Pharmaceutical Packaging

- Pharmaceutical materials must be contained, protected and labelled from the point of manufacture to the final point of patient use. Protection is necessary against physical, chemical, climatic and biological hazards. Product quality, safety and stability must be maintained throughout.
- The packaging must also be convenient in use in order to promote good patient compliance.
- Sterile products require effective closure systems to preclude microbial contamination and the pack itself must be capable of withstanding any sterilisation process required.

Manufacturers are responsible for presenting their commercial products in unit packages that will protect the products for their declared shelf-lives. If subsequent repackaging occurs, the responsibility for determining the shelf life of the product in the new pack lies with person who performs the repackaging procedure.
- A knowledge of packaging materials will ensure the adoption of a rational approach to the original choice of container and, if required, to the use of alternative packs.

Terminology

- Single-dose containers: hold a quantity of the preparation intended for total or partial use as a single administration.
- Multi-dose containers: hold a quantity of the preparation suitable for two or more doses.
- Well-closed containers: protect the contents from contamination with extraneous solids and liquids and from loss of contents under ordinary conditions of handling, storage and transport.
- Light-resistant containers: protect the contents from the effects of radiation of wavelength between 290 nm and 450 nm.
The nature and degree of protection required will influence the choice of layers. Cellulose film is clear and transparent conveying a bright appearance; however, it is subject to high moisture permeation. Aluminium is opaque, light-proof and provide good moisture protection but in thin films it is fragile. Paper has a good mechanical strength. Polyvinyl chloride (PVC) gives reasonable protection from moisture; the level of protection can be improved by using a polyvinylidene chloride (PVDC) coating to provide a PVC/PVDC laminate, both give clear films. In all cases polyethylene may be laminated to the other film materials to make heat sealing easier.

Special Types of Pack

- Strip packs:
  Comprise one or more sealed pockets of material, each of which contains a single dose of the product. Types of dosage forms that may be presented in strip packs include tablets, capsules, granules, suppositories, eye drops and (as a large sachets) liquid medicines. The pack is composed of two layers of film or laminate material; the later can be the same (e.g. an all aluminium pack) or dissimilar (e.g. cellulose film and aluminium layer).

- Blister packs:
  Consist of a base layer which contains cavities containing pharmaceutical products, and a lid that is sealed by heat, pressure or both. They are more rigid than strip packs and cannot be used for powders, semi-solids or liquids. Blisters are made on high speed machines and often form the basis of original packs. The base layer materials used in blister packs are similar to those used for strip packs, however, they must be able to withstand thermoformation (e.g. PVC/PVDC, aluminium, PVC, polypropylene (PP), Aclar). The extent of moisture protection afforded by the various materials used in the blister packs can vary widely depending on the methods and equipment used.

Airtight containers:- are impermeable to solids, liquids and gases under ordinary conditions of handling, storage and transport.

Sealed containers:- are containers closed by fusion of the material of the container.

Tamper-evident containers:- are closed containers fitted with a device that reveals irreversibly whether the container has been opened. (e.g. tear band lid, the break band, glue-end cartons, cellophane overwraps for cartons)

Child-resistant containers (CRCs):- are designed specifically to prevent children gaining access to potentially hazardous products.
The material most commonly used for the lid of a blister is aluminium coated with a heat–seal lacquer or laminated with a thin polyethylene membrane on the inside to provide a sealing bond with a base material.

✔ Tropicalised packs:-
Are blister packs that have an additional aluminium membrane sealed over the polymer membrane to provide greater climatic protection against high humidity.

✔ Pressurised packs:-
Expel the product through a valve mechanism, utilising the positive pressure of the propellant, a compressed or liquefied gas, which is contained in the pack. The container used may be metal, plastic or glass. Pharmaceuticals packed in this way include some inhalations, local anaesthetics, foams, creams, and particularly some treatments for asthma. The aerosol canister is fitted with an actuator that when pressed allows the valve to open, releasing the contents through the valve/actuator assembly. This may contain a metering device to provide uniformity of dosage.

There are two types of gas used to pressurise packs; the liquefied gases (e.g. CFCs) and the compressed gases (e.g. argon, nitrogen).
Pressurised packs are costly to produce and disposable can be a problem. However; they protect the product from moisture, light and microbial contamination and they prevent the loss of the volatile components.

✔ Original packs:-
Are commercially produced pharmaceutical packs for finite treatment periods that are intended to be dispensed in their original form. The batch number, expiry date and other manufacturers' information is thus always provided on the dispensed product. The primary container may be a bottle, a strip pack, a blister pack or another form of pack; the packs usually contain a patient information leaflet.
**Packaging Materials**

- **Glass containers:**
  Are particularly useful for liquid preparations owing to their rigidity, their superior protective qualities and their ability to allow easy inspection of the contents. Glass is impermeable to air and moisture, inert to most medicinal products and can be coloured to protect the contents from light of certain wavelengths. Moreover, glass can be sterilised by heat and ampoules can be hermetically sealed by fusion.

- **Plastic containers:**
  Plastic containers are now used for many different types of packs including rigid bottles for tablets and capsules, squeezable bottles for eye drops and nasal sprays, jars, flexible tubes, sachets, strip packs and blister packs. Plastic is a light, mouldable material which is usually very resistant to breakage.
  The plastics used in containers consist of one or more polymers, together with certain additives (e.g. plasticisers, lubricants, anti-static agents, mould-release agents, opacifiers, resins, stabilisers, antioxidants) if necessary.

Major disadvantages include fragility, weight and, for certain types of glass, its ability to release alkali to aqueous contents, especially during heat sterilisation.

There are four types of glass available for pharmaceutical packaging:

- **Type I:** (neutral or borosilicate glass) used for aqueous parenteral preparations.
- **Type II:** (treated soda-lime glass) also used for some aqueous parenteral preparations.
- **Type III:** (soda-lime glass) only used for non-aqueous parenteral preparations or for powders for injection.
- **Type IV:** (general purpose soda-lime glass) used for non-parenteral products.

Polymer materials used in pharmaceutical packaging include HDPE, LDPE, polypropylene, polystyrene, and poly (ethylene terephthalate) (PET). The selection of certain plastic type depends on the requirements of a pharmaceutical manufacturer for certain product.
**Metal containers:**

The collapsible metal tube, used for pharmaceutical ointments and creams, is made from aluminium. Rigid metal tubes, made from tinplate or aluminium, are mainly used in pressurised packs. The inner surface is coated with an epoxy resin or other suitable layer to provide product protection from the base layer.

Aluminium foil is used in strip and blister packaging. Laminates of aluminium foil with other film substrates adds strength to the relatively fragile aluminium component, which is used for its moisture barrier effect.

**Closures:**

Provision of an effective seal is the fundamental requirement of any closure system. The product content must be effectively contained and ingress of external substances must be prevented.

Closures for pharmaceuticals in bottles may take the form of:

1. **Threaded screw caps:** they may be child resistant or tamper-evident. They may be made from tinplate or aluminium. They may also be made from plastic, either a thermosetting or a thermoplastic material.

2. **Push-on or plug type closures:** are usually formed from thermoplastic materials. They often provide a better overall seal against the entry of moisture vapour than the traditional screw cap closure.

3. **Rubber stopper:** used for multidose injection vials and lyophilised preparations. The main advantages of rubber are its ability to reseal itself after penetration by a needle and its ability to withstand heat sterilisation. Rubber is also used in eye drop bottle closure and as a plunger in syringes. Rubber may be natural, butyl, or silicone.

- **Partial sleeves over the bottle neck and closure or full length sleeves over the majority of the container body and the closure provide a tamper-evident system.**

- **The types of child-resistant containers (CRCs) most often used pharmaceutically include push-down and turn caps and squeeze and turn caps.**

- **Metered-dose pump sprays are used for aerosols and for nasal sprays. Nasal sprays are typically based on plastic push-on or threaded screw closures.**
• **Labels and leaflets:**

Labelling is a critical aspect of the packaging operation. Overprinting of batch details and expiry information is now often done on-line using ink-jet or laser printing methods. The majority of labels used in pharmaceutical packaging are paper based. Information for the patients about their medicines may come in form of separate patient leaflets or patient support packs.

Critical print on labels, leaflets, and cartons can now be automatically checked on production lines using image scanning systems.

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