



PACK PERFECTION

THE PILLARS AND PITFALLS
OF BLISTER PACKING

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Blister packaging is one of the preferred methods for packaging pharmaceutical products today. In order to ensure the effectiveness of the blister pack, it is essential that careful consideration is given to the key stages of pack development, as well as potential pitfalls.

INTRODUCTION

Blister packaging has become one of the preferred methods of packaging pharmaceutical products, second only to plastic bottles, and made up 17% of the entire pharma packaging market in 2010. With its popularity continuing to rise, early adoption of the blister pack could enable manufacturers and the clinical trial sector to create a process model that can be maintained throughout the entire product lifecycle.

The growing trend towards blister packs is undoubtedly due to their ability to fulfil all the critical aspects of pharma packaging: uniformity, purity, integrity, safety and stability. Careful consideration should be given to these aspects at each stage of the pack design and development process. By focusing on four key pillars of good blister packing practice – material selection, package design, equipment and quality control – the following discussion serves as a guide to initialising blister pack development in any setting, and highlights potential pitfalls to avoid.

PILLAR 1: MATERIAL SELECTION

Selecting the appropriate materials is essential in producing the perfect blister pack. The water vapour transfer rate (WVTR) and oxygen vapour transfer rate (OVTR) of a blister pack is especially important. The chosen materials will need to provide a sufficient barrier to ensure the stability and shelf life of the specific product. And although there is a myriad of materials to choose from, in general, material choice should be dictated by the WVTR and OVTR requirements of the packaged product.

BASE MATERIAL

The best barrier material is cold formed foil (CFF) as it offers a barrier of nearly 100% from both oxygen and water, allowing the manufacturer to offer extended shelf life. Figure 1 shows the comparative barrier properties of different packaging materials and shows that CCF has a WVTR of virtually 0g/m²/day at 38°C/90%RH, while a standard mono PVC is at the other extreme, with a WVTR of 3.1g/m²/day at 38°C/90%RH.

However, there are also a number of disadvantages to

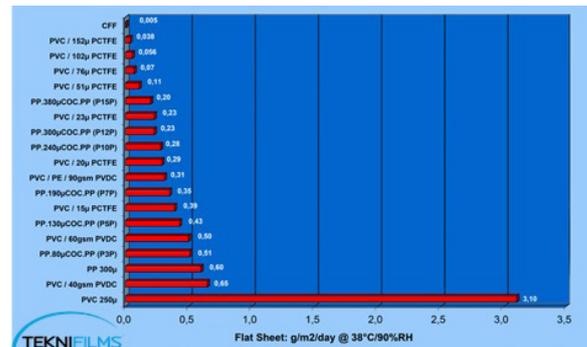


Figure 1: TEKNIFILMS - WVTR of materials

CFF. The cost, in particular is arguably the highest of all blister packing materials available. Furthermore, the footprint of the blister is considerably larger than packs made from other materials, impacting portability, shelf space requirements and, inevitably, distribution costs. In addition, the cold forming process is slower than other methods, thus the throughput of the production line is reduced. These factors, along with the non-transparency of the material, are some of the more prominent issues with CFF.

The recent introduction of high barrier polymers, such as polychlorotrifluoroethylene (PCTFE) and the next generation polyvinylidene chloride, has helped to bridge the gap between the conventional, low-cost thermoform materials and CFF. One of the main advantages of these high barrier laminates is the reduction in overall package size. The ability to form the cavity at a tighter angle produces smaller blister pockets and a tighter nested blister, helping to reduce shipping costs and shelf space in the pharmacy.

Inevitably, when selecting the base material, the manufacturer will have to compromise between cost, blister size and protection level.

LIDDING MATERIAL

The choice of lidding material is also very important in creating the perfect blister pack and depends on the application. Lidding foils normally fall under one of three types (see Table 1):

Push Through

The most cost-effective and readily available lidding material – this comes in a variety of thicknesses (15-20 micron being the most common) and the aluminium can be soft or hard tempered. This type of foil is usually selected where the blister pack is not required to be child-resistant.

Peelable

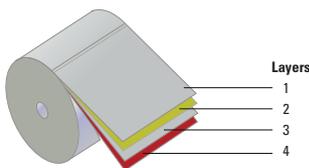
Peelable material is also a commonly used type of lidding foil, and comes in a variety of thicknesses. The aluminium is normally soft tempered and is usually selected when the product contained requires a child-resistant, yet elderly-friendly pack.

Peel-Push

This type of lidding foil is used where the pack is required to be child-resistant, yet elderly-friendly, and has the added benefit of providing extra security with regards to product access. It comes in a variety of thicknesses and the aluminium is normally soft tempered.

Table 1: Lidding material construction

Layers	Lidding type			
	Push through	Peelable	Peelable	Peel-push
1	Lacquer	Paper	Polyethylene terephthalate (PET) or paper	Paper
2	Aluminium	PET	Soft aluminium	PET
3	Heat seal lacquer	Soft aluminium	Heat seal lacquer	Peelable layer
4		Heat seal lacquer		Soft aluminium



PILLAR TWO: PACKAGE DESIGN

The blister pack design process requires considerable thought in order to ensure stability and shelf life of the product it contains.

Cavity design is a critical element, not only in its ability to protect the product from transport and handling damage, but also to protect against ingress of water and oxygen.

A well-designed cavity should have an even material thickness to help maintain the required protection

level as this is fundamental in helping to uphold the barrier, as well as the physical properties of the form. There are two key elements in the blister design which will guarantee a good material distribution of cavities: draw ratio and blister geometry. The following considers these elements for thermoform materials and Figure 2, part A, illustrates a good thermoformed pack.

DRAW RATIO

Draw ratio is vital in maintaining an effective barrier. As a rule of thumb, a draw ratio less than two will typically produce a pocket with good draw characteristics.

$$\text{Draw ratio} = \frac{\text{Form width}}{\text{Form depth}}$$

A ratio greater than two can cause the material to stress and stretch above acceptable levels, thus causing Problems with the form. Figure 2, part C shows an example of a cavity with a large draw ratio.

BLISTER GEOMETRY

There are a number of practical guidelines to follow to improve the formability of a thermoformed blister pocket:

Draft Angle

If possible, a minimum draft angle of 5° should be used (7° if using PCTFE laminates). Figure 2, part B, shows an example of bad draft angle.

Edge Fillet

A minimum fillet radius of 0.5mm will help the material flow into the pocket. A radius larger than this will cause the material flow with even greater ease.

Base of Pocket Geometry

Square-based pockets should be avoided where possible as spherical bases typically perform better. Similarly, a corner radius should be used with a minimum radius of 1mm on the base. This will also improve material flow.

It should be noted that CFFs have different characteristics in respect to draw ratio and blister geometry. For example, draw ratios for CFF are generally smaller, and cavity wall geometry ideally involves multiple draft angles.

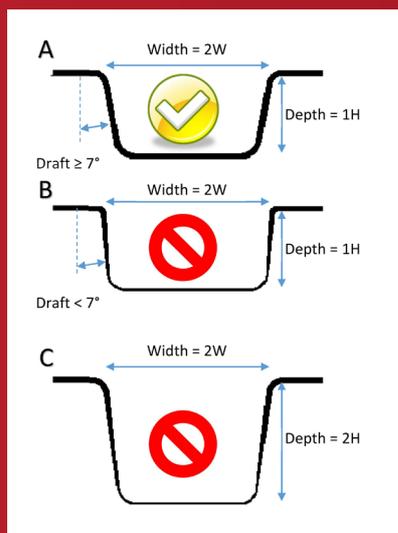


Figure 2: Examples of good and bad pocket designs. Part A demonstrates an example of a good cavity design. It shows a good draw ratio and draft angle leading to an even material distribution throughout the cavity profile. Part B provides an example of a bad cavity design. It demonstrates an overly aggressive draft angle, which has caused the thinning of the material/barrier at the base of the pocket. Part C shows an example of a bad cavity design. A bad draw ratio has caused thin material distribution at the base of the pocket

PILLAR THREE: EQUIPMENT

Once suitable materials have been selected and an appropriate design has been created, it is vital that the correct equipment is sourced to produce the blister. This is a complicated and time-consuming process but, briefly, some of the aspects that need to be taken into account include:

FORMING

The manufacturer should investigate in detail various elements and features of specific equipment in relation to their product and blister pack. For example, when looking at thermoforming equipment, the following elements of the forming process should be scrutinised:

- Preheat type (contact or non-contact)
- Preheat length (different materials have different requirements)
- Shrinkage of material post-forming (different materials behave differently post-forming)
- Chilling

SEALING

The sealing operation on most modern packaging lines falls into one of two categories: platen type or rotary type seals. Each has very different sealing characteristics (see Figure 3).

Rotary sealing type machines typically run at higher speeds than the intermittent platen type, and usually seal in a shorter time and at a lower pressure. This type requires a

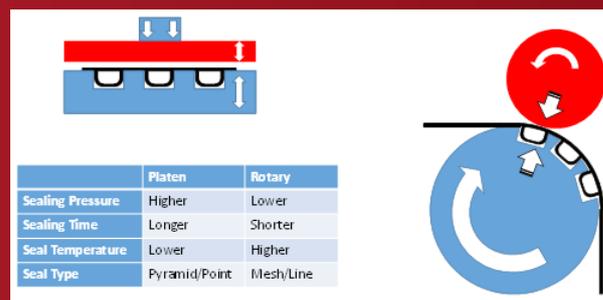


Figure 3: Comparison of intermittent platen sealing (left) and rotary sealing process (right)

higher seal temperature and a different knurl design to achieve effective pocket closure.

Meanwhile, the intermittent platen type requires a higher sealing pressure and longer sealing time than the rotary seal machine, but tends to use a lower seal temperature because of these longer dwell times. This type is most commonly seen in the clinical trial setting as it is more suitable for smaller batches than the rotary type.

PILLAR FOUR: QUALITY CONTROL

Once the blister pack goes into production, it is vital that what looks like the perfect blister on paper becomes, and remains, a perfect blister in reality.

To ensure the quality of the blister, every packaging process has a number of checkpoints where the quality of the materials and blister can be assessed. These include pin holes detection, print and cut registration, and final package integrity testing.

A package integrity test is often viewed as the most important step in the process check, as this is often the only time the completed blister is tested. This test is used to ensure the strength of the seal, check for channels/capillaries in the seal, and look for defects in the material caused during the packaging process.

There are a number of destructive and non-destructive package integrity tests available that range in sensitivity, technology and cost. These include blue dye, helium trace gas, force decay and laser/vision deflection. The most widely adopted method by pharmaceutical manufacturers is the traditional blue dye test, due to its low cost and ease of implementation. However, it is messy, subjective and wasteful, which has encouraged many manufacturers to look towards more technologically advanced options.

PACK PERFECTION

To develop and maintain the perfect blister pack that will provide uniformity, purity, integrity, safety and stability, while remaining cost-effective, requires careful consideration of the four pillars. Fundamentally, the manufacturer must take into account the patient, the product stability and the product application, as a blister pack can only be considered ideal if it fulfils the functions dictated by these elements.