



INDUSTRIAL PROCESS VALIDATION OF TABLET DOSAGE FORM: AN OVERVIEW

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ABSTRACT

In pharmaceutical organizations, validation is a fundamental segment that supports a company commitment to quality assurance. Validation is a tool of quality assurance which provides confirmation of the quality in equipment systems, manufacturing processes, software and testing methods. Validation assures that products with pre-determined quality characteristics and attributes can be reproduced consistently/reproducibly within the established limits of the manufacturing process operation at the manufacturing site. Validation of the individual steps of the manufacturing processes is called the process validation. Different dosage forms have different validation protocols. Here this article concentrates on the process validation of tablet dosage form, protocol preparation and regulatory basis for process validation in industry. It gives in detail the validation of each step of the manufacturing process of tablets through wet granulation.

Key words: Process validation, Tablet dosage form, Quality assurance, Protocol, Regulatory basis, Wet granulation.

INTRODUCTION

“A dosage form is the physical form of a dose of a chemical compound used as a drug or medication intended for administration or consumption.”

A tablet has numerous advantages over other dosage form, among which are simplicity, low cost, speed of production, patient convenience and stability of a drug substance in a drug dosage form. It comprises a mixture of active substances and excipients, usually in powder form, pressed or compacted into a solid. The excipients can include binders, glidants (flow aids) and lubricants to ensure efficient tabletting; disintegrants to promote tablet break-up in the digestive tract; sweeteners or flavours 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 (extending its shelf life), or to enhance the tablet's appearance^{1,2}.

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. 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, labelling and validation³.

Process validation establishes the flexibility and constraints in the manufacturing process controls in the attainment of desirable attributes in the drug product while preventing undesirable properties. This is an important concept, since it serves to support the underlying definition of validation, which is a systematic approach to identifying, measuring, evaluating, documenting, and re-evaluating a series of critical steps in the manufacturing process that require control to ensure a reproducible final product⁴.

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 pre determined specifications and quality characteristics⁵.”

Types of process validation^{6,7,8}

1. Prospective Validation: In Prospective Validation, the validation protocol is executed before the process is put into commercial use. During the product development phase the production process should be broken down into individual steps. Each step should be evaluated on the basis of experience or theoretical considerations to determine the critical parameters that may affect the quality of the finished product. A series of experiments should be designed to determine the criticality of these factors. Each experiment should be planned and documented fully in an authorized protocol.

All equipment, production environment and the analytical testing methods to be used should have been fully validated. Master batch documents can be prepared only after the critical parameters of the process have been identified. It is generally considered acceptable that three consecutive batches/runs within the finally agreed parameters, giving product of the desired quality would constitute a proper validation of the process.

2. 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 documented evidence to show that the production process is in a state of control.

3. Retrospective Validation: In retrospective validation, historic data taken from the records of the completed production batches are used to provide documented evidence that the process has been in a state of control prior to the request for such evidence.

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.

Stages of process validation⁴

The three stages of process validation are shown in Figure 1.

Stage 1 – Process Design or process pre-qualification: The commercial process is defined during this stage based on knowledge gained through development and scale-up activities.

Stage 2 – Process Qualification: During this stage, the process design is confirmed as being capable of reproducible commercial manufacturing.

Stage 3 – Continued Process Verification: Ongoing assurance is gained during routine production that the process remains in a state of control.

Stage 1 includes performing process understanding studies to establish all process parameters, determining which parameters are critical, and executing supporting validation studies. Pre-qualification activities involve the evaluation of process parameters and their ranges. The key to meaningful pre-qualification studies is a process pre-qualification plan that is based on a well-defined manufacturing process. Each parameter is assessed for its potential to affect (positively or negatively) the applicable process controls or quality attributes.

Stage 2 includes the performance of three consecutive runs at the intended commercial scale. The manufacturing process qualification is performed under a prospective protocol using the appropriate output and results from the stage 1 studies (i.e., critical parameters), in process controls and specifications, and any additional criteria specific to the process.

Stage 3 is the ongoing assessment of process performance through life cycle qualification and management of process changes. Critical process parameters are monitored routinely during batch release. After validation, all changes made to manufacturing procedures are assessed for impact to the validated process, and revalidation is performed as needed.

The regulatory basis for process validation^{5,6,9,10}

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, and 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 and/or process.

First, manufacturers are required by law to conform to cGMP regulations. Second, good business dictates that a manufacturer avoids the possibility of rejected or recalled batches. Third, validation helps to ensure product uniformity, reproducibility and quality.

Although the original focus of validation was directed towards prescription drugs, the FDA Modernization Act of 1997 expanded the agency's authority to inspect establishments manufacturing over-the-counter (OTC) drugs to ensure compliance with cGMP.

Once the concept of being able to predict process performance to meet user requirements evolved, FDA regulatory officials established that there was a legal basis for requiring process validation. The ultimate legal authority is Section 501(a)(2)(B) of the FD&C Act, which states that a drug is deemed to be adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing,

packing, or holding do not conform to or were not operated or administrated in conformity with cGMP.

The cGMP regulations for finished pharmaceuticals, 21 CFR 210 and 211, were promulgated to enforce the requirements of the act. 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 intended to possess (21 CFR 211.100(a) and 211.110(a)).

Strategy for industrial process validation of tablet dosage form^{5,6}

The strategy selected for process validation should be Simple and straightforward.

The following five points gives strategy for industrial process validation:

1. The use of different lots of raw materials should be included i.e., active drug substance and major excipients.
2. Batches should be run in succession and on different days and shifts (the latter condition, if appropriate).
3. Batches should be manufactured in the equipment and facilities designated for eventual commercial production.
4. Critical process variables should be set within their operating ranges and should not exceed their upper and lower control limits during process operation. Output responses should be well within finished product specifications.
5. Failure to meet the requirements of the Validation protocol with respect to process input and output control should be subjected to process requalification and subsequent revalidation following a thorough analysis of process data and formal discussion by the validation team.

Process validation protocol⁶

Validation protocol is a written plan stating how validation will be conducted, including test parameters, product characteristics, production and packaging equipment, and decision points on what constitutes acceptable test results. This document should give details of critical steps of the manufacturing process that should be measured, the allowable range of variability and the manner in which the system will be tested.

The validation protocol provides a synopsis of what is hoped to be accomplished. The protocol should list the selected process and control parameters, state the number of batches to be included in the study, and specify how the data, once assembled, will be treated for relevance. The date of approval by the validation team should also be noted.

In the case where a protocol is altered or modified after its approval, appropriate reasoning for such a change must be documented.

The protocol for process validation is given in tables 1, 2 and 3.

Industrial process overview of tablet manufacturing^{5,6,11}

Steps and process critical parameters during process validation of tablet manufacturing process are given in table 4.

1. Mixing or Blending: Materials that have similar physical properties will be easier to form a uniform mix or blend and will not segregate as readily as materials with large differences.

Parameters to consider:

Mixing or blending technique: Diffusion (tumble), convection (planetary or high intensity), or pneumatic (fluid bed) techniques can be used to mix or blend materials. Determine the technique that is required for the formulation or process objective. It may be different, depending on

whether you are mixing the drug and excipient for a direct compression formulation or adding the lubricant (e.g., magnesium stearate) to the granulation.

Mixing or blending speed: Determine the intensity (low/high shear) and/or speed (low/high/optimal shear) (rpm) of the mixing or blending. Mixing the drug and excipient will require more intense mixing than adding the lubricant to the final blend.

Mixing or blending time: How much mixing or blending is required to obtain a uniform mixture? The mixing or blending time will be dependent on the mixing or blending technique and speed. Experiments should be done to determine if the materials can be overmixed, resulting in demixing or segregation of the materials. Demixing can occur due to the physical property differences (e.g., particle size distribution and density). For example, demixing can occur in a direct compression formulation in which the drug substance is micronized (5 microns) and the excipients are granular (500–1000 microns).

Drug uniformity: Content uniformity is usually performed to determine the uniformity of drug throughout the mix or blend. Representative samples should be taken throughout the mix or blend. The sampling technique and handling of the materials are key in obtaining valid content uniformity results. Segregation of the sample can occur by overhandling, resulting in inaccurate results. For the final blend (blend prior to compression), the sample taken should be equivalent to the weight of a single tablet.

Excipient uniformity: Besides drug uniformity, excipients need to be uniform in the granulation or blend. Two key excipients are:

Lubricant: The lubricant needs to be distributed uniformly in the mixture/granulation for the high-speed compression operation. Uneven distribution of the lubricant can result in picking and sticky problems during compression. It can also lead to tablet performance problems (low dissolution due to excessive lubricant in some tablets).

Color: The colorant(s) need(s) to be evenly distributed in the mixture so that the tablets have a uniform appearance (e.g., color, hue, and intensity). The coloring agent may need to be prescreened or more uniformly dispersed in the blend prior to compression to avoid speckling or shading of the color.

Equipment capacity/load: The bulk density of materials or granules will affect the capacity of the equipment. If an excipient in the formulation affects the density of the final blend to a greater extent than any other ingredient, then a well-controlled density specification for that excipient may be warranted. Test different-sized loads in the mixer/blender (e.g., 30, 50, and 70% of working volume) for optimal mixing or blending. Undercharging or overcharging a blender can result in poor drug or tablet lubricant distribution.

2. Wet Granulation: What type of wet granulation technique will be used? Will it be of low shear (e.g., Hobart), high shear (e.g., Diosna, GEI-Collette) or fluid bed (e.g., Glatt, Fluid Air)? Each technique will produce granules with different physical properties and will require monitoring of different processing parameters. Wet granulation parameters to be considered during development and validation are:

Binder addition: Should the binder be added as a granulating solution or dry like the other excipients? Adding the binder dry avoids the need to determine the optimal binder concentration and a separate manufacture for the binder solution.

Binder concentration: The optimal binder concentration will need to be determined for the formulation. If the binder is to

be sprayed, the binder solution needs to be dilute enough so that it can be pumped through the spray nozzle. It should also be sufficiently concentrated to form granules without over wetting the materials.

Amount of binder solution/granulating solvent: How much binder or solvent solution is required to granulate the material? Too much binder or solvent solution will over wet the materials and prolong the drying time. The amount of binder solution is related to the binder concentration.

Binder solution/granulating solvent addition rate: Define the rate or rate range at which the binder solution or granulating solvent can be added to the materials. Can the granulating solution be dumped into the mixer or does it have to be metered in at a specific rate?

Mixing time: How long should the material be mixed to ensure proper formation of granules? Should mixing stop after the addition of the binder or solvent solution or should additional mixing be required? Granulations that are not mixed long enough can form incomplete or weak granules. These granules may have poor flow and compression properties. On the other hand, over mixing the granulation can lead to harder granules and a lower dissolution rate.

Granulation end point: How is the granulation end point determined? Is it determined or controlled by granulation end point equipment (e.g., ammeter or wattmeter)? Is it controlled by specifying critical processing parameters? For example, a drug or excipient mixture may be granulated by adding a predetermined amount of water (granulating solution) at a certain rate. The granulation is completed after mixing for a set time after the water has been added.

3. Wet milling: Does the wet granulation need to be milled to break up the lumps and enhance drying of the granulation? Wet granules that have a wide aggregate range can lead to inefficient drying (long drying times and partially dried large granules or lumps).

Factors to consider are:

Equipment size and capacity: The mill should be large enough to delump the entire batch within a reasonable time period to minimize manufacturing time and prevent the material from drying during this operation.

Screen size: The screen needs to be small enough to delump the material, but not too small to cause excessive heating of the mill, resulting in drying of the granulation.

Mill speed: The speed should be sufficient to efficiently delump the material without straining the equipment.

Feed rate: The feed rate of the wet granulation is interrelated to screen size and mill size and speed.

4. Drying: The type of drying technique (e.g., tray, fluid bed, and microwave) required for the formulation needs to be determined and justified. The type of technique may be dependent on such factors as drug or formulation properties and equipment availability. Changing dryer techniques could affect such tablet properties as hardness, disintegration, dissolution, and stability. The optimal moisture content of the dried granulation needs to be determined.

High moisture content can result in

- (1) Tablet picking or sticking to tablet punch surfaces and
- (2) Poor chemical stability as a result of hydrolysis.

An over dried granulation could result in poor hardness and friability. Moisture content analysis can be performed using the conventional loss-on-drying techniques or such state-of-the-art techniques as near infrared (NIR) spectroscopy.

Inlet/outlet temperature: The inlet temperature is the temperature of the incoming air to the dryer, while the outlet temperature is the temperature leaving the unit. The inlet

temperature is critical to the drying efficiency of the granulation and should be set high enough to maximize drying without affecting the chemical/physical stability of the granulation. The outlet temperature is an indicator of the granulation temperature and will increase toward the inlet temperature as the moisture content of the granulation decreases (evaporation rate).

Airflow: There should be sufficient airflow to ensure removal of moisture laden air from the wet granulation. Insufficient airflow could prolong drying and affect the chemical stability of the drug. Airflow and the inlet/outlet temperature are interrelated parameters and should be considered together.

Moisture uniformity: The moisture content could vary within the granulation. Heat uniformity of the dryer (e.g., tray), amount of granulation per tray, and incomplete fluidization of the bed are factors that could affect the moisture uniformity of the granulation.

Equipment capability/capacity: The load that can be efficiently dried within the unit needs to be known. A larger load will require more moisture to be removed on drying and will affect the drying time. In the case of fluid bed drying, a maximum dryer load is that load above which the dryer will not fluidize the material.

5. Milling: The milling operation will reduce the particle size of the dried granulation. The resultant particle size distribution will affect such material properties as flow, compressibility, disintegration, and dissolution. An optimal particle size/size distribution for the formulation will need to be determined. Factors to consider in milling are:

Mill type: What mill type (e.g., impact or screen) should be used? Each has several variants, depending on the means to reduce the particles. The type of mill can generate a different particle size/size distribution

Screen size: The selected screen size will affect the particle size. A smaller screen size will produce a smaller particle size and a greater number of fines.

Mill speed: What is the optimal mill speed? A higher mill speed will result in a smaller particle size and possibly a wider particle size distribution. It can also generate more heat to the product, depending on the screen size and feed rate, which could affect the stability of the product.

Feed rate: The feed rate is dependent on the mill capacity, screen size, and mill speed.

6. Lubrication

Selection of lubricant: what kind of lubricant should be used?

Grade of the lubricant used. Compatibility with other ingredients.

Amount of lubricant added: How much lubricant is required? Too much lubricant will form hydrophobic layer on the tablet resulting in dissolution problems.

Mixing time: How long should the material be mixed to ensure proper formation? Should mixing stop after the addition of the lubricant or should additional mixing be required? If not mixed long enough form problems like chipping, capping, etc.

7. Tablet Compression: Compression is a critical step in the production of a tablet dosage form. The materials being compressed will need to have adequate flow and compressibility properties. The material should readily flow from the hopper onto the feed frame and into the dies. Inadequate flow can result in “rat holing” in the hopper and/or segregation of the blend in the hopper/feed frame. This can cause tablet weight and content uniformity problems. As for the compressibility properties of the formulation, it should be examined on an

instrumented tablet press. Factors to consider during compression are as follows:

Tooling: The shape, size, and concavity of the tooling should be examined based on the formulation properties and commercial specifications. For intagliated (embossed) tablets, factors such as the position of the intagliation on the tablet and the intagliation depth and style should be examined to ensure that picking of the intagliation during compression or fill-in of the intagliation during coating does not occur.

Compression speed: The formulation should be compressed at a wide range of compression speeds to determine the operating range of the compressor. The adequacy of the material's flow into the dies will be determined by examining the tablet weights. Is a force feeder required to ensure that sufficient material is fed into the dies?

Compression/ejection force: The compression profile for the tablet formulation will need to be determined to establish the optimal compression force to obtain the desired tablet hardness

The following in-process tests should be examined during the compression stage:

- i. Appearance
- ii. Hardness
- iii. Tablet weight
- iv. Friability
- v. Disintegration
- vi. Weight uniformity

8. Tablet Coating: Tablet coating can occur by different techniques (e.g., sugar, film, or compression). Film coating has been the most common technique over recent years and will be the focus of this section.

Key areas to consider for tablet coating include the following:
Tablet properties: Tablet properties such as hardness, shape, and intagliation (if required) are important to obtain a good film-coated tablet. The tablet needs to be hard enough to withstand the coating process. If tablet attrition occurs, the tablets will have a rough surface appearance. For tablet shape, a round tablet will be easier to coat than tablets with multiple sides or edges because of the uniformity of the surface. For intagliated tablets, the intagliation style and depth should be developed to prevent fill-in or chipping of the intagliation.

Equipment type: The type of coater will need to be selected. Conventional or perforated pan and fluid bed coaters are potential options.

Coater load: What is the acceptable tablet load range of the equipment? Having too large a pan load could cause attrition of the tablets because of the overall tablet weight in the coater. In the case of a fluid bed coater, there may not be sufficient airflow to fluidize the tablets.

Pan speed: What is the optimal pan speed? This will be interrelated to other coating parameters, such as inlet temperature, spray rate, and flow rate.

Spray guns: The number and types of guns should be determined in order to efficiently coat the tablets. The spray nozzles should be sized properly to ensure even distribution over the tablet bed and to prevent clogging of the nozzles. The location and angle of the spray gun(s) should be positioned to get adequate coverage. Having the guns positioned too close together can lead to a portion of the tablets to be over wet.

Application/spray rate: The optimal application/spray rate should be determined. Spraying too fast will cause the tablets to become over wet, resulting in clumping of tablets and possible dissolution of the tablet surface. Spraying too slowly

will cause the coating materials to dry prior to adhesion to the tablets. This will result in a rough tablet surface and poor coating efficiency.

Tablet flow: The flow or movement of the tablets in the coater should be examined to ensure proper flow. There should be sufficient tablet bed movement to ensure even distribution of the coating solution onto the tablets. The addition of baffles may be required to provide adequate movement of tablets for tablet coating.

Inlet/outlet temperature and airflow: These parameters are interrelated and should be set to ensure that the atomized coating solution reaches the tablet surface and then is quickly dried.

Coating solution: The concentration and viscosity of the coating solution will need to be determined. The solution will need to be sufficiently diluted in order to spray the material on the tablets. The concentration of the coating solution will also determine the amount and volume of solution to be applied to the tablets. The stability of the coating solution should be investigated to establish its shelf life.

Coating weight: A minimum and maximum coating weight should be established for the tablet. Sufficient coating material should be applied to the tablets to provide a uniform appearance; however, it should not be great enough to cause fill-in of the intaglia.

Residual solvent level: If solvents are used for tablet coating, the residual solvent level will need to be determined.

Appearance testing of the tablets is critical during the coating operation. Items to look for include the following:

- i. Cracking or peeling of the coating
- ii. Intaglia fill-in
- iii. Surface roughness
- iv. Color uniformity
- v. Coating efficiency should be determined for the coating operation. The efficiency will determine the amount of coating solution coverage that may be required.

9. In-process tests

- i. Moisture content of “dried granulation”
- ii. Granulation particle size distribution
- iii. Blend uniformity
- iv. Individual tablet/capsule weight
- v. Tablet hardness
- vi. Tablet thickness
- vii. Disintegration
- viii. Impurity profile

10. Finished product tests

- i. Appearance
- ii. Assay
- iii. Content uniformity
- iv. Tablet hardness
- v. Tablet friability
- vi. Impurity profile
- vii. Dissolution

Process validation testing is generally done on the **first three batches** of product made in production-size equipment.

Revalidation testing is only done when a “significant” change has occurred. A significant change is one that will alter the in-process or final product specification established during the validation program or a change in formula, process, or equipment.

CONCLUSION

Tablet 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. The total program should begin with validation of the active pharmaceutical ingredient (API) characteristics so that this material will be uniform batch after batch, providing a solid footing upon which the dosage form will be built. Scientific information obtained during the preformulation stage can form the basis for a well-designed and comprehensive validation program. The parameters chosen must be relevant indicators of a controlled process. Continued awareness of validation requirements and a diligent application of validation principles will thus help to ensure that pharmaceutical products will be able to be developed and produced with the quality and reproducibility required from regulatory agencies across the world.

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Table 1: Protocol for title page in industry

Name of the company	
Process validation protocol	
Product:	Page No. : 1 of
Protocol No. :	Version No. :
Product name :	
Label claim :	
Master Formula Record (MFR) No. :	
Batch Manufacturing Record (BMR) No. :	
Effective Date :	

Table 2: Protocol approval

	Prepared By	Checked By		Approved By
Signature				
Date				
Name				
Department	Quality Assurance (QA)/Research and development (R&D)	R & D	Production	Quality Control
				Head – QA

Table 3: Table of contents

Sr. No.	Title	Page No.
1.	Protocol Approval Sheet	
2.	Table of contents	
3.	Objective	
4.	Scope	
5.	Validation term and responsibility	
6.	Steps for validation and acceptance criteria	
7.	Process flow chart	
8.	Procedure	
9.	Form – A : Review of raw material/packing material	
10.	Form – B : Evaluation of active raw material	
11.	Form – C : Evaluation of inactive raw material	
12.	Form – D : Qualification of equipment	
13.	Form – E : Test instrument calibration	
14.	Form – F : Dry mixing	
15.	Sampling point diagram of RMG	
16.	Form – G : Wet mixing	
17.	Form – H : Drying	
18.	Sampling point diagram of FBD	
19.	Form – I : Lubrication	
20.	Sampling point diagram of RMG	
21.	Form – J : Compression	
22.	Form – K : Coating	
23.	Form – L : Bulk packing	
24.	Re validation criteria	
25.	Change control	
26.	Stability	
27.	Deviations	
28.	Conclusion	
29.	Report and Approval	

Table 4: Steps and process critical parameters during process validation of tablet manufacturing process

Steps	Purpose	Control variable	Test parameters	Acceptance criteria
Dry mixing	Homogenous mixture	➤ Mixing time ➤ Impeller speed	Mixing time and speed	Mixing time:min. Impeller speed: (slow/medium/high)±5RPM. Content uniformity :90%-110% RSD : ±5%
Wet granulation	Convert powder to granules	➤ Time ➤ Temperature ➤ Solvent used	Mode and time of addition	Depending up on the formulation
Drying	Reduce moisture content to proper level for compression	➤ Inlet temperature ➤ Outlet temperature ➤ Drying time	Inlet/outlet temperature and drying time	Initial drying:°C Drying time:min. Final drying:°C±5°C Loss on drying :% below 3% or depending on formulation
Milling	Reduce particle size of dried granulation	➤ Mill speed ➤ Feed rate	Milling speed	Impeller speed : (slow/medium/high) Chopper speed: (slow/medium/high)
Lubrication	Provide granules suitable flow and compressibility	➤ Time ➤ Blender/granulator speed	Mixing time and speed	Mixing time:min. Speed:rpm. Content uniformity :
Tablet compression	Manufacture of compressed tablets	➤ Compression speed ➤ Compression force	Machine speed and compression force	Average weight:mg Uniformity of weight mg : Thickness :mm Hardness :N or Kp Disintegration time: NMT.....min. Friability : NMTw/w Assay : Dissolution:.....%
Tablet coating	Coating of tablet	➤ Pan speed ➤ Spray rate	Pan speed, inlet/outlet temperature, spray rate	Average weight :mg Weight of 20 tablets : ..mg Thickness :mm Disintegration time: NMT.....min. Assay : Dissolution:%

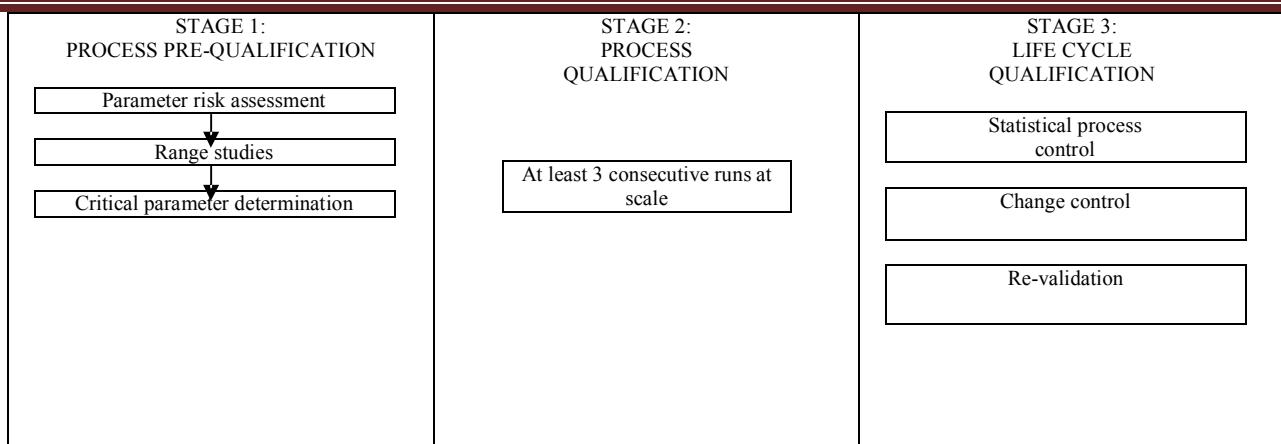


Figure 1: Three stages of process validation