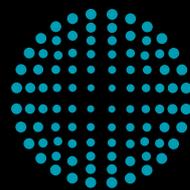


# CONTINUOUS MANUFACTURING



**FETTE**  
**COMPACTING**  
be efficient



# Continuous Manufacturing: consistent efficiency



## CONTINUOUS MANUFACTURING

Continuous Manufacturing is increasingly gaining in importance in the pharmaceutical industry. Apart from classic batch lines, recent years have also seen pharmaceutical manufacturers operating initial continuous production lines as a reaction to the increasing pressure on shorter time to market for new drugs, improved product quality, reduced costs and more flexible production methods. Consequently, increased number of OSD are being developed and produced using Continuous Manufacturing.

Initial experience gleaned by manufacturers confirms that considerable savings can be achieved with Continuous Manufacturing. Compared to batch equipment, continuous lines are significantly more space-saving which frees up space in expensive clean room areas. The continuous flow of materials does not require any storage space for intermediate products and makes it possible to scale batch sizes solely over the lines' runtime. Regulatory authorities such as the Food and Drug Administration (FDA) also support this comprehensive and reliable approach to production. These and many other advantages make Continuous Manufacturing a guarantor for efficiency in the future.

### **A new understanding of processes**

Continuous Manufacturing is accompanied by a new understanding of processes: the outlet product of one unit operation forms the direct inlet material for the next one. Unlike batch procedures, continuous lines are operated without interruption over a longer period of time. Many processes and components which would have been separate in the past are merging to form a single line, enabling a higher degree of flexibility in terms of production volumes as well as lower production costs. As a general rule, the more streamlined the design of the line as a whole, the greater the control afforded over the production process. For this reason, by using direct compression Fette Compacting is relying on the most compact and efficient method of Continuous Manufacturing in tablet production.



**TECHNOLOGY** stands for everything we offer in production technology – from tablet presses and capsule filling machines through Process Equipment to tableting tools and format parts.

**SERVICE** covers all the services related to machines, Process Equipment and installations such as spare parts supply, plant modernization and technical field service department.

**COMPETENCE** is the overarching idea behind all our process-related services. This includes training, product trials, application and Performance Consulting as well as engineering.

# Continuous Manufacturing: the advantages at a glance

## 1 Faster

- ▶ **Time-to-Market**  
Shorter time to market as formulation and drug product development can be done much faster and with less API on a Continuous Manufacturing line compared to batch processing. Moreover, product transfer from development to commercial production is done on the same equipment
- ▶ **Processing times**  
Shorter processing times as there is no need for intermediate product handling and storage. Production lead times drop from weeks to hours

## 2 More flexible

- ▶ **Batch sizes**  
Batch size is determined by runtime, not by equipment size
- ▶ **Production volume**  
Flexible control of the production volume

## 3 Safer

- ▶ **Process reliability**  
Safe and stable continuous processes thanks to on-line quality monitoring via PAT and Advanced Process Control (APC) technology
- ▶ **Operator protection**  
Improved operator safety through less contact with the processed substances

## 4 More efficient

- ▶ **CapEx & OpEx**  
Lower costs thanks to more efficient production and less demand for clean room areas
- ▶ **Product loss**  
Less product loss and minimum downtimes
- ▶ **Ecological footprint**  
Smaller ecological footprint thanks to energy-saving production processes

Using Continuous Manufacturing, batch sizes can be managed flexibly across the service life of the lines. An essential competitive advantage also lies in faster market launches of new products as the same line can be used for both development and production. Time-intensive scale-up processes are largely avoided. Last but not least, Continuous Manufacturing also offers advantages in terms of product quality as well as improving the ecological footprint using more energy-efficient processes.

# Direct compression: the shortest route

The transition from batch manufacturing to continuous, sees a growing switch from granulation based production processes to direct compression.

Compared to continuous granulation-based production, direct compression is the leaner way of manufacturing as some cost-intensive production steps are not passed. As the short production process comprising only three steps requires little equipment, spatial requirements are very low compared to other Continuous Manufacturing lines. Thanks to its reduced degree of complexity, direct compression allows fast product changes and better process control with shorter time to steady state, thanks to lower total hold-up mass in the direct compression line.

By using continuous tableting lines, Fette Compacting relies on the highly-efficient method of direct compression. After the dosing process, the powder is fed directly from the mixer into the tablet press without any additional granulation. For some years now, an increasing number of pharmaceutical producers have been giving preference to this fast and easy process over more complex production methods. The number of active and auxiliary substances which can be processed on direct compression lines has been increasing accordingly.

Direct compression is also a guarantor of quality: as the powder is fed directly in a continuous flow from the mixer into the tablet press, quality-impairing factors can be significantly reduced. For example, vibrations can be avoided during the transport of intermediate products which could cause them to segregate.

## Core element – tablet press

The core element of the direct compression lines offered by Fette Compacting is formed by the ultra-modern tablet presses in the FE Series. Coupled with a horizontal mixing system and ultra-precise dosing, they form a safe and efficient continuous line for an extensive capacity range.

## Direct compression line by Fette Compacting

- ▶ Raw material charging
- ▶ Dosing unit
- ▶ Mixing system
- ▶ Tablet press: FE Series
- ▶ Integrated control system
- ▶ At-line or in-line quality monitoring

## Technical data

- ▶ Throughput: 5-300gk/h
- ▶ Up to 7 LIW dosing units
- ▶ Exchangeable mixer
- ▶ Premixtures can be processed
- ▶ Package available for Multiple Unit Pellet System (MUPS)

Direct compression	Dry granulation	Wet granulation
▶ Dosing	▶ Dosing	▶ Dosing
▶ Mixing	▶ Mixing	▶ Mixing
▶ Tableting	▶ Roll compacting	▶ Wet granulation
▶ Optional: Coating	▶ Grinding	▶ Drying
	▶ Tableting	▶ Dosing
		▶ Mixing
		▶ Tableting



Direct compression line supplied by Fette Compacting: FE55 tablet press with dosing unit and mixing system

# PAT sensors: quality assurance in real time

A key advantage of Continuous Manufacturing is improved end product quality thanks to in-process real-time monitoring of Critical Quality Attributes (CQA's) such as blend uniformity and tablet content uniformity.

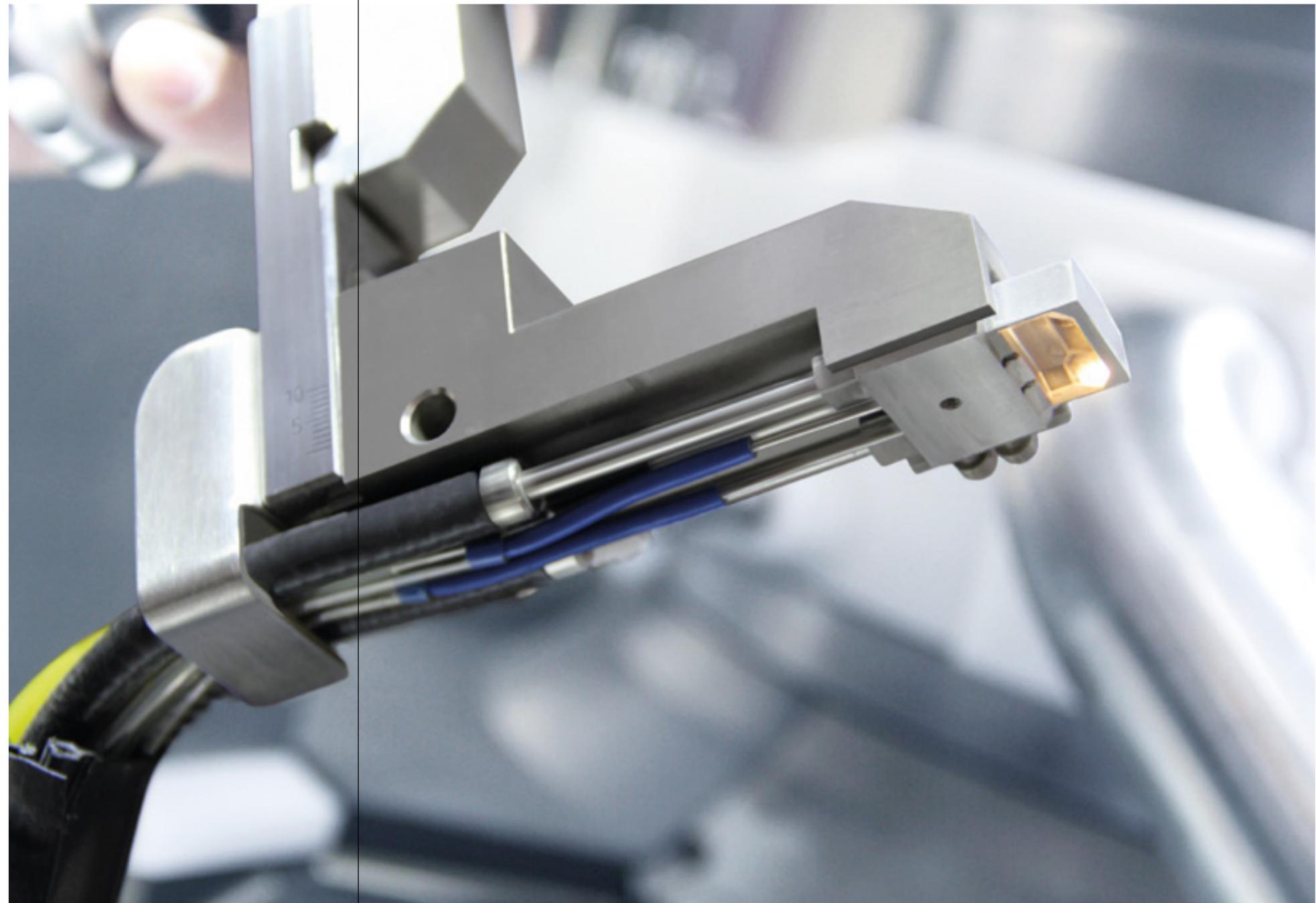
Fette Compacting primarily relies on near-infrared spectroscopy (NIR) for real-time analysis of powder and tablet quality.

The advantage of NIR technology is that many substances react well to its spectral range and the rays can penetrate deep inside the tablet without damaging it. NIR is also fast and therefore eminently suitable for high-performance machinery. Where NIR sensors reach their performance limits, Fette Compacting turns to Raman spectroscopy. Thanks to a strong laser, it is capable of accurately determining even tiny concentrations of substance. In special cases, methods such as Laser-Induced Fluorescence (LIF), UV, or terahertz spectroscopy can also be relied on.

The number and position of sensors used varies depending on the respective application. Especially during R&D, a sensor is often used after the mixer before the powder reaches the tablet press. Sometimes a sensor is also deployed at the Fill-O-Matic. The chemical properties of the finished tablet are examined in-line in the tablet press or at-line in the Checkmaster.

The NIR sensor in the tablet presses permit inspection of each individual tablet in terms of its API concentration and can reject single out-of-specification tablets. Moreover the data collected from all tables allows for further optimisation of the entire production process. This enables users to safeguard a high degree of process accuracy and product quality even during ongoing production processes.

The checkmaster NIR at-line tester is especially attractive for determination of content uniformity of the produced tablets, as single tablet spectroscopic measurements are coupled with physical single tablet measurements such as tablet size, weight, and hardness.



NIR measuring head for the tablet press in in-line mode

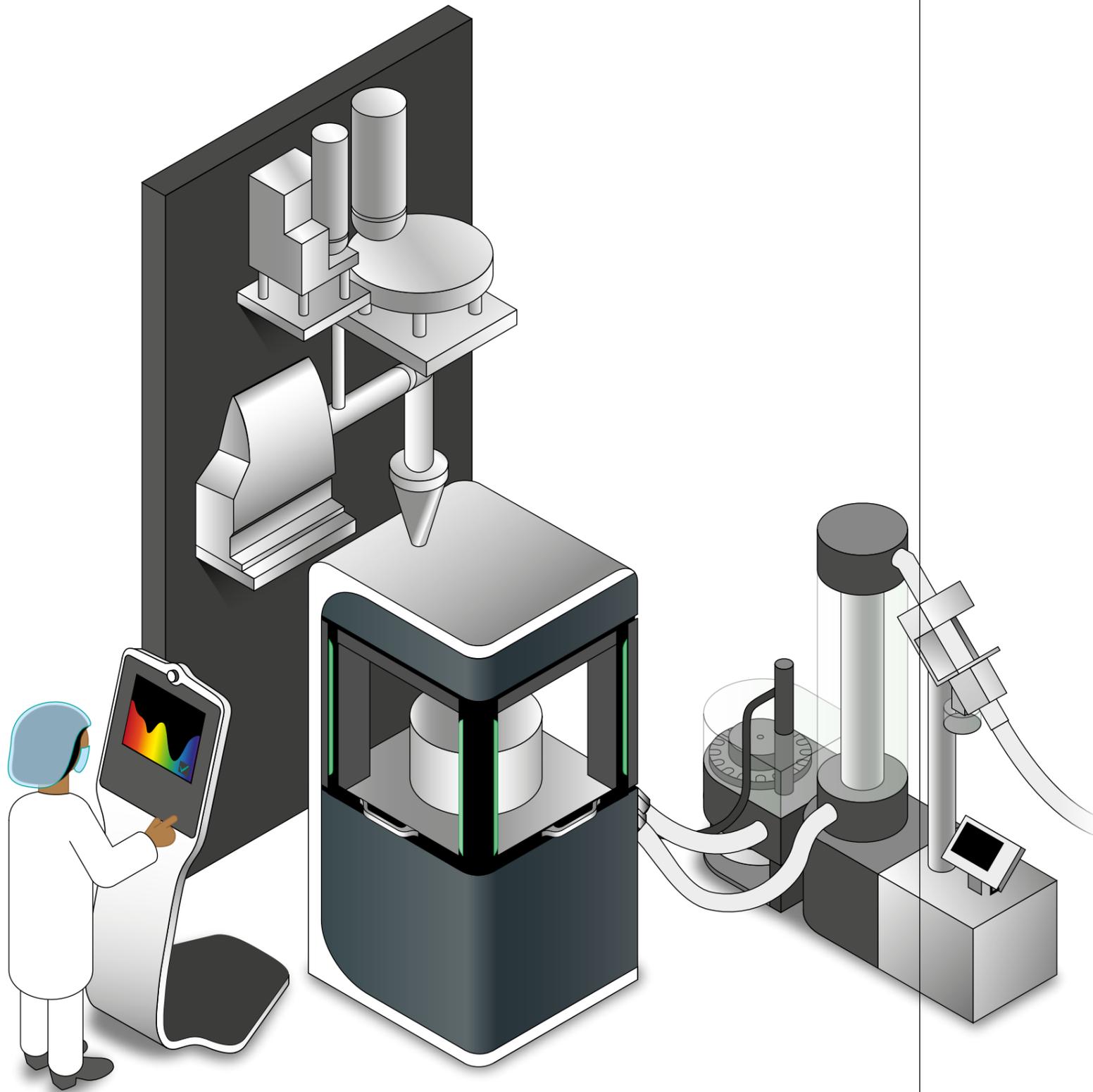


Checkmaster for analyzing active ingredients in at-line mode



Raman measuring in tablet press

# Service: until everything fits



Test continuous production line setup

Continuous direct compression is an innovative method of tablet production. But this method is not suitable for all formulations. Process experts at Fette Compacting examine processability in individual cases and support the entire development phase of the continuous line.

A test line for direct compression is available in the Competence Center in Schwarzenbek. The production line includes an FE Series tablet press, a mixing system, and up to seven dosing units. The plant can also be fitted with the requisite PAT system where customers can test the performance of individual components and the entire manufacturing line as well as collaborate with the application experts at Fette Compacting to intensify their process knowledge.

#### Test line at Technology Center in Schwarzenbek

- ▶ Feasibility study
- ▶ Evaluating individual components (dosing units, mixer, tablet press, PAT, etc.)
- ▶ Trial runs to gain process knowledge

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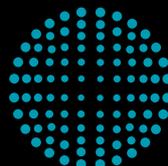
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