Brief review on Total Quality Management in Pharmaceutical Industries

Article · December 2022

DOI: 10.35629/7781-070510301037

6 authors, including:

Priyanka Parekar
Delonix Society's Baramati College of Pharmacy Baramati
7 PUBLICATIONS **10** CITATIONS
SEE PROFILE

Shivpuje Shivpuje
Swami Ramanand Teerth Marathwada University
22 PUBLICATIONS **64** CITATIONS
SEE PROFILE

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 1030-1037 www.ijprajournal.com ISSN: 2456-4494

Brief review on Total Quality Management in Pharmaceutical Industries

Alfa A. Jain[1*], Priti D.Mane-Kolpe[2], Priyanka B.Parekar[3],Ashwini V. Todkari[3], Komal T.Sul[3], Shivraj S. Shivpuje[4]

[1]*DKSS's Institute of Pharmaceutical Sciences and Research, Swami-Chincholi, Pune, Maharashtra, India 413130.*

[2]*DKSS's Dattakala college of Pharmacy, Swami-Chincholi, Pune, Maharashtra, India 413130*

[3]*Delonix Society's Baramati College of Pharmacy Barhanpur Baramati, Pune, Maharashtra, India 413133.*

[4]*School of Pharmacy SRTM University, Nanded, Maharashtra-431606.*

Submitted: 02-10-2022 Accepted: 12-10-2022

ABSTRACT:

The pharmaceutical products or drugs are directly delivered tocustomer's body system, so need to assured that products must meet their specifications such as quality, purity and safety. Maintaining quality of such products havegreat challenge for pharmaceutical Industries which could be achieved by total quality management (TQM).TQM an organizational approach that focuses on quality as an overarching goal, aimed at the prevention of defects than detection of defects. Quality assurance and quality control department in all pharmaceutical industry maintain such quality.

The success of quality management depends on various guidelines like Good Manufacturing Practices, Good Laboratory Practices, along with implementation of Total Quality Management, Six Sigma, Change Management/ Change control/ Deviation Management, Out of Specifications (OOS), Out of Trend (OOT), Corrective & Preventive Actions (CAPA).

Keywords: Total Quality Management, Out of Specification, Out of Trend, Pharmaceutical Industries and Corrective Action and Preventive Action.

I. INTRODUCTION:

The pharmaceutical industriesarevital segment of the health care system that conducts research, manufacturing and marketing of pharmaceuticals, biological products and medicinal devices used for the diagnosis as well as treatment of diseases [1].If products are not of appropriate quality then they could beresult in severe adverse effects or even death of the consumers or patients. Initially concept of total quality control is used that quality is assured just on basis of quality control parameters[2]. But this concept of TQM involves building quality in a pharmaceutical product as it involve complete records such as standard operating procedures for every step, validation records, master formula records and batch production records etc[3]. This review includes information about quality, quality management, current status and need of TQM. This article describes TQM as multifaceted approach for quality management of pharmaceuticals by utilizing various quality management approaches such as quality by design, good manufacturing practices, quality risk management etc. leading to high quality products[4, 5]. In figure 1Design Do Analyze Act (DDAA) cycle

II. THE BASIC COMPONENTS OF TQM

2.1 Design: Establish the processes necessary to carry out quality test.

2.2 Do: Implement the processes.

2.3 Analyze: Monitor and measure processes and products against Policies.

2.4 Act: Take action continuously for improving quality of product.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 1030-1037 www.ijprajournal.com ISSN: 2456-4494

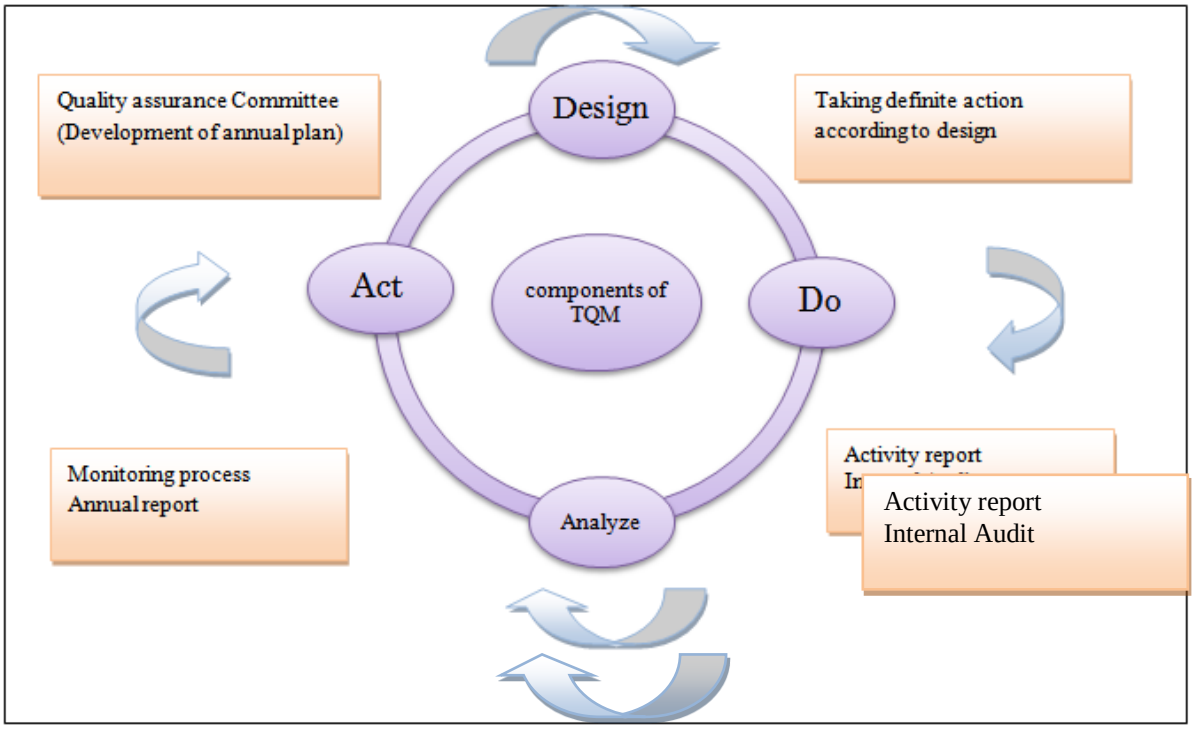
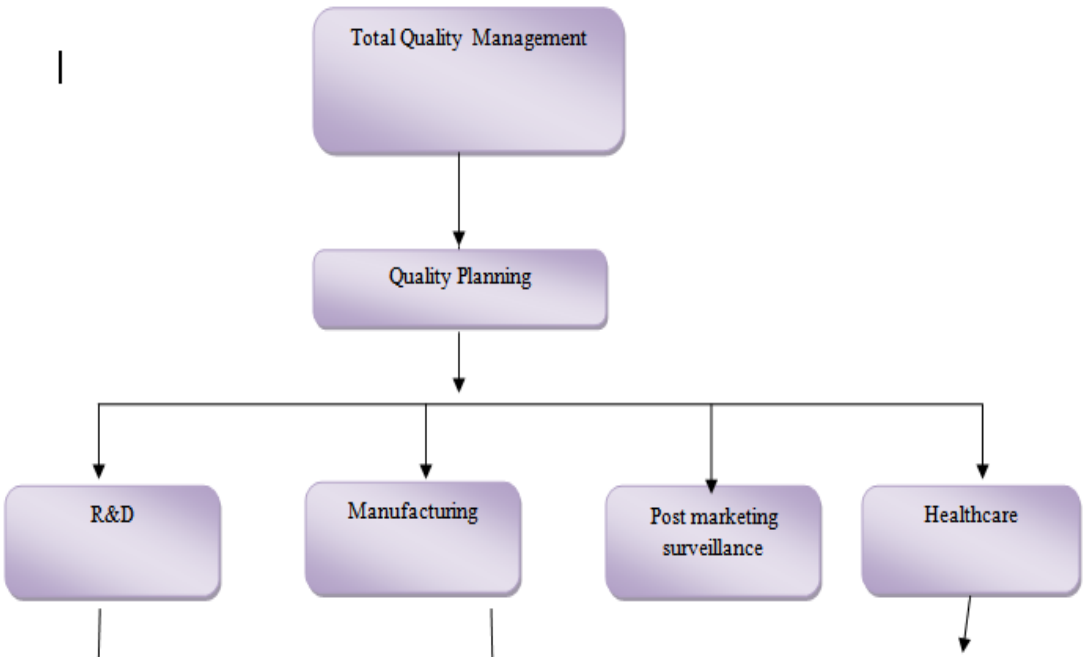


Figure 1: Design Do Analyze Act (DDAA) cycle

III. MANAGEMENT OF QUALITY IN DIFFERENT AREA OF PHARMACEUTICAL

Various phases of TQM approach are described figure 2.



International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 1030-1037 www.ijprajournal.com ISSN: 2456-4494

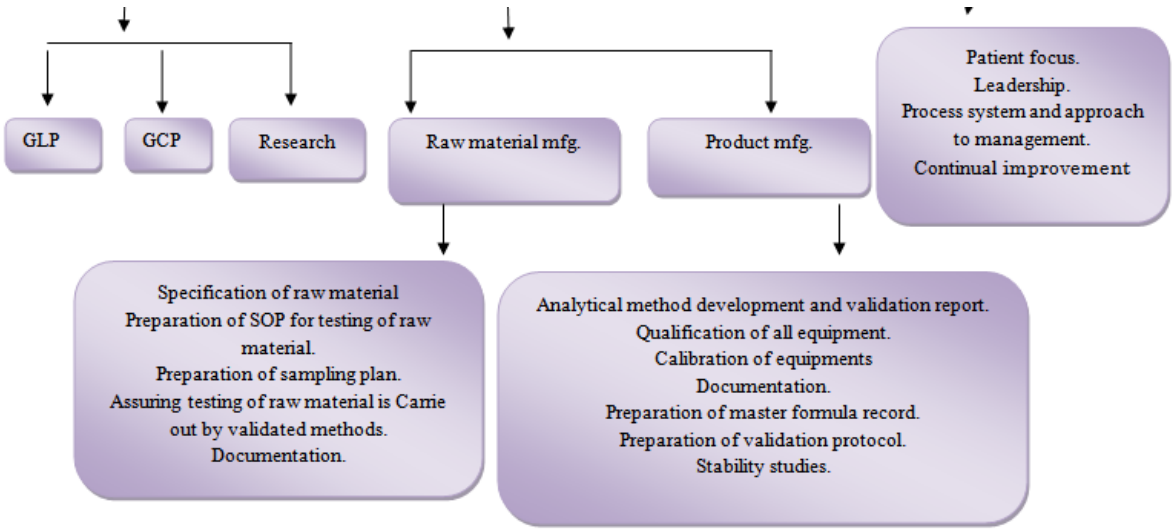


Figure 2: Various approaches in pharmaceutical industry

3.1Research and development:TQM also plays very relevant role in quality management in research and development process. It involves following points:

3.1.1 Good Laboratory Practices (GLP)

1. It strictly controls the use of animals during experiments in laboratory.
2. TQM in GLP involves following points.
3. Prepares protocol or master schedule sheet for the study.
4. Maintain copy of protocol, required for conducting study in the laboratory.
5. Periodic analysis of equipment through which study is to be carried out.
6. Documentation if any change in approved protocol of the study then there should be documentation along with reason for approval of the change. [6, 7].

3.1.2 Good Clinical Practices (GCP)

It strictly control over use of human beings in clinical trials. The approaches for GCP are almost similar to that of GLP. The major difference being that before involving any subject or human being into the clinical trials study. A complete duly filled informed acquiesce form should be taken from subjects along with their signature to make sure that subject is known about clinical trials study. These records should be documented [8, 9].

If patient rebel during the study then number of rebel along with reason should be documented.

3.2 Manufacturing:In production, it include manufacturing of both raw materials and API, production and packaging of dosage form, along with pilot plant scale up activities[10].

3.3 Post marketing surveillance:Management of quality is based on market survey which is based on post marketing surveillance, involves change control and its documentation if any change is required in the approved process[11].

3.4 Healthcare: Quality management in healthcare involves following points:

Patients focus: healthcare organization depends on the patients, should meet patients' requirements and aim to exceed their expectations[12].

3.4.1 Leadership: Leaders establish direction of the organization. It creates and maintain the internal environment in which people could be fully achieve the organization's objectives[13].

3.4.2 Process and system approach to Management:A desired result is achieved more efficiently when activities are managed as a process. Identifying, understanding, and managing the system for effectively archiving objective of organization[14].

3.4.3 Continual improvement: Continual improvement of the organization's means overall performance should be a permanent.

IV. IMPLEMENTATION OF QUALITY IN PHARMACEUTICAL INDUSTRY:

4.1 Six sigma

The six sigma could be defined as the methodology of continuous improvement aimed to reduce defects which could be used along with lean management principles. Six sigma principles are must in pharmaceutical industries in order to provide a zero defect product with quality, safety and

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 1030-1037 www.ijprajournal.com ISSN: 2456-4494

efficacy towards the consumer. Today, many companiesselect six sigma for improving efficiency of design, manufacturing, with reducing costs. This implementation of six sigma and lean management in together improves the entire quality of the pharmaceutical industry with a minimal cost [15, 16].

The six sigma is an essential tool for failure analysis to rectify the errors in most of the pharmaceutical industries and its implementation is an essential to enhance the customer satisfaction with reduce the cost[17].

Benefit: The successful cases of Aspen Medical Europe Limited (hereafter called Aspen Medical), are the best examples that explain the need of six sigma in a pharmaceutical industry. For a success of quality product with minimized cost[18].

To understand the six sigma for basic learners, it could be best understand with the help of given in Figure 3

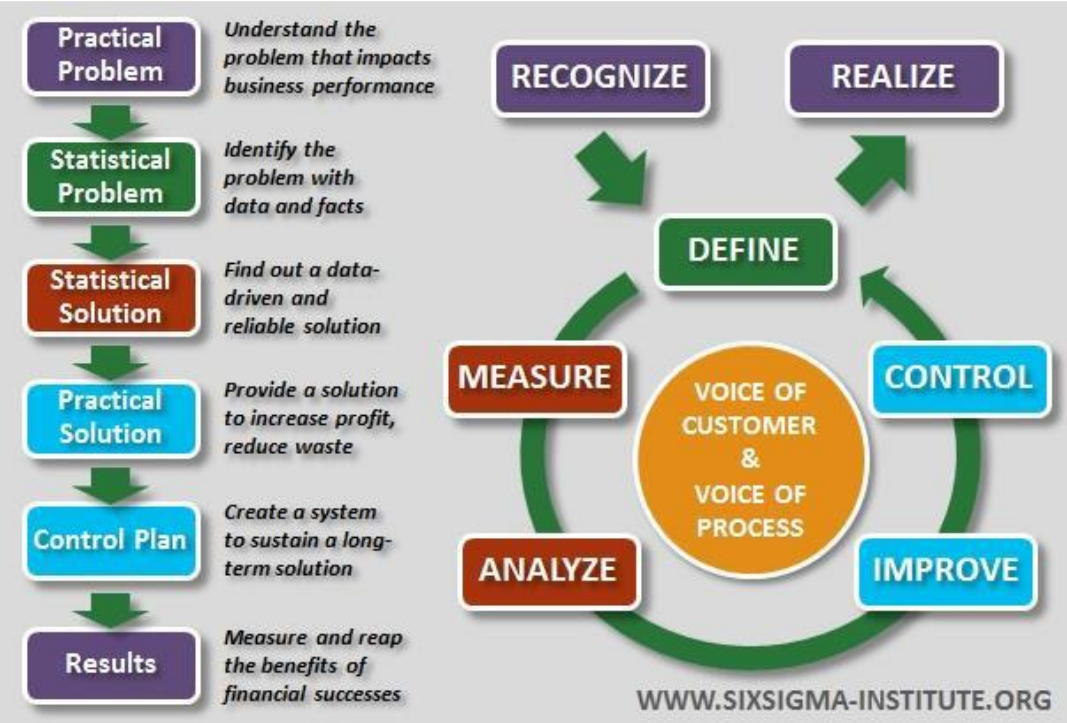


Figure 3: The basic concepts of six sigma and DMAIC principles[19]

4.1.1 Implementation of six sigma is perform by different ways in pharmaceutical industries:

Companies require employee with six sigma certification. It proof that employee has taken course of six sigma and has knowledge to run production process systematically.

Pharmaceutical companies that has offering six sigma course in their company. This help older employee to attain six sigma certification course and improve their performance.

Many companies send their employee for training for six sigma course[20].

4.2 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 arising of OOSin any procedure indicates that procedure are not in control which result in rejection of final products which could be an ultimate loss for any pharmaceutical industries. So that it is an important criteria to address the OOS results. This could be eradicate by laboratory investigation by changing the errors in the standard operating procedures and to address by quality control officer by additional laboratory testing[21].

In a deep study, the OOS could be eradicated in three phases-

Phase I: Laboratory investigation

Phase II: Full scale investigation

Phase III: Review of product development.

This OOS could be easily understand 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

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 1030-1037 www.ijprajournal.com ISSN: 2456-4494

package. It is addressed in this case study that investigation of OOS is an important criteria and reporting immediately the oos results to the authorities is an important agenda by the laboratory quality control staff [12][22]Figure 4.

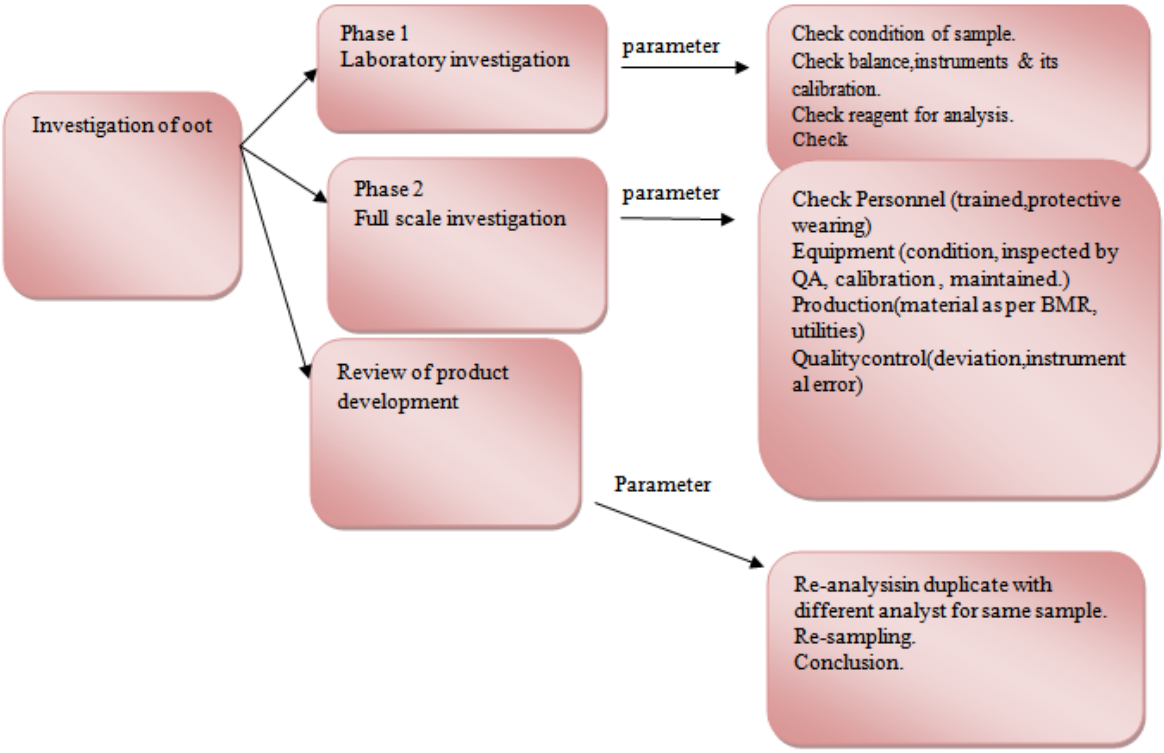


Figure 4: Out of specification

4.3 Out Of Trend (OOT): The Astra Zeneca defined OOT as an out of trend is an important regulatory or quality assurance parameter that is must to be addressed in a pharmaceutical industry in order to minize the errors and to deliver a stable pharmaceutical products. 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 [23, 24].

The OOT could be better understood by taking a case study as an example presented by Dr Pradeep, Quality control manager, Haffkine Bio-Pharma. Corp. Ltd., Mumbai.

Example-

The specificationlimit for assay is: 95.0-105.0% w/w of label claim and the result obtained was 95.8 % w/w, even though the results are within the specified limits but it is must to compare the result with the previous data, if it found the average value of the trend is 99.05 w/w, then this batch result of 95.8 w/w is called as Out of trend (OOT). The OOT can be best understood by reading various documented literatures, however OOTissues in most of the pharmaceutical issues like product stability, raw materials are less understood but became a hot core interest for regulatory authorities.

4.4 Corrective and Preventive actions (CAPA) :

The CAPA is an important quality management principle can be defined as corrective action to eliminate detected nonconformity and as an action to prevent the occurrence of non-conformity.

The CAPA could 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 lead 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

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 1030-1037 www.ijprajournal.com ISSN: 2456-4494

essential to prevent these type of mishaps and can produce zero defect and safe products to customer at economical rates[25].

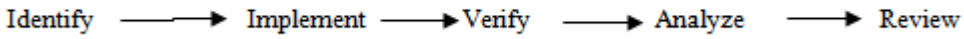
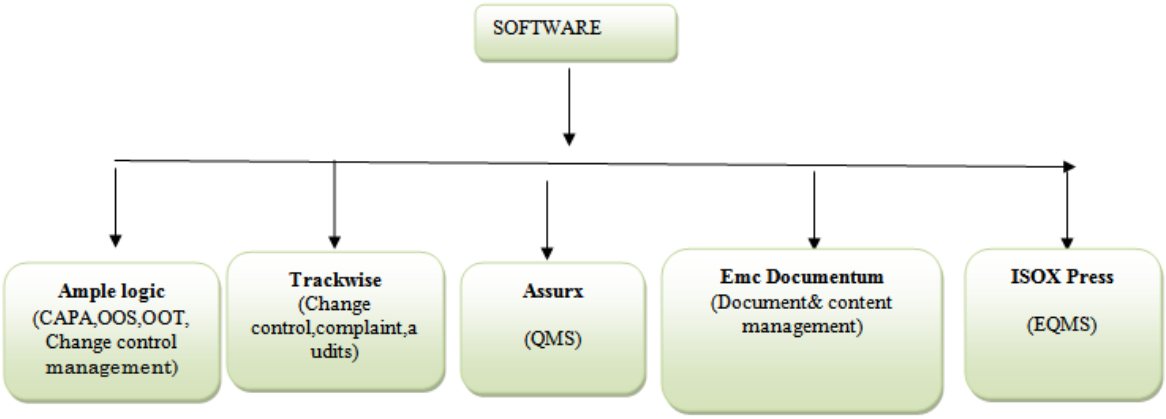


Figure **: CAPA: Five step process**

V. SOFTWARE USED FOR MANAGEMENT OF QUALITY IN PHARMACEUTICAL INDUSTRY:



5.1 Ample logic software: It provides,automated and computerized solution to pharmaceutical industries. It is used for various purpose likeCAPA,OOS,OOT etc.in implementation of quality in pharmaceutical industry[26].

5.1.1CAPA tracking software:This software helps by identifying and taking corrective action .Ample logic CAPA is important tool for better of business process used to design new pharmaceuticalproductsor redesigns existing one[27].
It has 3 important steps:
Identifying root cause of problem
Impact assessment
Recommending CAPA

5.1.2Change Control Management: Change control software will keep record of each & every change made to material,methods, equipment and software and that are properly documented, validated, approved and verified it[28].
This process starts by requesting change made by internal user client. Next option is called change control auto-motion that improves transparency throughout process.
In this way, change control is managed by using this software.

5.1.3out of specification (OOS): This software describes results are within range or out of range.This software has various key feature which are as follow:
a)**Simplified OOS**:-Reports provides information without manual data entry as everything is done automated with this feature issue are corrected on time & error are drastically reduced.
b)**Phase wise investigation:**Takes place by software when OOS is reported finally, it is subjected to future investigation with aid of this features tasks brought are re analyzed re-testing re-sampling & crosschecked for compliance with regulatory bodies.
c)**Automated alter & notification**:Uses are notify directly through emails that are seut automatically to users email account.
OOTsolution is to be transmitted into current process within a short, this compression tracking & trending will automatically generate metric reports & summarized reports with a click of a button.

VI. CONCLUSION:

The implementation of quality management systems in pharmaceutical industry is very essential in order to deliver a quality,safety and zero defect product at an economical rate.Also in order to minimize the mishaps or dangerous contaminations in a pharmaceutical products. These

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 1030-1037 www.ijprajournal.com ISSN: 2456-4494

principles are very much essential, The OOS & OOT are very much essential in a pharmaceutical company to give assurance on the quality of products. The change management system plays an important role in the pharmaceutical companies to come up with innovative, safe and clinically approved drugs at cheaper cost.

REFERENCES:

[1] B. Mazumder, S. Bhattacharya, A. Yadav, Total quality management in pharmaceuticals: a review, Total Quality Management.Vol-3, 365-375.

[2] A. Mitra,2016,"Fundamentals of quality control and improvement",John Wiley & Sons,vol-4,II, 25-30

[3] S. B. B. Bhandari ,A. Baldi, 2014, "Total quality management of pharmaceuticals: recent approaches and advancements total quality management of pharmaceuticals" recent approaches and advancements.Vol-4, II, 655-660

[4] P. Pandey ,G. Anju,2018," Quality Management System in Drug Industry" A Review, Biomedical Journal of Scientific & Technical Research,Vol-2,I, 2177-2179 .

[5] J. N. Morfaw,2009."Total quality management (TQM) A model for the sustainability of projects and programs in Africa" University press of America,Vol-1, 8-9

[6] M. Bajpai ,J. D. Esmay,2002,"In vitro studies in drug discovery and development: an analysis of study objectives and application of good laboratory practices (GLP)" Drug metabolism reviews, Vol- 34, 679-689.

[7] J. P. Myers, F. S. vom Saal, B. T. Akingbemi, K. Arizono, S. Belcher, T. Colborn, I. Chahoud, D. A. Crain, F. Farabollini, L. J. Guillette Jr,2009,"Why public health agencies cannot depend on good laboratory practices as a criterion for selecting data: the case of bisphenol A" Environmental health perspectives, Vol- 117, 309-315.

[8] L. Beghin, M. Castera, Y. Manios, C. Gilbert, M. Kersting, S. De Henauw, A. Kafatos, F. Gottrand, D. Molnar, M. Sjöström,2008,"Quality assurance of ethical issues and regulatory aspects relating to good clinical practices in the HELENA Cross-Sectional Study" International Journal of Obesity, Vol- 32, S12-S18.

[9] N. Bergamo, V. de Trespalacios, M. L. Marquez, S. Perez, S. Samaniego, E. Vander Elst,2001,"Good Clinical Practices (GCP) in Latin America: Prospects for regional harmonization: a challenge for the twenty-first century" Drug information journal: DIJ/Drug Information Association, Vol- 35, 27-34.

[10] A. Adamo, R. L. Beingessner, M. Behnam, J. Chen, T. F. Jamison, K. F. Jensen, J.-C. M. Monbaliu, A. S. Myerson, E. M. Revalor, D. R. Snead,2016,"On-demand continuous-flow production of pharmaceuticals in a compact" reconfigurable system, Science,Vol-352, 61-67.

[11] Y. Suzuki, M. Shibuya, S.-i. Satoh, Y. Sugimoto, K. Takakura,2007," A postmarketing surveillance study of fasudil treatment after aneurysmal subarachnoid hemorrhage" Surgical neurology, Vol-68,126-131.

[12] U. Varshney,2007,"Pervasive healthcare and wireless health monitoring" Mobile Networks and Applications, Vol-12, 113-127.

[13] K. Blanchard,2018,"Leading at a higher level: Blanchard on leadership and creating high performing organizations" FT Press,Vol-1, 6-7

[14] I. P. McCarthy ,B. R. Gordon,2011,"Achieving contextual ambidexterity in R&D organizations: a management control system approach" R&d Management,Vol-41, 240-258.

[15] H. De Koning, J. P. Verver, J. van den Heuvel, S. Bisgaard, R. J. Does,2006," Lean six sigma in healthcare" Journal for Healthcare Quality,Vol-28,4-11.

[16] L. Sehwail ,C. DeYong,2003, "Six Sigma in health care" Leadership in Health Services,Vol-1

[17] M. S. Raisinghani, H. Ette, R. Pierce, G. Cannon, P. Daripaly, 2005,"Six Sigma: concepts, tools, and applications" Industrial management & Data systems,Vol-1, 2-3

[18] S. Roan ,M. Jernelid,2009,"Six Sigma strategy applied to the pharmaceutical industry: how customers benefit," ed,Vol- 1, 2-4

[19] M. Chaitanya, S. Chinni, M. Jyothi, Y. P. Reddy,2018,"The Importance Of Quality Management System For a Successful Health Care Industry: A Review Based on Case Studies" Journal of Chemical and Pharmaceutical Research, Vol-10,143-149.

[20] M. T. Taner, B. Sezen, J. Antony,2007, "An overview of six sigma applications in

healthcare industry" International Journal of health care quality assurance,Vol-1, 5-6

[21] T. Appleton, P. Bryan, D. Contos, T. R. Henry, P. Lehmann, S. Ohorodnik, D. Reed, C. Robichaud, J. Schetter, N. South,2012,"Nonclinical dose formulation: out of specification investigations" The AAPS journal,Vol-14, 523-529.

[22] M. Kader,2016,"Mitigating the Risks of Generic Drug Product Development: An Application of Quality by Design (QbD) and Question based Review (QbR) Approaches" Journal of Excipients and Food Chemicals,Vol-7,915.

[23] M. Bašić ,B. Knežević,2018, "implementation of patient-satisfaction questionnaire at uhc zagreb," IN 18. hrvatska konferencija o kvaliteti I 9. znanstveni skup hrvatskog društva za kvalitetu međunarodni stručni i znanstveni skup

[24] M. J. Suh, S. S. Kim, M. S. Song, M. S. Yee, E. G. Oh, K. R. Shin, O. S. Kim, S. J. Lee, Y. J. Lee, H. S. Oh,2001,"An analysis on the contents and the trend of nursing research published in Journal of Korean Academy of Adult Nursing", J Korean Acad Adult Nurs,Vol-13, 571.

[25] G. Nahler,2009,"corrective and preventive actions (CAPA) Dictionary of Pharmaceutical Medicine", Springer,Vol-1, 40-40.

[26] D. Jackson,2012,"Software Abstractions: logic, language, and analysis." MIT press,Vol-1,141142.

[27] A. Kusinitz,2004"Understanding CAPA Requirements in a Software Context" Biomedical instrumentation & technology,Vol- 38,221-224.

[28] F. T. Rothaermel, 2016, Strategic management: concepts" McGraw-Hill Education,vol- 4,[14] 2-6 .

[29] Pravin P Karle, Shashikant C Dhawale, Vijay V Navghare, Shivraj S Shivpuje. 2021; Optimization of extraction conditions and evaluation of Manilkara zapota (L.) P. Royen fruit peel extract for in vitro α-glucosidase enzyme inhibition and free radical scavenging potential. Future Journal of Pharmaceutical Sciences, 7(1):1-10.

[30] MR Rao, S Shivpuje, R Godbole, C Shirsath. 2015; Design and evaluation of sustained release matrix tablets using sintering technique. International Journal of Pharmacy and Pharmaceutical Sciences, 8(2):115-121.

[31] MRP Rao, S Taktode, SS Shivpuje, S Jagtap. 2016; Optimization of Transmucosal Buccal Delivery of Losartan Potassium using Factorial Design. Indian Journal of Pharmaceutical Education and Research, 50(2): S132-S139.

[32] N Patre, S Patwekar, S Dhage, S Shivpuje. 2020; Formulation & Evaluation Of Piroxicam Bionanocomposite For Enhancement of Bioavailability. European Journal of Molecular & Clinical Medicine, 7(11): 9362-9376.

[33] SJ Wadher, SL Patwekar, SS Shivpuje, SS Khandre, SS Lamture. 2017; Stability Indicating Assay Methods for Simultaneous Estimation of Amoxicillin Trihydrate And Cloxacillin Sodium in Combined Capsule Dosage Form by UV-Spectrophotometric Method. European Journal of Biomedical and Pharmaceutical sciences, 4(10).

[34] Santosh A.Payghan Shivraj S. Shivpuje Shailesh L. Patwekar, Karna B. Khavane, Padmavati R. Chainpure. 2021; A Review on Different Preparation Method Used For Development of Curcumin Nanoparticles. International Journal of Creative Research Thoughts, 9(1):4088-4101.

[35] Zeba Ashfaq Sheikh P. R. Chainpure, S. L. Patwekar, S. S. Shivpuje. 2019; Formulation and evaluation of Garciniacambogia and Commiphoramukul Herbal tablets used for Anti- Obesity. International Journal of Engineering, Science and Mathematics, 8(4): 180-195.

[36] Sheetal Rathod P. R. Chainpure, S. L. Patwekar, S. S. Shivpuje. 2019; A Study Of Carica Papaya Concerning It's Ancient And Traditional Uses - Recent Advances And Modern Applications For Improving The Milk Secretion In Lactating Womens. International Journal of Research, 8(2):1851-1861.

[37] Shivraj S. Shivpuje Shailesh J. Wadher, Bhagwan B. Supekar. 2019; Development And Validation of New FT-IR Spectrophotometric Method For Simultaneous Estimation Of Ambroxol Hydrochloride And Cetirizine Hydrochloride In Combined Pharmaceutical. International Research Journal of Pharmacy, 10(3):110-114.

[38] Shivraj S. Shivpuje, Shailesh J. Wadher, Bhagwan B. Supekar. 2019; Simultaneous Estimation of Ambroxol Hydrochloride and Cetirizine Hydrochloride in Combined Solid

Tablet Formulations by HPTLC-Densitometric Method. Asian Journal of Biochemical and Pharmaceutical Research, 9(1):1-10.

[39] JW Sailesh, SS Shivraj, SI Liyakat. 2018; Development and Validation of Stability Indicating RP-HPLC Method for the Estimation of Simvastatin in Bulk and Tablet Dosage form. Research Journal of Pharmacy and Technology, 11(4): 1553-1558.

[40] Patil S. S. Shivpuje Shivraj S. Patre Narendra G. 2017; Development and Validation Of Stability Indicating HPTLC Method For Determination of Nisoldipine (Niso) In Tablet Dosage Form. European Journal of Biomedical and Pharmaceutical sciences, 4(12):462-468.

[41] Lamture Sima S. and Shaikh Isak Wadher Shailesh J., Kalyankar Tukaram M., Shivpuje Shivraj S., Khandre Supriya S. 2017; Development And Validation Of Stability Indicating Assay Method For Simultaneous Estimation Of Amoxicillin Trihydrate And Cloxacillin Sodium In Pharmaceutical Dosage Form By HPTLC. World Journal of Pharmaceutical Research, 10(6):1002-1014.

[42] W Shailesh, K Tukaram, S Shivraj, L Sima, K Supriya. 2017; Development and Validation of Stability Indicating UV Spectrophotometric Method for Simultaneous Estimation of Amoxicillin Trihydrate and Metronidazole In Bulk And In-House Tablet. World Journal of Pharmaceutical and Medical Research, 3(8):312-318.

[43] J Wadher Shailesh, M Kalyankar Tukaram, S Shivpuje Shivraj. 2017; Development and Validation of Stability Indicating Assay Method for Simultaneous Estimation of Amoxicillin Trihydrate and Cloxacillin Sodium In Pharmaceutical Dosage Form By Using RP-HPLC. World Journal of Pharmaceutical Research, 10(6):1002-1014.

[44] Priyanka B. Parekar, Shivraj S. Shivpuje, Vijay V. Navghare, Manasi M. Savale, Vijaya B. Surwase, Priti S. Mane- Kolpe, Priyanak S. Kale. 2022; Polyherbal Gel Development And Evaluation For Antifungal Activity, European Journal of Molecular & Clinical Medicine. 9(03): 5409-5418.