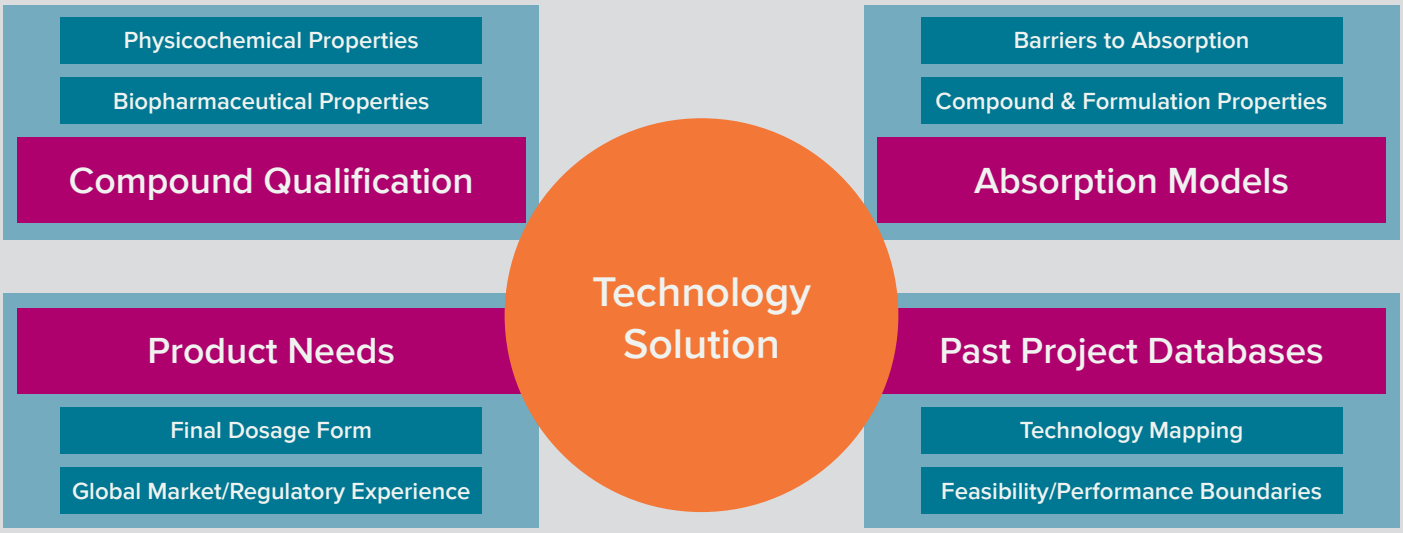
Bioavailability Enhancement Technologies

Capsugel® | Lonza Pharma & Biotech



Inputs required for optimal enabling technology selection

The increasing fraction of poorly water-soluble compounds in drug discovery has led to routine use of enabling technology to improve oral drug absorption and bioavailability (BA). Enabling technologies are being utilized to bring new compounds to market as well as repositioning existing compounds in life cycle management strategies.

At Lonza Pharma & Biotech, we appreciate that the choice of an optimal enabling technology can be complex, and therefore utilize a set of overriding principles in our design and development approach:

A full understanding of the BA-limiting factors is critical and includes physicochemical and biological challenges

The diverse needs of drug compounds cannot be addressed by a single technology

Development success, and rapid advancement of a compound, is more probable with matching the compound properties and product needs early in the development process

In many cases, more than one technology can be utilized successfully and commercial considerations such as desired dosage format can play a decisive role

Speed to clinic and market is best ensured by a focus on manufacturability during product design, thereby reducing the need for reformulation and facilitating rapid scale-up

We employ a proven design and development roadmap approach based on extensive depth in BA enhancement technologies, i.e.

A toolkit consisting of key technologies utilized in addressing dissolution rate, solubility and absorption challenges

Decades of experience in designing and developing drug products across a myriad of compound and target product profile challenges

Proprietary predictive modeling and technology selection methodologies developed through the study and advancement of thousands of compounds

Specialized and phase-appropriate equipment designed through extensive process design investment and science of scale studies

Incorporation of high containment capabilities for all enabling technologies from lab-scale to commercial-scale production of drug product intermediates

Lonza's integrated yet flexible offering ensures that we can meet your exact needs from product design through development to clinical and commercial manufacture. With the option of utilizing one partner throughout the drug development process, we can minimize complexity, risk and cost, while ensuring rapid advancement to clinical trials and commercialization.

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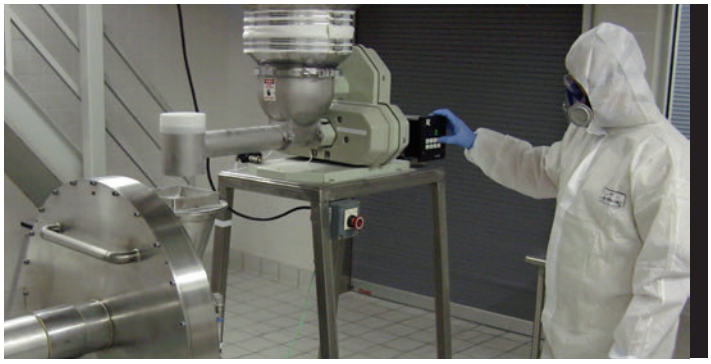
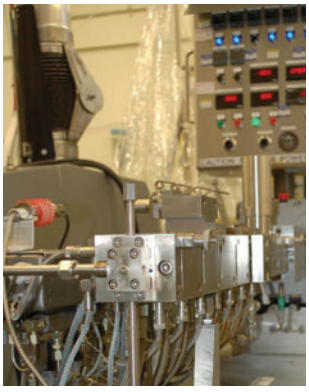


Micronization / Jet Milling

Micronization through jet milling is typically utilized for APIs (BCS IIa) that require a 1-10 micron average particle size in order to provide sufficient dissolution rate. At Lonza, we utilize two integrated particle engineering sites (Quakertown, Pennsylvania, USA and Monteggio, Switzerland) for jet milling, with expertise coming from decades of particle engineering experience. Both locations are full service providers of micronization with proprietary, phase-appropriate jet milling equipment in place to support the full product development cycle, from proof-of-concept studies through commercial manufacture.

Hot-Melt Extrusion



Effective delivery of many of BCS class II compounds with low solubility can be enabled with amorphous dispersions made by hot-melt extrusion (HME). HME manufacture of amorphous dispersion involves the melting of a drug substance with an appropriate polymeric excipient in a co-rotating twin-screw extruder. When cooled, the extrudate generally consists of a single-phase amorphous glassy matrix that can be milled to the desired particle size and incorporated into traditional tablet or capsule dosage forms. At Lonza, we use extruders at a wide range of scales using current Good Manufacturing Practice (cGMP) and development (non-cGMP) processes to produce extrudates for use in clinical studies and small-scale commercial levels (Bend, Oregon, USA).

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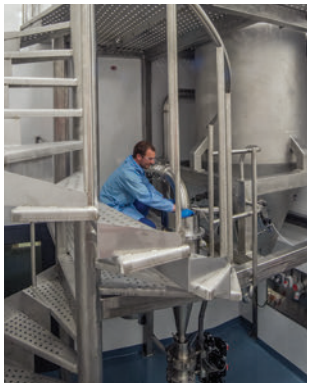
Spray-Dried Dispersions



Pioneered by Bend Research, Lonza's spray-dried dispersion (SDD) technology is a powerful tool in addressing low aqueous solubility. SDDs are obtained by dissolving drug and polymer in an organic solvent and then spray-drying the solution. The formulation and process conditions are chosen so that the solvent quickly evaporates from the droplets, allowing insufficient time for phase separation or crystallization. In addition to their proven performance in enhancing solubility, SDDs have demonstrated long-term stability, rapid scale-up and excellent manufacturability. At Lonza, we have decades of experience in SDD technology, with specialized phase-appropriate pharmaceutical spray dryers in place to support early feasibility assessments through clinical and commercial-scale supply (Bend, Oregon, USA).

Lipid-Based Formulations

Lipid-based formulations (LBF) have the capacity to address both physicochemcial barriers to absorption as well as attenuate biological obstacles to drug BA, particularly by reducing efflux, metabolism in the intestine, and/or increases the drug fraction entering the lymphatic system. Lonza has premier technology depth in LBF, with decades of formulation and scale-up experience utilizing lipid excipients, solvents and co-solvents. Specialized and phase-appropriate processing equipment is in place (Edinburgh, United Kingdom; Ploermel, France; Bend, Oregon, USA) to support LBF applications across liquid-filled hard capsule, soft gel, and lipid multiparticulate (LMP) formats from feasibility studies through to clinical and commercial scale manufacture.

Learn more about how Lonza's enabling technologies can address your bioavailability challenges