Review Article Available online www.ijrpsonline.com ISSN: 2249–3522

International Journal of Research in Pharmacy and Science

Process Validation of Solid Dosage Form: A Review

Sharma Ajay*, Saini Seema

Department of Pharmaceutics, Rayat Institute of Pharmacy, Rayat and Bahra Campus, Railmajra, Distt. Nawanshahar, Near Ropar, Punjab, India

ABSTRACT

Process validation emphasizes the role of objective measures and statistical tools & analyses and emphasizes knowledge, detection, and control of variability and gives assurance on consistent of quality/productivity throughout life cycle of product. Validation is the art of designing and practicing the designed steps alongside with the documentation and activity will consistently lead to the expected results. Validation and quality assurance will go hand in hand, ensuring the through quality for the products. Validation assures the products with predetermined quality characteristics and attributes can be reproduced consistently/reproducibly with in the established limits of the manufacturing process operation at the manufacturing site. This type of validation is based on the physics of compression. It often includes the qualification of systems and equipment. A properly designed system will provide a high degree of assurance that every step, process and change has been properly evaluated before its implementation. It is a requirement for good manufacturing practices and other regulatory requirements. Validation is required in order to move a product from development to commercial production. Different dosage forms have different validation protocols. Here this article concentrates on the process validation of solid dosage forms, protocol preparation, prerequisites and regulatory basis for process validation and role of validation team.

KEY WORDS: Process validation, Solid dosage form, Protocol, Prerequisites, Regulatory basis

***Corresponding Author**

Ajay Sharma
Rayat Institute of Pharmacy Railmajra,
Distt-SBS Nagar, Punjab, India
Contact number: 09888496816
Email: sharmaajay177@gmail.com

TABLE OF CONTENTS

1. INTRODUCTION

The principal objective of dosage form design is to achieve a predictable therapeutic response to a drug included in a formulation which is capable of large scale manufacture with reproducible product quality. Solid dosage forms include tablets and capsules. The manufacturing of solid dosage forms involves extensive powder handling. The powder must be blended for uniformity and converted into dosage form either through compression or encapsulation. Typical requirements include weighing, blending, granulation areas, compression/ encapsulation areas and coating areas. To ensure product quality, numerous features are required, like chemical and physical stability, suitable preservation against microbial contamination if appropriate, uniformity of dose of drug, acceptability to users including prescriber and patient, as well as suitable packing, labeling, and validation[1].

The concept of validation was first proposed by two Food and Drug Administration officials, Ted Byers and Bud Loftus in the mid 1970's in order to improve the quality of pharmaceuticals[2]. Assurance of product quality is derived from careful attention to number of factors including selection of quality parts and materials, adequate product and process design, control of the process and in process and end product testing. Due to the complexity of today's medical products , routine end product testing alone is not sufficient to assure product , routine end product testing alone often is not sufficient to assure product quality for several reasons[3,4].

According to US FDA in 1978,

"A validation manufacturing process is one which has been proved to do what it purports or is represented to do. The proof of validation is obtained through the collection and evaluation of data, preferably, beginning from the process development phase and continuing the production phase. Validation necessarily includes process qualification (the qualification of materials, equipment, system, building, personnel), but it also includes the control on the entire process for repeated batches or runs"[5].

Process validation is defined as the collection and evaluation of data, from the process design stage through commercial production, which establishes scientific evidence that a process is capable of consistently delivering quality product. Process validation involves a series of activities taking place over the lifecycle of the product and process. Process validation is a term used in the medical device industry to indicate that a process has been subject to such scrutiny that the result of the process (a

product, a service or other outcome) can be practically guaranteed. This is vitally important if the predetermined requirements of the product can only be assured by destructive testing.

Process validation establishes the flexibility and strict control in the manufacturing process control in the attainment of desirable attributes in the drug products while preventing undesirable properties [6].

The requirement of process validation appears of the quality system (QS) regulation. The goal of a quality system is to consistently produce products that are fit for their intended use. Process validation is a key element in assuring that these principles and goal are met[7]. Process controls include raw materials inspection, in-process controls and targets for final product. The purpose is to monitor the on-line and off-line performance of the manufacturing process and then validate it. Even after the manufacturing process is validated, current good manufacturing practice also requires that a well-written procedure for process controls is established to monitor its performance[8].

The United State Food and Drug Administration (USFDA) has proposed guidelines with the following definition for process validation- Process Validation is established document evidence which provides a high degree of assurance that a specific process consistently produces a product meeting its predetermined specification and quality attributes [6,9].

2. REASON FOR PROCESS VALIDATION

The possible reason of performing process validation may include:

• New product or existing products as per SUPAC changes.

• Change in site of manufacturing.

• Change in batch size.

• Change in equipment.

• Change in process existing products.

• Change in composition or components.

• Change in the critical control parameters.

• Change in vendor of API or critical excipient.

• Change in specification on input material.

• Abnormal trends in quality parameters of product through review during Annual Product Review (APR).

• Trend of Out of Specification (OOS) or Out of Trend (OOT) in consecutive batches[10].

3. PHASES OF VALIDATION

3.1 Design Qualification (DQ)

Document verification of the design of equipment and manufacturing facilities.

3.2 Installation Qualification (IQ)

Documented verification of equipment of system design and adherence to manufacturer's recommendations.

3.3 Operational Qualification (OQ)

Documented verification of equipment or system performance in the target operating range.

3.4 Process performance qualification (PQ)

Documented verification that equipment or systems operate as expected under routine productions the operation is reproducible, reliable and in a state of control.

4. PROCESS/ PRODUCT VALIDATION

Validation is establishing documented evidence which provides a high degree of assurance that a specific system will consistently produce a product meeting its predetermined specifications and quality attributes.

4.1 Process Validation Phases

The activities relating to validation studies may be classified into three:

4.1.1 Phase1: This is the Pre-validation Qualification Phase which covers all activities relating to product research and development, formulation pilot batch studies, scale-up studies, transfer of technology to commercial scale batches, establishing stability conditions and storage, and handling of in-process and finished dosage forms, equipment qualification, installation qualification master production document, operational qualification and process capacity.

4.1.2 Phase 2: This is the process validation phase. It is designed to verify that all established limits of the critical process parameter are valid and that satisfactory. Products can be produced even under the worst conditions.

4.1.3 Phase 3: Known as the validation maintenance Phase, it requires frequent review of all process related documents, including validation of audit reports, to assure that there have been no changes, deviations failures and modifications to the production process and that all standard crepitating procedures (SOPs), including change control procedures, have been followed. At this stage, the validation team comprising of individuals representing all major departments also assures that there have been no changes/deviations that should have resulted in requalification and revalidation.

A careful design and validation of systems and process controls can establish a high degree of confidence that all lots or batches produced will meet their intended specifications. It is assumed that throughout manufacturing and control, operations are conducted in accordance with the principle of good manufacturing practice (GMP) both in general and in specific reference to sterile product manufacture[11, 12].

5. TYPES OF VALIDATION

Validation can be prospective, concurrent, retrospective or revalidation (repeated validation), computer system validation.

5.1 Prospective validation: Prospective validation is defined as the establishment of documented evidence that a system does what it purports to do based on a pre planned protocol. This validation is usually carried out prior to the introduction of new drugs and their manufacturing process. This approach to validation is normally under taken when ever new formula, process or facility must be validated before routine pharmaceutical formulation commences. In fact validation of process by this approach often leads to transfer of the manufacturing process from the development function to product. The objective of prospective validation is to prove or demonstrate that the process will work in accordance with a validation master plan or protocol prepared for pilot product trails.

5.2 Retrospective validation: Retrospective validation is defined as the establishment of documented evidence that a system does what it purports to do on review and analysis of historical information. The sources of such data are production, QA and QC records. The issues to be addressed here are changes to equipment, process, specification and other relevant changes in the past.

5.3 Concurrent validation: It is similar to the prospective, except the operating firm will sell the product during the qualification runs, to the public as its market price. This validation involves

in process monitoring of critical processing steps and product testing. This helps to generate and documented evidence to show that the production process is in a state of control.

5.4 Revalidation: It is the repetition of a validation process or a part of it. This is carried out when there is any change or replacement in formulation, equipment plan or site location, batch size and in the case of sequential batches that do not meet product specifications and is also carried out at specific time intervals in case of no changes [11, 13, 14].

5.5 Computer system validation: Computer validation encompasses computers, which directly control process or system or collect analytical data. Computer validation includes the qualification of all software and hardware, which has an impact, direct or indirect on the quality of product. The validation approach to programmable logic controller (PLC) hardware and personal computers (PCs) is similar, both to one another and to general overall approach top validation, in that the end user should define each requirement [15].

6. STRATEGY FOR VALIDATION OF METHODS

The validity of a specific method should be demonstrated in laboratory experiments using samples or standards that are similar to the unknown samples analyzed in the routine. The preparation and execution should follow a validation protocol preferably written in a step by step instruction format as follows:

- Develop a validation protocol or operating procedure for the validation.
- Define the application purpose and scope of method.
- Define the performance parameters and acceptance criteria.
- Define validation experiments.
- Verify relevant performance characteristics of the equipment.
- Select quality materials, e.g. standards and reagents;
- Perform pre-validation experiments;
- Adjust method parameters and/or acceptance criteria, if necessary;
- Perform full internal and external validation experiments;
- Develop SOPs, for executing the method routinely;
- Define criteria for revalidation.
- Define type and frequency of system suitability tests and/ or analytical quality control (AQC) checks for the routine; and

- Document validation experiments and results in the validation report [16].

7. REGULATORY BASIS FOR PROCESS VALIDATION

The concept of process validation from its beginnings in the early 1970s through the regulatory aspects associated with current good manufacturing practice (cGMP) regulations and the application thereof to various analytical, quality assurance, pilot plant, production and sterile product and solid dosage forms considerations. In the early 1990s, the concept of preapproval inspection (PAI) was born and had as one of its basic tenets the assurance that approved validation protocols and schedules were being generated and that comprehensive development, scale-up, biobatch and commercial batch validation data were required in order to achieve a successful regulatory PAI audit.

There are several important reasons for validating a product or process. First, the manufacturers are required by law to confirm to cGMP regulations. Second, good business dictates that a manufacturer avoids the possibility of rejected or recalled batches. Third, validation help to ensures product uniformity, reproducibility and quality. But the original focus of validation was directed toward prescription drugs, the FDA modernization act of 1997 expanded the agency's authority to inspect establishment manufacturing over the counter (OTC) drugs to ensure compliance with cGMP.

FDA has the authority and responsibility to inspect and evaluate process validation performed by manufacturers. The cGMP regulations for validating pharmaceutical (drug) manufacturing require that drug products be produced with a high degree of assurance of meeting all the attributes they are intented to possess. FDA regulations describing current good manufacturing practice (CGMP) for finished pharmaceuticals are provided in 21 CFR parts 210 and 211.

The CGMP regulations require that manufacturing processes be designed and controlled to assure that in-process materials and the finished product meet predetermined quality requirements and do so consistently and reliably. Process validation is required, in both general and specific terms, by the CGMP regulations in parts 210 and 211. The foundation for process validation is provided in § 211.100(a), which states that "[t] here shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity. This regulation requires manufacturers to design a process, including operations and controls, which results in a product meeting these attributes [17, 18, 19, 20].

8. SAMPLING PROCEDURE

A significant improvement in sampling can be achieved by use of sampling thief, some times known as grain thief as per historical reasons. This device consists of two tubes one fitting tightly inside the other and with long holes cut through the tubes in corresponding positions. One end of the outer tube is fitted to a point to facilitate insertion in to a bulk powder. Sampling procedure consisting of inserting the device in to powder, rotating the inner tube to open the holes, allowing the powder to enter the tube rotating the inner tube once more to close the holes and finally removing the thief from the bulk powder.

Although the thief sampling is better method, that merely scooping off top of a bulk powder, it is still an interior technique even though most thief's are relatively sharp ends, the act of plunging the thief through the bulk powder must tub the sample to some degree, compression force propagates a head of the thief as it is pressed in to the bulk thus potentially changing the strata of bulk and altering the valve of the powder as the outer walls of the thief., further more because large particles will flow more easily than small particles, an open thief liable to be filled preferentially with course fraction of the particle distribution.

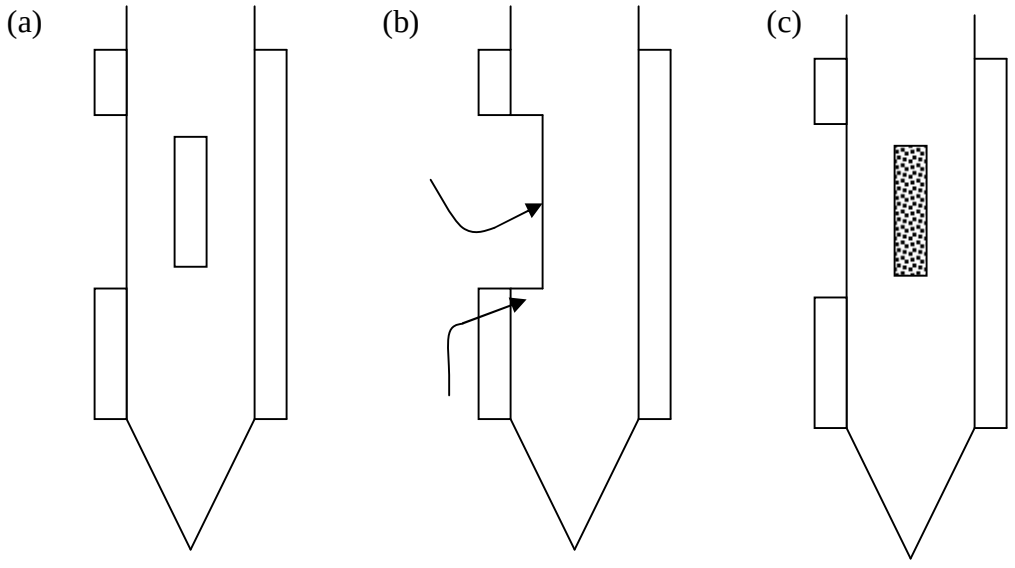

Fig.-1 Sampling thief

8.1 Operation of sample thief (sample rod):

a) The sleeve was rotated so that the interior compartment is isolated from the bulk powder, while in the closed position; the thief is plunged into the central mass of the powder.

b) Once the thief is as the desired position, the unit is rotated so that the interior compartment is now exposed to the bulk provider flows into the thief compartment of its own accord.

c) Once the interior compartment of the thief is failed, the sleeve of the thief is rotated so that the interior compartment is again isolated from the bulk powder. The thief then with drawn from the powder, and the sample is analyzed [21].

9. VALIDATION TEAM

A multidisciplinary team is primarily responsible for conducting and supervising validation studies. Personnel qualified by training and experience in a relevant discipline may conduct such studies. The working party would usually include the following staff members such as;

Head of quality assurance.

Head of engineering.

Validation manager.

Production manager.

Specialist validation discipline: all areas.

The validation team should:

Prepare the site validation master plan with the specific requirements as per the company policy.

- Meet regularly, In accordance with a defined schedule, to discuss the progress and compliance with the validation plan and schedule.
- Determine the systems / equipment to be qualified / validated and the extent of validation to be carried out.
- Determine the frequency of validation.
- Prepare and evaluate the suitability of the protocols.
- Verify the adequacy of the tests used for proving that the objectives are achieved.
- Complied reports should be checked and approved by validation team members.

Maintain records of validation studies and inform to the Corporate Quality Assurance of progress in terms of validation plan and schedule [22].

10. PREREQUISITES FOR SUCCESSFUL VALIDATION:

There are thirteen tools or elements that are required for conducting effective validations. Each are presented and discussed in the following sections

10.1 Understanding:

Perhaps the single most important element required is a good understanding of what validation is? This understanding activity goes beyond the basic definition of validation, beyond the concept of "requiring a minimum of three runs". This understanding must be anchored by sufficient years of practical experience and knowledge. It will permit sound and logical decisions, even under the most intense situations.

Given the fact regulated drug manufacturers must perform validations, it is very important that this understanding be shared through out the organization.

- Why can't the laboratory use the piece of equipment undergoing validation?
- Why can't the facility be used before the laboratory has competed analysis of the microbial data?
- Why are validations so expensive?

If the entire company is fairly educated on what validation entails, less time will be required defending validations actions.

10.2 Communication:

One of the best methods of improving environmental understanding is through communication. Communication is essential for any activity that requires more than one resource to complete. This point is understandable considering that conducting effective validation involves multi – departments. One of the keys to proper communication is locating the right communication vehicle. Most organizations communicate through one or more of the following methods.

- Conversations
- Memos
- Periodic meetings
- Training sessions

10.3 Experience:

A firm must have resources with solid validation experience in order for their validation program to be successful.

10.4 Cooperation and focus:

Multitude of departments that some times interact during the course of executing validation program are project management, accounting, validation, quality control, project engineering, process engineering, quality assurance, facilities, regulatory, etc. it is safe to assume that these departments have an array of priorities, and typically they are not the same as validation's.

If some one fails to approve the protocol or to sample per the protocol, the cost of validation will undoubtedly increase because more time will be spent seeking approvals. Likewise, time will be spent justifying and writing the explanation for why a sample was not initially collected. Cooperation is essential and critical. Therefore, each member must be focused on the overall tasks, and willing to cooperate 100%.

10.5 Resources:

In reality, it does not matter how much knowledge, experience, and understanding a firm has, if they don't allocate the proper resources for conducting effective validations.

Resources mean personnel who will plan and execute, equipment on which validations will be performed on, materials, with which to conduct validations, laboratories that will perform necessary analysis, funding to pay for the validations, and time in which to perform validations. Validations can often begin, but can not be completed if any one of these resources are missing.

10.6 Budget:

It is important to understand that a successful validation must be done to completion. Typically, it should not be limited by a budget assembled by personnel who have no appreciation for what is required to successfully complete validation. Further, it is important to understand that validations cost money.

Consider how projects are funded within corporations. Each department has to prepare an annual budget for anticipated expenses. It is very important that the anticipated costs are shared with upper management to assure that ample support or funding exists. From a corporate standpoint, each one of the validation elements requires time, and therefore has an associated cost. Thus, it is essential that they are reflected in the validation budget.

10.7 Plan:

Conducting validations within most companies will involve a number of departments and disciplines. These disciplines need a plan in order to get good team synergy. Further, this plan must be communicated in order to be accepted and successful.

- When should the analytical laboratory receive the samples?
- How should a deviation be handled?
- How will chamber temperatures be monitored?
- When will the first event occur?
- Will manufacturing assistance be required to execute the validation protocols?

It is essential that the lead validation resource know the answer to each of the above questions, and assures that they are shared in pre-validation planning sessions

10.8 Training:

Training is essential for any successful validation. Typically this training initiates with in the validation group. It is essential that the lead validation resource for a given validation project initiate, facilitate, coordinate and/or communicate the need for resource training as required by validation event. Actually, the requirement for training goes beyond the act of mere teaching. The regulating bodies require proper documentation be assembled and maintained to serve, as proof that key resources have undergone required training. Proper should minimally include employee identification, a description of training course, and the data on which training occurred.

10.9 Standard Operating Procedures (SOPs):

SOPs capture activities that routinely occur within an organization. Departments charged with abiding by or following these SOPs must first be trained against these SOPs. Many SOPs are typically the offspring of a successful validation. In most cases, equipment operation procedures are drafted for use during the initial phases of qualification. These SOPs often are not finalized until after the equipments OQ event. A case in point would be an SOP for set- up and operation of a new piece of equipment. Often, the vendor manuals or the specifications will convey how the equipment is operated. In the OQ phase, this information is usually transcribed for use in the form of a draft SOPs. Once the OQ steps are completed, the result should be an SOP that is finalized, approved, trained upon, and implemented for routine use. The expectation is that these SOPs are finalized before the equipment is used to support process validation.

10.10 Quality Control Lab Support:

During most validations, some laboratory testing will be required. In most cases this testing is handled by the QC group. QC is expected to provide results in timely manner. So often, the wait for the receipt of analytical results causes the entire validation project to come to halt. Because validations are based on the results obtained. In addition, QC input is required during protocol preparation. If the QC lab lacks organization, maturity, technical competency, appropriated methods, etc. an initiative has to be undertaken to attain laboratory support through a contract laboratory.

10.11 QA Support:

All validation resources may not be the best for adhering to compliance procedures. It is therefore up to QA to thoroughly police the protocols before, during, and after execution.

This policing must be against internal SOPs and external regulations. The expectation is that QA will enforce any relevant compliance issues, and will there by prevent an unwanted discovery by auditing bodies. If an auditor uncovers a number of compliance issues, the department that will often be held accountable is QA. It must be understood that a good QA resource often is not a resource that most other departments would choose as their best buddy during working hours. However, their value to success of the organization's validations must not be minimized.

10.12 Permission to conduct preliminary runs:

When a system undergoes validation, the desire is that its operation is then faultless. Validations require practice. Given the fact that validations are typically expensive, it should be understood that anything that would assure that the costs are minimized would be an asset. Therefore, it is advisable that permission be attained to perform some form of preliminary runs. These runs can be used to provide operator training, to investigate values recommended by specifications or vendors equipment manuals, and/ or explore any limits proposed for validation.

10.13 Realistic completion dates:

Typically, the expectation is that once the requisite time has been allotted to complete three runs, the system under validation is released and ready for use. Unfortunately, this is rarely the case. For example, a cleaning validation activity will require time to complete the following activities, including:

- Training
- Conducting cleaning events
- Gather cleaning samples

- ❖ Obtain the microbial challenge results
- ❖ Evaluate results
- ❖ Write conclusions
- ❖ Seek and attain post execution approval.

Therefore, it should be relatively easy to see it requires much longer than the three, basic runs. Validation resources typically provide input on validation tasks. The firm must understand that this is often a lose/lose situation because if the planning resource is overly optimistic, disappointment will result when the completion date is not met. Oftentimes, commercial campaigns are planned, based up on the projected completion date. These campaigns may involve contractual commitments. If the dates are not met, money will be forfeited.

If the resource is overly pessimistic, chances are that the environment will not be ready to react when validation is completed well before the projected date. In this case, campaigns may not be pursued in a timely manner, and therefore, the opportunity to earn money may be lost. Either one of these extremes causes some degree of disarray.

Thus, it is the responsibility of the lead validation resource to accurately plan, communicate, and realistically reflect the time required to complete validation [23, 24, 25].

11. VALIDATION REPORT

A written report should be available after completion of the validation. If found acceptable, it should be approved and authorized (signed and dated). The report should include at least the following:

- Title and objective of study.
- Reference to protocol.
- Details of material.
- Equipment.
- Programmes and cycles used.
- Details of procedures and test methods.
- Results (compared with acceptance criteria).
- Recommendations on the limit and criteria to be applied on future basis [26, 27].

12. DOCUMENTATION

Documentation at each stage of the process validation lifecycle is essential for effective communication in solid dosage form projects. Documentation is important so that knowledge gained

about a product and process is accessible and comprehensible to others involved in each stage of the lifecycle. In addition to being a fundamental tenet of following the scientific method, information transparency and accessibility are essential so that organizational units responsible and accountable for the process can make informed, science-based decisions that ultimately support the release of a product to commercial scale. The degree and type of documentation required by CGMP is greatest during process qualification, and continued process verification. Studies during these stages must conform to CGMPs and must be approved by the quality unit in accordance with the regulations (21 CFR 211.22 and 211.100) [28, 29, 30, 31].

13. PROTOCOL FOR PROCESS VALIDATION OF SOLID DOSAGE FORM (CAPSULES)

Raw material
↓
Dispensing
↓
Movement of Raw material to production area
↓
Dry granulation (Blending + Mixing)
↓
Compression
↓
Strip packaging

Figure: Process overview

14. CONTROL PARAMETERS FOR CONSIDERATION IN SOLID DOSAGE FORMS DEVELOPMENT

UNIT OPERATION	PROCESS VARIABLE	METHOD RESPONSES
Dry mixing	Mixing time	Power consumption
Granulation	Load, speed, binder, Addition rate, Granulation time, Amperage Reading of impeller & chopper	Power consumption
Drying	Load, inlet temperature, Air flow rate, drying time	Moisture content/ LOD
Blending(mixing)	Load, speed, mixing time	Blend uniformity
Compression	Press speed, feed rate, precompression force, compression force	Moisture content, hardness, disintegration, content uniformity,dissolution

15. CONCLUSION

Process validation is the key element in the equality assurance of pharmaceutical product as the end product testing is not sufficient to assure the quality of finished product. Process Validation is the most important and recognized parameters of cGMP. Process validation involves a series of activities taking place over the lifecycle of the product and process. Solid dosage form validation should be part of a comprehensive validation program within an industry. The multidisciplinary validation team must identify the product and process characteristics that must be studied and incorporate specific validation tests to ensure that that product will meet all quality, manufacturing, and regulatory requirements.

16. ACKNOWLEDGEMENT

The author is highly thankful to the Director, Rayat Institute Of pharmacy and the management for providing us all the facilities.

17. REFERENCES

1. Aulton ME. Pharmaceutics, the science of dosage form design, international edition, 2nd edition, Churchill Livingston (Elsevier), 2006:1.
2. http://en.wikipedia.org/wiki/validation (drug manufacture); Dated:20th september ,2011.
3. Ramamurthy S, Saravanakumar M. “Validation”, The Eastern Pharmacist; 1997.p.476.
4. Satish M, Vadya R, Paras R, Fernandes SN, Amonkar N. The Eastern Pharmacist. 1994; 37 (443): 51-53.
5. Patel RC, Bhuva CK, singh RP, Dadhich A, Sharma A. Pharmaceutical Process Validation, Pharmatutor ART – 1053.
6. Nash RA, Wachter AH. Pharmaceutical process validation. 3rd edition New York: Marcel Dekker; 2003: 159-180. Rev Res, 2010; 4(2): 145-154.
7. Guidance for Industry: Process Validation: General Principles and Practices. U.S. Department of Health and Human Services, Food and Drug Administration, Centre for Drug Evaluation and Research (CDER), Centre for Biologics Evaluation and Research (CBER), Centre for Veterinary Medicine (CVM), January 2011.
8. Chow S. Pharmaceutical Validation and Process Controls in Drug Development. Drug Inf J 1997; 31: 1195-201.
9. Dashora K, Singh D, Saraf S. Validation- The essential quality assurance tool for pharmaceutical industries, 2005; 3: 45-47.

10. Alam S. Pharmaceutical Process Validation: An Overview. J Advanced Pharm. Edu. Res., 2012; 2(4): 185-200.
11. Fetterolf DM. Developing a sound process validation strategy. Int Biopharm, The science and business of Biopharmaceuticals 2007; 20.
12. Sharma SK. "Validation of Pharmaceutical products and processes". The Eastern Pharmacist; 2001: 263.
13. Jeena S. Industrial process validation of solid dosage form- An overview. Int J Pharm Sci Rev Res 2010;4:145-154.
14. Guidelines for process validation of pharmaceutical dosage form, Drug sector SFDA, version 2; 2010.
15. Guidelines on General Principles of Process Validation, Food and Drug Administration, Maryland, 1984, 4-25.
16. Jatto E, Okhamafe AO. An overview of pharmaceutical validation and process controls in drug development. Trop J pharm Res 2002; 2: 115-122.
17. Aleem H, Zhao Y, Lord S, McCarthy T, Sharrat P. Pharmaceutical process validation: An overview. J. Proc. Mech. Eng, 2003; 217: 141-151.
18. Nash RA, Alfred HW. Pharmaceutical process validation, 3rd ed. Marcel Dekker, New York, 2003: 159-180.
19. Kathiresan K, Kiran K. Basics of validation- Pharmaceutical Prospective, 1st ed. KK Publishers, Chidambaram, 2005: 32-36.
20. Champan KG. A history of validation in the United States, Part 1, Pharm. Tech. 1991;15: 82-96.
21. Berman J, Planchard JA. Marion Merrell Dow Inc., Formulation Development Department, 1995; 21(11):1257-1283.
22. Kumar NL, Moorthy DG, Kumar RS, Sekaran CS. An overview of pharmaceutical validation: quality assurance view point, 2011; 1(4): 1003-1014.
23. Tetzlaff RF, Sheppard RE, Leblanc AJ. Prospective on the systemic GMP inspection approach and validation development. Pharm. Tech. 1993: 100-116.
24. Leblane DA. Establishing scientifically justified acceptance criteria for cleaning validation of finished drug product. Pharm. Technol. 1998; 23: 13-148.
25. WHO Expert Committee on Spacifications for Pharmaceutical preparations, 34th Report, WHO Technical Report Series no. 863, Annex 6, WHO, Geneva, 1966: 80-96.
26. South African Guide to Good Manufacturing Practice. Pretoria: Medicines Control Council, 1996.

27. Good Manufacturing Practices for Pharmaceutical products, WHO Expert Committee on specifications for pharmaceutical preparations, 32nd Report, WHO Technical Report Series no. 823, WHO, Geneva, 1992; 14-96.
28. U.S. Food and Drug Administration. Guidelines on General principles of Process Validation; U.S. FDA: Rockville, MD, May, 1987.
29. www.processvalidation.com
30. www.picscheme.org
31. Chaitanya kumar G, Rout RP, Ramtake S, Bhattachaiya S, Process Validation, The Indian pharmacist, 2005: 14-19.