

Chapter-3

Pharmaceutical Technology

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Drug Formulation Development

Definition:

Pharmaceutical Formulation: *It is the process in which different active chemical substances are combined together to produce a medical compound (or) medical drug.*

Pharmaceutical formulation:

• **There are two types of Pharmaceutical Formulation. They are as follows:**

Oral formulation:

i) The most important characteristic for oral formulation is that it must be overcome the problems which are associated with oral administration.

ii) The most critical problem is rate of drug solubility

iii) Drug solubility can be controlled through particle size and crystal form.

iv) The oral formulation is divided into two parts.

They are as follows: i) Tablet form ii) Capsule form.

Topical medication forms: This type includes several parts as the following:

i) Cream ii) Ointment iii) Gel iv) Paste v) Powder

Major types of Formulation

- ❖ Drug substance in capsules/bottles
- ❖ Blends in capsules/bottles
- ❖ Dry granulation in capsules/bottles
- ❖ Sterile liquid formulation
- ❖ Sterile freeze-dried formulation
- ❖ Sterile colloidal formulation
- ❖ Sterile viscous formulation

Pharmaceutical Products:

Antibiotics:

i) Penicillin ii) Streptomycin iii) Tetracycline iv) Chloramphenicol

Other Synthetic drugs:

i) Sulpha drugs

Examples: sulfamethoxazole, sulfathiazole, sulfaguanidine, sulfacetamide sodium.

ii) Anti-TB drugs

iii) Analgesics

iv) Anesthetics v) synthetic antimalarials vi) Gastrointestinal drugs

❖ Vitamins

❖ Synthetic Hormones

Tablet-Formulation

A tablet contains the following ingredients:

- i) 5-10% of the drug active substance
- ii) 80% of fillers, disintegrants, lubricants, glidants and binders.
- iii) 10% of compounds which ensure easy disintegration, disaggregation and dissolution of the tablet in the stomach or the intestine.

- ❖ The dissolution time can be modified for a rapid effect or for sustained release.
- ❖ Special coatings can make the tablet resistant to the stomach acids.
- ❖ It only disintegrates in the duodenum, jejunum and colon as a result of enzyme action or alkaline pH.

Tablet Ingredients

In addition to active ingredients, tablet contains a number of inert materials known as additives or excipients. Different excipients are:

1. Diluent
2. Binder and adhesive
3. Disintegrants
4. Lubricants and glidants
5. Colouring agents
6. Flavoring agents
7. Sweetening agents

Topical

Some drugs can be applied directly to where they are needed. These are called **TOPICAL**.

❖ It can be used to treat eye, ear or skin problems.

Topical preparations are available in different forms:-

- **CREAMS** – the drug is dissolved in water and mixed with oil or fat. Creams spread easily and penetrate the outer layers of the skin.
- **OINTMENTS** – the drugs are present in a base of wax or fat. They do not penetrate the skin.
- **POWDERS** – fine powders to apply to the skin e.g. flea powders.
- **MEDICATED SHAMPOOS** – drugs mixed with detergents which penetrate the coat. Shampoos are left in contact with the skin for the recommended amount of time and then should be rinsed off thoroughly.
- **SPRAYS** – a way of applying liquids in fine droplet form e.g. flea sprays.

Drug Design and its classifications

Drug design:

It is the process of producing or invention of novel (or) new medical product and the design of this new product completely based on the knowledge of biological target.

Moreover, this process sometimes known as rational drug design.

Classification of Pharmaceutical Formulation and Drug Design:

Drug design:

There are two major classifications of drug design. They are as follows.

i) Ligand-based drug design ii) Structure-based drug design.

❖Ligand-based drug design:

In this branch or type of pharmaceutical formulation the design of the drug will be made or built depends on the knowledge of what binds to it.

❖Structure-based drug design:

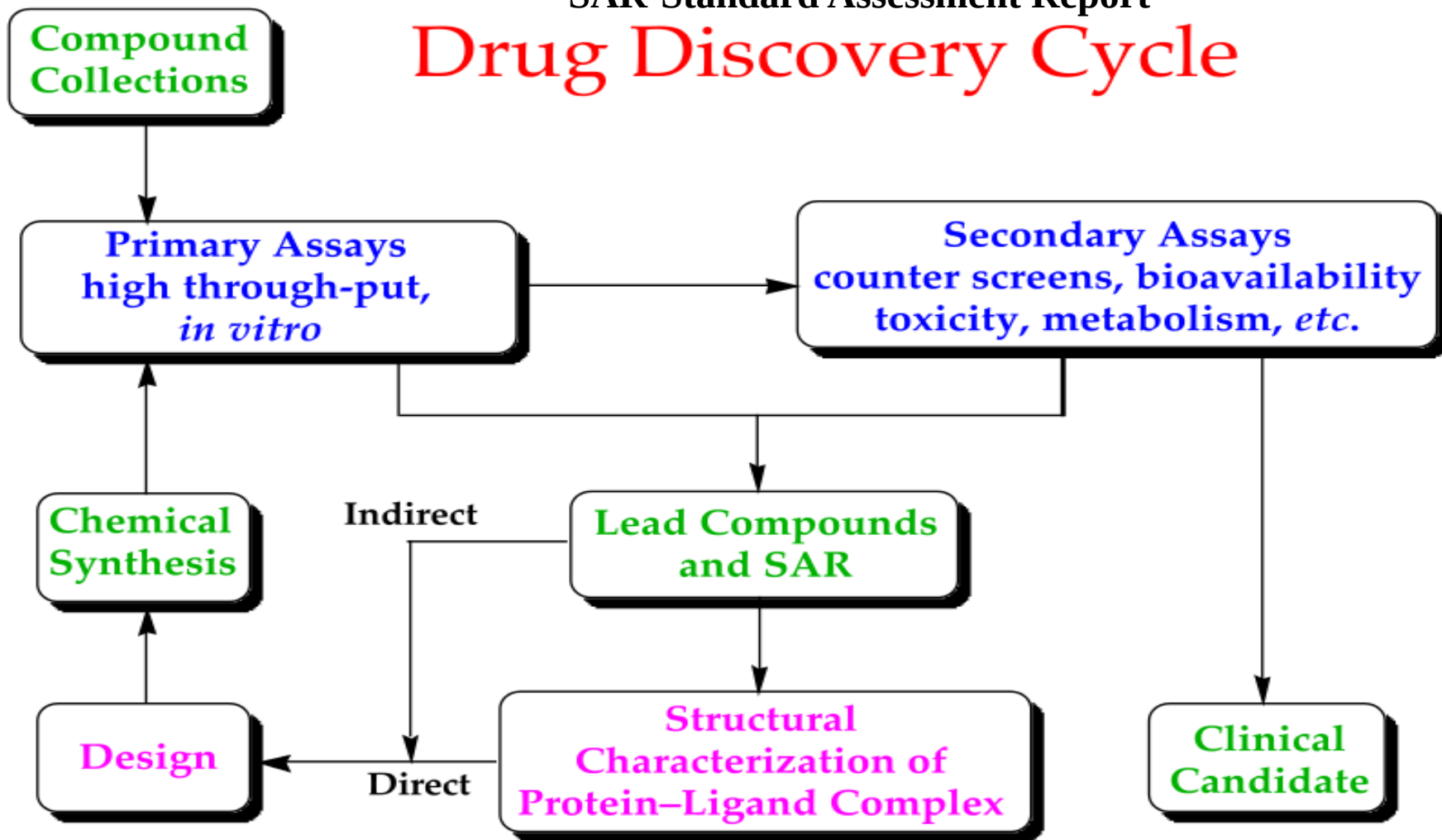
This type of drug design will depend on the information related with the three dimensional structure of the biological target. These information will be obtained by using methods like X-ray or NMR.

Process Development

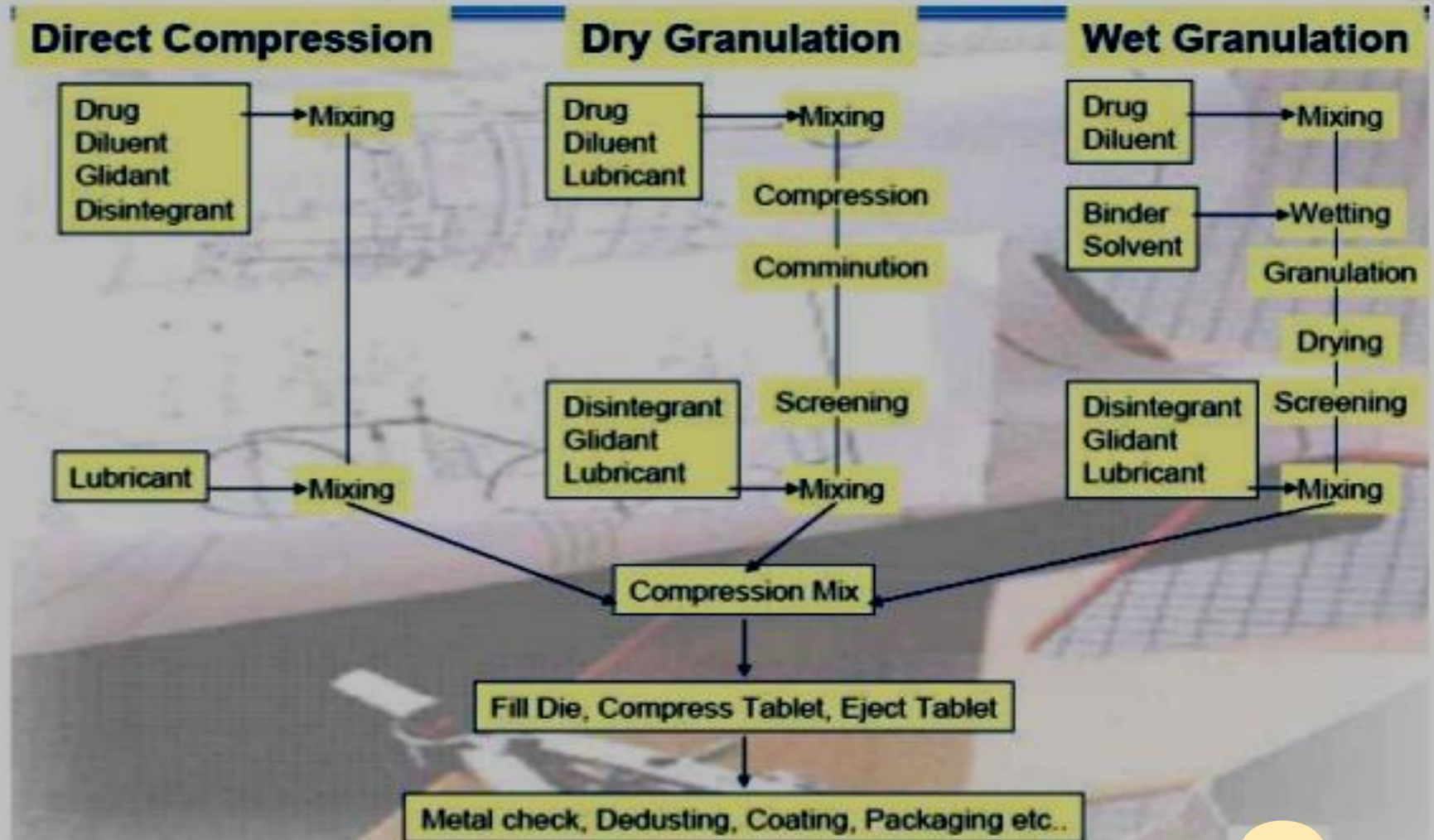
Schematic Diagram of Drug Discovery cycle

SAR-Standard Assessment Report

Drug Discovery Cycle



Tableting methods



Drug Regulatory Affairs(DRA)

Drug Regulatory Affairs(DRA) is a process of interaction of company with Drug Regulatory Authorities and Internal Departments of the Organization.

- ✖ **On what Issues does DRA department provide assistance? :**
- ✖ Licensing
- ✖ Registration
- ✖ Development
- ✖ Manufacturing
- ✖ Quality Guidance
- ✖ Pricing Marketing
- ✖ Pharmacovigilance

What is Dossier ?

Dossier is a collection or file of documents that contains all the technical data of pharmaceutical product to be approved / registered / marketed in a country.

It most commonly called as Registration Dossier,

In US : New Drug Application (NDA),

In EU : Marketing Authorization Application (MAA)

❖ DMF-Drug Master File

❖ CTD-Common Technical Document

Pharmaceutical Quality Control

Analysis are as follows:

- **Karl Fischer Water Determination**
- **Heavy Metals Analysis**
- **Identification of elements**
- **Loss on Drying**
- **Optical Rotation**
- **pH**
- **Titrations**
- **Ultraviolet Spectroscopy**
- **X-Ray Powder Diffraction**
- **Thermal Analysis (DSC and TGA)**
- **Particle size by sieve and laser diffraction**
- **Liquid and Solid-state NMR**

Quality Assurance

Quality assurance is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product. With regard to pharmaceuticals, quality assurance can be divided into major areas: development, quality control, production, distribution and inspections.

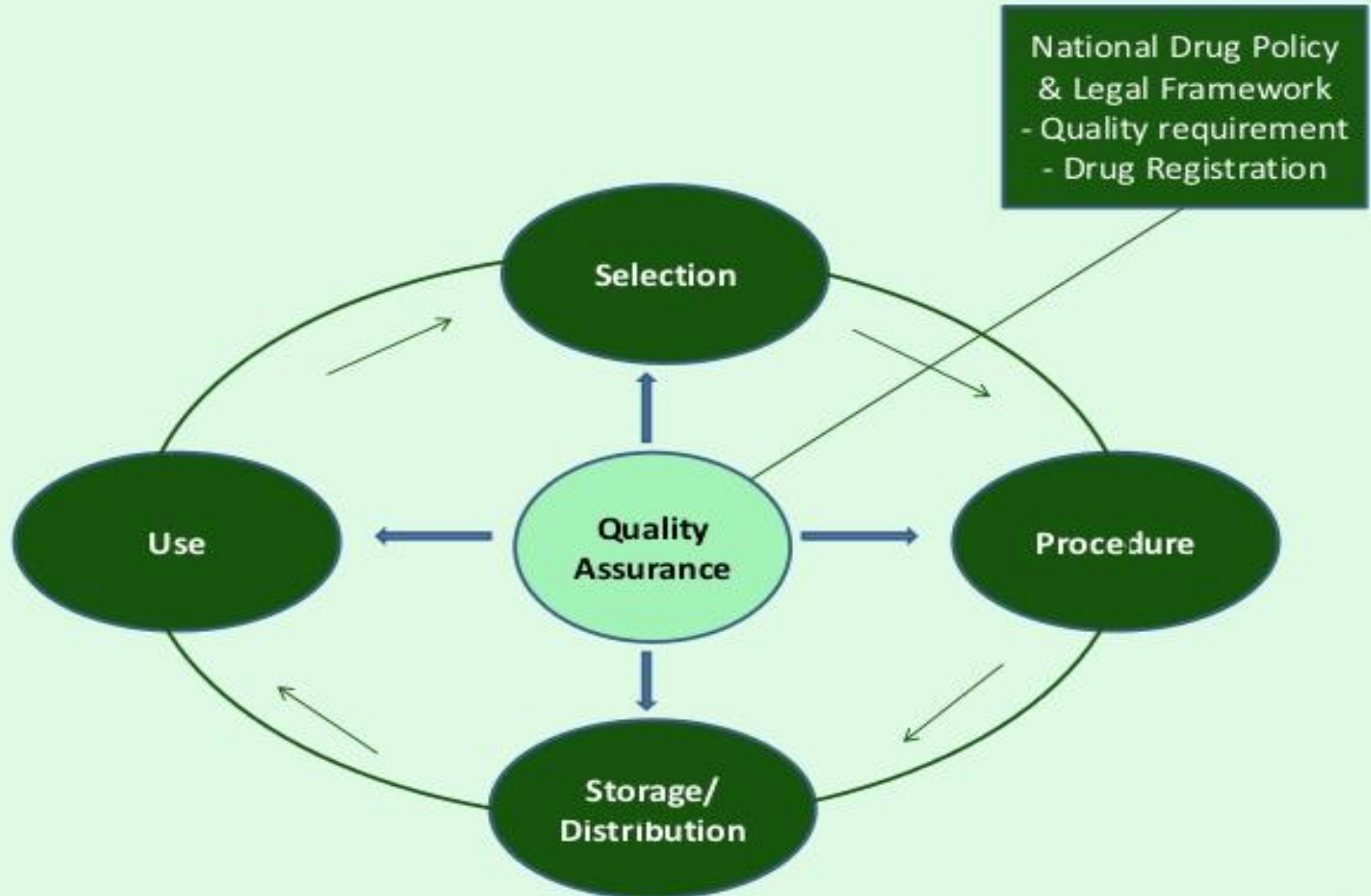
The 5 M's of Quality

- Man
- Material
- Machinery
- Manuals/Methodology (SOP)
- Motivation

QA Activities

1. Technology transfer
2. Validation
3. Documentation
4. Assuring quality of products
5. Quality improvement plans

Flow Sheet-Quality Assurance



Package Engineering

Definition: Packaging is the science, art and technology of enclosing or protecting the Pharmaceutical products.

❖ **Packaging can be described as a coordinated system of preparing goods or transport, warehousing, storage, sale and end use.**

NEED OF PACKAGING

- Physical protection
- Barrier protection
- Agglomeration
- Security
- Convenience
- Dose control

CHARACTERISTICS

- Protection From Environmental Conditions
- Non-reactive With The Product
- Not Impart Taste Or Odor to the Product
- Non-toxic,
- Adoptable To Commonly Employed High Speed Packaging Equipments
- Meet Applicable **Tamper Resistance** Requirements

Packaging basic Types

PACKAGING TYPES:

- **Primary packaging** is the material that first envelops the product and holds it.



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- **Secondary packaging** is outside the primary packaging –used to group primary packages together



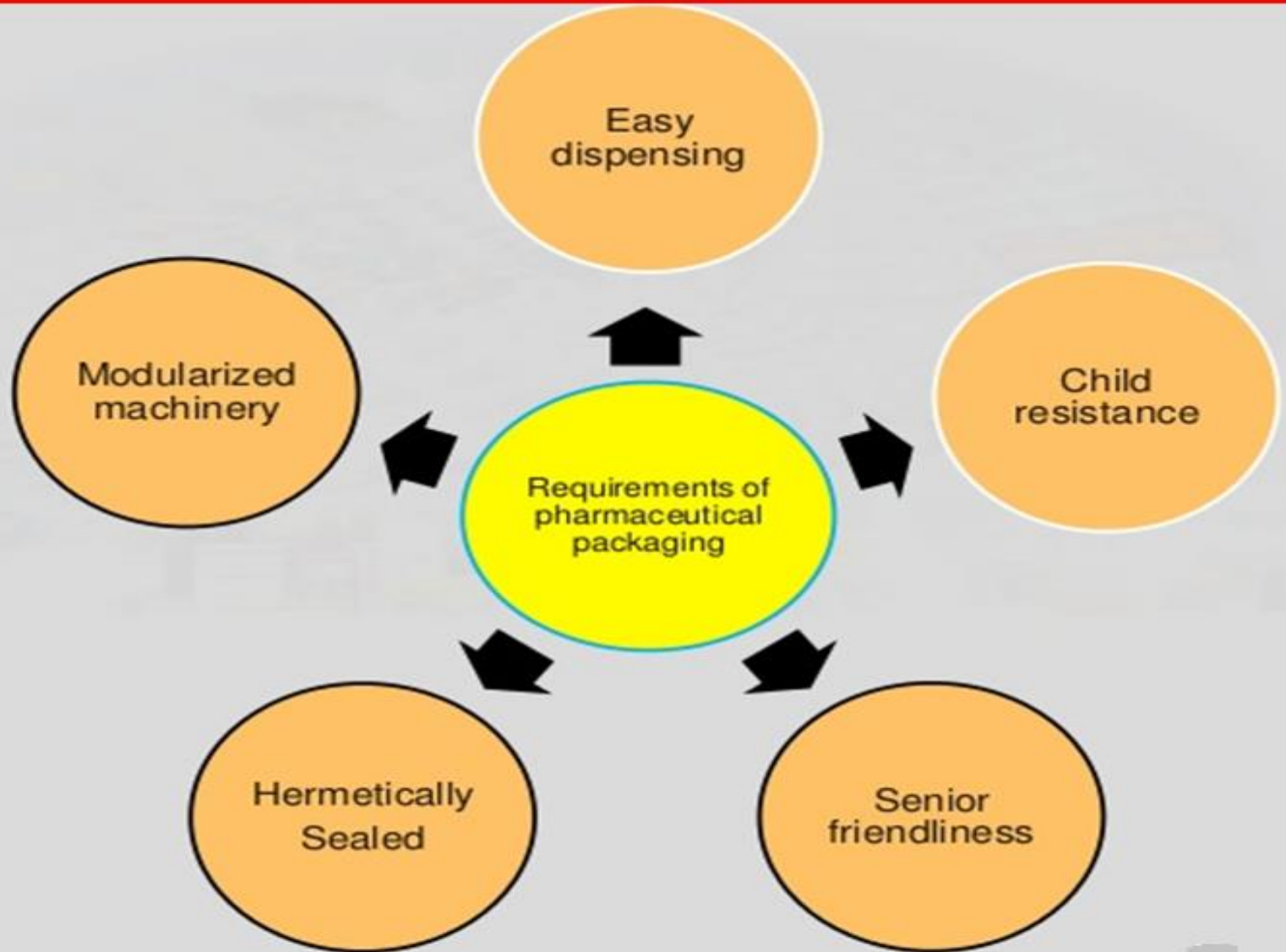
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- **Tertiary packaging** is used for bulk handling, warehouse storage and transport shipping. The most common form is a palletized unit load that packs tightly into containers.



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Requirements of Pharmaceutical Packaging



Major types of Packaging

- Strip packaging (Blister Packaging)
- Bottle packaging

Blister Packaging Materials:

- i) Monolayer PVC
- ii) PVC/PVDC duplex
- iii) PVC/PE/PVDC triplex
- iv) PVC/ChlorotriFluoroethylene
- v) Polystyrene
- vi) Aluminium blister foil

Bottle Packaging Materials

COMMONLY USED MATERIALS:

- Glass
 - type III (solids)
- Plastic
 - low density polyethylene (LDPE)
 - high density polyethylene (HDPE)
 - polypropylene (PP)
 - polyester PET,
 - Cyclo-olefin copolymer (COC)

COMMERCIAL PACK DEVELOPMENT

- **Approach:**

1. Identify Pack Options

2. Material Selection & Testing

3. Development Stability Testing

4. Controls Defined

5. Pack Selection

GLASS

- Widely used.
- **Advantages of glass:**
 - It allows easy inspection of the containers contents
 - variable shapes.
- **Disadvantage of glass:**
 - It is fragile
 - It is expensive when compared to the price of plastic

GLASS COMPOSITION

- Silica (SiO_2) 59-75 %
- Calcium oxide (CaO) 5-12 %
- Sodium oxide (Na_2O) 12-17 %
- Alumina (Al_2O_3) 0.5-3.0 %
- **Other oxide :**
 - Barium oxide (BaO)
 - Boric oxide (B_2O_3)
 - Potassium oxide (K_2O)
 - Magnesium oxide (MgO)

PLASTIC:

LDPE.

- It is a thermoplastic made from the monomer ethylene.
- Density range of 0.910–0.940 g/cm³.
- **Not reactive** at room temperatures, (except by strong oxidizing agents).
- No branching.
- Withstand temperatures of 80 °C continuously.
- Made in translucent or opaque variations.

Testing of Packaging

- ❖ Water vapour Transmission rate
- ❖ Temperature and Relative Humidity
- ❖ Oxygen Transmission rate
- ❖ Blister scan

Analytical Development

Method Development and Validation:

Drug development methods include chromatographic, spectroscopic, “wet-chemical” and modern titration techniques.

Chromatographic analysis:

Liquid Chromatography:

- ❖ UV and Diode Array
- ❖ Mass Spectrometry
- ❖ Refractive Index (RI)
- ❖ Multi Angle Light Scattering (MALS)
- ❖ Fluorescence
- ❖ Conductivity

Gas Chromatography

- ❖ Flame ionization (FID)
- ❖ Flame photometric (FPD)
- ❖ Thermal conductivity (TCD)

Ion Chromatography

❖ Spectroscopic, diffraction and thermal techniques such as NMR, XRD, FTIR and DSC are also applied to assess the chemical and polymorphic purity of both drug substances and drug products.

Thank you

