



RESPIRATORY DRUGS (DPI)

Milling, classifiying & mixing

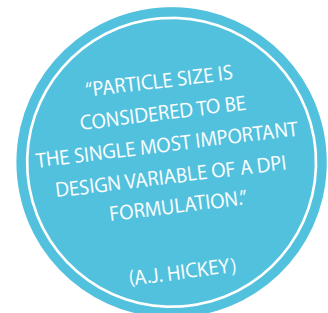


**HOSOKAWA
MICRON GROUP**

PROCESS SOLUTIONS FOR DPI FORMULATIONS

A guide to select the proper process equipment.

To ensure proper delivery, inhalation products require active pharmaceutical ingredients (APIs) and carriers to be sized precisely and mixed carefully. When selecting processing equipment, it is essential to consider all aspects of the materials involved and the final product requirements. Those aspects may include, for example, cohesiveness, flow properties, particle size distribution, the amorphous content of the API and property enhancing additives. The Hosokawa Group provides the DPI manufacturing industry with milling, classifying and mixing solutions.



MILLING & CLASSIFYING

Active Pharmaceutical Ingredients (APIs)

The typical fineness requirement for the API is in the range of 1-5 μm . Besides this challenging high fineness, a steep particle size distribution is required. Hosokawa Alpine offers different technologies to achieve this.

The spiral jet mill is the most common jet mill used for micronisation of fine particles in the pharmaceutical industry. Without movable parts or drives, it is easy to inspect and clean.

The fluidised bed opposed-jet mill is the first choice whenever a sharp top cut and steep particle size distribution are in focus and a wide range of fineness requirements 4-150 μm should be achieved in one machine.

For highly potent APIs, Hosokawa Alpine offers containment integrated milling systems.

Carriers

Carrier production often combines milling, classifying and sometimes mixing to avoid fine dust. The typical fineness is in the range of 40-200 μm with a minimum amount of fine particles.

Pin mills are the proven technology for carrier production. When steeper particle size distribution or higher-end fineness is required, an impact mill with an integrated air classifier can be preferable. To eliminate any significant amount of fine dust still left, a second classifying step can further improve the particle size distribution.



» Cyclomix, 5 litres



» Mini Cyclomix lab mixer

KEY FEATURES CYCLOMIX

- » Perfect dispersion of fines
- » Accurate temperature control with jacketed vessels
- » Creates homogeneous mixtures without lumps
- » Reproducible processes
- » Filling rates between 30-100%
- » CIP- and SIP-able designs

KEY FEATURES MINI CYCLOMIX

- » Compact table top design
- » Exchangeable product bowls, available in 0.1, 1 and 2 litres
- » Online filling and discharging (contained)
- » Touch panel operation
- » Recipe Management, data logging and data export

MIXING

Mixing formulations for dry-powder inhalers is a delicate matter. Delivering a fully homogeneous blend, without deterioration of the particles is a prerequisite.

To disperse the actives in the carrier, a certain amount of mechanical energy is required to break the cohesive forces between the particles. Applying too much energy however, results in excessive adhesive forces between the carrier and the actives, restricting the separation during inhalation.

Cyclomix high shear impact mixer

Finding the right balance for the required mixing energy calls for a very efficient mixer. Hosokawa Micron's Cyclomix high shear impact mixer has proven to be perfectly suitable for this application.

The Cyclomix combines impact mixing by knife blades and shear mixing by paddles. It has proven to be suitable for other processes as well, such as coating, bonding, rounding and densification.

Custom production scale

Clinical trial batches can be processed in a mixer of 5 litres. These units are built and documented according to cGMP guidelines. Standard sizes on a larger scale are: 1, 5, 15, 50, 100 litres and larger. Larger production scale units are fully custom-built.



» 75 litre Cyclomix system

HOSOKAWA MICRON GROUP WORLDWIDE



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Milling, classifying

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