, it is very much essential to implement the concept of six sigma along with lean management systems. The six sigma is an essential failure analysis tool to rectify the errors in most of the small medium industries and its implementation is essential even in pharmaceutical industries to increase the customer satisfaction and to reduce the cost.

Six Sigma involves two methods:

5.2.1 DMAIC

This abbreviation involves five phases for an improvement cycle define, measure, analyze, improve and control.

5.2.2 DMADV

This abbreviation involves five phases define, measure, analyze, design and verify.

5.3 QRM [16]

It is not always appropriate nor always necessary to use a formal risk management process (using recognized tools and/or internal procedures, e.g., standard operating procedures (SOPs)). The use of an informal risk management process (using empirical tools or internal procedures) can also be considered acceptable. The two primary principles of QRM are that the evaluation of the risk to quality should be based on scientific knowledge which ultimately linked to the protection of the patient and the level of effort, formality and documentation of the QRM process should be commensurate with the level of risk.

Initiating QRM Process → Personnel involved in QRM →Knowledge of the product and process →Risk assessment → risk control →Risk Review → Verification of QRM process and methodologies → Risk communication and documentation

5.4 QbD

In this progressively non-stop manufacturing environment, QbD uses a data-driven approach to deliver better understanding of manufacturing processes, reduced likelihood of batch failures, more efficient and effective control of change, as well as greater return on investment, time and cost savings. ICH Q8 defines design space from the concept that quality cannot be tested into product but has to be built in by design. Based on the ICH Q8; which concerns pharmaceutical development with targeting designing quality into the ingredients, formulation and manufacturing process to deliver the intended performance of the product. In these situations, opportunities exist to develop more flexible regulatory approaches. The design and conduct of pharmaceutical development research should be consistent with their intended scientific purpose.

5.4.1 Process capability analysis

Process capability analysis is a set of tools used to find out how well a given process meets a set of specification limits. In other words, it measures how well a process performs. In practice, it compares the distribution of sample values—representing the process outcome—to the specification limits**,** which are the limits of what we want achieved. Sometimes it compares to a specification target as well.

Process capability indices are usually used to describe the capability of a process. There are a number of different process capability indices, and whether you calculate one or all may depend on your analysis needs. But to calculate any process capability indices you assume stability of your process; for unstable processes process capability indices are meaningless. So, a first step in process capability analysis is a check for stability throughout the process.

5.4.2 Change control/Change Management

Change control is "A process that confirms the changes to material, means, equipment and software are properly documented, validated, permitted and visible". This can be defined as a systemic approach concerned with change in organization's aims, processes or protocols.

Change management system is a formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect the validated status of facilities, systems, equipment or processes. The intent is to determine the need for action that would ensure and document that the system is maintained in a validated state.

The main aim of this change management also known as restructuring management is to implement plans for achieving, controlling and the change and to help the people to familiarize with the new system. This includes planned protocols to demand a change and also a proper step to request and follow them up. The changes made to control the established processes must be recorded, reviewed and approved by the quality assurance unit.

Benefits of change management process:

- It permits the firm to measure the total influence of a change.
- The firm can respond quicker to client demands.
- Shortcomings in the process can be reduced.
- Variations can be applied without undesirably affecting the regular process in company.
- It helps an organization to line up current resources within the system.
- Timeline to implement the change will be reduced.
- Customer service and effective service will increase to clients and customer.
- Organizational effectiveness and efficiency are continued or even improved by allowing the concerns of employees.
- Proper change management process lowers the risk associated with the process and change.
- Employees will be aware about the change associated with the company and performance of employee will also increase.
- Company revenue also increases.
- Generates chance for the growth of "best practices", leadership development, and team development [15].

5.5 Out of Specification (OOS)

OOS can be defined as those outcomes of any procedures which may fall out of specified parameters, which are represented in the official monograph or compendia. The recurrent arising of oos in any process indicates that protocols/sops are not in control which result in refusal of final products which will be an ultimate loss for any company including pharmaceutical industries. This can be done by laboratory study by changing the errors in the SOPs and to address by quality control officer by supplementary laboratory testing.

The major goals of the investigation are to determine the root cause of existing potential problems. A written plan should be present prior to the investigation and it should be defined objectively.

5.5.1 Laboratory investigation

The objective of the investigation is to determine the root cause of the OOS results. The source of each OOS result should be identified either as an aberration of the measurement process or an aberration of the manufacturing process.

The laboratory investigation mainly consists of three parts:

- Phase I: Laboratory investigation (Identifying and assessing OOS test results)
- Phase II: Full-scale OOS investigation (Investigating OOS test results)
- Phase III: Investigation (Resampling)

The step-wise procedure for phase I is as follows

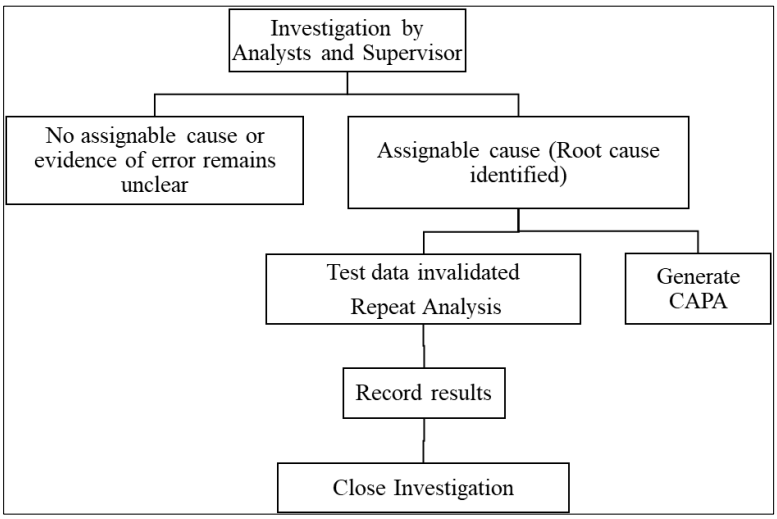

Figure 1 Phase I Diagram

The step-wise procedure for phase II is as follows:

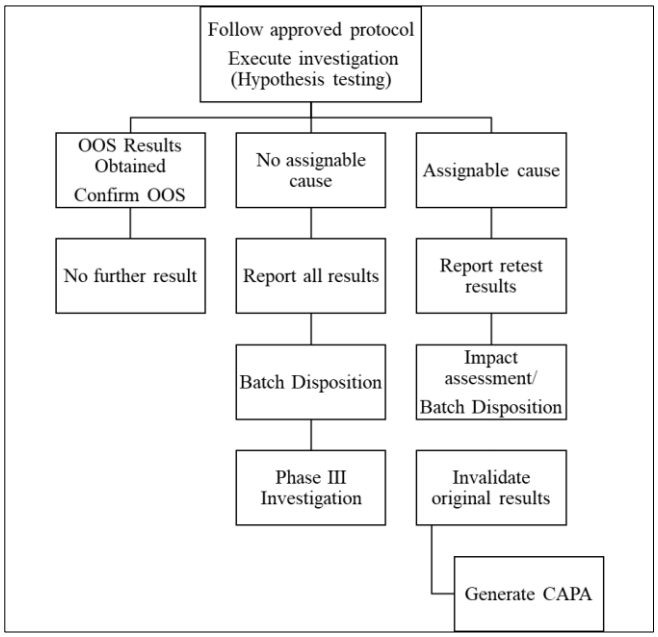

Figure 2 Phase II Diagram

The step-wise procedure for phase III is as follows

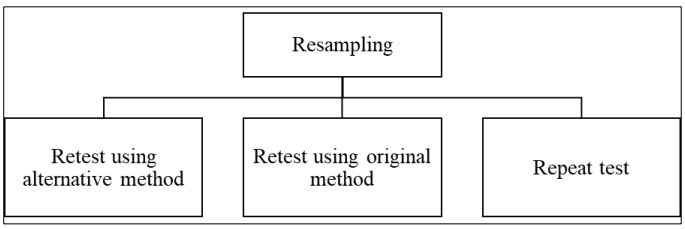

Figure 3 Phase III Diagram

5.6 Out of Trend (OOT)

OOT is an important governing or quality assurance constraint that is must to be addressed in a pharma industry in order to diminish the errors and to deliver an unchanging pharma product. Thus, OOT result is a stability result that does not follow the probable trend, either in comparison with other stability batches or with respect to old results or existed results. This is a task in pharmaceutical companies always to recognize OOT stability data and how to report this OOT stability results. The identification of out of trend results is a very stimulating task in the degradation and impurity analysis.

5.7 Corrective and Preventive Actions (CAPA)

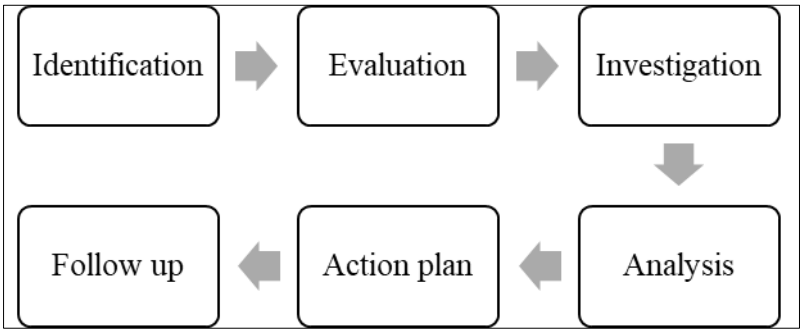

Figure 2 CAPA process

CAPA an important quality management value can be defined as a corrective action to reject defected nonconformity and as an action to prevent the incidence of nonconformity. The corrective actions help to eradicate the roots of a detected nonconformity or other unwanted situation and should avoid the reappearance of the same issues. Whereas the preventive action is to abolish the source of a, potential nonconformity or other undesired possible outcomes. The CAPA can be effectively implemented to assure satisfactory quality and regulatory requirements by the following basic steps :[9,12].

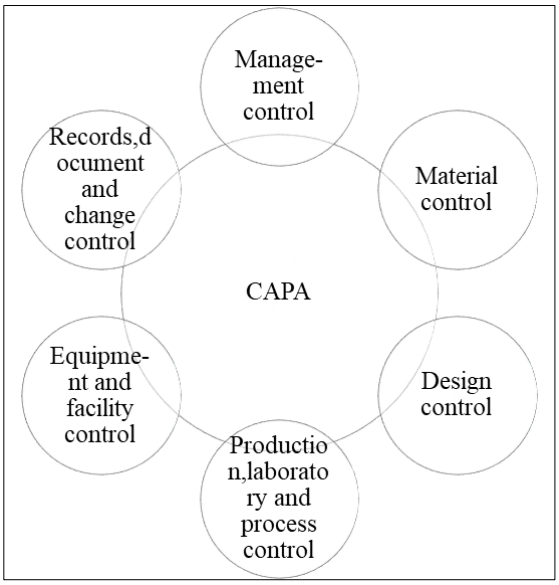

Figure 3 Relationship of CAPA with quality subsystems

CAPA is considered as important element of an effective QMS and should have a close connection with other quality subsystems.

5.8 Hazard Analysis and Critical Control Point

The Hazard Analysis and Critical Control Point (HACCP) methodology was known to be a safety management system used in the food industry. Their main aim is to prevent known hazards and to reduce the risks that they will cause at specific points in the food chain. HACCP is a systematic method for the identification, assessment and control of safety hazards. The hazards are classified as biological, chemical, or physical agents or operations that might cause illness or injury if not controlled. The HACCP system is based on seven principles:

- Conduct a hazard analysis.
- Determine the critical control points (CCPs).
- Establish target levels and critical limit(s).
- Establish a system to monitor the CCPs.
- Establish the corrective action to be taken when monitoring indicates that a particular CCP is not under control.
- Establish procedures to verify that the HACCP system is working effectively.
- Establish documentation concerning all procedures and keep records appropriate to these principles and their application.

5.8.1 Process analytical technologies

Process analytical technologies play a key role in enabling “quality by design” and scientific aspect of manufacturing. Its main aim is to understand and control the manufacturing process through the application of integrated chemical, physical, microbiological, mathematical and risk analysis methods. It has been applied in non-pharma industries for many years, yielding cost savings and manufacturing efficiencies. The implementation of process analytical technology

is bringing lots of benefits and improvements for many pharmaceutical processes. The benefits are lower production cycle times, improved manufacturing efficiency, reduced rejects and increased production operating time.

5.8.2 Lean Manufacturing

Lean manufacturing is about eliminating waste across an entire company and focusing on the big picture through learning how to do more with less. Lean manufacturing key benefits are eliminated waste, improve quality, reducing cost and reducing time.

5.8.3 ISO

ISO 9001 is defined as the international standard that specifies requirements for a quality management system (QMS). Organizations use the standard to demonstrate the ability to consistently provide products and services that meet customer and regulatory requirements. It is the most popular standard in the ISO 9000 series and the only standard in the series to which organizations can certifies 9001 helps organizations ensure their customers consistently receive high quality products and services, which in turn brings many benefits, including satisfied customers, management, and employees. Because ISO 9001 specifies the requirements for an effective quality management system, organizations find that using the standard helps them in organize a QMS, create satisfied customers, management, and employees, continually improve their processes and save costs.

6. Applications of Pharmaceutical Quality Management System

It is related to drug products, including biological and biotechnological products, throughout the product lifespan the systems supportive to the development and manufacture of pharmaceutical drug substances. It includes:

6.1 Pharmaceutical development

- Manufacturing and development of APIs.
- Manufacturing of medical delivery kits.
- Development of delivery systems.
- Pilot plant scale up activities.
- Formulation manufacturing process.
- Development of medical devices for accurate dosing.

6.2 Analytical method development

During manufacturing process:

- Acquisition and control of materials.
- Provision of facilities, utilities, and equipment.
- Production (packaging and labelling).
- QC and QA.
- Release.
- Storage.

During product technology transfer:

During product discontinuation:

- Retention of sample and related documentation.
- Continued product assessment and reporting [17].

7. Conclusion

Quality is still very important and strategics component of competitiveness. We can find quality as a component In Global Competitiveness report which determines countries growth towards innovation economy.

One of the most popular quality management systems in the words is ISO 9001 standard. It has many benefits that make it so popular within entrepreneurs. Overall, the conclusion is that different ways of working with QMS does not only impact the value of QMS per se, rather it also influences management's respect for and view of quality management.

Compliance with ethical standards

Acknowledgments

We are thankful to pioneer Pharmacy Degree College for valuable support and guidance.

Disclosure of conflict of interest

The author declare that they have no conflict of interest.

References

[1] Pandey P, Goyal A. Quality Management System in Drug Industry: A Review, Biomedical Journal of Scientific & Technical research. 2018; 2(1): 2177-2179.

[2] Kushare S, Darekar A. Quality Assurance and Quality Management in Pharmaceutical Science and Pharmaceutical Industry, Journal of Drug Delivery and Therapeutics. 2019; 9(2): 537-542.

[3] Baldi A, Bhandari S. Total Quality Management of Pharmaceuticals: Recent Approaches and Advancements, International Journal for Pharmaceutical and Allied Research. 2014; 4(2): 655-663.

[4] Patil D. Quality Management and Quality Assurance in Pharmaceutical Development, Academic Journal of Pharmaceutical Sciences. 2019 Jan; (1): 16-21.

[5] Sharma S, Bodla RB. Pharmaceutical Quality Management System: A Review, International Journal of Drug Regulatory Affairs. 2014; 2(3): 67-68.

[6] Savale SK., QBD: Approach used in Development of Pharmaceutical Formulations, Asian Journal of Biomaterial Research. 2017; 3(6): 11-24.

[7] Q10 Pharmaceutical Quality System, ICH Tripartite Guidelines, International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human use. 2009.

[8] Sharma P. An Analytical Study of Quality Management in Pharmaceutical Industries, International Journal of Management Research & Review. April 2017; 7(4): 482-489.

[9] Rompicherla N, Paul E. The significance of Quality Metrics in a Pharmaceutical Quality Management System-A case-based study, Indian Journal of Pharmaceutical education and Research. July 2020; 54(3): 798-808.

[10] Saudagar R, Doltade M. Role of Quality Assurance Department in Pharmaceutical Industries: A Review, Journal of drug Delivery and Therapeutics. 2019; 9(3): 678-683.

[11] Corinne Lee Siong, Chan Wan Kai, Quality Systems Implementation in the Pharmaceutical Industry, University of Mauritius Research Journal. 2009; 15: 436-457.

[12] Chaitanya MVNL, Chinni S. The Importance of Quality Management system for a successful Health care Industry: A Review Based on Case Studies, Journal of Chemical and Pharmaceutical research. 2018; 10(8): 143-149.

[13] Bhaskar M, Bhattacharya S. Total Quality Management in Pharmaceutics: A Review, International Journal of PharmaTech Research. 2011; 3(1): 365-375.

[14] Charde MS, Bande RT. Six Sigma: A novel approach to pharmaceutical industry, International Journal of Advances in Pharmaceutics. 2013; 2(6): 71-74.

[15] Lokesh MS, Gupta V Quality Management System in Change Control at Industry Level: An Overview, International Journal of Pharmacy and Pharmaceutical Sciences. 2015; 7(5): 13-19.

[16] Hemant Kumar S, Paneesh C. Handling Out-of-Specification during Laboratory Incidence, Journal of Global Trends in Pharmaceutical Sciences. 2019; 10(3): 6591-6597.

[17] Dubey N, Gupta H. Pharmaceutical Quality Management System: Current Concept, Journal of Advanced Pharmacy Education & Research. 2011; 2: 120-124.