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# PROCESS VALIDATION OF ORAL DOSAGE FORM (TABLET)

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## ABSTRACT

To persist in the direction of be present in spirited market and to be flourishing, it be necessary to construct elevated point of product quality Validation is one of the important steps in achieve and maintain the excellence of the ultimate result consignment before batch. Not counting apparatus, we cannot fabricate a product. By authenticate every step of creation method we are able to assure that the finishing product is of top feature. This appraisal provides information on objectives and revenue of process justification, type of method validation and regulatory phase.

**KEYWORDS:** Process validation, instrument, solid dosage form.

## INTRODUCTION

The key objective of dosage structure create to reach an expected of assistance response to a drug comprise in a formulation which is proficient of bulky scale fabricate with reproducible product superiority. Solid dosage forms comprise tablets and capsules. The developed of solid dosage forms encompass broad handling residue. The grind must be combine for standardization and changed into dosage form whichever during compression or encapsulation (Alam 2012). Classic needs contain weighing, blending, granulation areas, compression area and covering area. To certify result value, various characteristics are obligatory, similar to chemical and physical instability, appropriate conservation alongside microbial blot if correct, consistency of dose of drug, adequacy to user include prescriber and patient, as well as appropriate filler, category, and justification (Ahir et al. 2014).

The idea of rationale was initial recommended with two Food and Drug Administration official, Ted Byers and Bud Loftus in the mid 1970's in instruct to increase the quality of pharmaceuticals. Assurance of product quality is consequential since careful understanding to number of factor including assortment of quality part and equipment, sensible product and method design, control of the process and in process and end product testing (Ajay & Seema 2013) Due to the complexity of today's therapeutic products, routine end product testing simply is not satisfactory to guarantee of product, routine end product testing alone often is not adequate to assure product quality for copious reason.

## SEVERAL DEFINITION OF VALIDATION

**According to FDA,**

Assertion of product quality is derive since attentive and complete interest to a quantity of effect factors, through: variety of quality process during in-process and end-product test.

**According to US FDA in 1978,**

"A validation developed process is one which has be prove to make what it significances or is in material form to do. The evidence of justification is obtain during the assortment and estimation of statistics, rather, establishment from the method increase stage and progressing the manufacture period. Validation essentially includes method qualification but it also includes the control on the total course of action for frequent batch or run".

**European Commission - 1991,**

"Act of representative, in agreement of GMPs to facilitate any" process essentially lead to conventional marks.

**European Commission - 2000 - Validation** -"Measure verification that the practice, operate in predictable parameter, can carry out economically and reproducibly to construct a therapeutic product assembly its determined stipulation and quality attribute".

**WHO guidelines** Term justification as "Validation is standard act of prove to any procedure, method, equipment, material, movement in fact lead to the usual results". Validation act of proving, in agreement of GMPs that any process accurately lead to ordinary results. Documented proof that the process, operated with in predictable parameters, can perform successfully reproducibly to produce a healing product assembly its programmed stipulation and quality attribute (Surbhi et al., 2012).

## OBJECTIVES OF PROCESS VALIDATION

- To bring into the light software confirmation and justification and to argue the difference between them.
- To give details the program review method.
- To give details stopped analysis as a authorization technique.
- To depict the sanitary room software development process.

## ADVANTAGES OF PROCESS VALIDATION

1. It is uncomplicated process and humidity susceptible and heat susceptible products can also be handle.
2. Prolonged actual time inspection and regulation of process.
3. Reduction the hazard of avoid trouble and thus assure the soft organization of the process.
4. Better capability to statistically assess process routine and product variables e.g. persons; signify; series; organize limit.
5. Improve statistics and assessment ability and distended confidence about process reproducibility and product quality.
6. Superior capability to set objective parameters and control restrictions for regular production, associate among validation result (Sharma et al. 2015).

## IMPORTANCE OF PROCESS VALIDATION

- Government regulation
- Rapid automation.
- Improved employee awareness .
- Easier preservation of equipment's.
- Improved output.
- Reduction in quality cost.
- Less failures of process thus less complaints.
- Process optimization.

## TYPES OF VALIDATION

### Analytical Validation

Analytical validation is the assessment of invention value characteristics through testing, to establish reliability is being maintain during the creation life series and that the precision, accuracy, specificity, LOD, linearity, selectivity, strength, purity and measurement has not been compromise. The analytical method gives the detail stepladder obligatory to complete

an analysis. This may contain research of samples, standards and reagents, use of equipment and use of method for the estimate and several supplementary (Ojha et al., 2014).

**Equipment Validation**

Validation of equipment's is known as qualification. It is separated into Installation Qualification(IQ),Operational Qualification (OQ), and Performance Qualification (PQ).An installation document documents agree static traits of a facility or item in the direction of demonstrate to installation of the part have be properly achieve in addition to the mechanism specification of the manufacturer contain be meet. Subsequent headed for deception it must be definite to the equipment be capable of bring functioning series as exact keen on achieve command. This is calling Operational Qualification. The Performance Qualification be disturbed with demonstrate the method being complete in the appliance as it is hypothetical to do (Verma et al., 2014).

**Process Validation**

Process validation is "A predictable method which provide a superior amount of assurance that a precise practice will constantly generate a result summit its encoded measurement and inferiority attribute".

**VARIETY OF PROCESS VALIDATION AS FOLLOW**

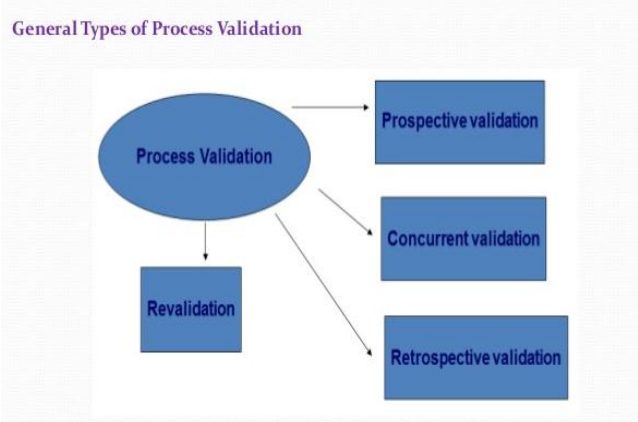



**Fig.1 General Type of Process Validation**

**(a) Prospective validation**

It is term like the association of acknowledged evidence to a creature do pardon? It reason stand leaving scheduled pre-planned procedure. This approach to justification is usually undertake at any time a fresh method, process or facility have in the direction of validate previous to marketable routine pharmaceutical formulation commences (Manubhai et al.

2012). During the product expansion phase the production process should be cracked down into individual steps. Every footstep must be evaluating going on the root of occurrence or else hypothetical consideration to control the decisive parameter so as to possibly will influence the quality of the ended product. A sequence of experiment has to be premeditated to establish the criticality of this factor. Both trial should be intended and accepted completely in an official protocol (Sharma et al. 2015).

**(b) Retrospective validation**

It is definite as the institution of predictable proof to a scheme do what it rationale to do base on re-examine with laboratory analysis of chronological information. This is achieving by the re-evaluate of the historical mechanized testing statistics to confirm that the method have constantly remain in organize. Designed in favour of the idea of conservative validation study, it is consider satisfactory to facilitate information from a smallest amount of ten uninterrupted batch formed be utilize. While not as much of than ten batches be presented, it is consider to facilitate the data are inadequate to express retrospectively with the intention of the method is completely under rule. In such cases the cram have to be supplement among statistics generate with coexisting or probable validation(Kaustubh et al. 2014).

**(C) Concurrent validation**

Concurrent validation is used for creating predictable verification that a capability and processes do what they significance to do, based on in sequence generate during actual assertion of the process. This advance involve monitor of significant handing out stepladder with finish product trying of current fabrication, to prove that the built-up progression is within a circumstances of control (Ram et al. 2015).

**(d) Revalidation**

Re-validation is typically achieved to the authentication of initial validation for a Periodic review. Re-validation provides the sign to facilitate change within a course of action and the progression atmosphere that are presented do not harmfully affect process characteristics and product quality.

**STEP OF PROCESS VALIDATION**

Readily available be three stage of method validation they be.

**Step 1:** method design or pre-qualification: The advertisement practice is clear for the period of this phase base scheduled the knowledge gained through development and scale up activities.

**Step 2:** method qualification: in this phase, the development intend is established as being able of reproducible industrial developed.

**Step 3:** Continued development certification: in progress assertion is gain through usual invention that the method remnants in a situation of control.

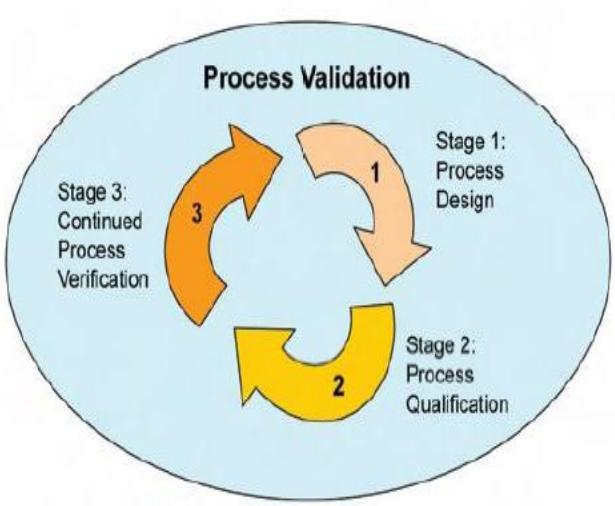



**Fig.2 Step of process validation**

**PROCESS PERFORMANCE QUALIFICATION**

This verify with the aim of the system is repeatable furthermore be constantly produce a quality product. These training declare, through proper presentation list also correlated citations, to facilitate equipment, supplementary system and sub-systems have been made to order exactly. The finish marks be to every prospect operation determination be dependable and within arranged operational limits. At various stages in a validation workout there are needs for protocols, documentation, procedures, specifications and acceptance criteria (Sindhur et al., 2012).

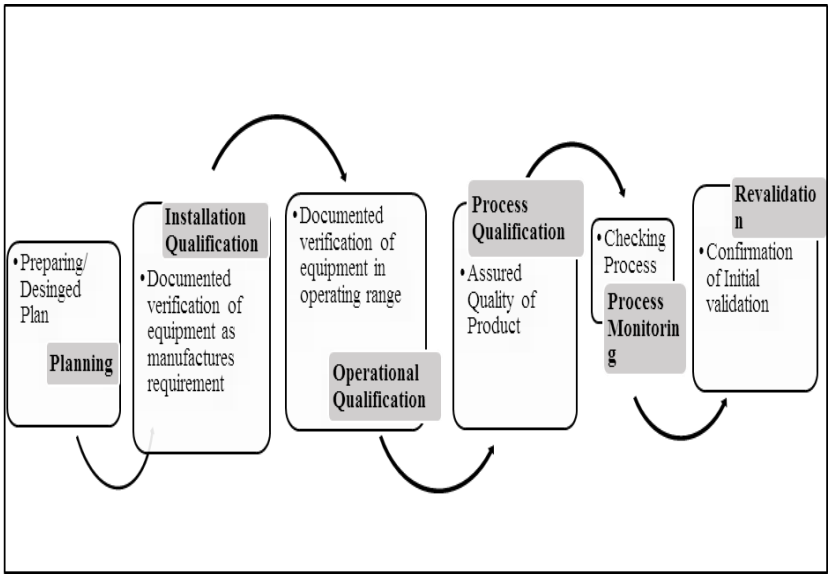



**Fig. 3 Life cycle of Process Validation**

Tablets are comprises of mixture of active ingredients and excipients which are compacted or mould keen on a cylindrical or biconvex solid. The benchmark aim of this dosage structure is to accomplish a conventional restorative reaction to a drug which is integrated into a formulation which is able of bulky magnitude built-up with reproducible product superiority. Their expenditure is smallest of all the oral dosage form. They are lightest and dense of all oral dosage form (Harsimranjit et al. 2012).

Identify the key physicochemical property of the drug substance that desires in the direction of considered in developing the formulations of tablet, such as the following.

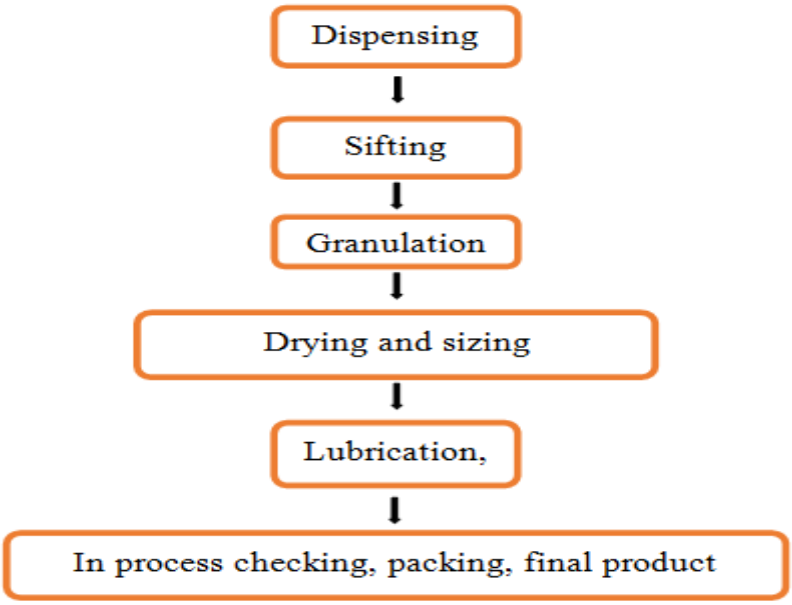
1. Solubility of the drug material all through the physiological pH variety: - Depending on the solubility of the drug, a stabilizer possibly will be essential to improve dissolution.
2. Particle range allotment as well as shell region: The particle range allotment of the drug can establish what category of an excipients (e.g., microcrystalline cellulose) to employ. (Paruchuri et al. 2012)
3. Morphology: stipulation of the drug is unstructured or has dissimilar polymorphs; certain excipients may perhaps be present use to stop renovation of the drug to last physical forms.
4. Tapped and bulk density: An Excipient (e.g.,diluents) that has a parallel bulk density while the drug may be selected to diminish separation, particularly among a direct compression formulation. (Sandhya et al. 2015).
5. Material flow and compressibility: A liberated flow, extremely compressible matter such as microcrystalline cellulose may be use intended for drugs among pitiable flow or compressibility properties.

6. Hygroscopicity: exceptional ecological functioning state of affairs may be requisite ensure that humidity is not pick up for the period of material storage or managing and during the construct of the tablet dosage form.

7. Melting point: If the drug have a low melting point, a straight compression formulation can require to be residential as a substitute of a damp granulation formulation to keep away from drying the substance and potentially melt or mortifying the drug (Bs & Vm 2010).

**Approach for the manufacturing progression justification of tablet dosage form**

1. The make use of of changed a lot of rare objects must be integrated.
2. Batch has to be run in sequence in dissimilar shift and time.
3. Batch must be manufactured within equipment's and conveniences with the purpose of premeditated for the trade manufacturing.
4. Fundamental method parameter has to set within their working range and should not undertake higher and lower limits of these ranges for the duration of the process.
5. Stoppage to assemble the necessity of procedure with admiration to the course of action input and output must be subjected to development requirement and consequent revalidation.(Goněc et al. 2014)




**PROCESS VALIDATION PROTOCOL**

It be a in black and white preparation which states that how will be the validation directed with experiment parameter, design type, manufacture and wrapping equipment's and the getting criteria. This document gives the crucial steps of the developed procedure with the

purpose of should be calculated and permissible series of unpredictability and the method in which the structure is to be tested. The confirmation procedure delivers a synopsis of hope what is to be gifted(Teresa & College n.d.). It must inventory the particular progression and control parameter. State the numeral of batch which is to be comprised in to a study and identify how the statistics once assembled and be treating for application. The date of agreement of protocol should be noted down in the confirmation team. In the case where the protocol is changed or modified suitable reasons for such change must be documented (Ahir et al. 2014) Process parameters involved in tablet manufacturing: The create of oral solid dosage form as capsules and tablet is a complex multi-stage process under which the initial supplies adjust their physical features a approach to of times earlier than the final dosage form is designed. Traditionally, tablets encompass by granulation, a process that communicates two primary basics to formulate: compatibility and fluidity. Both wet granulation and dry granulation are use. Irrespective of whether tablets are made by direct compression or granulation, the first step, milling and mixing, is the same; subsequent step differ (Thaduvai et al. 2012).

## TYPICAL OPERATIONS IN WET GRANULATION, DRY GRANULATION AND DIRECT COMPRESSION

### Wet granulation

The unique portions of wet granulation process involve the wet massing of the powder, wet sizing or milling, and drying. The wet granulation technique employs a solution, suspension, or slurry containing a binder, which is usually added to the powder mixture; however the binder may be incorporated dry into the powder mix, and the liquid may be added by itself (A NKS et al. 2014).

### Dry granulation

In this procedure the granulation is produced not by adding a binder. Here compact huge mass of the combination as well as consequently crush also sizing this piece to small granules takes place. The primary powder particles are aggregate under high pressure. Which include mainly two process. Either a huge tablet (acknowledged as a slug)is produced in a heavy-duty tableting press (a process known as slugging)or the powder is squeeze involve two roller to create a sheet of objects(Ram et al., 2015).

**Direct compression**

Some granule chemical similar to potassium chloride, potassium iodide and ammonium chloride have special property that they are free flow as well as consistent in nature which allow them to be compacted directly into tablet machine without any need for wet or dry granulation (Bhattacharjee et al., 2011).

**Table: 1 comparative study of the process parameters for different granulation processes.**

| Wet granulation | Dry granulation | Direct compression |
|---|---|---|
| Milling and mixing of drugs and excipients. | Miling and mixing of drugs and excipients | Milling and mixing of drugs and excipients |
| Preparation of binder solution | Compression into slugs or roll compaction | Compression of tablet |
| Wet massing by addition of binder solution or granulating solvent. | Milling and screening of slugs and compacted powder | |
| Screening of wet mass | Mixing with lubricant and disintegrate | |
| Drying of wet granules | Compression of tablet | |
| Screening of wet mass | | |
| Blending with lubricant and disintegrate to produce " running powder" | | |
| Compression of tablet | | |

**Table 2: Different Process Validation Parameters involved in the mfg of a tablet.**

| Sr. No | Process step | Control Variables | Measured responses(test) |
|---|---|---|---|
| 1 | Pre-blending | Blending time, RPM, Loading Size, Order of addition. | Blend uniformity |
| 2 | Granulation | Mixing speeds, Amount of granulation fluid, Feed rate, Granulation time | Drug distribution, Water/solvent content, Appearance |
| 3 | Drying | Initial temperature, Outlet temperature, Drying temperature. | Particle size distribution, Densities, Loss on drying. |
| 4 | Milling | Screen size, Milling speed, Feed rate. | Particle size, distribution/shape, Loos/tapped densities |
| 5 | Lubrication | Blending time, Blender speed, Load size | Particle size, distribution/shape, Loos/tapped densities, Flow properties. |

| | | | |
|---|---|---|---|
| 6 | Tableting | Compression rate, Granule feed rate, Pre-compression force, Compression force. | Appearance, Weight variation, hardness/friability, thickness, Moisture content, Disintegration/dissolution, Assay/dose uniformity. |
| 7 | Coating | Pan load, Inlet/exhaust temperature, Inlet exhaust humidity's, Pan speed, Atomizing pressure | Percent weight gain, Thickness, Dissolution, Assay, Degradation level, residual solvent. |

## CONCLUSION

Solid dosage form validation should be part of a inclusive validation program within an industry. The multidisciplinary validation group necessity recognize the product and method character to should be study as well as include particular validation test towards ensure that the product will collect every feature, manufacturing as well regulatory needs. Finally, it can be concluded that Process validation is a key component in the quality assurance of pharmaceutical product because the finish product test be not satisfactory towards assure quality of completed result.

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