improve the product's security from pilferage and deliberate contamination and safeguard the product's legitimate user. Ideally, packs would be completely tamper-proof, though this is probably impossible to achieve against determined malice.

The primary pack must be compatible with the product, and take nothing out of the product and add nothing in. Drug absorption or adsorption into the pack would reduce product potency, while chemicals leaching out of the pack and into the product could induce drug degradation. In addition, the primary pack must protect the product against atmospheric factors, such as extremes of temperature, light, moisture, oxygen, carbon dioxide, particulates (e.g. dust, dirt), as well as biological hazards, such as microorganisms, insects and rodents, and enable product stability.

Drug molecules can undergo chemical reactions triggered by light, heat, moisture, or atmospheric gases, such as oxygen (see Chapters 48 for more details). For example, light can provide the energy necessary for a drug isomer to change its configuration. Protection from light is usually achieved by using an opaque or amber-coloured container. Oxygen can cause drug degradation via oxidation. Carbon dioxide can dissolve in the water in unbuffered aqueous products, and lower their pH by forming carbonic acid. Water can cause drug degradation via hydrolysis. Moisture gain into a product can also cause dilution of liquid products, wetting of solid products and an aqueous environment can support microbial growth. Solvent loss from a product can also occur if the container is permeable. Secondary packs also contribute to protection against atmospheric factors to some extent, although their major role is to provide protection against mechanical hazards, such as shock (e.g. when dropped), compression, vibration, abrasion, puncture, etc., during handling, storage and transport.

Closures

A closure is a device – e.g. stopper, lid, top or cap – which is used to close a container, and is an integral part of the pack. The word 'pack' therefore covers both the container and the closure. Without the latter, the functions of a pack, such as containment, presentation, protection and convenience, cannot be fulfilled, and like the container, the closure must be inert, compatible with the contents, and protect the latter against environmental hazards, such as oxygen, light, moisture, etc.

Certain closures must maintain sterility, e.g. in multi-use parenteral vials. A good seal between the container and the closure prevents anything from leaking out or gaining access into the pack, and is obtained by a snug fit between the inner face of the closure and the external face of the container finish. Resilient liners inside the closure are sometimes used to achieve a snug fit, although many plastic closures are internally moulded to achieve a good seal and are liner-free.

The closure has to be user-friendly, allow easy opening to legitimate consumers and be easy to reclose (for multi-unit packs), as well as child-resistant, tamper-resistant and tamper-evident. Closures may also include dispensing devices, e.g. a pump on bottles containing creams. The outer surface of the closure may also be ribbed to allow good grip when opening by twisting. Pharmaceutical closures are mostly made of plastic (thermosets and thermoplastics), although metal is also used, e.g. on parenteral vials.

The word 'closure' does not always refer to a stopper-type device. Metal tubes have two closures – a cap at one end while the other end of the tube is sealed by folding and crimping. Flexible packaging, such as pouches, sachets and blister packs do not contain a closure as defined above. They are instead sealed by heat and/or pressure, or with adhesives, and are non-reclosable packs.

Packaging materials

Once the function(s) of the desired packaging has been defined, selection of the primary packaging material is the first step in the packaging process, and takes into account the dosage form, the route of administration, drug/product stability, need for terminal sterilization and for visual inspection of the packaged medicine, patient compliance and convenience, aesthetics, cost, environmental-friendliness, etc. Liquids, which are in constant intimate contact with the primary pack, as opposed to solids such as tablets and capsules, require greater quality from a pack in order to 'take nothing out of the product or add nothing in'.

Injectable liquids require even greater quality from the pack compared to oral liquids, to maintain sterility and freedom from other possible contaminants, such as extraneous particulates. Medicines which are terminally sterilized in their final packs need to be made from materials that can withstand the sterilization procedure.

Semi-solids need to be able to be dispensed from the container, under slight pressure, e.g. squeezing of a tube. Drugs which are sensitive to atmospheric