

CASE STUDY:

Beyond the Package: Use of Active Material Science Solutions to Solve DPI Challenges with Moisture Ingress and its Impact on Delivered Dose and Particle Size Distribution

Situation

Inhaled drug delivery systems face unique stability challenges that need to be managed in order to meet label claim dosages and improve patient compliance. For dry powder inhalers, keeping the powder formulation dry is a key element to controlling build up of the powder in the delivery channel and maintaining the integrity of the API. A leading developer of inhaler devices and dry powder formulations came to Aptar CSP Technologies with a unique problem that went beyond keeping the formulation in their reservoir-based DPI dry. Once the inhaler was removed from its original packaging, the multi-dose DPI needed maintained environmental protection and precision moisture control that was not attainable with standard desiccant solutions.

Challenge

Like most dry powder inhalation systems, the drug product using this device was sensitive to moisture. However, the API was also sensitive to over drying, which meant that the developer needed a solution to keep RH levels within a specific range both during storage and use life. The specifications required two years of shelf life with at least three months of use life for the multi-dose system. The RH needed to be below 20% but more than 10% during storage, and not above 50% during use. The solution had to account for 120 patient uses that exposed the API to an ambient environment for 20 seconds per dose. This required a solution that could not only maintain a consistent but low RH over the course of multiple doses, but bring the environment back to the precise RH conditions required after ambient environment exposure within two hours (Figure 1). Traditional desiccant solutions were unable to provide the precise microclimate needed to protect the efficacy of the API.

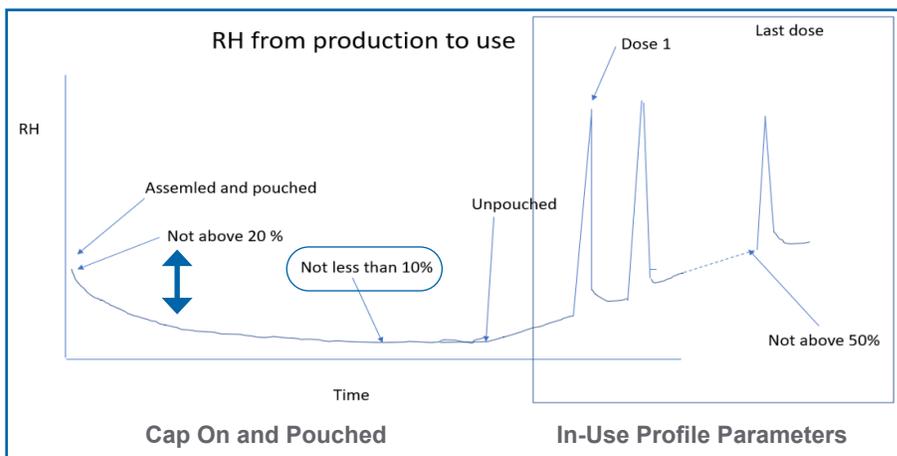


Figure 1: Sponsor RH Specifications

Solution: Active Material Science Technology

Aptar CSP Technologies' active material science solutions deliver a proven, customizable and seamlessly integrated method for protecting sensitive products in the pharmaceutical and drug delivery device industries. The company's proprietary Activ-Polymer™ platform technology has the ability to incorporate single or multiple chemistries into a polymer solution that retains the performance of the chemistries while maintaining the physical properties of the polymer. This offers tremendous manufacturing flexibility as the polymer can be extruded into a film, injection molded or blow molded, and even melted into a liquid like compound.

In this application, Aptar CSP co-developed an integrated solution with the customer, developing an injection molded active component to replace an existing plastic part in the dry powder inhalation device (Figure 2). The Activ-Polymer™ material was custom formulated to adsorb tailored amounts of moisture at a controlled rate to deliver the precise microclimate needed to protect the API within the device, without impacting the device design.

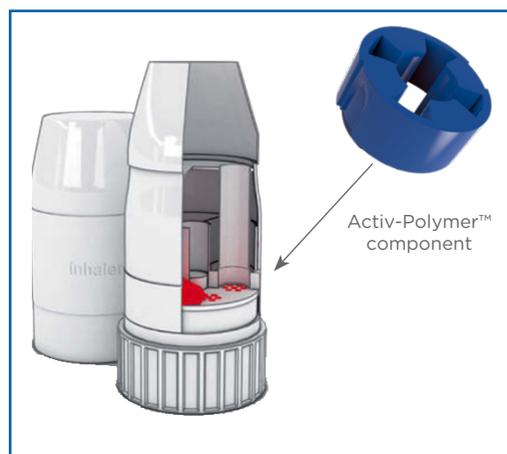


Figure 2: Rendering of DPI cross section and custom Activ-Polymer™ component to replace current plastic part

Selection of 3-Phase Activ-Polymer™ Formulation:

In order to choose the right formulation for this project, Aptar CSP first studied the behavior of various actives to meet kinetic requirements. Device samples with and without Activ-Polymer™ material were placed in a climatic chamber set to 30°C/80% RH to compare performance. The samples with no desiccant protection at all allowed the RH% to increase to over 40% after 14 days, which will negatively impact the API's stability. Those with Activ-Polymer™ material delivered acceptable results, but required fine tuning of the formulation to meet the specific target RH% range the sponsor required.

DATA REVIEW:

Custom Formulating Activ-Polymer™ Material for Precision Microclimate Protection Over Time

Once the proper active was selected, Aptar CSP needed to determine the proper formulation for this use case. CSP measured the moisture adsorption kinetics of five different 3-Phase Activ-Polymer™ formulations, capturing the RH adsorption weight gain as a function of time (Figure 3). Formulation 4 delivered a solution that can quickly adsorb and release moisture, adsorb 100mg in 2 hours without any pre-loading, and act as a buffer to maintain the necessary RH inside the DPI in the required time. Studies determined that in order to control the RH in the packaging during shelf life (2 years) between 10% and 20%, the Activ-Polymer™ component needed to be pre-loaded with a defined amount of moisture. Several studies were performed to evaluate the amount of moisture pre-loading. Sample A (low pre-loading) of Formulation 4 was determined to maintain the desired specifications (Figure 4). This formulation was co-molded into an active component that replaced a plastic part in the device, seamlessly integrating the protective technology.

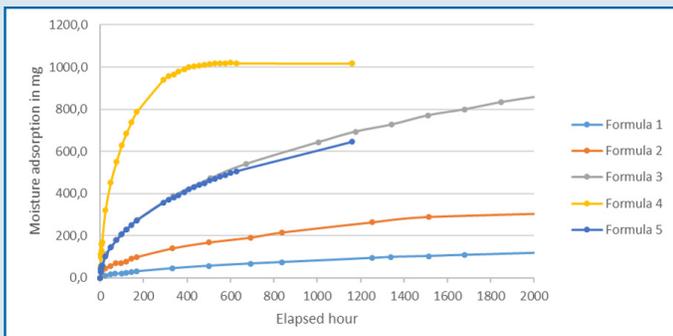


Figure 3: Moisture Adsorption Kinetics of 3-Phase Activ-Polymer™ Compound at 30°C/80%RH Performed with Sponsor Molded Part

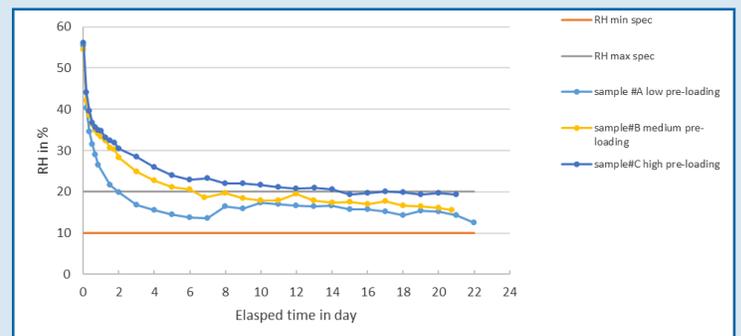


Figure 4: RH% in Sealed Aluminum Bag at 30°C/80%RH with 3-Phase Activ-Polymer™ Component Formula 4, Various Moisture Pre-Loading

Results

Aptar CSP delivered a custom-engineered, active molded component that replaced a current part in the DPI. The active component delivered a buffered solution to protect the API from moisture, while not over drying, throughout storage and use life, meeting the sponsor’s precise specifications (Figure 5).

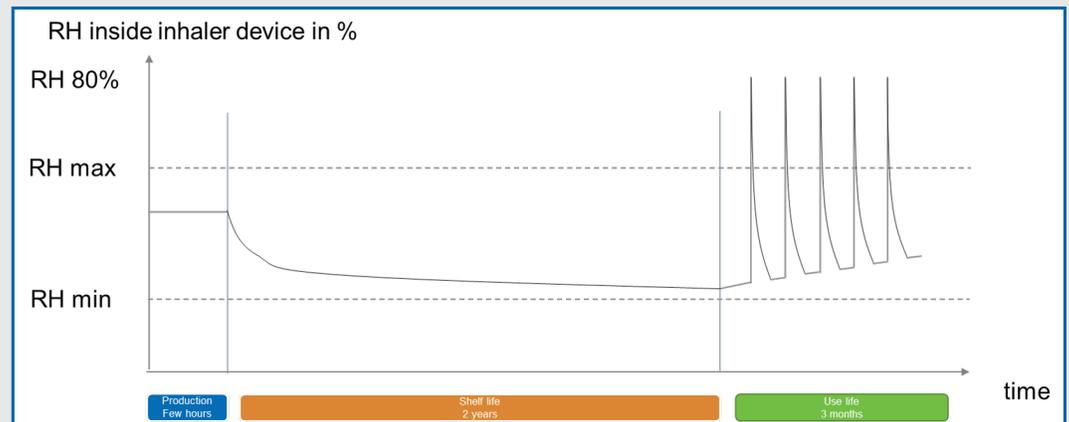


Figure 5: RH% Inside DPI with Activ-Polymer™ Component Throughout Storage and Use Life

Conclusion

Leveraging active material science technology to protect dry powder inhalation devices is a cutting-edge method for ensuring drug product stability. This technology not only helps drug developers leverage flexible solutions to meet stability requirements and attain drug approval, but also delivers an optimal patient experience, protecting dosage in a manner that is invisible to the end user. Aptar CSP’s custom-formulated solutions deliver a controlled and precise microclimate to mitigate risks associated with not only relative humidity, but VOCs and other environmental factors. The technology’s flexible format and highly-engineered chemistries provide a truly custom solution for active protection without impacting device design.

