

Rethinking Drug Product Delivery & Packaging: New Solutions to Old Challenges



Billy Abrams | Senior VP Business Development | March 17, 2020

The Problem: Maintaining Product Integrity Against Moisture & Oxygen

- API stability
- Minimize degradants
- Physical properties that can impact performance
 - Compaction
 - Dissolution
 - Flow



The Solution

Aptar CSP Technologies' 3-Phase Activ-Polymer™ Platform Technology



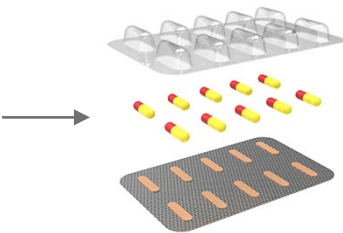
Platform Technology Serving Broad Therapeutic Areas



Oral Solid Dose / Probiotics / Diagnostics

Activ-Blister™ Solutions*

** FDA Approved Packaging for HIV Drug Commercializing in Q2 2020*



Activ-Vial™ Bottles

Injection molded bottles and vials with Activ-Polymer™ Sleeve



Dermal / Transdermal / Inhalation / Medical Device / Diagnostics

Activ-Film™ Material

Activ-Film™ material affixed to the foil pouch to scavenge Moisture and Oxygen simultaneously

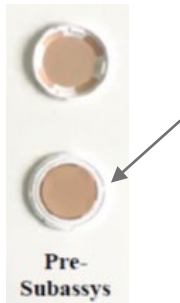
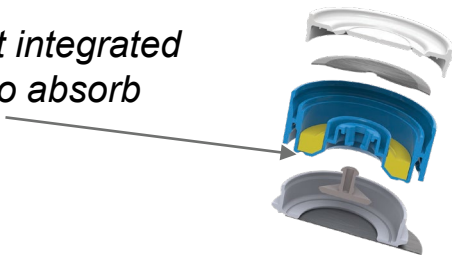


Activ-Film™ material affixed to test strip

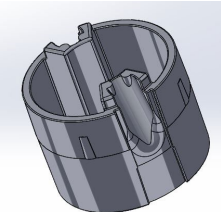
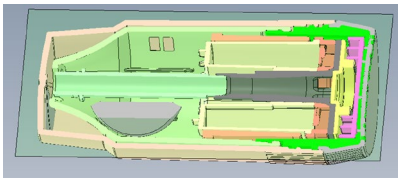


3-Phase Molded Components

Molded component integrated into MAP devices to absorb moisture



Internal component to control RH in reservoir-based dry powder inhaler

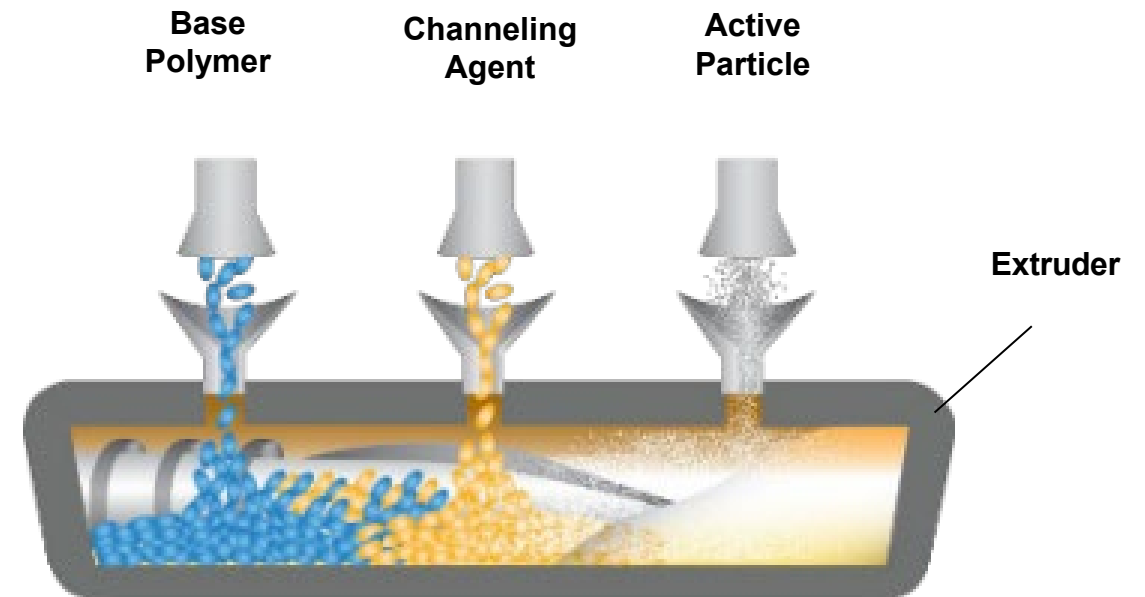


3-Phase Activ-Polymer™ Material = Platform Material

Material Science: Adding Chemistry to Polymers

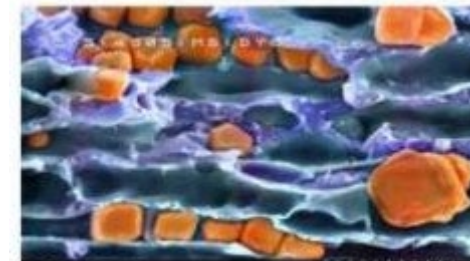
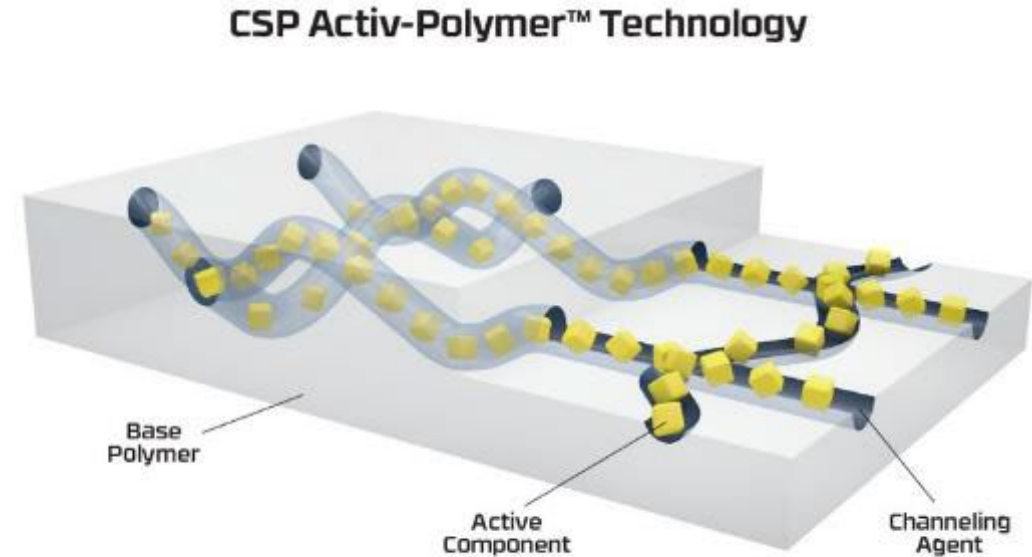
3-Phase Polymers

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™ Material

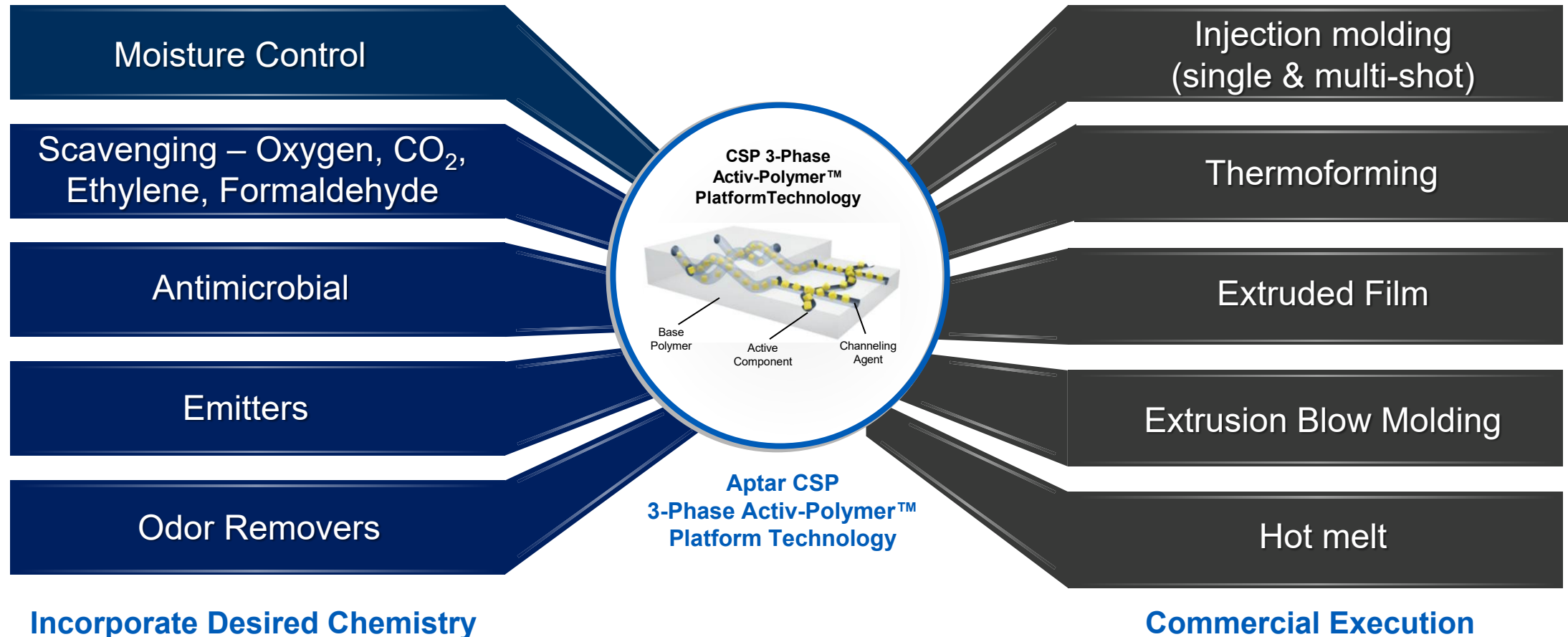
- Channels created within a polymer allow movement of gases
- “Active” particles are added to the polymer in order to:
 - **Adsorb** or **Absorb** (moisture, gases, reactive impurities, odors, formaldehyde and other volatiles)
 - **Release** (aromas, biocides, nutrients, carbon dioxide)
- **Gas diffusion** is controlled through the channel composition



PP/PEG/Molecular Sieve Film

Active Packaging Platform Technology

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.



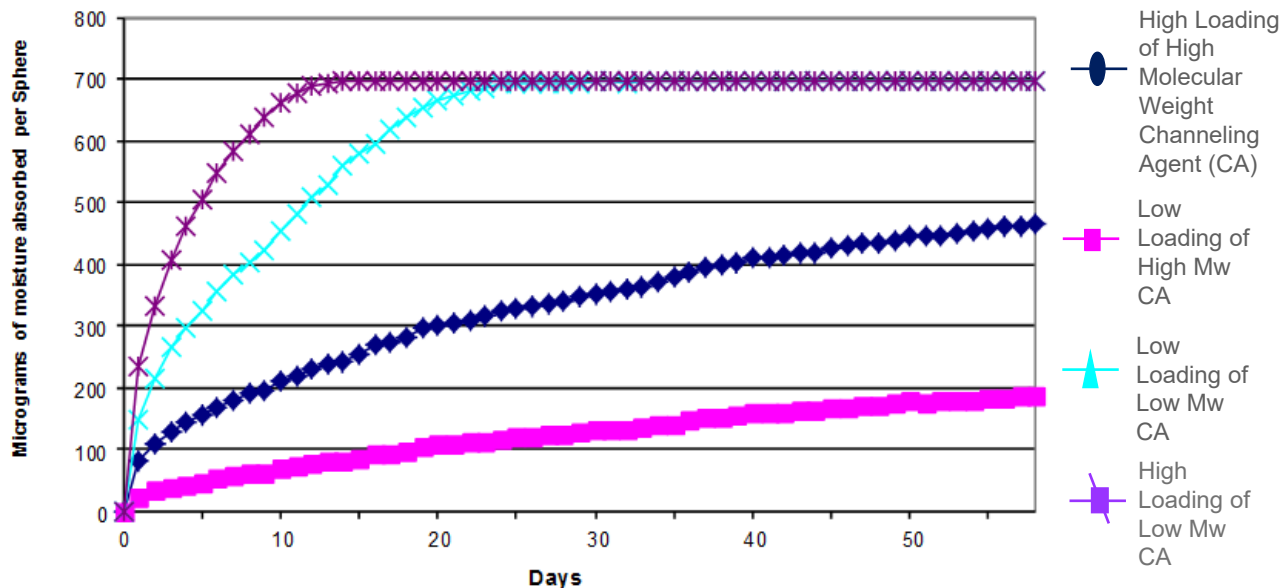
Active Packaging – Putting Chemistry into Polymers

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

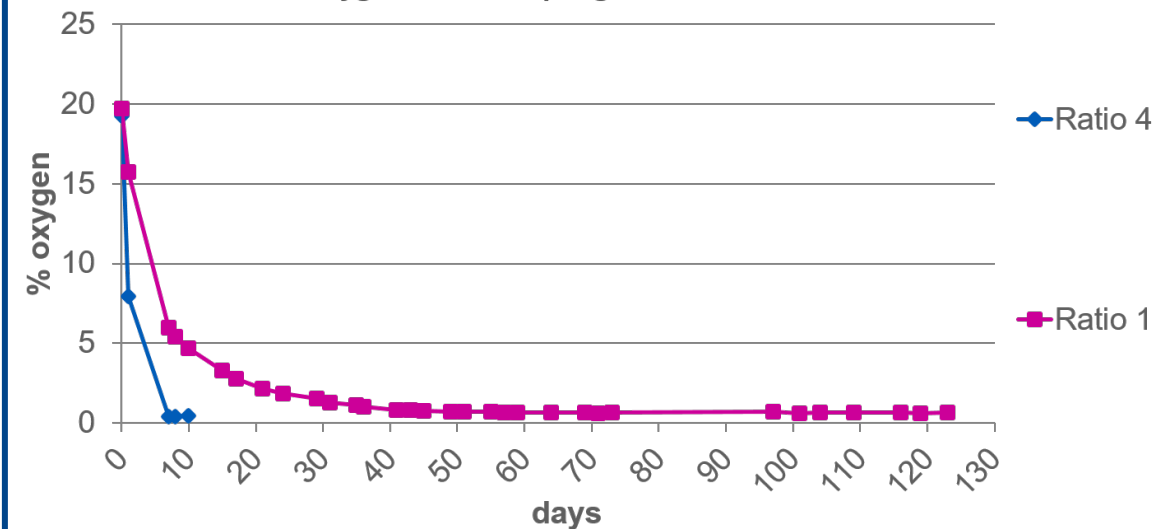
Customized Absorption Rates

ACTIV-TAB Sphere (0.00565gram) Rate of Absorption at 10% RH and 72 °F.
(Desiccant percentage and Polymer remain constant for each formula)



Oxygen Scavenging Customization

M0047
(Ratio represents =Total capacity of piece/available oxygen volume)
Oxygen absorbed per gram of film=30cc

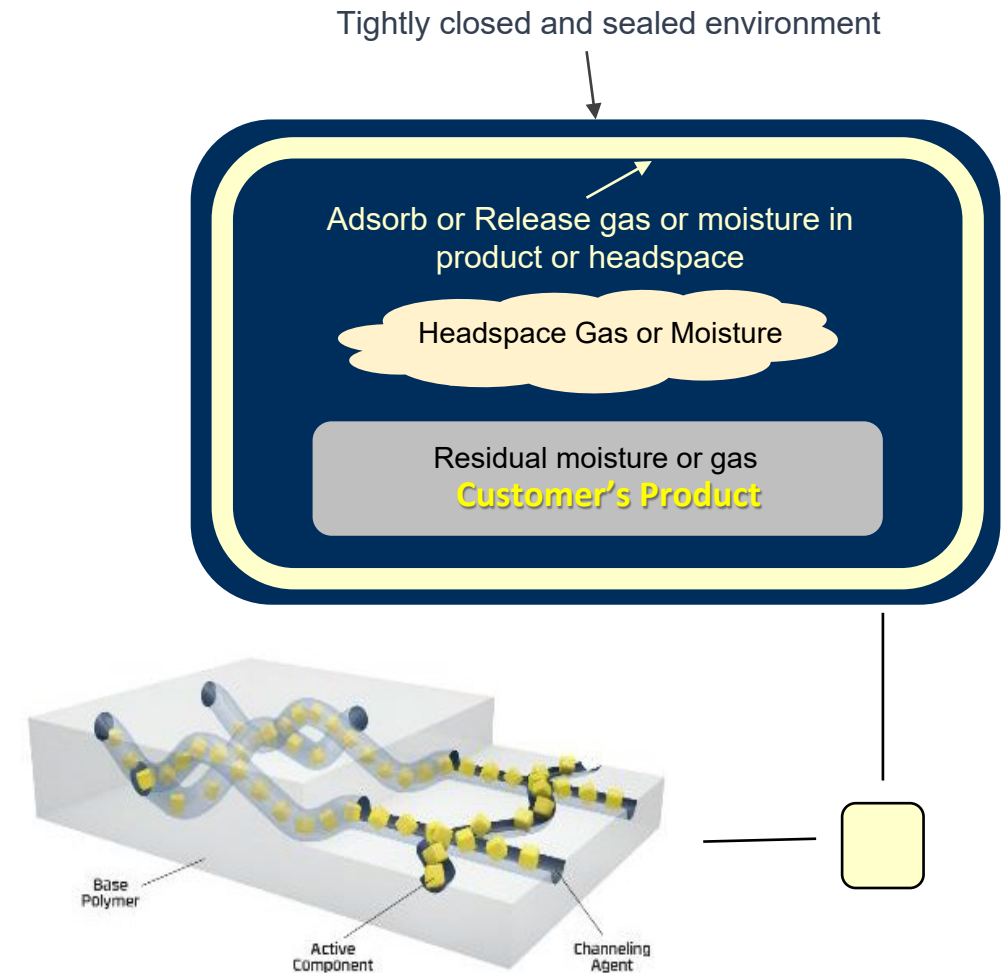
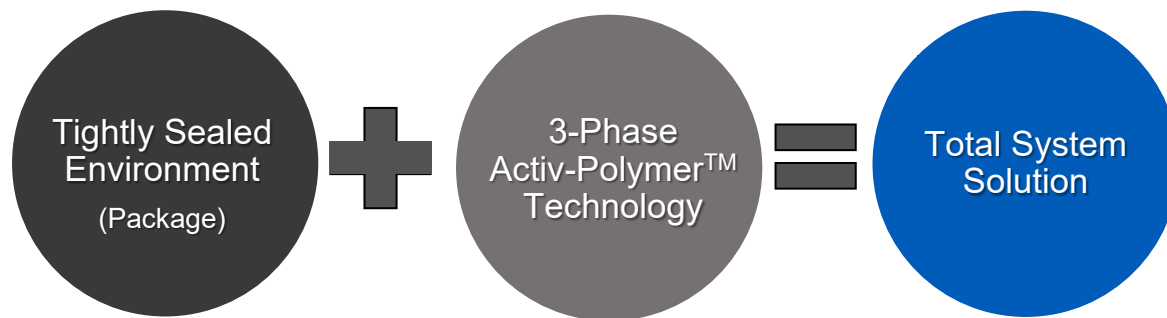


Active Packaging – Putting Chemistry into Polymers

Tightly Sealed Environment

Utilizing **3-Phase Activ-Polymer™** technology requires a **tightly sealed environment**

- Chemistry required determined
- Gas or moisture transmission rates are reviewed
- Focus on seals associated with package
- Amount of **3-phase material** required will depend on how **tight** of an **environment** it will be placed in



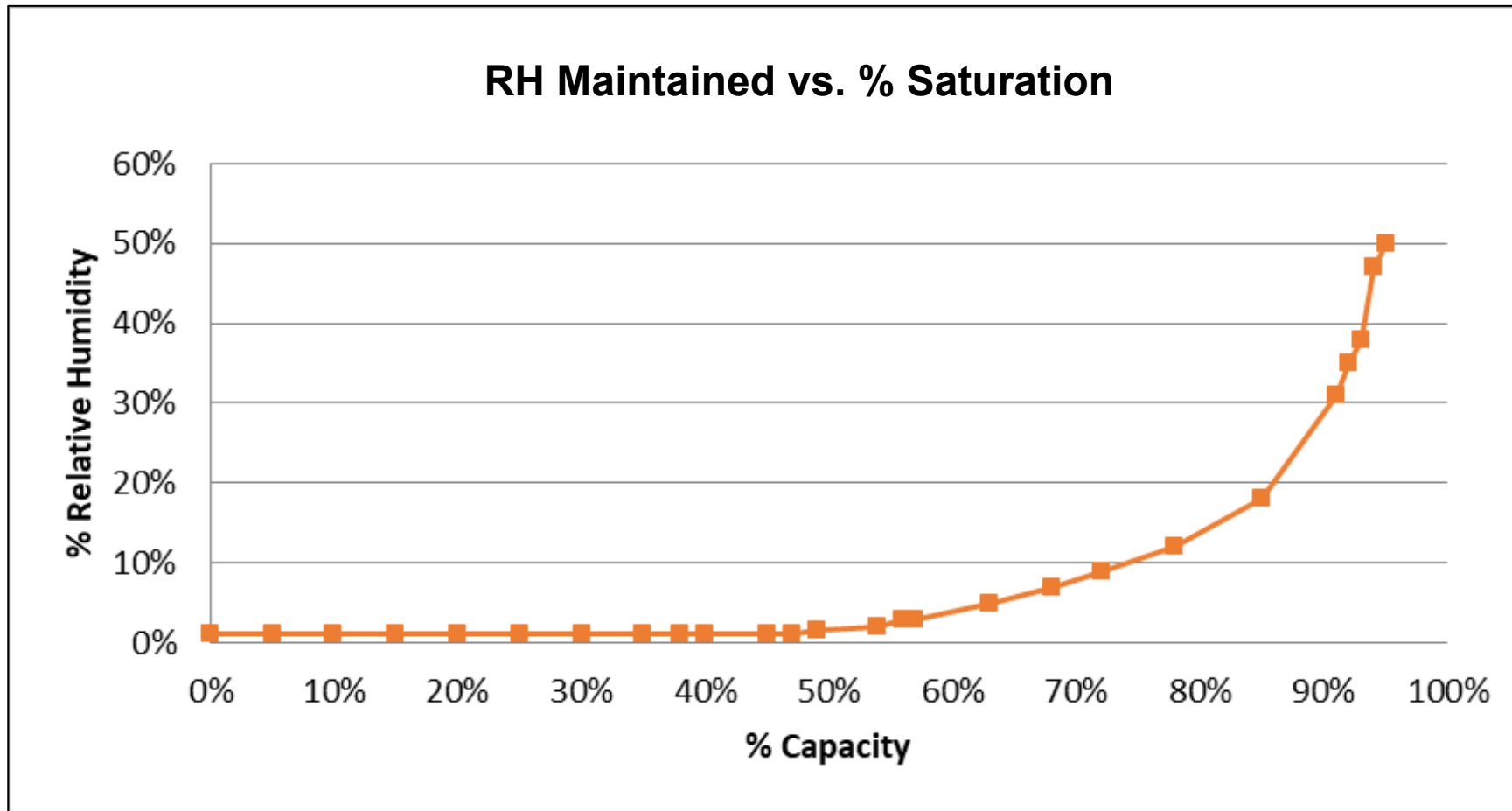
- Can product be over-dried?
- What is acceptable Water Activity (A_w) level of the project?
- At what RH level will A_w create physical stability issues?
- Chemical stability modeling with services like FreeThink Technologies' *ASAPprime*®

Moisture Ingress

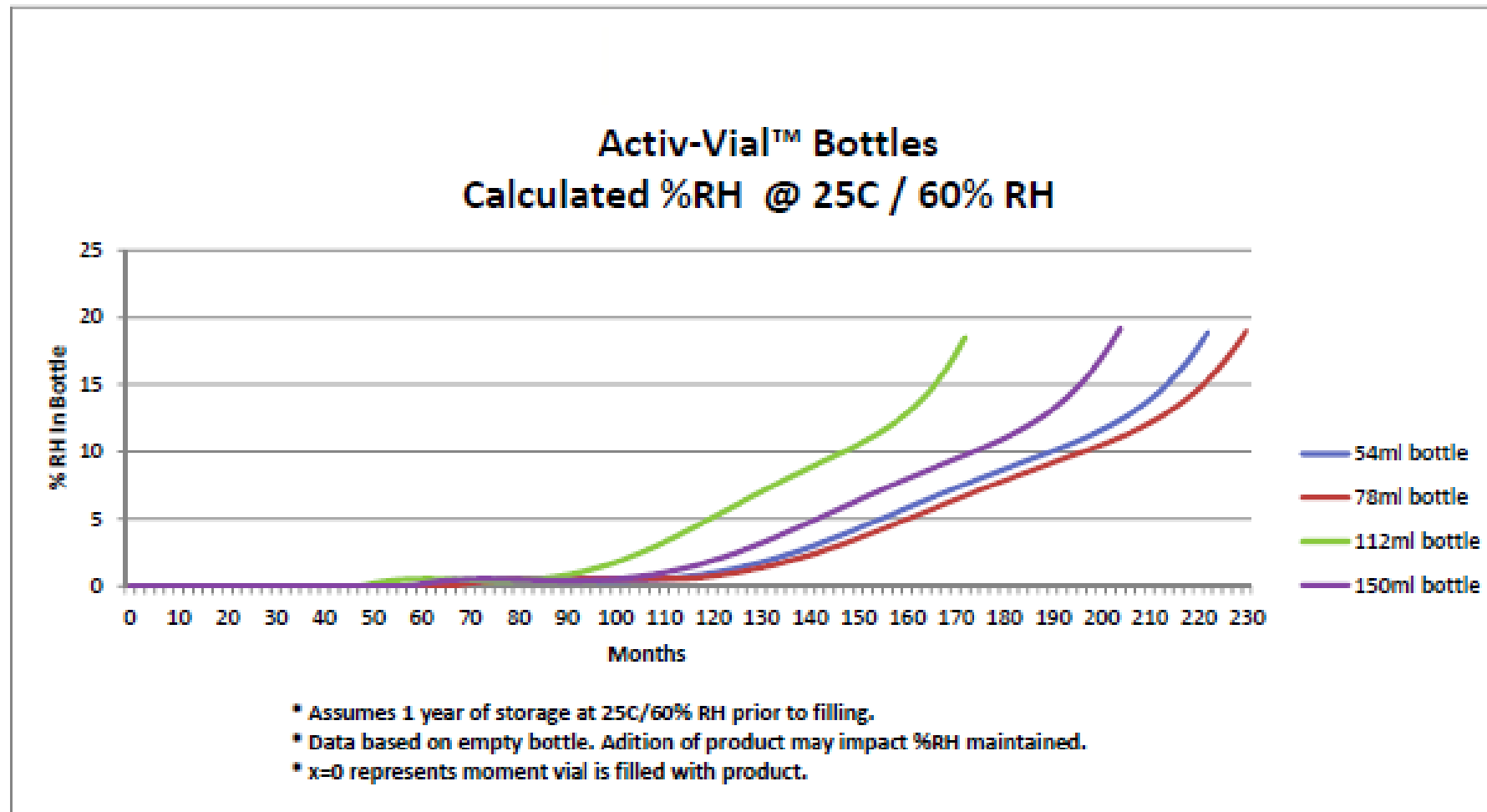
- Moisture ingress is defined as the amount of moisture per day adsorbing into the desiccant plastic through the seal and vial walls.
- Driving force – Moisture content gradient between the external and internal headspace of vial
- Proportional relationship across different conditions exists, allowing for testing and conversion between various conditions
- Ingress testing performed at 30°C/80%RH (24.37 g/m³) and 22°C/80%RH (15.58 g/m³)

ICH Zone	Conditions	Moisture Content (g/m ³)
II	25°C/60%RH	13.87
III	30°C/35%RH	10.66
IV	30°C/65%RH	19.80
Accelerated Testing	40°C/75%RH	38.47

RH Maintained

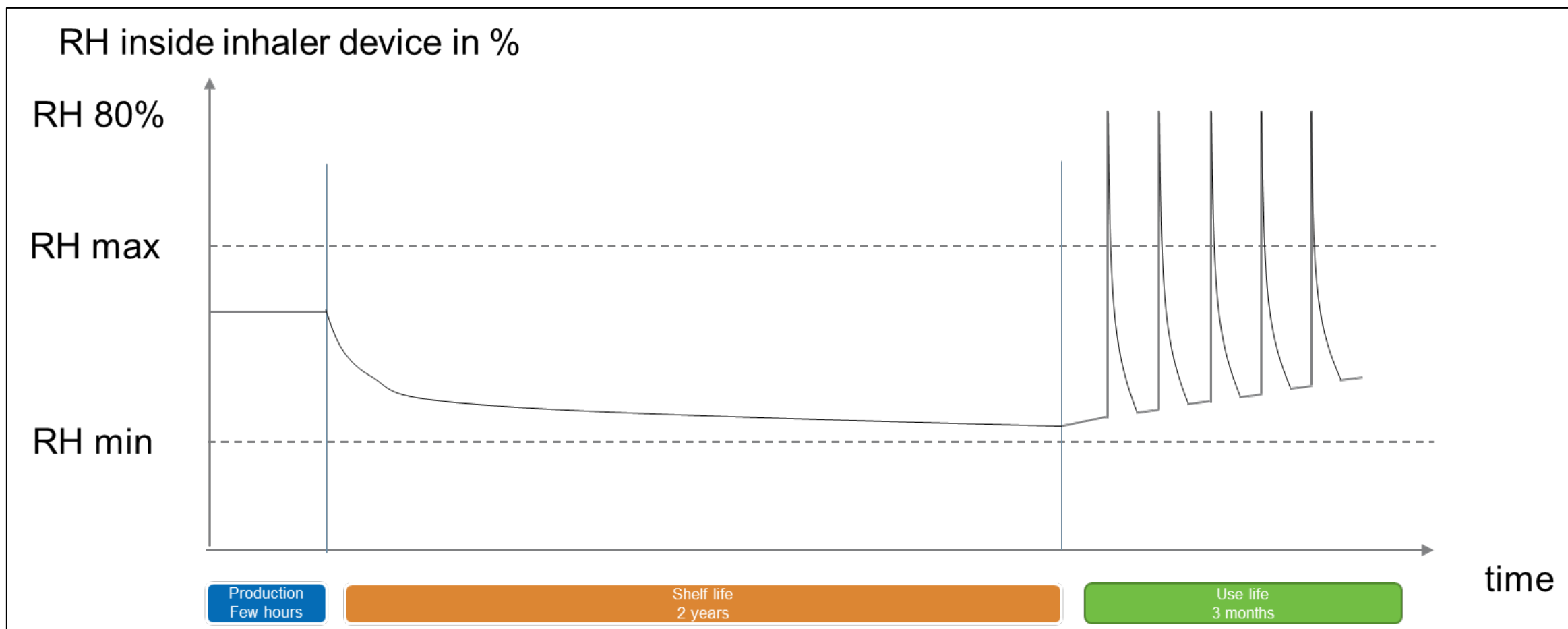


RH Maintained



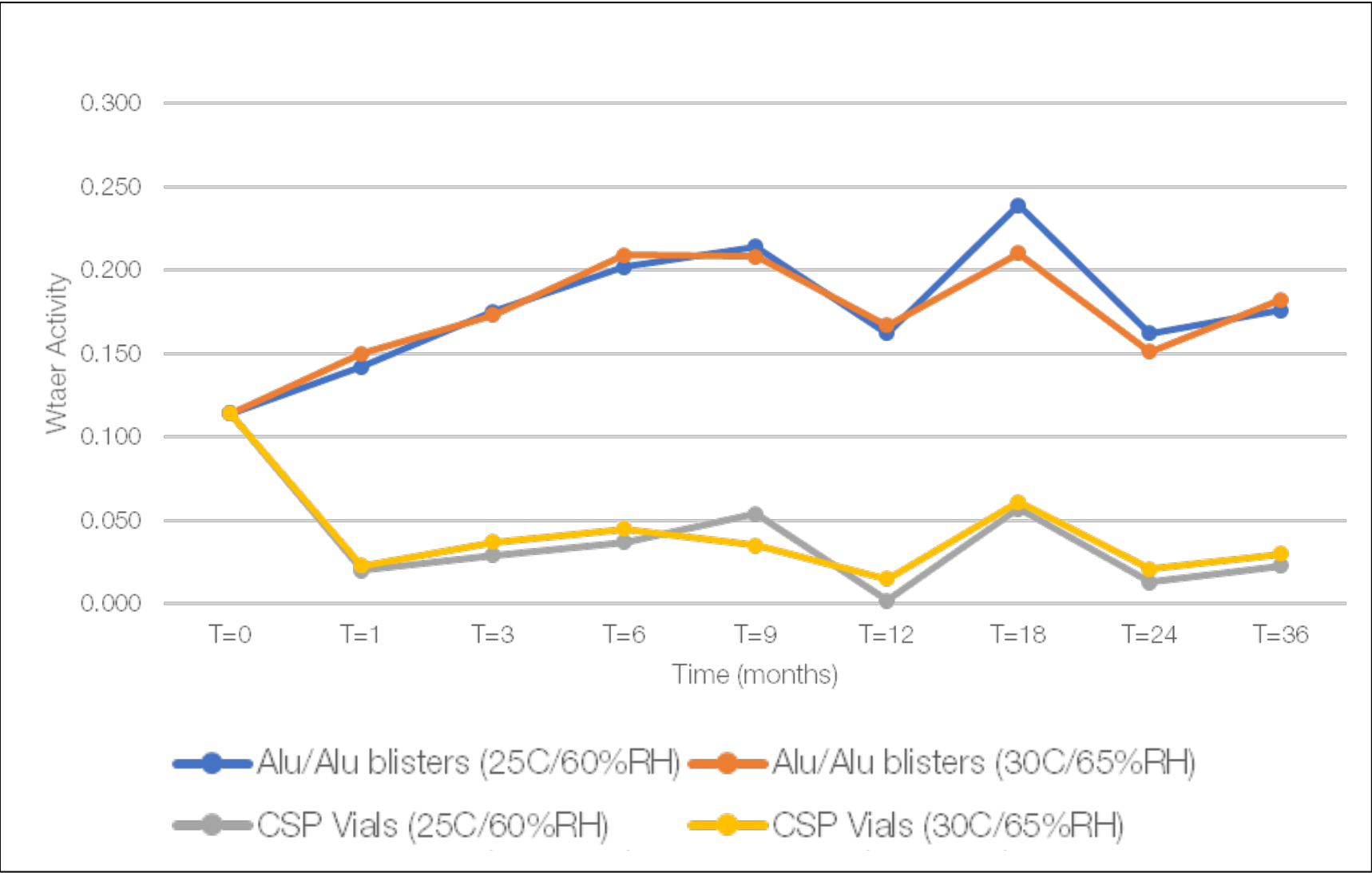
Buffered RH Solutions for Products Susceptible to Over-Drying

RH inside an inhaler using a custom CSP 3-Phase Activ-Polymer™ component throughout the storage and use life of the device.



Probiotic Capsules – Water Activity

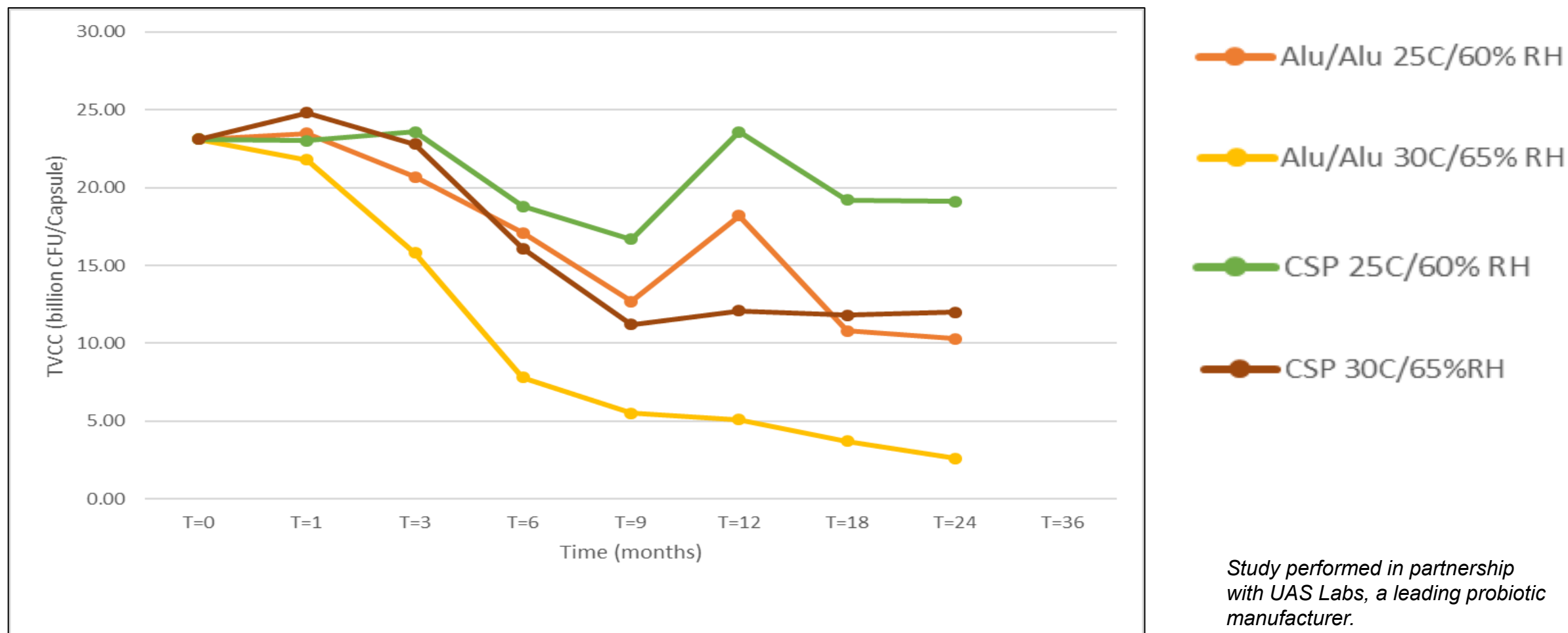
(CSP vs Alu/Alu Blisters)



Study performed in partnership with UAS Labs, a leading probiotic manufacturer.

Probiotic Capsules – Strain Potency

(CSP vs Alu/Alu Blisters)



Predictive Stability

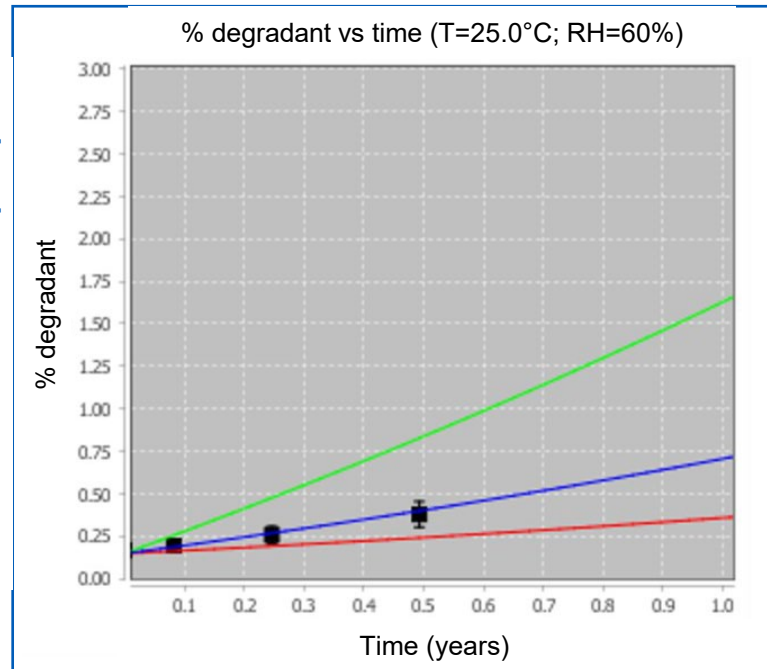
ASAP^{prime}® predictions compared to degradant growth in tablets stored under ICH stability conditions.

Blue lines show the mean prediction while green and red lines show the 95% confidence interval.

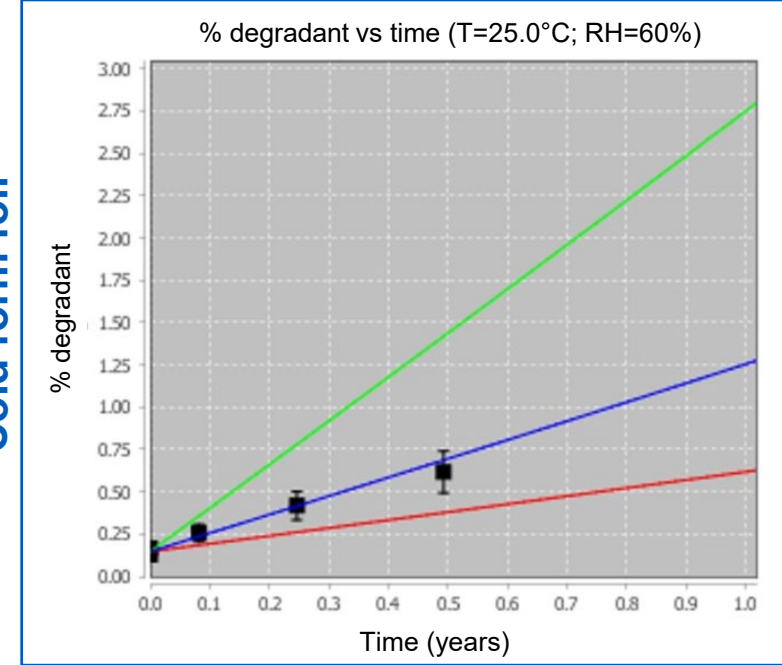


Study performed in partnership with FreeThink Technologies.

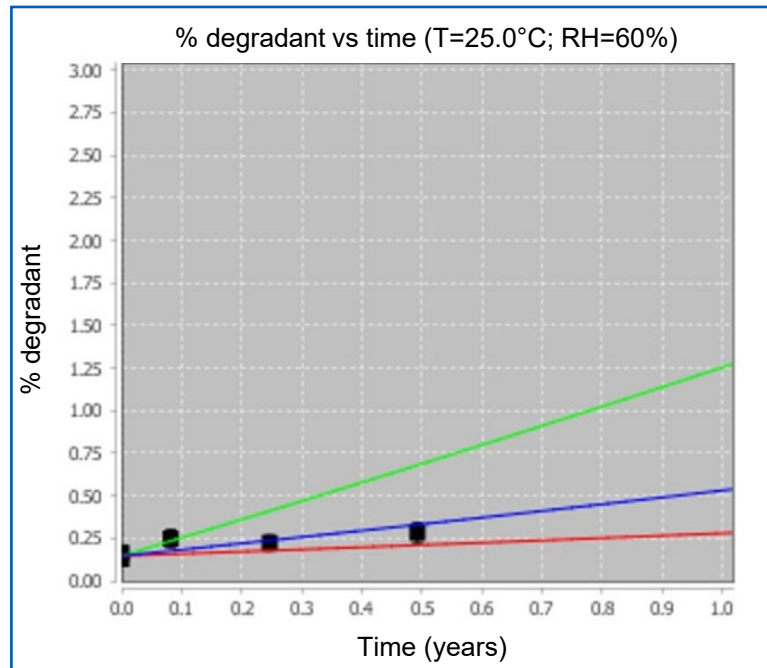
Activ-Blister™
Formulation 1 (SG)



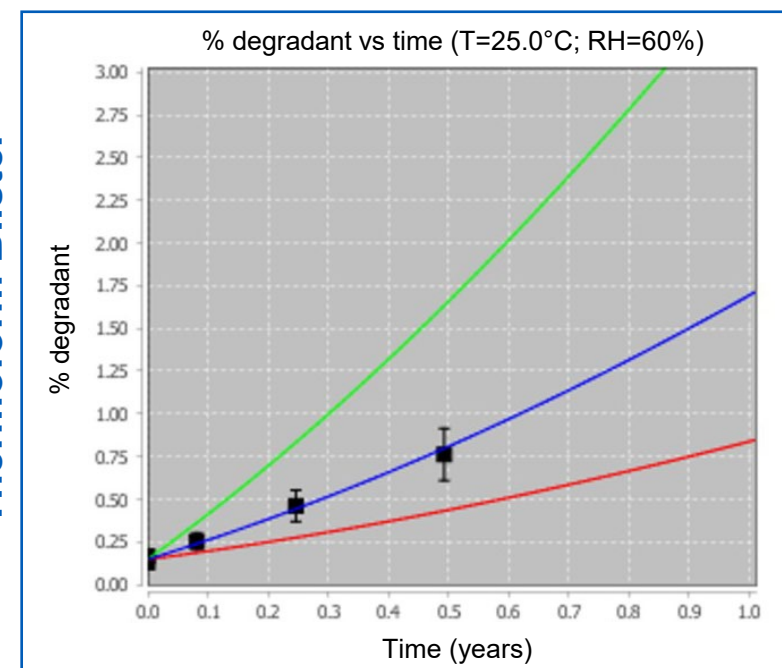
Cold form foil



Activ-Blister™
Formulation 2 (MS)



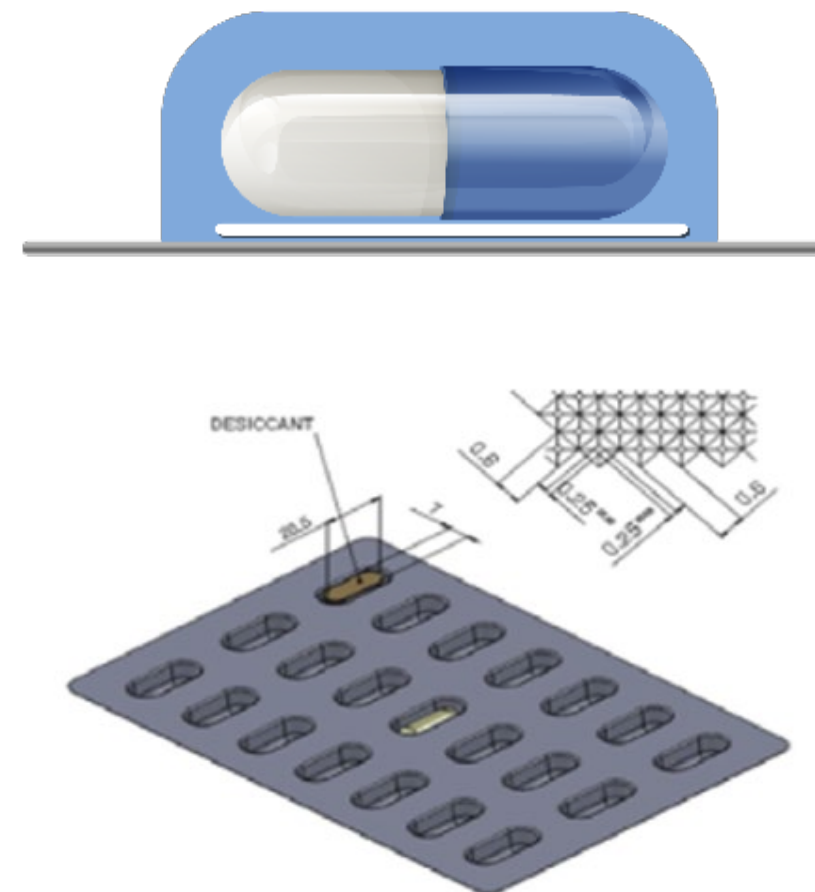
Thermoform Blister



Results compared to Aclar-type thermoformed blisters

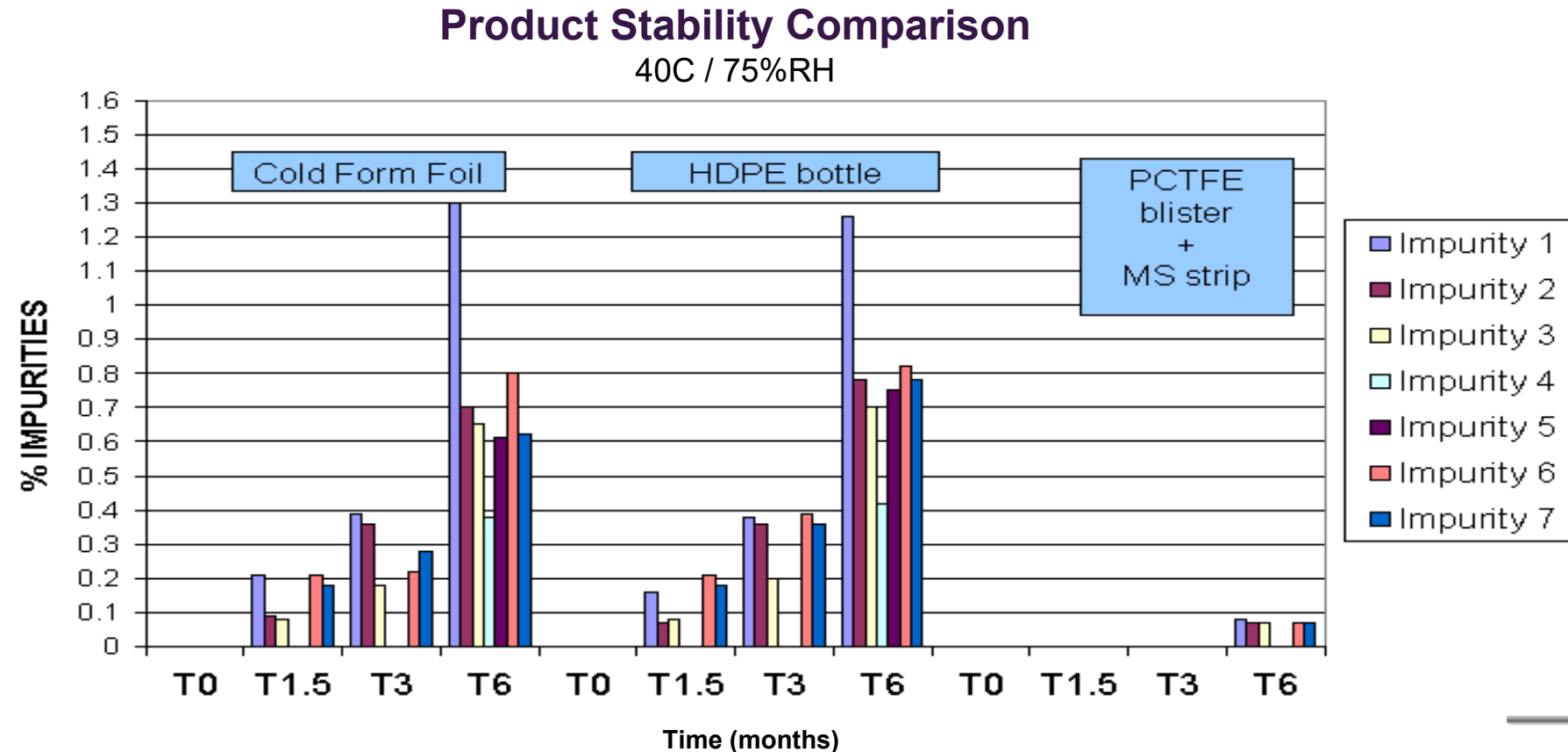
Aclar® type	Temp/RH (°C/%RH)	Days to saturation
Rx160	25/60	209
Rx160	30/65	71
Rx160	40/75	21
UltRx2000	25/60	370
UltRx2000	30/65	220
UltRx2000	40/75	71
UltRx6000	25/60	1036
UltRx6000	30/65	647
UltRx6000	40/75	209

Assume ~6.6mm x ~13mm x 1mm piece
for Size 0 capsule



Activ-Blister™ Solutions

Results compared to other solutions



NOTE: Pharmaceutical Requirements:

- Total substances <1.0%
- Unknown individual impurities <0.1%

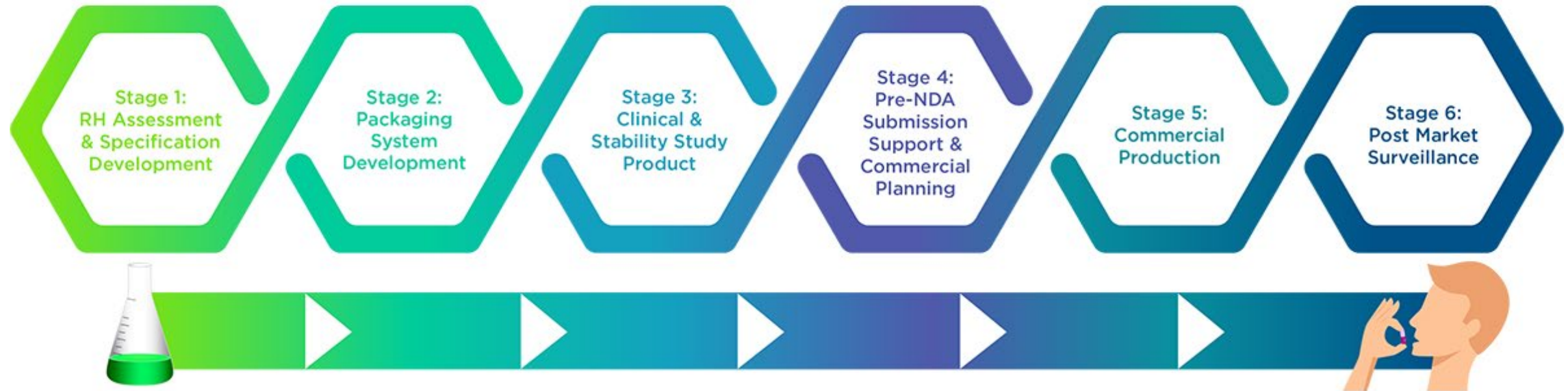
* Data/Graphics courtesy of Tekniple

Award-Winning *Xcelerate* Development Services

Complete solution from R&D stability to product launch

Optimized active packaging development process offering end-to-end support, expediting speed-to-market.

Xcelerate Development Services



***Xcelerate* Development Services awards:**

Pharma Manufacturing magazine 2019 All-Star Innovator Award

Medicine Maker magazine 2019 Innovation Award

3-Phase Activ-Polymer™ Solutions

Value for Drug Product Delivery & Packaging

1. Can be used to manage RH and oxygen
2. Multiple, customized formats available to suit any drug packaging need
3. Proven use across a range of commercialized products





Questions?