

## Successful Pharmaceutical Packaging The Right Approach to Calculating Your Protection Needs

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Pharmaceuticals are subject to a variety of degradation pathways that compromise drug safety and shelf-life. By far the greatest degradation is caused by hydrolysis and oxidation. However, other mechanisms include racemization, photodegradation, elimination, and complexation. A number of active packaging components are available to help maintain pharmaceutical integrity; however, determining the optimal solution requires a calculated analysis that joins the expertise of packaging engineers and pharmaceutical formulation chemists.

Sorbents such as desiccants and oxygen absorbers represent a class of active packaging components that can be used to guard against the effects of degradation. These ensure the integrity of packaged pharmaceuticals.

Sorbents are considered “active” because they respond to changes in the headspace of packaging relative to outside conditions. Packaged sorbents are manufactured from silica gel, molecular sieve, and a variety of oxygen-absorbing compounds.

Active sorbents have high adsorbing capacity and take up little space. When incorporated successfully into a package, they can significantly reduce the rate of degradation, resulting in an improvement in pharmaceutical quality, safety, shelf-life, stability, and usability.

Sorbents come in different delivery formats, including canisters and packets, as well as a new compressed density format. Determining the

correct active formula requires manufacturers to consider a variety of factors.

### Modeling Moisture and Oxygen Ingression

To optimize package protection for solid-dose formulations, pharmaceutical manufacturers need to employ moisture and oxygen ingress modeling techniques to analyze the rates of degradation for a given pharmaceutical. The rationale behind modeling is based on a number of factors. Oxidative changes can cause a loss of pharmaceutical potency after several weeks, whereas two to three years of shelf-life may be required depending on distribution channels. Modeling also determines steady-state levels of oxygen within bottles, moisture permeation across bottle walls and material permeability.

Ingress modeling provides a calculated moisture or oxygen ingress value using established Moisture Vapor Transmission (MVTR) and Oxygen Transfer (OTR) rates. MVTR and OTR rates are applied to the proposed package and, with the inclusion of other sources of moisture or oxygen, are used to determine the appropriate amount of sorbent material to be used.

Desiccant and oxygen absorber requirement calculations rely on interdependent dynamic modeling, which judges the interaction of package permeability with the adsorption and de-sorption

properties of the pharmaceutical formulation.

Ingress modeling results and related sorbent product recommendations allow packaging engineers and formulation chemists to quickly understand what their theoretical sorbent requirement will be for a proposed package. It also allows them to demonstrate these findings using a



small-scale, “proof-of-concept” accelerated stability test.

Ingress modeling requires specialized equipment as well as skilled analysis by people experienced in packaging challenges and analytical chemistry. It is crucial to find a packaging solutions provider proficient in both of these areas of expertise.

### Examining the Whole Process

When shaping a degradation-prevention program, it is also critical that manufacturers consider the *whole* manufacturing process. What might work in one part of the operation may not work at another end - solutions determined upstream may have unintended consequences downstream.

For example, ingress modeling may propose a two-gram unit sorbent that does not fit into the neck of a proposed pharmaceutical bottle. Another critical consideration is the type of automation found in a packaging line. A sorbent format may not work at high speeds with certain automated equipment. Other times, a “double drop” of sorbents may be required, depending on the bottle dimensions, or the pharmaceutical.

An active packaging solution must consider all parts of the manufacturing process, from the pharmaceutical formulation to the packaging environment and to the distribution chain. When developing the optimum package protection, the best approach to take is a multi-disciplinary one that considers the knowledge and experience of packaging engineers, formulation chemists, analytical chemists, and the sorbent supplier.

### Consider Changing Protection Strategies

Pharmaceutical manufacturers often assume that it is time consuming and expensive to change strategies once an active packaging protocol has been established and approved. This is not typically true. In fact, changing course may significantly streamline operations and improve product quality, and often can be more cost-effective. The most time-consuming aspect of switching strategies is finding out what needs to be done.

Current FDA guidance has made changing desiccant, or oxygen absorber, formats a relatively simple procedure. Often it is a simple matter of an annual reporting change. It is important; however, to

work with a packaging partner who understands the regulatory roadmap. All products should be 21 CFR-compliant and supported by a Type III Drug Master File (DMF) on file with FDA.



Protecting pharmaceuticals from degradation is important to ensure commercial success. When used appropriately, active packaging is an important part of the complete solution. As with any evolving technology, a change may appear daunting but can, in fact, improve operations. The bottom line is to consider the whole gamut of factors involved in pharmaceutical degradation, and every aspect of upstream and downstream processing. Calculating these factors with a modeling system, supported by a knowledgeable partner, can lead to a more shelf-stable, and safer, product.

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