Career Point International Journal of Research(CPIJR)
©2022 CPIJR | Volume 4 | Issue 1 | ISSN : 2583-1895

A Brief Review on Pilot Plant Scale - Up Technique for Solid Dosage Form

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Abstract *The pilot plant method is a way to create products on a smaller scale because it helps to identify variables that can affect large-scale production, such as equipment speed variations, procedures, personnel needs, space requirements, formula reviews, raw materials, and the creation of responsible and practical manufacturing processes. The solid dosage form pilot plant approach offers recommendations for mass industrial output. The last twenty years have seen incredible breakthroughs and improvements in pharmaceutical research, giving us the ability to produce new treatments quicker than ever before. Other pilot plants are built-in labs employing stock lab equipment. These numerous parameters, such as mixing, drying, granulation, and compression, among others, have an impact on the solid dosage form. The pharmaceutical business values pilot plants highly because they guard against batch failure and other processes.*

Key words- Pilot plant, Plant, solid dosage form, drying, blending.

I. INTRODUCTION-

1. PLANT - A site where the five elements—matter, method, machines, money, and a person—combine to produce a good.

2. Pilot Plant: This is a tiny industrial facility where issues were discovered and resolved.

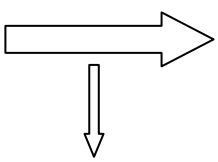
Or

When implementing a new process on a broad industrial scale, a tiny programme called a "pilot plant" is utilised to learn more about its ethics.

Or

It is the plant, connection between research laboratory to commercial scale production.

R & D Production



Pilot Plant

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Scale- up – It means Research to developed process.

Or

Increasing the batch size is known as scale – up.

1.2 Difference between Laboratory scale formulations(LSF) vs. Large scale production (LSP)

1. Batch size/volume/number of units
2. Container material
3. Equipment design
4. Processing arrangements
5. Processing speed and time
6. Operating controls e.g. Temperature and Humidity

1.3 Objectives-

1. To provide therapeutic dosage forms that are both physically and chemically stable.
2. Suitable processing equipment selection and validation. Selection, approval and validation of raw material specification.
3. Evaluation and validation of process as well as production control.
4. Evaluate and determine the product formula's capacity to withstand batch-scale conversion.
5. Find mistake in small scale and assure the quality in large scale.

1.4 This pilot can be used for –

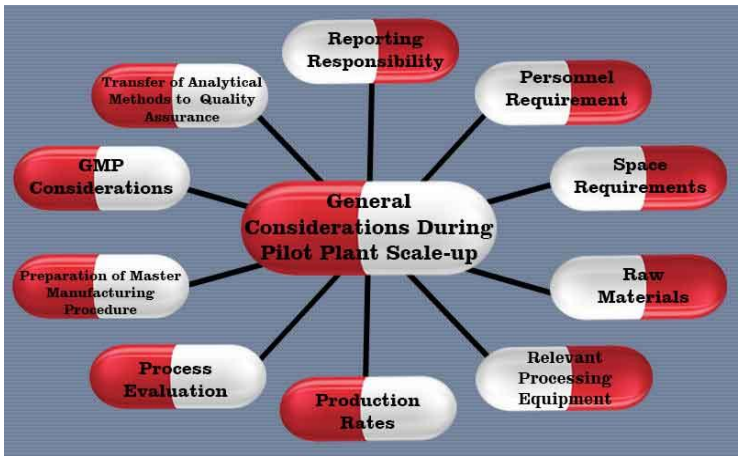
1. Analyze the outcomes of laboratory research, product development, and manufacturing procedures.

2. Creating small amounts of goods for shelf-based research, storage stability, restricted market testing, sensory, chemical, and microbiological analyses.

3. Identify marketable byproducts that need treatment before being released.

4. Provide records that may be used to help you decide whether to go through with the whole manufacturing process; if you make the right choice, you can design and construct a full-size plant from scratch or make modifications to an existing one.

2. GENERAL CONSIDERATION



2.1 REPORTING RESPONSIBLITIES –

1. Research &Development team with a diverse staff.

2. Even when the switch from development to production is complete, a facilitator of product development may still produce and provide assistance.

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2.2 PERSONAL REQUIREMENTS-

1. Scientists with experience in actual production environments as well as in pilot plant operations are preferred.

2. Because they must comprehend both the intent of the formulator and the attitude of the production staff.

3. The team must have some engineers on staff, and scaling up also requires an understanding of engineering theory.

2.2.1 SPACE REQUIREMENT

1. Management and data processing
2. Physical assessment region
3. Standard equipment floor space
4. A storage space

1. **Administration and record processing** –

a) Both scientists and technicians should have access to adequate offices and desk space.

b) The area need to be close to the workplace.

2. **Physical evaluation area-** Equipment used for physical testing should be given top place. such as a pH metre or digital balance.

3. **Standard equipment floor space** –

a) a) A separate pilot plant area has the machinery required to produce all different kinds of dosage forms.

b) Median length and complete length manufacturing device is vital in estimation the consequences scale-up of studies method and process.

c) Equipment used should be made movable where ever possible.

d) Space for cleansing of the instruments ought to be additionally provided.

4. **Storage area** –

a) This area should be provided with an approved and unauthorized area for active and auxiliary ingredients..

b) It should be provided for the warehouse of the raw material, end Manufacturing produced goods from the pilot plant and materials from the pilot scale-up batches.

c) Packaging space must also be provided.

2.3 RAW MATERIAL

1. The pilot plant's approval and validation of raw materials for active ingredients and excipients is one of its functions or responsibilities.

Why? ⇩

2. It is not necessarily which raw materials are used in pilot plant scale for further used in commercial scale.
3. Particle size is important for formulation of product like particle size, particle shape can lead to variations in bulk density, static charge, solubility rate, flow characteristics, etc.
4. Very small particles have developed due to the static charges and decrease the solubility of drugs.

2.4 RELEVANT PROCESSING EQUIPMENT:

1. The simplest, most cost-effective machinery that can produce goods that meet the requested standards is utilised.
2. The size of the machinery should be determined by the size of the manufacturing batches.
3. The procedure won't develop the scale-up if the equipment is extremely little.

2.5 PRODUCTION RATES:

The main aim of production rates is quality with speed.

1. Product is loss at some stage in the producing with inside the equipment.
2. The two batches are prepared for given time for cleaning the equipments between the batches.

2.6 PROCESSE EVALUATION

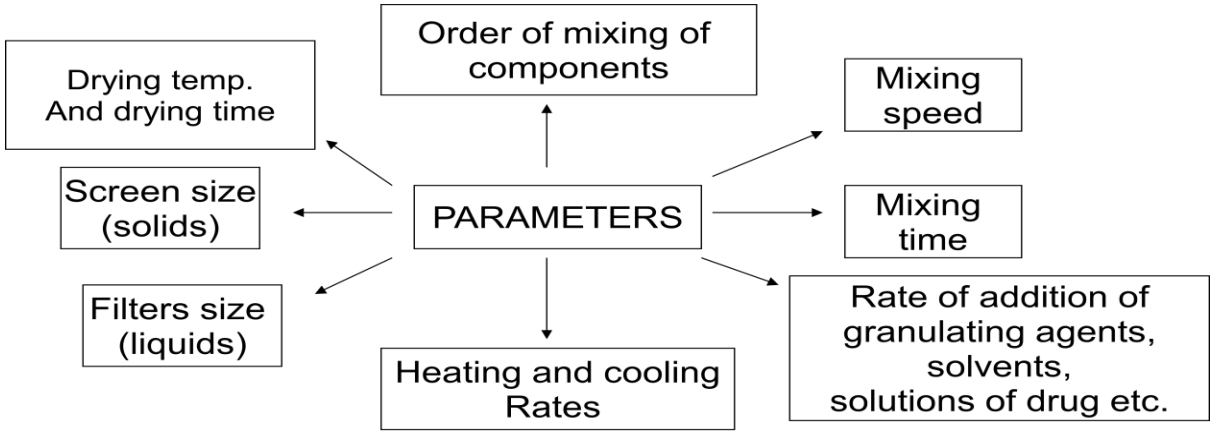


Figure 2.2 – Process evaluation parameters during pilot plant

2.7 MASTER MANUFACTURING PROCEDURE PREPARATION:

It consists of

1. The weight sheets for chemicals. How many chemicals are required in a batch should be stated, along with their quantity and possible use sequence.
2. The guidelines for sampling
3. Developing and finishing product requirements.
4. Manufacturing instructions should be written in a language that the operator can comprehend and are referred to as SOPs.

5. It has a variety of parameters for temperature, heating and cooling rates, addition rates, and blending periods and speeds.
6. Appropriate documentation has to be done.

2.8 PRODUCT UNIVORTY AND STABILITY: -

1. The physical and chemical stability of the products is the most crucial aspect of the pilot plant.
2. As a result, stability testing should be done on each pilot batch that represents the final formulation and production process.
3. Final formulations should also include stability studies.

2.9 GMP CONSIDERATIONS:

2.9 GMP CONSIDERATIONS,

It should be a component of scale-up efforts to:

1. Schedule preventive maintenance on a regular basis.
2. Conduct regular process reviews and revalidations
3. Appropriately documented quality working processes.
4. Employing knowledgeable, technically skilled employees
5. Enough resources are provided for staff training
6. A clear procedure for technology transfer
7. Approved cleaning techniques.
8. Proper equipment placement facilitates material flow and reduces cross-contamination.

2.10 ANALYTICAL METHODS ARE TRANSFERRED TO QUALITY ASSURANCE:

Method for transferring quality assurance was created by the analytical research section.

1. The following elements are included in the transfer procedure.
2. Go through the procedure to confirm that the right analytical tool is on hand.
3. Employees need to be trained to administer the exam.
4. The test's dependability should be examined.
5. Before transferring, the test technique should be evaluated.

2.10 TRANSFER OF ANALYTICAL METHODS TO QUALITY ASSURANCE:

Analytical research department developed method to transfer Quality assurance.

1. Transfer process includes the following aspects.
2. Review the process to make sure that the proper analytical instrument is available.
3. Personnel should be trained to perform the test.
4. Reliability of the test should be checked.
5. At last assay procedure should be reviewed before transfer.

3. PILOT PLANT SCALE – UP FOR SOLIDS (TABLETS):

1. In scaling up the manufacture of tablets and capsules from experimental laboratory batch sizes to intermediate and large scale production, each stage of the operation must be carefully considered.
2. Same manner, equal device however distinct overall performance while quantity of substances improved significantly, may also contain a prime manner alternate that make use of strategies and device that had been both unavailable or improper on a lab scale.
3. The following are the standard unit operations concerned in manufacturing of solid dosage forms.

Stages of Production of Tablets:

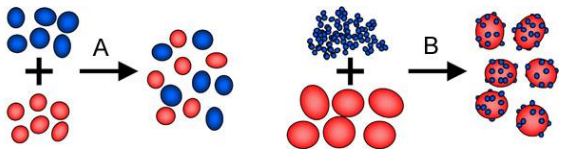
3.1 Material Handling -

1. The matters are actually poured via hand, but middle- or wide ranging operations, Pick - up of this materials frequently turn out to be required.
2. If many materials are used to change the process to stop contaminant.
3. It should be ensure correct quantity of substances to be reached in specific palace.
4. It should be selected for the system depends upon the property of substances.
5. There is minimal lack of material.
6. More superior techniques of dealing with substances which include vacuum loading systems, metering pumps, screw feed device.

3.2 Reduction of Particle Size– Various particle size measurements are used to reduce size reduction such as milling, mixing, homogenizing, etc. Particle size reduction is important for granulation process because various factor affecting of the formulation like dissolution, disintegration etc.

3.3 Dry Blending

1. Dry mixing method makes use of a binary cohesive powder combination which include unlike molecule sizes.
2. It is well known that finer particles adhere preferentially on the surface of the coarse particles. It is also called as bilateral blend.

3. 

4. It should be used for powder for encapsulation or to be granulated ensure good drug distribution.
5. Inadequate mixing at this level should bring about discrete part of the batch being both excessive or low in potency. It should be ensure that all the ingredients are free of aggregates.
6. Screening and/or milling of the ingredients usually makes the process well grounded and reproducible.
7. These equipments are used -V-blender, Double cone blender, Ribbon blender, Slant cone blender, Bin blender.

SCALE-UP CONSIDERATIONS

a) Time of blending.

b) **Blender loading**.

c) Size of blender.

3.4 GRANULATION:

Important instructions during the granulation

a) To expansion fine properties of the material,

b) To increase the bulk density of the powders,

c) To change the particle size distribution,

d) Invariable dispersion of active pharmaceutical ingredient.

3.4.1 Wet granulation- binder solution is added to wetting and binding of a powder blend. The wet mass is prepared, screened and dried to obtained granules.Equipment used in wet granulation process-

a) Sigma blade mixer

b) Planetary mixer

Factor affecting scale up process-

a) Granulating time

b) Granulating temperature

3.5 Drying: Drying is the major critical procedure after granulation however numerous element thinking about in drying operations are air flow, air temperature and intensity of the granulation.

Fluidized Bed Dryer:

• Optimum loads - rate of airflow.

• Inlet air temperature.

• Humidity.

Fig – 3.1 Fluidized bed dryer

3.6 Slugging: Slugging is a pre-compression technique for the formation of greater big tablets (slugs), typically of variable weight, because of bad waft of the drug powder. The ensuing slugs are ultimately damaged down into granules, which can be recompressed to attain the finishing tablets. This is completed on a tablet press designed for slugging, which operates at pressures of approximately 15 heaps, as compared with a regular pill press, which operates at stress of 4heaps or less. If too much quality powder is generated all through the milling operation, the substances need to be screened and finely recycled via the slugging operation.

3.7 Dry Compaction - In a process using counter-rotating rollers, the formula's components are continuously surpassed to generate a sheet of stable mass that is then

densified. The feed materials may be compressed into dense briquettes (almond or stick-shaped) if the rollers have grooved or etched surfaces, or into dense ribbon-like materials termed flakes (easy rolls), depending on the kind of rollers being used. Similar milling, sizing, lubrication, and compressing of the condensed materials results in the tablets. Curler compaction is necessary to increase the bulk density of materials with a very low density to a level that allows encapsulation or compression. In order to create a granulation with the necessary tableting or encapsulating qualities, pilot plant staff should assess if the final drug combination or the active entity may be handled in this way more effectively than by normal processing.

3.8 Compression: The final check of the tablet method and granulation may be compressed on a high-velocity tablet press. Compression parameters may be evaluated with the aid of using press velocity same to standard manufacturing velocity. Then detect the problems such as,

• Sticking to punch surface
• Tablet hardness
• Capping
• Weight variation

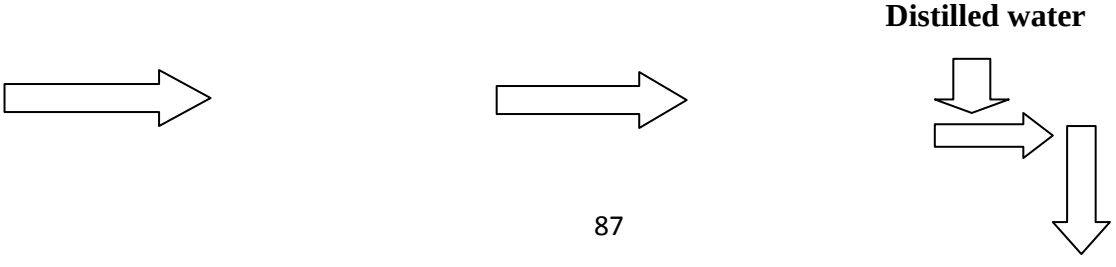
Granules must be delivered at adequate rate

3.9 Tablet Coating: Many changes in Sugar coating (Carried in conventional coating pans), due to new developments in coating technology (Conventional sugar coating pan changed to perforated pans or fluidized-bed coating columns), changes in safety and environmental regulations

Pan and fluidized coating:

• Optimum tablet burden.
• Working tablet bed temperature.
• Drying airflow velocity and temperature.

General Flow Chart –



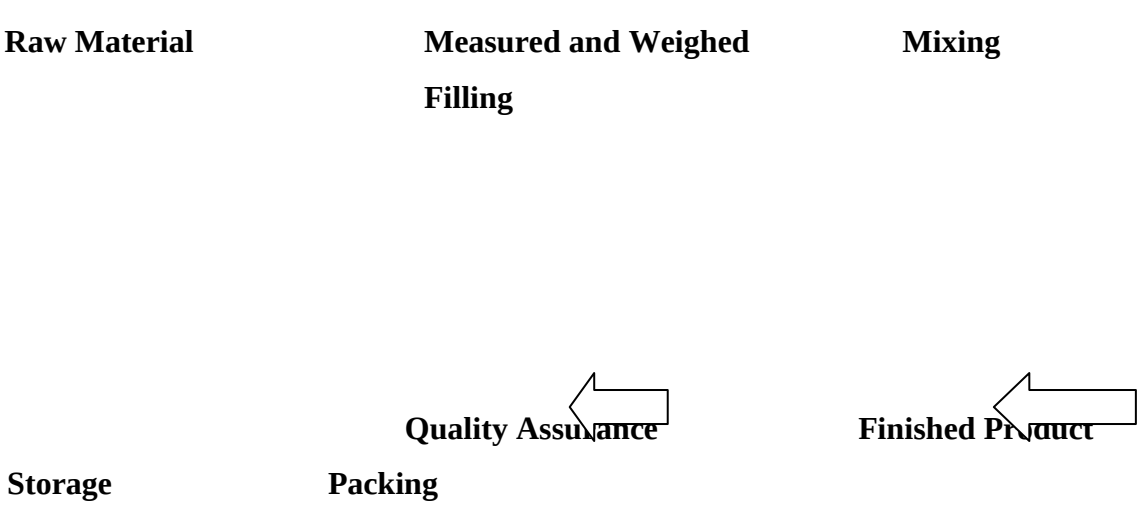


Fig – 3.2 Flow chart of solid dosage form

4.0 Encapsulation of hard gelatine capsule – Both tablet and capsules are produced from ingredients that may be either dry blended or wet granulation to produce dry powder or granules. These are various factor which affect good flow characteristics like bulk density, particle size distribution and compressibility. There are two types of equipments used in capsule filling operation, Zansai machine. and Hofliger kark machine.

Scale up considerations-

1. Bulk density
2. Powder flow
3. Lubricant distribution
4. Compressibility
5. Size and type of equipment used in blending.

CONCLUSION- Pilot plant scale up techniques is important for development for large scale production. The various variable like granulation feed rate, coating, rate of air flow, temperatures and humidity play an important role in pilot plant technique. With the help of pilot plant technique, we can increase our working efficiency. The significance of pilot plant scale up studies give range of relevant processing equipments and other infrastructure facility layout.

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