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REVIEW ARTICLE

INDUSTRIAL PROCESS VALIDATION OF TABLETS: AN OVERVIEW

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ABSTRACT

The validation is a Fundamental segment to support the commitment of company towards quality assurance. It also assures that product meets its predetermined quality specification and quality characteristics. Validation of individual steps of manufacturing is known as process validation. Product quality is the mainstay of pharmaceutical industries and is derived from careful attention to a number of factors including selection of quality parts and materials, adequate product and manufacturing process design, control of the process variables, in-process and end-product testing. By validating each step of production process we can assure that the final product is of best quality & provides information on validation of tablet dosage form which has a numerous advantages over other dosage forms. The objective is to present a review and to discuss aspects of validation in terms of pharmaceutical unit operations like those individual technical operations that comprises of various steps involved in product design and evaluation and provide information on validation of tablet dosage form which have numerous advantages over other dosage forms.

KEY WORDS: Quality, process variables, process validation, manufacturing, dosage forms, guidelines.

INTRODUCTION:

The prime objective of any pharmaceutical plant is to manufacture products of requisite attribute and quality consistently, at the lowest possible cost. Numerous features are required to ensure product quality, such as 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].It is through careful design and validation of both the process and process controls that a manufacturer can establish a high degree of confidence that all manufactured units from successive lots will be acceptable. Successful validation of a process may reduce the dependence upon intensive in-process and finished product testing. In most cases, end-product testing plays a major role in assuring that quality assurance goals are met; i.e., validation and end-product testing are not mutually exclusive[2].

The FDA in "Guidelines on General Principles of Process Validation "defines process validation as establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality characteristics. According to EMEA, "Process validation can be defined as documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce a medical product meeting its predetermined specifications and quality attributes"[3].

OBJECTIVES OF PROCESS VALIDATION:

- In addition to the individual equipment, the manufacturing process must be validated.
- The goal is to create a robust manufacturing process that consistently produces a drug product with minimal variation that adheres to quality criteria of purity, identity, and potency.
- Engineers should draft and execute a validation plan for the manufacturing process in order to satisfy guidelines. The validation plan usually involves just a PQ section.
- Just as equipment validation, after the initial validation, major changes will result in the need for subsequent revalidation.
- Process validation will ensure a robust product which is highly reproducible over time.

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 incipient.
- Change in specification on input material.

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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[5].

BENEFITS OF PROCESS VALIDATION:

- Consistent through output.
- Reduction in rejections and reworks.
- Reduction in utility cost.
- Avoidance of capital expenditures.
- Fewer complaints about process related failure.
- Reduced testing process and finished goods.
- More rapid and accurate investigations into process deviation.
- More rapid and reliable start-up of new equipment.
- Easier scale-up from development work.
- Easier maintenance of equipment.
- Improve employee awareness of processes.
- More rapid automation[6].

THE PROCESS VALIDATION HAS 4 TYPES:

1) Prospective validation: - In prospective validation the validation protocol is executed before the processes put into the commercial use. During the product development stage 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 finished product.

2) Concurrent validation: - It is similar to 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 which helps to generate documented evidence to show that production process is in a state of control.

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

4) Revalidation: - It is the repetition of validation process or 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[7].

Stages of process validation: - There are 3 Stages of process validation they are

Stage 1:- **Process design or pre-qualification**: The commercial process is defined during this stage based on the 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.

Tablets are comprises of mixture of active ingredients and excipients which are compressed or molded into a cylindrical or biconvex solid. The principle objective of this dosage form is to achieve a predictable therapeutic response to a drug which is included into a formulation which is capable of large scale manufacturing with reproducible product quality. Their cost is lowest of all the oral dosage forms. They are lightest and compact of all oral dosage form[8,9,10].

THE 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, 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))[12,13,14,15]

STRATEGY FOR THE INDUSTRIAL PROCESS VALIDATION OF TABLET DOSAGE FORM:

- The use of different lots of Raw material should be included.
- Batches should be run in succession in different shifts and days.
- Batches should be manufactured in equipments and facilities that are designed for the commercial manufacturing.
- Critical process parameters should set within their operating Ranges and should not undergo upper and lower limits of these ranges during the operation.
- Failure to meet the requirement of protocol with respect to the 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.[12,13] .

PROCESS VALIDATION PROTOCOL:

It is a written plan which states that how will be the validation conducted including test parameters, product characteristics, production and packaging equipments and the acceptance criteria. This document gives the critical steps of the manufacturing process that should be measured and allowable range of variability and the manner in which the system is to be tested. The validation protocol provides a synopsis of hope what is to be accomplished. It should list the selected process and control parameters. State the number of batches which are to be included in to a study and specify how the data once assembled and be treated for relevance. The date of approval of protocol should be noted down by the validation team. In the case where the protocol is altered or modified appropriate reasons for such change must be documented.

PROCESS EVALUATION AND SELECTION:

Determine the unit operations needed to manufacture the tablets and their critical process parameters.

1). Mixing or Blending

The mixing or blending unit operation may occur once or several times during the tablet manufacture. For example, a direct compression formulation may involve one blending step in which the drug and the excipients are blended together prior to compression. A wet granulation formulation may require two mixing/blending steps: (1) prior to granulating to have a uniform drug/excipient mixture, and (2) after milling the dried granulation to add other excipients, such as the lubricant. Some or all the items provided in this section may therefore be pertinent for validation, depending on the mixing or blending objective.

The following physical properties of the drug and excipients are factor in creating a uniform mix or blend: Bulk density Particle shape Particle size distribution Surface area.

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.

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 excipients 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 (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 over mixed, 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 over handling, 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 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 overwet 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 is 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: critical process parameters which are needed to be considered during wet milling in process validation 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 picking or sticking to tablet punch surfaces and poor chemical stability as a result of hydrolysis. An over dried granulation could result in poor hardness and friability. Moisture content analysis can he performed using the conventional loss-on-drying techniques or such state-of-the-art techniques as near infrared (NIR) spectroscopy. Parameters to consider during drying are:

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 (evaporization 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. Particle size testing will need to be conducted and the results examined when substituting mill types.

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: 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). 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 compression 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.

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 particle size/size distribution or level of lubricant may need to be adjusted in order to have a robust process on a high-speed compressor.

7). Tablet Compression

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- Tooling
- Compression speed
- Compression/ejection force

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

- Appearance
- Hardness
- Tablet weight
- Friability
- Disintegration

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 will 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: 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 greatenough to cause fill-in of the intagliation.

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:

1. Cracking or peeling of the coating.
2. Intagliation fill-in.
3. Surface roughness.
4. Color uniformity.

Coating efficiency should be determined for the coating operation. The efficiency will determine the amount of coating solution overage that may be required.

9. In-Process Tests

Moisture content of "dried granulation": Loss on drying (LOD) can be used to determine whether or not the granulation solvent has been removed to a sufficient level during the drying operation (usually less than 2% moisture).

Granulation particle size distribution: An extremely important parameter that can affect tablet compressibility, hardness, thickness, disintegration, dissolution, weight variation, and content uniformity. This parameter, which can be done by sieve analysis, should be monitored throughout the tablet validation process.

Blend uniformity: Samples of the blend are taken and analyzed to ensure that the drug is uniformly dispersed throughout the tablet/capsule blend. The proper blend time must be established so that the blend is not under- or over mixed. The sampling technique is critical for this test to be valid.

Individual tablet*:* the weight of individual tablets is determined throughout compression/encapsulation to ensure that the material is flowing properly and the equipment is working consistently. The individual weight should be within 5% of the nominal weight. Weight fluctuations or frequent machine adjustments suggest that the formulation/process (e.g. poor granulation flow) is not optimized and/or that the equipment may need maintenance.

Tablet hardness: Tablet hardness is determined periodically throughout the batch to ensure that the tablets are robust enough for coating, packing, and shipping and not too hard to affect dissolution.

Tablet thickness: Tablet thickness is also determined periodically throughout the batch and is indirectly related to the hardness. It is another indication of whether or not the formulation has proper flow and compression properties.

Disintegration: Disintegration is determined during the manufacture as a predictor of tablet performance.

10. Finished product tests

Appearance: The tablets should be examined for such problems as tablet mottling, picking of the monogram, tablet filming, and capping of the tablets. If the tablets are colored, the color quality needs to be examined.

Assay: This test will determine whether or not the product contains the labeled amount of drug.

Content uniformity: Samples are taken across the batch profile (beginning, middle, and end) and analyzed to ensure that the dosage forms comply with compendial standards 15% of the labeled amount) or more stringent internal limits. It will indicate whether there is demixing during the manufacturing operation (i.e., segregation during flow of granulation from a storage bin).

Tablet hardness: A critical parameter for dosage form handling and performance.

Tablet friability: Friability is an important characteristic on the tablets' ability to withstand chipping, cracking, or "dusting" during the packaging operations and shipping.

Dissolution: Dissolution is important to ensure proper drug release characteristics (in vitro availability) and batch-to-batch uniformity.

These key test parameters are the yardsticks by which the major processing variables in solid dosage forms are evaluated. Some processing variables are:

Mixing time and speed in blenders and granulators Solvent addition rates in granulators Time, temperature, and airflow conditions in dryers and coaters Screen size, feed rate, and milling speed in mills Machine speed and compression force in tablet presses

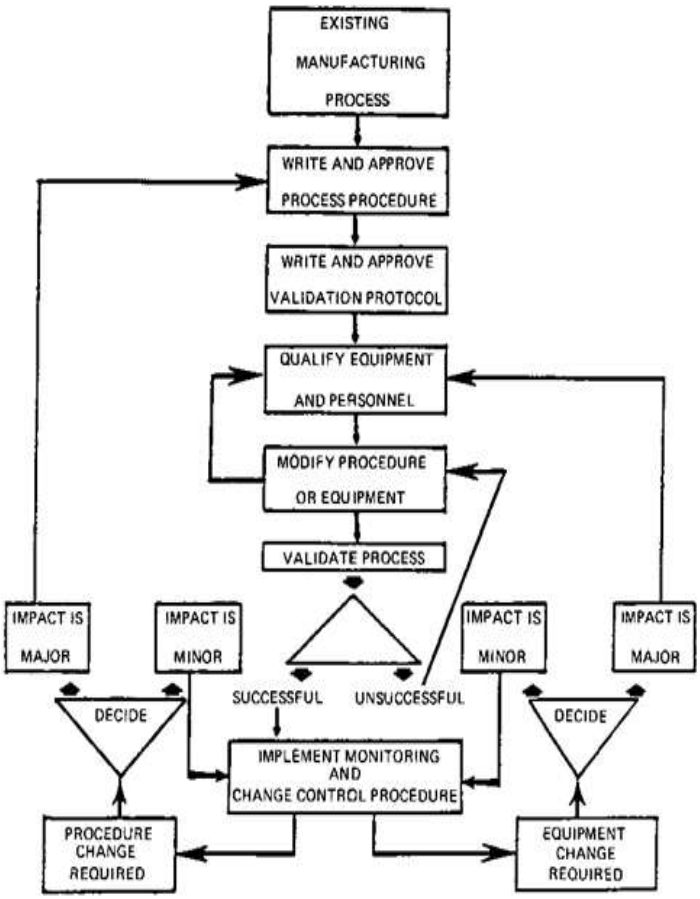

Figure 1: validation of existing manufacturing process.

ANNUAL PRODUCT REVIEW:

Annual Product Quality Review is an annual quality review of licensed medicinal product which is conducted with the objective of verifying the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished product to highlight any trends and to identify product and process improvements. The Annual Product Quality review (APQR) is an effective quality improvement tool to enhance the consistency of the process and the overall quality of the product. The PQR will capture a broader view of product data, capturing trends and will help determine the need for revalidation and changes, if any.

The Product Quality Review Report should contain at least the following details:

- A review of starting materials and product contact primary packaging materials used for the product, especially those from new sources.
- A review of critical in-process controls and finished product results
- A review of all batches that failed to meet established specification(s) and their investigation
- A review of all significant deviations or non-conformances, their related investigations, and the

Effectiveness of resultant corrective and preventive actions taken

- A review of all changes carried out to the processes or analytical methods
- A review of Marketing Authorization variations submitted/granted/refused, including those for third country (export only) dossiers.
- A review of the results of the stability monitoring programme and any adverse trends
- A review of quality-related product returns, complaints and recalls and the investigations performed at the time
- A review of adequacy of any other previous product process or equipment corrective actions
- For new marketing authorizations and variations to marketing authorizations, a review of post-marketing commitments

The qualification status of relevant critical equipment and utilities, e.g. HVAC, water, compressed gases, etc.[20, 21, 22, 23]

CONCLUSION:

Validation is the commonest word in the areas of drug development, manufacturing and specification of finished products. Tablet dosage form should be integral part of the comprehensive validation program me within the industry. The total program me should begin with the validation of API so that material will remain uniform from batch to batch. The scientific information which is obtained during the preformulation stage can form the basis for the validation program me Validation of a new or existing product involves the efforts of scientists at various stages of the product development life cycle. Scientific information obtained during the preformulation stage can form the basis for a well-designed and comprehensive validation program. 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.

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

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