PILOT PLANT
SCALE- UP TECHNIQUE

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Definitions

- **Plant**:- It is a place were the 5 M's like money, material, man, method and machine are brought together for the manufacturing of the products.
- **Pilot Plant**:- It is the part of the pharmaceutical industry where a lab scale formula is transformed into a viable product by development of liable and practical procedure of manufacture.
- **Scale-up**:- The art for designing of prototype using the data obtained from the pilot plant model.

Objective

- To try the process on a model of proposed plant before committing large sum of money on a production unit.
- Examination of the formula to determine it's ability to withstand Batch-scale and process modification.
- Evaluation and Validation for process and equipments
- To identify the critical features of the process.

- Guidelines for production and process controls.
- To provide master manufacturing formula with instructions for manufacturing procedure.
- To avoid the scale-up problems.

STEPS IN SCALE UP

Define product economics based on projected market size and competitive selling and provide guidance for allowable manufacturing costs

Conduct laboratory studies and scale-up planning at the same time

Define key rate-controlling steps in the proposed process

Conduct preliminary larger-than-laboratory studies with equipment to be used in rate-controlling step to aid in plant design

Design and construct a pilot plant including provisions for process and environmental controls, cleaning and sanitizing systems, packaging and waste handling systems, and meeting regulatory agency requirements

Evaluate pilot plant results (product and process) including process Economics to make any corrections and a decision on whether or not to proceed with a full scale plant development

Why conduct Pilot Plant Studies?

- A pilot plant allows investigation of a product and process on an intermediate scale before large amounts of money are 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 scale processing plant from laboratory data alone with any degree of success

A pilot plant can be used for

- Evaluating the results of laboratory studies and making product and process corrections and improvements
- Producing small quantities of product for sensory, chemical, microbiological evaluations, limited market testing or furnishing samples to potential customers, shelf-life and storage stability studies
- Providing data that can be used in making a decision on whether or not to proceed to a full-scale production process; and in the case of a positive decision, designing and constructing a full-size plant or modifying an existing plant

General considerations

1. Reporting Responsibility

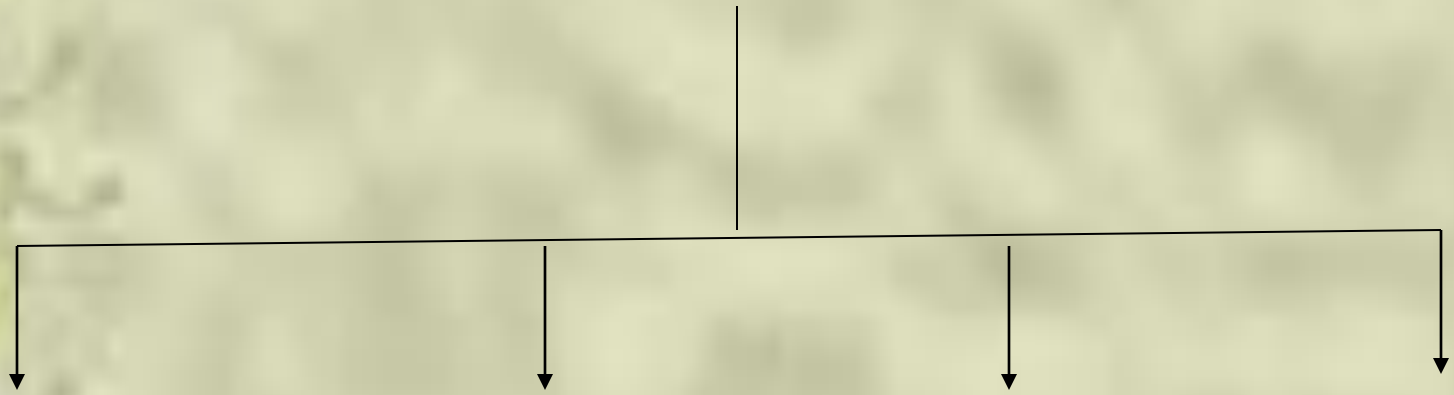
R & D group with separate staffing

The formulator who developed the product can take into the production and can provide support even after transition into production has been completed

2. Personnel Requirement:-

- Scientists with experience in pilot plant operations as well as in actual production area are the most preferable
- As they have to understand the intent of the formulator as well as understand the perspective of the production personnel.
- The group should have some personnel with engineering knowledge as well as scale up also involves engineering principles

3. Space Requirements



- Administration and information processing
- Physical testing area
- Standard equipment floor space
- Storage area

❑ Administration and information process:

Adequate office and desk space should be provided for both scientist and technicians.

The space should be adjacent to the working area.

❑ Physical testing area:-

This area should provide permanent bench top space for routinely used physical- testing equipment.

❑ Standard pilot-plant equipment floor space:-

Discreet pilot plant space, where the equipment needed for manufacturing all types of dosage form is located.

Intermediate – sized and full scale production equipment is essential in evaluating the effects of scale-up of research formulations and processes

Equipments used should be made portable where ever possible. So that after use it can be stored in the small store room.

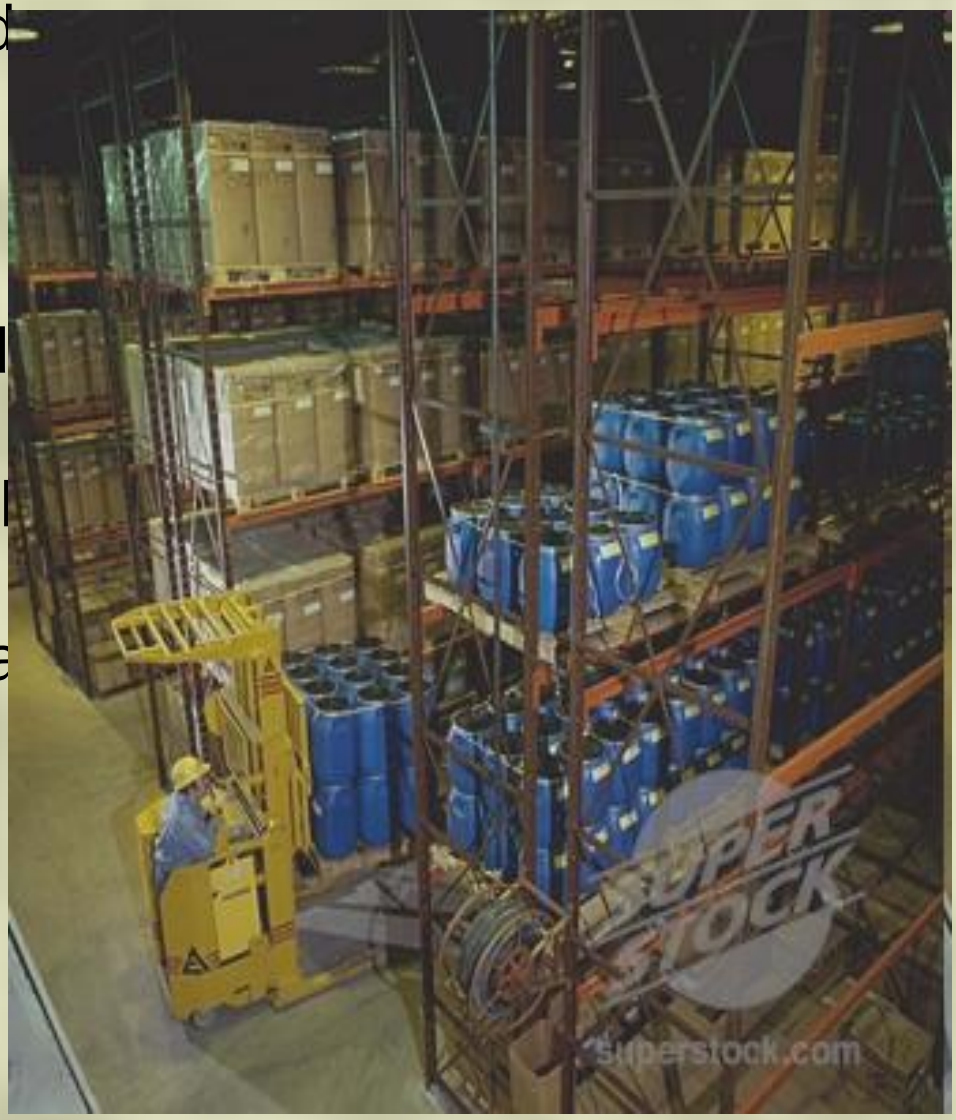
Space for cleaning of the equipment should be also provided.

❑ Storage Area:-

It should have two areas divided as approved and unapproved area for active ingredient as well as excipient.

Different areas should provided for the storage of the in-process materials, finished bull products from the pilot-plant & materials from the experimenta scale-up batches made in the production.

Storage area for the packing material should also be provided.



4. Review of the formula:

A thorough review of the each aspect of formulation is important.

The purpose of each ingredient and it's contribution to the final product manufactured on the small-scale laboratory equipment should be understood.

Then the effect of scale-up using equipment that may subject the product to stresses of different types and degrees can more readily be predicted, or recognized.

5. Raw materials:-

One purpose/responsibility of the pilot-plant is the approval & validation of the active ingredient & excipients raw materials.

Why?

Raw materials used in the small scale production cannot necessarily be the representative for the large scale production

6. Equipment:-

The most economical and the simplest & efficient equipment which are capable of producing product within the proposed specifications are used.

The size of the equipment should be such that the experimental trials run should be relevant to the production sized batches.

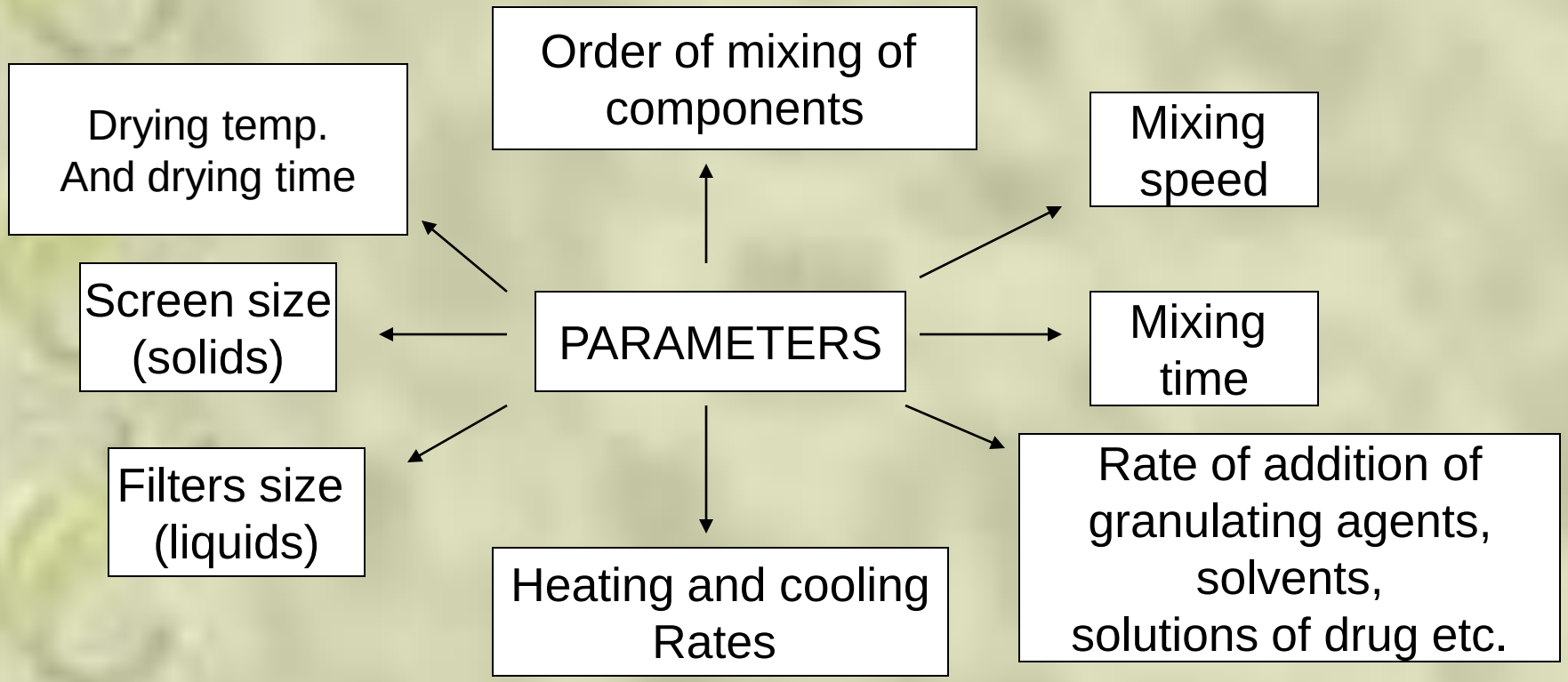
If the equipment is too small the process developed will not scale up,

Whereas if equipment is too big then the wastage of the expensive active ingredients.

7. Production Rates:-

The immediate as well as the future market trends/requirements are considered while determining the production rates.

8. Process Evaluation:-

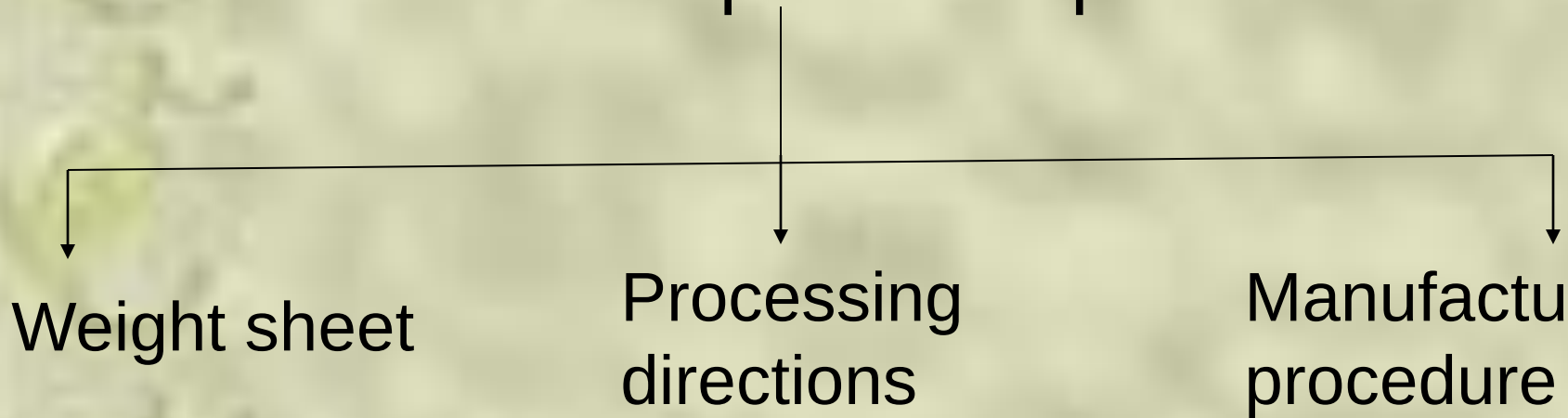


- Why to carry out process evaluation????

- The knowledge of the effects of various process parameters as few mentioned above form the basis for process optimization and validation.

9. Master Manufacturing Procedures:-

The three important aspects



- The **weight sheet** should clearly identify the chemicals required In a batch. To prevent confusion the names and identifying nos. for the ingredients should be used on batch records.
- The **process directions** should be precise and explicit.
- A **manufacturing procedure** should be written by the actual operator.
- Various specifications like addition rates, mixing time, mixing speed, heating, and cooling rates, temperature, storing of the finished product samples should be mentioned in the batch record directions.

10. Product stability and uniformity:-

The primary objective of the pilot plant is the physical as well as chemical stability of the products.

Hence each pilot batch representing the final formulation and manufacturing procedure should be studied for stability.

Stability studies should be carried out in finished packages as well.

GMP CONSIDERATION

- Equipment qualification
- Process validation
- Regularly schedule preventative maintenance
- Regularly process review & revalidation
- Relevant written standard operating procedures
- The use of competent technically qualified personnel
- Adequate provision for training of personnel
- A well-defined technology transfer system
- Validated cleaning procedures.
- An orderly arrangement of equipment so as to ease material flow & prevent cross- contamination

Advantages

- Members of the production and quality control divisions can readily observe scale up runs.
- Supplies of excipients & drugs, cleared by the quality control division, can be drawn from the more spacious areas provided to the production division.
- Access to engineering department personnel is provided for equipment installation, maintenance and repair.

Disadvantages

- The frequency of direct interaction of the formulator with the production personnel in the manufacturing area will be reduced.

- Any problem in manufacturing will be directed towards it’s own pilot-plant personnel's.

Important Questions

- What is the significance of pilot plant scale up with routine production procedure ?
- What do you mean by pilot plant scale up and give examples ?

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