

Rethinking Dry Powder Inhaler Packaging: New Solutions to Old Challenges

Aptar 
CSP Technologies



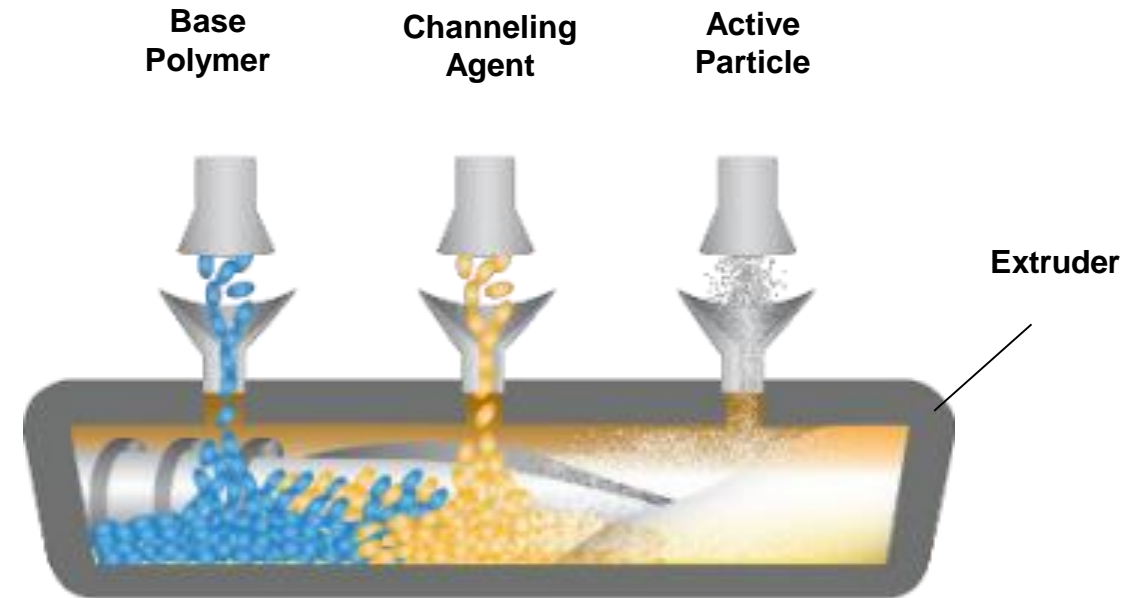
François Bidet | VP Business Development | 5th February 2020

3-Phase Activ-Polymer™ Material = Platform Material

Material Science: Adding Chemistry to Polymers

3-Phase Polymers

1. Majority Polymer: Base structure component
2. Particle: Adsorbing / absorbing – active component
3. Minority Polymer / Channeling Agent: Immiscible in majority polymer

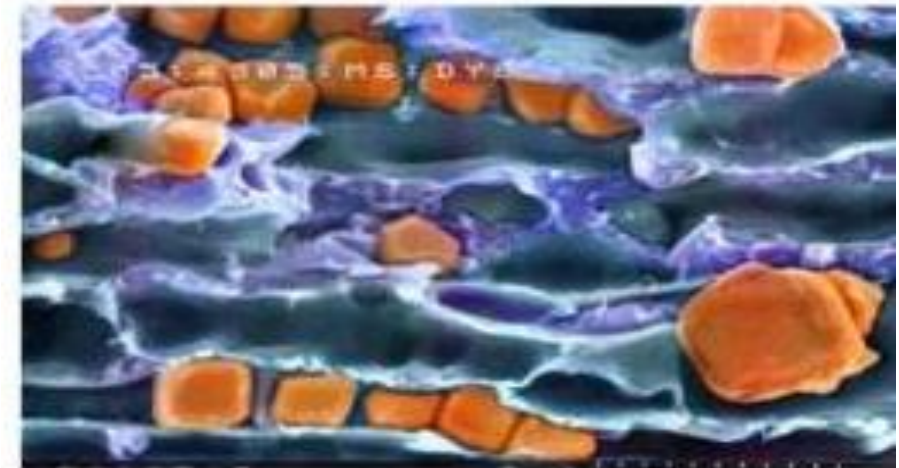
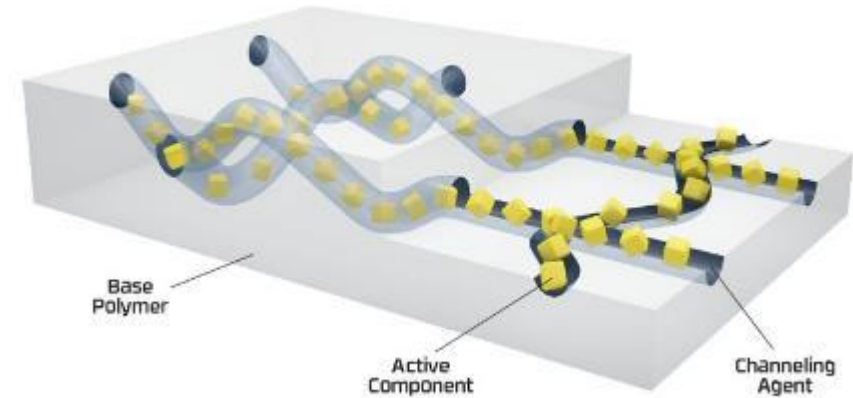


3-Phase Activ-Polymer™ Applications

- Channels created within a polymer allow movement of gases
 - **Moisture Control**
 - **Scavenge:** odors, formaldehyde, and VOCs
 - **Release/Emitting :** aromas, biocides, nutrients, carbon dioxide
 - **Antimicrobial :** pathogen reduction

- **Gas diffusion** is controlled through the channel composition

CSP Activ-Polymer™ Technology



PP/PEG/Molecular Sieve Film

Platform Technology Serving Broad Therapeutic Areas

Material science deployed in key therapeutic areas → Activ-Vial™, Activ-Seal™, Pharmapuck™, and Activ-Film™

Transdermal



Hormone Patch



Drug delivery



Anti-Fungal



Diagnostics



Blood Glucose Testing



Probiotics



Dietary Supplement



Medical Device



Implant Neurostimulator



Management of Moisture in Dry Powder Inhalers

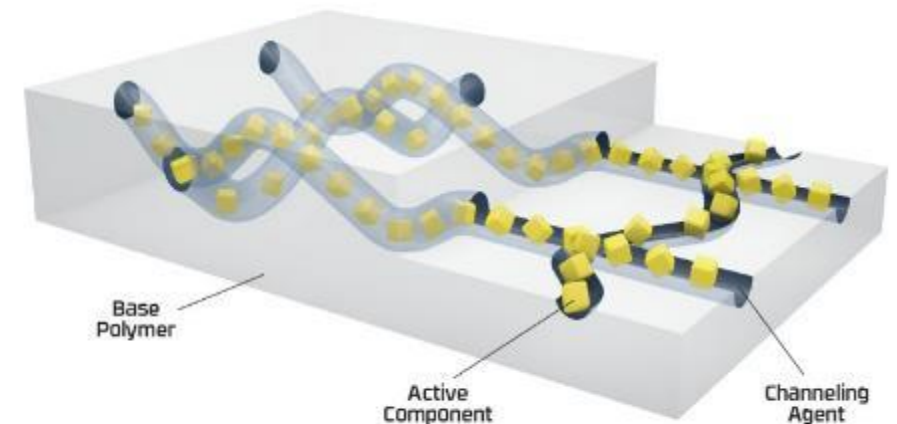
- Dry Powder Inhalers are sensitive to moisture level
- Depending on device and formulation, level of moisture should be controlled for optimal drug delivery
- Residual Humidity (RH) could be very low (<1%) or need to be in a controlled RH (Equilibrium Relative humidity between 10 & 20%)
- RH management should be adapted to devices (Reservoir DPI, Capsule-Based DPI, Blister...)

Why Use Active Packaging for DPI?

- Confined space of packaging
- Ability to control RH level
- DPI growth across all regions
- Rise of biologics and pro-drugs
- Access to ICH Zone 3 and 4 climates
- Ease of use
- Avoid complicated packaging
- Reduce development and reformulation
- Secure shelf life extension



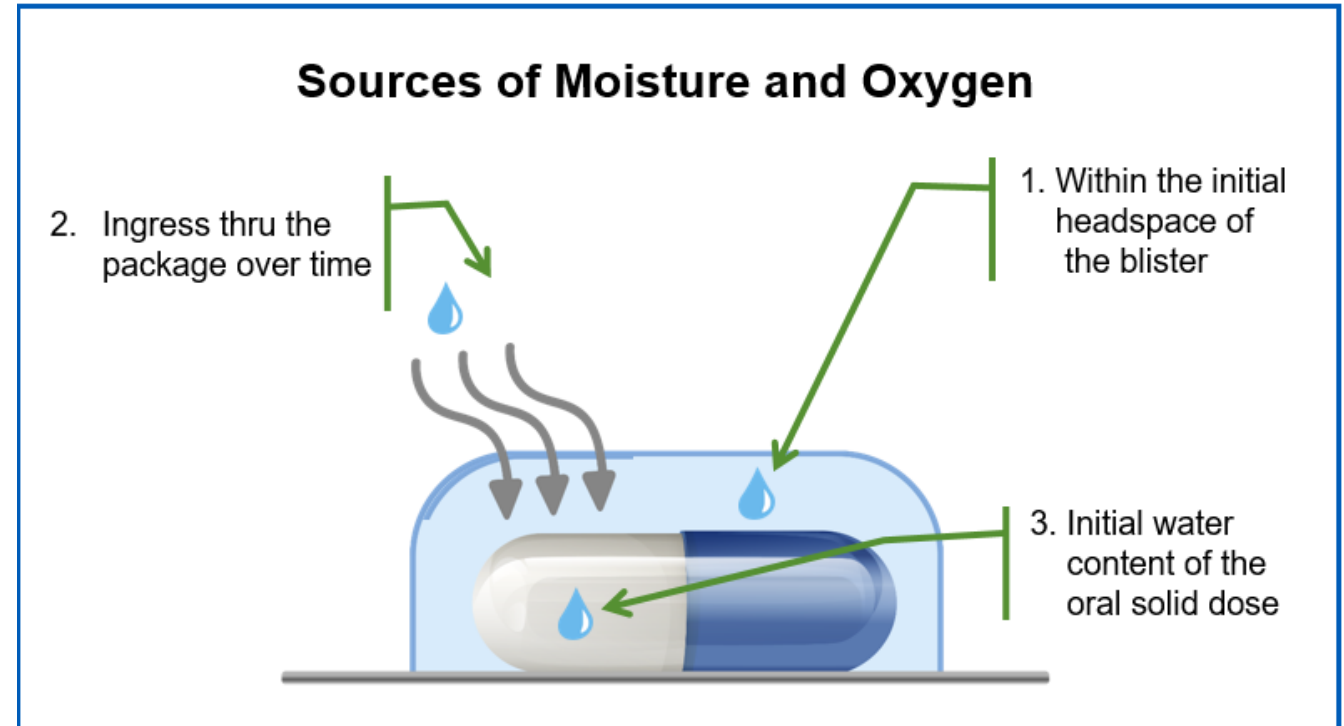
CSP Activ-Polymer™ Technology



Protecting Capsule-Based DPI from O₂ / Moisture

Blister Headspace Management Challenges:

- Confined space of packaging
- Possible need to minimize oxygen and moisture
- Minimize production impact
- Avoid complicated packaging
- Avoid lengthy development and reformulation



Activ-Blister™ Solutions = Protection with Flexibility

- Management of all sources of moisture & oxygen
 - Silica Gel and Molecular Sieve desiccants
 - Combination options available (e.g. moisture + oxygen)
- Customized capacity and uptake rates
- Oxygen products do not require moisture to be active
- Integrate into existing and new packaging lines



Active Packaging – Putting Chemistry into Polymers

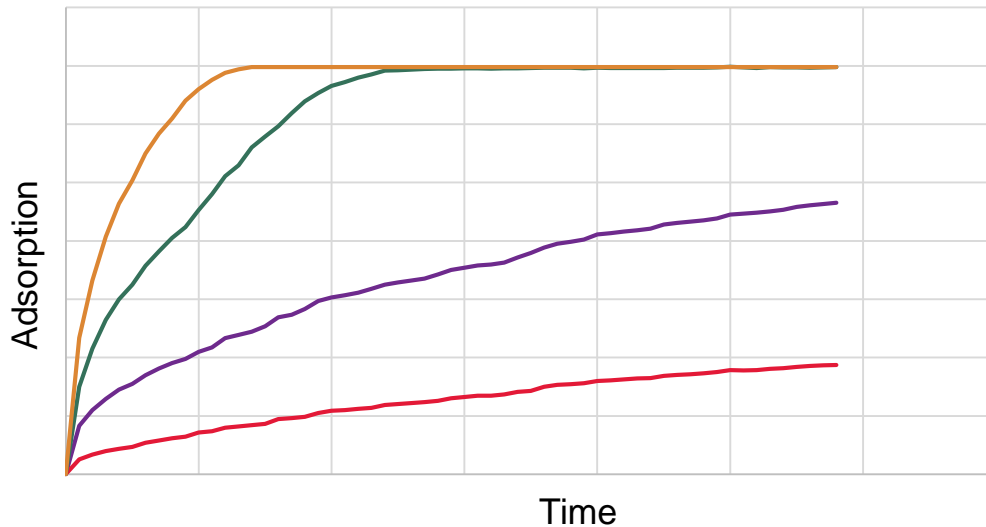
3-Phase Activ-Polymer™ Material

3-Phase Activ-Polymer™ material allows the **control of kinetics** based upon formulation

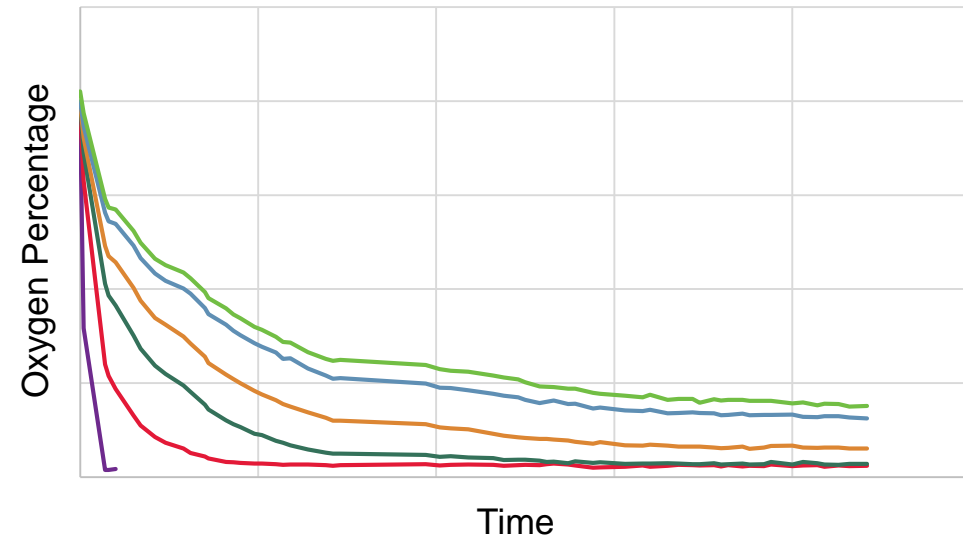
- Uptake rate can be increased or decreased
- Capacity can be increased or decreased



Moisture Adsorption Kinetics



Oxygen “Pull-Down” Performance



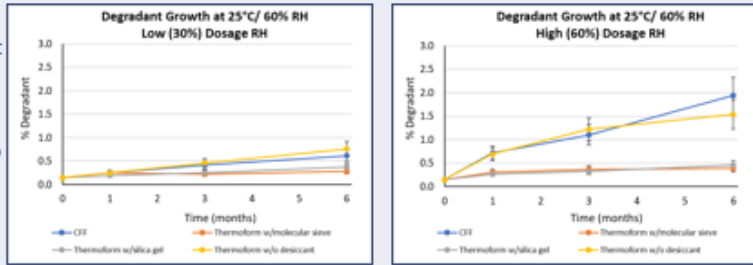
Activ-Blister™ Solutions Provide Superior Protection of a Model Drug Product Over Cold-Form Foil*

RESULTS

Growth of main degradant in tablets stored under ICH stability conditions under different packaging configurations.

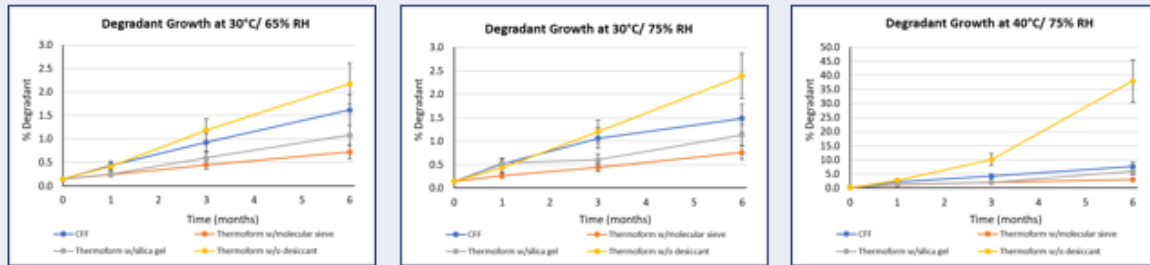
Probability of passing with a 2-yr shelf life at 25°C/60% RH, 30% dosage RH:

- Molecular sieves: 99%
- Silica gel: 95%
- Cold-form foil: 71%
- Thermoform alone: 24%



Activ-Blister™ with molecular sieves result in the lowest degradant growth.

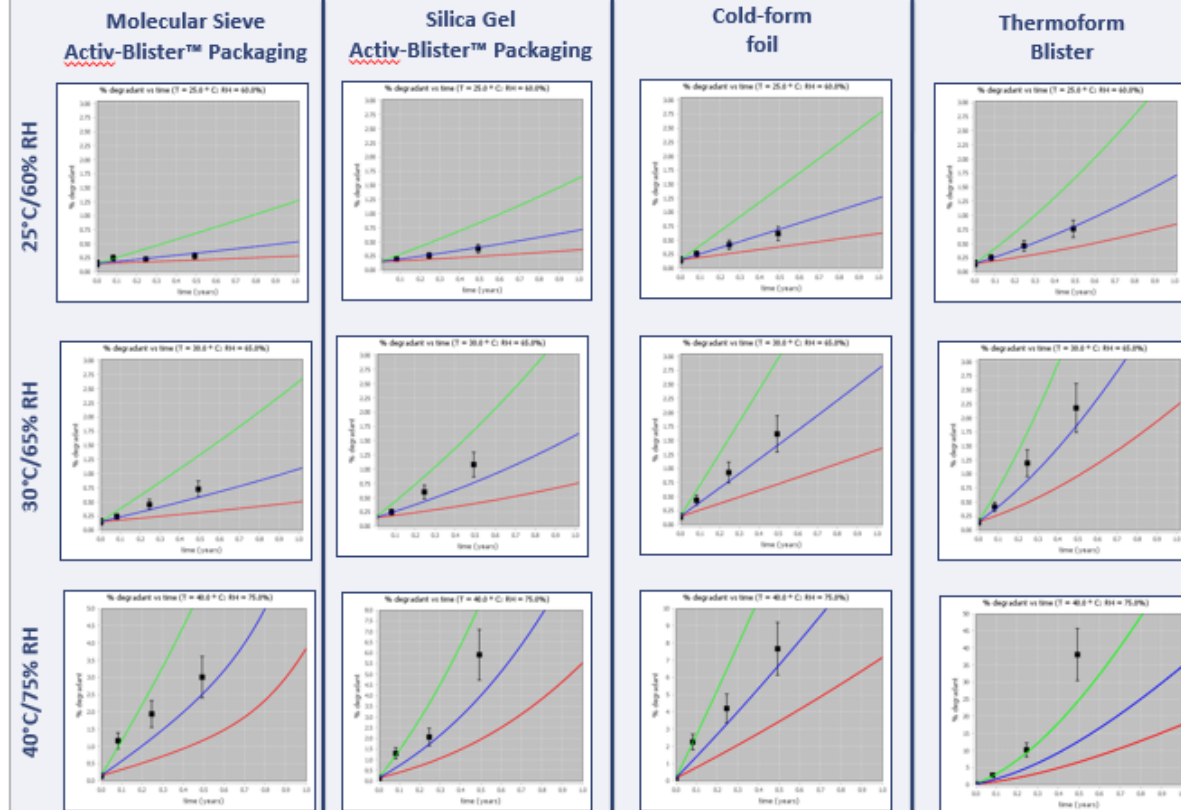
Impact of Activ-Blister™ highest with high dosage RH (60% RH).



Molecular sieve Activ-Blister™ Solutions > **Silica gel Activ-Blister™ Solutions** > **Cold-form foil** > **Thermoform**
 Most protective to degradation ← → Least protective to degradation

RESULTS (cont.)

Selected ASAPprime® predictions compared to degradant growth in tablets stored under ICH stability conditions. The blue lines show the mean prediction while green and red lines show the 95% confidence interval.



Note: The 40°C/75% RH conditions have differing scales due to the wide range of degradation

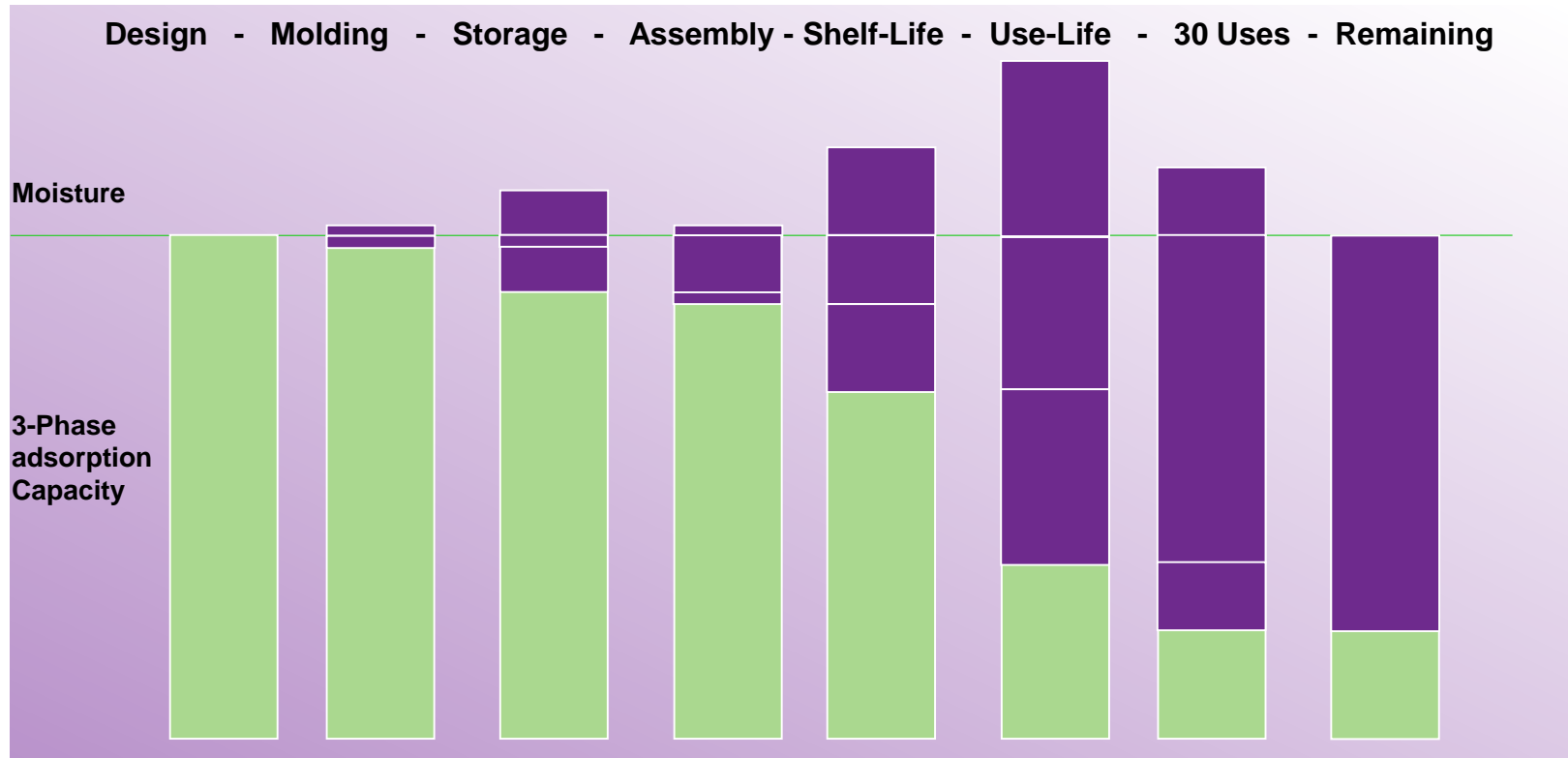
*Poster presented at SOS Conference 2019 (Amsterdam) by Maria Krisch (FreeThink Technologies Inc.) et al

Reservoir DPI Case Study: Summary Findings

- Initial testing with molecular sieve indicated API powder was too dry
- Determined API required a given relative humidity range
- 3-Phase Activ-Polymer™ molded part should be pre-loaded with a controlled moisture level
- 3-Phase Activ-Polymer™ molded part should have high and quick water adsorption capacity at 20-50% RH
- Adsorption kinetics play an important part of design
- 3-Phase Activ-Polymer™ material can be designed to:
 - Maintain targeted RH to better preserve API
 - Reduce the RH level between 2 inhalations
 - Withstand desired shelf-life and use-life

Impact on DPIs = Multi-Dose Blister-Based DPI

- Activ-Polymer™ material into the device
- Fully integrated to carefully calculated moisture scavenging
- Can be tailored for specific API requirements

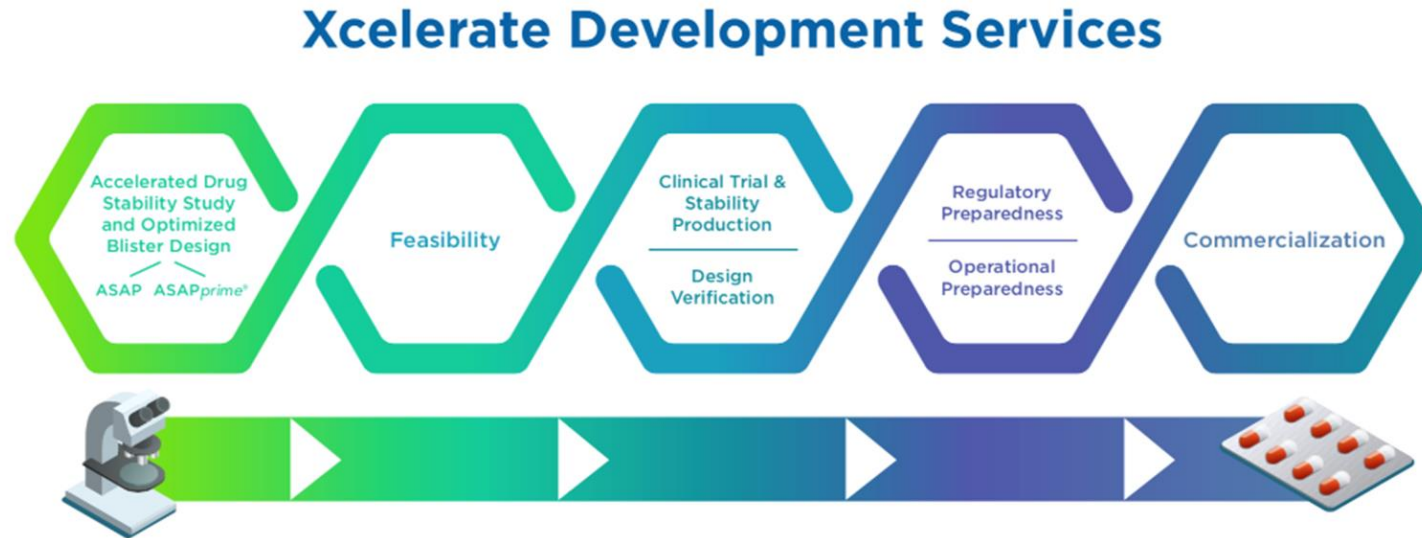


Key Findings

- Effective Sealing of External Openings
- + Low MVTR
- Administration of standard and very moisture sensitive formulations

Aptar CSP Offer: Xcelerate Development Services

- Development Services with Free Think Inc
- Complete solution from Stability Challenge to Production Launch
- Designed for new applications and existing packaged products



Xcelerate's customized process is intended to determine a drug product's moisture and oxygen sensitivity using highly accelerated stability studies open to specified environmental conditions such as temperature, relative humidity, and oxygen level, then uses modeling to create theoretical package designs. Once the optimal packaging sorbent levels are determined, laboratory, clinical, and stability study sample supplies are meant to be prepared for confirmation or actual use.

Any questions, please contact us at

info.pharma@aptar.com