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Review Article

INDUSTRIAL PROCESS VALIDATION OF SOLID ORAL DASAGE FORM: A REVIEW

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ABSTRACT

Validation is the important step in gaining and maintaining the quality of the final product. Validation of the individual steps of the processes is called the process validation. Different dosage forms have different validation protocols. Validation is therefore is one element of quality assurance programs and is associated with a particular process therefore word validation simply means "assessment of validity" or action of proving effectiveness. Validation thus provides a higher degree of assurance that the manufacturing process consistently meets the pre-determined specifications and the quality products output can be used to increase productivity, its consistent quality and decreasing the need for processing and market complaints of the drug product. This overview examines the need for pharmaceutical validation, the various approaches and steps involved.

Keywords: Validation, strategy, planning, essentials of validation.

INTRODUCTION

The prime objective of any pharmaceutical plant is to manufacture products of requisite attribute and quality consistently, at the lowest possible cost. Although validation of drug products have been conducted in the pharmaceutical industry for a long period of time, there is an ever increasing interest in validation owing to their industry's greater emphasis in recent years on assurance of quality and productivity improvement. Validation is a necessary part of the quality assurance program and is a fundamental to an efficient production operation. Process validation establishes the flexibility and constraints in the manufacturing process controls and in the attainment of desirable attributes in the drug product while preventing undesirable properties during manufacturing. This is an important concept, and it serves to support the underlying definition of validation, which is a systematic approach to identifying, measuring, evaluating, documenting, and re-evaluating series of critical steps in the manufacturing process that require control to ensure a reproducible final drug product. USFDA defined process validation as "establishing documented evidence which provides high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality characteristics. Solid dosage forms include Tablets and capsules[1-3].

The manufacturing of solid dosage forms or drug products involves extensive powder handling. The powder must be blended for uniformity and converted into the dosage form either through compression or encapsulation. Typical requirements include weighing, blending, mixing/granulation areas compression/encapsulation areas, and coating areas[4].

Instead of the ongoing development of more sophisticated solid drug delivery systems, tablets are still by far among the most prevalent solid dosage form. The emphasis will be on the practical inspectional requirements and theoretical approach that does not reflect the practicals and problems encountered when validating actual production operations. A tablet is a pharmaceutical dosage form. It comprises a mixture of active substances and excipients, usually in powder form, pressed or compacted into a solid dosage form. The excipients can include binders, glidants (flow aids) and lubricants to ensure efficient tabletting, disintegrants added to promote tablet break-up in the digestive tract; sweeteners or flavors to enhance taste, and pigments to make the tablets visually attractive. A polymer coating is often applied to make the tablet smoother and easier to swallow, to control the release rate of the active ingredient, to make it more resistant to the environment by extending its shelf life, or to enhance the tablet's appearance[5].

Planning for Validation

All the validation activities should be planned properly. The key elements of a validation programme should be clearly defined and documented in a validation master plan (VMP) or other similar equivalent documents. The validation master plan is a document which summarizes the company's overall philosophy, intentions or approaches that are used for establishing performance adequacy. A validation master plan should be agreed upon by management. A validation master plan should provide an overview of the entire validation operation and its organizational structure, its content and planning. The main elements include the list inventory of the items to be validated and planning schedule. The validation master plan should not repeat information documented elsewhere but should refer to existing documents such as policy documents, SOP's and validation protocols[6,7].

The following are the most common types of validation plan documents:

- SVMP (site validation master plan)
- VMP (validation master plan)
- VP (validation plan)
- VPP (validation project plan)

Essentials of Validation

Validation is an important part of quality assurance. It involves the systematic study of systems, facilities and processes its goal is to determine that whether they perform their intended functions adequately and consistently as specified. A properly validated process is the one which has been demonstrated to provide a high degree of assurance that uniform batches will be produced so that they that meet the required specifications and has therefore been formally

approved. The term Validation in itself does not improve processes but confirms that the processes and formula have been properly developed and are under control. Adequate validation is very beneficial to the owner manufacturer in many ways:

- Adequate validation deepens the understanding of processes and decreases the risk of preventing problems and thus help in assurance of smooth running of the process.
- It minimizes the risk of defect costs.
- This also minimizes the risk of regulatory noncompliance.

Validation should thus be considered in the some situation outlined below:

- In case of totally new process.
- When equipment is new.
- The Process and equipment which have been altered to suit changing priorities.
- In case of Process where the end-product test is poor and an unreliable indicator of product quality.

In case when any new manufacturing formula or method of dosage preparation is adopted, steps must be taken to demonstrate its suitability for routine processing and the defined process should be shown to yield a product which is consistent with the required quality. The extent to which deviations from chosen parameters may influence product quality should also be evaluated. In production, tests are performed each time on a batch to batch basis using specifications and methods devised during the development phase. The objective is to monitor the process continuously. When certain processes or products have been validated during the development stage, it is not always important to revalidate the whole process or product if similar equipment is used or similar products have been produced[8].

Process validation

Process validation is an important concept and it serves to support the underlying definition of validation, which is a systematic approach to identifying, measuring, evaluating, documenting, and re-evaluating the series of critical steps involved in manufacturing process of dosage forms that require control to ensure a reproducible final product

Process Validation is the "Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes" FDA Guideline, 1987.In its new guidelines FDA had made some changes in the process validation and defined it as "The collection and evaluation of data, from the design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products".

Types of Process Validation

The various types of process validation are outlined below

Prospective or Pre marketing Validation: In this type of validation experimental plan called the validation protocol is executed before the process is put to commercial use. Maximum of the validation efforts need some degree of prospective experimentation so as to generate validation support data. It is generally considered acceptable that the three consecutive batches of dosage forms runs within the finally selected parameters, that gives the product of the desired quality would constitute a proper validation of the process. It is suggested that the validation batches made should be of the same size as the intended production scale batches, when this is not practical[9].

Concurrent Process Validation: Concurrent validation is carried out during routine production activity. The document requirements are same as prospective validation. It is same as that of the prospective validation, except the operating firm will sell the product during qualification runs. The decision to carry out concurrent validation must be justified, documented approved by authorized person. This type of validation involves in process monitoring of critical processing steps and product testing, this helps to generate the document evidence to show that the production process is in a state control[10].

Retrospective Process Validation: In case of Retrospective validation the historic data is taken from the record of completed production batches are used to provide the documented evidence that the process has been in the state of control prior to the request for such evidence. is defined as the. The sources of such data may be the production, QA and QC records.

This type of validation is acceptable only in case of well-established processes, without any change in the composition of the product, operating procedures and Equipment. The source of data for this type of validation may be include batch documents Process control chart, logbooks, process capability studies. Those Batches which are selected for retrospective validation should be representative of all batches made during the review period including any batches that fail to meet the specification[11].

Revalidation: Revalidation is the repetition of a validation process or a part of it. This is carried out when there are any changes or replacements in the formulation or equipment plan and equipment site of location. It also provides the evidence that the changes in a process-introduced may be intentionally or unintentionally and do not adversely affect process characteristics and product quality. Revalidation may be needed in the following cases:

- Change in formulation.
- Changes in the procedure or quality of pharmaceuticals ingredients.
- Change in equipment, addition of new equipment and major breakdown.
- Major change of process parameters, change in site, batch size change.

Strategy for Process Validation of Solid Dosage Form

The strategy the process validation should be simple and straight forward. The following few points give the strategy for process validation[12-15].

- The use of the lots of different raw materials should be included. Eg. Active drug substances and excipients.
- Batches of the medicine dosage form should be manufactured in the equipment and the facilities designated for eventual commercial production.
- Critical process variables of manufacturing process must be set within their operating ranges and should not exceed their control limits during the process operation and responses of output should be well within finished product specifications.

- Batches should be run in succession and on different days and shifts (the latter condition, if appropriate).
- In case of Failure to meet the requirements of the Validation protocol with respect to the process input and output control should be subjected to process requalification and the subsequent revalidation following a thorough analysis of process data and formal discussion by the validation team.

Phases in Process Validation

Phase 1: This is the pre- validation qualification phase and it covers all activities relating to product research and development, formulation pilot batch studies, scale-up studies, 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[16].

Phase 2: This is a process validation phase. This phase 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.

Phase3: This phase is known as validation maintenance phase and this phase requires frequent review of all process related documents, including validation of audit reports, so as to assure that there have been no changes, deviations and modifications to production process and that all standards crepitating (SOPs),including change control procedures have been followed. At this stage the validation team comprising of individual 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 system and process control 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 principles of good manufacturing practices both in general and in specific reference to sterile product manufacture. The responsible authorities for process validation is a validation working party that convened to provide progress, community and ultimately approve the entire effort including all of the documentation generated. The working committee should include the following members of the company[17]:

- Quality Assurance Head
- Engineering Head
- Production Head
- Validation Specialist all discipline
- Validation Manager

Validation Protocol

The validation protocol should satisfy the following in detail[18]:

- General information
- Objective
- Background/revalidation
- Summary of development and technical transfer form R&D or another site activity to justify in process testing and controls any previous validations. Before formal cleaning validation programs were instituted, visual inspection was the primary means of determining equipment cleanliness.
- List of equipments and their qualification status
- Facilities qualification
- Process flow chart
- Manufacturing procedure narrative
- List of critical processing parameters and critical excipients
- Sampling, test and specification
- Acceptance criteria

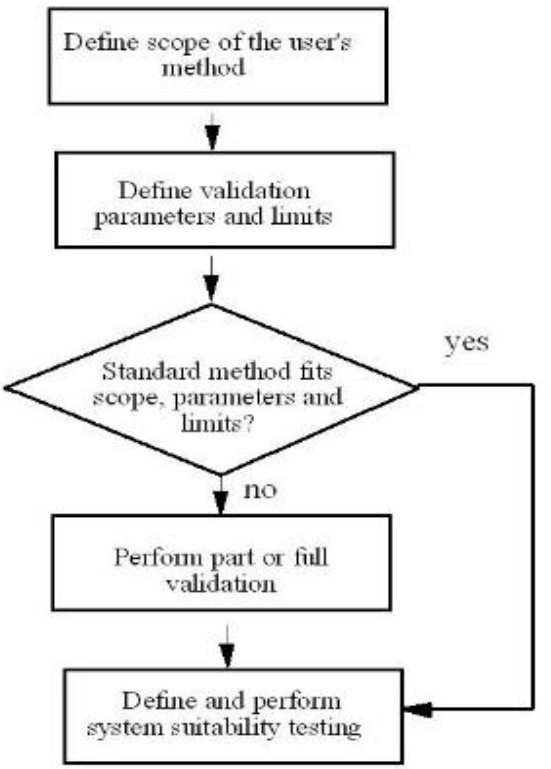

Figure 1: Validation Plan

CONCLUSION

It is concluded that the Process validation is an important part of among all validation like equipment validation, cleaning validation, vender validation etc. Process validation is a step to assure the identity, strength, purity, safety and efficacy of pharmaceutical drug product validation is the most common word in the drug development, manufacturing and specification of finished product.

From the review study it is concluded that the pharmaceutical validation and process controls are important to assure that the drug product meet standards for the identity, strength, quality, purity and stability.

REFERENCES

1. Nash RA and Wachter AH. Pharmaceutical Process Validation; 3rd Edn; Marcel Dekker publication. 2003; 432 – 434.
2. Kiran K and Kathiresan K.Basic Principles of Validation. 2005;1:35-36.
3. Aulton ME. Pharmaceutics, the science of dosage form design, international edition, second edition, Churchill Livingston (Elsevier), 2006: 1.
4. Levin M, Pharmaceutical process scale-up, Marcel Dekker, Inc., New York 2002: 313.
5. www.processvalidation.com as on 29-03-2013.
6. Satyabrata jena, Arjun G, Anil kumar ravipati N V, Satish kumar D,Vinod K R, David Banji. Industrial Process Validation of Solid Dosage Forms–An Overview International Journal of Pharmaceutical Sciences Review and Rsearch. 2010, 4(2).
7. www.picscheme.org as on 31-03-2013.

8. Committee on Specifications for Pharmaceutical Preparations. Good Manufacturing Practices for Pharmaceutical Products. WHO Technical Report Series no. 82. Geneva: World Health Organization, 1992, pp 14-79.
9. Chao, A. Y., St. John Forbes, E., Johnson, R. F., Von Doehren, P., Prospective Process Validation. In: I. Berry, R. A. Nash, eds. Pharmaceutical Processing Validation, Vol. 23, Marcel Dekker, New York, April 1993; 227–248.
10. Nash, R. A., Process Validation of Pharmaceutical Ingredients. In: Nash, R. A., Wachter, A. H., Pharmaceutical Process Validation, Vol.129, An International 3rd Edition, Revised and Expanded, Marcel Dekker, New York, March 2003, 809-813.
11. Avallone, H. E., Retrospective Validation, NAPM Meeting, Port Chester, New York, September 1983, 29-32.
12. US Food and Drug Administration. Guideline on General Principals of Process Validation; U.S. FDA Rockville, MD, May, 1987.
13. Chaitnya Kumar G, Rout RP, Ramtake S, Bhttachaiya S, Process Validation, The Indian Pharmacist, Aug 2005: 14-19.
14. Kathiresan K, Kiran K, Basics of Validation- Pharmaceutical Perspective, first edition, K.K. Publishers, Chidambaram, 2005: 32-46.
15. www.wikipedia.com as on 02-04-2013.
16. Harder SW. Encylopedia of Pharmaceutical Technology. Swarbrick KJ, Boylon J C. (Eds). Marcel Dekker, Newyork, 1995; 2: 447-456.
17. Nash RA, Alfred HW, Pharmaceutical Process Validation. 3rd Edition, Marcel Dekker, New York, 2003; 159-180.
18. South African Guidelines for good manufacturing practice, Medicinal Control Council, Pretoria, 1996.

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