

Sorbent Technology Embraces QbD and Modeling

MULTISORB'S ADRIAN POSSUMATO ADDRESSES NEW TECHNOLOGIES IN SORBENTS AND DESICCANTS AND HOW PACKAGING SOLUTIONS ARE CHANGING TO MEET INDUSTRY NEEDS.

By Michele V. Wagner, Senior Digital Editor

AT THIS year's Interphex show in New York, we caught up with Adrian Possumato, global director, healthcare packaging of Multisorb Technologies, to discuss the company's latest sorbent and desiccant technologies and how the industry is moving towards QbD-driven packaging.

PhM: *How are the needs of the industry changing in terms of packaging solutions using sorbents and desiccants?*

A.P.: We're seeing an increased use of sorbents (i.e., desiccants, oxygen absorbers, hydrocarbon absorbers) and intelligent sorbents, which are designed to provide a specific management outcome by controlling the level of moisture, oxygen, and/or hydrocarbons in pharmaceutical packaging.

Some of the factors driving the trend are:

New Chemical Entities. The R&D pipeline isn't as robust as it was 10 years ago. Drug substances that were shelved years ago due to significant chemical instability are getting a second look due to the more advanced drug formulation and sorbent technologies available.

New Formulation Technologies. In the case of some solid oral dose products, proprietary sustained-release, targeted-release, rapid-release, and tamper-resistant formulation technologies are being employed for both new and existing drug substances. Many of these products have very specific chemical and physical stability challenges, which can be addressed through the use of sorbent technology.

Drug/Device Combination Products. In the case of certain dry powder inhalers and active transdermal drug delivery systems, incorporation of intelligent sorbents is essential to ensure both physical and chemical stability of not only the products' primary shelf life, but also

throughout consumer use.

Generic Drug Products. While the patents for many drug substances are expiring, separate patents governing the use of specific drug product formulation additives are still valid. Without the use of these stabilizing additives, the drug product can suffer significant chemical degradation sometimes involving multiple degradation pathways. Except for amorphous drug substances, aggressive moisture management can reduce chemical degradation.

Combination Drug Products. We're seeing a number of combination drug products where two drug substances are combined in a single dosage form. As one would suspect, these formulations can be quite complex and often require very specific sorbent functions. Multifunctional intelligent sorbents can be used for such formulations.

Additionally, we are noticing that more manufacturers are considering the use of sorbent technologies earlier in the development process. This change is propelled by the availability of value-added services such as pseudo-empirical modeling, which predicts the stability outcome of a

drug product susceptible to moisture and/or oxygen degradation under given conditions.

PhM: *How does pseudo-empirical modeling and stability testing ensure effective drug packaging?*

A.P.: Pseudo-empirical modeling simply takes the guesswork out of the equation. Very often, formulation chemists hit a roadblock in trying to achieve the required chemical or physical stability profile of their drug product formulation. They rely on package engineers to incorporate sorbent technologies in clinical or commercial packaging to help make the difference between the actual



DESICCANTS

and desired stability outcomes.

Pseudo-empirical modeling involves the use of empirically-derived measurements of the drug product, its packaging, and our sorbent to predict a specific moisture or oxygen management outcome in the drug product and packaging headspace under accelerated or RT stability conditions. In the case of moisture, we use our validated SimulSorbSM modeling program to predict the equilibrium relative humidity (ERH) in the package headspace and drug product free moisture level for the desired shelf-life. Often this information alone allows the formulation chemist to determine if a stability solution has been attained. However, one can predict degradation through further stoichiometric calculations in the manner in which free moisture induces the chemical degradation pathway(s) is known.

Similarly, our SimulOxSM service provides an approach for the management of oxygen in pharmaceutical packaging. For example, maintaining the stability of a drug product formulation requires controlling the oxygen concentration in a pharmaceutical package's headspace over time.

PhM: What are the biggest challenges and risks when dealing with the hydrocarbon management of sorbents?

A.P.: We have observed that hydrocarbons in a drug product package are often the result of the volatilization of residual solvents used during the organic synthesis of the drug substance or related to the chemical degradation or interaction of some packaging materials. While this can sometimes relate to a drug product stability issue, the goal of hydrocarbon management is usually odor control. However, in some instances we've been challenged with removing moisture and oxygen while allowing a specific volatilized hydrocarbon to remain in the package headspace. This is where multifunctional intelligent sorbents have proven to be effective when preceded by the use of our SimulSorb and SimulOx pseudo-empirical modeling programs.

PhM: How do the SimulSorb and SimulOx services help companies maintain compliance?

A.P.: Our SimulSorb and SimulOx pseudo-empirical modeling services are used to predict stability outcomes of a drug product through its primary and often secondary (consumer use) stability profiles. It is said that knowledge is power, and predicting a moisture- or oxygen-management outcome to directly or indirectly forecast a stability outcome of a drug product is extremely useful for many areas of a pharmaceutical manufacturer's business.

Additionally, the same knowledge is very useful in all areas of compliance especially with sorbent handling procedures during commercial packaging operations.

PhM: Is there any time-savings using the SimulSorb and SimulOx service for sorbent ranging studies? Any cost-savings?

A.P.: The SimulSorb and SimulOx pseudo-empirical modeling services typically save our customers 6-12 months of development time by eliminating costly and time-consuming sorbent ranging (stability) studies. Saving development time translates into earlier regulatory filing, review, approval, and market launch.

Because the market rewards the first to arrive, these services offer improved cash flow to our customers, especially in cases where companies have been struggling for years to arrive at a drug product stability solution.

PhM: How did you develop your QbD Calculations through Operations program for your sorbent systems?

A.P.: Our QbD Calculations through OperationsSM program is designed to help pharmaceutical companies identify and incorporate the right sorbent solution to preserve the efficacy of their drug products. It involves two basic components:

Calculations refer to the use of our SimulSorb/SimulOx pseudo-empirical modeling services. It involves integrated mathematical modeling using empirically-derived measurements of the specific drug product, its packaging, and our sorbent/intelligent sorbent product. This process is critical in helping companies determine the right sorbent solution for their products.

Operations imply the use of our sorbent and/or intelligent sorbent product solutions with industry-standard dispensing machinery for a turn-key implementation at the clinical and commercial packaging operations level. This part of the program results in the integration of the identified sorbent solution to the manufacturer's product packaging.

We are effectively providing turn-key, downstream operations solutions as established with the upstream, R&D calculations.

PhM: How important do you think incorporating QbD standards into your packaging technology is within the industry?

A.P.: I think the industry is at the point where the use of a QbD program like *Calculations through Operations* is a must as it serves as the bridge between the formulation development and package engineering groups and the package engineering and packaging operations groups.

In a very competitive, resource-limited pharmaceutical industry that has far fewer drug product candidates now than previous years doing it right the first time through QbD is essential.