

New Drug Applications Demand Intelligent Sorbents

Novel formulations and drug-delivery systems require optimized packaging protection.

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Dropping a sorbent into pharmaceutical packaging is the traditional approach for preventing product damage from moisture and maintaining shelf life and product efficacy. However, new formulations and packaging configurations, coupled with the ever-present pressures to speed new drugs to market, are requiring that sorbents become intelligent. Rather than simply serving as a moisture absorber, sorbents need to fill the role of environmental managers. They need to provide a specific range or steady-state level of protection to pharmaceutical packaging that is increasingly taking different, more-innovative shapes.

An intelligent sorbent is designed to provide a specific management outcome. It could control the level of moisture, oxygen, and/or hydrocarbons in the package. A sorbent might be used to maintain a specific humidity range to maintain a drug's stability, or reduce or eliminate volatilized hydrocarbons. In some cases, it is necessary for a sorbent to carry out multiple protective functions.

Given that the pharmaceutical landscape has been changing rapidly, packaging solutions are required to become more innovative. For instance, dry-powder inhalers (DPIs) are a relatively new addition to the market—and they have specific sorbent needs. New devices in development are changing the format of the sorbent itself, requiring in some cases that it be customized

and incorporated into a packaging design much earlier in the process.

Another important trend to note in this marketplace is the rise of generics. Manufacturers need to be aware of intelligent sorbent solutions as they

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work to meet packaging protection needs for a variety of formulations competing with those that are coming off patent.

A NEW ERA OF UNSTABLE FORMULATIONS

Many new drugs coming onto the market are based on chemistries that were in preclinical discovery stages years ago but abandoned because at the time, the drug chemistries were considered too unstable. Thanks to new formulation and packaging technologies, some of these molecules are being reintroduced into drug product formulations that can be tested clinically and eventually marketed in commercial packaging presentations.

These formulations are putting

increasing pressure on the packaging engineers who are charged with keeping them stable. These engineers increasingly need to work with formulation chemists to understand the specifics of the compounds they are packaging. The standard tools at their disposal—traditional desiccant products—may no longer satisfy all of their package-protection needs.

In most cases, the goal of a sorbent is to prevent chemical and/or physical degradation from taking place within a pharmaceutical package. An aggressive and active sorbent that dries an environment works well for some drug formulations because it reduces molecular mobility and inhibits the chemical and/or physical reactions that can lead to product degradation. However for an increasing number of formulations, overdrying can degrade a drug product as well; for example, the aqueous base coating on the surface of a tablet may begin to crack. For gelatin capsules in particular, over-desiccation can cause physical and aesthetic damage. In these cases, aggressive moisture management can cause serious problems.

OXYGEN ABSORPTION, HYDROCARBON MANAGEMENT, AND MOISTURE CONTROL

For solid-dose drugs subjected to oxidative and moisture-mediated degradation, sorbents can be customized to perform the role of specialty oxygen absorbers. They can be

developed to eliminate oxygen from the packaged environment while managing free moisture and maintaining a specific equilibrium relative humidity (ERH) in the package. This is critical to ensuring the integrity of drug compositions requiring management of both oxygen and moisture.

An important function of the modern-day sorbent involves hydrocarbon management. Residual solvents used while synthesizing drug substances or active pharmaceutical ingredients can form volatilized hydrocarbons that end up in the bottle's headspace. This produces a noxious odor that must be removed through the use of activated carbon. In these instances, an intelligent sorbent can be tailored to perform the dual function of removing odors while maintaining moisture control.

It is important to determine the type of hydrocarbon management needed for a particular product, as this will determine an intelligent sorbent's configuration. For example, a sorbent made from a specific type of molecular sieve could be configured to function as a hydrocarbon scrubber, which removes formaldehyde. Sorbent functionality also depends upon the specific need. In some cases, it may be necessary to remove hydrocarbons but to retain water molecules, in which case a sorbent must be constructed so that it does not overdesiccate a product.

THE CASE OF DRY-POWDER INHALER SYSTEMS

An increasing number of new pharmaceuticals and medical devices have unique environmental-management needs. These include transdermal patches or combination products with an electrical component that needs protection from corrosion caused by volatilized hydrocarbons. A range of such similar applications can be successfully stabilized using a moisture-regulating (to a specific ERH) oxygen absorber that also absorbs volatilized

hydrocarbons.

An example of intelligent sorbents can be seen in the special requirements for new respiratory drug-delivery systems, such as DPIs. A reservoir-style DPI might meter out drug doses from a central chamber, or the medication may come in the form of individual, premeasured doses, whereby each dosing format incorporates a separate sorbent.

For dry-powder formulations, a moisture-management system is needed to prevent the drug product from becoming hydrated and the particles agglomerating, or clustering together. The potency and stability of the particles must be maintained so that the air-flow dispersion of the drug is accurate and consistent. A simple sorbent consisting of silica gel or molecular sieve may lead to overdrying, reducing the relative humidity of the container holding the powder down to a very low percentage. This excessively dry state could promote static charge of particles when dissimilar materials in a device (e.g., plastics and foil) come in close proximity. The triboelectrification that might result could compromise the performance of the DPI device by reducing the amount of drug product that is inhaled.

An intelligent sorbent can be configured within a DPI system to regulate moisture to a more desirable range, depending on the specific chemistry of the product and application requirements. The sorbent can also be tailored to device design; an example could be a compressed-solid format, incorporating a blend of silica gel and carbon-based compounds, that is fitted into a molded cavity of the device.

SORBENT STRATEGIES REQUIRE EARLY PLANNING

As manufacturing increases for generic drugs, more companies are

facing numerous formulations with different stability challenges that require intelligent sorbents. A one-size-fits-all approach to packaging protection is not a viable strategy. This is also true for the new drug formulations and new delivery technologies coming onto the market. A significant number of resources go into packaging, and without careful planning and consideration of all the factors required for protecting a drug, the result may be a product with compromised stability.

A sorbent packaging strategy must be intelligent, and it must be optimized based on the specific application. It must consider the product, its chemistries, delivery system, required shelf life—essentially the entire life cycle of a product from manufacturing to end use. It's a common mistake to assume a sorbent's function is simply to absorb or adsorb excess moisture, or that the answer to an unstable chemical compound is simply to insert additional sorbents into a package. Though most often sorbents are inserted into packaging at or near the end of the packaging line, the choice of sorbent strategy cannot be an afterthought.

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