PILOT PLANT SCALE UP TECHNIQUE :-

Introduction :- In Pharmaceutical Companies, the demand of any Pharmaceutical dosage form product is Essential for the growth of the management.

⇒ But the main Problem generates in the large Scale production is the accuracy in the Product. If we can produce the drugs initially at large rate, the chances of the drug degradation became maximize.

⇒ To reduce the loss of time, material and money in direct large Scale productions, we use Pilot Plant Technique, to produce the product at a Small level, after the Successful production of product, It can Scale up (increase) to produce at large level.

Plant :- The Place where the money, material, man, method and machine (5M) work together to produce the Products

→ Include Standard procedures and good laboratory practices.

Pilot Plant :- It is the method or Technique used to produce the required product at small level, before the production of large Scale products.

⇒ Part of the Pharmaceutical Industry, also Include Testing of products.

Scale Up :- The process of production of products at large Scale or level by designing a prototype by using Pilot Plant data.

SIGNIFICANCE OF PERSONNEL REQ., SPACE REQ., RAW MATERIAL REQ.

Pilot Plant Technique helps to reach a Basic or good Qualitative type for RND (Research and development) to produce the product at large level

OBJECTIVE

⇒ Find the Error on documentation Base and make profit on large Scale.

⇒ For finding of functioning of Equipments, and changes to be done.

⇒ To produce the product Stable at Physico-chemical level.

⇒ Evaluation and Validation.

⇒ To reduce Pharmaceutical Error in the testing also.

⇒ To Identify the critical features of the process and documented

⇒ To decrease the time, Material and money wastage.

STEPS IN SCALE UP

Make a defined budget on the Basis of marked requirement, Selling and Manufacturing costs etc.

+

At Same time, Planning can be conduct for lab Studies (Pilot Plant) and Scaling up.

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Define the rate-controlling Step in the process (that effects the product Stability) + Documented

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Conduct Preliminary Studies at Small level

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Design and construct a pilot plant System having provision for process and Environment control, cleaning, Sanitizing etc Systems

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Evaluate pilot plant results to proceed with a large scale plant development

GENERAL CONSIDERATIONS

① Reporting Responsibility ; Include Research and development group staff and developor or formulator who develop the product

⇒ RND gaves formulas and procedure for the Product making.

⇒ The formulator can development the product

② Personnel Requirement :-

Number of the worked required to produce the product in whole operation.

⇒ workers include trained, operator, chemist, Senior officer etc.

⇒ The Experienced Scientist Required to produce the products in Production Region.

⇒ Trained Engineer Required for machine operation.

⇒ Trained chemists also need for chemical Evaluations

③ Space Requirement :- The proper area must be Evaluate as based to the production Requirement.

→ Include Administration and Information processing.
→ Testing area Required.
→ Standard processing area required.
→ Storage area requirement.

④ Review of Formulae :- Checking of the all documented Based contents before the formulation of products.

→ Verify the drug or salt formulae.
→ Checking up of calculations
→ Checking up of Interaction between two materials, Chemicals.

⑤ Raw Material :- Issue the raw material according to the production need and record by the Pilot Plant level.

⑥ Equipment :- A Suitable Equipment can help to produce product in a required time.

→ Machine or Equipment decides the time and quantity to produce the product.

(7) Production Rate :- Suitable time should be decided in which the product with good Stability can be produced.

(8) Process Evaluation :- order of component mixing, speed, time, addition of Excipients, Filter (for liq.) and Screen Size (for Solid), temp. can be Evaluated firstly.

(9) MMP (Master manufacturing Procedure)

after Procedure, the SOP can formed include quantities, processing and Steps in procedure.

(10) Product Stability and uniformity :-

By Biological, Physical and chemical testing, the Stability, Quality and uniformity can be Evaluated.

SCALE UP TECHNIQUE FOR LIQUID ORALS :-

Liquid Orals :- The physical form of drug product that is pourable, flowable.

→ Liquid orals may be dispersions or solutions.

→ Dispersion phase having 2 phases.

→ Solution is a homogeneous mixture of 2 or more substances.

→ They may be newtonian or pseudo flow forms of liquid.

Liquid Manufacturing Process Steps :-

1. Required material Planning
2. Liquid preparation (Suitable)
3. Filling and Packing
4. Quality Assurance (Testing)

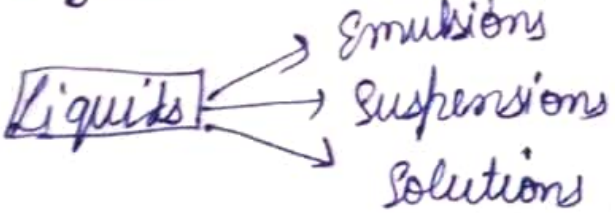
☆ Critical Aspects that Effect Manufacturing

⇒ Physical Plant: heating, ventilation and air controlling System can be maintained to avoid Physical or chemical unstability of ingredients.

⇒ Liquid: Material used in suitable Liquid Type also can be Evaluate to produce a Stable product

Exam: In Suspensions, the excipients can be used to enhance API and Vehicle Connection, Buffering system used to maintain PH etc.

→ Critical Points can be Noted to avoid degradation.



⇒ Equipment: Evaluation and proper set-up of the Equipment also decrease the degradation risk of the Material.

General flowchart : (For equipment use)

Raw Material → Measure and weighed

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Mixing ← Distilled H_2O

↓

Filling

↓

Packing

↓

Product Storage

↓

Quality Tests.

⇒ QA :- (Quality Assurance)

→ QA refers to test the product quality on documentation base

→ QA checks or Tests :-

- Drug dissolution in Solution
- drug potency in suspension
- Temperature uniformity in Emulsion
- Final volume
- Stability Etc.

PILOT PLANT SCALE UP CONSIDERATION FOR SOLID :-

☆ Solid :- The unit solid dosage form having a Preventive, curable and diagnostic purpose in our Body.

exam - Tablets or capsules

→ The main aim is to Ensure the production of a Stable product.

☆ Critical Aspects for Solids :-

⇒ Physical Plant :- The cleanliness maintainance, Equipment, and other aspects that can play role in safe production of drugs must Evaluated.

⇒ Solids :- To produce the Stable, Qualitative dosage form, the required + Suitable excipients must required for good API and Vehicle Interaction, Integrety etc.

⇒ Features of manufacturing place :

- Proper lighting fitting
- Proper draining facility.
- Area should be air conditioned and humidity controlled.

⇒ Equipments :- (Functioning)

- Material handling System
- Mixing
- Granulation
- Drying
- Reduction of Particle Size
- Blending
- Compression
- Tablet coating.

① → Material handling system used to handle material such as Ingredients, raw material, etc.

→ Include transfer, delivery and mixing of materials etc.

② Mixing is the Blending or Addition of 2 or more ingredients for enhance flow property, content uniformity, lump free mass etc.

→ V-blender, Sigma Blade Blender, Bin Blender etc used for mixing or Blending.

(3) Granulation is the technique used to separate the equal size particles from mixture.
→ wet or dry granulation methods used for ~~gra~~ granulation.
→ Enhances the particle distribution uniformly, Reduces dust production etc.
→ Also improves flow property.
→ Sigma blade mixer used for wet granulation.
→ Microwave, Spray dryer etc used for dry granulation.

(4) Drying is process of removal of moisture from the particles.
→ hot air oven and fluid bed dryer used to dry the substance.
→ It reduces the degradation and microbial contamination of the substances.

(5) Particle Size Reduction: The process of decrease the size of particles uniformly.
→ used to enhance Quality, flow property, Surface area etc.
→ hammer mill, mechanical Sieving and Screening devices used for Particle Size Reduction

(6) Blending :- Mixing of substances and make uniformity of Bulk.

→ used for uniform distribution of all the contents.

(7) Tablet coating :- The layering on the surface of Tablets to reduce the bitter or unpleasant Taste and enhance its appearance.

→ different polymers etc used to coat the Tablets.

PILOT PLANT SCALE UP CONSIDERATION For Semisolid

↳ Mixing Speed
↳ Mixing Equipment (could be able to move Semisolid mass from outside walls to centre and from Bottom to top)
↳ Motors (Drive mixing System with appropriate handling system at its most viscous stage)
↳ heating and cooling process
↳ Product transfer
↳ Addition of Active Ingredient
↳ Temperature range
↳ Product Viscosity
↳ Product Compatibility.

SUPAC GUIDELINES

SUPAC - Scale up and post Approved Changes.

SUPAC guidelines involves the changes have to be done in the Scale up process and also after the Scale up approval.

→ Regarding the composition, manufacturing process or Place can be changed through the SUPAC guidelines.

→ SAPAC is a guideline guidance document that contain Procedure that how to Submit the changing critesia document to approve the Required changes.

#PURPOSE : Gave Instructions, how the changes can be done even after the Approval of the Scale Up Technique Documennent (Previous)

→ Changes can be involves
- ↳ Components / Composition
- ↳ Scale up or Scale down
- ↳ Manufacturing process or Equipment.

☆ NDA (New drug Application), ANDA (Abbreviated new drug Application), AADA (Abbreviated Antibiotic drug Application) can be used to approve the changes.

SUPAC Guidelines Involves

☆ Level of Changes
- → Minor (small Change)
- → Moderate Change
- → Major Change.

☆ Tests
- → Application / Compendial Test
- → In Vitro dissolution
- → In Vivo

☆ Filling
- → Annual report
- → Changes being effected Supplement
- → Prior Approval Supplement.

☆ Level of Changes : It Define the type of change can be want to have, Small or Large etc. type.

- Level 1 (Minor) Change
- Level 2 (Moderate) Change
- Level 3 (Major) Change

Level 1 :-

→ Level Change can not Effect the Product Quality

→ Level of changes can be file in Annual reports in case of Level 1 changes.

Level 2 :-

→ Moderate changes can /may be effct the Product Quality.

→ These can be filed in the "changes being effected Supplement" or in "Prior Approval Supplement".

→ These changes tests can depend upon the Therapeutic range of the Supplement.

Level 3 :-

→ Major changes can impact more the Quality of the Product

→ It can be filed in "Prior approval supplement"

Factor Involve Level of changes

① Site change / Manufacturing area

- Level 1 Change involve single facility but change in Area of a Procedure
- Level 2- Changes involve campus to campus or Industry to Industry at neighbour or nearer area
- Level 3 - changes involve sites 1 to other at farer distant.

② Changes in Batch Size :- (up or Low)

- Level 1 - Batch Size changes upto 10 time.
- Level 2 - Batch Size changes more than 10 time.

③ Manufacturing → Equipment Change
→ Process change

↳ Equipment change

- Level 1 - from non Automated to Automated (same design & working principle)
- Level 2 - Change from non Automated to Automated Equipment with Change in Design & working principle.

- Process change
  - Level 1 - Changes within Applicatn & validation Range (Mixing time, Rotation speed)
  - Level 2 - Changes Beyond Application & validation Range
    - eg. (Now change in Mixing or Rotation speed time)
  - Level 3 - Change whole manufacturing Procedure
    - eg. wet granulation changes to the direct compression

ADVANTAGES OF SUPAC GUIDELINES

* Generally, If changes can be require, the written Information is require from Initial Stage to final but In SUPAC guidline, only the Information that we want to change can be Submitted Instead of whole written Procedure.

INTRODUCTION TO PLATFORM TECHNOLOGY

Platform Technology :- It is a tool that can be used to Enhance the drug's Safety, efficacy, efficiency and quality in the drug product Development.

→ Used as a Valuable Tool.

→ Platform Technology can used as Base in the Development of other new Techniques.

★ Exam. Of Platform Technologies :-

① Nanotechnology - Small/Tiny particles used to Destroy the cancer cells directly travel to the cancer cells.
→ Redua Toxicity and better outcomes
→ Mainly used in Target Therapy Development.

② Microsphere Technology :- Also small molecules formed that can Deliver on Target Site.

③ Liposomal Technology : used to Improve drug Delivery and Target Delivery
→ Improve Pharmacokinetic Parameter (ADME)

④ Hot melt Extrusion Technology :- Solid molecular Dispersion can be Developed by Technology that work better than Solvent based ~~pa~~ products.

→ have Sustained, Modified and Targeted Delivery.

⑤ Sustained release Formulation Technology :- Advance Technology used for Prolong Action of drug at the uniform level to the Target Site.

exam- only once a day Tablet can be intake for whole day Action on the Site.

→ Improve safety profile, uniform drug effect, drug Concentration is Stable.

⑥ Orally Disingrating formulation Technology :- Technology used to form Dosage form that Disintegrate in the mouth and produces effect in Body.

⑦ Inhalation Technology :- The Dosage forms used by Inhale through nose and directly target the Lung Disease / Respiratory Disorders like Asthma, COPD etc

(8) Sprinklers :- Generally like sprays and mostly used for childrens by dissolving or sprinkle the drugs in the food.

(9) Stem cell Based products :- Step cells from Bone Marrow used in the Thera-peutic Application that treats many disorders.

(10) Effervescent Technology :- The dosage form can dissolve very readily, result in Enhance the Effect and also having impleasant taste masking property.