



## PAT AND CAPA: OVERVIEW FOR INDUSTRIAL AND ANALYTICAL APPLICATIONS

**Chandni Chandarana<sup>1\*</sup> and Mehali Patel<sup>2</sup>**

<sup>1</sup>Assistant Professor, Department of Quality Assurance Techniques, Smt. BNB Swaminarayan Pharmacy College  
Salvav, Vapi, Gujarat, India.

<sup>2</sup>Student, Smt. BNB Swaminarayan Pharmacy College Salvav, Vapi, Gujarat, India.

**\*Corresponding Author: Chandni Chandarana**

Assistant Professor, Department of Quality Assurance Techniques, Smt. BNB Swaminarayan Pharmacy College Salvav, Vapi, Gujarat, India.

Article Received on 09/12/2017

Article Revised on 30/12/2017

Article Accepted on 21/01/2018

### ABSTRACT

Nowadays PAT and CAPA are in major use by most of pharma industries for better and higher yield in production section and financial profit. These designs are based on analytical data analysis and process validation. Implementing PAT and CAPA is quite lengthy procedure but is very beneficial in industrial application. PAT can be implemented right from the starting of the production till end where the finished product is obtained. CAPA can be Implemented, pre and post operational ways. This review article gives information about PAT and CAPA implementation in pharmaceutical industries and some analytical approaches. PAT and CAPA can be applied in each and every steps involved in any industries starting from raw material analysis to finished end product. In this review we will see overview on PAT and CAPA implementation and application of their in pharma field.

**KEYWORDS:** PAT (Process Analytical Technology), CAPA (Corrective And Preventing Action).

### INTRODUCTION

#### **PAT :- (Process Analytical Technology)**

Process analytical technology (PAT) is a system or process of designing, analysing and controlling manufacturing throughout process. PAT involve the use of raw material properties, process examination, manufacturing parameters and chemometric techniques to produce finished products of acceptable quality and purity. PAT is a system used for improving quality of raw materials as well as finished products to pharmaceutical industries in manufacturing field. It is also useful in reducing manufacturing cost by eliminating errors in process. PAT is employed by means of use of data analyser in production area.

#### **CAPA :- (Corrective and Preventive Action)**

Corrective action is steps taken for eliminating the causes of an existing error in manufacturing procedure. It also ensure the recurrence of errors or undesirable situations. Whereas preventive action are steps taken to eliminate the potential errors in process. The preventive action is designed to prevent the occurrence of situations of errors in process of manufacturing area which is not yet exist. CAPA is process of eliminating causes in manufacturing procedure. It ensure the reduction in errors in manufacturing area

### Implementation of Pat

#### **1. Basic Acknowledge**

The PAT guidance stress on the need to create a wide explanation of the below given concept beyond pharmaceuticals manufacturing procedure to decide the standards laborious to process and product purity.

The information given by the PAT Application is followed in three main types:

- It is a foundation for robust process and product design.
- It provides continuous learning throughout the product life cycle.
- It assists and explains various advantageous ways for novel new application.

The procedure of experiments, and evaluation of analytical measurement data are valuable parts of building the knowledge base.

#### **Examples of sources of variation**

- Difference in the raw material provider manufacturing processes that impact the chemical and physical parameters of the provided materials.
- Time difference in manufacturing event (e.g., between equipment maintenance events).
- Effects linked to planned changes to equipment / analyser hardware and software of the system.

- Employee's ways of working (i.e., various mid setup of employee in manufacturing area).
- Fluctuation in environmental factors (e.g. temperature, humidity and other environmental factors).
- Long term usage of certain instrument may leads to deterioration of product.

## 2. Process examination and control

The understanding of interrelation between unit operation and product is the basic essential need for the scheme of the process examination, process control and Quality Assurance variables used in production. PAT is an in-process application in which the outcome received by the on time analysis of laborious process control steps are used to control the process in various methods. Throughout manufacturing, procedure parameters are calibrated (within the limits) to get the required product quality at the end of procedure. The automated system required for this level of process control are accessible nowadays and are used widely in the field of chemical industries. Updated Technologies used in PAT include: Near infra red (NIR), Raman spectroscopy, UV – visible Spectrophotometer, Fourier Transform Infrared (FTIR), XRay Powder Diffraction (XRPD), Terahertz Pulse (TP) spectroscopy, NIR microscopy, Acoustic Resonance (AR) spectrometry, thermal effusivity, etc. In which NIR spectroscopy is the most trendy and widely used technique.

## 3. Calibration of PAT system

The calibration plan for a PAT system, include the calibration of Software for data analysis, Process analyser hardware and software Process control. Software IT systems for the regulation, storage and backup of outcome.

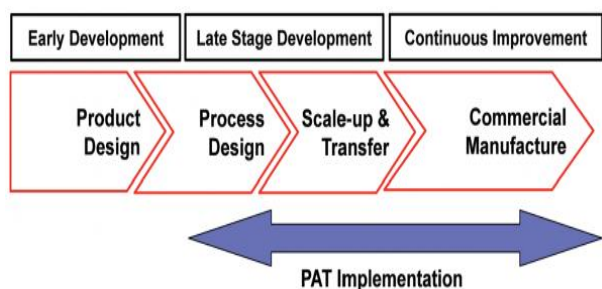


**Figure 1: Implementing of product lifecycle.**

## Implementation of Capa

Implementing corrective or preventive action is efficient technique for quality assurance and systematize framework is achieved in seven basic steps:

- The detection of the difficulties, non-acceptance, or incident or the probable difficulties.
- Determination of level of the fault and possible impact on the industry.
- The evolution of a procedure with several roles.
- Executing full Analysis of the fault with proper documenting procedure.

- Providing an Action Plan including all the parameters that must be proceeded to correct and/or prevent the problem.
- The Implementation of design requires pre-verification of procedure.

## Identification

The first step in the task is to find the fault. It is necessary to describe the situation that fault exists. This must involve the reference of the data, a wide clarification of the fault, proof for fault that is present.

**Report Source** Reporting the reference of the data available can be very useful when conducting an investigation into the fault and implementing the action plan that is provided. It will also provide data for determination of the potency of the quality system and increase the finishing of the steps taken to the proper employee or departmental area.

Corrections/Corrective and preventive actions for Quality affairs, hazards and non-acceptance should be identified from the following:

- Purchaser survey and regular inspections
- Internal Audits
- Purchaser protest
- Purchaser returns
- Product recalls
- Output of management reviews
- Any other GMP issues / observations and non-conformances.

## Representation of the fault

A thorough representation of the fault The representation should be abbreviated but must consists of enough information by which fault can be easily understood from reading the explanation.

## Proof

List out the determined data accessible that gives explanation of fault which is present

## Elucidation

The condition that has been reported and registered in the "Identification" section should now be explored to elucidate first, the need for action and then the level of action required. The impression of the fault and the actual threat to the industry and/or purchaser must be explored.

## Power Impact

Part of the elucidation is a particular explanation of particularly why the problem is a concerned. This may include the possible impact that the problem may have in terms of finance, work, product quality, protection, reliability, and purchaser approval.

## Controlling of Threat

Using the final data of the impact validation, the possibility of the problem is controlled. The stage of

threat that is related with the fault may affect the steps that are taken.

### Remedial Action

On the basis of result obtained, the impression and fault are evaluated, it may be detected that sudden other way of action is in needs a solution until a full investigation and a permanent solution is applied.

The actions that are taken are recorded. This records will become part of the 'Action Implementation' and 'Follow Up' sections of the CAPA action.

### Responsibilities /Resources

An important part of the investigation procedure is to assign responsibility for conducting each aspect of the investigation. Any additional resources that may be required is also identified and documented. For example, specific testing instrument or external analysis may be required.

### Investigation procedure form

A standard "Investigation Procedure" forms is included. This is a record of action, for the investigation into the fault. There should be involvement of the overall objective and the instructions for conducting the investigation. The individual responsible for the investigation and an expected completion record should also be entered

### Investigation

In this step of the process a procedure is recorded for implementing an investigation into the fault. A record gives idea about the investigation is finished and nothing is missed.

### Aim of the investigation

The first step in the investigation is to state a motto for the action. In the "Identification" section the problem was defined and the current situation stated. The objective is a statement of the desired outcome of the corrective or preventive action. State what the situation will be when the action is complete. This may be a statement in the form of: "the problem will be corrected, all effects of the fault identified and rectified, and controls will be in place to prevent the situation from repeating again.

### Investigation Procedure

A general commands are introduced in form, what should be done to identified the contributing and main cause of the fault. The investigation procedure will defer, depending on the conditions.



Figure 2: Implementing CAPA system in closed loop.

### Application of Pat

Revolutions in the process analytical chemistry (process analyzers) and in our power to entrap and analyze large amount of data have served as the main criteria for adaptation of PAT in the pharmaceutical industry. The attribute of PAT is that, quality is improved in the product, preferably being analysed before dispatch of product. The PAT framework consist of threat managing, at/on-line trace detectors that assist in monitoring/ managing /designing of the process and forecast of process working. Various analytical techniques are being used in the pharmaceutical industry, including Fourier transform infra-red spectroscopy (FTIR), UV-spectroscopy, gas chromatography, high performance liquid chromatography (HPLC), X-ray diffraction spectroscopy, and NIR spectroscopy

### Application of Capa

- **Pharmaceutical Development**-final Product or process variant is consider. Implementing CAPA is useful where corrective actions and preventive actions are incorporated into the renewal design and development process
- **Technology improvement** -CAPA can be used effectively for feedback, feedforward and continual improvement.
- **Commercial Manufacturing**-CAPA should be used and the effectiveness of the actions should be calculated.
- **Product Discontinuation**-CAPA should be in regular use even after product has been manufactured. The product Impression in the market should be remembered as well as other products which may influence purchaser.

### CONCLUSION

PAT and CAPA implementation is easy and very beneficial in industrial manufacturing point of view. Commercial benefits are received after applying PAT and CAPA system in analytical and production area. Any error in procedure, raw material, equipment, even in finished product can be analysed and improved by implementing these both systems together. Pre and Post manufacturing analysis can be easily performed. Validation and elucidation of raw material and finished product can be easily performed.

## REFERENCES

1. Kamble R, Sharma S, Varghese V, Mahadik KR, "Process Analytical Technology (PAT) in pharmaceutical development and its application" *International Journal of Pharmaceutical Sciences Review and Research*, 2013; 23: 212-223.
2. Tenzin Tashi, Vitalis B Mbuya, H V Gangadharappa, "Corrective Action and Preventive Actions and its Importance in Quality Management System: A Review" *International Journal of Pharmaceutical Quality Assurance*, 2016; 7(1): 1-6.
3. Gupta S, Gupta N. V, "Corrective and Preventive Action: A Key to Pharmaceutical Industry", *International Journal of Pharm Tech Research*, 2016; 9(3): 406-414.
4. Davies B, "Process Analytical Technology: A Framework for Innovative Pharmaceutical Manufacturing" *Thermo Fisher Scientific*.
5. Morris J, Chen Z, Lovett D, "Process Analytical Technologies (PAT) and Quality by Design", 2009; 26-28.
6. Alexey L, Oxana R, "Process Analytical Technology: a critical view of the chemometricians" *Journal of chemometrics*, 2012; 26: 299-310.
7. Stelzer T, Shin Yee Wong, Chen J, Myerson A, "Evaluation of PAT Methods for Potential Application in Small-Scale, Multipurpose Pharmaceutical Manufacturing Platforms" *Organic Process Research & Development*, 2016; 20: 1431-1438.
8. Jaime I. Aponte S, "Evaluation and assessment of the current use of CAPA tools in the regulated industry", 2012.
9. Dr. Berkeley W, Dr. John B, Manley J, "PAT and green chemistry: The intersection of benign by design and quality by design", 2009.
10. Lawrence X. Yu Robert A. Lionberger, Andre S. Rawa, Rosario D'Costa, Huiquan Wu ,Ajaz S. Hussain, "Applications of Process Analytical Technology to Crystallization Processes", 2003.
11. Markens U, "CAPA management in a GMP environment", 2014.
12. Markku K, Kurkinen M, Weymarn N, Niemela P "Process analytical technology (PAT) needs and applications in the bioprocess industry", 2016.
13. Rathore A, Bhambure R, V. Ghare, "Process analytical technology (PAT) for biopharmaceutical products", 2010.
14. Chew W, Sharratt P, "Trends in process analytical technology", 2012.
15. Scott B, Wilcock A, Process analytical technology (PAT) *J Pharm Sci Technol*, 2006; 60(1): 17-53.
16. Rajabhadur VA, Dewangan P, Process Analytical Technology Helps Pharmaceutical Companies Capture Process Knowledge and Achieve Operational Excellence.
17. PAT Initiative Expected to Invigorate Pharmaceutical industry with Improved Quality, Better Efficiency and Improved Profits, White paper, 1-8.
18. International Conference on Harmonization (ICH) Q11, Development and Manufacture of Drug Substances Draft Guideline, May, 2011.
19. A practical approach to PAT implementation Highlights of Advances in the Pharmaceutical Sciences: An American Association of Pharmaceutical Scientists (AAPS) Perspective 2007 and obacco/ CDER/ ucm1 28080. htm Accessed on 25 may, 2013.
20. Ghorab MK, Chatlapalli R, Hasan S, Nagi A , Application of thermal effusivity as a process analytical technology tool for monitoring and control of the roller compaction process, *AAPS Pharm Sci Tech*, 2007; 8(1): E155-E161.
21. Rick EC and Egan JC, the Impact of Process Analytical Technology, (PAT) On Pharmaceutical Manufacturing, 2009.
22. R.M Baldwin, Inc.' Preventive / Corrective Actions (CAPA) Guidelines.
23. Guidance for Industry Q10 Pharmaceutical Quality System, April EMEA, ICH Q 10: Pharmaceutical Quality System, European Medicines Agency, Westferry Circus, Canary Wharf, London, UK, 2008; 4-20.
24. Vikram C, Anil K S, Ravindran A, Piyush T and Mona N. Investigating Out-of-Specification Results and Development CAPA Program for Pharmaceutical Industries: An Overview. *Journal of Der Pharmacia Lettre*, 2011; 3(2): 368-382.
25. Triadaphillou S, Martin E, Montague G, Norden A, Jeffkins P, Stimpson S *Biotechnol Bioeng*, 2007; 97(3): 554-567.