



Continuous Processing

MODCOS for Continuous Oral Solid Dosage Production



Why continuous production



Why Continuous Production?

Saving manufacturing costs

- High productivity because of substantial time and cost saving
- Rapid process development, limited API consumption and therefore more efficient
- Smaller footprint and therefore less room for the plant, compared with a batch installation

Improving quality

- Consistent high product quality through continuous real time process monitoring and control
- Significantly reduced scale-up issue and risk because scale-up is done by scale out of manufacturing time
- No process knowledge gap between development and commercial scales



Why Continuous Production?

Requirements for continuous production

- Real process understanding
- Advanced PAT and control technology
- New thinking from equipment suppliers
- New thinking from development, manufacturing, quality and regulatory teams

Regulatory body

- Basically the FDA as regulatory body is encouraging manufacturers to adopt continuous manufacturing

The FDA is encouraging manufacturers to adopt continuous manufacturing, which can streamline QbD development and NDA submission.



Glatt Continuous Philosophy / Concept



Glatt Continuous Philosophy / Concept

Integrated modular continuous systems

- Continuous processing is offered as full / partial system or individual unit operation allowing modular expansion over time
- Glatt and best third-party equipment is integrated into one cohesive system
- Each process unit has its own control system with local panel
- Each process unit can be operated in integrated mode or in local mode
- Fluid bed machine can be operated in continuous or batch mode
- We offer three different granulation methods
- Integrated control system with PAT measurement, traceability and documentation, based on residence time and residence time distribution in the entire line.



Glatt Continuous Philosophy / Concept

Line definition by throughput

- **S-line - 1 up to 15 kg/h**
Development, clinical test phase, new products
- **M-line - 5 up to 50 kg/h**
Development, clinical test phase, new products
- **L-line - > 50 kg/h**
Existing products and block busters



Glatt Continuous Philosophy / Concept

Proposal for a m-line installation, up to 50 kg/h



Glatt. Integrated Process Solutions.



Glatt Continuous Philosophy / Concept

Proposal for a s-line installation, up to 15 kg/h (completely mobile)



Glatt. Integrated Process Solutions.



- Loss in weight feeder
- Twin screw execution
- Quick change design for easy cleaning
- Feeder sizes from 50 g/h up to 300 kg/h



Continuous dry mixing



- Continuous dry mixer
- Throughput: 2 - 50 kg/h
- speed: 400 - 900 UpM
- additional ports possible
- Easy cleanability



Continuous Granulation

Three different granulation methods:



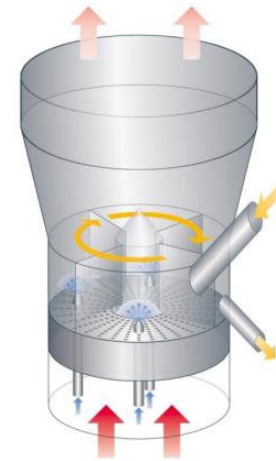
Twin Screw Extruder

High shear Granulate



Dry Mix / Wet Granulator

Mid shear granulate



Fluid Bed Granulation

Low shear granulate

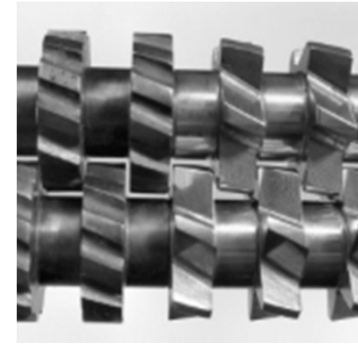
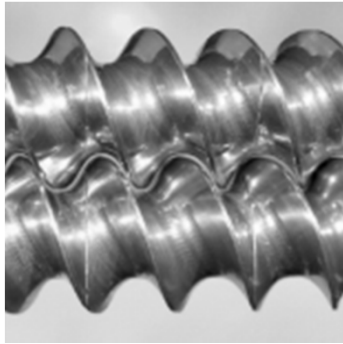


Twin Screw Extruder Granulation



- Throughput: TSG 16 2 - 15 kg/h
 TSG 24 5 - 50 kg/h
- speed: 100 - 1000 rpm
- Various ports for adding powder and liquid
- high shear forces





twin screw extruder for hybrid operation



wet granulation



hot melt extrusion



Single Shaft Wet Granulation

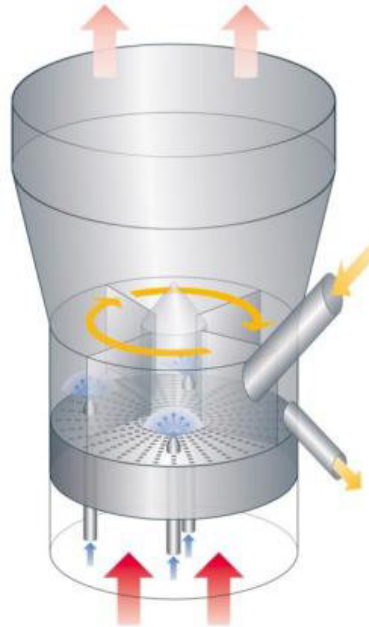


- Throughput: 2 - 25 kg/h
- speed: 400 - 900 rpm
- additional ports possible
- Easy cleanability
- Mid shear forces



Fluid Bed Granulation

- Granulation process insert for GPCG Fluid bed dryer
- 4 static chamber module
- Conical chamber shape
- Variable number of nozzles





Fluid Bed Drying

GPCG 10 → Modcos m-line for multi application

**BATCH
GOES
CONTI**



Batch Execution



Conti Execution



Fluid Bed Drying

GPCG 2 → Modcos s-line for multi application

**BATCH
GOES
CONTI**



Batch Insert



Conti Drying Insert



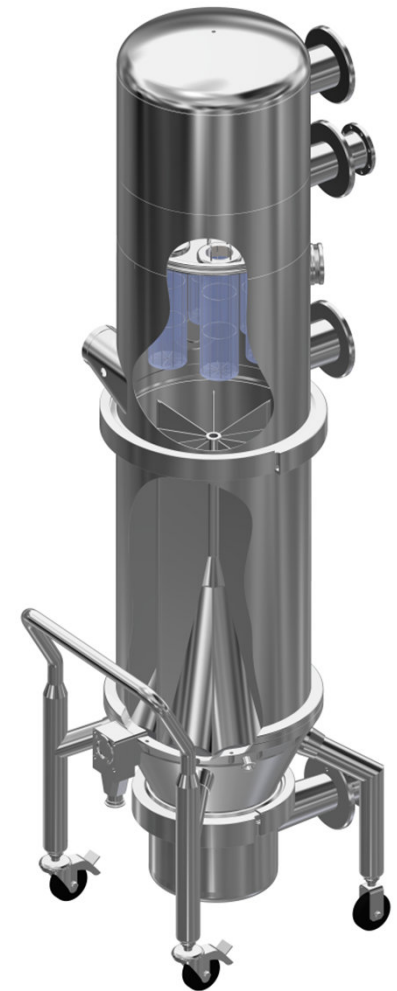
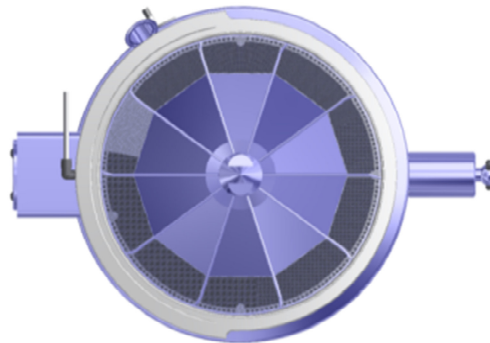
Conti Granulation Insert





Fluid Bed Drying

- 10 chamber rotating module (carrousel)
- Conical chamber shape
- Very narrow residence time distribution





Controlled Product Conveying

- Glatt rotary valve
- Vacuum barrier
- Shock pressure barrier
- Flame arrester
- Continuous discharger



Product Conveying and Milling



Vacuum conveyor with conical mill

- Small surfaces (cleaning)
- Variable speed adjustment
- Fully closed design

Compression: partnership with Fette

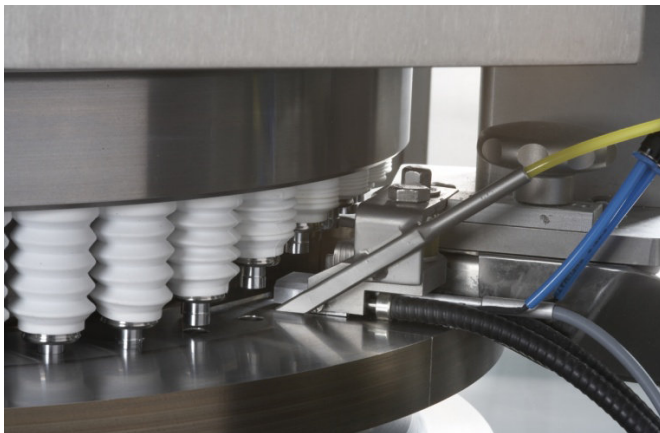


- Works continuous by design
- Magnesium spraying system available
- Data Acquisition und Management (SQL)



At-line Quality control with NIR-Checkmaster

- Checks four parameter (Weight, Hardness, Thickness, Diameter)
- API content with NIR-Transmission optional
- Automatic Sampling
- Integrated control loops



In-line API content in tablet press

- Measurement in reflection
- 100% Control
- patented



PAT



PAT Systems

- **Particle size and size distribution:**
 - Eyecon from Innopharmalabs, optical system
- **Moisture content:**
 - TEWS, microwave measurement technology
- **Content uniformity / Blend homogeneity**
 - Sentronic, NIR measurement technology
 - Alternativ: Raman, laser based optical measurement technology



Controls



Controls



- Based on latest GlattView MEGA Version
- Integrated mode of all Process units
- Local mode of each process unit
- Communication to the process units via Profibus
- Communication to PAT sensors via Ethernet

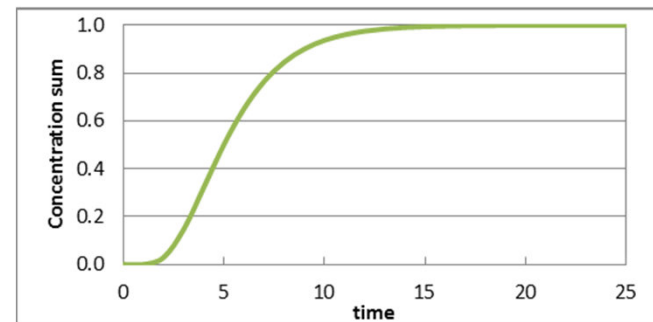
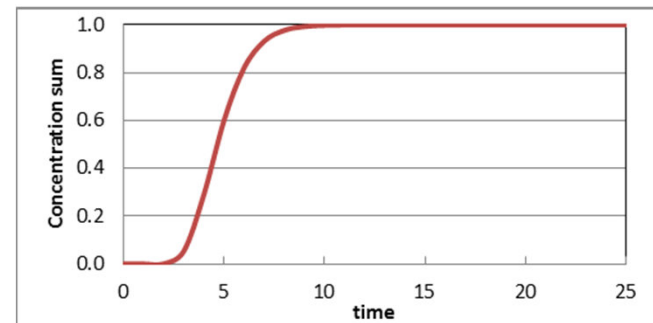
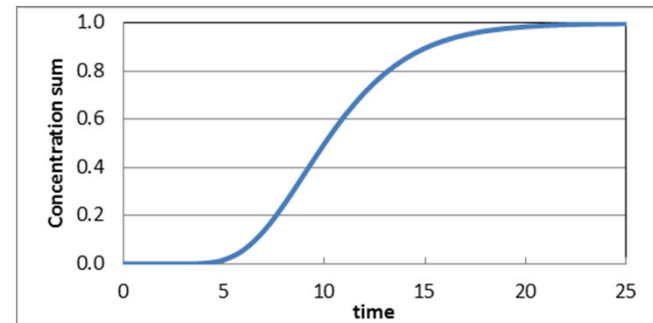


Traceability / Documentation

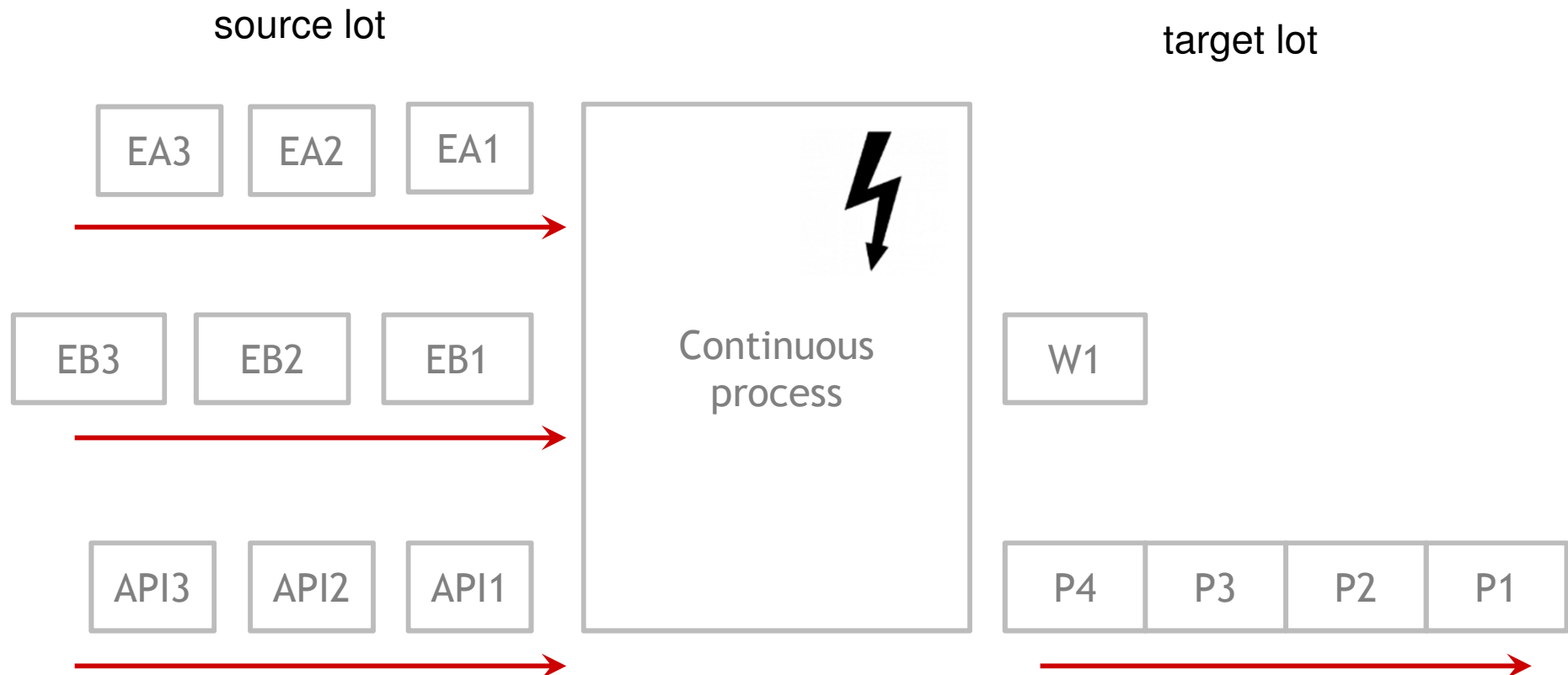


Residence Time Behaviour

Each process unit has its individual residence time behaviour



Influence of the residence time (distribution)?
When do we find source lots in the finished target lots?





OOS Tracking / Controlling

- Keep the continuous process as long alive as possible
- OOS product discharge before or behind tablet compression (recommendation)
- OOS product gets a virtual “OOS stamp” and the controls tracks it through the continuous line until discharge to waste
- Every process parameter can be supervised,