Packaging

Fig. 9.1 Metric medicine bottle.

9.4 Glass vial.
Introduction

• Why should you be aware of packaging?
  ✔ Packaging of extemporaneous preparations.
  ✔ Repackaging of bulk medicines.

The expiry date of the repackaged medicines must not exceed 12 months unless justified for longer periods.
Introduction

The container must:

• Maintain the quality, safety and stability of the medicine.

• Protect the product against:
  ✓ physical damage,
  ✓ chemical and microbial contamination,
  ✓ light, moisture and oxygen as appropriate

• Be user friendly, easy to open and reclose.

• Other factors such as cost and the need for both child resistant closures and tamper –evident seals.
Each container is labeled with the:

• Identity and quantity of the medicine.
• Batch no.
• Appropriate storage instructions.
• Product expiry date
• Requirements for handling and storage.

Limitation of repackaging: e.g.

• glycercyl trinitrate tablets...... volatile drug.
• Sterile products; not always possible.
Primary and secondary packaging

1. Primary packaging: Which are in direct contact with the product (bottle, closure, blister.....).

Primary containers must:
• Protect the medicine from damage and from extraneous chemical and microbial contamination.
• Support use of the product by the patient.

Primary containers must NOT:
• allow product leakage,
• chemically react with the product,
• release components
• uptake product components.
Primary and secondary packaging

2. Secondary packages:

Are additional packaging materials that improve the appearance of the product and include outer wrappers or labels that do not make direct contact with the product. Also can also supply information about the product and its use. They should provide evidence of tampering with the medicine.
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<th>Type</th>
<th>Examples of use</th>
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<td>Glass</td>
<td>Primary</td>
<td>Metric medical bottle, ampoule, vial</td>
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<tr>
<td>Plastic</td>
<td>Primary</td>
<td>Ampoule, vial, infusion fluid container, dropper bottle</td>
</tr>
<tr>
<td>Plastic</td>
<td>Secondary</td>
<td>Wrapper to contain primary pack</td>
</tr>
<tr>
<td>Board</td>
<td>Secondary</td>
<td>Box to contain primary pack</td>
</tr>
<tr>
<td>Paper</td>
<td>Secondary</td>
<td>Labels, patient information, leaflet</td>
</tr>
</tbody>
</table>
Terms of containers

• **Single-dose containers** hold the medicine that is intended for single use. e.g. glass ampoule.

• **Multidose containers** hold a quantity of the material that will be used as two or more doses. e.g. multiple dose vial or the plastic tablet bottle.

[Image of various medical containers]

[Image of a sterile glass vial]

Terms of containers

• **Well-closed containers** protect the product from contamination with unwanted foreign materials and from loss of contents during use.

• **Airtight containers** are impermeable to solids, liquids and gases during normal storage and use. If the container is to be opened on more than one occasion it must remain airtight after re-closure.

• **Sealed containers** such as glass ampoules are closed by fusion of the container material.
Terms of containers

- **Tamper-evident containers** are closed containers fitted with a device that irreversibly indicates if the container has been opened.

- **Light-resistant containers** protect the contents from the effect of radiation at a wavelength between 290 nm and 450 nm.

- **Child-resistant containers**, commonly referred to as CRCs, are designed to prevent children accessing the potentially hazardous product.
Terms of containers

- **Blister packs** are composed of a base layer, with cavities that contain the pharmaceutical product, and a lid. This lid is sealed to the base layer by heat, pressure or both. They are more rigid than strip packs and are not used for powders or semi-solids. Blister packs can be printed with, day and week identifiers to produce calendar packs. These identifiers will support patient compliance.

[Image of blister packs]

Terms of containers

- **Tropicalized packs** are blister packs with an additional aluminum membrane to provide greater protection against high humidity.

- **Strip packs** have at least one sealed pocket of material with each pocket containing a single dose of the product. The pack is made of two layers of film or laminate material. The nature and the level of protection that is required by the contained product will affect the composition of these layers.
Terms of containers

• **Original packs** are pharmaceutical packs that are commercially produced and intended for finite treatment periods.

• **Pressurized packs** expel the product through a valve. The pressure for the expulsion of the product is provided by the positive pressure of the propellant that is often a compressed or liquefied gas.
The selection of packaging for a pharmaceutical product is dependent on the following factors:

- The nature of the product itself: its chemical activity, sensitivity to moisture and oxygen, compatibility with packaging materials
- The type of patient: is it to be used by an elderly or arthritic patient or by a child?
- The dosage form
- Method of administering the medication
- Required shelf life
- Product use, such as for dispensing or for an over-the-counter product.
Packaging materials

Glass

Glass is the preferred packaging material. Glass does have several advantages:

• It is inert to most medicinal products,
• Impervious to air and moisture,
• It allows easy inspection of the container contents,
• It can be colored to protect contents from harmful wavelengths of light,
• Easy to clean and sterilize by heat,
• It is available in variously shaped containers.
Packaging materials

Glass

Disadvantages of glass:

• Fragile: glass fragments and cracks
• Expensive in comparison to plastic.
• Heavy (transport cost)
• Certain types of glass release alkali into the container contents,

The chemical stability of glass for pharmaceutical use is given by the resistance of the glass to the release of soluble minerals into water contacting the glass. This is known as hydrolytic resistance.
Packaging materials

Glass

Type I glass:

Composition: Neutral glass, borosilicate glass (silica (silicon dioxide, SiO₂) and boron oxide).

Advantages:
• It possesses a high hydrolytic resistance.
• It is the most inert type of pharmaceutical glass.
• It has the lowest coefficient of thermal expansion (and hence suitable for sterilization by heat.....for ampoules and vials).

Disadvantages:
• It has very high glass transition temperature so needs complicated processing.
• And therefore expensive.

Uses:
• Type I glass is suitable for packing all pharmaceutical preparations.
• It is widely used as glass ampoules and vials to package fluids for injection.
• In contrast to the other types of glass (type II and III), this type has no/little amounts of basic oxides, so it is used to package solutions that could dissolve basic oxides in the glass.
Packaging materials

Glass

Type II glass

**Composition:** soda-lime-silica glass.

Soda (Na$_2$CO$_3$) is used to decrease the glass transition temperature of silica. However, soda would increase water solubility of silica, so lime (CaO) is used to increase the hydrolytic resistance. This type would also contain other oxides.

**Advantages:**

- This glass has a lower melting point than Type I glass. It is thus easier to produce and consequently cheaper.
- High hydrolytic resistance due to surface treatment of the glass.

**Uses:**

- Type II glass used to package aqueous preparations.
- However, as it contains basic oxides, it is **not** used to package parenteral formulations with a pH <7 (i.e. acidic); this would increase the pH of the formulation and could affect the drug stability and potency.
- It is the glass used to produce containers for eye preparations and other dropper bottles.
Packaging materials

Glass

Type III glass

**Composition:** soda-lime-silica glass: It has a similar composition to Type II glass but contains more leachable oxides.

**Properties and uses:** Type III glass offers only moderate resistance to leaching and is commonly used to produce dispensary metric medical bottles. It is also suitable for packaging non-aqueous parenteral products and powders for injection.
Packaging materials

Glass

Types of glass containers

Bottles:
These are either amber metric medical bottles or ribbed (fluted) oval bottles. Both types is supplied with a screw closure.

Amber metric medical bottle are used for packaging a wide range of oral medicines.

Ribbed oval bottles are used to package various products that should not be taken orally; this includes liniments, lotions, inhalations and antiseptic solutions.

Containers for Parenteral products:
Small-volume parenteral products, such as subcutaneous injections, are typically packaged in various containers made of Type I glass. Glass ampoules for single use, Multiple-dose vials for more than one use.
Ribbed oval bottle.

Fig. 9.1 Metric medicine bottle.
Packaging materials

Glass

Types of glass containers

Jars:
Powders and semi-solid preparations are generally packed in wide-mouthed cylindrical jars made of clear or amber glass.

Dropper bottles:
Eye drop and dropper bottles for ear and nasal use are hexagonal-shaped amber glass containers fluted on three sides. They are fitted with a cap, rubber teat and dropper as the closure.

http://www.amazon.co.uk/GLASS-AMBER-BOTTLE-DROPPER-PIPETTE/dp/B003ODUKBY
Packaging materials

Plastics

Two classes of plastics:
Thermosets (screw caps) and Thermoplastics.

The advantages of plastics for packaging:
1. Release few particles into the product
2. Flexible and not easily broken
3. Are of low density and thus light in weight
4. Can be heat sealed.
5. Are easily moulded into various shapes
6. Suitable for use as container, closure and as secondary packaging
7. Cheap.
Packaging materials

**Plastics**

**The disadvantages of plastics are:**

1. They are not as chemically inert as Type I glass
2. Some plastics undergo stress cracking and distortion from contact with some chemicals
3. Some plastics are very heat sensitive
4. They are not as impermeable to gas and vapor as glass
5. They may possess an electrostatic charge which will attract particles
6. Additives in the plastic are easily leached into the product
7. Substances such as the active drug and preservatives may be taken up from the product.
<table>
<thead>
<tr>
<th>Plastic polymer</th>
<th>Properties</th>
<th>Uses</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-density polyethylene (LDPE)</td>
<td>Soft, flexible and easily stretched.</td>
<td>Squeeze bottles as eye drop bottles.</td>
<td>Disadvantages of PE (LDPE and HDPE): •Softened by flavoring agent and aromatic oils, •Unsuitable for packaging oxygen sensitive products, •Adsorb antimicrobial preservative agents, •Crack on contact with organic solvents.</td>
</tr>
<tr>
<td>High-density polyethylene (HDPE)</td>
<td>Strong, stiff, less permeable to gases than LDPE.</td>
<td>Bottles for solid dosage forms</td>
<td></td>
</tr>
<tr>
<td>Polypropylene</td>
<td>Strong and stiff, good resistance to cracking when flexed</td>
<td>Used for closures with hinges. Used also for tablet containers and IV bottles</td>
<td></td>
</tr>
<tr>
<td>Polyvinyl chloride (PVC)</td>
<td>Rigid</td>
<td>Laminate (for blisters) and the main constituent of IV bags.</td>
<td></td>
</tr>
<tr>
<td>Polystyrene (PS)</td>
<td>Clear, hard, brittle with low impact resistance.</td>
<td>Used for tubes and amber-tinted bottles. It is also used for jars for ointments and creams with low water content.</td>
<td>Its use in drug packaging is limited due to its high permeability to water vapor</td>
</tr>
</tbody>
</table>
• Closures
• Collapsible tubes
• Unit dose packaging (blister, strip)
• Paper
• Patient pack dispensing
Storage and stability of medicines

Medicines DO NOT keep indefinitely. Some can be kept for only a short time. There are 6 general causes for the limited time for which medicines can be kept and these are:

• Loss of drug (such as hydrolysis or oxidation).
• Loss of vehicle (such as evaporation of water or other volatile ingredients).
• Loss of uniformity (such as caking of a suspension or creaming of an emulsion).
• Change in bioavailability (particularly with tablets where ageing van reduce availability).
• Change of appearance (such as colour changes).
• Appearance of toxic or irritant products (as a result of a chemical change).
General notes for storage and expiry date

- Storing in a cool place means 8-15 °C, in a refrigerator means at 2-8 °C.
- Expiry date is the date after which the medicine should not be used. The expiry date is calculated from the shelf life at the time of preparation.
- Shelf life is normally the time that a medicine can be kept before the potency has fallen to 90% of the original.
- Shelf life for manufactured products is based on accelerated stability studies (Arrhenius plot).
- The shelf for extemporaneous preparation may be found in an appropriate monograph, if available. If no monograph is available, the product is labeled with as short an expiry date as possible.
- Freshly prepared is defined as prepared no more than 24 hrs before issue.
- Recently prepared is defined as discarded after 4 weeks.
Shelf life

Log scale

\[ t = \frac{2.303}{K} \log \frac{C_0}{C_t} \]