Top Five Enemies of Blister Packaging

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Introduction

There are five threats to the integrity of a blister package: temperature, time, humidity, UV light, and oxygen. Each one of these "enemies" represents a major decay mode for a drug product, an obstacle to be overcome before eventual consumption. Theoretically, all five can be controlled with good technical data and a high-performing blister package, but things can (and often do) go awry when theory meets practice.

FDA Quality by Design principles can act as core guidance in product design and understanding, including identification of critical material attributes (CMAs).

Background

Real-world challenges in packaging loosely group into two overlapping approaches: one approach is to over-package to be sure of hitting shelf-life requirements, while the other camp guesses at the required packaging and takes their chances. Both approaches suffer problems that are indicative of the changing times: for starters, overpackaging has lost favor as both industry and lawmakers pivot towards environmentally friendly alternatives that reduce waste and inefficiency. Meanwhile, members of the second camp fail to meet quality demands, causing them to default to the first approach, or in the worst case, suffer packaging failures.

These scenarios are avoidable by starting with FDA Quality by Design (QbD) core principles as guidelines to create packaging solutions that are neither overkill nor inadequate but well suited to the task. Instead of falling back on the most intensive solutions, such as cold form foil (CFF), the preferred approach is to make an informed decision, driven by data and backed by QbD core principles.

Time

The first enemy of product stability is time. One of the most promising advances in tackling this challenge is the incorporation of technology into packaging. New smart packaging for food can accurately calculate the expiry due to the proliferation of microbes and send the information to a smartphone, using a tag that costs about 2 cents. The same technology can be applied to medicine and is expected to be part of a $60B industry by the end of 2022.

Moreover, placing sensors in packages allows monitoring inside warehouses, enabling a better understanding of drug quality within the rows and stacks. This translates to more efficient management of stock, faster turnover, and better time-sensitive decisions—without sacrificing quality.

Temperature

Temperature is already being monitored for some drug products and APIs before they reach the consumer. Temperature sensors on pallets may become unnecessary when sensors are incorporated at the level of individual blister packs. Details collected by increasingly small devices could easily pinpoint parts of shipments that have frozen or overheated, removing the need to discard entire shipments in the case of temperature excursions.

Smart temperature monitoring could be a major cost-saver in the case of sensitive and expensive medications. Not just a win for manufacturers, the technology could alert consumers to temperature excursions after the product has reached their hands. A blister pack that can report to its owner that it was left in a hot car too long can help prevent the ingestion of ruined medication.

Humidity

Humidity is a key factor because it influences moisture vapor transmission rate (MVTR), the parameter most likely to cause unacceptable penetration of water through blister packs, potentially causing degradation. In some situations, the excipients or delivery system may be compromised instead, as tablets meant to function as a slow-release delivery mode swell, soften, and release the API faster than intended.

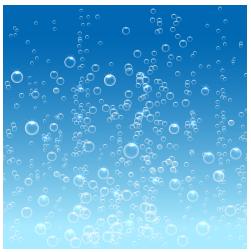
Problems resulting from moisture diffusing through the film can usually be targeted through the proper selection of moisture barriers. Monolayer films manufactured from PVC, polyester, or polypropylene, offer a basic level of moisture vapor protection that can be adequate for less sensitive materials and extremely cost-effective. Multi-layer barrier films can be used for more sensitive products. Multi-layer structures often include PVdC coatings or laminations made with Aclar® films to provide a diffusion-resistant barrier. The choice of barrier material and thickness is determined by the results of stability studies and can target a specific market (i.e. thicker Aclar® films can handle tropical Zone 4 environments). Underneath the Aclar® or PVdC is usually a base layer of PVC or polyester that provides structure and support to allow processing on common form/fill/seal equipment. Together, these measures can prevent hydrolysis from becoming an issue.

UV Light Transmission

UV light transmission is another decay mode that must be addressed for successful product delivery since many drugs are degraded by exposure to wavelengths under 400 nm. Fortunately, UV light protection is relatively straightforward, with several good choices available. Films can deliver varying degrees of light protection derived from UV absorbers and pigments used in the base film of a multilayer structure or within a single monolayer film.

In some cases, adequate protection can provide by coloring the granules used during film production or from a UV protection additive applied during the production of PVC intended for films. Many engineers will default to the information contained in USP 671 (Container Performance) to determine their requirements. A film with a single "food-approved" UV absorber combined with an amber pigment will typically meet USP 671 requirements and will sufficiently attenuate the percentage of light transmission.

Oxygen Transmission



Oxygen transmission rate (OTR) is an area where the need for an effective barrier in packaging has gained attention since many drugs suffer degradation and loss of efficacy through oxidation. Combinations of multiple-layer films that provide protection are often compositionally similar to those mentioned above for moisture protection. PVdC-coated films offer good mid-range oxygen protection, while laminated films with EVOH layers are becoming more common in pharmaceuticals.

These films tend to work well when designed in a manner to protect EVOH from losing its oxygen barrier when ambient moisture rises. Multi-layer structures that use Aclar® to protect the EVOH from moisture allow EVOH to protect the drug from oxygen. These types of barrier films pose a sophisticated engineering challenge, since achieving the desired outcome relies on selecting a base film that machines well and follows QbD principles, while utilizing effective layer arrangements to deliver the functionality needed to prevent degradation of the drug. That can be a lot to juggle when trying to develop a simple, cost-effective blister pack.

Conclusion

When it comes to drug product development strategies, meeting the highest standards of pharmaceutical packaging is crucial. Gone are the days of passive packaging. Far more is required than what meets the eye: packages need to protect drug content, degrade quickly in the environment, actively inform consumers, and even provide feedback to material handlers and manufacturers who want to know about their fate downstream.

Rondaxe can help guide you through the development and challenges of your blister package. We understand the intricacies of this process and we have experience on all sides of the equation when it comes to drug production, packaging, and distribution. We'll help you find a solution that balances your needs and ensures safe, reliable delivery to patients.