

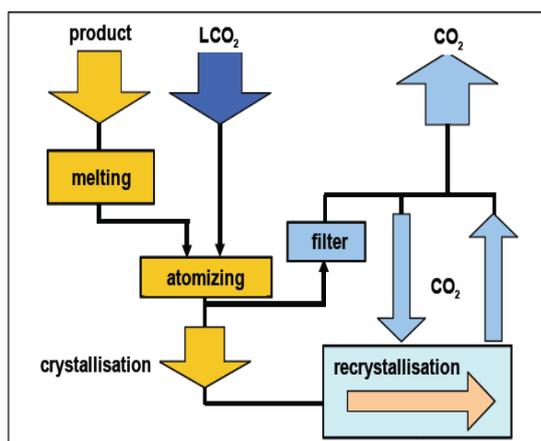
Innovative Process Development and Products

SiTec signed a cooperation agreement with **Messer Group**, in-licensing a novel, solvent-free, near or supercritical fluid technology, for the development of pharmaceutical products as fine powders or microspheres with improved drug delivery properties. *SiTec* is closely collaborating with **Messer Italia SpA** for operations in the biopharmaceutical sector.

About VarioSol®

VarioSol® is a **novel cryospraying technology** for the production of pharmaceutical micronized powders, based on the use of near-critical carbon dioxide. In such conditions, CO₂ has favourable physical properties, as a spraying agent and refrigerant. In the VarioSol® process the product is either melted, dispersed, or dissolved in a feeding vessel at controlled temperature, and subsequently sprayed, under controlled pressure, into a spraying tower, where it comes in contact with expanding supercritical CO₂. The expanding fluid atomizes the sprayed product into very fine particles, while cooling it down to temperatures <0°C.

Using cold exhaust gas for controlled recrystallisation



Variosol Basic Process Design



Variosol Lab-Scale Equipment

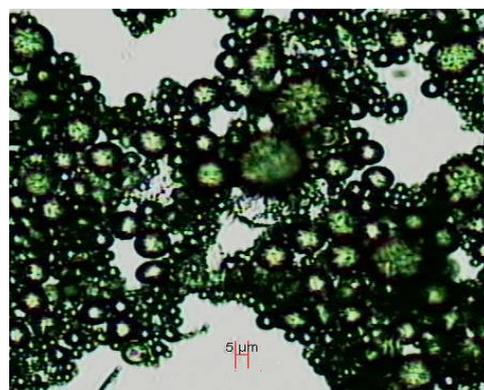
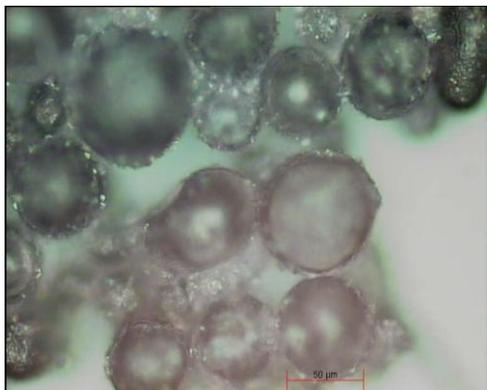
VarioSol® is owned by **Messer Group GmbH**, protected by several patents and patent applications, and licensed worldwide to **SiTec** for pharmaceutical and biotech applications.

VarioSol® Advantages

- ❑ **Drug and excipients crystallization temperature can be modified**, by varying the ratio of product mass to cryogenic fluid. Unlike conventional spraying, it is possible to crystallize materials with low melting point, allowing the development of solid products with improved drug delivery and stability properties, based on self-emulsifying lipids, lipid-polymer blends, and polymers with low Tg.
- ❑ **VarioSol® can facilitate the formulation of thermolabile molecules** otherwise damaged by hot processing, like melt extrusion. This can be accomplished by means of the cryogenic conditions created by expanding CO₂.
- ❑ **Particles can be produced without the use of organic solvents** in the process. Size typically ranges between 5-10 µm to 80-100 µm, with narrow size distributions. Particle properties can be modified to the needs of specific products and dosing routes.
- ❑ **Process is fast with high recovery yields**. Lab-scale equipment size allows to process batches from about 20g to 1Kg, in limited space and with low investment costs.
- ❑ **Process is scalable with same basic equipment design**. Pilot scale processing typically features product output from 5 to 30 kg/h

Pharmaceutical Applications of Variosol®

- ❑ *Improved solubilization and absorption of poorly soluble (BCS Class II), and poorly absorbable (BCS Class III) drugs.*
- ❑ *Controlled drug dissolution and release, for reduced dosing frequency*
- ❑ *Microencapsulation and delivery of biological drugs*
- ❑ *Preparation of fine particles for delivery of inhalable products*



Amphiphilic microparticles obtained with two different nozzles types