

110% MIXING SOLUTIONS



ystral Machines, Systems and Applications in Pharmaceutical Industry

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Jetstream Mixer in Pharmaceutical Industry

Homogenous mixing with Jetstream Mixer

- Vertical circulation, highest number of vertical revolutions (no horizontal rotation, no separation, no vortex)
- Completely homogenous mixing from bottom to top in shortest time (10 times faster than normal agitator)
- Independent from filling level (even during emptying at minimum levels)
- No vortex, no air incorporation
- No baffles required, easy to clean
- Perfect for suspensions which tend to sediment
- Ideal to mix high + low viscous, heavy + light liquid etc.
- Faster temperature exchange cooling / heating
- Turbulent **micro mixing** in the mixing head
- Homogenous and laminar **macro mixing** in the whole tank
- For scale-up: $P/V = \text{constant}$



Jetstream Mixer in Pharmaceutical Industry

Jetstream Mixer installation

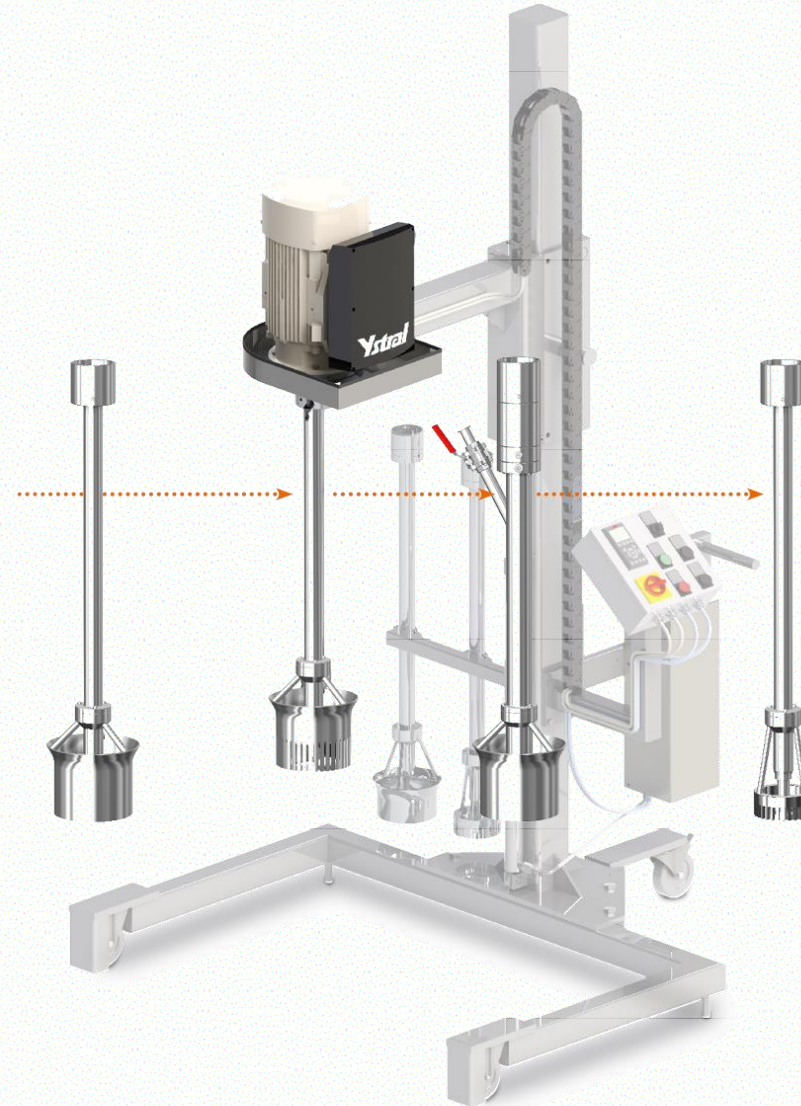
- Top entry
- Side entry
- Bottom entry



Jetstream Mixer in Pharmaceutical Industry

Jetstream Mixer installation

- On a lift for mobile vessels
- Multipurpose = exchangeable tools:
 - *Jetstream mixer*
 - *Dispermix*
 - *Disperser*



Jetstream Mixer in Pharmaceutical Industry

Jetstream Mixer in movable liquid containers



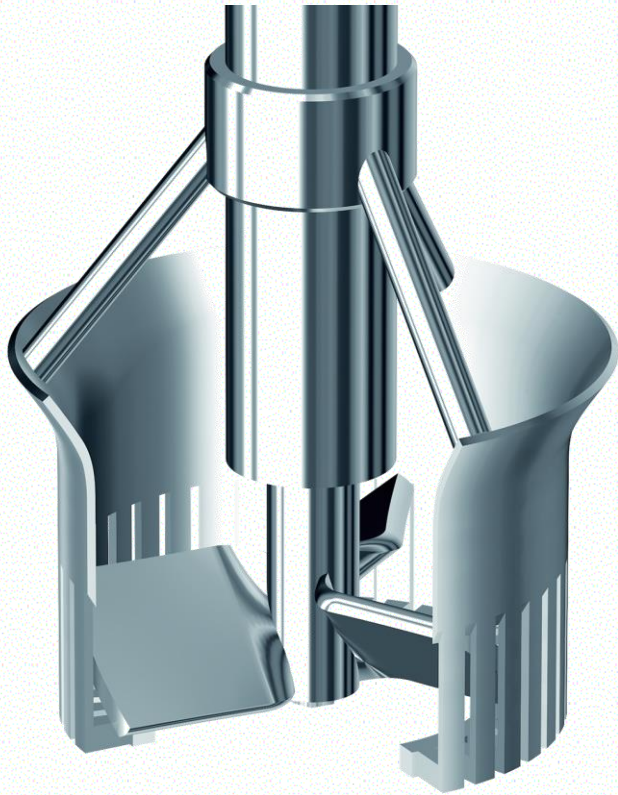
Mixing and Dispersing with Dispermix



- Two operations parallel at the same time inside the tank
- Completely homogenous mixing and simultaneous Dispersion
- Jetstream Mixing: vertical circulation, completely homogenous, no vortex, no air, no baffles, independent from filling level ...
- Dispersion: permanent partial stream dispersion / emulsion



Execution: Coarse, Fine and High Shear Dispermix

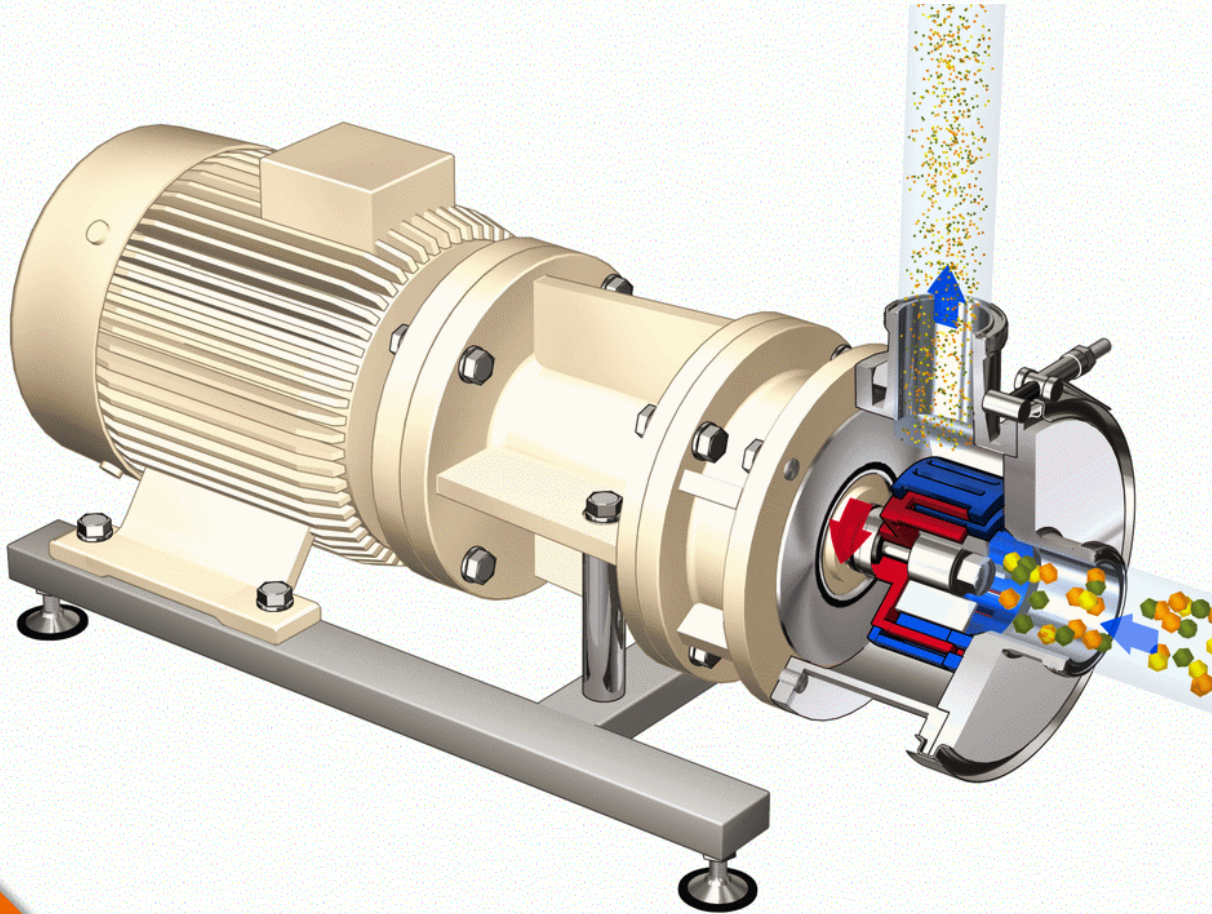


- Desagglomeration
(thickeners, sticky, lumpy ingredients, flakes, pieces...)
- Prevents from reagglomeration
- Prevents from creaming
(instable emulsions with no or low amount of emulsifier)
- Ideal for spray dry emulsions, Pickering Emulsions, Coacervation
- Shear can be switched off:
normal rotation: **With Shear**
reverse direction: **No Shear**



In-Line Dispenser

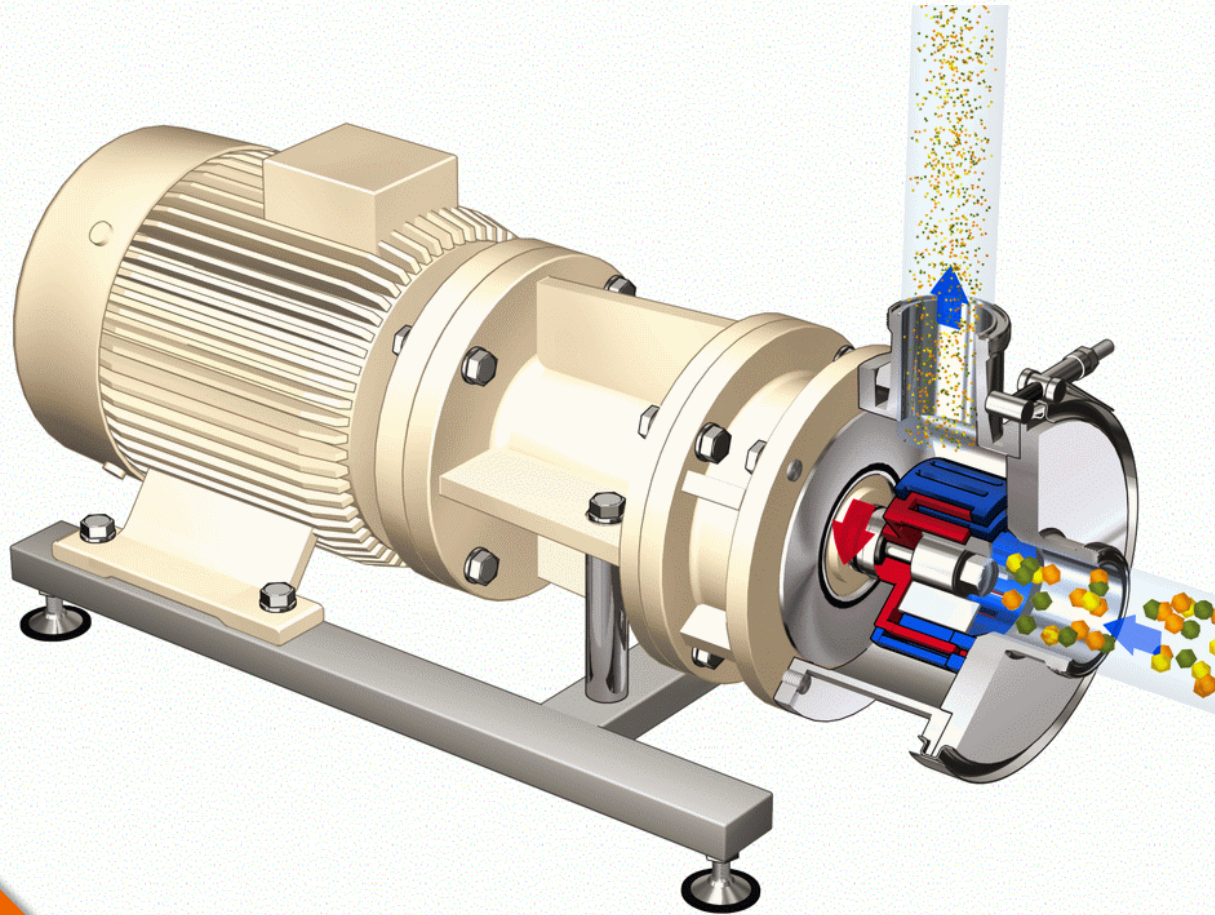
Dispersion, Emulsification and Controlled Drop Size Distribution



- Full Stream Dispersion
- 100% identical shear conditions
- 10 different sizes
- Interchangeable tools
(different slot sizes, up to 6 dispersing rings, up to 3 stages, optional pumping)

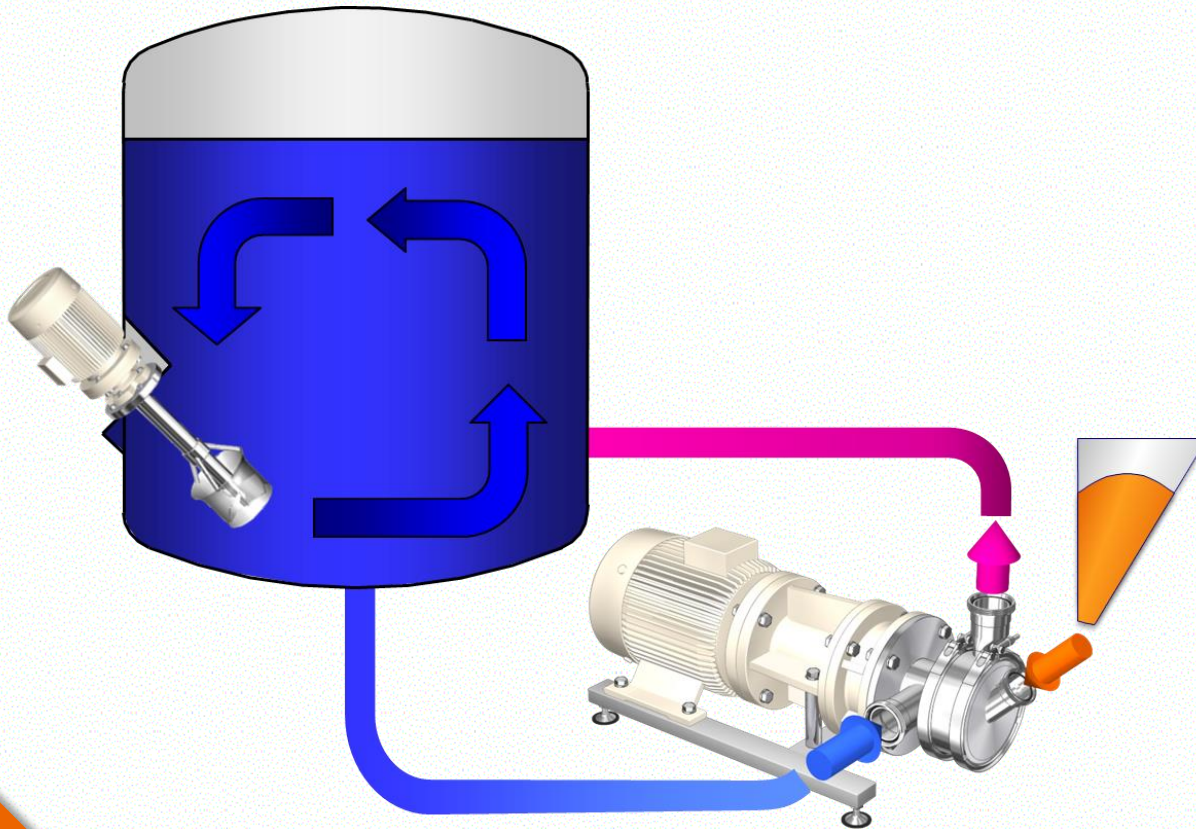
In-Line Disperser

Dispersion, Emulsification and Controlled Drop Size Distribution



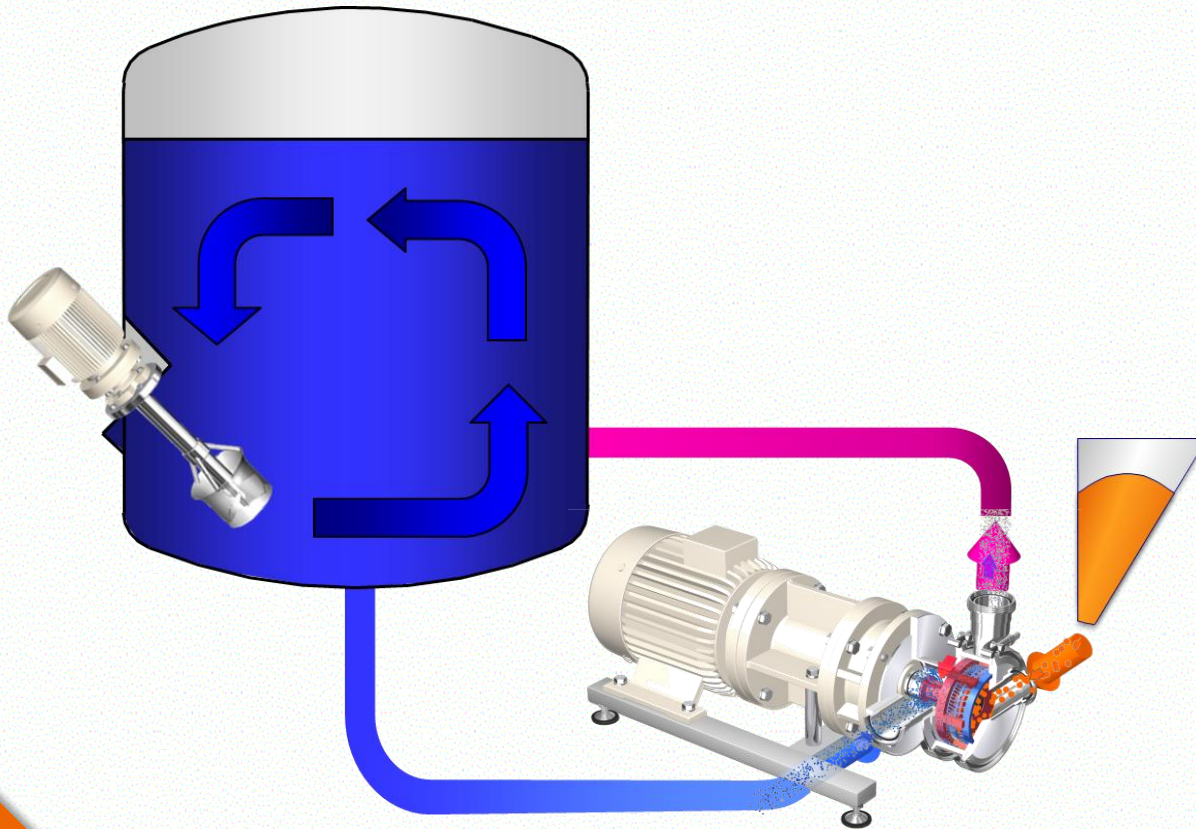
- Full Stream Dispersion
- 100% identical shear conditions
- 10 different sizes
- Interchangeable tools
(different slot sizes, up to 6 dispersing rings, up to 3 stages, optional pumping)
- Flow rates from 100 to 50.000 l/h
- Shear rates up to 100.000 s^{-1}
- Shear speeds up to 50 m/s
- Shear Frequency up to 6000 Hz
- Specific Energy 1 ... 100 MJ/m³
- Real Hygienic Design

Powder induction with Conti-TDS



- Liquid recirculated
- Vacuum created in the mixing head
- Dust- and loss-free powder induction
- Independent from batch size and filling level
- Manual or automatic powder feeding from powder hopper, bag tip station, container, big-bag, isolator, bag, suction hose etc.
- Powder-Liquid Dispersion under controlled shear and maximum vacuum expansion
- Further circular dispersion possible

Powder induction with Conti-TDS

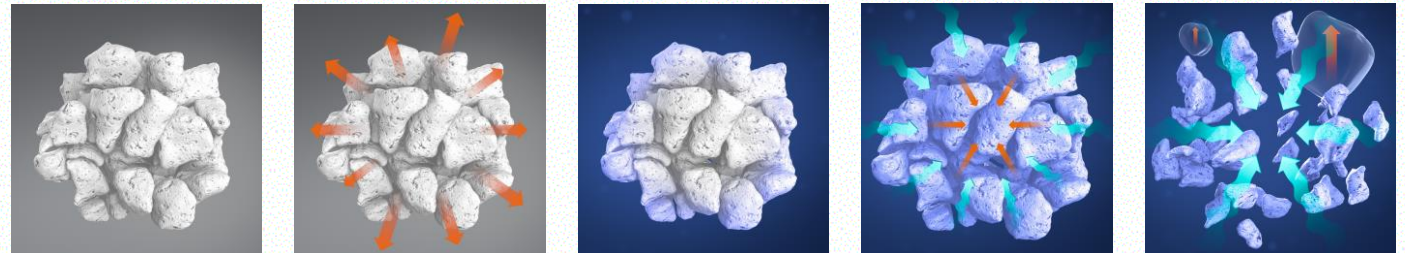


- Liquid recirculated
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- Manual or automatic powder feeding from powder hopper, bag tip station, container, big-bag, isolator, bag, suction hose etc.
- Powder-Liquid Dispersion under controlled shear and maximum vacuum expansion
- Further circular dispersion possible
- One machine for one or more tanks
- For vacuum or pressurized tanks, long distances, high pressure losses:
Combination with pumps

Powder induction with Conti-TDS



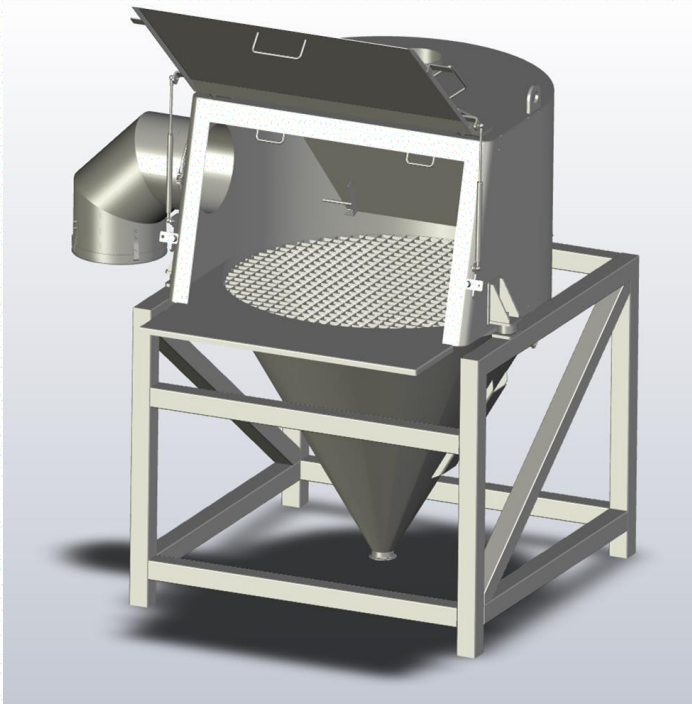
- Powder contains air between particles and inside agglomerates
- Vacuum expansion separates particles in moving powder on the way into the dispersing zone
- Even inside agglomerates: air expands
- Complete wetting under maximum vacuum
- Complete penetration, desagglomeration



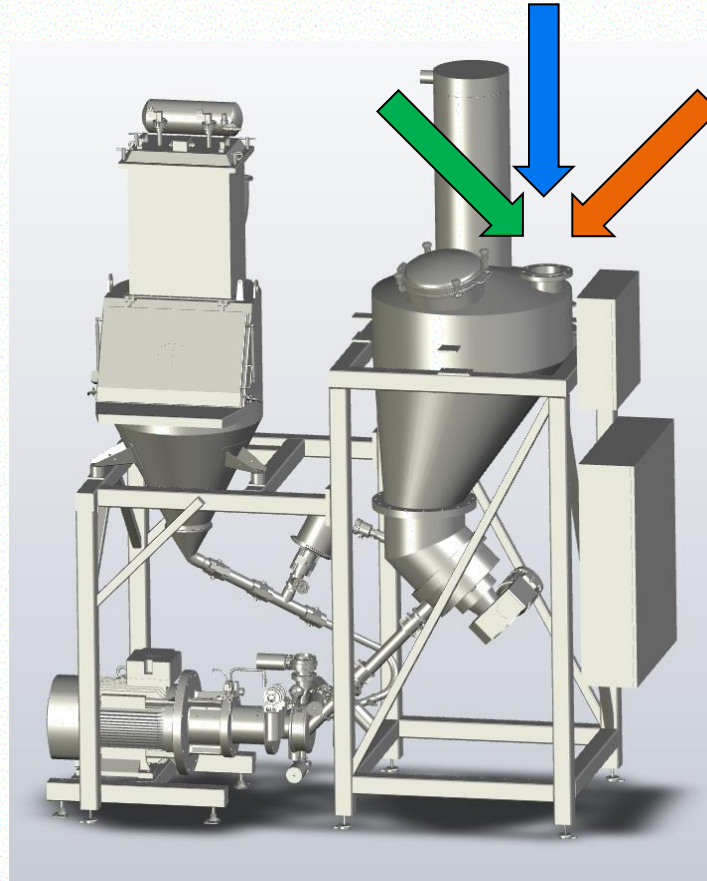
See: ystral.com/en/company/videos: Basics of powder wetting

Powder Handling Components

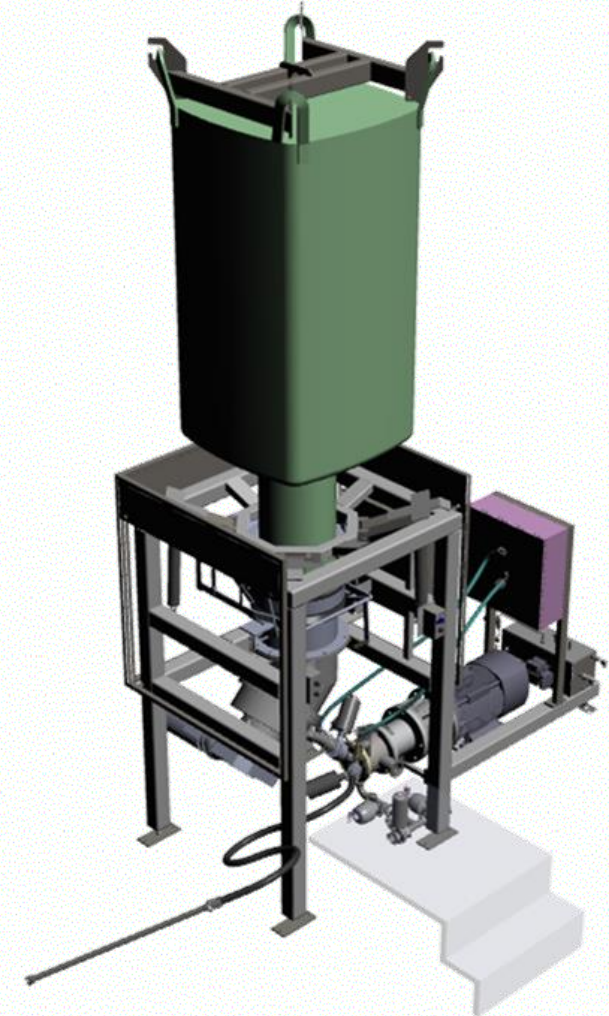
Bag-tip station



Bag-tip + automatic feeding



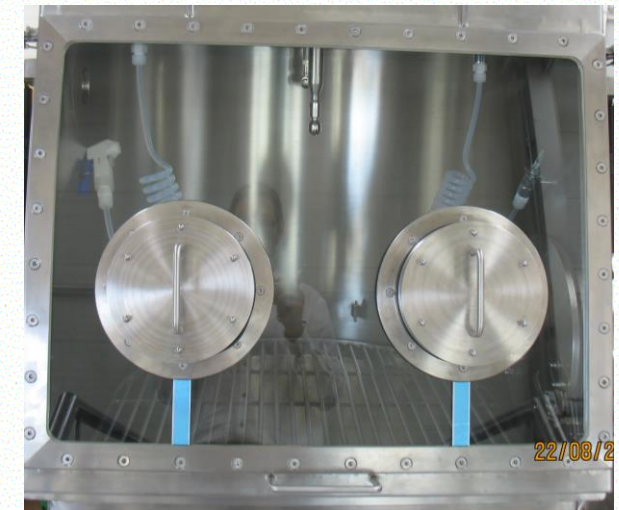
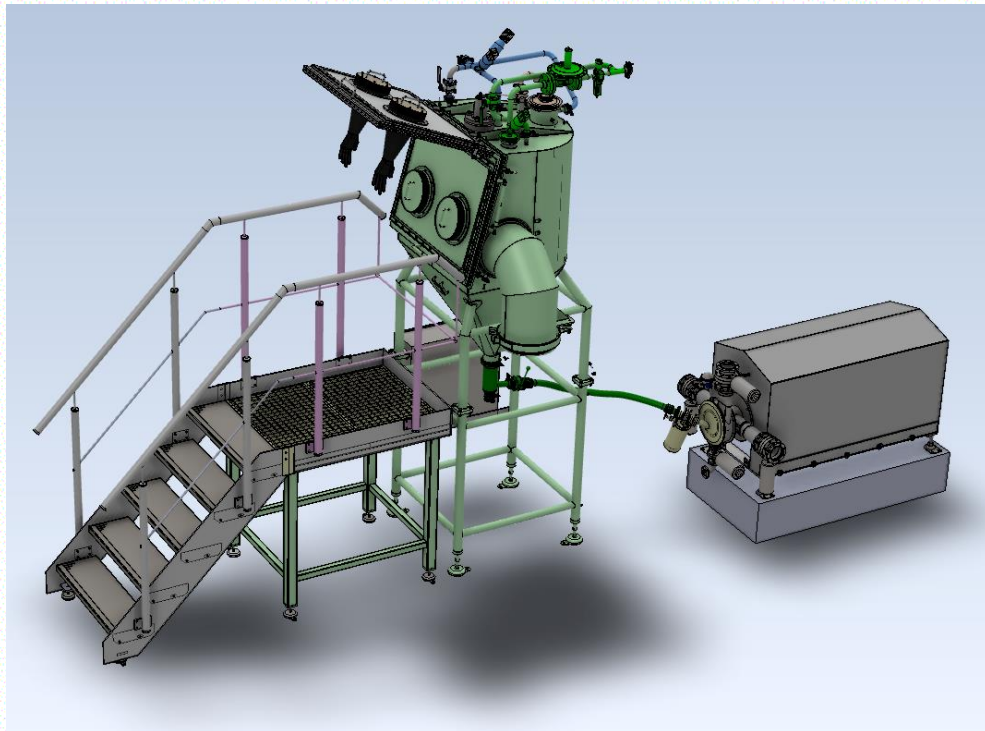
Big-bag + suction hose



Many different versions of all these systems available

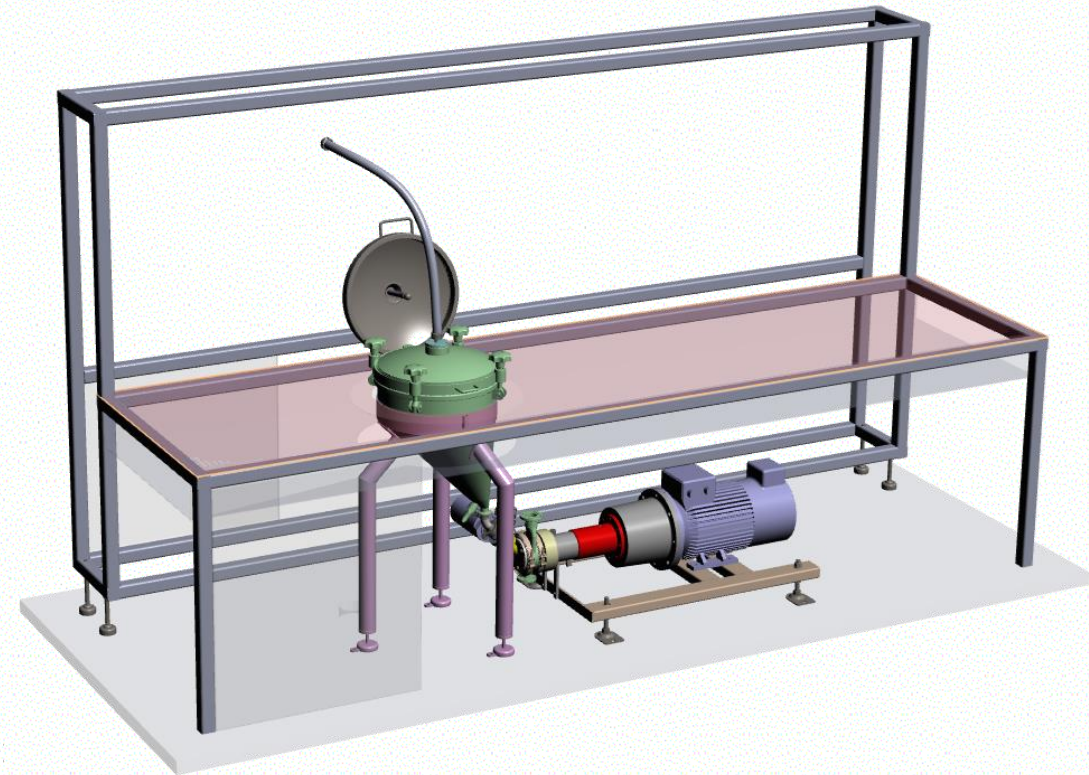
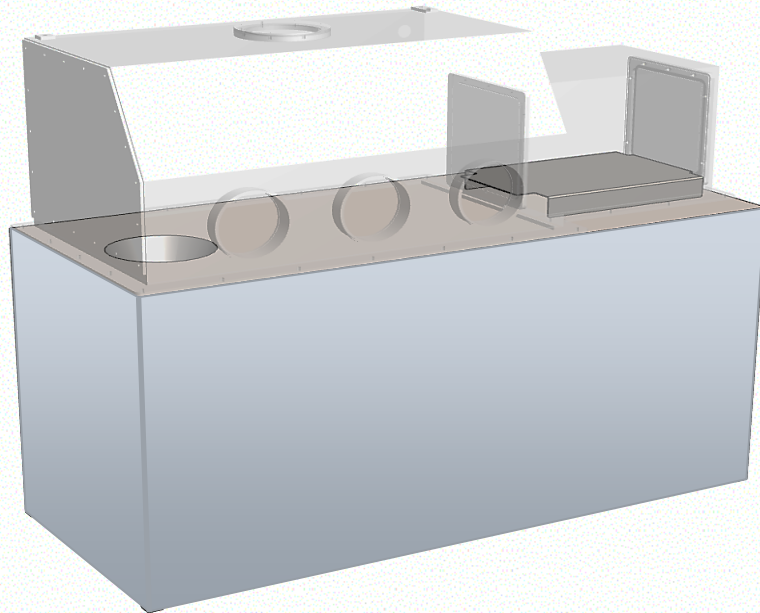
Powder Handling Components

Glove box isolator



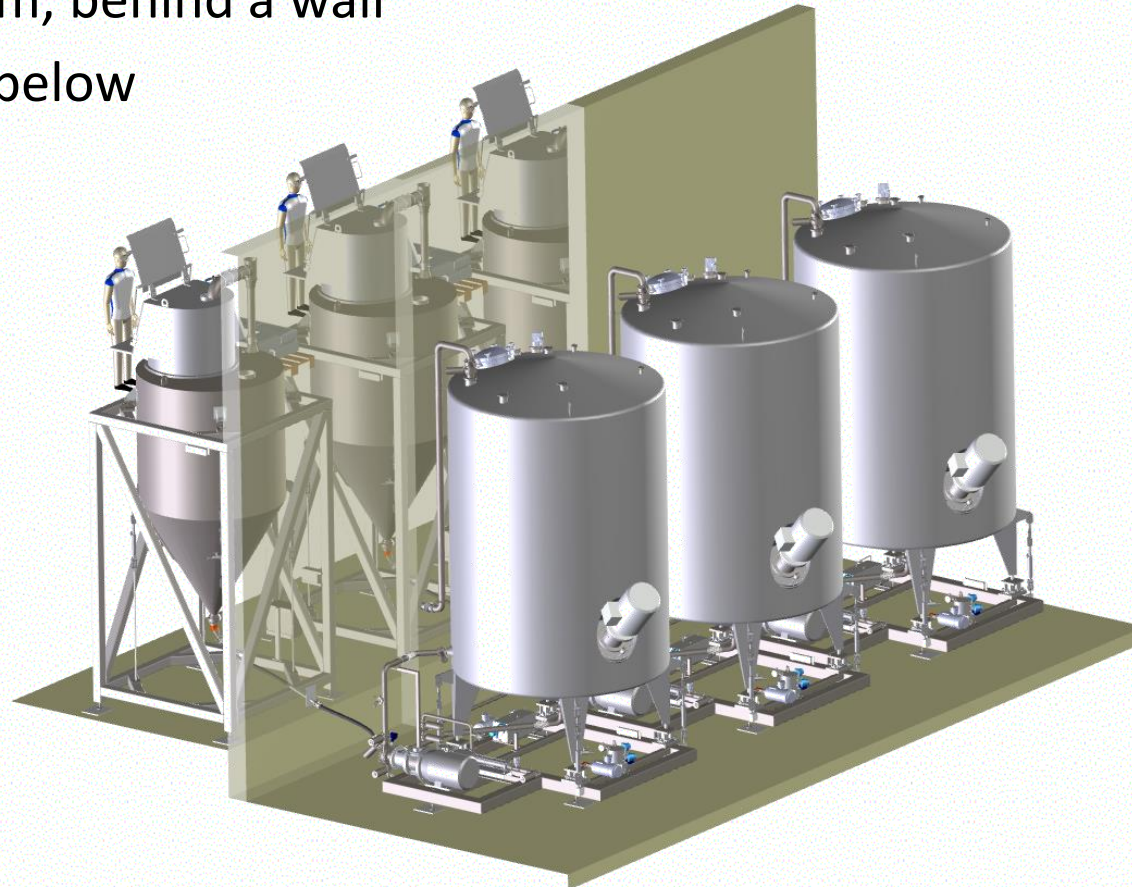
Conti-TDS installation - separate from powder handling area

- Sealed encapsulation below table with glove box
- ... or below open powder handling table inside the clean room
- Outside half suit isolator



Conti-TDS installation - separate from powder handling area

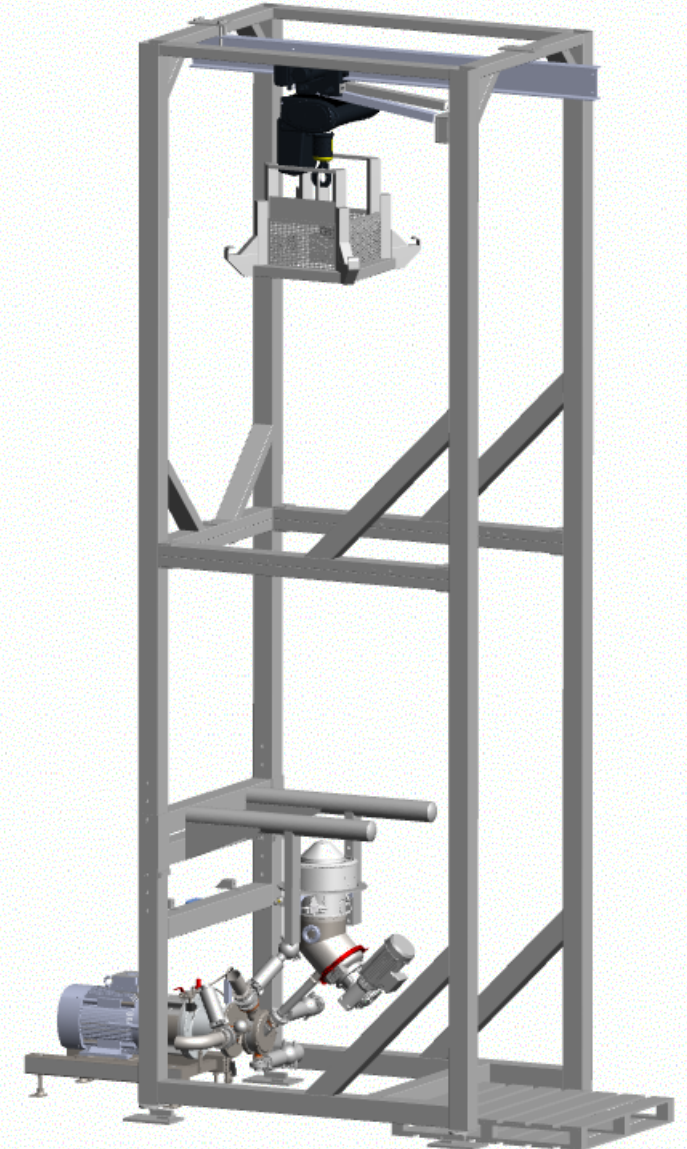
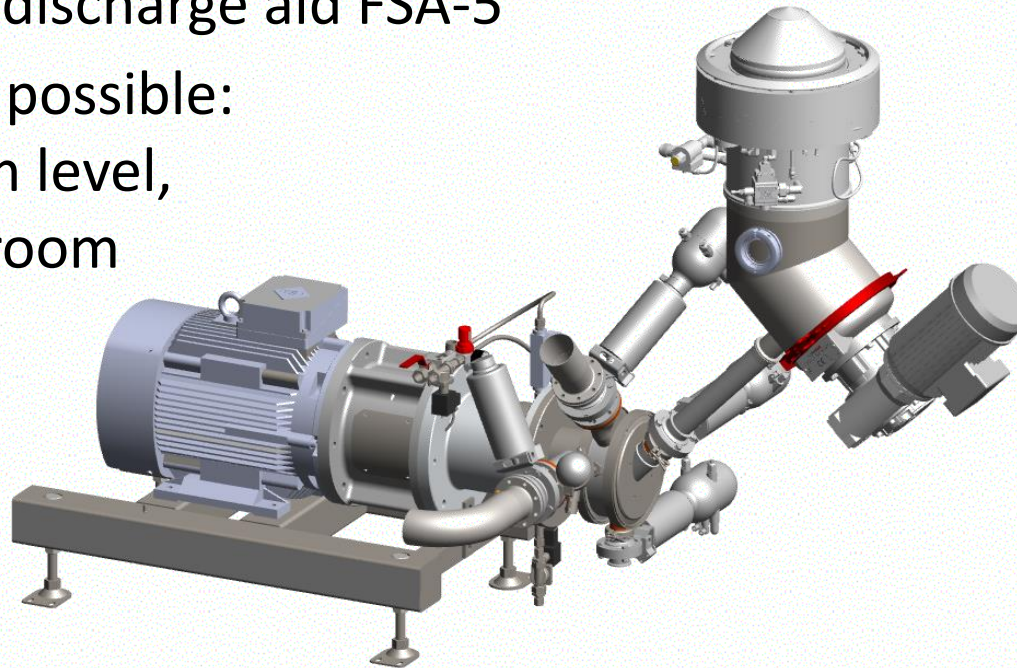
- Separate room, behind a wall
- Or one level below



Powder Handling Components

Big-Bag discharging with active / passive valve

- Passive valve to be clamped in the big-bag outlet spout
- Sealed big-bag connection
- Conti-TDS for induction and dispersion
- Fluidization and discharge aid FSA-5
- Split installation possible:
BBHS clean room level,
Conti-TDS tech-room
or lower level



Powder Handling Components

Hermetic container unloading and dispersion system

- Hermetically sealed against the ambient
- Powders, granules, chips, with agglomerates
- Conti-TDS for induction and dispersion
- Powder fluidization and discharge aid FSA-5
- Container: vacuum control and protection
- Integrated load cells
- For limited room height
- CIP, including powder port
- Options:
 - *Complete encapsulation for installation in clean room environment*
 - *Split installation: Upper part clean room level, lower part tech-zone level*

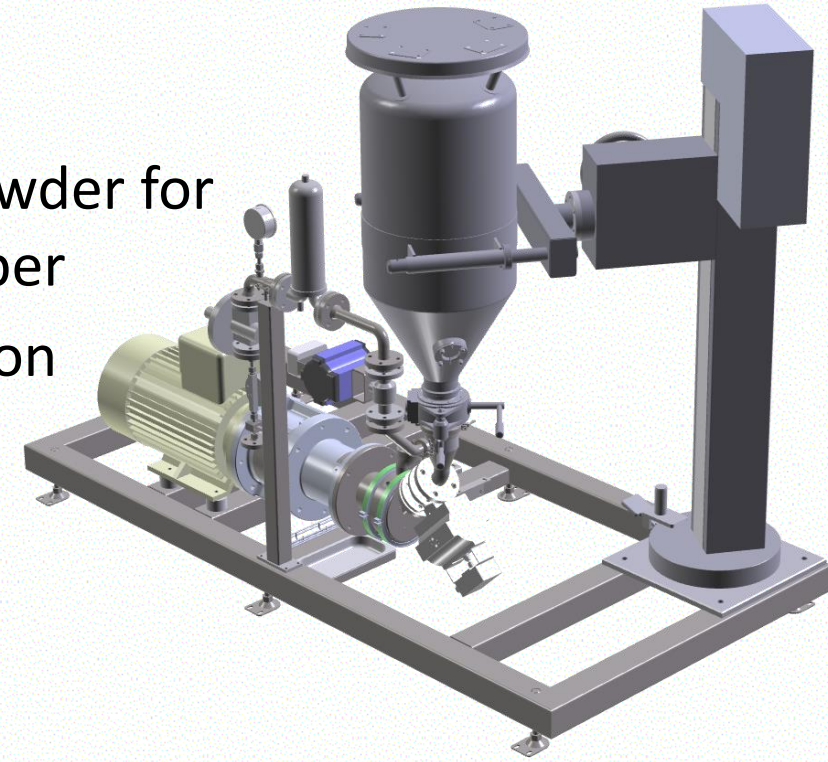


Powder Handling Components

Hermetic container unloading and dispersion system



- Hermetically sealed against the ambient
- Powders, granules, chips, liquids
- Split butterfly valve
- Typically unloading the complete powder for one batch into an intermediate hopper
- Conti-TDS for induction and dispersion
- Controlled container venting if inducted directly from the container



Machines and Complete System Design

Hygienic design

- 3A labeled
- FDA conform materials
- 1.4404 / ASTM 316L, polished
- Material Certification
- Aseptic connections
(11864, 11853, EHEDG Clamp seal)
- GMP
- With drain valve or self draining
- Easy to disassemble/assemble
- Easy to clean, CIP / SIP
- DQ, IQ, OQ documentation



Trends in Pharmaceutical Manufacturing with ystral machines

- Ingredient addition without opening the tank
- Less or no preservatives
 - *No microbial contamination during powder induction with Conti-TDS*
 - *Powders and liquids added without opening the tank = No contact with air borne germs!*
- Less or no emulsifiers
 - *Pickering emulsions, stabilizing particles instead of emulsifiers*
 - *Narrow drop size distribution to avoid Ostwald ripening*
- Replacement of bacteriologically critical ingredients
 - *Instead of organic ingredients or thickeners new polymers, silica, inorganic thickeners*
 - *Requiring dispersion under optimum conditions with Conti-TDS*
- Customized, specialized, personalized batches
 - *Small, made to order, flexibility and independence from batch size*
- Digitization, Batch control and documentation, Digital Technologies

Trends in Pharmaceutical Manufacturing – not required with ystral machines

- Production based on small volume batches
to avoid scale up issues between clinical trials and large-scale batches
- Quasi continuous production lines based on small batches

Conti-TDS and Z-Inline working outside the tank independent from batch size

Jet stream mixer and Dispermix: $P/V = \text{constant}$

→ Scale up under identical conditions

Stable Quality in Pharmaceutical Manufacturing – with ystral Conti-TDS

- Quality is created in the process – not with quality check and adjustment
- Constant quality is based on constant conditions – totally independent from the operator
- Manual powder handling affects the quality exceptionally
- In traditional powder addition on a liquid surface the operator has enormous influence
 - *Slow / fast*
 - *Steady / with interrupts*
 - *From high above / directly on the surface*
 - *In a vortex with additional air / without air*
 - *Creating agglomerates / no agglomerates ...*

→ **Conti-TDS = outside the tank and independent from batch size**

→ **Powder induction conditions determined by the machine = always constant**

→ **Completely independent from operator**

→ **Guarantees reproducible consistent quality**



Complete Systems

PiloTec Plant 10 to 50 liters

- Based on PiloTec and X50 Multipurpose mixer
- Exchangeable tools
- Integrated control
- Heating/cooling
- Product development and small batch production
- Powder from mobile hopper, container or suction hose
- Low/medium/high shear inline dispersion



Complete Systems

Chewable tablets formulation

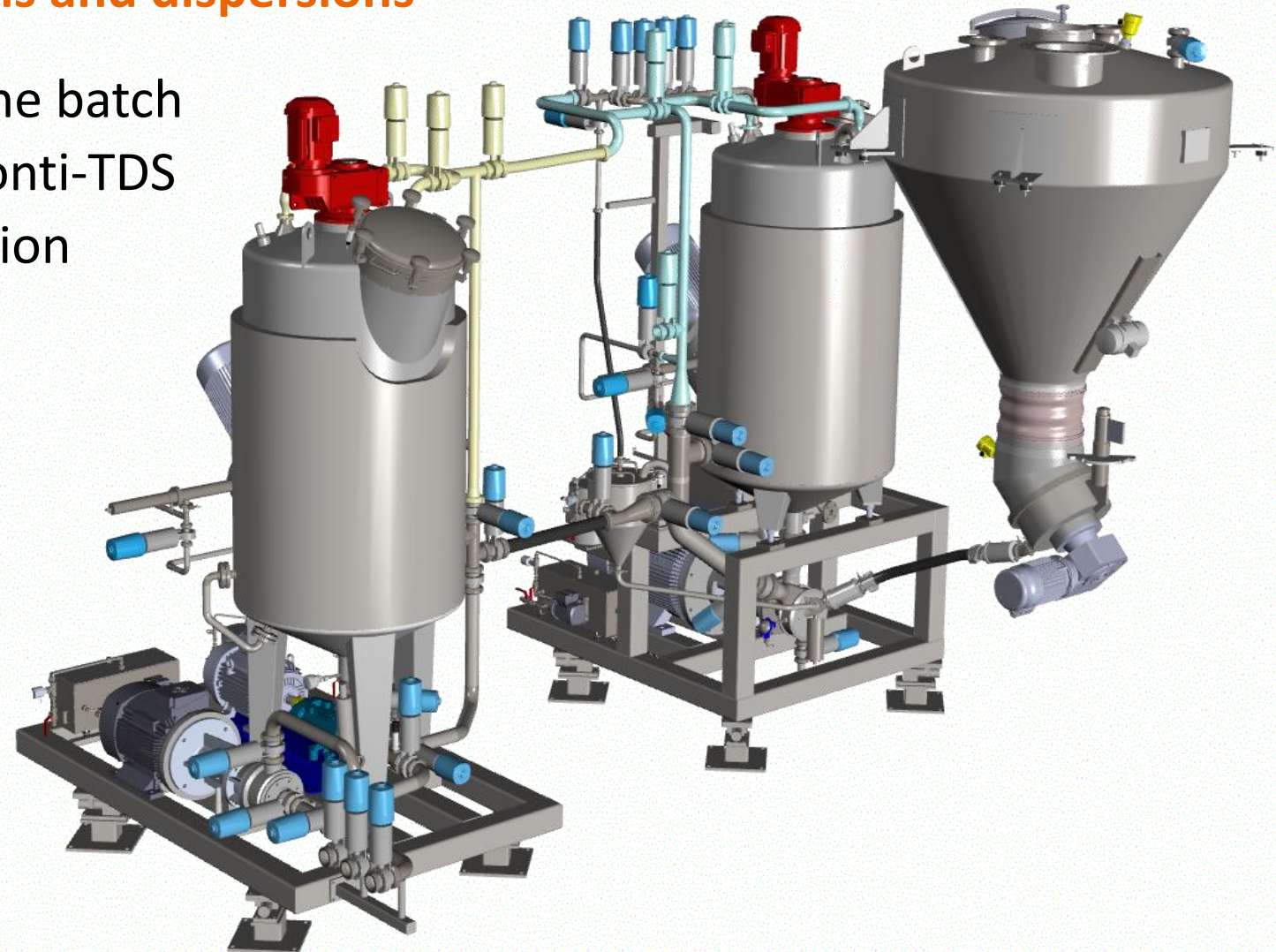
- Organic thickener polymer induction with Conti-TDS-3
- Bag tip station on load cells
- Active ingredient preparation and dispersion in the small units at the side
- Liquid and powder handling in separate rooms with a wall in between



Complete Systems

Medium and high viscous emulsions and dispersions

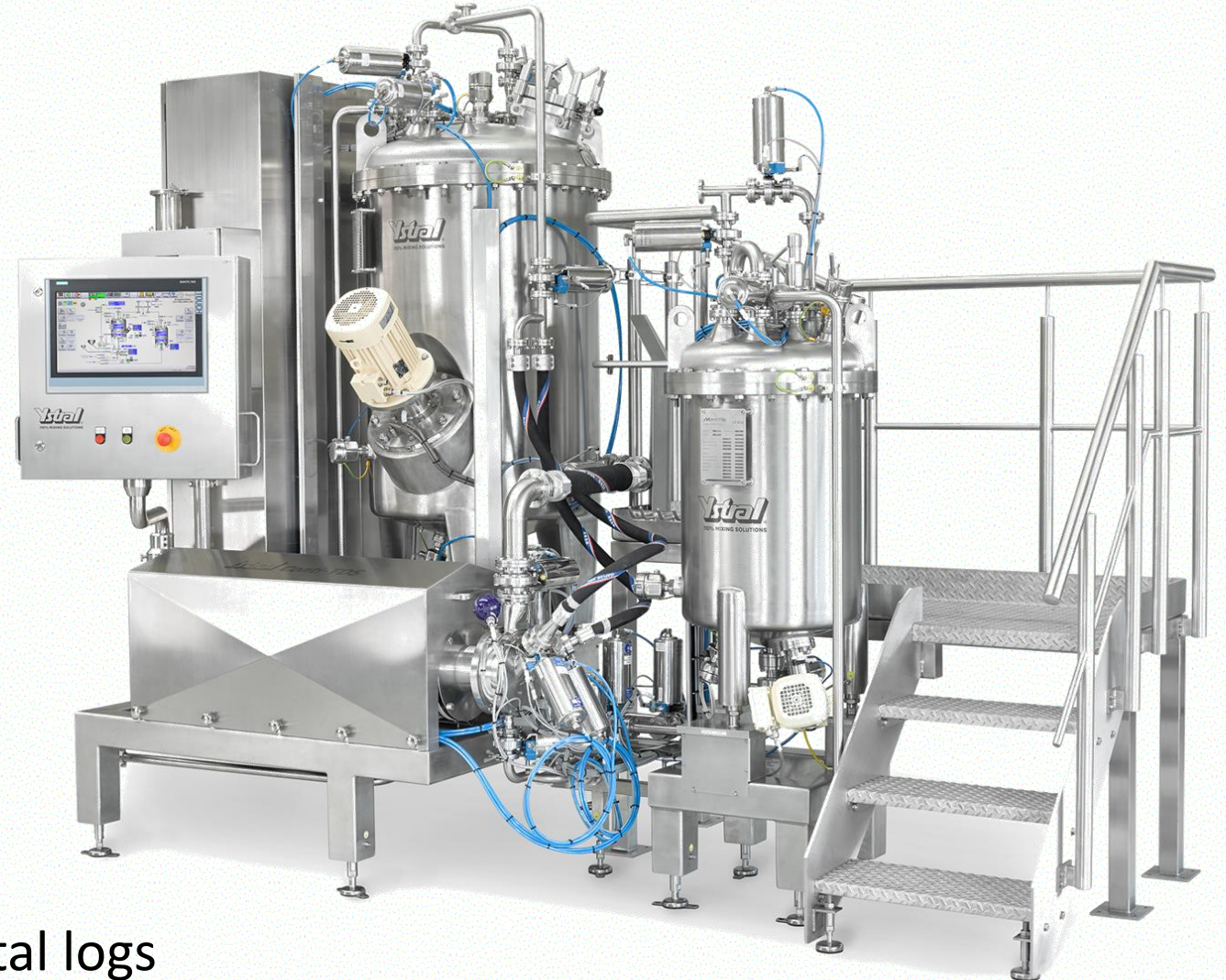
- Preparation of the powder for one batch
- Induction and dispersion with Conti-TDS
- High shear dispersion and emulsion with Z-inline in a separate tank



Complete Systems

Tablet coating, lacquer, polishing

- Extremely flexible system
- 80% time saving
- 60% energy saving
- Emulsions in nanometer range
- 90% higher storage stability
- 100% reproducible process
- Automatic cleaning
- Automatic control
- Generation of tamper-proof digital logs



Tablet coating and micro encapsulation liquid

- Mobile system with process tanks in two different sizes
- Designed to move on a floor scale
- Conti-TDS-2, Jet stream mixer
- ATEX (GD)
- Massive time reduction, especially for the thickener (from hours to minutes)
- One Conti-TDS for two tanks enables optimum dispersion of powders in different liquid/liquid combinations (to prevent competitive absorption and partial desolvation phenomena)



Complete Systems

Vacuum process system



- Powder and liquid induction, dispersion and emulsification
- Heating, cooling
- Vacuum, Pressure
- Conti-TDS below the vessel, Dispermix and anchor stirrer



Complete Systems

Vacuum process system

- Powder dosed in the powder hopper
- Induction, dispersion and emulsification
- Heating, cooling
- Vacuum, Pressure
- Precise dosing
- Complete system on load cells
- Conti-TDS below the vessel,
Jet stream mixer and anchor stirrer
- Ex-proof execution
(in this case US-ex)



Parenteral Nutrition

- Dextrose, Mannitol, Sorbitol, Amino acids
- Emulsions
- Dispersion in WFI with Conti-TDS

Injection, infusion

- Salt, electrolytes
- Dextran, Starch (HES)
- Induction, dissolution with Conti-TDS

Blood plasma

- Sugar with Conti-TDS, under process vacuum



Enteral Nutrition

- High concentrations of proteins, amino acids, dextrose, sugar etc.
- Conti-TDS with special direct injection head for pure proteins
- No additional air, no foam stabilization
- Accelerated hydration of proteins
- Hydrolyzation under high shear with less enzymes, less acid, lower temperature



Hard and soft gelatin capsules

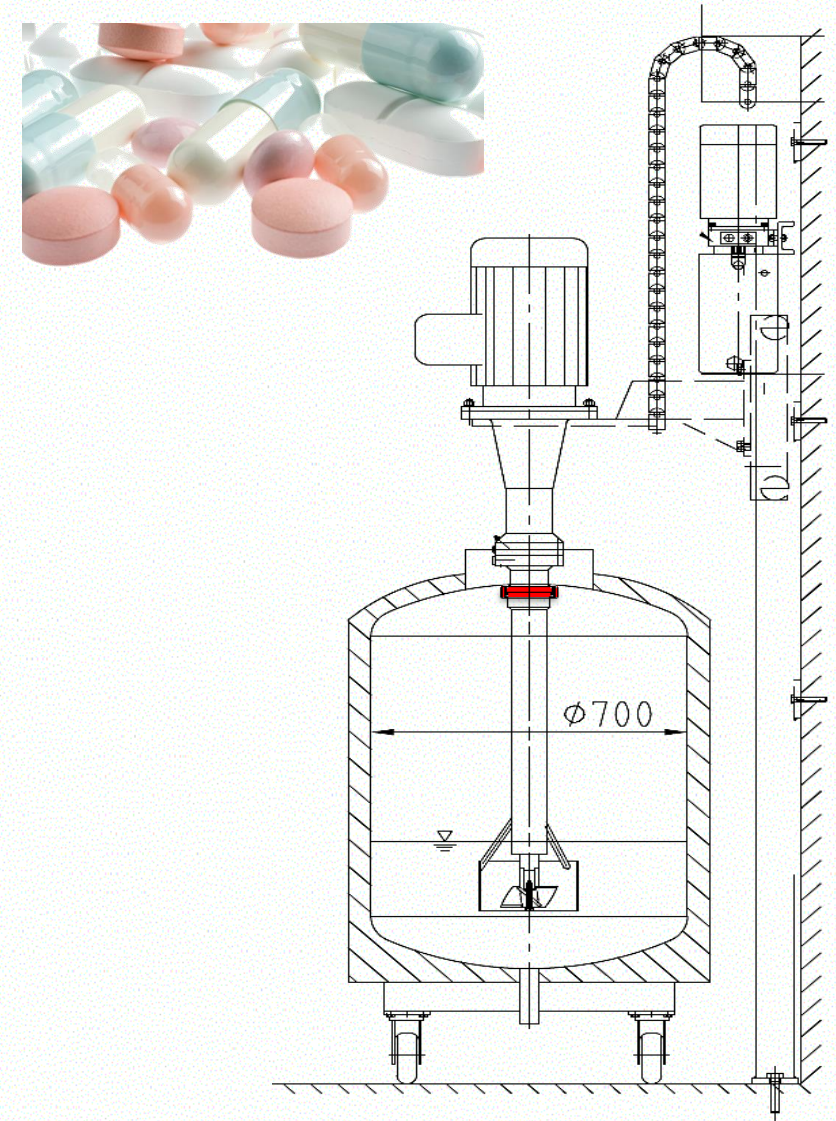
- Jet stream mixer on a lift for mixing and coloring extremely high viscous gelatin gel in mobile vessels
- Quick coupling to disassemble the shaft for cleaning and inspection inside and outside

Enteric coatings for gelatin capsules and tablets

- Induction and dissolution of HPMC, Eudragit and other polymers with Conti-TDS
- Aqueous and non aqueous

Tablet coating, polishing

- Flexible and variable complete systems for all types of tablet coatings (examples see pages 27-29)



Oral liquid formulations

- Dust free powder induction from bags and containers without lifting them above the open tank
- Even agglomerated powders without problems
- Precise viscosity control with Conti-TDS

Granulation syrup and binder

- Starch, Dextrose, Maltodextrin, Cellulose ethers etc. in high concentrated syrup and binder solutions with Conti-TDS
- Water and alcohol based

Spray dry emulsions, Microencapsulation emulsions

- Powder induction with Conti-TDS
- Emulsions – Conti-TDS and/or Z-Inline Disperser
- Stable agitation and coacervation with Dispermix



Pharmaceutical Gel, Embrocation Gel, Pain Relieve Gel

- Water based, oil based, emulsions
- Organic or inorganic thickeners with Conti-TDS
- For Example: Single tank saponification process for Ibuprofen Gel saves several process steps and process tanks

Povidone, PVP-Iodine Preparations

- Extremely sticky material
- Conti-TDS with direct injection head, initially developed for PVP induction



More examples for Conti-TDS applications:

- Inhalations
 - *Liquid is a gaseous propellant, only under pressure it is liquid*
- Vitamin products
 - *High dust explosion potential, low MIE (Minimum Ignition Energy)*
- Nicotine, Hormone, Penicillin products
 - *Dust free powder handling, bad flow behavior*
- X-ray-contrast agent
 - *Heavy barium sulfate powder*
- Sanitizer, Disinfectant
 - *Polymer thickener induction*
- ...

110% MIXING SOLUTIONS



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