Industrial Solutions
Process Technologies

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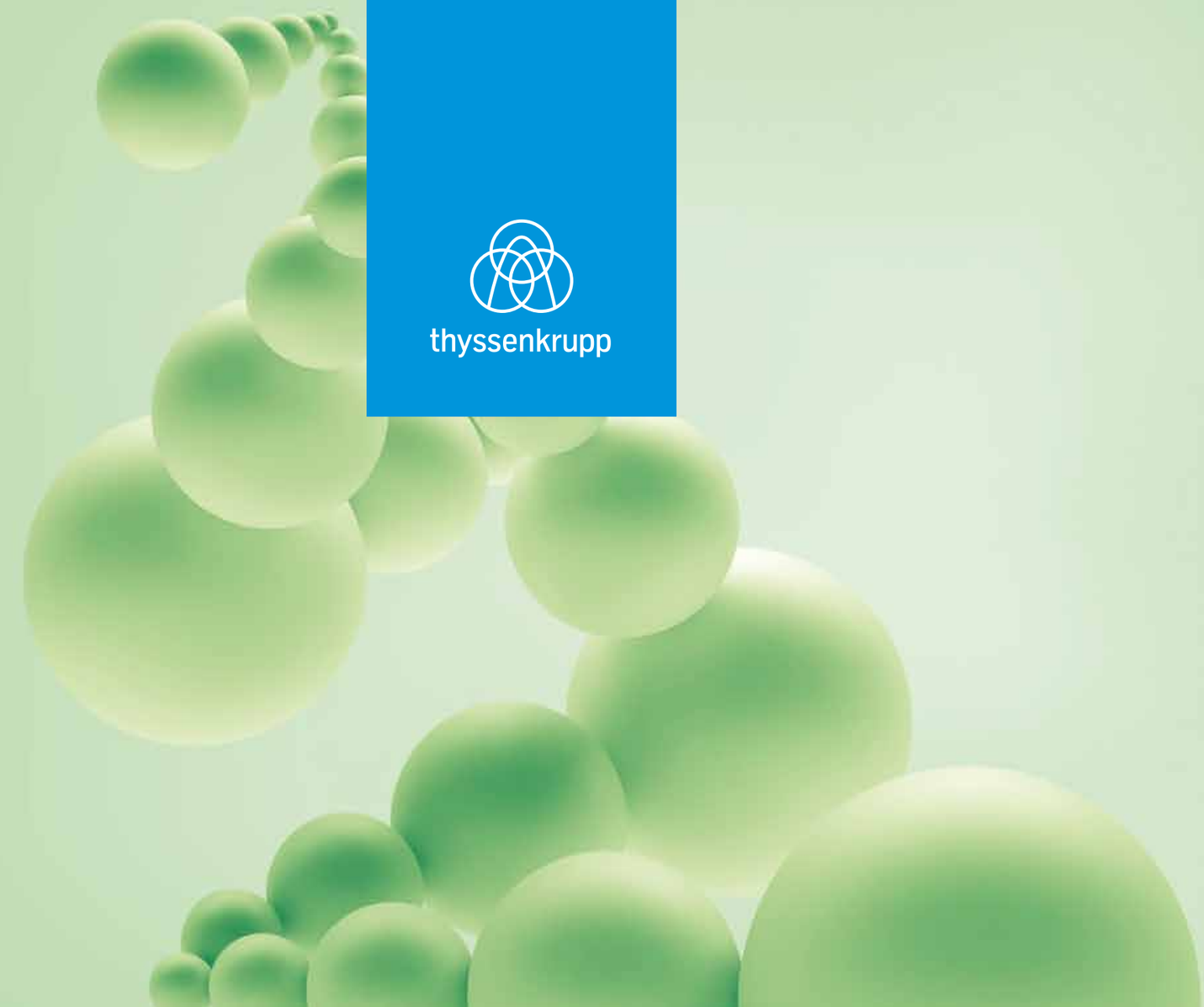
Industrial Solutions

Particle formation

Hygienic design

thyssenkrupp



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Particle design using supercritical fluids

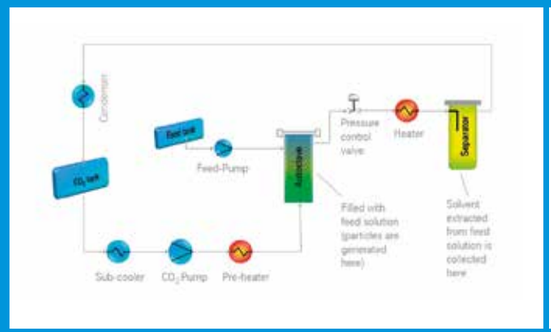
Numerous processes with supercritical CO_2 have been developed which allow the generation or modification of fine particles with defined particle size distributions in micro- and even nano-scale of certain shape and/or determined morphology. This new technology is of highest relevance to generate pharmaceutical products and substances. The dosing and release properties of active pharmaceutical ingredients (APIs) are significantly influenced by the particle properties. New drugs with exact and controlled properties will be possible in the near future by using these new processes complementing traditional granulation and spray drying processes.

Characteristics of high pressure micronisation:

- Physical characteristics when applying supercritical fluids to melts/solutions:
  - reduction of viscosity
  - reduction of surface tension
- Quick super-saturation by pressure change and contact to supercritical fluid, respectively
- High nucleation rate, small growth rate
- Particles in micro- or nano-scale possible

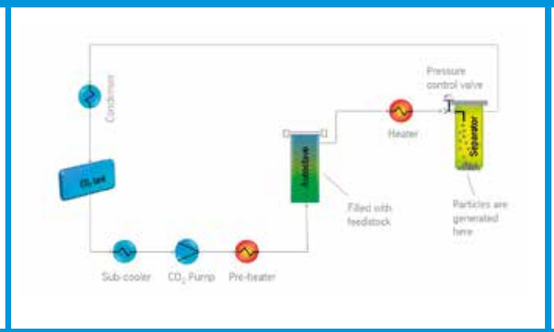
Advantages of supercritical processes

- Size: micro- to nanometer
- Narrow size distribution adjustable
- Control of geometry (spherical, needle, etc.)
- Morphology (smooth, porous, massive) controllable
- Applicable to difficult substances, for example with high melting points or high viscosity
- No thermal stress due to mild temperature conditions
- No oxidation due to inert atmosphere
- Possibility of generation of composites
- CO_2 acting as germicide



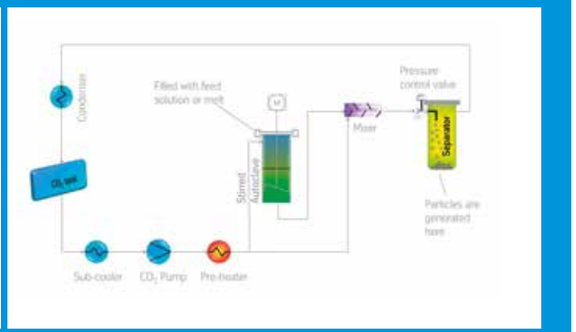
RESS-process (Rapid expansion of supercritical solutions)

A soluble substance is dissolved by supercritical CO_2 in the autoclave. The solution flows to the spray tower (separator), where the pressure is decreased and the dissolved substance becomes insoluble and precipitates as fine particles.



GAS-process (Gas antisolvent crystallization)

In the GAS-process the active substance, which is insoluble in supercritical CO_2, is dissolved in a solvent. This solution is fed into the autoclave. CO_2 is fed into the autoclave in parallel. The CO_2 dissolves the solvent and reduces the solubility of the active substance until it precipitates in the autoclave. Solvent and CO_2 leave the autoclave. After reducing the pressure CO_2 and solvent are separated in the separator.



PGSS™-process (Particles from saturated solutions)

A solution or melt is filled into the autoclave and mixed with supercritical CO_2. After the solution has been saturated, it is mixed with CO_2 and fed into the spray tower. Pressure decrease in the nozzle leads to an expansion of the CO_2 and thus to the generation of fine particles.

Plants and equipment for pharmaceutical applications

Components and plants for particle design

While standard supercritical extraction equipment is suitable for foods, the pharmaceutical industry has higher requirements concerning materials, surfaces, prevention of dead space, cleanability, process controls documentation and others.

Uhde High Pressure Technologies has developed hygienic high pressure pipe fittings and valves, modified experienced equipment like the clamp closure system for high pressure vessels and uses innovative manufacturing procedures like orbital welding of pipes.

Plants are designed to allow easy draining of the process fluids. CIP and WIP features can be implemented.

Design, manufacturing and documentation of plants will be carried out according to current Good Manufacturing Practice cGMP.

Pharmaceutical plants from Uhde High Pressure Technologies fulfill all demands on FDA, EMEA, cGMP, GAMP etc. SPS, SCADA and visualization fulfill the requirements of 21 CFR Part 11, GAMP.

Picture top left: polished full stainless steel quick acting clamp closure

Picture center left: orbital welding of pipes

Picture bottom left: high pressure fittings with elastic metal seals