



# Everything for Inhalation

# Integrated Inhalation Development Services

	PRE-CLINICAL	CLINICAL	COMMERCIAL
<b>Drug Substance</b> <ul style="list-style-type: none"> <li>• Polymorph control</li> <li>• Small-scale to commercial manufacturing</li> </ul>			
<b>Particle Engineering</b> <ul style="list-style-type: none"> <li>• Wet Polishing</li> <li>• Jet Milling</li> <li>• Spray Drying</li> <li>• Particle size control</li> <li>• Scalability</li> </ul>			
<b>Drug Product</b> <ul style="list-style-type: none"> <li>• Blending (low and high shear)</li> <li>• Precision capsule filling (100% fill weight check)</li> </ul>			

## Particle Engineering Technologies

### Unprecedented particle size control

- Median particle size control down to 0.1  $\mu\text{m}$
- Spans down to 0.6
- At any scale

### Advanced Engineered Particles for low and high dosages

- Microencapsulation
- Nanocoating

### API alone

### Control over interfacial properties

#### STRENGTHS

##### Jet Milling

- Simple
- Solvent free

##### Wet Polishing

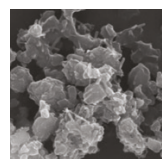
- Reduced amorphization
- PSD control
- Reproducibility
- Scalability

##### Spray Drying

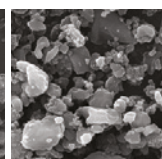
- PSD control
- Reproducibility
- Scalability
- Thermo-labile compounds

#### JET MILLED API

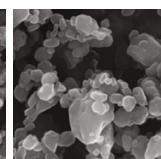
#### WET POLISHED API



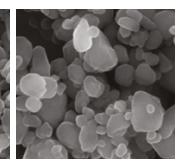
JM Fluticasone Propionate (FP) 2 $\mu\text{m}$



JM Mometasone Furoate (MFA) 2 $\mu\text{m}$



WP FP 2 $\mu\text{m}$



WP MFA 2 $\mu\text{m}$

# Everything for Inhalation

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Inhalation drug product development at Hovione has a strong focus on formulation for Dry Powder Inhalers (DPI), particularly for capsule-based and reservoir-based DPIs.

From formulation composition optimization and precision capsule filling with 100% fill weight check, to analytical characterization and scale-up to a commercial scale, Hovione can take your product from the early proof of concept stages up to a fully developed and scaled process. Together with our API and Particle Engineering capabilities, this means that your product can be fully developed and produced at Hovione, from API synthesis, to size reduction and final drug product.

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# Carrier-based Formulations

## Blending

Most carrier-based formulations are lactose-based and they can carry different inhalation grades of lactose, typically a combination of coarse and fine lactose, and a range of API percentages. The lactose grades for your specific product will be carefully chosen to provide the best possible aerodynamic performance and stability through the life cycle of your product. With our low-shear and high-shear blenders (Turbula and Diosna), we are equipped to perform blend production from very small batches of only a couple grams up to a fully commercial scale on the kilogram range. Our cGMP blending equipment (Diosna P1-6 and Diosna PVAC 10-60) will allow production of blends from 150 g up to 15 kg (per batch).

## Capsule filling

Also on the capsule filling side of the process, we offer a range of different pieces of equipment that can satisfy your demand. From a lab-scale weight-based Quantos capsule filler, that is semi-automatic and will fill up to 100 capsules per hour, to a capacitance-based (MultiNett system) pilot scale FlexaLab (MG2) that will fill up to 3 000 capsules per hour with 100% fill weight verification, Hovione can guarantee production of batches of up to 10 000 capsules, both in R&D and cGMP environments, so your development and clinical supply can be fully covered. With a recent investment on a Tekna (MG2) capsule filler, we now have the capability of going up to 70 000 capsules per hour and assure your low volume commercial supply of a capsule-based formulation for DPI.

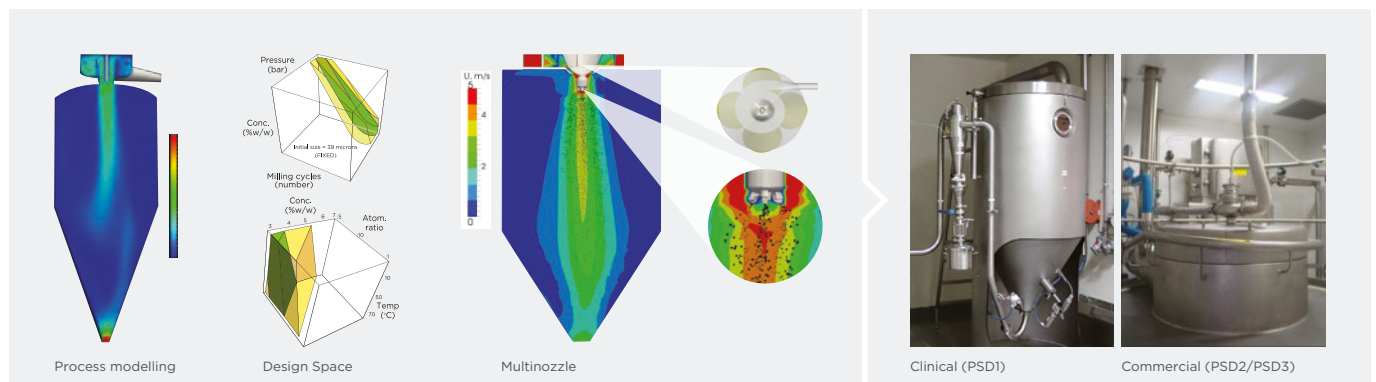
# Carrier-free Formulations

## API-alone formulations

For the kind of applications where no excipients can be used, for example proteins which are denatured when in contact with lactose and other sugars, you may need to develop an API-alone formulation. In this case, due to the necessary small size of the API particles for pulmonary delivery, the formulation can become too cohesive. Therefore, the properties of the powder need to be optimized in order to provide an appropriate aerodynamic performance. With Hovione's extensive expertise in Particle Engineering technologies, we are capable of achieving the best possible performance for your product. Spray drying, wet or dry milling, among others, can be applied to fine-tune the particle interactions and optimize the efficiency of delivery.

## Composite particle formulations

For the platform of composite particle formulations, the optimization of the formulation in terms of composition and ratio of excipients and the particle engineering steps are both carried out simultaneously using spray drying technology. This allows the application of Hovione's strong expertise in spray drying directly to your formulation, which goes hand in hand with the application of QbD principles. From internal predictive tools using CFD and statistical modelling, to scale-up methodologies specific for inhalation particles, including patented multinozzle and taylor-made cyclone approaches, excellent control over the process as well as optimization of the final product performance can be guaranteed.



# State-of-the-Art Analytical Characterization for Dry Powder Inhalation

## Particle/Physical Characterization

- PSD by Laser Diffraction (Malvern and Sympatec)
- Computerized microscope imaging for particle characterization
- DVS
- Ultra-picnometer
- XRPD
- DSC
- Thermogravimetric analysis
- Scanning electron microscopy
- Surface area by BET & Raman spectroscopy

## Formulation Characterization

- Fast Screening, Andersen Cascade and Next Generation Impactors
- Dosage Unit Sampling Apparatus (DUSA)
- Dissolution testing
- Breath simulators (closer to in vivo deposition)

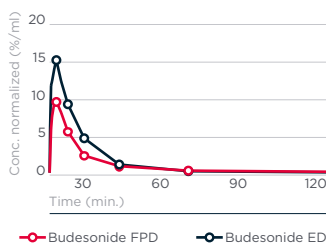
## Biopharmaceutical Characterization

## Microbiology

# Beyond Cascade Impaction Evaluation

The use of anatomical throat models and breathing simulators allows formulation development under conditions mimicking different target patient populations.

Dissolution testing is an integral part of the development of inhalation formulations.



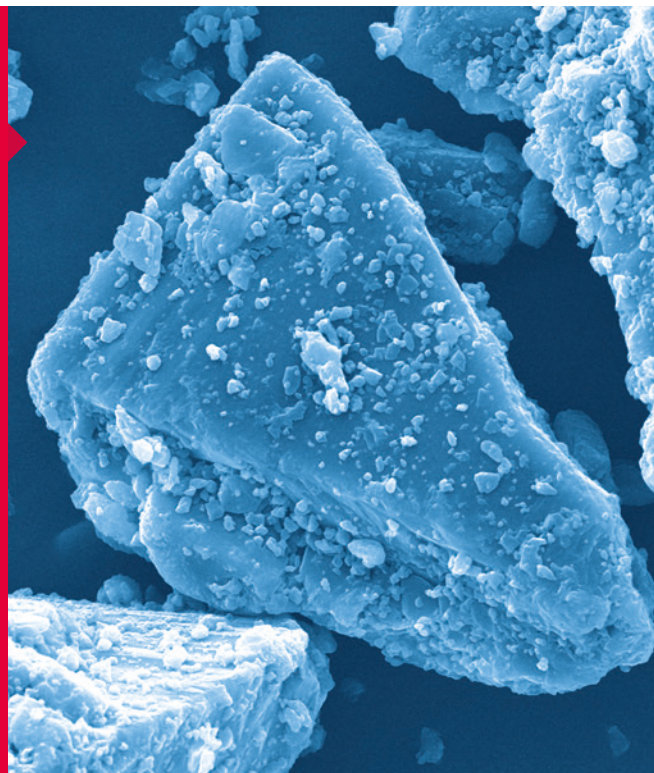
Breathing simulator

# Portfolio of Off Patent APIs

## Expertise in Customized APIs for Inhalation

Hovione's inhalation APIs are designed at the particle level to bring unique performance to your formulation.

- Acclidinium
- Beclomethasone
- Fluticasone
- Glycopyrrolate
- Indacaterol
- Mometasone
- Olodaterol
- Salbutamol
- Salmeterol
- Tiotropium
- Umeclidinium
- Vilanterol





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