PILOT PLANT SCALE UP FOR LIQUID ORALS

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INTODUCTION

Liquid dosage forms comprise of non-sterile solutions, emulsions and suspension.

The considerations for pilot plant scale up of liquid orals are as follows-

1) The physical form of a pourable drug product shows Newtonian or pseudo plastic flow behavior and takes the shape of its container at room temp.

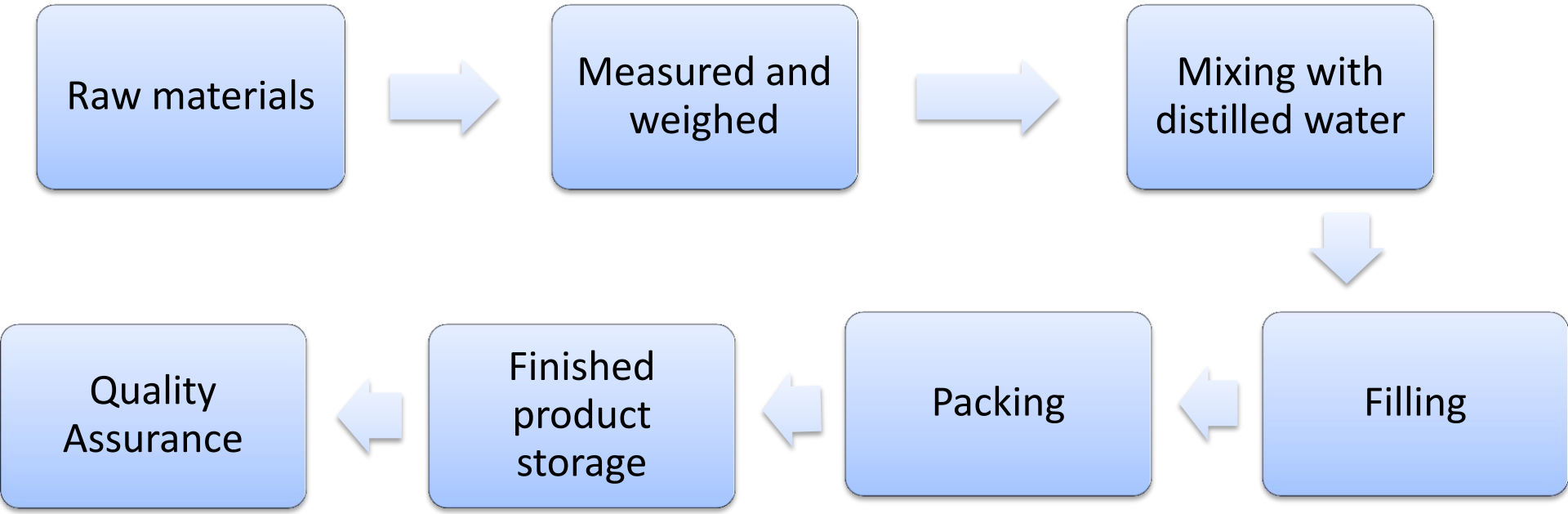
2)Liquid orals may be solutions or dispersed systems.

3)Two or more phases, with one phase distributed in another, are present in dispersed system.

4)A homogeneous mixture of two or more substances is referred to as solution.

Steps of Liquid Manufacturing Process

- Liquid manufacturing process involves the following steps-



1) Raw Materials

One responsibility of pilot plant is the approval and validation of the active ingredient and excipient raw materials used in pharmaceutical product

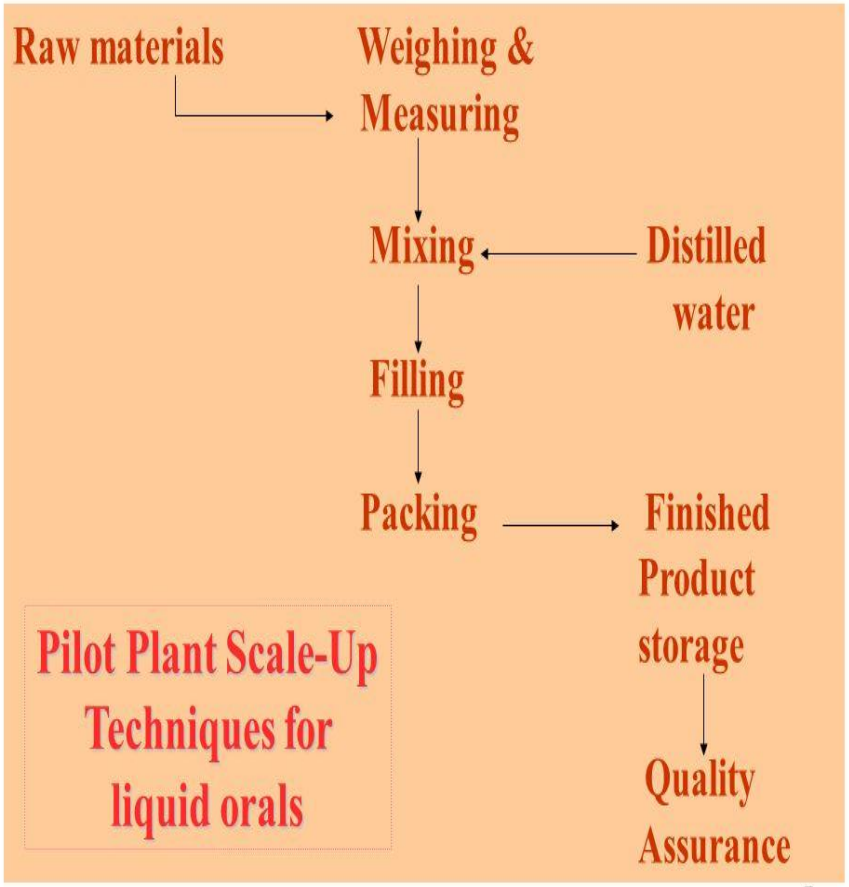
- **SOLVENTS**-Water, alcohol, glycerol, polyethylene glycol ,polypropylene glycol.
- **PRESERVATIVES**-Benzyl alcohol, chloro cresol, benzoic acid.
- **ANTIOXIDANTS**-Ascorbic acid, sodium thiosulphate, sodium metabisulpahte.
- **ORGANOLEPTIC AGENT**-colouring agent, flavouring agent, sweetening agent.

2)Relevant Processing Equipment

- Almost all formulation development work is carried out on small relatively simple laboratory equipments.
- The equipments that is most economic, the simplest, the most efficient should be selected.
- Liquid pharmaceutical processings tanks,kettles, pipes, mills,filter housing and so forth are most frequently fabricated from stainless steel.
- Ease of cleaning should be considered if multiple products are to be manufactured in the same equipment.

Stages of Operation

A. Tank selection
B. Mixing
C. Filtration and Clarification
D. Transfer and Filling.



3)Process Evaluation

- Items that should be examined includes the following-
  - Mixing speed
  - Mixing time
  - Rate of addition of solvents, solution of drugs, slurries etc..
  - Heating and cooling rates
  - Filter size
  - Filling

4)GMP Consideration

- Equipment qualification
- Process validation
- Regular process review and revalidation
- Relevant written SOP
- Adequate provision for training of personnel
- A well defined technology transfer system
- An orderly arrangement of equipments.

5) Quality Assurance

- Dissolution of drugs in solution
- Potency of drugs in suspension
- Temperature uniformity in emulsion
- Microbiological control
- Product uniformity
- Final volume
- Stability

Pilot scale up for Suspension

- A pharmaceutical suspension is a coarse dispersion in which internal phase (therapeutically active ingredient) is dispersed uniformly throughout the external phase.
- Formulation aspects of suspension-

Purposes	Agents
Facilitating the binding between API and vehicle	Wetting agents and salt formation ingredients.
Protecting the API	Buffers, polymers and antioxidants.
Maintaining the suspension appearance	Colouring agents, suspending agents and flocculating agents.
Masking the unpleasant taste or odour	Sweeteners and flavouring agents.

Filling and Operation

- Filling- important parameter in the transfer of liquids from tank to tank into containers.
- The selection of equipment depends on characteristic of liquid such as viscosity, type of packaging , surface tension.
- Gravimetric(specific weight)
- Volumetric(specific volume)
- Constant volume filling.

Pilot plant scale up for Emulsion

- An emulsion is a thermodynamically unstable system consisting of at least two immiscible liquid phases one of which is dispersed as globules in the other liquid phase stabilized by a third substance called emulsifying agent.
- Formulation aspect of emusion-

Purposes	Agents
Particle size	Solid and droplet particles.
Protecting the API	Buffers,antioxidants and polymers.
Maintaining the appearance	Colouring agents,emulsifying agents, penetration enhancers and gelling agent.
Masking the unpleasant taste and odour	Sweeteners and flavouring agents.