CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://zenodo.org/records/10674856

https://www.iajps.com/volumes/volume11-january-2024/60-issue-01-january-24/

Available online at: http://www.iajps.com *Review Article*

A REVIEW ON PILOT PLANT SCALE UP TECHNIQUES AND PLATFORMTECHNOLOGY

B.Mahammad Thowsif*[1], Dr. BV.Ramana[2]

[1]Student Dr. K.V.Subbareddy Institute of Pharmacy

[2]Principal and Professor, Department of Pharmaceutics, Dr .K.V. Subbareddy Institute of Pharmacy

Abstract:

In modern context, as per market demand there is surely an augmentation or decrease in production, this is called SUPAC. Distinct recommendations are made for those diverse sorts of SUPAC in by various regulating organizations for manufacture of items. Here SUPAC guidelines and post approval adjustments are provided for production in this review study. determined that SUPAC guideline line offer benefits as: This Review Focus on Reduced processing period for site transfers, saving operational overhead & maintenance expenditures. More quicker deployment of equipment and method improvements, better yield & Reduce failure investigations. More quicker adoption, increase in lot sizes and Manufacture of fewer un commercial stability batches and Reducing stability testing/costs.

Keywords : *Pilot plant techniques ,solid dosage form, tablet compression, SUPAC, Post approval changes, Lot size , Site Transfer, Stability.*

Corresponding author:

B.Mahammad Thowsif,

Student,

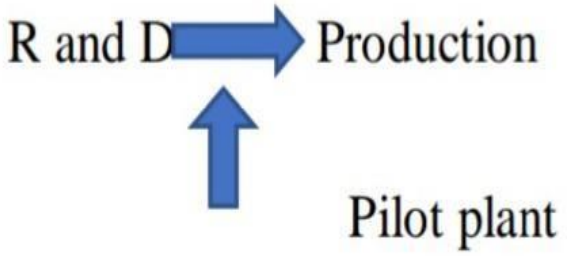
Dr. K.V.Subbareddy Institute of Pharmacy

QR code

Please cite this article in press B.Mahammad Thowsif et al., A Review On Pilot Plant Scale Up Techniques And PlatformTechnology, Indo Am. J. P. Sci, 2024; 11 (01).

INTRODUCTION:

Pilot plant: Defined as a part of the pharmaceutical industry where a lab scale formula is transformed into a viable product by the development of liable practical procedure for manufacture." R & D Production.



A pilot plant is a pre-commercial production system that employs new production technology and/or produces small volumes of new technology-based products, mainly for the purpose of learning about the new technology. The knowledge obtained is then used for design of full-scale production systems and commercial products, as well as for identification of further research objectives and support of investment decisions. Other (non-technical) purposes include gaining public support for new technologies and questioning government regulations. Pilot plant studies must include a close examination of formula to determine its ability to withstand batch scale and process modifications; it must include a review of range of relevant processing equipment also availability of raw materials meeting the specification of product and during the scale up efforts in the pilot plant production and process control are evaluated, validated and finalized.[1]

A pilot plant allows investigation of a product and process on an intermediate scale before largely are committed to full scale production. Pilot plant scale up techniques consist manufacture of experimental formulation on high speed production instrumentation, with an efficient manner. It is a requirement for equipment analysis and establishes documented evidence with high degree of assurance that produce a product which meets predetermined specifications and quality attributes. Pilot plant is a pharmaceutical plant, which is used to obtain experimental data on a new process, to produce a new dosage form. The rapid development of modern economy and technology the energy crisis, air pollution from the combustion of fossil fuels, volcanoes and wildfires. The solid and liquid particles suspended in air (aerosols) and water pollution from waste water because of Marine Dumping, Oil leaks and Spills and Global Warming have become increasingly serious. So, the current study of pilot plant was designed to obtain the pharmaceutical using of water efficiency using water conservation strategy and at source effluent treatment for reusable in manufacturing unit and save the maximum water, because water is the main source of pilot plant.[2]

Why conduct Pilot Plant Studies?

- A pilot plant allows investigation of a product and process on an intermediate scale before largeare committed to full-scale production.
- It is usually not possible to predict the effects of a many-fold increase in scale.
- It is not possible to design a large complex food processing plant from laboratory data alone with any degree of success.

The Pilot scale studies must comprise;

- Current Good Manufacturing Practices (cGMP) environment,
- Highly trained and competent staffs,
- Equipment support,
- Facility of thorough and careful study of the formula.

The criteria that need to be determine for effective product scale up include;

- The prerequisites,
- Training,
- The reporting connections,
- Responsibility of staff.

The pilot plant, supply and processing methods must be examined, verified and completed throughout the scale up. and plant plays a significant part in the technology assessment, scale up but also transfer operations of new goods.

Pilot plant scale up processes includes:

The primary actions take place during scaling up at the initial stages are;

- Technical factors of process development,
- Technical considerations of scaling up,
- Organization responsibility,
- Determination of responsibilities of technology transfer team,
- Technology transfer documents,
- FDA pre-approval inspection preparation.

Major technical aspects:

- The scaling up an pilot plant contains important technical factors that include;
- In early development,
- Identification of important components,
- Control of essential components,
- Identification of formulation variables,

- Control of formulation variables,
- Modeling a pilot plant equipment to production regions equipment.
- Identification of important process parameters.
- Identification of operating ranges for the pilot plant equipment
- Collection of data on Product and process.[3]

Objectives of Pilot plant scale up:

- Avoidance of the challenges linked with the scale-up.
- Production and processes controls guidelines preparation.
- To identify the important elements of the process,
- Preparation and supply of Master Manufacture Formula for manufacturing.
- Evaluation and Validation of process and equipment.
- Examination of a formula for determine the batch stability.

Significance of Pilot Plant:

- Standardization of formulae.
- Review of range of relevant processing equipment's.
- Optimization and control of production rate.
- Information on infrastructure of equipment's during the scale up batches physical space required.
- Identification of critical features to maintain quality of a product.
- Appropriate records and reports to support GMP.[4]

General consideration:

1. Reporting responsibility.
2. Personnel requirement.
3. Space requirement.
4. Review of the formula.
5. Raw material.
6. Equipment.
7. Production rate.
8. Process evaluation.
9. Master manufacturing process.
10. Product stability and uniformity.

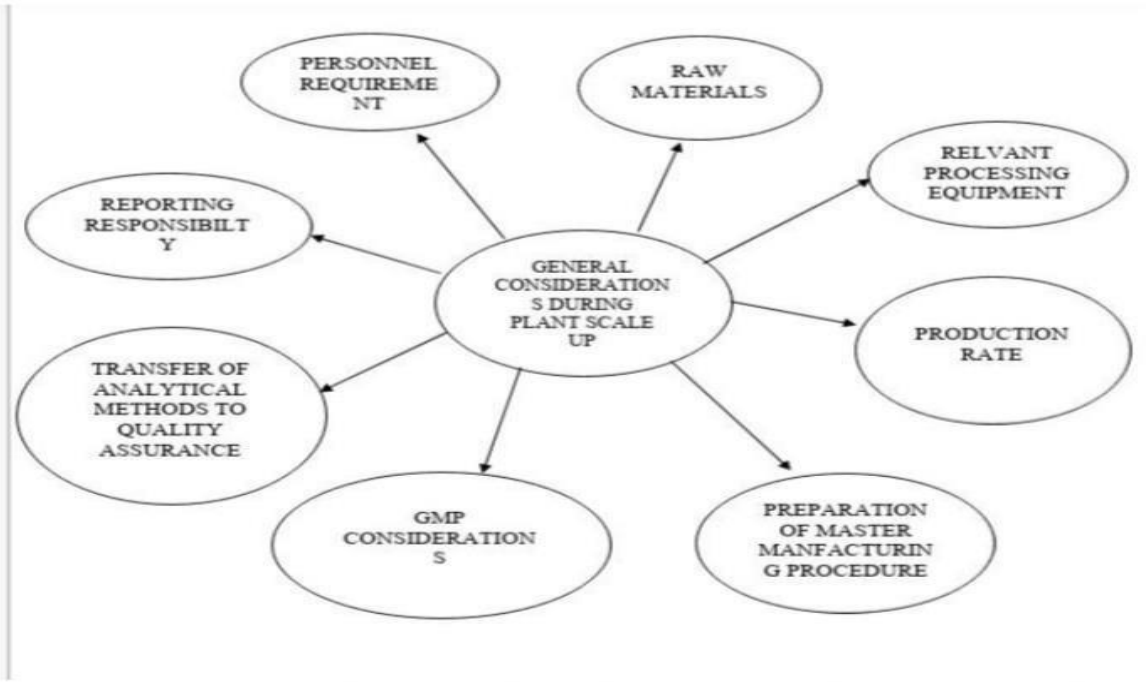


Figure 1: General consideration during pilot plant scale

Reporting responsibility:

- R and D group with separate staffing.
- The formulator who developed the product can take into the product and can provide support even after transition into production has been complete.

Personnel requirements:

- In pilot plant techniques, scientists will be well experience and actual production area are the most preferable -As they have to know the goal of the formulator as well as understand the view of the production personnel.

Space requirements:

A. Administration and information process: Sufficient office and desk space should be provided for both scientist and technician. The space should be close to the working area.

B. Physical testing area: This area should issue permanent bench top for regularly used physical testing equipment.

C. Standard equipment floor space: Equipment used should be made movable where ever possible so that after use it can be stored in the small store room. Space for cleaning of equipment should be also provided.

D. Storage area: It should have two areas;

> Approved area

> Unapproved area

Different areas should supply the storage of in-process material finished bulk products from the pilot plant and materials from the experimental scale up batches made in the production. storage area for the packaging material should also be provided.

Review of the formula:

A minute analysis of each feature of formulation is main.

- The cause of each ingredient and it "s present to the final product manufactured on the small-scale laboratory equipment should be understood.
- Then the result of scale up using equipment that may subject the product to stresses of different types and degrees can more readily be predicted.

Raw materials:

One authority of the pilot plant is the approval and validation of the active ingredient and excipients raw materials. Raw materials used in the small-scale production can't require to the large scale production.

Equipment:

Equipment should be inexpensive, simplest and systematic equipment are used.

- The size of the equipment should be such that the experiment trials run should be applicable to production sized batches.
- If the equipment is too small the process developed will not scale up- if equipment is too big then the wastage of the expensive active Ingredients.[5]

Production rate:

The quick and future market trends are considered while determining The production rate.

Process evaluation:

Process evaluation Parameters:

i. Order of mixing of components

ii. Mixing speed

iii. Mixing time

iv. Rate of addition of granulating agents, solvents, solutions of the drug etc.

v. Heating and cooling rates.

vi. Screen size

vii. Filters size

viii. Drying temperature and drying time

Master manufacturing procedure:

1. Weight sheet sampling directions.

2. Processing and procedure.

3. Manufacturing.

Main aspects

The weight sheet should clearly identify the chemical required in a batch.

The process direction should be exact and clear.

Manufacturing procedure should be written by the real operator.

Product stability and uniformity:

The goal of pilot plan is the physical and chemical stability of the product. Hence, pilot batch constitute the final formulation and manufacturing procedure should be studied for stability.[6]

GMP consideration:

Include,

>Equipment qualification.

>Process validation.

>Regularly process review and revalidation.

>Relevant written standard operating procedures.

>The use of competent technically qualified personnel.

>As well-defined technology transfer system.

>Validated cleaning procedures.

>Equipment qualification.

ADVANTAGES:

- Members of the production and quality control divisions can quickly observe scale of runs.

- Supplies of excipients, drugs, cleared by the quality control division, can be drawn from the more spacious areas provided to the production division.
- Explosion to engineering department personnel is provided for equipment installation, maintenance and repair.

DISADVANTAGES:

- The frequency of direct inter-connection of the formulator with the production personnel in the manufacturing area will be decrease.
- Some difficulty in manufacturing will be directed regarding its sown pilot plant procedures.

PILOT PLANT-PREDETERMINE FOR IMPROVEMENT. [7]

- Pilot vegetation are at the point of an exceptional evolution read about the 10 factors that will affect the design, construction and operation of those next-technology gadgets.
- I even have visible many adjustments in pilot plant over the path of my carrier, but I are expecting that we are at the verge of an extraordinary evolution of these gadgets.

My crystal ball sees 10 key factor influencing next-generation pilot plant:

1. Outsourcing,
2. Automation,
3. Fugitive emissions,
4. Multiple trains,
5. Online analytical capabilities,
6. Safety and control system interaction,
7. Wireless technology,
8. Instrument availability,
9. Instrument multi-functionality,
10. Unit size.

PILOT PLANT SCALE UP CONSIDERATIONS FOR SOLIDS: [8]

- ✓ The primary duty of the pilot plant group of workers is to make sure that the newly formulated tablets advanced by way of product development personnel will prove to be successfully, economically and continually reproducible on a manufacturing scale.
- ✓ The design and creation of the pharmaceutical pilot plant for tablet development should incorporate functions important to facilitate upkeep and cleanliness.
- ✓ If feasible, it must be positioned on the ground floor to expedite the transport and shipment of substance. Each stage taken into consideration cautiously from experimental lab batch length to intermediate and large-scale manufacturing. Some process, identical device however one of a kind performance while quantity of material increased drastically.
- ✓ May content major procedure trade that utilises strategies and device that were either unavailable or improper on lab scale.

LAYOUT OF PILOT PLANT:

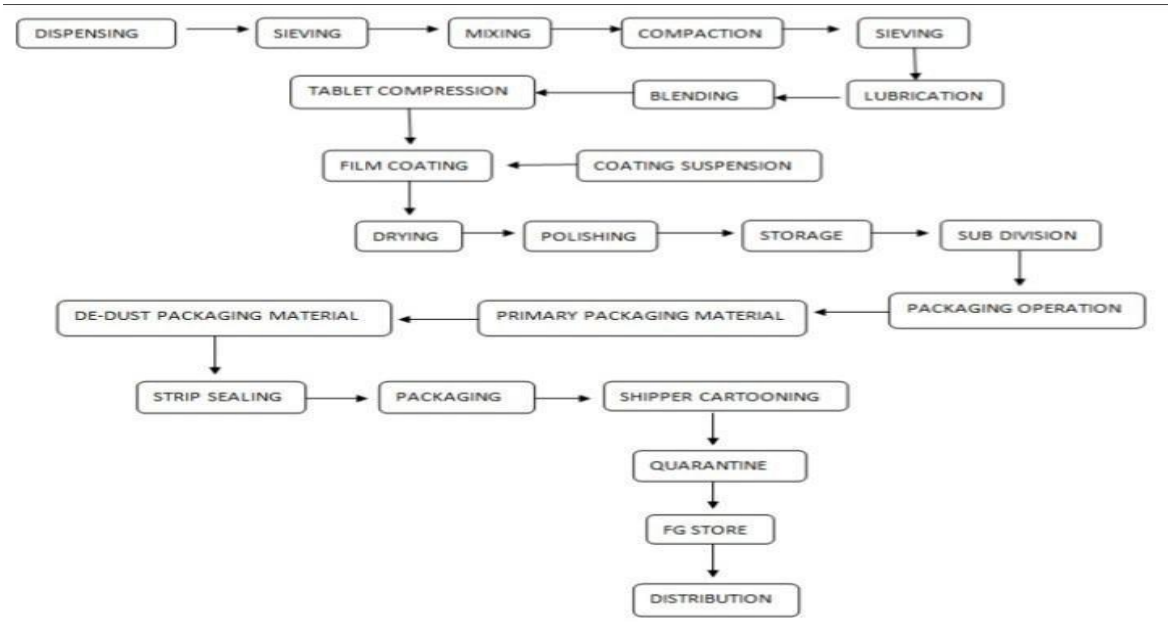


Figure 2: Preparation of solid dosage forms

STAGES OF PRODUCTION OF TABLETS:

1. Material handling system
2. Dry blending
3. Granulation
4. Drying
5. Reduction of practical size
6. Blending
7. Slugging (dry granulation)
8. Dry compaction
9. Compression

Material Handling:

The handling of ingredients is significantly different and important to manage cautiously in largescale and medium-sized manufacturing first from laboratory scale the features of materials including density, size, form as static charge must have been taken into consideration when implementing the processing stages such;

- Lifting and tilting of drums,
- Vacuum loading system,
- Screw feeding systems,
- Metering pump systems.

Each material handling system should deliver the precise quantity of the component to the destination. The cross contamination should be avoided whenever a system involves exchange of material for more than a product phase. This is done by usage of proven cleaning technique for the equipment.

Chemical Weighing:

The improper substances and amounts can result in cross contamination or products containing products during chemical weighing.

A central weighing department ought to have for all the processing regions due to following benefits;

- Centralization of duty,
- Avoidance of duplicate weighing facility,
- Lower labour cost.

A chemical weighing department should be constructed to offer supervision, checkers, lightening, dust collection, sufficient sanitation, correct weighing equipment, provision for sink and drain board, cabinets, vacuum supply system, printing scale facility with meters for liquids. During weighing of dye but very powerful medications, an separate room should be supplied.[10]

Tablet mixing and Granulation:

Blending and Granulation:

Powders to be utilized as encapsulated or for being granulated must be carefully mixed to guarantee optimal medication distribution. Improper blending at this point might result in discrete areas of the sample either be high or low on potency to prevent drug content fluctuation. Steps are also made to guarantee that all the components are free of. The lumps and agglomerates may be eliminated by conducting screening or milling of the materials should be done to prevent flow difficulties, quasi compression and encapsulation processes, to promote content homogeneity of the product. In blending, segregation and mixing process takes place which relies on particle size, shape, hardness and density.

Dry Blending and Direct Compression:

- Different blenders used in blending include V-blender, double cone blender, Ribbon blender, Slant cone blender, Bin blender,
- Different blenders used in blending include V-blender, double cone blender, Ribbon blender, Slant cone blender, Bin blender,
- The elements influencing the optimization of mixing operation with direct compression materialsare;
- The sequence of adding ingredients to the blender.
- The mixing speed - Planetary type mixer, Tumbling Mixer, Cone Type Mixer.
- The mixing time –It impacts compressibility of Finished Material.
- The use of additional dispersion equipment with the mixer - Use chopper cell in Twin Shell Mixer.
- The mixing action - Controlled either by Mechanics of the Mixer.
- The blender loads Maximum operating volume and usual functioning range.[11]

Slugging (Dry Granulation):

- The dry powder can really be compacted directly owing to inadequate flow and compression characteristics.
- The slugging is done by utilizing the Tablet Press of 15 tons.
- During compression, slugs were broken down by Hammer Mill having acceptable particle size distribution.
- The granulation by dry compaction may also be performed by moving powders between tworoller which exert pressure of 10 Tones per linear inch.

Wet Granulation:

- The most prevalent grounds claimed to warrant granulating are;
- To give excellent flow characteristics to the material,
- To improve overall apparent density of the particles,
- To modify a particle size distribution,
- Uniform distribution of active substances.

Traditionally, wet granulation has been carried out utilizing Sigma blade mixer and Heavy-duty planetary mixer. Wet granulation may also be made utilizing tumble blenders equipped with highspeed chopper blades. More recently, the usage of multifunctional "processors" that are capable of executing all activities necessary to create a completed granulation, such as dry blending, wet granulation, drying, sizing or lubrication inside a continuous process in a single equipment.

- The elements that influence the Fluidized Bed Granulator include;
- Process Inlet Air Temperature,
- Atomization Air Pressure,
- Air Volume,
- Liquid Spray Rate,
- Nozzle Position and Number of Spray Heads,
- Product and Exhaust Air Temperature.[12]

Drying:

The most popular traditional technique of drying a granulation remains the rotating hot air oven, that is heated whether by steam or electricity. The main parameters that consider a part of scaleup of such an oven drying process include airflow, air temperature, or the depth of granulation on the trays. If the agglomeration bed is far too wide and too dense, the dryer would be ineffective, but if soluble dyes also included, migration of the color to a surface of both the granules. Drying periods at specific temperatures and airflow levels must be defined for every product, and for each individual oven load. Fluidized bed dryers are just an appropriate option to a circulating hot air oven. The main criteria examined as part of scaling up fluidized bed dryer are optimal loads, rate of airflow, input air temperature and humidity. The specifications to be regarded for drying process through using Tray Dryer for scale up are Air flow, Air temperature, Depth of a granulation just on trays, Monitoring of the drying process through the use of temperature and moisture probes but also Drying times at stipulated temperatures and air flow rates for every product. The Parameters to be addressed for the drying process by utilizing a Fluid Bed Dryer for scale up are Optimum load, Air Flow Rate, Inlet Air Temperature and Humidity of the entering air.

Reduction of Particle size:

Compression variables that may be impacted by the particle size distribution include flow ability, compressibility, uniformity of tablet weight, content uniformity, tablet hardness, and tablet colour uniformity. First stage in this method is to figure out the size distribution of granulation to use a succession of "stacked" sieves with decreasing mesh apertures. Particle size reduction of the dry granulation of production size batches may be carried out by running the all material through with an oscillating granulator, a hammer mill, a mechanical sieving device, or in some situations, a screening device. As part of the scale-up of a milling or sieving process, the lubricants and glidants, which in the laboratory are normally applied directly to the final blend, are usually added to the dried granulation during the sizing procedure. This is done because some of these additives, notably magnesium stearte, tend to agglomerate when introduced in high amounts to the granulation in a blender.

Facilities:

- To minimise cross contamination in scale up and to assist the cleaning of equipment properly, following facilities must be supplied that are;
- Presence of separate room with availability of extra space,
- Must have granulation as unit operation,
- Must have washing and drainage facilities,
- Must have cold, hot water and steam supply system,
- Platform should be of stainless steel or non-dust material system,
- Air condition system is encouraged but if lacking, window must be screened,
- Use of a multipurpose processing system.[13]

Granulation Handling and Feed System:

The handling of the final granulation in the compressed area is either by Hand scooping for tiny level or through sophisticated automated handling system using vacuum or mechanical system for big size. The features the material like size, size distribution that flow property impacts the tablet attributes like medication standard consistency, tablet weight, thickness and hardness. For effective cleaning, advanced material handling systems such long lengths transfer tubes, valves, vacum but also pneumatic pumps should be employed.

Tablet Compression:

- The tablet press binding precedent duties as during compression are;
- Filling of an empty die cavity with granulation.
- Pre-compression of granulation.

Compression of granules.

- Ejection of the tablet from the die cavity and take-off of the crushed tablet.
- The lengthy trial runs at press speeds is often chosen to find out the probable compression difficulties such as clinging towards the punch

surface, tablet hardness, capping, and weight fluctuation discovered.

- High-speed tablet compression relies on the capacity of the press to communicate with granulation.[14]

During choice of high speed press parameters that should be examined are;

- Granulation feed rate.
- Delivery mechanism should not modify the overall particle size distribution.
- System should not create separation of fine and coarse particles.
- It should produce static charges.
- The die feed system is able to feed the die cavities sufficiently in the brief length of time whilethe die is traveling beneath the feed frame.
- The smaller the tablet, the more difficult it is to obtain a consistent high press rate.
- For high-speed machines, triggered die feed systems with such a range of feed paddles withvariable speed capacities, are essential.
- Compression of the granulation normally happens as a single event when the heads of thepunches travel over the lower and beneath the top pressure rollers.
- This allows the punches to penetrate the die to a predetermined depth, compacting thegranulation to the thickness of the gap specified between the punches.
- The rapidity and dwell time between when the press event happens is regulated by the speed of the press is turning and by size of compression rollers.
- Larger the compressions roller, the much more progressively compression force applied and released.
- Slowing down the press speed or utilizing bigger compression rollers will typically minimizecapping in a formulation.
- The last process is the ejection of compressed tablets from die cavity.
- During compression, the granulation is compressed to form tablet, linkages within compressible material must be created which results in sticking.
- High amounts of lubricant or over mixing may result in a soft tablet, reduction in wet ability of the powder and an extension of the dissolving period.
- Binding to die walls may also be addressed by making the die to be 0.001 to 0.005 inch broader at the top section than at the middle in order to release pressure during ejection.

Tablet Coating: *[15]*

Many improvements in Sugar coating (Carried in conventional coating pans), owing to new advancements in bringing greater (Conventional sugar-coating pan converted to perforated pans and fluidized-bed coating columns), changes in safety and requirements. The development of new polymers have led in a move between aqueous coating material to aqueous film coating. The tablets must be adequately hard to survive the tumble to which they are exposed whether in the coating pan or the coating column. Some tablet core materials are inherently hydrophobic, and in these circumstances, filmcoating with an aqueous system may need particular formulation of the tablet core and/or the coating solution. A film coating solution may have been discovered to perform well with a specific tablet in a small lab coating pan but may be absolutely inappropriate on a production scale. To promote the efficient coating the tablet should not be constructed as flat surface or sharp edges.

Encapsulation of Hard Gelatin Capsules:

The High-Speed machine is used to create the capsule by employing the processed powder blend with following particle properties such particle size distribution, bulk density, compressibility to enhance excellent flow property. This promotes the creation of compacts of the proper size and of sufficient cohesion to be filled into capsule shells.

Filling of capsule is done by two filling systems;

- Zanasi or Martelli create slugs in a dosator.
- Hof liger-Karg Machine

Weight fluctuation in capsules may happen owing to inadequate flow characteristics, incorrect lubrication and plug adhering to the dosator plunger surface. Overlay lubrication may produce issues in weight fluctuation, disintegration, dissolution and Bioavailability. The properties of granulation and the completed products are highly impacted by the kind and size of equipment used for mixing, granulating, drying, sizing and lubricating.

For better encapsulation, required of controlled environmental conditions that includes Controlled humidity (RH 45 to 55 %) system in processing and encapsulation (RH 35 to 65 %) room and adequate temperature condition of 15 to 25 °C.

PILOT PLANT SCALE UP CONSIDERATIONS FOR LIQUID ORALS: [16]

The physical structure of a pharmacological product that may be included displays Newtonian or Pseudo plastic flow behavior.

The oral liquid dosage forms classify as Monophasic and Biphasic. The Monophasic is of simple solutions. The Biphasic is suspension and emulsion. Liquid preparation for oral use is usually Solutions, Emulsions or Suspensions containing one or more drug forms in suitable vehicle. The preparation for oral use are either supplied in finished form or with excipients or it may also prepare just before use by dissolving powder in vehicle stated on label.

The liquid preparation for oral use consists of antimicrobial preservative, antioxidants, dispensing agent, suspending agent, thickening agent, emulsifying agent, buffering wetting, solubilizing, stabilizing, flavoring and sweetening with suitable coloring agent. They may be single dosage or multiple dosage preparation. The devices used are spoon or cup, oral syringe, dropper, etc. The liquid of should be uniformity of mass, uniformity of mass of doses delivered by measuring devices, container with proper labeling.

- It conforms to its container at room temperature.
- Liquid dosage forms may be distributed systems or solutions.
- In scattered systems there are two or more phases, where one phase is disseminated in another.
- A solution refers to two or more substances combined homogeneously.

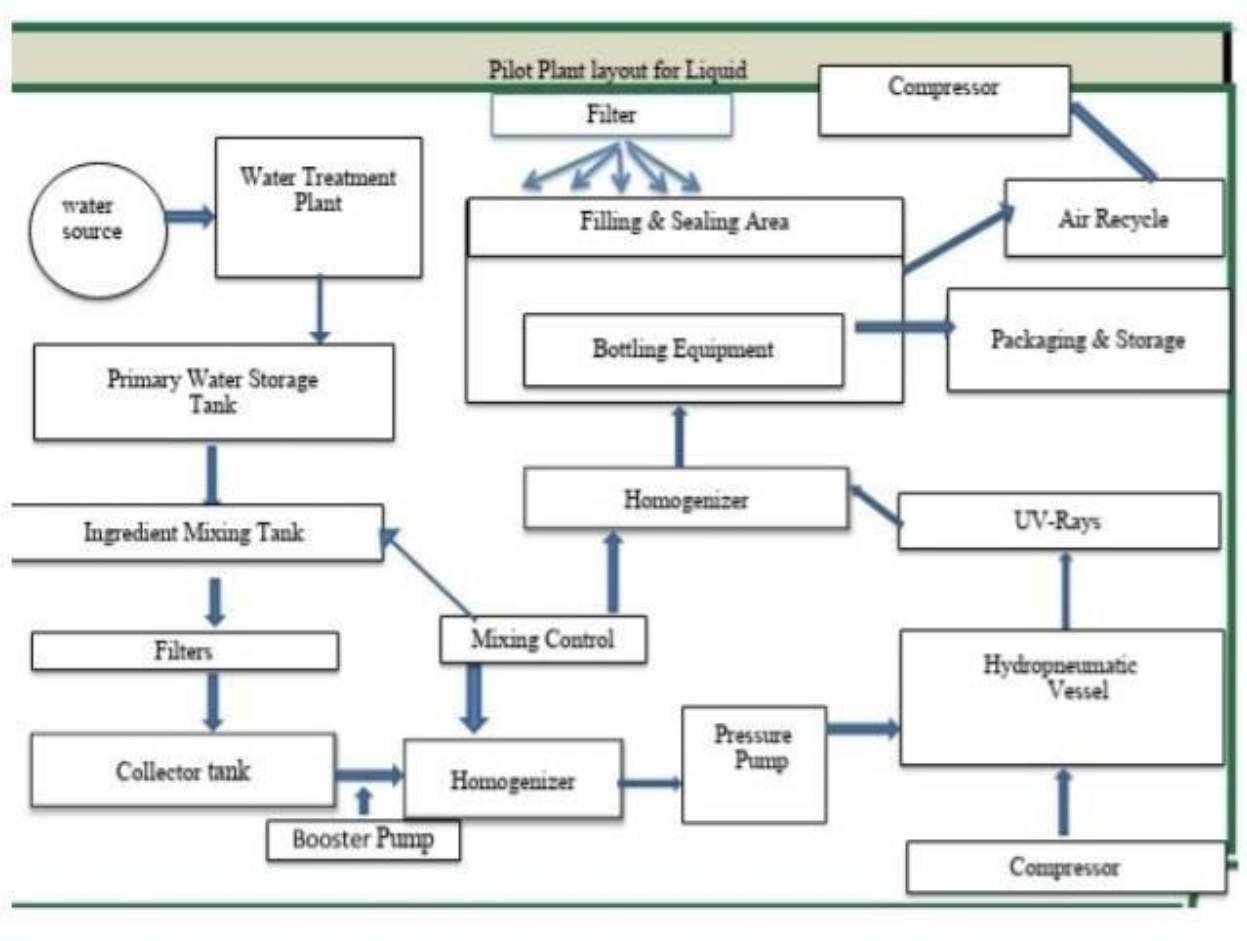


Figure 3: Pilot plant layout for liquid

Steps of liquid manufacturing process:

- Planning of material needs.
- Liquid preparation.
- Filling and Packing.
- Quality assurance.
- Critical features of liquid manufacturing.
- Physical Plant.
- Heating, ventilation, and air regulating system.

The impact of extended processing durations at suboptimal temperatures should be evaluated in terms of repercussions on the physical or chemical stability of components as well as product.[17]

Solution:

The parameters to be considered are for scaling up of solutions are;

- Impeller diameter.
- Tank size (diameter) (diameter).
- Number of impellers.
- Impeller type.
- Mixing capabilities of impeller.
- Rotational speed of the impeller.
- Height of the filled capacity of the tank.
- Number of baffles.
- Transfer system.
- Clearance between Impeller Blades and wall of the mixing tank.

Filtration device (should remove desirable elements but should not eliminate active or adjuvant substances) (should remove desired materials but should not remove active or adjuvant ingredients). Passivation of Stainless Steel (Pre-reacting the SS with acetic acid or nitric acid solution to eliminate. the surface alkalinity of the Stainless Steel) (Pre-reacting the SS with acetic acid or nitric acid solution to remove. the surface alkalinity of the Stainless Steel).

Suspension: [18]

The criteria to be considered are for scaling up of suspension are ;

- Versator (To prevent air entrapment) (To avoid air entrapment).
- Wetting of suspending agent.
- Addition and dispersion of suspending agents.
- Selection of the equipment according to batch size.
- Time and temperature necessary for hydration of the suspending agent.
- Mixing speeds (High speed should not be utilised since it leads to air entrapment) (High speed should not be used as it leads to air entrapment).
- Mesh size (Must be able to remove the foreign particles and sieve determined depending on manufacturing batch size testing) (Must be able to remove the foreign particulates and sieve selected based on production batch size trials).

Emulsion:

The parameters to be examined are for scale up of emulsion are ;

- Homogenizing equipment.
- Temperature.
- Mixing equipment.
- Phase densities.
- In-process or final product filters.
- Phase volumes.
- Screens, pumps and filling equipment.
- Phase viscosities.

The layout of pilot plant of liquids consists of the equipment such as tanker, mixer, homogenizer, filtrationassembly. [19]

TANKER: It should be according to batch size preparation of the drug. It should not produce any additive to the product. It is made up of stainless steel of different grades and lined with Teflon and glass if high viscosity liquid then high electrical stirrers are used.

MIXER: Here simple mixing is done to increase mixing of liquid. There should be proper adequate clean up procedure. At high viscosity air entrapment occur it can be minimized by reduce agitator speed by caring out mixing process in closed tank under vacuum homogenizer. There should be a variety of equipment should be used for better results. Filtration and Clarification should require careful evaluation to exhibit high purity of drug as their laboratory counterparts. It should be checked periodically to know the purity of substance.

The advantages of liquid dosage form are immediate available for absorption in the body, easy route of administration.

PILOT PLANT SCALE UP CONSIDERATIONS FOR SEMI SOLIDS: [20]

Semi solid dosage forms are the topical dosage forms that are intended for the therapeutic, protective, or cosmetic functions. Few examples are Ointments, paste, creams, plasters, suppositories, gels and rigid foams.

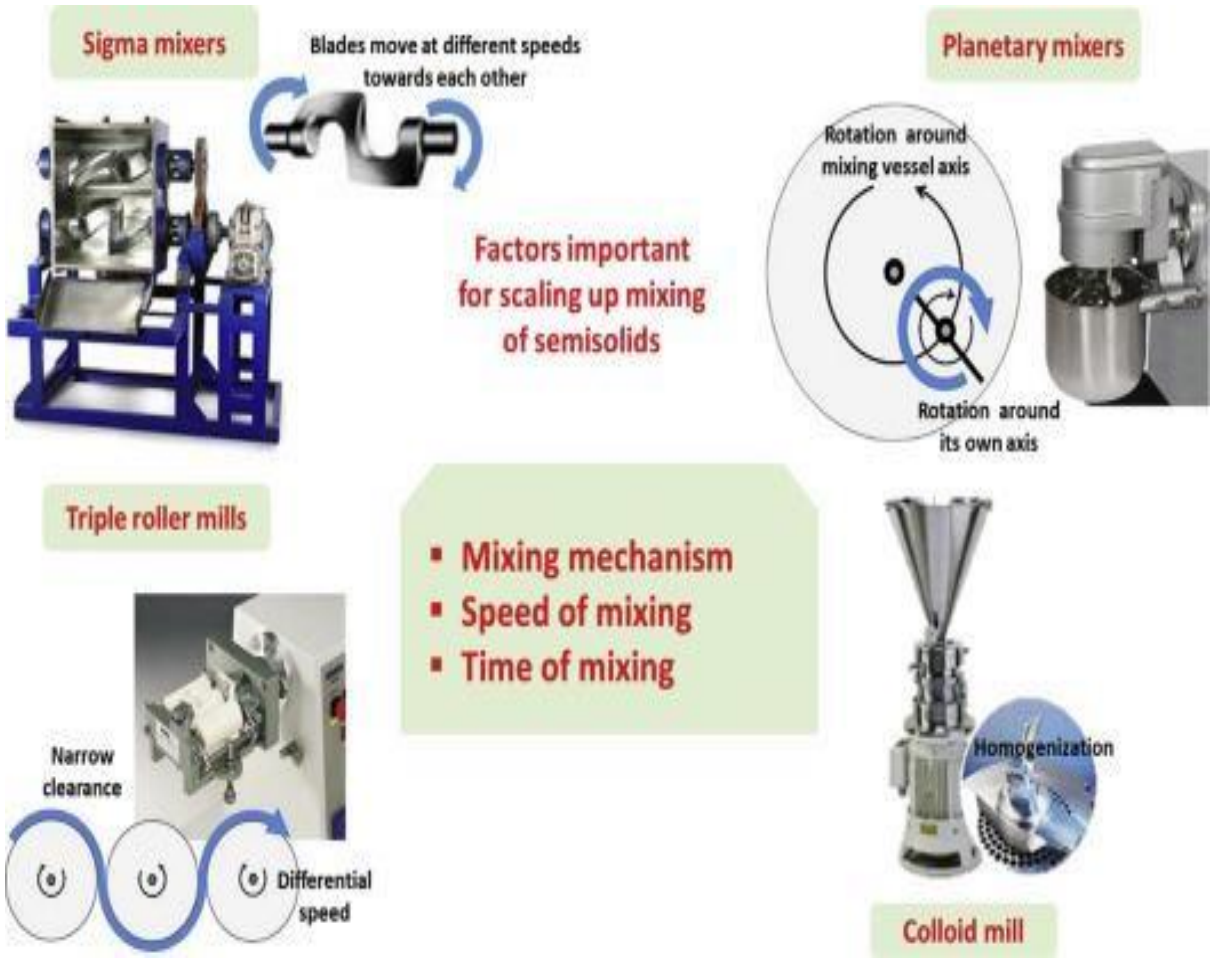
Semisolids are the complex formulations which are having complex structural elements. They are of two phases-oil in water one is a continuous phase also known as external phase and the other is a dispersed

phase also known as internal phase.

Semi solid dosage form products are mostly administered topically or by the insertion method into an orifice of the body.

The following parameters have to be addressed during the scale up of semisolid goods;

- Mixing speed.
- Mixing apparatus,
- Motors
- Heating and cooling procedure.
- Component homogenization.
- Product transfer.
- Addition of active ingredients.
- Working temperature range.
- Shear during handling and transfer from manufacturing to holding tank to filling lines.
- Transfer pumps.
- Following criteria must be consider for selecting the size and kind of pump,
- Product compatibility with the pump surface.
- Product viscosity.[21]



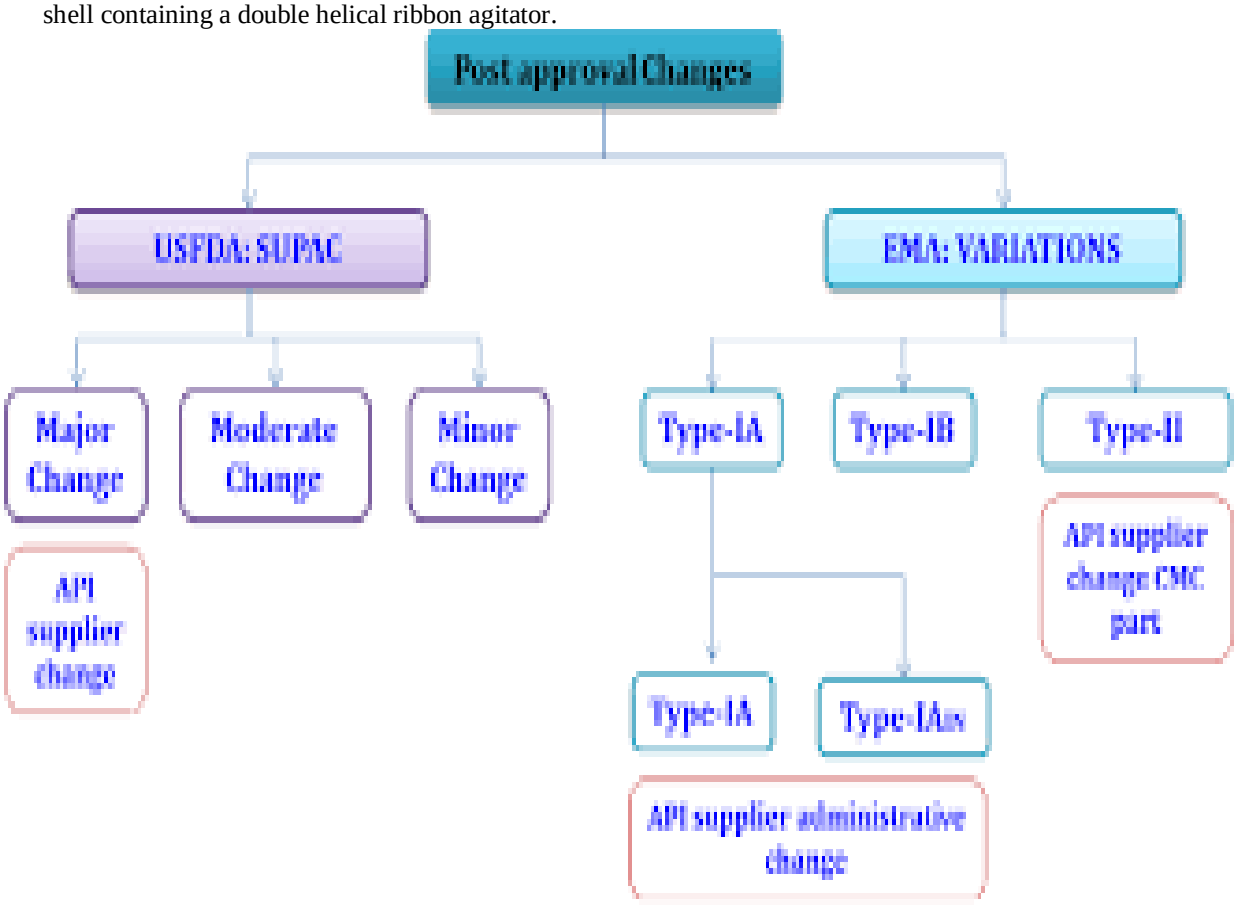
The Equipment's used in semi-solid dosage form are:

1. Agitator mixer: This agitator is a machine used in a tank for mixing numerous process media together. It works through mechanical mean by rotating an impeller to impart energy to the media which interact and mix the ingredients. An agitator consists of shaft, impellers, motor and gear box.
2. Roller mill: It is a form of compression mill which use single, double or triple cylindrical wheels arranged horizontally. It is rotated through there long axis in opposite pairs or against flat plates which is used to crush or grind several materials. One roller is run by motor and other by friction. The stress and attrition are employed in the procedure of milling which are rotate at distinct speeds.
3. Ribbon agitator: The mechanism involved is shear that is transfer by moving blades in a fixed shell. The functions are paste mixers, vacuum dryer, granulators. The mixing is completed within 15 mins or less. It consists of U-shaped shell containing a double helical ribbon agitator.
4. Colloidal mill: It is used to reduce the particle size of solid forms of the pharmaceutical ingredients which are present in different liquid or solid forms. It works on the principal of rotor-stator. Generally it is used in production of sterile products.
5. Sigma mixer: It works on the principle of shearing and tearing.

SUPAC (SCALE UP AND POSTAPPROVAL CHANGES) GUIDELINES: [22]

SUPAC reflects the adjustments proposed by the US FDA at the time of scale up or approval of NDA / ANDA.

In the process of producing a new medicinal product, the batch sizes employed in the early human trials are modest and the size of the batches is progressively raised (Scale-up) (Scale-up). The scale-up procedure and the adjustments made after approval in the composition, manufacturing method, manufacturing equipment, and change of location have become known as Scale-Up and Post approval Changes, or SUPAC.



The SUPAC Guidelines specify;
The degree of alterations - Minor, Moderate and Major Changes. Test - Application test, in vitro dissolution and in vivo.
Filing - Annual report, changes being implemented supplement and Prior Approval Supplement. The amount of adjustments may effect on formulation and quality performance in following levels;

- Level 1: unlikely to have discernible Impact.
- Level 2: might have substantial influence.
- Level 3: likely to have substantial effect.

These guidelines include suggestions for post approval adjustments in;

- The components or makeup alter,
- The place of production change,
- The scale-up of production change,
- The manufacturing (process and equipment) modification.
- The components or composition changes.
- This section focuses on changes in excipients in the drug product.

SUPAC-MR - Excipient critical or non-critical to the Modified drug release. Changes in non-release and release controlling excipients.
SUPAC-SS - Changes in preservative in semisolid formulations. SUPAC-IR Changes for immediate-release solid oral dose forms.
The location changes of manufacture:
Changes in location of the site of manufacturing, packaging activities and/or analytical testing laboratory. Do not include any scale-up adjustments, changes in production (including process and/or equipment), or changes in components or composition.
Current Good Manufacturing Practice (CGMP) inspection.

- Level I Changes; Classification-Single facility with the same equipment, standard operating procedures (SOP's), ambient conditions (e.g., Temperature and humidity) and controls, and people common. Test Documentation - Application/ compendia requirements in chemistry,dissolution and in vivo Bioequivalence – None.
- Level II Changes; Classification–Same continuous campus, Common staff, No additional modifications. Test Documentation– Application/ compendial requirements Notification of Location of new site Updated batch records.
  SUPAC – MR - Multi-point dissolution profiles (15,30,45,60 and 120 min) USP buffer medium at pH 4.5-7.5 for extended release). Three different Media (e.g., Water, 0.1N HCl, and USP buffer medium at pH 4.5 and 6.8for delayed release) until 80% of Drug Released.
- Level III Changes; Classification – Different campus, Different staff. Test Documentation – Application/compendial criteria. Notification of Location of new site. Updated batch record.
  SUPAC - IR: Multi-point dissolution profile in the application/compendial medium. SUPAC - MR: Multi- point dissolution profiles (15, 30, 45, 60 and 120 min) USP buffer medium at pH 4.5-7.5 for prolonged release). Three different Media (e.g., Water, 0.1NHCl, and USP buffer media at pH 4.5 and 6.8 for delayed release) till 80 % of Drug Released.

Changes in Batch Size (Scale-Up/Scale-Down):
Post-approval modifications in the size of a batch from the pivotal/pilot scale bio batch material to bigger or smaller production batches require for submission of additional information in the application. Scale- down below 100,000 dose units is not addressed by this advice.

- *Level I Changes;* Classification- Change in batch size, up to and including a factor of 10 times the size of the pilot/bio batch. Test Documentation – Updated batch records application/compendial requirements stability. Filing Documentation- Annual report (long term stability data) (long termstability data).
- *Level II Changes;* Classification- Adjustments in batch size beyond a factor of ten times the size of the pilot or bio batch, No further changes.[23]

Manufacturing Changes:
Production modifications may alter both equipment employed in the manufacturing process and the process itself.
Equipment;

- Level I Changes: Classification- Alternate equipment of the same design and concepts as automated equipment. Test Documentation – Updated batch records, Application/compendial requirements and stability. Filing Documentation- Prior approval supplement with rationale for modification; yearly report (long-term stability data) (long-term stability data).
- Level II Changes: Classification- Change to equipment of different design and concept. Test Documentation – Updated batch records, Application/compendial requirements and stability. SUPAC – IR - Multi-point dissolution profiles in various mediums. SUPAC – MR - Multi-point dissolution profiles in various mediums. Filing Documentation Annual report and modifications being Effected Supplement.[24]

Process;

- Level I Changes: Classification- Alternate equipment of the same design and concepts as automated equipment. Test Documentation – Updated batch records, Application/compendial requirements and stability. Filing Documentation- Annual report.
- Level II Changes: Classification- This category contains process alterations including adjustments such as mixing times and operating speeds outside the application/ validation limits. Test Documentation – Updated batch records, Application/compendial requirements and stability. SUPAC - IR - Multi-point dissolution profile. SUPAC- MR - Multi-point dissolution profiles in various mediums. SUPAC – SS - In vitro release test Documentation. Filing Documentation- Changes being implemented supplement; yearly report (long term stability data) (long term stability data).
- Level III Changes: Classification- Changes in the kind of process utilised (e.g. wet granulation to direct compression) (e.g. wet granulation to direct compression). Test Documentation – Updated batch records, Application/compendial requirements, stability, bio-study and IVIVC. SUPAC - IR - Multi-point dissolution profile. SUPAC- MR - Multi-point dissolution profiles in various mediums. Filing Documentation- Prior approval supplement with reason; yearly report (long-term stability data) (long-term stability data).

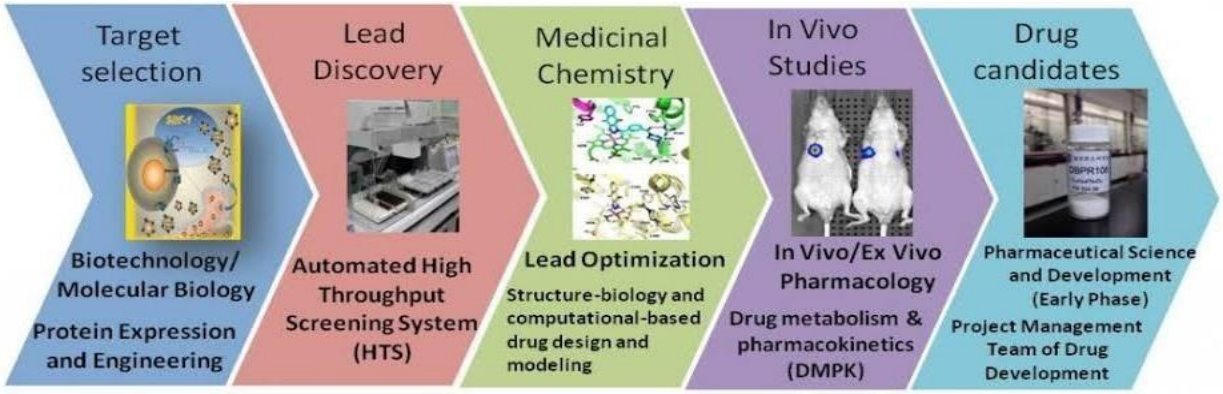
PLATFORM TECHNOLOGY:

Platform technologies are systems that disperse the system out into several levels of abstraction. This is done in order to distinguish between basic – platform – functions, and the application layer that sits on top of, and relies upon, these underlying common services.[25]

Pharmaceutical Platform technologies are regarded a helpful tool to increase efficiency and quality in medicinal product development. The underlying notion is that a platform, in conjunction with a risk-based strategy, is the most systematic manner to exploit existing knowledge for a given new molecule. Platform technology is becoming a common industrial approach for bio processing.

- *Importance platform technology:*

Platform firms move quicker than their conventional competitors. When your core goods and services constantly change, it drives your staff and your business to accept change swiftly.[26]



- *Types of platform technology:*

1. Computing Platforms.
2. Database Platforms.
3. Storage Platforms.
4. Application Platforms.
5. Mobile Platforms.
6. Web Platforms.
7. Nano technology.

CONCLUSION:

Pilot plant scale up considerations for solids, liquids, semisolids is discussed here. The main objective of pilot plant is "Find mistakes on a small scale and make profit on large scale". The significance of pilot plant scale up studies gives review of range of relevant processing equipment, Optimization and control of production rate, Information on infrastructure of equipment's. This also gives detail information about dosage form such as solids, liquids and semisolid dosages their types, equipment's used in their preparations, infrastructure of pilot plant layout.

REFERENCES:

1. Roop K Khar, Farhan J Ahmad, A Vashishtha, S. Harder, GV Buskirk, JV Battista. Pilot Plant Scale-up and Production Management. In: Roop K Khar, SP Vyas, Farhan J Ahmad, Gaurav K Jain, Editors. Industrial Pharmacy. 4 th edition. New Delhi: CBS Publishers &Distributors Pvt Ltd, 2013. pp. 947-1002.
2. Dhobale AV, Mahale AM, Shirsat M, Pethkar S, Chakote V. Recent Advances in Pilot Plant Scale Up Techniques - A Review. Indo Am J Pharm Res 2018; 8(4): 1060-1068.
3. Gomez AL, Strathy WA. Engineering Aspects of Process Scale-Up and Pilot Plant Design.In: Michael Levin, editor. PharmaceuticalProcess Scale-Up. New York: Marcel Dekker Inc;2002. p. 311-324.
4. Shah VP, Skelly JP, Barr WH, Malinowski H, Amidon GL. Scale-up of Controlled ReleaseProducts - Preliminary Considerations. Pharm Technol 1992; 16(5):35-40.
5. FDA. Center for Drug Evaluation and Research,Guidance for Industry: Immediate Release Solid OralDosage Forms. Scale-up and Post-Approval Changes:Chemistry, Manufacturing and Controls, In VitroDissolution Testing, and In Vivo BioequivalenceDocumentation [SUPAC-IR]; 1995.
6. Mounica NVN, Sharmila RV, Anusha S, Evangeline L, Nagabhushanam MV, Nagarjunareddy D, et al. Scale up and Postapproval changes (SUPAC) Guidance for Industry: A Regulatory note. Int J Drug RegulAff 2017; 5(1): 13-19.
7. Sherman R. Technology & Product Architectures. In: Business Intelligence Guidebook. Science Direct; 2015.
8. S. Henricks. The Possibilities and Challenges of Spray Drying, Advancing Process Solution Pharmaceutical Technology, Europe, Reprinted May 2010.
9. Vyas SP, Khar RK. Controlled Drug Delivery: Concepts and Advances. Lasted. Vallabh prakashan, 2002,156-189.
10. Shargel L, Yu ABC. Modified release drug products. In: Applied
11. Biopharmaceutics and Pharmacokinetics. 4th ed. McGraw Hill. 1999; 169-171.
12. Ratner BD, Kwok C. Characterization of delivery systems, surface analysis and controlled release systems. In: Encyclopaedia of Controlled Drug Delivery, Vol-I. Published by John Wiley & sons. 1999; 349-362.
13. Nandita GD, Sudip KD. Controlled-release of oral dosage forms, Formulation, Fill and Finish 2003, 10-16.
14. Malamataris S, Karidas T, Goidas P. Effect of particle size and sorbed moisture on the compression behaviour of some hydroxypropyl methylcellulose (HPMC) polymers, Int J Pharm 1994, 103, 205-215.
15. Gohel MC, Parikh RK, Padshala MN, Jena GD. Formulation and optimization of directly compressible isoniazid modified release matrix tablet, Int J Pharm Sci 2007, 640-644.
16. Levina M, Palmer F, Rajabi-Siahboomi A. Investigation of directly compressible metformine HCl 500 mg extended release formulation based on hypromellose, Controlled Release Society Annual Meeting 2005, 1-3.