Reimagining Probiotics Protection with Breakthrough Active Material Science Technologies

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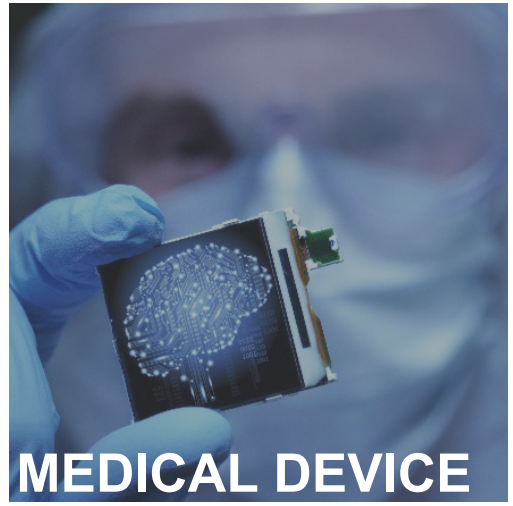
Aptar CSP Technologies

About Aptar CSP Technologies

- Joined **AptarGroup** in August 2018
- Premier active **material science solutions expert** delivering innovative, highly-engineered, **active packaging** solutions
- Headquarters Auburn, Alabama, USA, with **+500** dedicated employees in **4** countries
- **+1.2** billion components manufactured annually, **4** manufacturing locations worldwide (US, France & China)
- **+ 600** worldwide patents
- **ISO-9001**, **ISO-13485** and **ISO-14001** certified

Broad Therapeutic Expertise

Aptar CSP Technologies



Platform Technology Serving Broad Therapeutic Areas

Aptar CSP Technologies

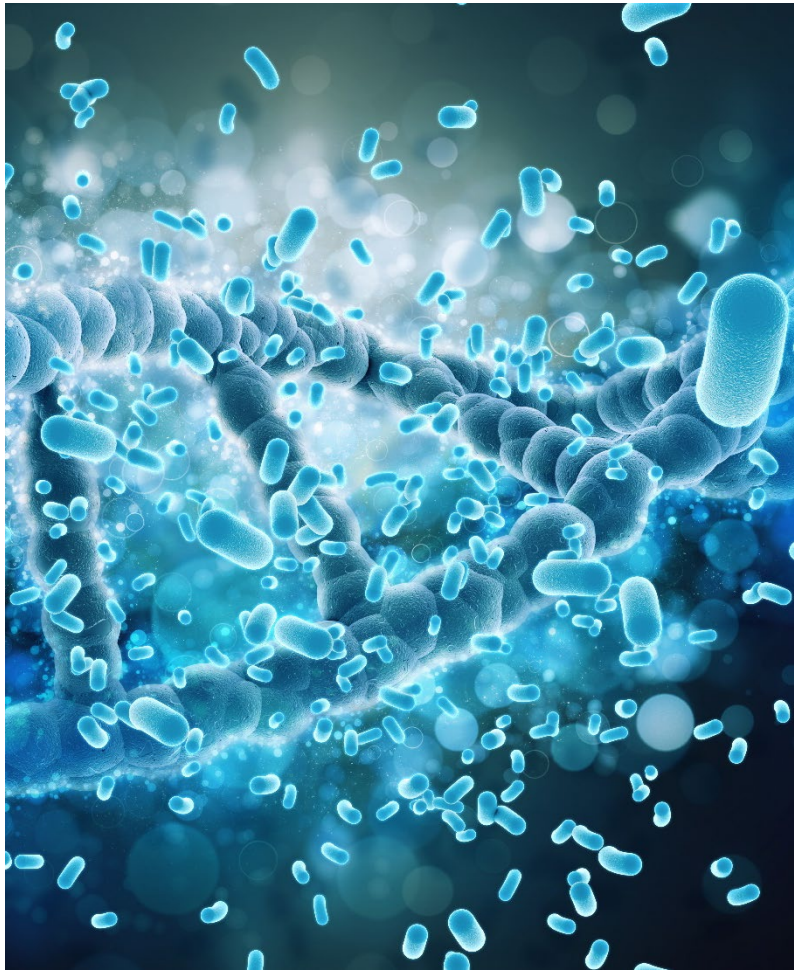
Oral Solid Dose	Dermal Drug Delivery	Drug Delivery Systems	Diagnostics	Probiotics	Medical Device & Implants
Immunodeficiency Treatment	Hormone Patch/ MAP Device	Inhalation/ Nasal Drug Delivery	Blood Glucose Testing/COVID Testing	Dietary Supplement	Implant Neurostimulator

Packaging of Probiotics Formulations Constraints

- Most probiotics strains are sensitive to moisture and temperature
- Some strains like Next Generation Probiotics (NGPs) are also very sensitive to oxygen and light
- Traditional packaging like bottles or coldform (alu/alu) blisters do not address initial moisture content
- Finished products storage at +4°C is less compatible with modern life
- To mitigate risk, manufacturers increase the number of strains/CFUs

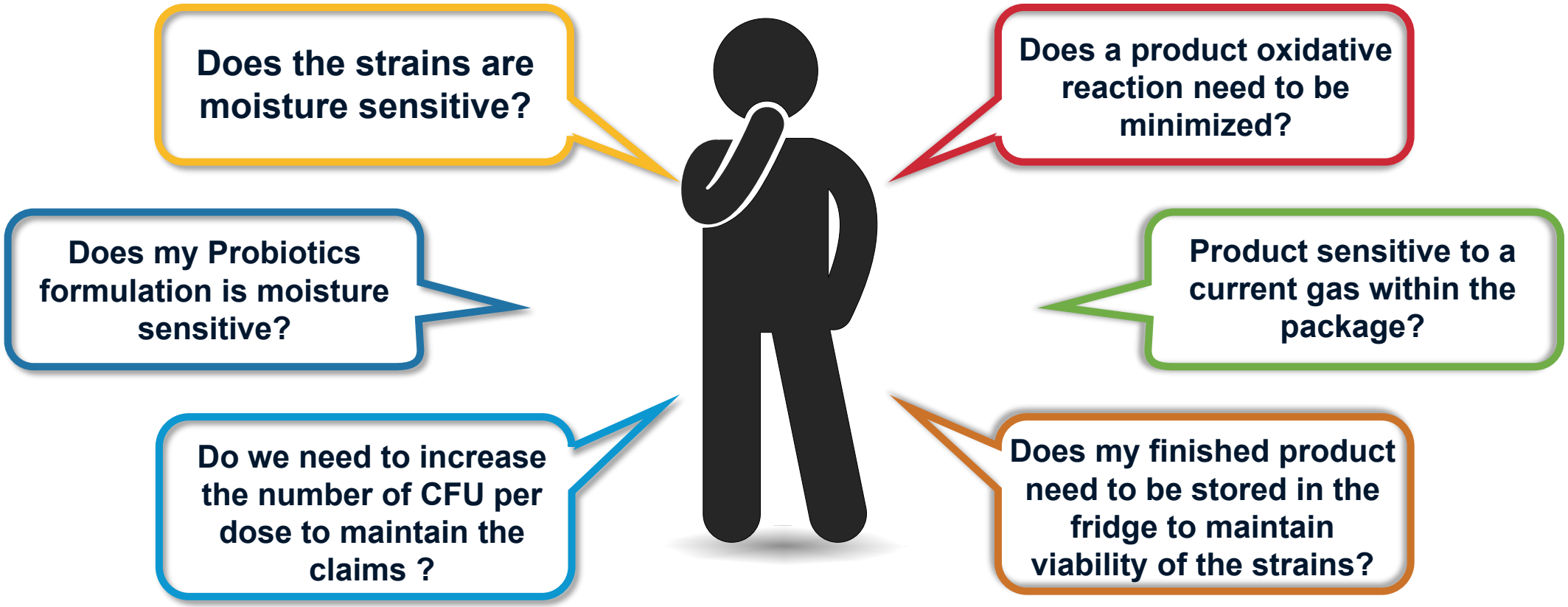
? Is it safe?

Is it cost effective?



Determining the Need for Active Packaging in Probiotics

Aptar CSP Technologies



Do you have a package or device that is tight and has headspace?

3-Phase Activ-Polymer™ Technology: The Solution to These Challenges

Active Material Science Platform Technology

Material Science: Adding Chemistry to Polymers

3-Phase Activ-Polymer™ Material

1

MAJORITY POLYMER

Base Structure Component

2

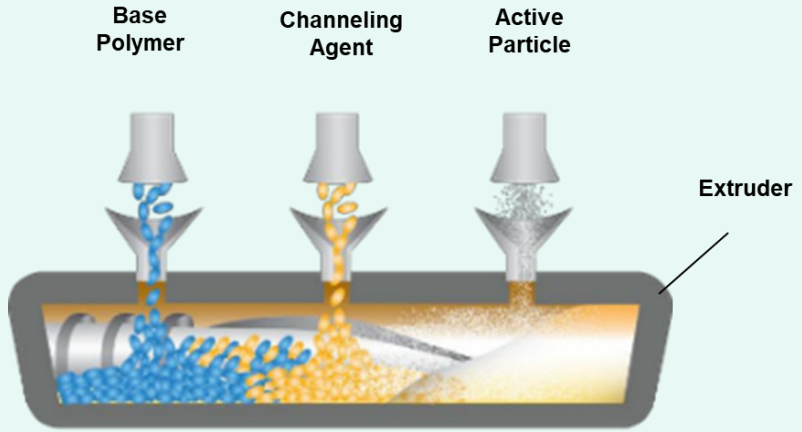
PARTICLE

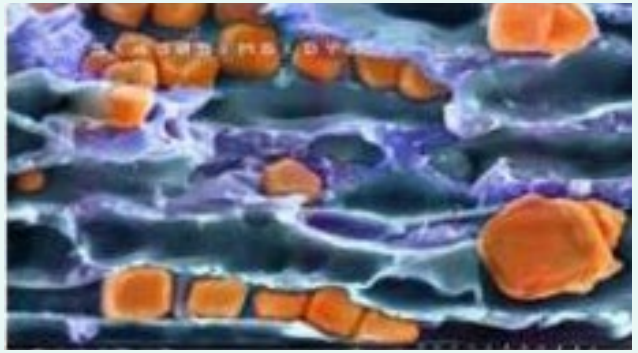
Adsorbing/Absorbing – Active Component

3

MINORITY POLYMER/ CHANNELING AGENT

Immiscible in majority polymer





Active Material Science Platform Technology

Material Science: Adding Chemistry to Polymers

3-Phase Activ-Polymer™ Material

1

MAJORITY POLYMER

Base Structure Component

2

PARTICLE

Adsorbing/Absorbing – Active Component

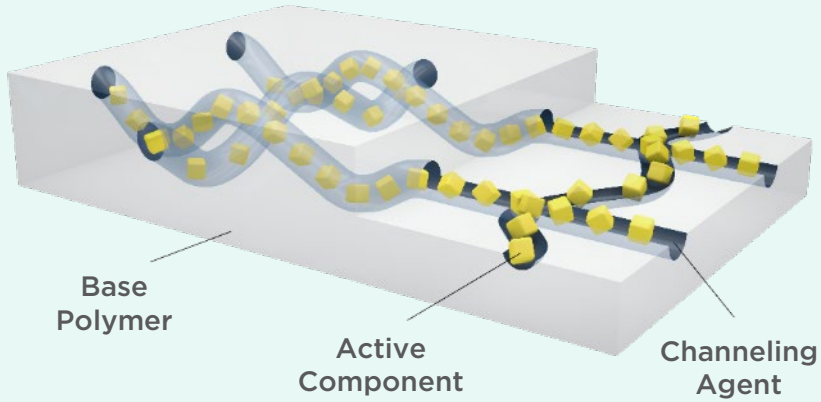
3

MINORITY POLYMER/ CHANNELING AGENT

Immiscible in majority polymer

HOW IT WORKS:

- Channels created within a polymer allow movement of gases
- "Active" particles are added to polymer to:
  - **Adsorb** or **Absorb** (moisture)
  - **Scavenge** (gases, odors, reactive impurities, formaldehyde, other VOCs)
  - **Release/Emit** (aromas, biocides, antimicrobials, nutrients, CO_2)
- **Gas diffusion** is controlled through the channel composition
- Allow **high load of active compound** in limited headspace



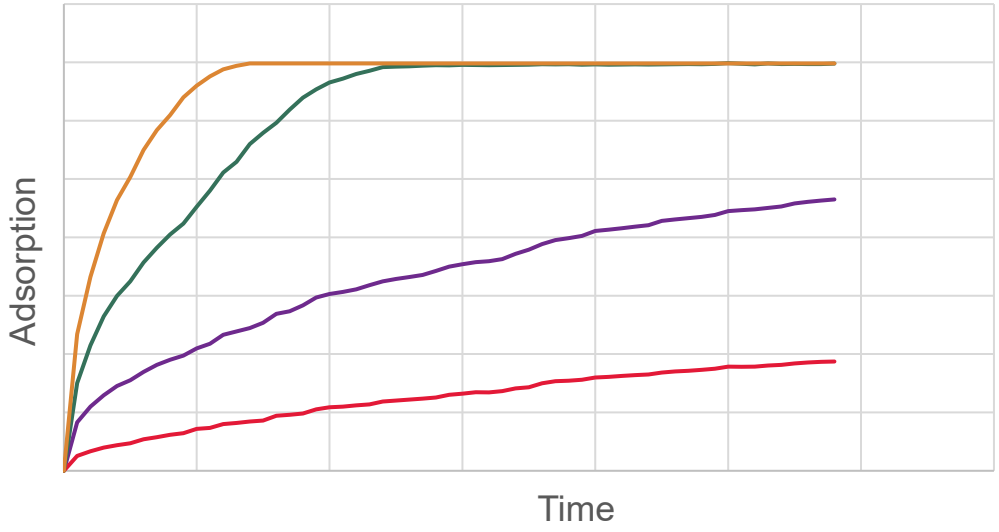
Active Packaging – Putting Chemistry into Polymers

3-Phase Activ-Polymer™ Material

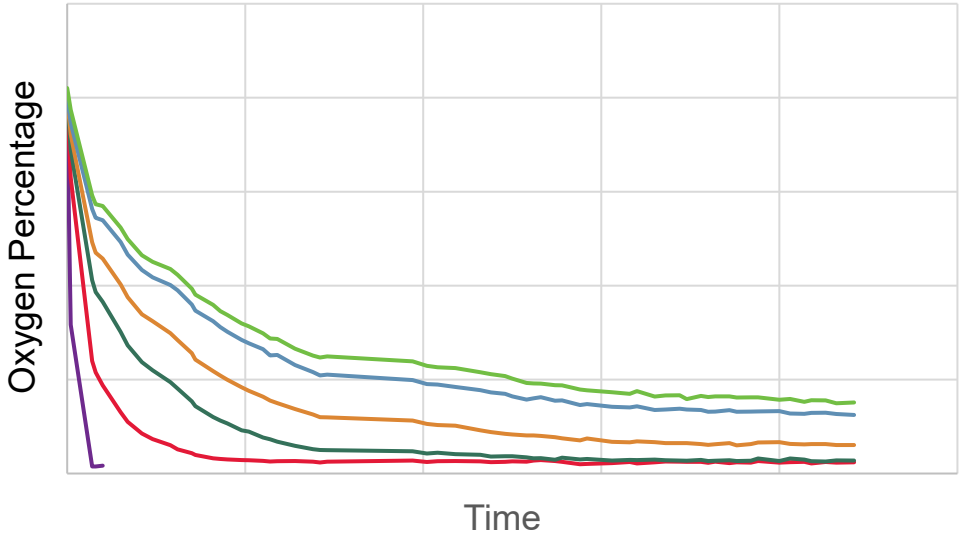
Allows the **control of kinetics** based upon formulation:

- Uptake rate can be increased or decreased
- Absorption capacity can be increased or decreased
- Buffered RH solutions for products susceptible to over-drying

Moisture Adsorption Kinetics



Oxygen “Pull-Down” Performance

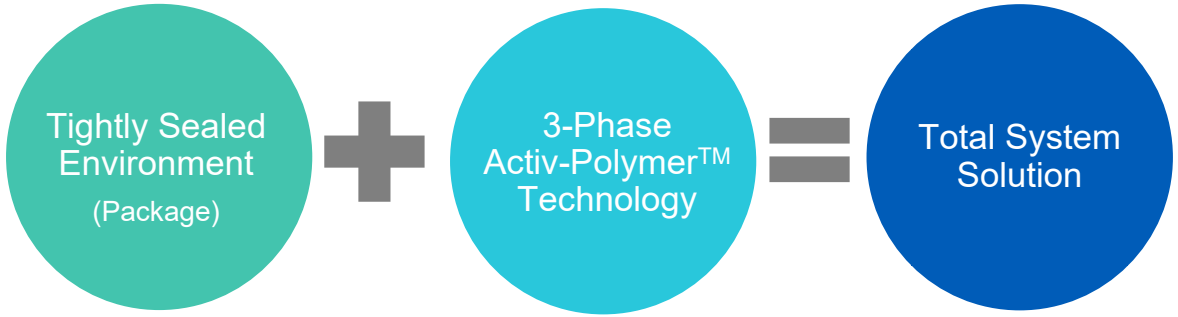


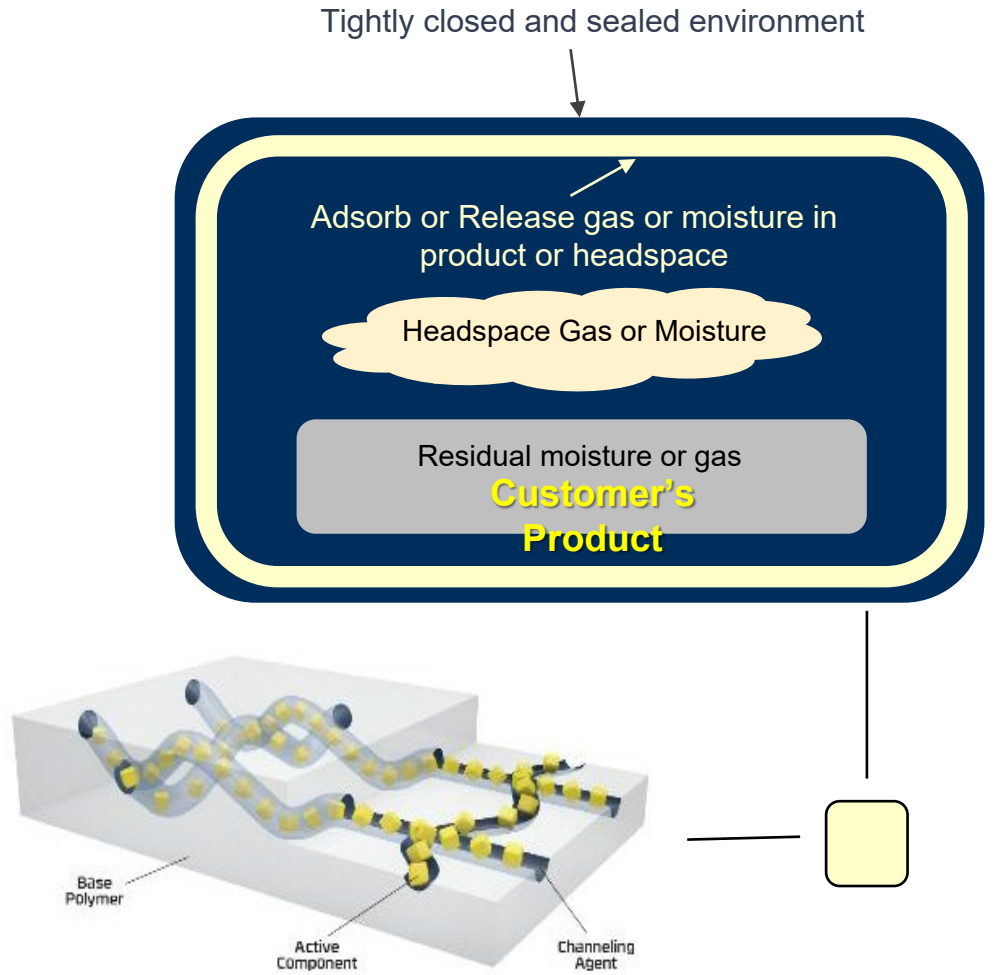
Active Packaging – Putting Chemistry into Polymers

Tightly Sealed Environment

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

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





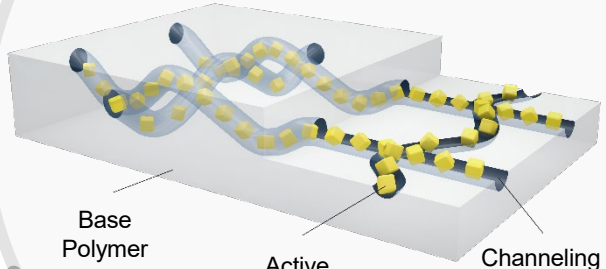
Active Material Science Platform Technology

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

Incorporate Desired Chemistry

- Moisture Control
- Scavenging - Oxygen, CO_2, Ethylene, Formaldehyde
- Antimicrobial
- Emitters
- Odor Removers

Aptar CSP 3-Phase Activ-Polymer™ PlatformTechnology



Commercial Applications

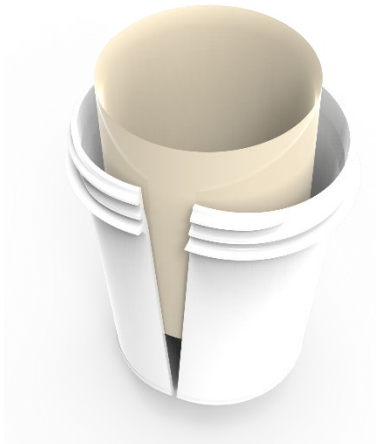
- Injection molding
- Thermoforming
- Extrusion Film
- Extrusion Blow Molding*
- Hot melt*

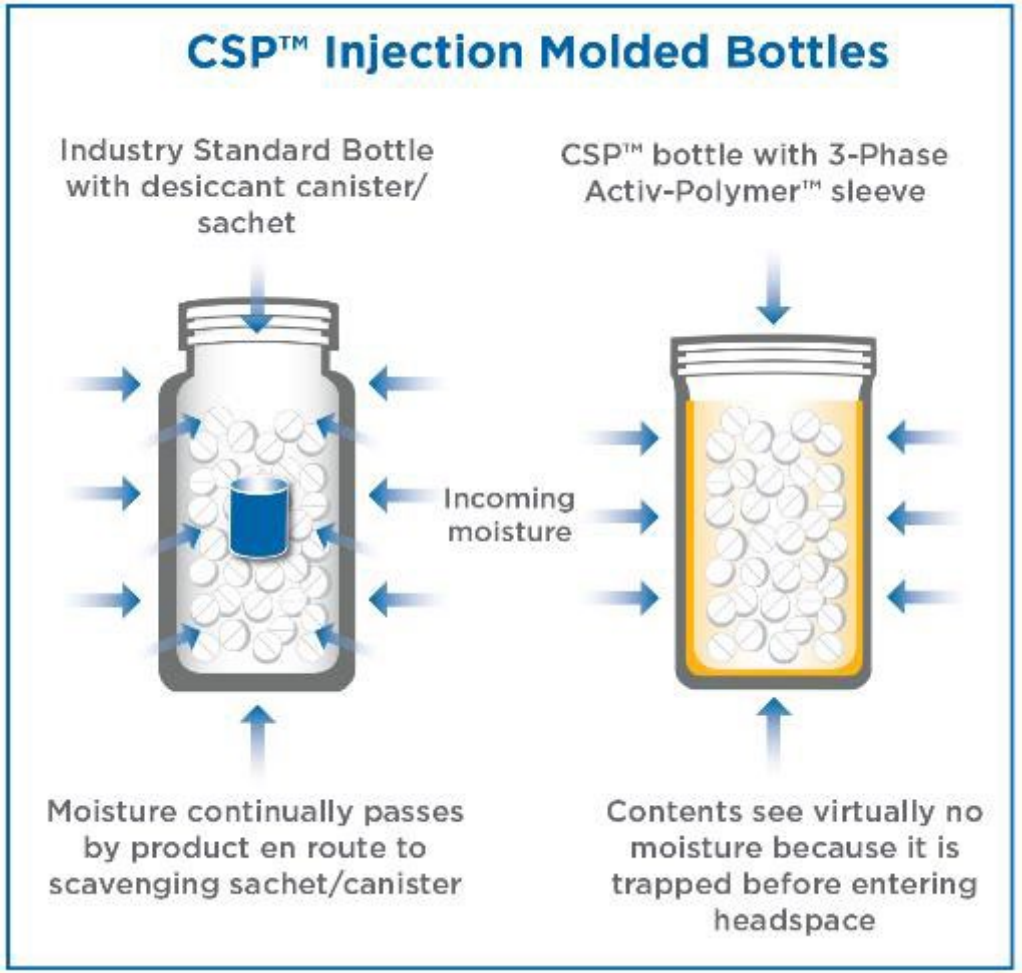
*Applications in development

Probiotics Formulations
Activ-Vial™

Technology Applications

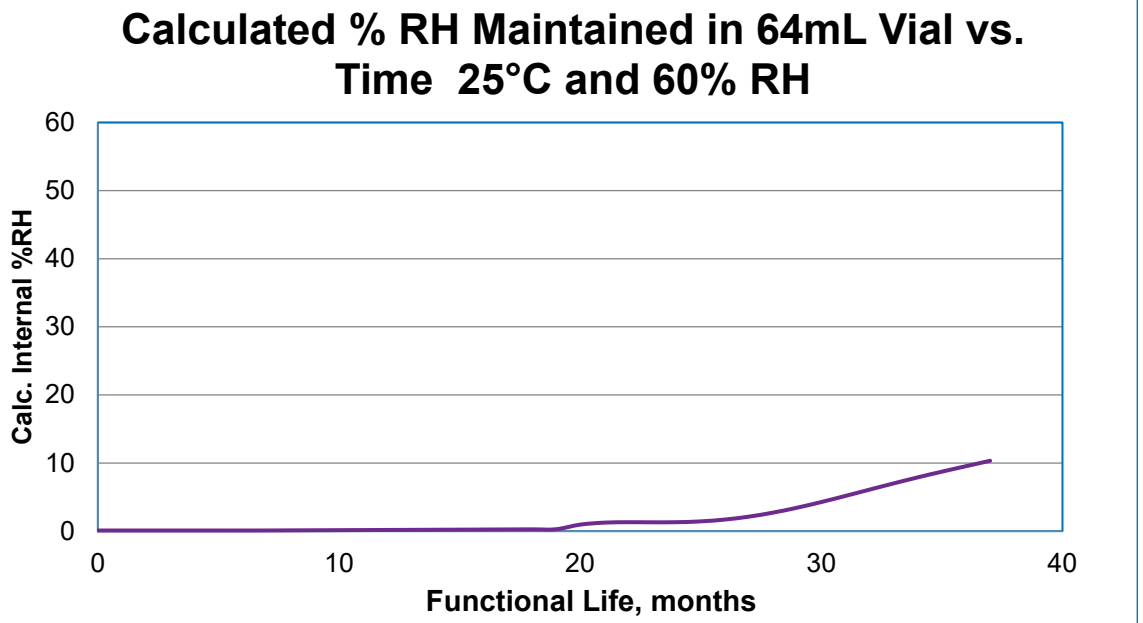
- **CSP™ Flip-Top Activ-Vial™** with integrated 3-Phase Activ-Polymer™ sleeve
- Patented “Close In The Mold” Technology Ensures **Moisture-Tight Seal**
- Maintains seal integrity throughout shelf life and consumer use life
- Child-Resistant/Senior-Friendly Closures
- Screw-Top versions also available



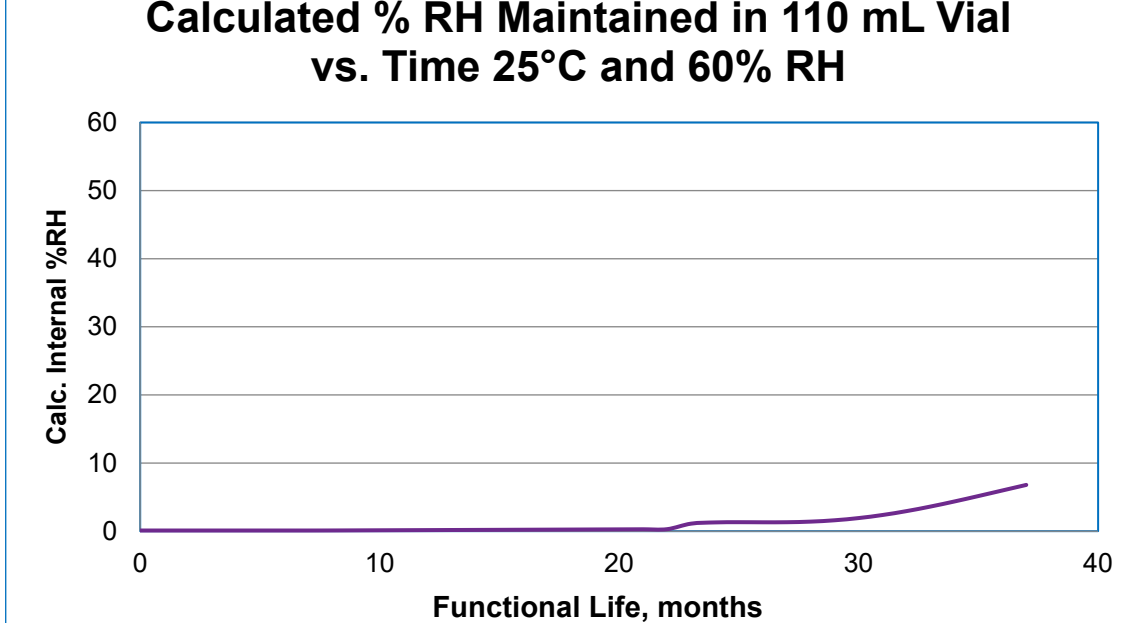


CSP™ Bottles Calculated RH Maintained

64ml and 110ml



- Data based on empty containers. Addition of product may impact %RH
- Data based on CSP's internal testing of bottles for foil seal integrity.
- Based on minimum capacity and maximum moisture ingress per container



- Data based on empty containers. Addition of product may impact %RH
- Data based on CSP's internal testing of bottles for foil seal integrity.
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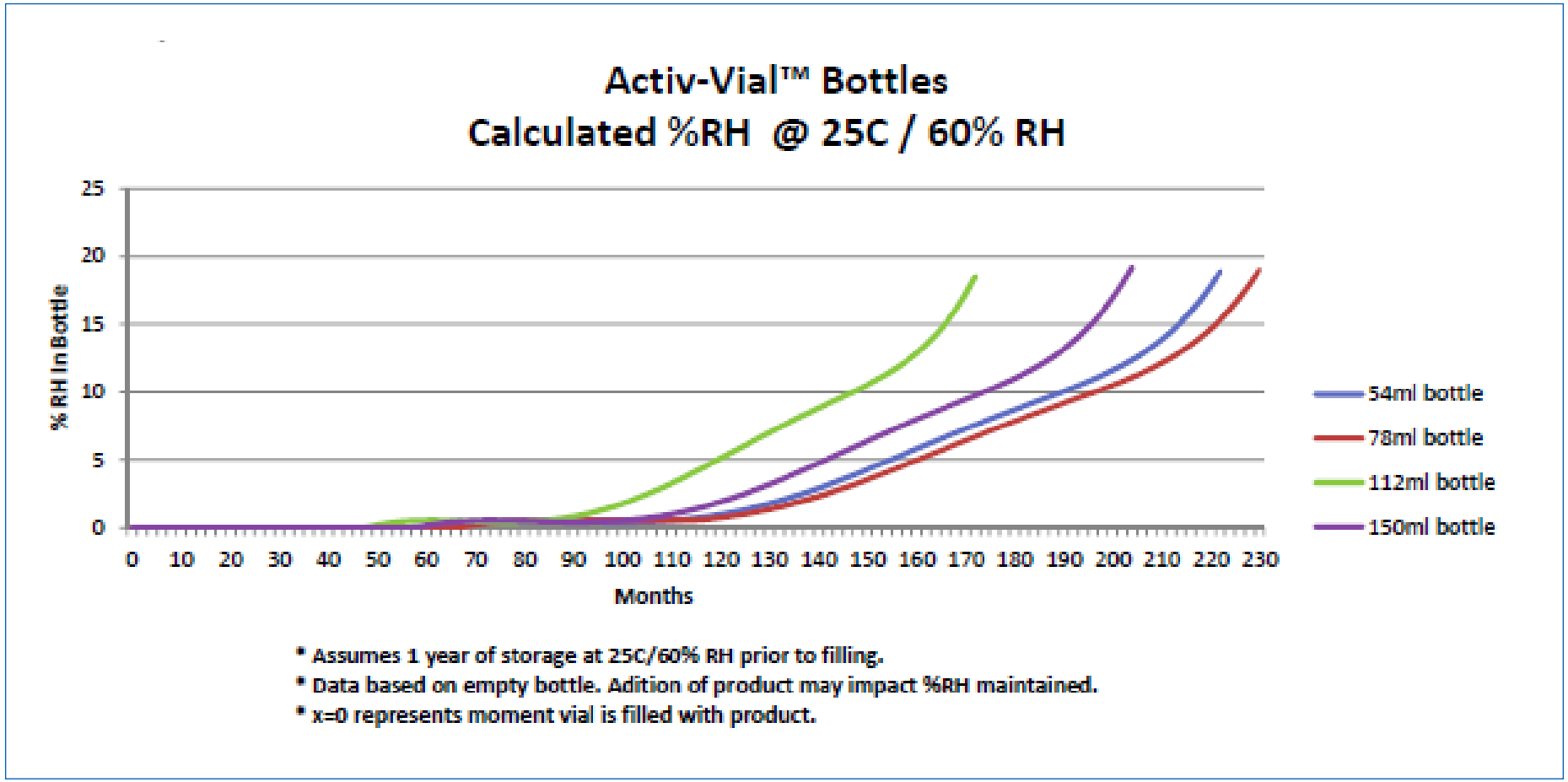
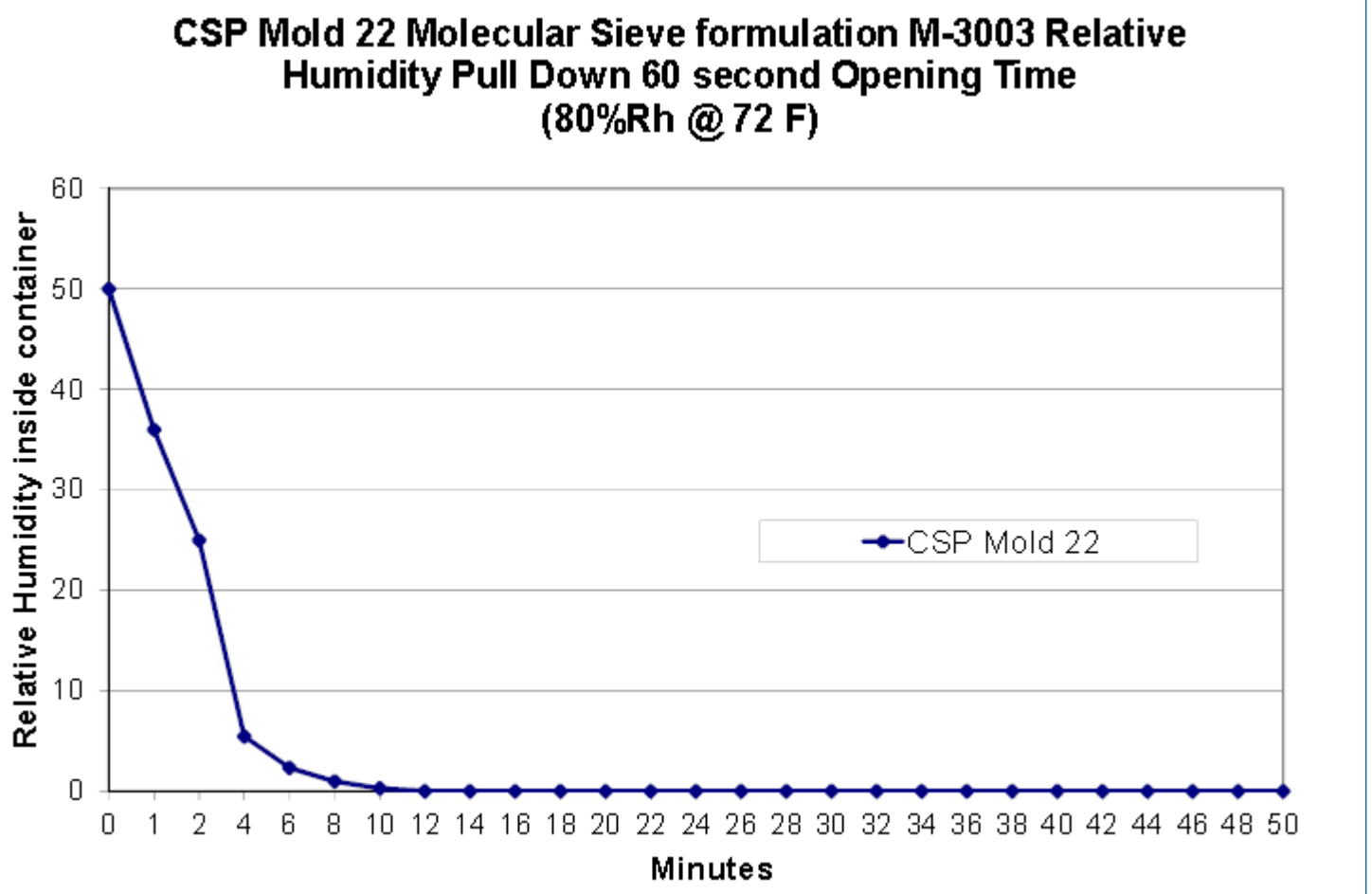
CSP™ Bottles RH Maintained

54ml, 78ml, 112ml, 150ml



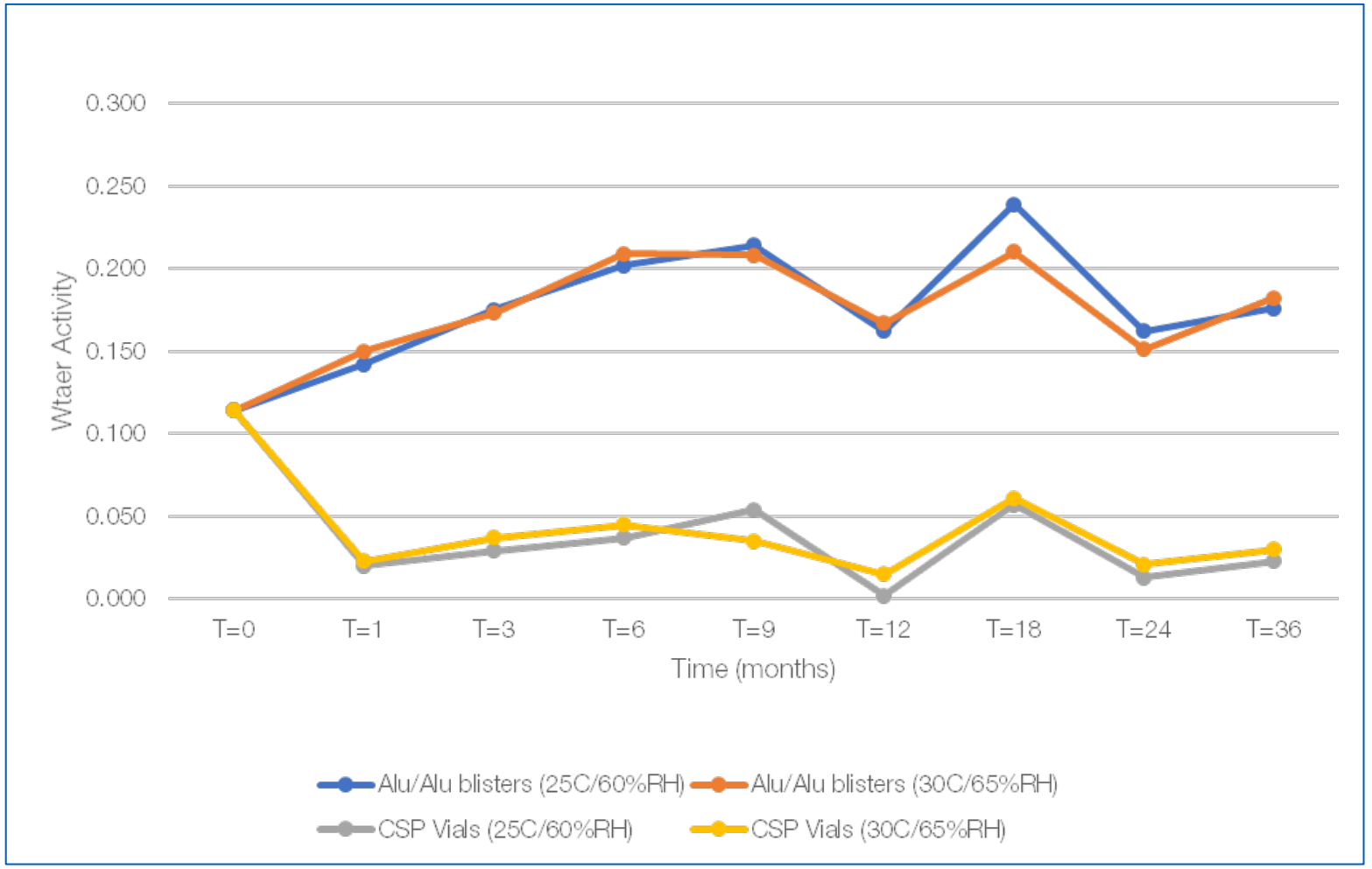
Humidity Control During Use Life

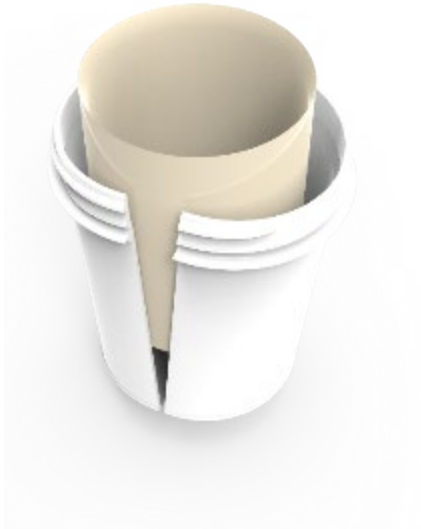


Probiotics capsules will remain dry during all use life

Probiotic Capsules – Water Activity

(CSP™ Activ-Vial™ vs Alu/Alu Blisters)

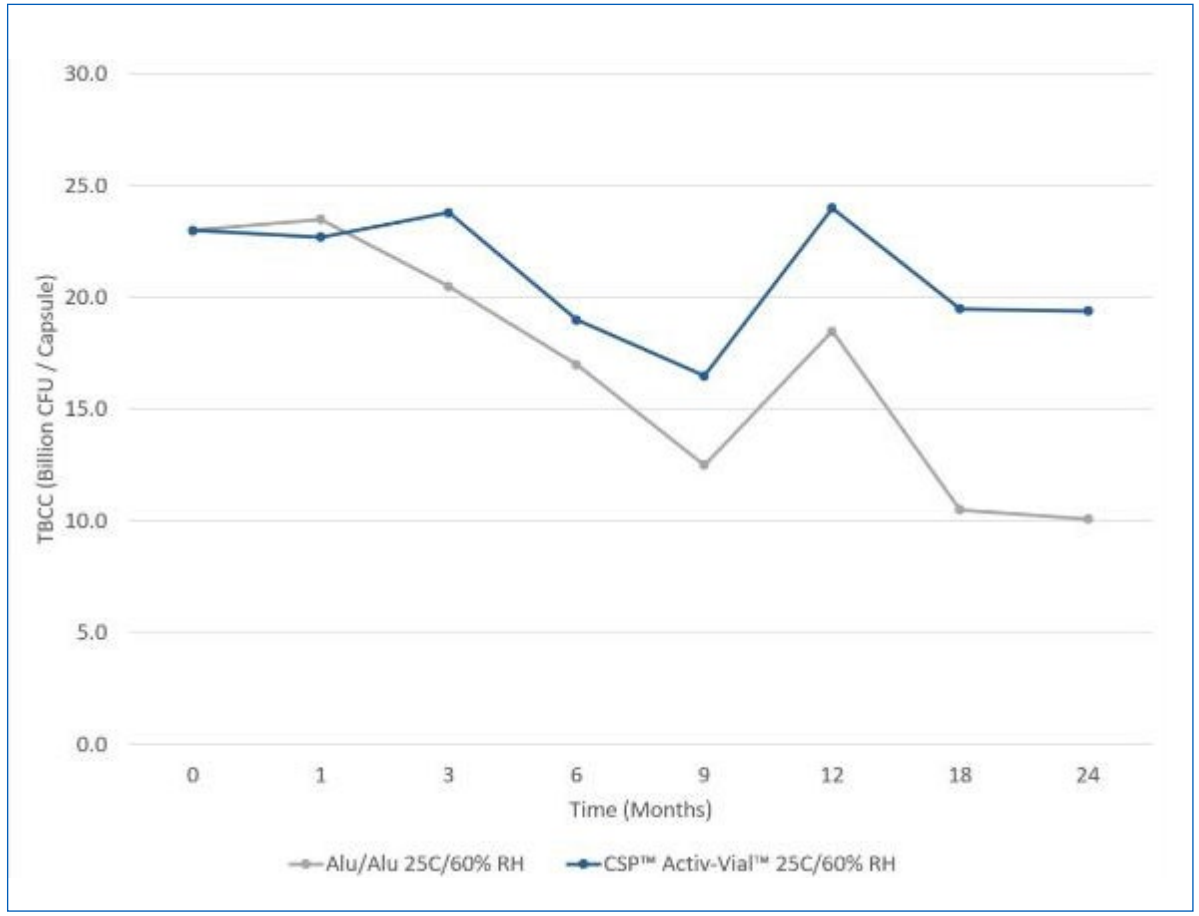


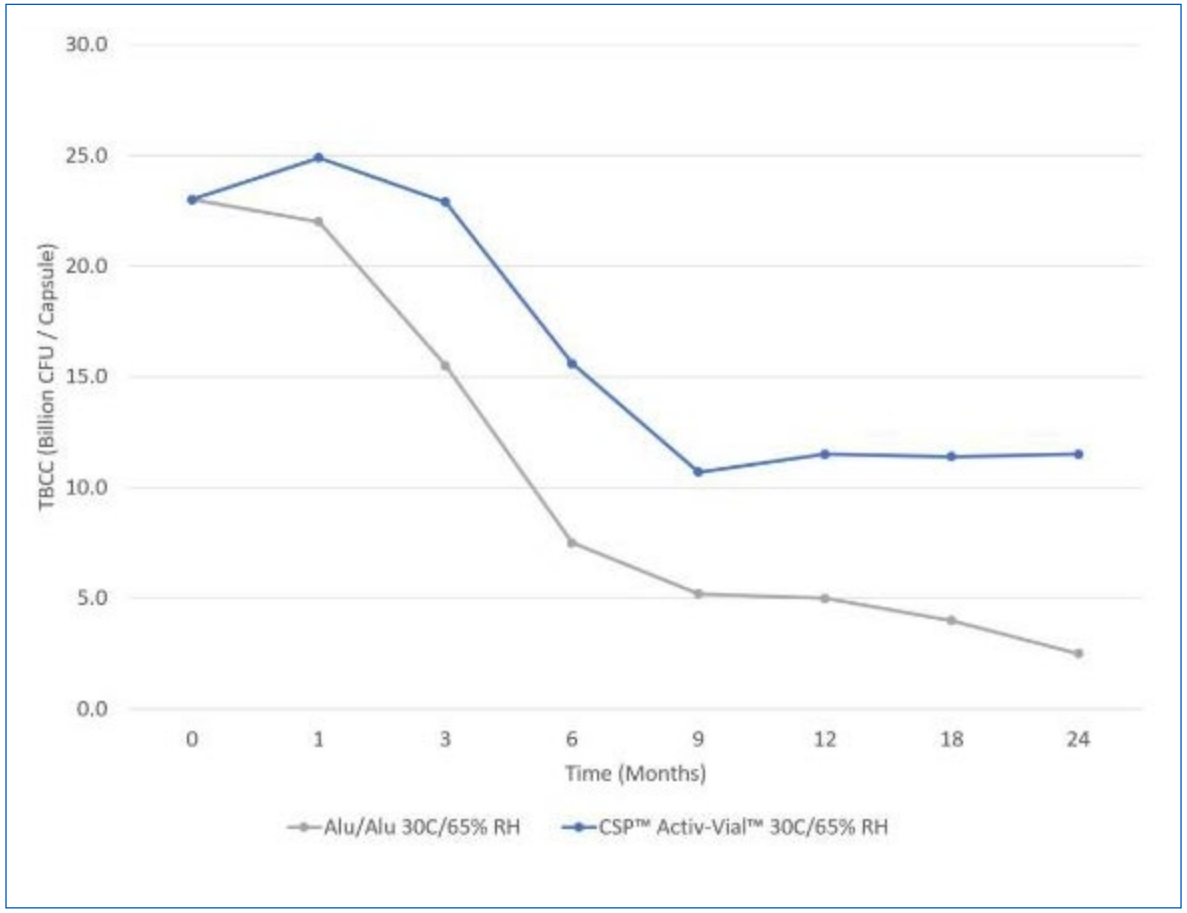


Study performed in partnership with UAS Labs, a leading probiotic manufacturer.

Probiotic Capsules – Strain Potency

(CSP™ Activ-Vial™ vs Alu/Alu Blisters)





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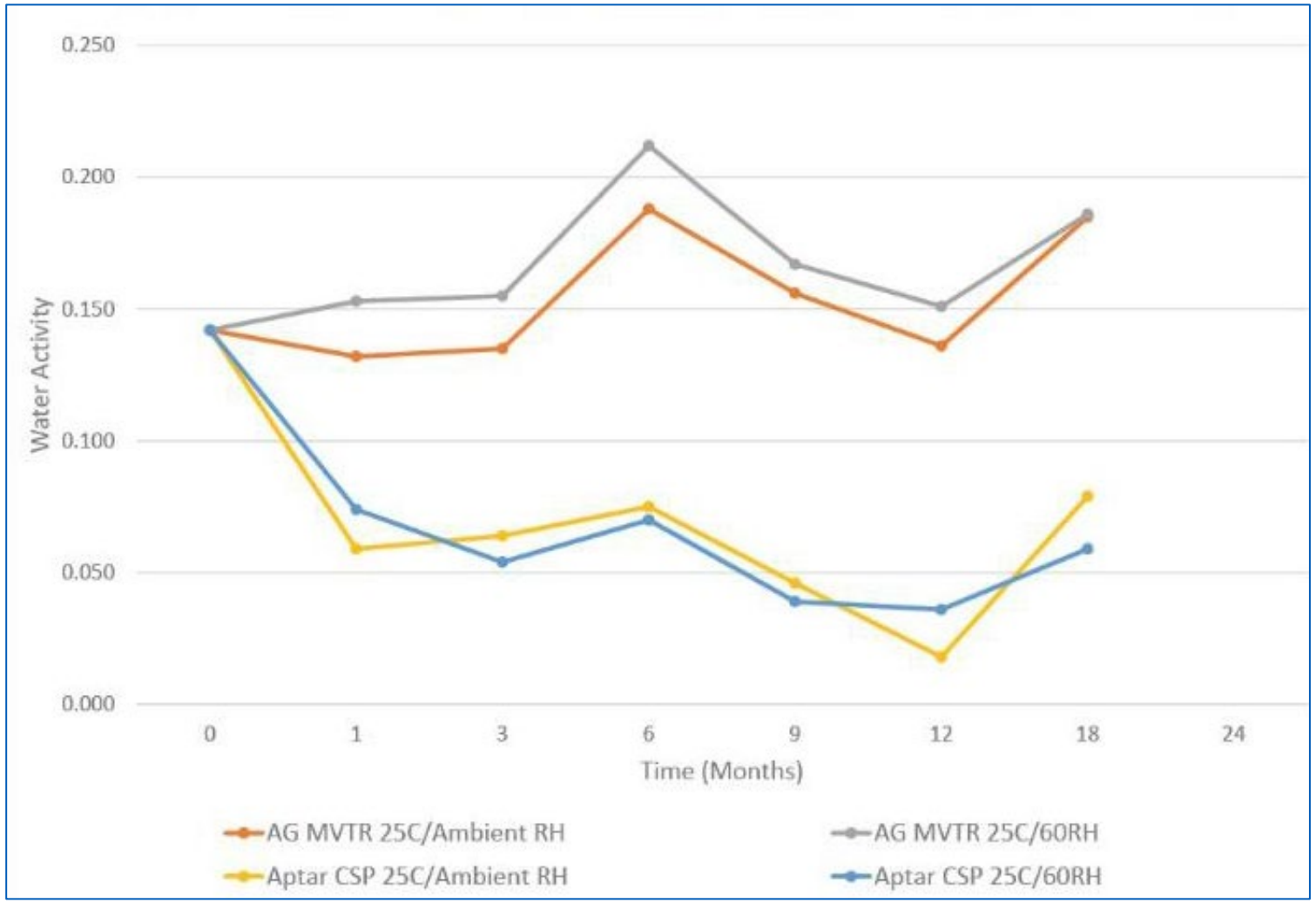
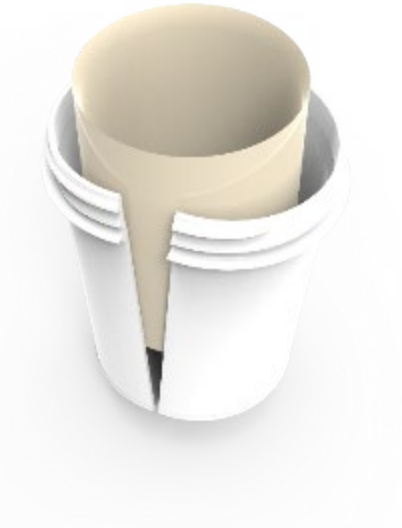
Water Activity in Probiotics + Cranberry

CSP™ Activ-Vial™ vs. Amber Glass with Desiccant





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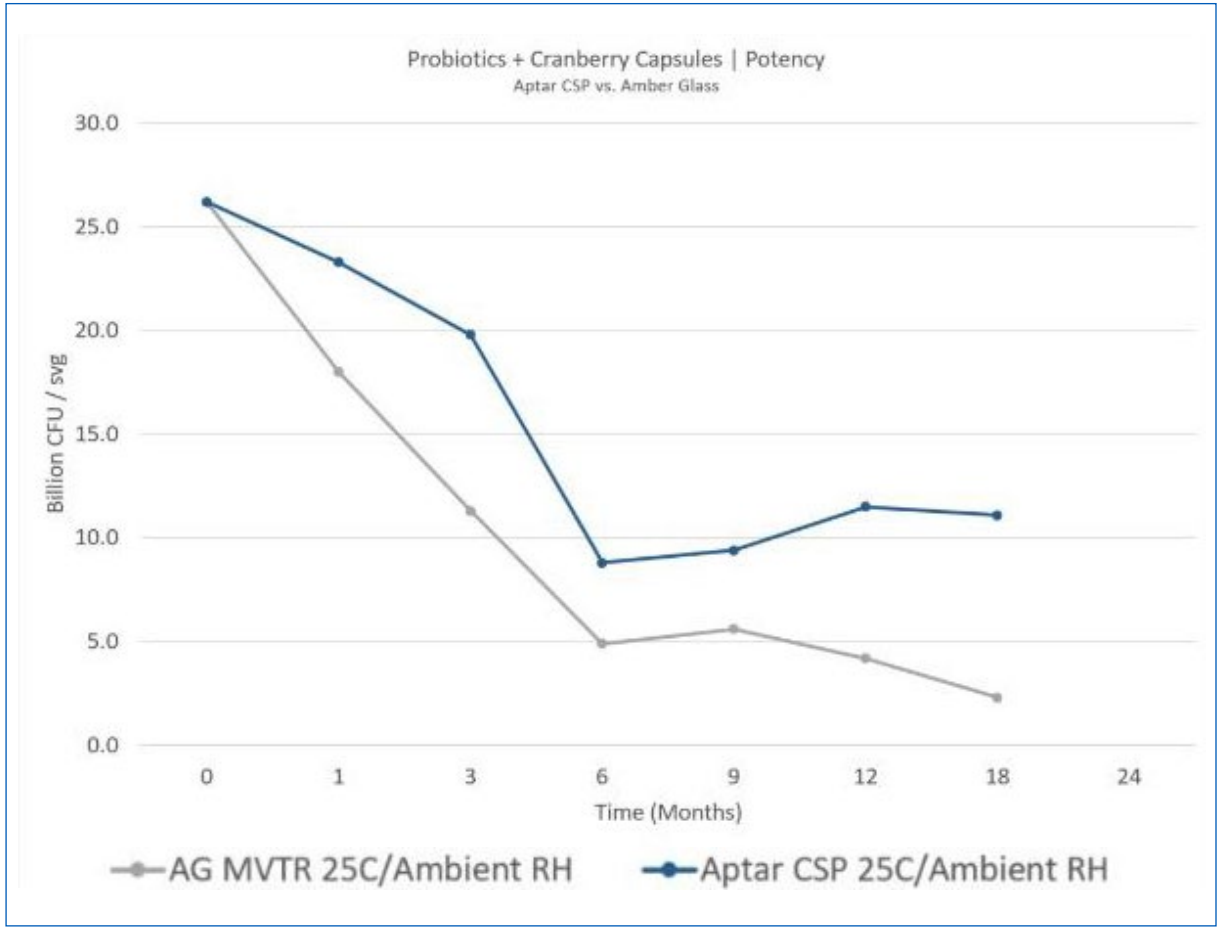
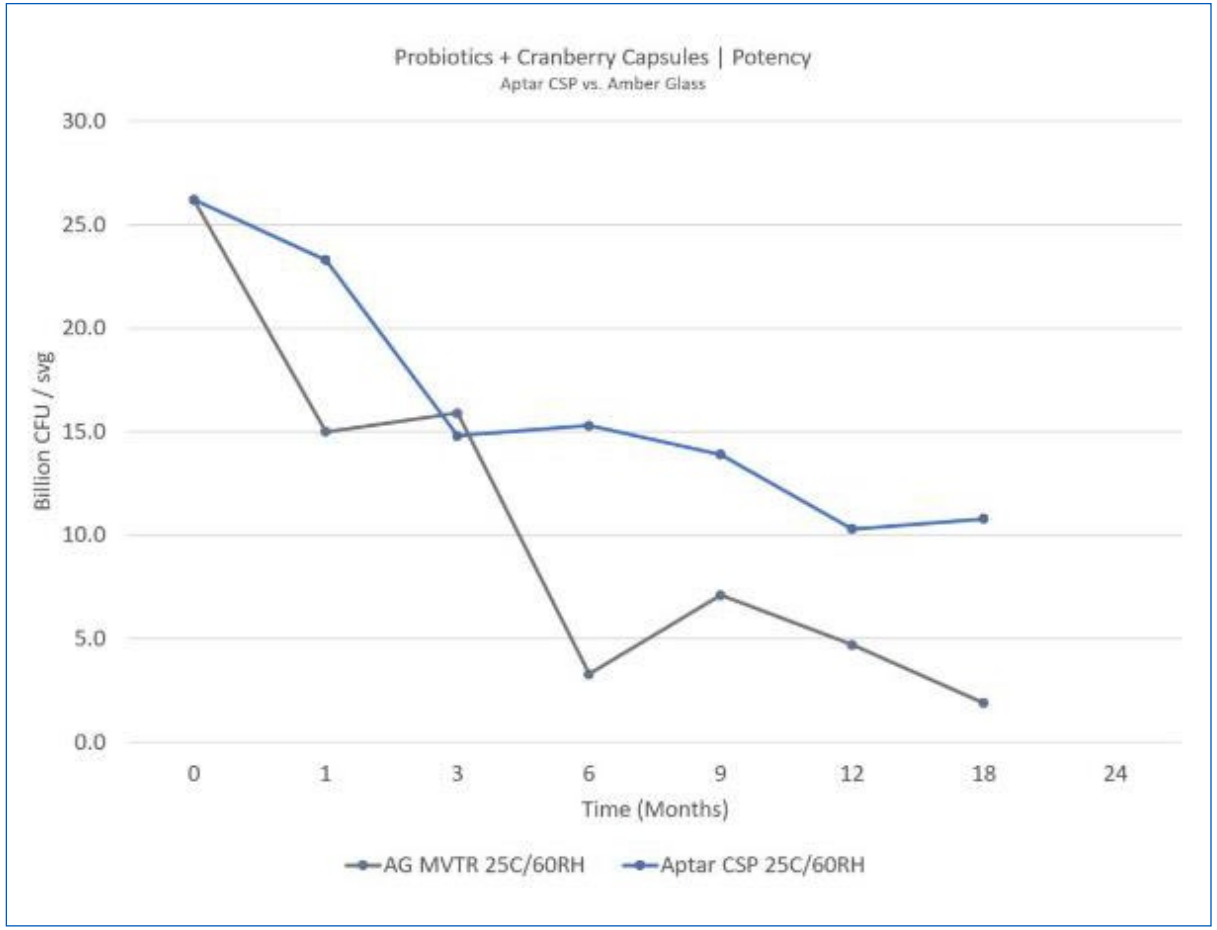
Potency of Probiotics + Cranberry Capsules

CSP™ Activ-Vial™ vs. Amber Glass with Desiccant





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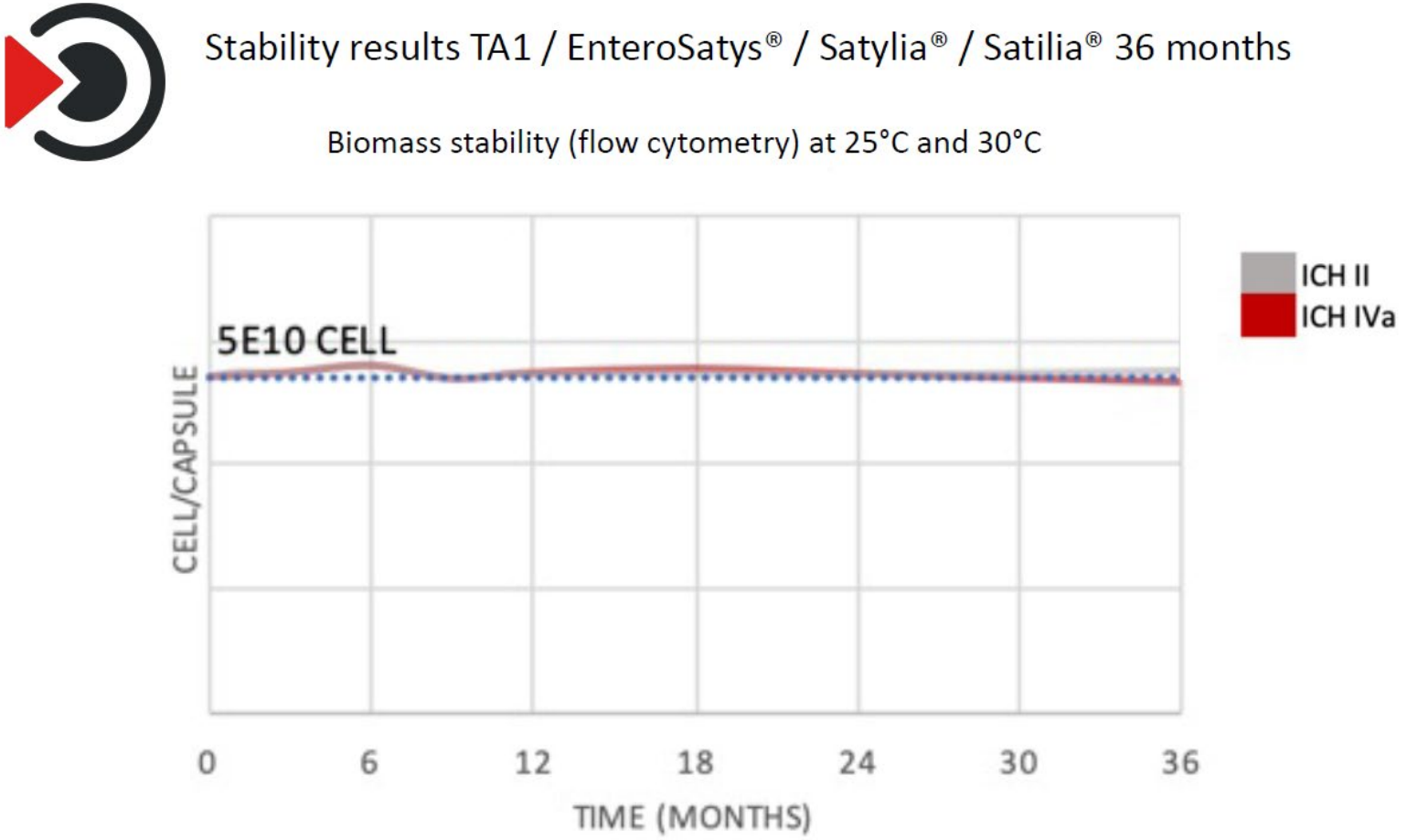
3 Years Stability Results

In collaboration with Targedys (France)



3 Years Stability Results

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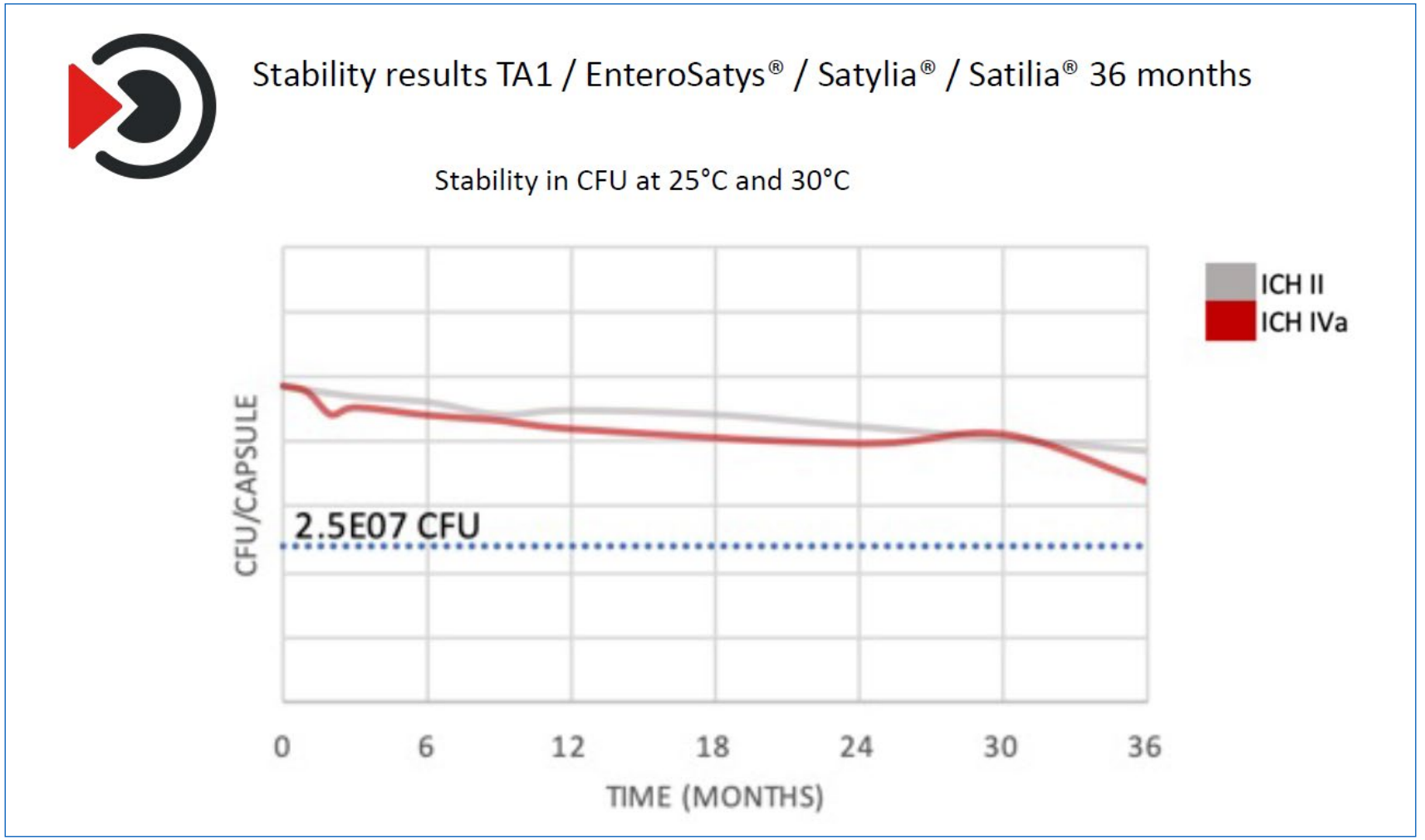


Probiotics Formulations
Activ-Polymer™ Molded Components

Probiotics Applications: Molded Components

- Can be integral device component (ex: reconstitution cap or straw)
- Adsorbs **moisture, O_2, odors, etc.**
- Maintains very tight dimensional tolerances

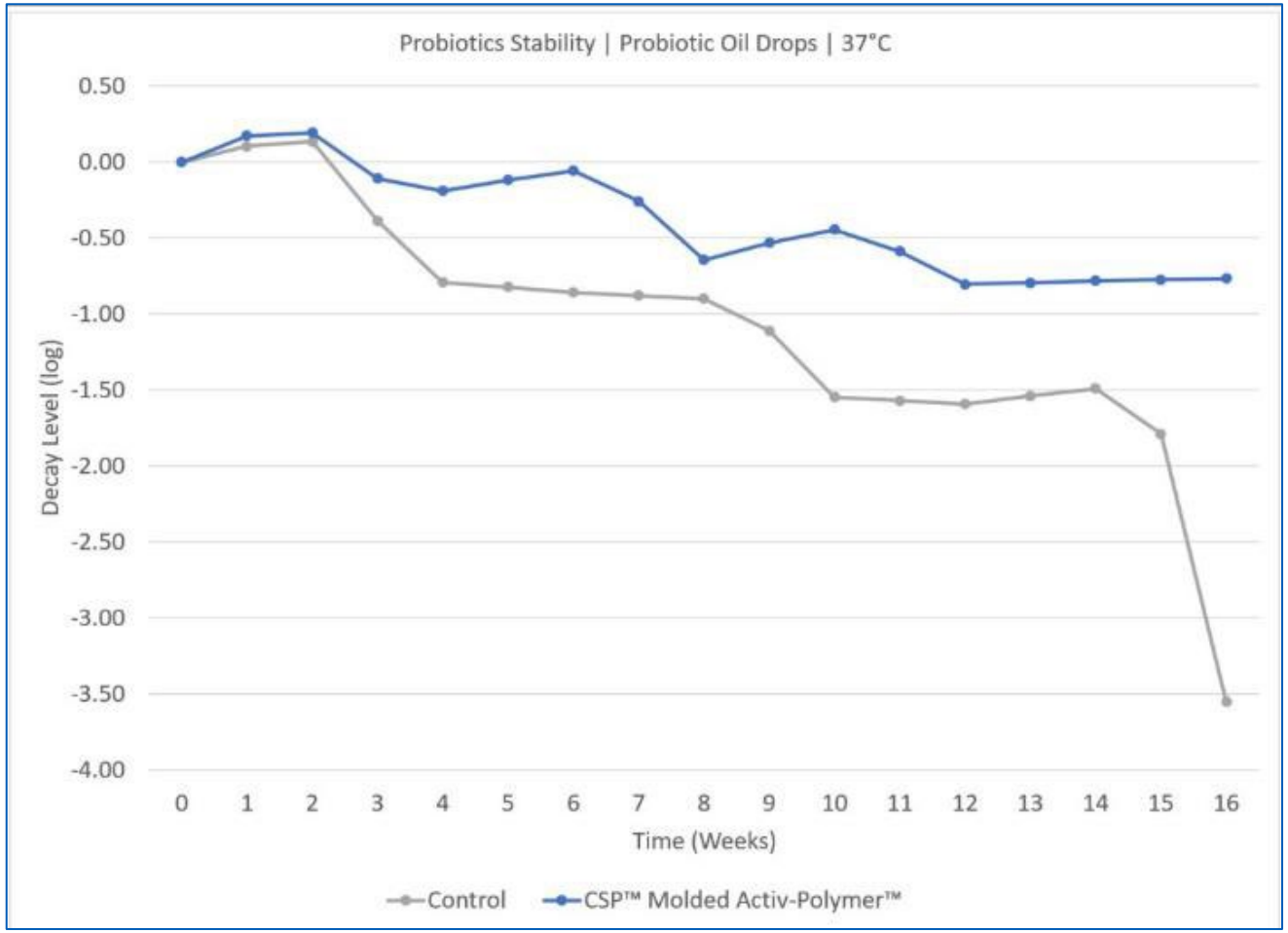
Activ-Tab™
Probiotics Oil Suspension

Bormioli 3 Phase
Probiotics Powder

X-Straw
Drug or Food Supplements Administration

Probiotic Oil Drops Stability

(CSP™ Molded Activ-Polymer™ vs. Control)



CSP™ Molded Activ-Polymer™ in graph uses 1 Tablet:

- 3mm thick x 8mm OD
- 0.2 gram

Data courtesy of

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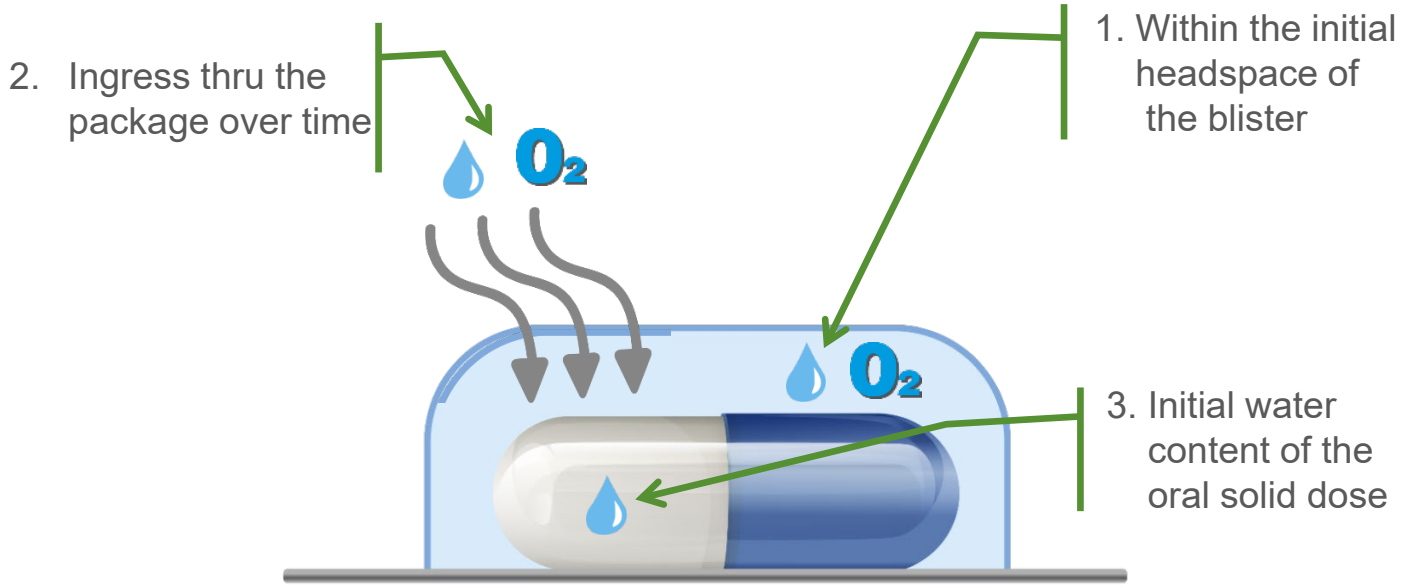
Probiotics Formulations
Activ-Blister™ Solutions

Probiotics Application Activ-Blister™ Solutions

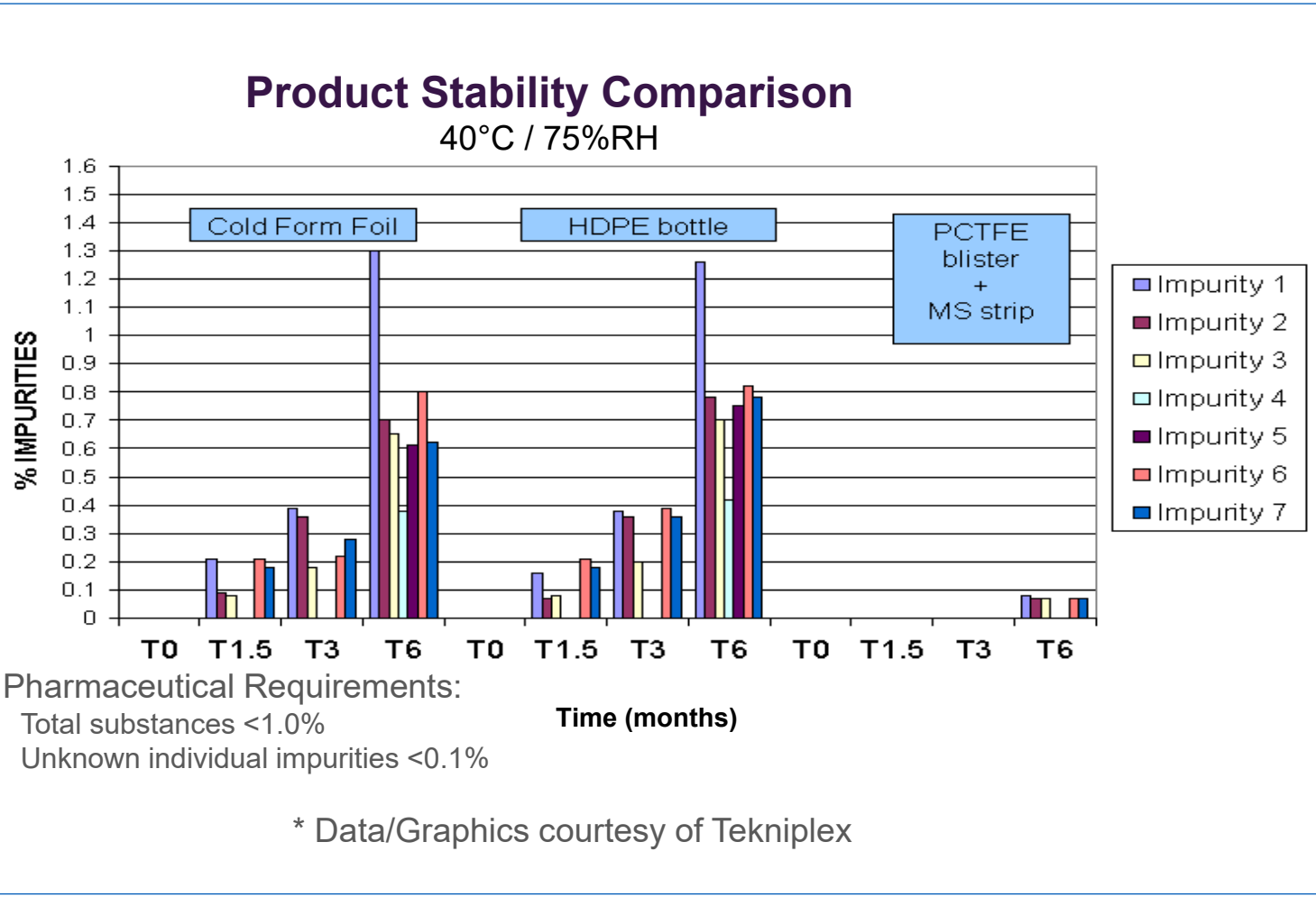
- Incorporating 3-Phase Activ-Film™ into blister packaging solutions
- 3-Phase Activ-Film™ heat staked to foil
- Protects product from moisture, oxygen, CO_2, reactive impurities and odors
- **Active headspace protection** achieved without extra steps (e.g. gas flush/purging, secondary packaging, or refrigeration)
- **Size reduction** → move from cold-form foils to thermoforms for a smaller blister footprint (**40-60% smaller)**

Sources of Moisture and Oxygen



Activ-Blister™ Solutions

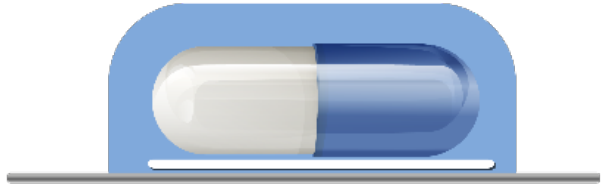
Results compared to Cold Form Blisters and HDPE Bottles



NOTE: Pharmaceutical Requirements:

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

* Data/Graphics courtesy of Tekniplex

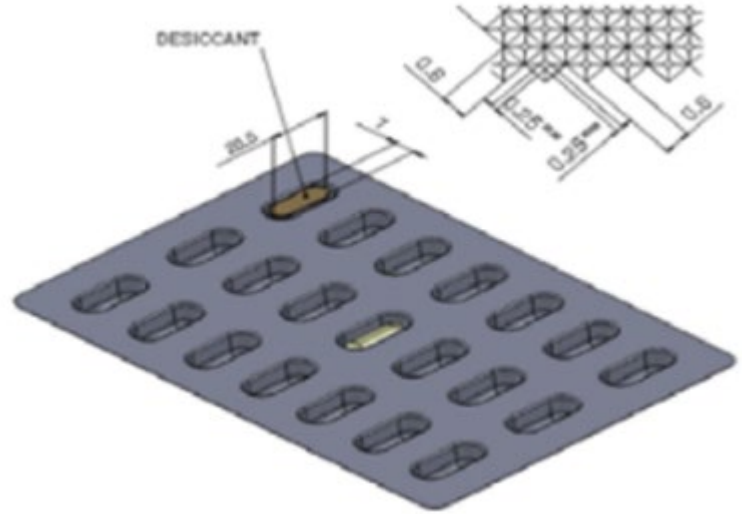


Activ-Blister™ Solutions

Results of Aclar-type thermoformed blisters + Activ-Film

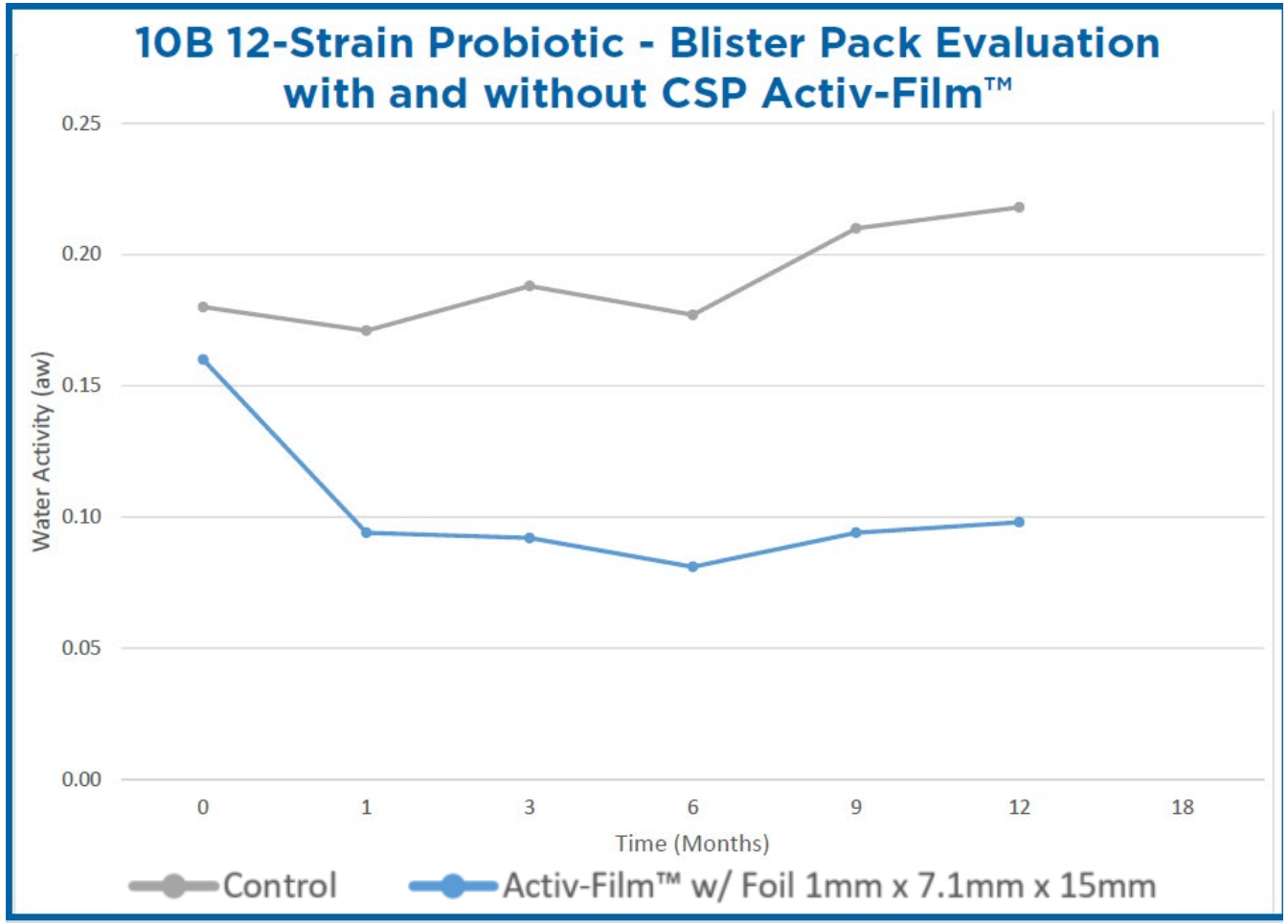
Aclar® type	Temp/RH (°C/%RH)	Days to saturation
Rx160	25/60	209
Rx160	30/65	71
Rx160	40/75	21
UltRx2000	25/60	370
UltRx2000	30/65	220
UltRx2000	40/75	71
UltRx6000	25/60	1036
UltRx6000	30/65	647
UltRx6000	40/75	209

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



Probiotic Capsule Water Activity

(Standard PVC.PvdC Blister Packaging vs. Activ-Blister™ Packaging with CSP Activ-Film™)



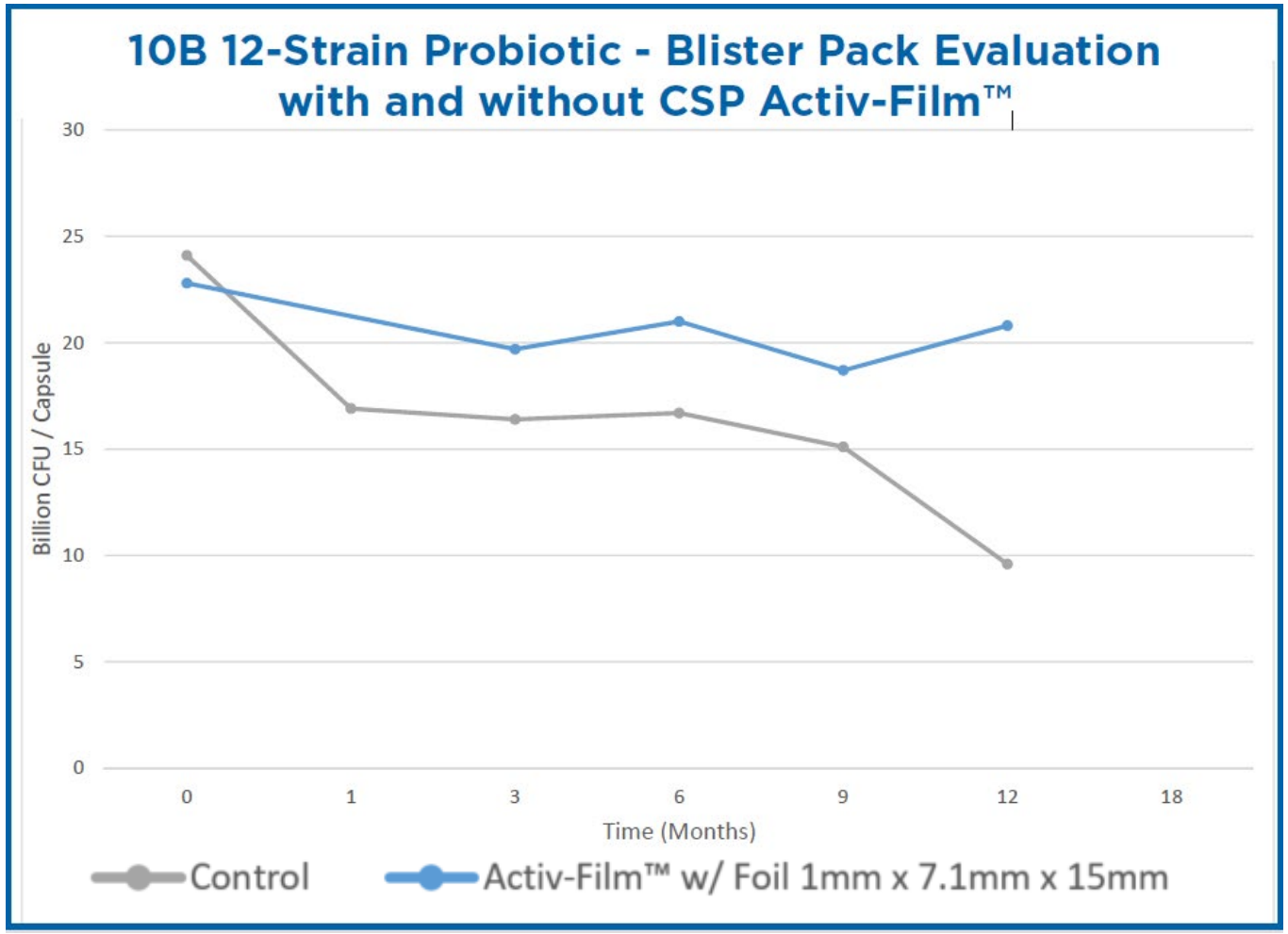
Storage Conditions:
22°C ± 2°C
40% ± 5% RH

Data courtesy of

MERICAL

Probiotic Capsule Potency

(Standard PVC.PvdC Blister Packaging vs. Activ-Blister™ Packaging with CSP Activ-Film™)



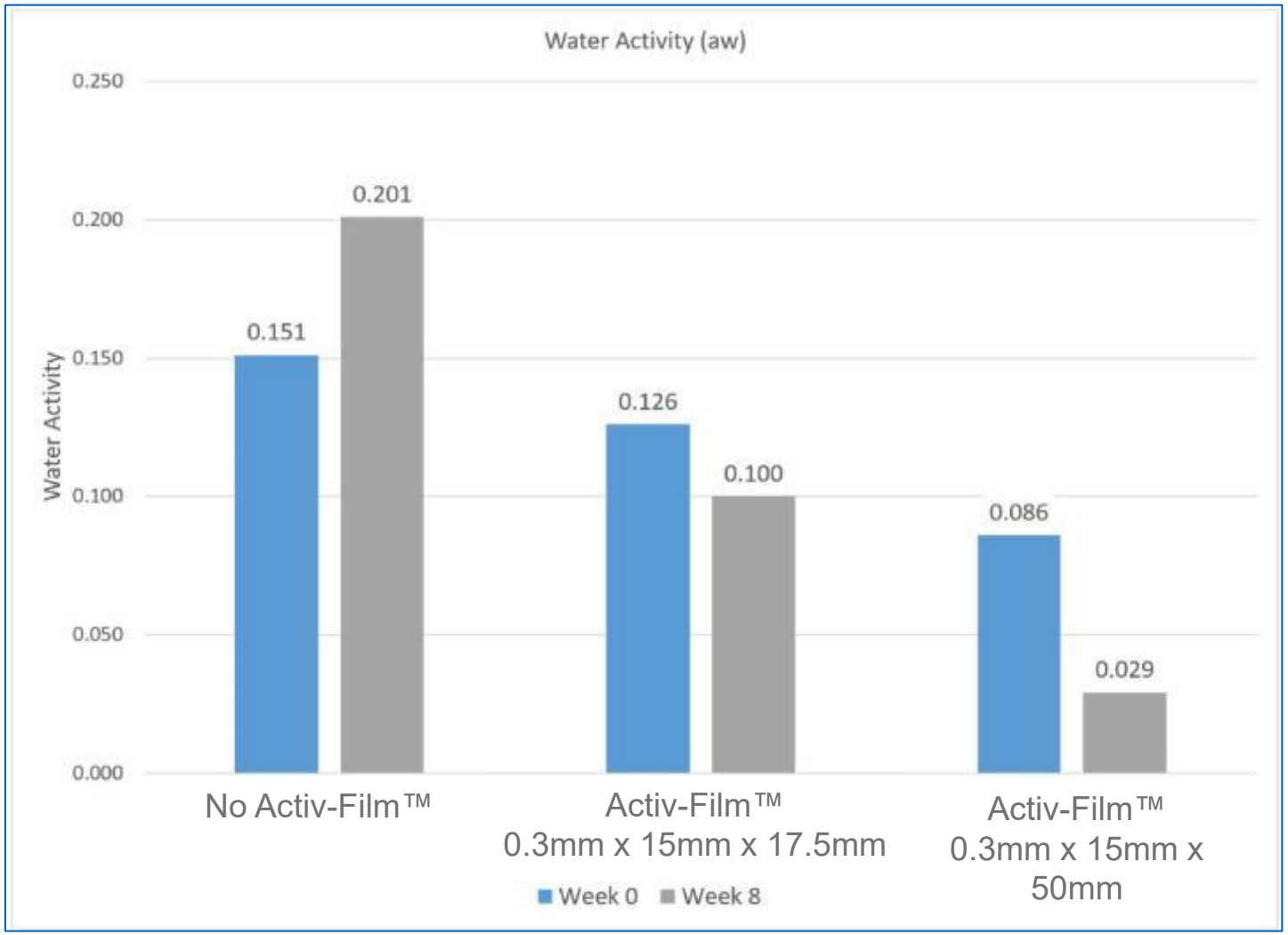
Storage Conditions:
22°C ± 2°C
40% ± 5% RH

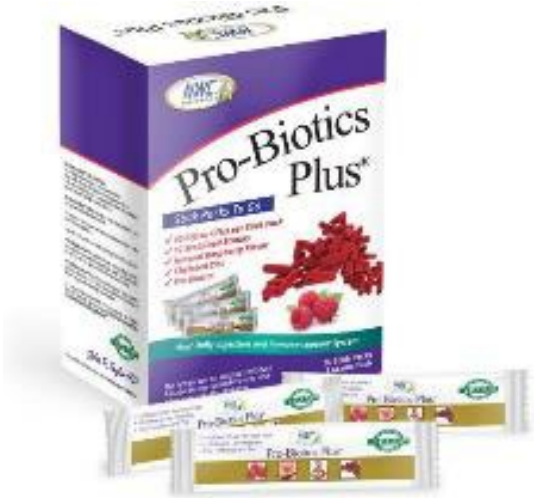
Data courtesy of

MERICAL

Probiotic Stick Pack Water Activity

(CSP™ Activ-Film™ vs. No Activ-Film™, Ambient Conditions)





Data courtesy of

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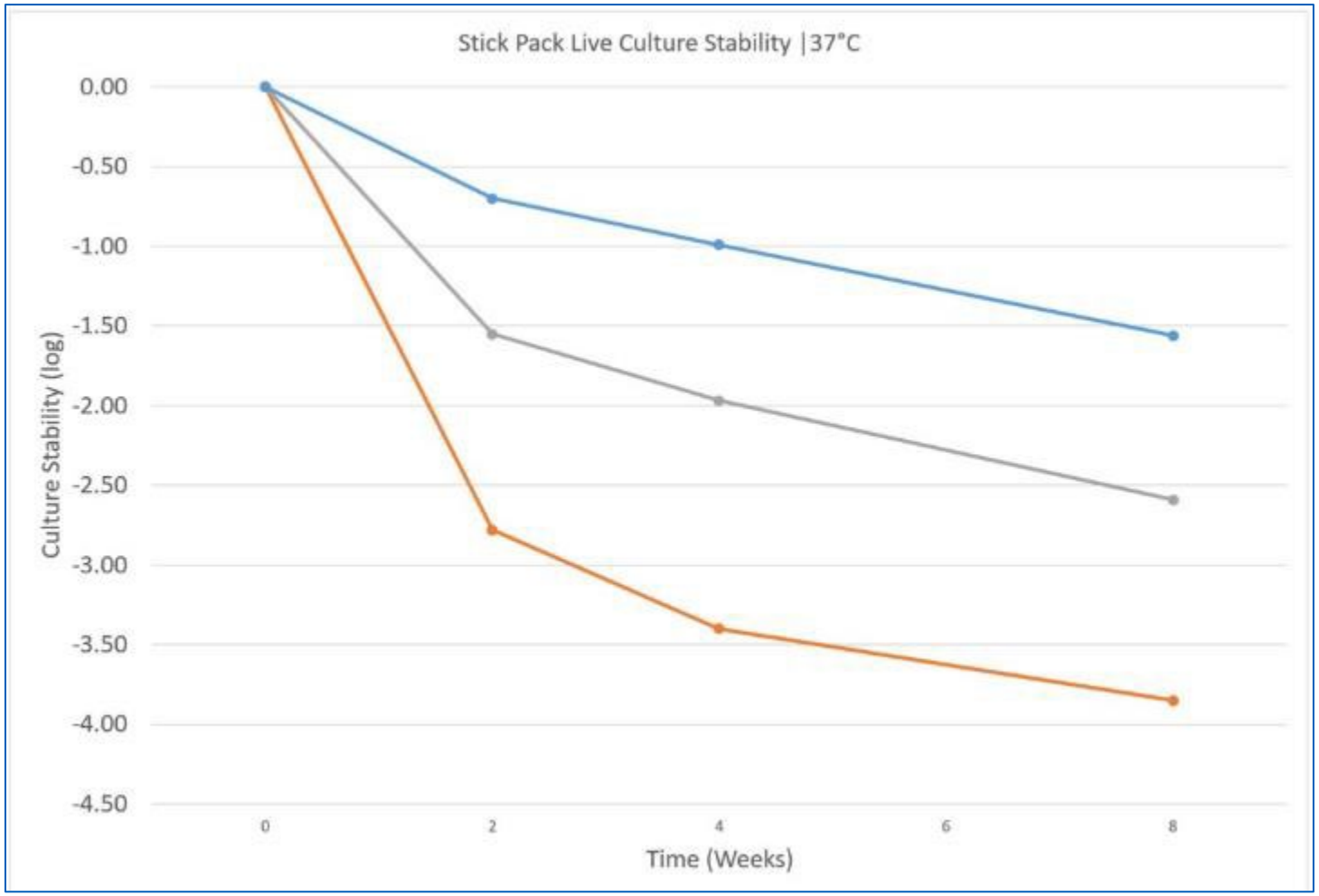
Probiotic Stick Pack Stability

(CSP™ Activ-Film™ vs. No Activ-Film™)



No Activ-Film™

Activ-Film™ 0.3mm x 15mm x 17.5mm

Activ-Film™ 0.3mm x 15mm x 50mm

Data courtesy of

glac
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Thank you for your attention!

François Bidet

VP Business Development

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