

**Honeywell Aclar® Films**



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## **Blister Packaging of Oral Solids – Challenges for the Pharma Industry and Patient Implications**

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## Abstract

This paper considers the challenges facing the pharmaceutical industry in implementing a blister packaging strategy that: protects advanced solid oral drug delivery systems from physical or chemical degradation; creates market advantage through product globalisation; and enhances the effectiveness of therapy for patients. It looks at how companies are leveraging production and marketing value through ultra high barrier films within thermoform solutions such as Honeywell Aclar® films.

High barrier blister packaging technology offers opportunities for process rationalisation. This technology also provides a pathway to market oral solid drug therapies that are more effective and the ability to package emerging solid dosage forms that are moisture, oxygen and/or even light sensitive.

## Introduction

Over the past 40 years, blister packs have been adopted globally by the pharmaceutical industry because of the flexibility in design and high productivity that the process delivers for the packaging of oral solids.

The inherent unit dose concept provides visual and haptic evidence of the number of doses taken, making it easy for patients to follow their therapy by swallowing an oral dosage. It is a comfortable and a familiar means of taking medication – and is one of the main reasons why the majority of marketed medicines have been presented as tablets and capsules over many decades.

Looking at companies' drug development pipelines, it can be noted that the absolute number and the

percentage of oral solids in those pipelines versus other dosage forms is declining. At the same time, the number of oral solid drugs requiring high to ultra-high barrier protection to maintain stability and achieve shelf life targets is growing substantially. Today it is harder than ever before to develop a solid oral formulation that can be marketed in blister packs without having a sufficiently high level of barrier protection.

As demonstrated in this white paper, primary packaging choices and pack design have significant implications on pharmaceutical stakeholders and patients, and may supplement efforts in drug formulation.

# Trends in Oral Delivery

## **More sophisticated drug formulation technology**

For drug substances to work they need to be absorbed within the body, otherwise they pass through the gastrointestinal tract and are excreted without causing any pharmacological effect. For the growing number of poorly soluble drug substances it is a challenge to arrive at a viable formulation. Reducing drug particle size down to submicron level is the first and most critical step to enhancing dissolution rate. Efforts to enhance solubility include changing the physical form by either adopting a less stable polymorph or the amorphous phase of a given API. Most often, the drug release profile is controlled with the aid of hydrophilic polymers. For example, third generation solid dispersions consist of finely dispersed drug particles that are embedded in polymeric carriers aided by surfactants. Obviously, from a packaging perspective, without moisture barrier protection the hydrophilic polymers may absorb water during storage and become prematurely plasticized. This affects the physical stability and - in turn - the performance of the entire formulation. With the decrease of drug particle size, the affective surface of all drug particles in the dosage is greatly enhanced; therefore if the drug molecule exhibits a moisture or oxygen-sensitive chemical group the likelihood for chemical degradation is increased. As a result, both pharma and drug delivery companies are increasingly looking to blister packaging made from high or ultra-high barrier films because they enable a consistent performance of the drug product and maintain product integrity during the targeted shelf-life.

## **Growing number of life-cycle management (LCM) projects**

Numerous LCM projects focus on reducing the frequency of drug administration with an anticipated gain in patient compliance and improved treatment outcomes. Modified Release (MR) formulations such as Controlled Release (CR) or Extended Release (ER), Fixed Dose Combinations (FDCs) and Oral Dispersible Tablets (ODTs) are the most prominent categories. It is observed that nearly every drug product launched in these LCM categories was in blister packs made from some level of high or ultra-high moisture barrier films.

## **Bigger dosages sizes resulting in bigger packs**

Tailoring the drug release profile quite often results in bigger dosage sizes due to the elevated amounts of high performance excipients and API required for a viable formulation. The same holds for any efforts to enhance drug dissolution rate by creating sub-micron drug particles, as this involves a greater increase in the overall drug surface requiring higher amounts of excipients to be matched. Similar arguments apply for FDCs and low potency APIs. Dosages are getting significantly bigger as are pack sizes. It is well known that most people with a chronic condition prefer small packs as they enable discretion, portability and convenience. Ironically, packs that are too bulky may even compromise patient compliance efforts in drug delivery (i.e. MR).

## **Beyond moisture sensitivities**

Quite a few formulations consist of APIs that are not only moisture sensitive but also exhibit sensitivities to oxygen and/or light. Drug products containing vitamins are often found in blister packages made with multi-layer films that provide either a combination of moisture and oxygen barrier or even moisture, oxygen, and light barrier.

# Blister Packaging Criteria – The Industry Drivers

## Globalization

A growing number of drug products are now marketed globally. In many cases the barrier protection of primary packaging used in moderate climatic zones is not sufficient in the hot and dry or hot and humid regions. Consequently, high and ultra-high moisture barrier films such as Aclar® films are growing in adoption and are outperforming the mid and low barrier categories in terms of number of oral solids launches.

## Complexity reduction

Establishing a limited number of agreed “first intent” primary packaging standards has become common practice within many pharmaceutical companies. Key selection criteria for primary packaging materials include the capability to offer stability in all climatic zones and to meet the needs of both marketing and packaging operations stakeholders. Additionally, there are ongoing efforts to reduce complexity by limiting the number of agreed variants down to a select few in order to drive both a reduction in cycle time and in the analytical costs inherent in parallel stability testing. The downstream benefits for packaging operations are gains in operational equipment efficiency (OEE) via faster change-overs, easier site transfer projects, and overall economies of scale.

## Reduction of cost of goods

Moreover, the productivity targets for packaging operations are getting more ambitious year by year. Increasing output with existing manufacturing facilities or meeting production budgets with lower capital expenditure are key drivers. As a result, packaging processes and equipment are selected with regards to achieving significant reductions of Cost of Goods (CoGs).

## Gains in pack sustainability

A growing number of pharmaceuticals companies have defined a sustainability strategy that achieves demonstrable reductions of consumed energy and waste, particularly with regard to packaging. This results in a concerted effort to introduce smaller and slimmer packs.

## Prevention of medication errors

Many oral solid brands are available in more than one tablet or capsule strength. Proper colour coding of the outer carton and /or potential colour differences in the dosage itself combined with clear blister packaging films has proven to be helpful in the effort to prevent medication errors.

## Child Resistance

Designing packages that are difficult for a child to open while also being easy for the user to open, in particular the elderly, remains a challenge. Although there are now numerous blister packaging solutions available that are both child resistant (US 16 CFR 1700-F=1 standard) and ‘senior-friendly’, companies continue to dedicate time and effort to creating a package that meets all requirements.

# Blister Packaging Criteria – The Patient Benefits

A high percentage of prescribed drug therapies do not achieve optimum outcomes for simple reasons like patient forgetfulness. To compensate, pharmaceutical companies are looking to maximize the benefits of oral therapies to better match users' lifestyles.

In addition, there is a high likelihood that a patient who experiences packaging-related issues during his/her therapy will not adhere to it and consequently will not enjoy optimum treatment outcomes. This greatly affects

longer-term therapies as the physician may not be inclined to refill the prescription, resulting in a lost patient from a brand owner's perspective. In the meantime there is a growing acknowledgement among brand managers of prescription medicines that the pack design itself can add to more successful therapies resulting in better treatment outcomes and higher revenues. A highly successful and well known example of this is Pfizer's Z-Pak® wallet, which is an antibiotic packaged in a pre-regimented unit-dose format.

## High-Barrier Packaging Choices

There are various pack presentations available that meet the functional requirement of providing high moisture, oxygen and light barrier protection. This includes amber glass bottles with metal-screw caps; multi-layer HDPE bottles; Cold Formed Foil (CFF) blisters; and blister-packs made from high barrier thermoforming films.

High barrier thermoforming and cold forming are the most dominant packaging technologies for moisture-sensitive oral solids outside the United States.

CFF will continue to be an option for the stability testing of formulations that are highly sensitive to moisture, oxygen and light.

Aclar® films laminated with PVC as well as PVdC-coated PVC are the most prevalent polymeric films used in thermoformed blister application. Aclar films exhibit the highest moisture barrier at any given thickness of the

barrier film layer. If oxygen barrier is needed there are solutions available that include an additional polymer such as EVOH or even PVdC. The high and ultra-high barrier film ranges start at Aclar film thicknesses of 51 micron and PVdC-coating weights of 120g.

The benefits common to all polymer-based thermoforming films are summarized as follows:

- Small blister footprint compared to CFF – even at big tablet and capsule sizes. For very large tablets and capsules, a reduction of blister footprint up to 65% can be achieved – the average is about 55%.
- Gains in user acceptance as they enable patient's discretion, portability and ease of dose extraction.
- Reduction in material use, from forming film to lid-stock and carton board – up to 60%.
- Reduction in energy use and carbon footprint – up to 25%.
- Gains in productivity on blister packaging lines – up to 200%.

## Conclusion

Value creation in drug delivery has traditionally focused on developing advanced solutions that meet the unmet needs of patients. Achieving better treatment outcomes has an impact on society as a whole: patients and their families live longer together and enjoy a better quality of life; social systems can plan for lower costs for acute care and assisted living; employers benefit from lower absenteeism rates; and physicians can provide better care and support for patients. There are growing efforts of pharmaceutical companies to enhance treatment effectiveness and improve outcomes under real life conditions of patients – outside of controlled clinical trial settings.

## About Author

Dr. Thomas Dries is member of Honeywell's Global Healthcare and Packaging team. In his role as Market Development Manager for Europe, Thomas promotes the values of Honeywell's high moisture barrier Aclar® films for key stakeholders in pharmaceutical companies.

In June 2003 Thomas was elected as Chairman of the Healthcare Compliance Packaging Council of Europe. He was re-elected in 2007.

## About Honeywell

Honeywell Specialty Materials is a global leader in providing customers with high-performance specialty materials, including fluorine products; specialty films and additives; advanced fibers and composites; intermediates; specialty chemicals; electronic materials and

Blister packaging has become a more important piece in this equation than ever before. Thermoforming films are enablers for optimizing blister pack designs more holistically, with decisions based on understanding and meeting patient needs, while at the same time offering opportunities for significant productivity gains in packaging operations. The success story of polymer-based films for blister packaging will continue, particularly as a result of the new generation films that provide global packaging solutions for advanced drug delivery systems.

Thomas is a polymer physicist by education. He spent more than 15 years in various R&D roles, mainly in the area of polymer films, and more than 10 years in Marketing of films for the packaging of foods and medicines.

chemicals; and technologies and materials for petroleum refining and petrochemical production.

For more information on Aclar® films please visit: [www.aclaradvantage.com](http://www.aclaradvantage.com)

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