



Stability, flowability, dissolution rate and bioavailability (BA) are all critical performance parameters impacted by the size distribution of particles. As part of our integrated product development services, Capsugel offers premier particle engineering capability through micronization, from early stage design through scale-up and commercial quantities. We are well versed in particle size reduction to low-micron or sub-micron levels — which plays an important role in effective drug delivery.

### Advanced Capabilities

Micronization and nano-milling are critical components of our bioavailability enhancement suite, and typically utilized with BCS class IIa compounds. Wet ball/ bead/pearl milling are used as a top-down approach to produce low micron or sub-micron particle size material and optimize dissolution performance. Bottoms-up particle engineering approaches for the production of nanocrystals through precipitation from supersaturated solutions are also utilized in addressing BA challenges. These approaches complement our other technologies, including solid dispersion (spray-dry dispersion and hot-melt extrusion technologies), lipid-based formulations, and nanocrystal technologies.

### Wide-Ranging Applications

Micronization and nano-milling are used routinely in many applications in solid oral and other dosage forms.

Enhance BA through dissolution optimization for oral drugs

Help solubilize and stabilize poorly soluble compounds in the development of multiparticulate systems, as well as drug emulsions and suspensions

Improve the palatability properties of a compound

Generate particles fine enough to be properly delivered to the lungs (for inhalation product development)

Help ensure absorption of a drug across the skin (in the development of transdermal products)

### Wet-Milled Suspension Equipment



Bend Research Mill  
Nominal API per batch\*  
0.02 – 0.5 g  
Nominal Volume per batch\*  
0.5 – 5 mL



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# Particle Size Engineering Through Micronization

## Center of Excellence for Micronization and Nano-Milling

Our Center of Excellence in Quakertown, Pennsylvania (USA) is a full-service provider of particle size reduction and particle size control technologies. With more than two decades of manufacturing experience, we can develop a robust process for any point during development, including R&D, pilot and commercial scale. Our micronization and nano-milling capabilities are fully integrated into overall product development.

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FDA registered and excellent inspection record

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115,000 square feet

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7 cGMP suites with independent air handling units, HEPA filtration, temperature and humidity control

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Phase-appropriate equipment for all stages of drug product development

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Proprietary mill designs and processing

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High containment capability

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## Micronization Range

Micronization through jet milling — where material is fed into a grinding chamber and particles are accelerated via compressed gas to create a tornado-like flow path — is used for APIs that require 1-10  $\mu\text{m}$  average particle size. Large particles migrate to the outside of the mill via centrifugal force; particle attrition occurs over time from continuous particle collisions and inner-particle abrasion. Micronized particles migrate to the center of the mill via drag force pulled at the mill outlet. Particle sizing and distribution is optimized by the variation in mill pressure, feed rate and proprietary mill design attributes.

## High Potency Compounds

High containment capabilities support particle size reduction of highly potent and cytotoxic compounds. A range of mechanical and jet milling capabilities are available within an isolator designed to meet containment levels down to 1  $\mu\text{g}/\text{m}^3$  at scales from 2-100 kg batch sizes. The isolator provides a negative pressure nitrogen environment, double HEPA filtration, RTP transfer ports and CIP capability.

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Demonstrated containment down to <10  $\text{ng}/\text{m}^3$

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Capable of multiple mills 2", 4" or 10" jet mills

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Continuous processing via RTP ports and interlocked Airlock

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## Nano-Milling

The Netzsch Delta Vita media mill, a nanoparticle milling solution, provides additional size reduction to nano-scale particles for development and production quantities. The Delta Vita is used for wet grinding of batches ranging from 15 mL to approximately 60 L, complementing our BA enhancement suite of technologies. This allows for ample milling energies (or tip speeds) to generate sub 1  $\mu\text{m}$  particles and stabilize them into a suitably formulated solution.

Learn more about how Capsugel's micronization and nano-milling can enhance your product development.

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