Manufacturing Consideration

- The manufacturing process for liquid preparations for oral use should meet the requirements of Good Manufacturing Practice (GMP).
- In the manufacture of liquid preparations for oral use, measures are taken to:
  - ensure that all ingredients are of appropriate quality
  - minimize the risk of microbial contamination
  - minimize the risk of cross-contamination

Steps of Liquids Manufacturing Process

- **Planning of Material Requirements:** Research and development of protocols and selection of materials; acquisition and analysis of raw materials; physical plant design, building, and installation; equipment selection and acquisition; personnel selection and initial training; and monitoring information system.

Raw Materials : Incoming raw materials should be tested as per specifications that is identity, purity, uniformity and microbial contamination .

Equipments : The following types of equipments may be used in the manufacture of liquid formulations:

- Mixing tanks (SS 316 Stainless Steel) equipped with an agitator.
- Measuring devices for large and small amount of solids and liquids. 3. Afiltration system e.g. filter press

Cleaning of equipments

- All equipments must be thoroughly cleaned and sanitized before use.
- Disinfectants used: Dilute solutions of H2O2, phenol derivatives.
- Sterilized by:Alcohol, boiling water, autoclaving, steam or dry heat.

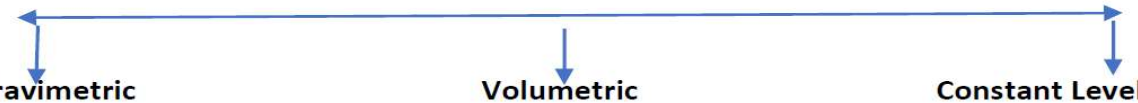
Cont.

- **Liquid Preparation**
- Research and development of protocols concerning liquid compounding;
- scale - up of the bulk product compounding;
- physical plant control and maintenance;
- equipment maintenance and renovation;
- continuous training of personnel and
- personnel compensation plan;
- supervision of system reports.

Cont.

- **Filling and Packing:**
- Research and development of protocols concerning filling and packing;
- scale-up of the finished drug product filling and packing;
- physical plant control and maintenance;
- equipment maintenance and renovation;
- continuous training of personnel and personnel compensation plan;
- supervision of system reports.

Filling and Packing



Gravimetric

Containers are filled with liquids to a given weight.

Usually limited to large container filling or highly viscous products.

Cannot be used in high speed, automatic equipment

Volumetric

Containers are filled with liquids to a given volume.

Filled amount is measured by the stroke of the piston and cylinder assembly.

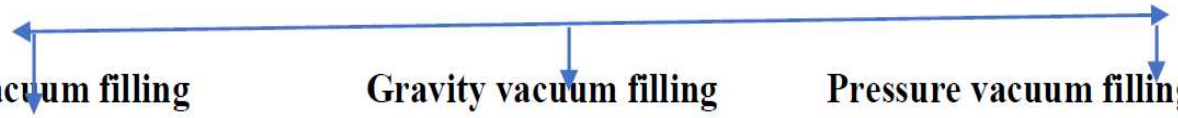
Problems may arise when containers used are not dimensionally uniform.

Constant Level

Filled amount is verified by adjusting the height to which the container is to be filled.

Variation in container dimension may result in variations in the net fill per unit.

Techniques of Filling



Vacuum filling

Vacuum developed within the container causes liquid to flow from tank to container.

Gravity vacuum filling

Bulk liquid tank is placed above filling stem so that liquid flows to the container due to force of gravity.

Pressure vacuum filling

Pressure applied to bulk liquid tank and vacuum developed in the container results in pressure difference so that liquid flows to the container.

Evaluation Tests for Syrups

A concentrated solution of a sugar, such as sucrose, in water or other aqueous liquid, sometimes with a medicinal agent added; usually used as a flavored vehicle for drugs.

Transmittance of light: A light transmittance meter is a newer tool that is used to check syrup color. In a light transmittance meter, a syrup sample is checked for color by passing light through the sample. The percent of light transmission is compared to light transmission rates set for different grades.

Visual inspection: With a visual inspection, the ingredients and the final products are carefully examined for purity and appearance. The physical appearance of products for patient adherence and compliance is critical so it should be

- Good looking
- Elegance in appearance

Sucrose concentration: The determination of sucrose concentrations is also very important in quality control testing of syrups. If the concentration of sucrose in the syrup is very high it may crystallize the syrup and fewer sucrose concentrations give favor for the microbial growth.

There is no specific method for the determination of sucrose in syrup, HPLC and UV spectroscopy for this purpose are used.

pH measurement: The measurement and maintenance of pH is also a very important step in quality control testing. Generally, there are two different types of methods used in the measurement of pH.

Methods for pH measurement:

- The simplest and cheapest is to dip a piece of pH paper into the sample. The paper is impregnated with chemicals that change color and the color may be compared to a chart supplied with the paper to give the pH of the sample.
- If the greatest accuracy is required a pH meter should be used. A typical pH meter consists of a special measuring glass electrode connected to an electronic meter that measures and displays the pH reading.

Physical stability in syrups: The syrups must be stable physically.

Example:

- Its appearance (no crystallization and microbial growth)
- Colour must be completely soluble with other ingredients
- Odor and taste(palatable).
- The solid material is completely miscible in liquid