

# Capsugel<sup>®</sup> Dry-Powder Inhalation Capsule Portfolio

External Launch Presentation

November 12, 2019



# Presenters Bio



**Business  
Development  
Lead**



**Technical  
Lead**

# Why the Interest in DPI Today?

Capsugel® Zephyr™: Dry-Powder Inhalation Portfolio - November 12, 2019

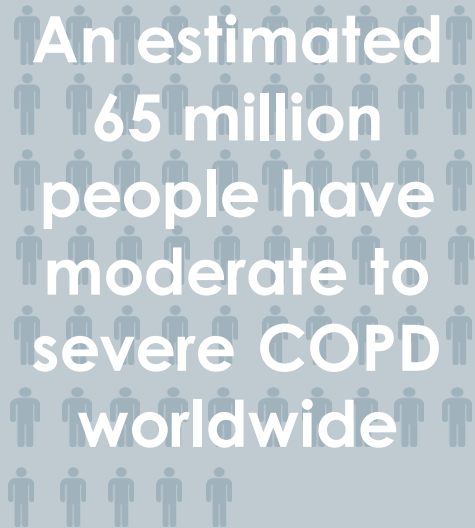


# Trends in Pulmonary Pathologies

## Global Statistics

Capsule  
Delivery  
Solutions

**Lonza**  
Pharma & Biotech



An estimated  
65 million  
people have  
moderate to  
severe COPD  
worldwide

About 334 million  
people suffer from  
asthma



Respiratory  
diseases make up

5  
—  
30

most common  
causes of death

3<sup>rd</sup>

Leading cause of death worldwide,  
and the numbers are increasing

14%

Of children are affected globally and  
it is the most common chronic  
disease of childhood.

10%

Of all disability-adjusted life-years  
(DALYs), a metric that estimates the  
amount of active and productive life  
lost due to a condition.

[https://www.who.int/gard/publications/The\\_Global\\_Impact\\_of\\_Respiratory\\_Disease.pdf](https://www.who.int/gard/publications/The_Global_Impact_of_Respiratory_Disease.pdf)

# Increased Interest for the Pulmonary Route

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## Systemic Application

- A non-invasive 'needle-free' delivery system
- Suitable from small molecules to very large proteins
- Enormous absorptive surface area, highly permeable membrane in the alveolar region
- Slow clearance in the lung results in prolonged residency in the lung
- Low enzymatic environment that is devoid of hepatic first-pass metabolism



## Pulmonary Diseases

- High concentration directly to the disease site
- Minimizes risk of systemic side effects
- Rapid clinical response
- Bypass the barriers to therapeutic efficacy
- Achieve a similar or superior therapeutic effect at a fraction of the systemic dose

# A Wide Variety of Inhalation Delivery Technologies

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## Pressurized metered dose inhalers (PMDI)



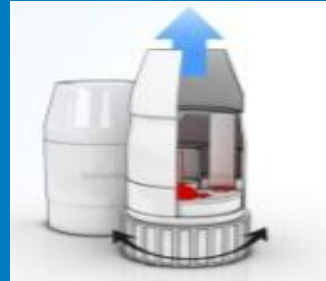
Commonly used in **emergency treatment**

### Market share

33% drug sales & 69% of inhalers sold

## Dry powder inhalers (DPI)

*3 main types*



Reservoir



Capsule



Blister

Mainly used in **preventive therapy**

### Market share

51% drug sales & 24% of inhalers sold

## Non-Portable Nebulizer Devices



Used in **emergency & preventive treatments**

### Market share:

9% of drug sales & 5% of inhaler sold

## Soft Mist Inhaler (New generation PMDI)



Used in **preventive therapy**

### Market share:

7 % of drug sales & 2% of Inhaler sold

Source: IMS

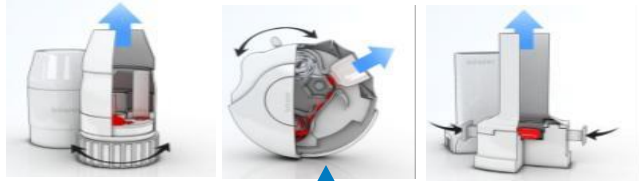
# Benefits of Capsule-Based DPI Systems

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## Dry-Powder Inhaler



Patient  
Compliance



- No need for coordinated device actuation and patient inhalation
- Open the path for **connected device** and improved patient compliance



- Ease of use, **commitment**, **self-assessment** of full medication dose delivered

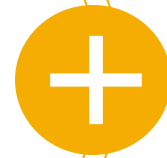
## Capsule-Based DPI



Cost-  
Effective



- Device flow-rate/inhalation requirements **can be adapted** to targeted patient population
- **High dose** carrying capacity
- Different level of **sophistication** available



- **Easy to manufacture** (standard filling equipment)
- Wide offer of **off-the-shelf devices**

Compatibility



- Potential **drug stability** advantage



- Compatible with **standard** carrier-based formulations and **new engineered particles** (Jetmill, Spray-Dried), ideal platform for combination drugs

Eco-  
Friendly



- No propellant



- **Re-usable** device, **biodegradable** capsule

# What is Capsugel® Zephyr™?

Capsugel® Zephyr™: Dry-Powder Inhalation Portfolio - November 12, 2019



# Capsugel® Zephyr™ Portfolio Products

## Coni-Snap®



Coni-Snap® Gelatin DPI

- **VP:** the cost-effective solution for less challenging formulations
- **Target segments:** Innovators & Generics
- **Target geographies:** worldwide

## Coni-Snap®



Coni-Snap® Gelatin-PEG DPI

- **VP:** the more robust gelatin-based solution
- **Target segments:** Generics
- **Target geographies:** worldwide



Vcaps® DPI

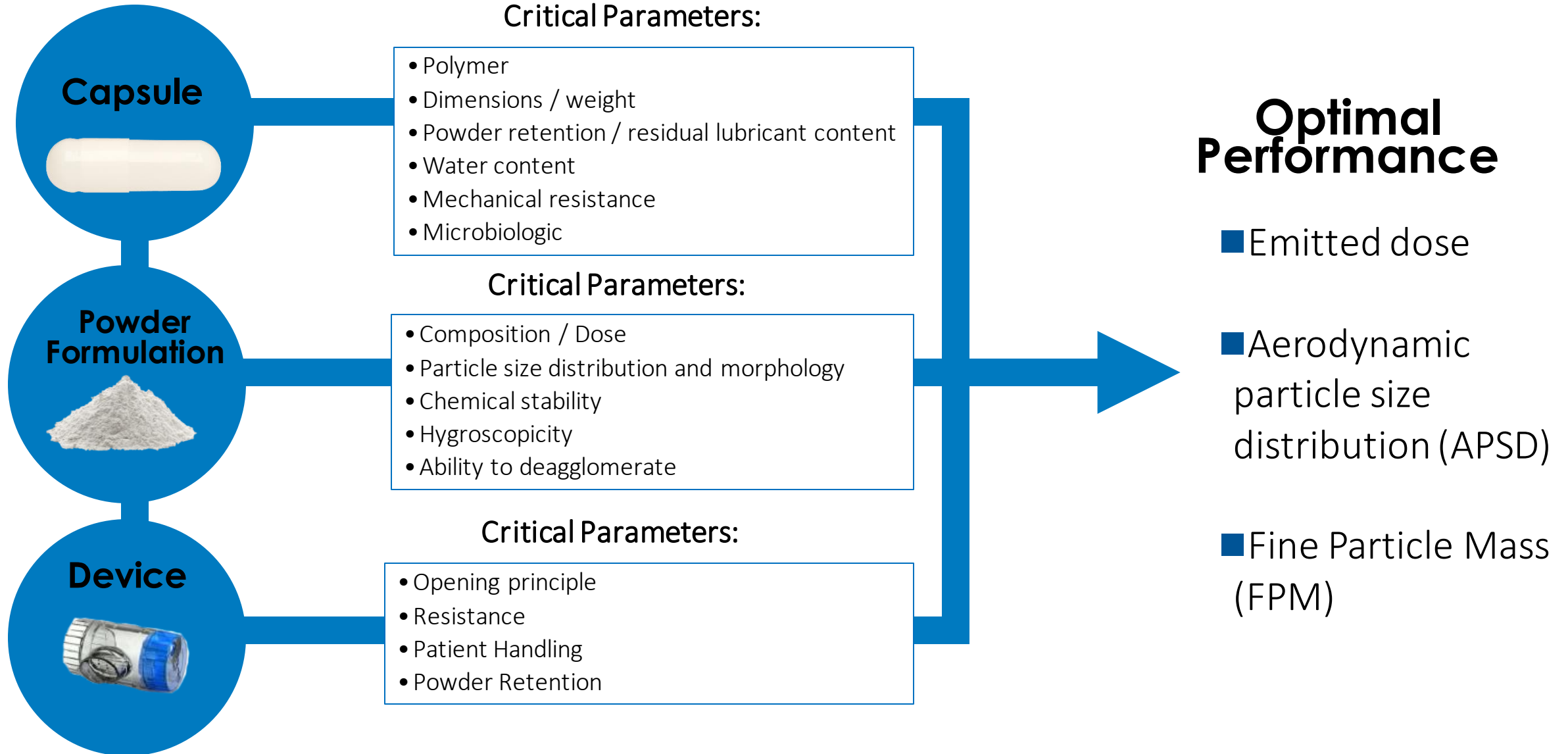
- **VP:** the superior HPMC performer with very low powder retention
- **Target segments:** Innovators & Generics
- **Target geographies:** worldwide



Vcaps® Plus DPI

- **VP:** the glossy and transparent HPMC capsule with consistent performance
- **Target segments:** Innovators & Generics
- **Target geographies:** worldwide

# Critical Parameters and Performance



# Capsule Specifications

- Dimensions of capsules are available in the respective [Technical Reference Files](#)



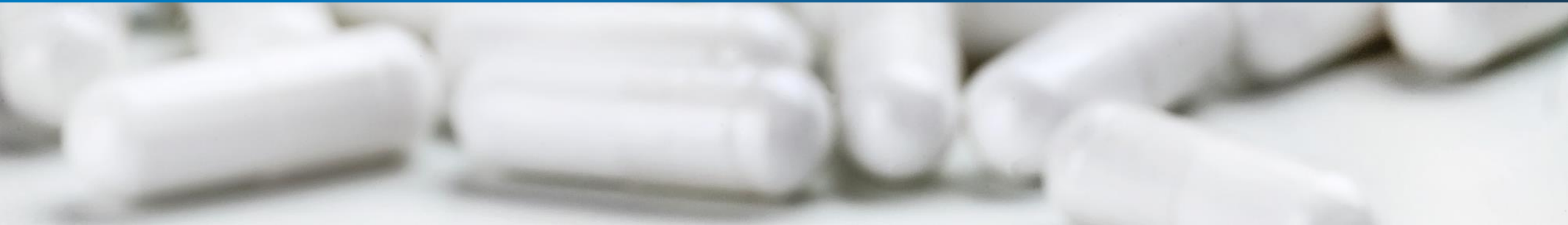
- In addition to specifications and information available in the Technical Reference File of Capsugel® Coni-Snap® Hard Gelatin Capsules, Vcaps® and Vcaps® Plus HPMC capsules, below specifications apply:

Test	Specification	Method reference	
		Coni-Snap® Hard Gelatin Capsules	Vcaps® / Vcaps®PlusHPMC Capsules
Lubricant content	Less than 500 ppm	CP019b	VCP016B / VCPP016B
Total viable aerobic count			
Total Aerobic Microbial Count	Less than 100 cfu per gram	CP031	VCP031 / VCPP031
Total Yeasts/Moulds Count	Less than 10 cfu per gram	CP032	VCP035 / VCPP035
Specified micro-organisms			
Bile-Tolerant Gram-Negative	Absence in 1 gram	CP048	VCP048 / VCPP048

Inhalation microbiological quality through respecting applicable GMP and Capsugel® standards, without use of preservatives, ethylene oxide or irradiation treatment

# DPI Capsule Performance

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# Powder Retention – Visual aspect

## Internal Lubrication Impact



*Capsules filled with lactose blend for DPI applications, closed, shaken, then opened, emptied and assembled.*

Consistency of internal lubrication process drives optimal consistent performance.

# LOD Customization Capabilities



Often, **capsule LOD** must be adapted to **specific formulation requirements** (filling properties, stability)



To find out best range, **water activity** measures can be performed in-house

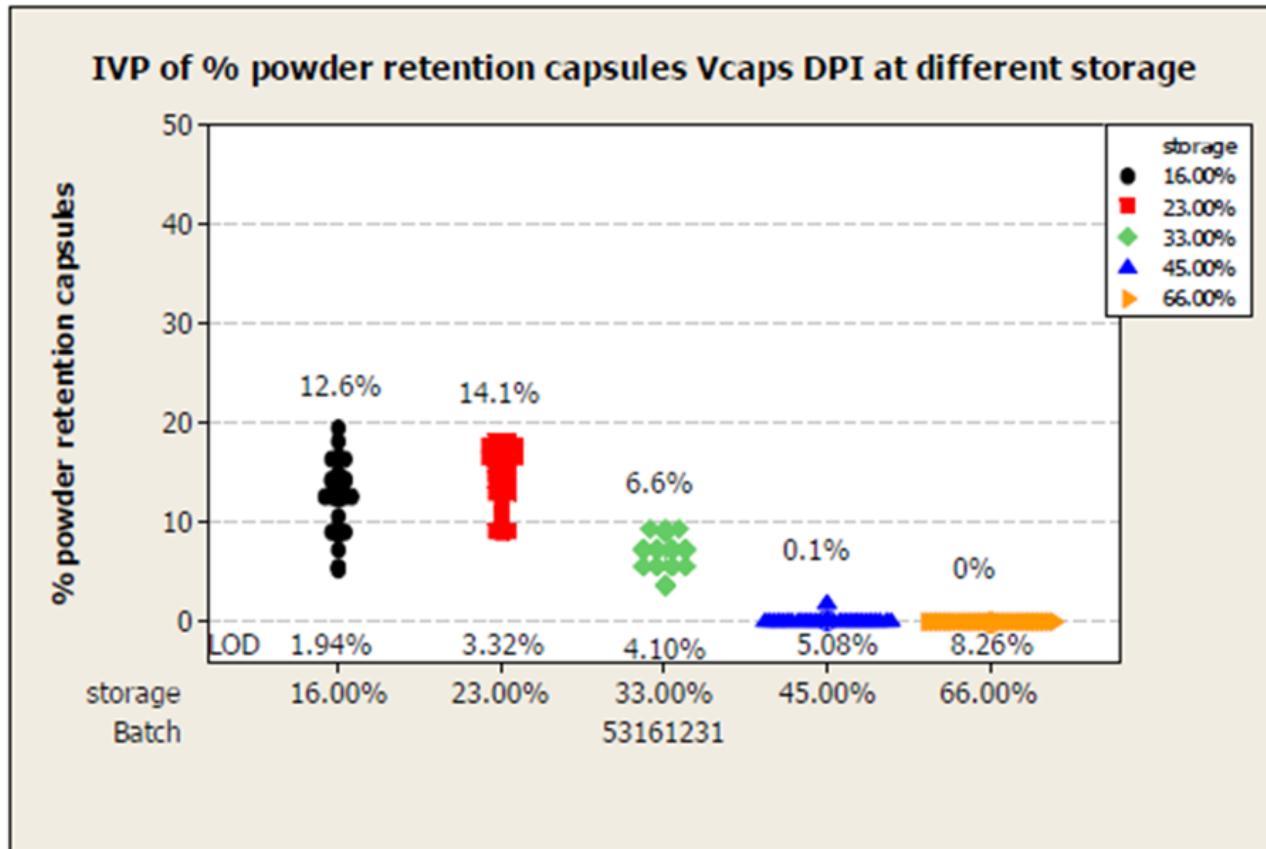


We deliver **LOD range** customization

# LOD Customization for Optimal Performance

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## Conclusion:

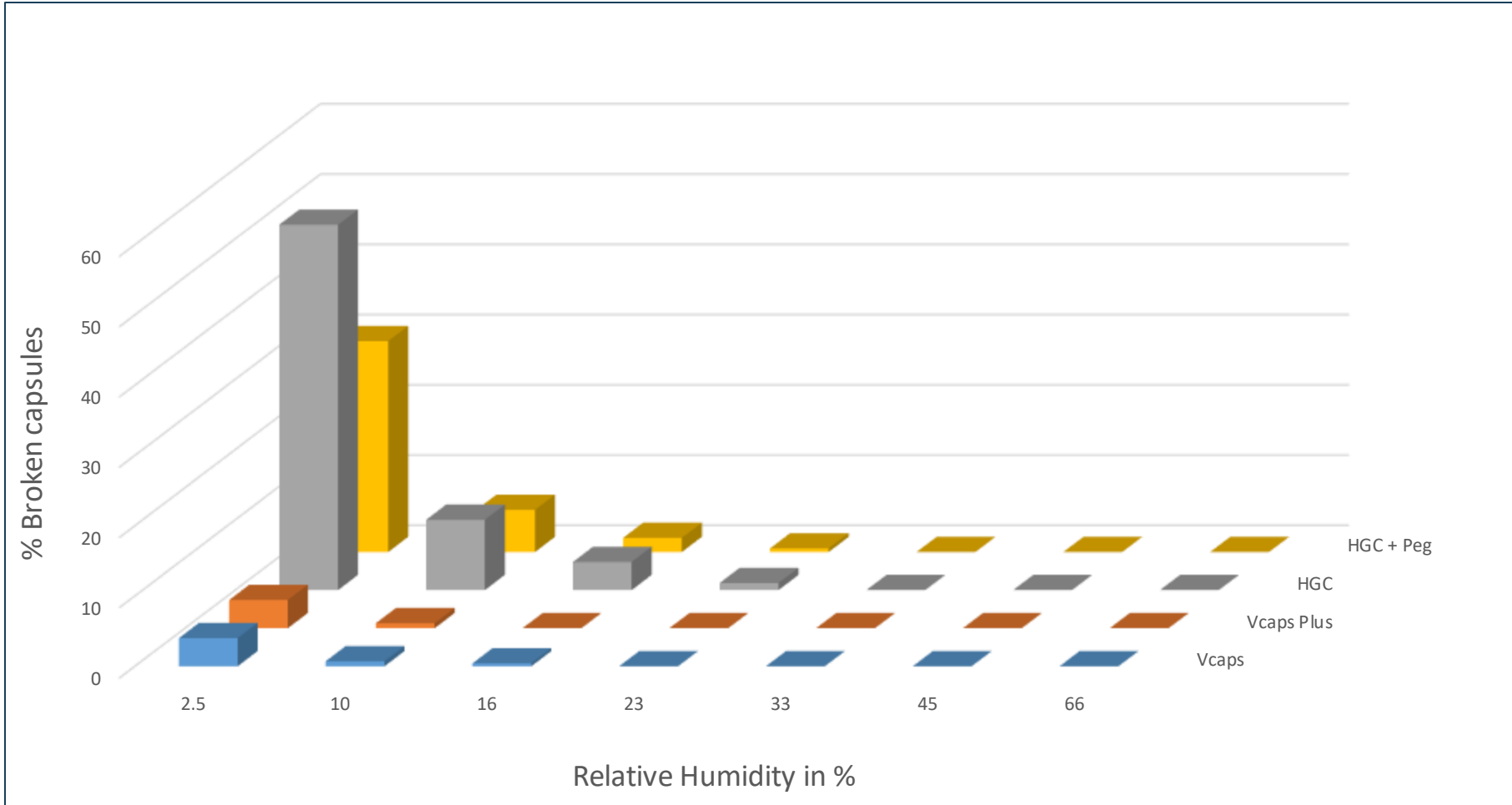
- Powder retention increased with decrease of LOD > Static effect
- Low LOD can be a solution for specific situations, but lower is not always better
- Water Activity measure allows to define the best compromise.

*Powder retention and water content of HPMC capsules (Vcaps<sup>®</sup> DPI) filled with 25.0 ± 1 mg 150 mesh lactose at different RH conditions (n=20)*

# Capsule Mechanical Performance

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Capsule interactions with environmental conditions have a decisive influence during shelf-life, packaging, deblistering and actuation phase

*Capsule brittleness in function of Relative Humidity, measured by tube test on 50 capsules*

# Performance With Different Inhalation Devices

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RS01 (Plastiaple)



Capsuhale  
(RPC – Formatec)



Handihaler®  
(Boehringer Ingelheim)



Twister™ (Aptar)



Rotahaler (Cipla)

	Puncturing <sup>(1)</sup>		
Capsules conditioning	23%RH	33%RH	45%RH
RS01	Good for HPMC capsules	Good for HPMC capsules	Good for HPMC, PEG & gelatin capsules
Capsuhale	Good for HPMC & PEG capsules	Good for HPMC & PEG capsules, acceptable for gelatin capsules	Good for HPMC, PEG & gelatin capsules
Handihaler	Good for HPMC capsules acceptable for other capsules	Good for HPMC & PEG capsules, acceptable for gelatin capsules	Good for HPMC, PEG & gelatin capsules

(1) Puncturing: 15 capsules were tested and observed after use for absence of particle; when a minor particle is missing for a few capsules only, the test is rated “acceptable”

	Opening <sup>(1)</sup>		
Capsules conditioning	23%RH	33%RH	45%RH
Twister	Good for HPMC & Gelatin capsules, acceptable for PEG capsules	Good for HPMC, PEG & gelatin capsules	Good for HPMC, PEG & gelatin capsules
Rotahaler	Good for HPMC, PEG & gelatin capsules	Good for HPMC, PEG & gelatin capsules	Good for HPMC, PEG & gelatin capsules

(1) Opening: : 15 capsules were tested and observed after use; when a minor part of the capsule is missing (capsule partly broken when opening) for a few capsules only, the test is rated “acceptable”

## CONCLUSIONS:

- Capsugel® capsules are adapting to a broad spectrum of device solutions
- Industry choice of device and capsules for DPI will be driven by the moisture sensitivity of the formulation
- Preferences in the targeted population to select between puncturing or opening devices

# Capsule Filling Machine Evaluation

Capsugel® capsules have been tested on a broad range of capsule filling machines and exhibit excellent machinability performances. Some of the brands include:

- Bosch
- IMA Group
- Harro Hofliger
- MG2
- Capsugel® filling machines

Our Technical Service Engineers can offer you their experience and knowledge in optimizing and setting up the triangle machine/capsule/powder according to your needs.

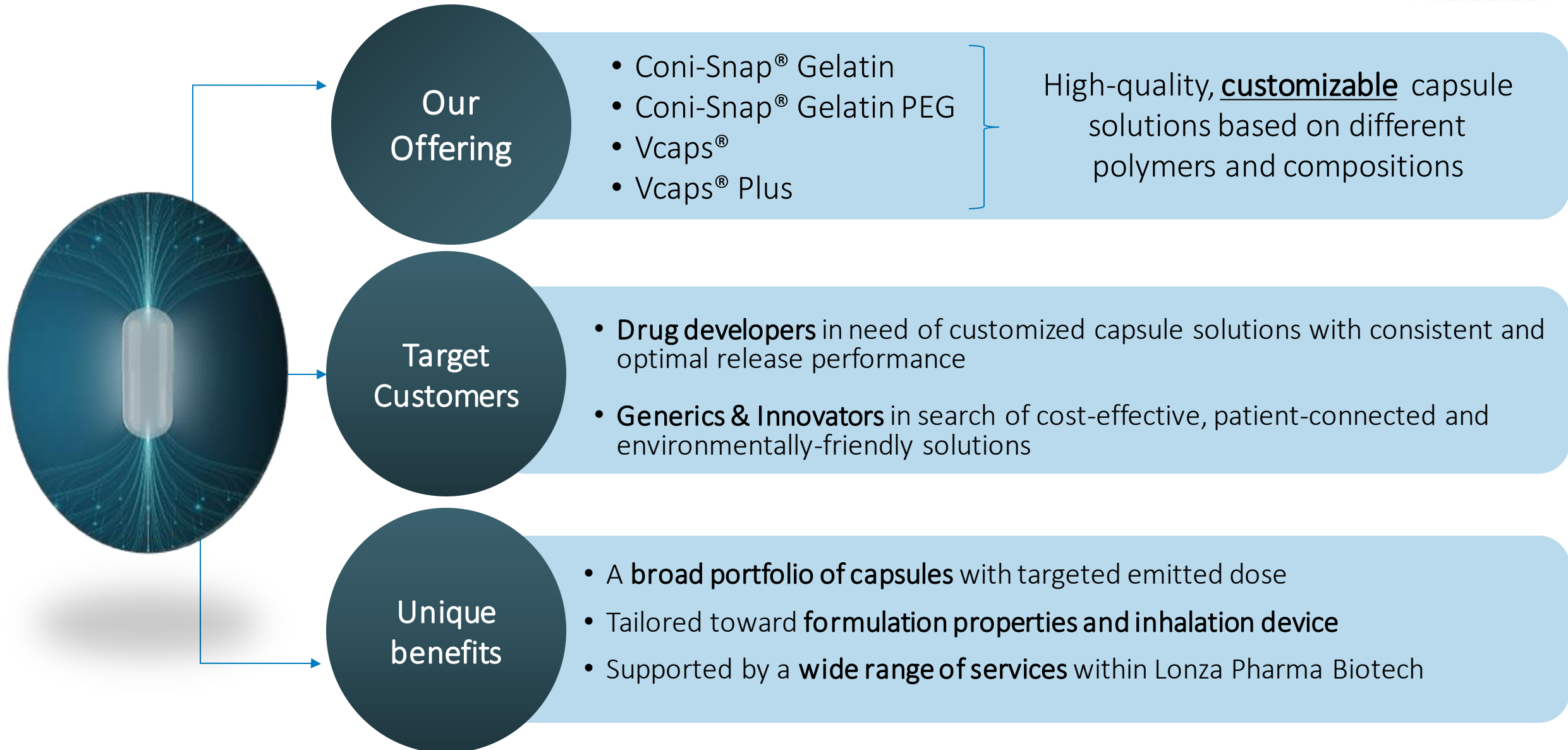


# Capsugel® Zephyr™ Summary

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# Capsugel® Zephyr™ in a Nutshell...



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# Questions?

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